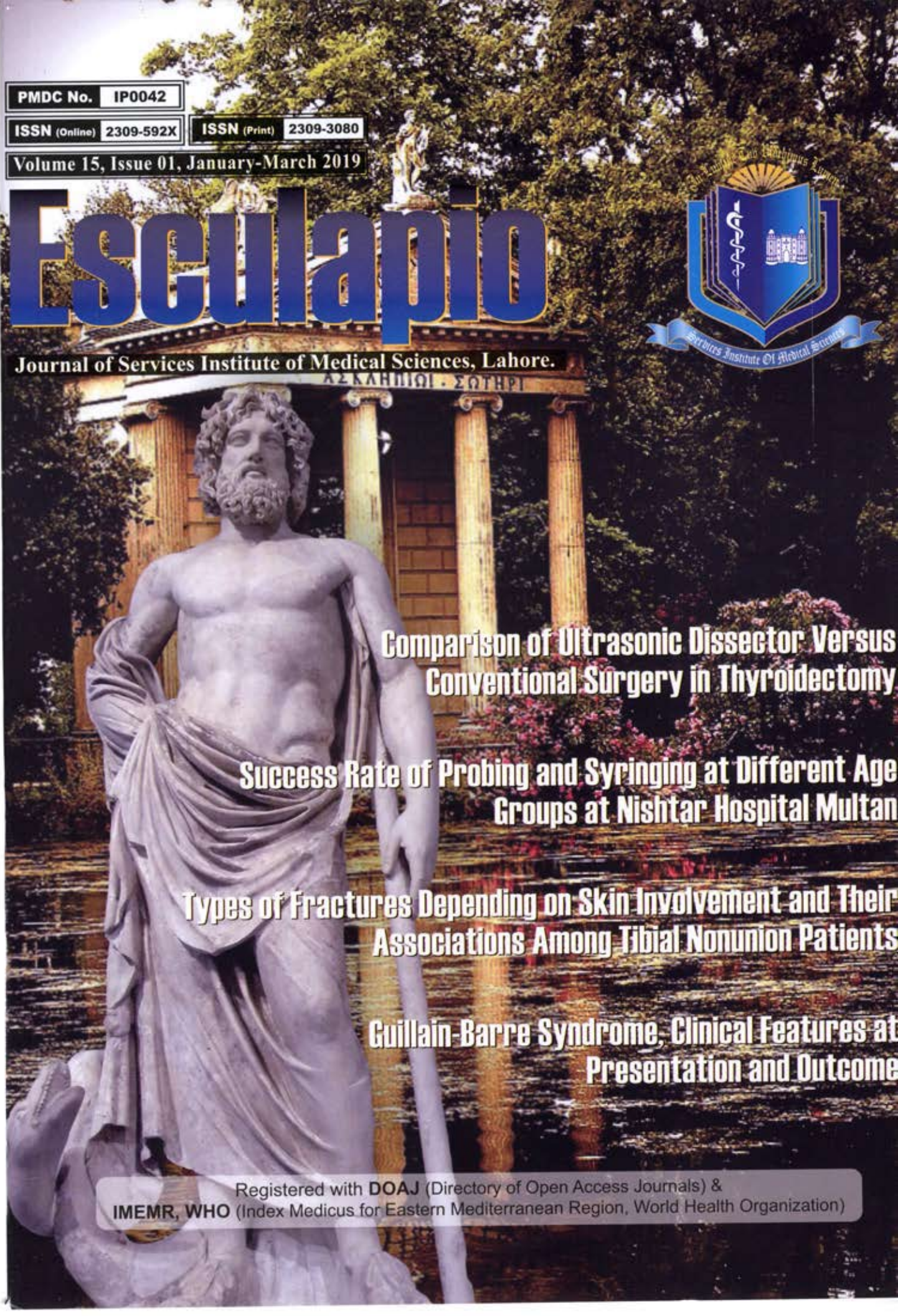
PMDC No. IP0042

ISSN (Online) 2309-592X ISSN (Print) 2309-3080

Volume 15, Issue 01, January-March 2019

Esculapio

Journal of Services Institute of Medical Sciences, Lahore.



Comparison of Ultrasonic Dissector Versus Conventional Surgery in Thyroidectomy

Success Rate of Probing and Syringing at Different Age Groups at Nishtar Hospital Multan

Types of Fractures Depending on Skin Involvement and Their Associations Among Tibial Nonunion Patients

Guillain-Barre Syndrome, Clinical Features at Presentation and Outcome

Registered with **DOAJ** (Directory of Open Access Journals) &
IMEMR, WHO (Index Medicus for Eastern Mediterranean Region, World Health Organization)

CONTENTS

ESCULAPIO

JOURNAL OF SERVICES INSTITUTE OF MEDICAL SCIENCES, LAHORE.

VOLUME. 15 JANUARY - MARCH 2019 ISSUE. 01

FOUNDER

Prof. Faisal Masud
(Vice Chancellor King Edward Medical University)

PATRON

Prof. Mahmood Ayyaz
(Principal SIMS & Professor of General Surgery)

EDITOR-IN-CHIEF

Prof. Mian Sajid Nisar
(Medicine, Pakistan)

ASSOCIATE EDITORS

Prof. Tayyiba Wasim
(Gynaecology, Pakistan)

Prof. Tayyaba Khawar Butt
(Pediatrics, Pakistan)

Dr. Anjum Razzaq
(Institute of Public Health)

ASSISTANT EDITORS

Prof. Dr. Muhammad Nadeem Aslam (Surgery, Pakistan)
Dr. Sobia Qazi (Medicine, Pakistan)
Dr. Amtuf Mussawar
Dr. Satia Waheed

INTERNATIONAL EDITORS

Dr. Bilal Ahmed (Medicine, USA)
Dr. Hamda Saleh (Nuclear Medicine, Australia)
Dr. Raza Hashmi (Cardiology, USA)
Dr. Nadeem Ahmad Khan (Gastroenterology, USA)

PUBLISHED BY

SERVICES INSTITUTE OF MEDICAL SCIENCES, LAHORE.
SECRETARIATE
MEDICAL UNIT IV, CONTACT NO. 042-99204879

ONLINE EDITION

VISIT THE WEBSITE FOR ONLINE ARTICLES AND SUBMISSION
WWW.ESCULAPIO.PK

PRINTED BY

TALAL PUBLISHERS
29 BASEMENT, ROSE CENTRE, KABIR STREET,
URDU BAZAR LAHORE, 0300-4327951

COMPOSED BY

AMEER ALI

REVIEW BOARD

Prof. Dr. Mumtaz Hasan *(Lahore)*

Prof. Dr. Anwar A. Khan *(Lahore)*

Prof. Tahir Shafi *(Lahore)*

Prof. Dr. Shamim Ahmad Khan *(Lahore)*

Prof. Dr. Iqbal Butt *(Lahore)*

Prof. Dr. Rashid Latif Khan *(Lahore)*

Prof. Dr. Tahir Saeed Haroon *(Lahore)*

Prof. Dr. Farrukh Khan *(Lahore)*

Prof. Dr. A. H. Nagi *(Lahore)*

Prof. Dr. Kartar Dhawani *(Karachi)*

Prof. Dr. Abdul Malik Achakzai *(Quetta)*

Prof. Dr. Fareed A. Minhas *(Rawalpindi)*

Prof. Dr. Zafar Iqbal *(Lahore)*

Prof. Dr. Alaf Khan *(Peshawar)*

Prof. Dr. Shabbir Nasir *(Multan)*

Prof. Khalid Bashir *(Lahore)*

Prof. Dr. J. P. Long *(UK)*

Prof. Dr. Harry Minhas *(Australia)*

Prof. Dr. Sasleri *(UK)*

Dr. Zia Farooqi *(Lahore)*

Maj. Ge. Dr. Naseem-ul-Majeed *(Rawalpindi)*

Brig. Dr. Mowadat H. Rana *(Rawalpindi)*

Brig. Dr. Muhammad Ayub *(Rawalpindi)*

EDITORIAL ADVISORY BOARD

Prof. Dr. M. Shahzar Anwar *(Urology)*

Prof. Dr. Alia Bashir *(Gynecologist)*

Prof. Dr. Abdullah Haroon *(Neurosurgery)*

Prof. Dr. Faiza Bashir *(Pathology)*

Prof. Dr. Najla Shore *(Physiology)*

Prof. Muhammad Amjad *(ENT)*

Prof. Khalid Waheed *(Ophthology)*

Prof. Muhammad Mujeeb *(ENT)*

Prof. Mehmood Ayaz *(Surgery)*

Prof. Dr. Farid Ahmad Khan *(Plastic Surgery)*

Prof. Kamran Khalid Chima *(Pulmonology)*

Prof. Rubina Sohail *(Obs. Gynae)*

Prof. Muhammad Imran *(Medicine)*

Prof. Kaukab Sultana *(Biochemistry)*

Prof. Muhammad Arif Nadeem *(Medicine)*

Prof. Ali Raza Hashmi *(Orthopaedic)*

Prof. Humayun Iqbal Khan *(Paediatric Medicine)*

Prof. Shahbaz Aman *(Dermatology)*

Prof. Naila Asad *(Anaesthesia)*

Prof. Tehreem Fatima *(Anatomy)*

Prof. Shumaila Seemi Malik *(Radiology)*

Prof. M. Waris *(Surgery)*

Dr. M Shafique *(Physiology)*

Dr. Nayyara Tahir *(Pharmacology)*

Dr. Afshan Shahid *(Community Medicine)*

Dr. M. Adnan Aslam *(Nurology)*

Dr. Zahid Rafique *(Nephrology)*

DISCLAIMER

Whilst every effort is made by the publisher, editors and editorial advisory board of the journal that no inaccurate or misleading data, opinion or statement appears in this journal, yet, they wish to make it clear that all the information appearing in the articles herein are the responsibility of authors, co-authors and contributors concerned. The publishers, editors and editorial advisory board accept no responsibility whatsoever for the consequences of any such inaccurate or misleading data, opinion or statement. Chief Editor.

Esculapio - Volume 15, Issue 01, January - March 2019

Reviewl Article

INFLAMMATORY BIOMARKERS FOR PARKINSON'S DISEASE

Asad Mumtaz, Sana Umar and AbuBakar Siddique

Abstract: Parkinson disease (PD) is caused by degeneration of dopaminergic neurons. Clinically it is characterized by bradykinesia, rigidity and resting tremors. The central hallmark of the PD is accumulation of alpha synuclein (α-SN). Aetiology of the PD includes exposure to the environmental toxins, low serum urate, genes and sporadic forms of the disease. Till date PD is a clinical diagnosis with almost 80% of dopaminergic neurons disintegrated when motor signs begin to appear. Therefore, there is urgent need for the definite biomarkers that indicate death of the dopaminergic neurons and provide accuracy in diagnosis. The cerebrospinal fluid (CSF) and imaging biomarkers are already available with varying and inconsistent results. Genetic biomarkers have also significantly contributed in revealing the physiological and pathological process underlying the PD. Most important of them is the leucine rich repeat kinase (LRRK2) which has role in both sporadic and familial forms of the PD. Inflammation appears also to be an important player in PD pathogenesis. The crosstalk between immune system of the CNS and peripheral immune system results in generation of cytokines and chemokines that are useful inflammatory biomarkers. Importantly LRRK2 expressed in different immune cells of the innate immunity which further strengths the role of inflammation in the PD pathogenesis. Hence inflammatory biomarkers could aid in early diagnosis of the PD, helps in identification of new pathways and novel therapeutic targets. Key words Parkinson disease (PD), leucine rich repeat kinase(LRRK2), MRI, innate immunity.

Introduction

PD is a neurodegenerative disorder, where the accumulation of α-SN aggregates is a central hallmark of the disease pathogenesis. However, the precise pathophysiological processes remain largely unidentified yet.[1] It is one of the most prevalent neurodegenerative disorders worldwide, affecting about 2%-3% of community older than age 65.[1] Until now 20 genes have been associated to the familial forms of the PD, whereas more than 20 genetic loci linked to increased susceptibility for the development of the PD were identified from genome-wide association studies (GWAS). Some of these genes seem to be particular relevant for the disease, including for example α-SN, glucocerebrosidase (GBA), parkin (PARK2), Pten-induced kinase 1 (PINK1), microtubule-associated protein tau (MAPT) and LRRK2.[2] The onset of PD can be characterised as juvenile (age < 21 yr), early onset (2150 yr) and late onset (generally >60 yr). In addition mutation carriers are clinically indistinguishable from idiopathic PD.[3] The clinical identification of PD is mainly based on the motor symptoms, which normally appears when 60-70% of the dopaminergic neurons are already deteriorated in the substantia nigra.[4] This depletion translates into the PD distinct motor signs, such as bradykinesia, rigidity and tremor.[5] Clinically PD is detected according to the UK Brain Bank Society Criteria based on motor signs and its upgrading by dopaminergic medication.[6] Besides disabling motor symptoms, PD development also comprise of noteworthy non-motor symptoms (NMS), such as depression, anxiety, fatigue, and cognitive decline.[7,8] The neuropathological alterations linked to these NM seems to result from α-synuclein containing Lewy bodies and Lewy neurites in the peripheral autonomic nervous arrangement and from the neuronal loss in the dorsal motor nucleus of the vagal nerve, the olfactory bulb, and the lower brainstem nuclei that control random eye movement (REM) sleep atonia.[4] The NMS anomalies of the PD includes dysautonomia, hyposmia, and REM sleep behaviour disorders (iRBD), that have been linked to the PD in people and cohort studies. Inflammation appears also to be an important player in PD pathogenesis. Immune alterations have been reported in the peripheral immune system, with altered cytokine levels and monocyte and lymphocyte subsets. Old age is the main risk for development of the PD. Similar to other immune cells, microglia exhibit age-dependent alteration. Studies from human and animal models suggest that inflammation-derived oxidative strain and cytokine-dependent toxicity add to nigrostriatal

path deterioration Furthermore, degeneration of dopaminergic neurons that releases of reactive oxygen species (ROS), chronic activation of microglia, and mitochondrial dysfunction all seems to contribute towards the neuroinflammation observed in the PD patients. [9] The inflammation statistics so far has largely focus on the risk of developing the PD. However, the significant issue is whether the immune reaction manipulates the pace of the PD development after its clinical identification. This issue is of special significance since the treatment should start with immunomodulatory drugs in the early phase of the PD. However, prior to this, proper immune-related biomarkers needs to be identified to ease the prospective tests of immuno-modulatory therapies to hinder disease progression in the PD patients. Inflammation biomarkers of the PD have achieved attention as probable, early markers of neurodegenerative disease course and may have a prognostic value. So far, the detection of biomarkers for the PD has focused exclusively on neuronal proteins (e.g., α-SN, tau, and β-amyloid). This is because these proteins are acknowledged to play a role in the primary pathophysiology of other neurodegenerative diseases including the PD.[9] Collectively, the data suggest that immune activation happened in the PD and play a vital role in its development in the central nervous systems (CNS) as well as the peripheral nervous system (PNS). Here we discuss recent advances in novel inflammatory significant biomarkers and how the cross-talk between the immune system of the brain and peripheral immune system give rise to the inflammatory biomarkers. Importantly cells of the immune system are potential biomarkers involved in the progression of the PD and will be discussed in detail here. Finally, the perspectives linked with inflammation biomarkers and therapeutic significance related to the PD will be concluded.

I. PD & biomarkers

a.CSF and blood based biomarkers in PD:

Biomarkers in body fluids and tissues may provide an effective route to detect proteins and other molecules correlated with the early diagnosis and progression of PD.[18] As multiple disease processes might coexist in PD, combination of different biomarkers that reflect each contributing pathogenic mechanism is likely to be the most appropriate approach. For example, tau and α-SN pathology coexist in PD, as well as in AD and dementia with Lewy bodies (DLB).[19] In the cerebrospinal fluid (CSF), α-SN and related molecules emerge as the most promising biomarkers,[19] although several others were also investigated such as urate or Aβ42 among others. [20] Data showed decreased tau and α-SN in the PD but inconsistency was found regarding other biomarkers i.e Aβ42, DJ-1, 8-OHdG and urate in the PD and related disorders. Nevertheless, these CSF biomarkers provide good indication of cellular turn over regarding pathways in the aging brain and subsequently the disease prognosis.

b.Genetic Biomarkers of PD:

Increasing evidence suggests that both genetic and environmental factors contribute to the aetiology of the PD. This means if a person suffered PD due to duplications, triplications or missense mutations in a gene even in these patients, age-related physiological alteration or environmental exposures contribute to the disease progression.[21] Several loci termed as PARK accounting for PD were identified in the last years. Almost half of the genes identify for PD affects the patients in a dominant manner and rest half exerts their expression in a recessive pattern.[21] The clinical symptoms varies with respect to genetic mutation in the PD. Some of the patients show more of the autonomic and resting tremors features than the others and vice versa however the decline in quality of life remains the same with the passage of time.[22] This suggests that pathogeneses varies with mutation in genes and not only disintegration of dopaminergic neurons but involvement of some other parts of the CNS occurred in the PD. The effect of the genetic alteration in the PD patients with regard to the symptoms could help in the clinical diagnosis in the future. However, the genetic testing for the PD currently used as a research tool. Some of the important genes with their inheritance and clinical features are summarized in **Table-1.**

II. Imaging Biomarkers of PD

It is well established that PD results from disintegration of dopaminergic neurons in the CNS[23] Collectively dopaminergic, serotonergic and cholinergic neurons contribute to the overlapping clinical features and presentation observed in the PD and parkinsonism. Thus, it is imperative to scan the vital structures of the brain supplied by these neurons to check their integrity in the aging brain. Substantia nigra pars compacta is especially important with regards to the dopaminergic neurons. Caudate, putamen, and Raphe nuclei are vital with regard to serotonergic neurons in patients with tremor-

Table-1: The genes with their inheritance pattern, clinical features and pathogenesis Adapted and modified.[22] Abbreviations: AD: autosomal dominant, AR: autosomal recessive.

Gene	Age of onset with inferitance	Features	Pathogenesis
SNCA	Early onset with AD	Classical PD to a more atypical	Diffuse lewy body (DLB)
PARKIN	Very early onset with AR	Classical PD	Inactivation of its E3 ligase function
PINK1	AR	Atypical features	Typical LB pathology
DJ-1	Very early onset with AR	EOPD	Increase oxidative stress and mitochondrial damage
LRRK2	AD	Classical PD	Diverse pathology comprising Lbs pathology and tauopathy with neurofibrillary tangles
Vacoular protien sorting associated protien 35 (Vps-35)	Old onset with AD	Classical PD	Disturs endosomal lysomomal trafficking

Table-2: Table described different imaging modalities with their functions specifically in the PD and related parkinsonism. (modified from literature).[25]

Imaging Modalities	Assessment in the PD and parkinsonism
SPECT	DAT-SPECT is particularly useful for the differential diagnosis between PD and nondegenerative parkinsonism, such as drug-induced parkinsonism, essential tremor (ET), dystonic tremor, or psychogenic parkinsonism
PET	PET measures the integrity of dopaminergic, serotonergic and cholinergic neurons in the PD and parkinsonism. It also assess the role of glutamatergic transmission, Cannabinoid type 1 receptors, opioid receptors A, adenosine receptors and Sigma 1 receptors.
Volumetric MRI	Gray matter (GM) changes have been assessed with voxel-based morphometry and cortical thickness analyses in PD.
T2 and T2*, and susceptibility -weighted imaging (SWI)	Iron accumulation in the brain can be detected in brain nuclei using sequences sensitive to local magnetic field in homogeneities.
Diffusion-weighted imaging and diffusion tensor imaging (DTI)	Useful to detect changes in white matter (WM) integrity in the PD and related disorders.
Functional MRI (rs-fMRI)	Measure the blood oxygenation level-dependent signal when subjects are positioned in the scanner in an awake-state without performing any particular task.
Task-Related Functional MRI	Investigate brain activity in patients with PD in order to elucidate pathophysiological mechanisms underlying PD symptoms and complications.

dominant PD. Putamen, the insular cortex, and the supplementary motor area and lower in the caudate nucleus, the orbitofrontal cortex, and the middle temporal gyrus are important in relation to the cholinergic neurons.[24] Imaging could provide information in the PD patients regarding anatomy and functional status of the whole brain and its important structures. PET radioligand scan applied can check the integrity of the projecting neurons in these brain regions. Proton magnetic resonance spectroscopy (1H-MRS) show gross physical changes (structural MRI) and metabolic changes at synaptic levels.[24] Studies have shown mixed and inconsistencies in results when comparing PD and healthy controls and between PD and parkinsonism.[25] Nevertheless, imaging provides good picture of the anatomical, metabolic and integral changes to study the disease details thus enhancing our diagnostic and treatment precision. **Table-2** highlights some of the functional performance of different imaging modalities in the PD patients.

II. Importance of LRRK2 gene in PD Neuroinflammation:

There are many genes involved in aetiology of the PD but the LRRK2 is only gene discovered so far with familial and sporadic form of the PD. The clinically indistinguishable symptoms of the LRRK2 from the idiopathic form of the disease points towards the same pathogenic process. LRRK2 has established role in inducing mitochondrial functioning, inflammatory responses, apoptosis, deregulating the immune system and endocytosis.[22] The role of the LRRK2 in immune system has been established too. It is well documented that LRRK2 expressed on the immune cells. The highest expression found in the macrophages followed by the B-cells and the dendritic cells.[28] The macrophages and DCs are the antigen presenting cells (APCs) of the innate immune system that are professional in presenting cells to the adaptive immune system. The function of microglia in the CNS is the same as that is performed by the macrophages in the peripheral immune system. Presentation of the processed antigen by the

macrophages activates the T-lymphocytes of the adaptive immunity that release cytokines to activate B-cells to generate immunoglobulin against the antigen. Importantly the antibodies produce by the B-cells can crossed the BBB and exert their influence via Fc receptors present in the microglia.[29] Figure 2 describes the axis through which B-cells antibodies activates the inflammatory process in the CNS. However the influence of the LRRK2 mutation in the B-cells antibodies differentiation process is still unclear.

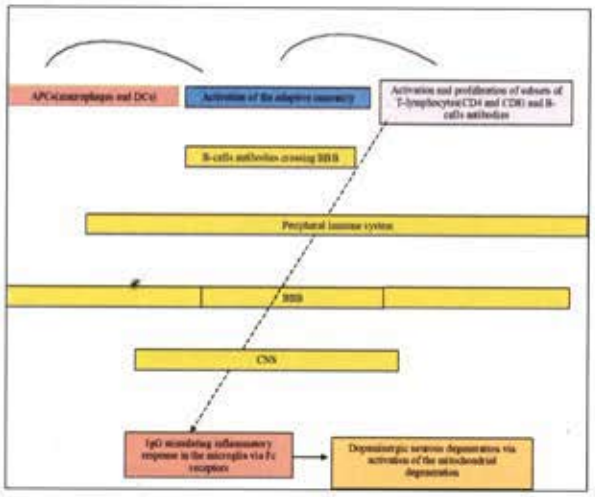


Fig-1: Schematic diagram showing the crossing of activated antibodies(IgG) that has specification for the Fc receptors in the microglia.

II. Biomarkers of immune dysregulation:

Studies showed a role of innate and adaptive immune system dysregulation in the development of the PD and its progression. The macrophages, neutrophils, natural killer cells, T-cells and B-cells have documented role at the cellular level. [30] T lymphocytes have a vital role in igniting and worsening of the PD. Importantly the T-cells occupies different dopaminergic receptors on their surface. With the introduction of most commonly used drug levodopa in the PD, a change happened in these receptors. With this alteration the a-synuclein presented to the T-cells with the help of MHC processed in a different way via dopaminergic receptors than it was done previously leading to abnormality in the pathways. Indeed, a-synuclein is a pathological hallmark of the PD and its proper disposition is vvital to halt the neuronal disintegration in the PD. Figure 3 depicts the simple pathway of discarding of a-synuclein via T-cells and the potential biomarkers originating in doing so. An important aspect in diagnosing the PD is its early detection with non-motor symptoms(NMS) as they precede the development of motor signs many years. Different cytokines have been found in the PD with non motor features. C-reactive protein (CRP), interleukin-6, tumor necrosis factor-alpha, eotaxin, interferon gamma-induced protein-10, monocyte chemotactic protein-1 (MCP-1), and macrophage inflammatory protein 1-β are in higher amount in the CSF of the PD patients. These cytokines are related with the NMS of depression, anxiety, fatigue, and cognition.[29]

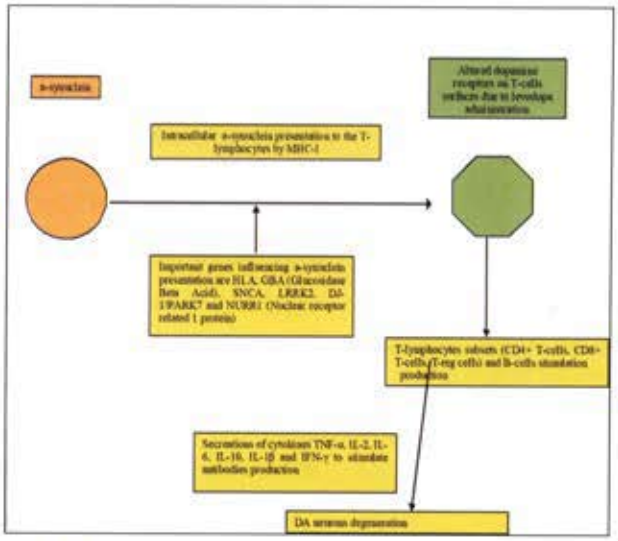


Fig-2: Immune system dysregulation generates specific biomarkers in the form of T and B lymphocytes and their subsets. The cytokines and important genes influencing the pathways provides special biomarkers for the PD.

II. Human leukocyte antigen(HLA) association to neuroinflammation in the PD:

The overexpression of PD linked genes disturb the countenance of pro-inflammatory cytokines. Besides this there are immunological genes that have a role in inflammatory process of the PD. The HLA complex is a gene complex encoding the MHC proteins which are accountable for the regulation of the immune system in humans. Association between PD and the HLA region was found on chromosome 6p21.3. It is particularly strong for sporadic and late-onset PD and men. Studies has identified four loci, including the HLA region, that contain a secondary independent risk variant for PD. This exerts an effect independently of the primary risk allele. The antigen-presenting cells, including microglia in the brain interact with T-cell receptors protein chains encoded by the closely linked HLA-DRA and HLA-DRB.

III. Conclusion and future directions:

To date PD is a clinical diagnosis and there is an urgent need to develop biomarkers that shows death of dopaminergic neurons well before the symptoms appears. Aging is the physiological process and biggest risk factor for the PD. The discovery of LRRK2 as a neurodegenerative process. Moreover whether inflammation in the CNS accelerate the neurodegeneration after its clinical identification needs investigation. This query is important in order to elucidate the role of anti-inflammatory and immunomodulatory therapy to slow the neurodegeneration in the PD.

Culprit gene for idiopathic and sporadic forms of the PD opens the gate for better understanding of the PD. In addition the LRRK2 expression in the immune cells (mononuclear, dendritic, T and B lymphocytes) further enhances the role of inflammation in the PD. The periphery inflammation is ill-studied in the PD and parkinsonism especially in the early prodromal phase when the NMS dominates. This is vital since most of the movement controlling neurons have been damaged when the motor signs starting to appear in the PD. However, efforts with large cohorts required to detect the inflammatory cytokines and chemokines at NMS stage of the PD. Since current drugs recommended for the PD depends on the disease features but levodopa remains the first choice of the treatment among clinicians. The studies of different genes and their influence on the inflammatory cells especially B cells provides new pharmacological targets and subsequently delaying the neurodegenerative process. Moreover whether inflammation in the CNS accelerate the neurodegeneration after its clinical identification needs investigation. This query is important in order to elucidate the role of anti-inflammatory and immunomodulatory therapy to slow the neuro-degeneration in the PD.

Department of Neurology
Services Institute of Medical Sciences Lahore
www.esculapio.pk

References

1.CH WilliamsGray, R Wijeyekoon. Serum immune markers and disease progression in an incident Parkinson's disease cohort (ICICLE PD).Disorders, 2016 Wiley Online Library.

2.Jean-Marc Taymans, Eugénie Mutez, Matthieu Drouyer, William Sibran and Marie-Christine Chartier-Harlin. LRRK2 detection in human biofluids: potential use as a Parkinson's disease biomarker? Biochemical Society Transactions (2017) 45 207212

3.Philippe Rizek MD, Niraj Kumar MD DM, Mandar S. Jog MD. An update on the diagnosis and treatment of Parkinson disease. CMAJ 2016. DOI:10.1503

4.Barbara Schormair, David Kemlink, Brit Mollenhauer, Ondrej Fiala, Gerrit Machetanz , Jan Roth, Riccardo Berutti, Tim M. Strom, Bernhard Haslinger , Claudia Trenkwalder , Daniela Zahorakova, Pavel Martasek , Evzen Ruzicka, Juliane Winkelmann. Diagnostic exome sequencing in early-onset Parkinson's disease confirms VPS13C as a rare cause of autosomal-recessive Parkinson's disease. Clin Genet. 2017 Sep 1. doi: 10.1111/cge.13124

5.J Campolo, R De Maria, L Cozzi, M Parolini. Antioxidant and inflammatory biomarkers for the identification of prodromal Parkinson's disease- Journal of the 2016 - Elsevier

6.Trezzi Jp1, 2, Galozzi S3, Jaeger C1, Barkovits K3, Brockmann K4,5, Maetzler W4,5, Berg D4,5,6, Marcus K3, Betsou F2, Hiller K1,7,8, Mollenhauer B9,10. Distinct metabolomic signature in cerebrospinal fluid in early parkinson's disease. Mov Disord. 2017 Aug 26.

7.Liu C, Cholerton B, Shi M, Ginghina C, Cain KC, Auinger P; Parkinson Study Group DATATOP Investigators, Zhang J.CSF tau and tau/Aβ42 predict cognitive decline in Parkinson's disease.Parkinsonism Relat Disord. 2015 Mar;21(3):271-6. doi: 0.1016/j.parkreldis. 2014.12.027.

8.D Lindqvist, S Hall, Y Surova, HM Nielsen. Cerebrospinal fluid inflammatory markers in Parkinson's diseaseassociations with depression, fatigue, and cognitive impairment.Brain, behavior, and, 2013 Elsevier.

9.Lori N. Eidson,George T. Kannarkat,Christopher J. Barnum,Jianjun Chang,Jaegwon Chung,Chelsea Caspell Garcia, Peggy Taylor,Brit Mollenhauer, Michael G. Schlossmacher,Larry Ereshefsky, Mark Yen, Catherine Kopil, Mark Frasier, Kenneth Marek, Vicki S. Hertzberg and Malú G. Tansey. Candidate inflammatory biomarkers display unique relationships with alpha-synuclein and correlate with measures of disease severity in subjects with Parkinson's disease. Journal of Neuroinflammation 201714:164.

10.Diane B. Miller and James P. O'Callaghan. Biomarkers of Parkinson's disease: Present and future. Metabolism. 2015 Mar; 64(3 0 1): S40S46.

11.Rachael A Lawson,1 Alison J Yarnall,1 Gordon W Duncan,1,2 David P Breen,3 Tien K Khoo,4,5 Caroline H Williams-Gray,3 Roger A Barker,3 David J Burn,1 On behalf

of the ICICLE-PD study group. Stability of mild cognitive impairment in newly diagnosed Parkinson's disease. J Neurol Neurosurg 2017 jnnp.bmj.com

12.Sharvari Lotankar, Kedar S Prabhavalkar, Lokesh K Bhatt.Biomarkers for Parkinson's Disease: Recent Advancement. Neurosci. Bull. DOI 10.1007/s12264-017-0183-5

13.Simon Sjödin , Oskar Hansson, Annika Öhrfelt , Gunnar Brinkmalm , Henrik Zetterberg, Ann Brinkmalm, Kaj Blennow . Mass Spectrometric Analysis of Cerebrospinal Fluid Ubiquitin in Alzheimer's Disease and Parkinsonian Disorders . Proteomics Clin Appl. 2017 Oct 3. doi: 10.1002/prca.2017

14.Mollenhauer B, Caspell-Garcia CJ, Coffey CS, Taylor P, Shaw LM, Trojanowski JQ, Singleton A, Frasier M, Marek K, Galasko D; Parkinson's Progression Marker Initiative.Longitudinal CSF biomarkers in patients with early Parkinson disease and healthy controls. Neurology 2017 Oct 13 pii: 10.1212/WNL

15.Bowman GL. Biomarkers for early detection of Parkinson disease: A scent of consistency with olfactory dysfunction. Neurology 2017;89:13

16.Jesper F. Havelund 1, Niels H. H. Heegaard 2,3, Nils J. K. Færgeman 1 and Jan Bert Gramsbergen. Biomarker Research in Parkinson's Disease Using

17.Metabolite Profiling. Metabolites 2017, 7, 42; doi:10.3390/metabo 7030042

18.Han W, Sapkota S, Camicioli R, Dixon RA, Li L. Profiling novel metabolic biomarkers for Parkinson's disease using in-depth meta bolomic analysis. Mov Disord.-2017 Sep 7. doi: 10.1002/mds.27173.

19.Weidong Le, Jie Dong, Song Li, Amos D. Korczyn. Can Biomarkers Help the Early Diagnosis of Parkinson's Disease? Neurosci. Bull. DOI 10.1007 /s12264-017-0174-6

20.Lucilla Parnetti, Anna Castrioto, Davide Chiasserini, Emanuele Persichetti, Nicola Tambasco, Omar El-Agnaf and Paolo Calabresi. Cerebrospinal fluid biomarkers in Parkinson disease. Neurol. 9, 131140 (2013);

21.Radu Constantinescu and Stefania Mondello. Cerebrospinal fluid biomarker candidates for Parkinsonian disorders. Fronteirs in neurology Jan 2013

22.Sushil Sharma, Carolyn Seungyoun Moon , Azza Khogali , Ali Haidous, Anthony Chabenne, Comfort Ojo, Miriana Jelebinkov, Yousef Kurdi , Manuchair Ebadi. Biomarkers in Parkinson's disease (recent update). Neurochemistry International 63 (2013) 201229

23.K. Kalinderi, S. Bostantjo poulou,L. Fidani.The genetic background of Parkinson's disease: current progress and future prospects. Acta Neurol Scand DOI: 10.1111/ane.12563

24.Guangwei Du, Mechelle M. Lewis, Christopher Sica, Lu He, James R. Connor, Lan Kong, Richard B. Mailman, and Xuemei Huang. Distinct Progression Pattern of Susceptibility MRI in the Substantia Nigra of Parkinson's Patients. Movement Disorder. Vol. 00, No. 00, 2018

25.Marios Politis1 , Gennaro Pagano, Flavia Niccolini. Imaging in Parkinson's Disease. International Review of Neurobiology 2017 Elsevier Inc. ISSN 0074-7742

26.Neeraj Joshi Sarika Singh. Updates on immunity and inflammation in Parkinson disease pathology. J Neuro Res. 2017;112.

27.Gardet, A., Benita, Y., Li, C., Sands, B.E., Ballester, I., Stevens, C., Korzenik,J.R., Rioux, J.D., Daly, M.J., Xavier, R.J. and Podolsky, D.K.(2011).LRRK2 isinvolved in the IFN-γ response and host response to pathogens.Journal of [1] of Immunology, 185:55775585

28.Feng Y, Li L, Sun XH.(2011). Monocytes and Alzheimer's disease.Neuroscience Bulletin,27(2): 115-122.

29.Li Chen, Mingshu Mo, Guangning Li, Luan Cen, Lei Wei, Yousheng Xiao, Xiang Chen, Shaomin Li,Xinling Yang, Shaogang Qu and Pingyi Xu. The biomarkers of immune dysregulation and inflammation response in Parkinson disease. Chen et al. Translational Neurodegeneration (2016) 5:16

30.Lindqvist D1, Hall S, Surova Y, Nielsen HM, Janelidze S, Brundin L, Hansson O. Cerebrospinal fluid inflammatory markers in Parkinson's disease--associations with depression, fatigue, and cognitive impairment. Brain Behav Immun. 2013 Oct;33:183-9. doi: 10.1016/j.bbi.2013.07.007. Epub 2013 Jul 31.

Original Article

COMPARISON OF ULTRASONIC DISSECTOR VERSUS CONVENTIONAL SURGERY IN THYROIDECTOMY

Imdad Ahmad Zahid, Zeeshan Ahmad, Asif Iqbal and Javed Raza Gardezi

Objective: To compare the results of ultrasonic dissector or conventional-surgery in terms of shorter operative time, hospital study and average drain output and to evaluate the incidence of postoperative complications.

Methods: A prospective randomized trial was conducted at surgical Unit-II of Services Hospital, Lahore. Duration of study was two years. After approval from ethical committee 100 patients with thyroid disease were included. These patients were divided in Ultrasonic Dissector (UD) group & Conventional Surgery (CS) group (50 each). In UD group patients were under went thyroidectomy with use of harmonic scalpel while in CS group patients were operated with suture ligations of vessels along with use of monopolar or bipolar cautery. All the data was collected on self designed proforma & SPSS 20 version was used for data analysis.

Results: The mean age of patients was 30 ±17 with dominant female gender. In UD group the mean operative time was 50.4 ± 7.41 minutes which was significantly lower than in CS group which was 88.6±3.89 min. Drain output was 23.9±15 ml & 33.7 ±30.2 ml in UD and CS group respectively with p- value of 0.024. P-Value was significant (<0.000) for hospital stay. Most common complication was parathyroid injury (12% cases in UD group & 16.0% in CS group). Hematoma & seroma formation was noted in 12% in each group.

Conclusions: We concluded that the use of Ultrasonic Dissector significantly decreases operative time compare to Conventional Surgery techniques. It is also safer in terms of reducing the incidence of postoperative complications.

Keywords: ultrasonic dissector, conventional surgery and thyroidectomy.

Introduction

Almost a century ago Kocher described the procedure for thyroidectomy.[1] Thyroid is one of the most vascular glands in the body with relatively little and difficult operative field.[2] Meticulous hemostasis during surgery is always a key factor for a successful outcome. In conventional-surgery (CS) of thyroidectomy the techniques used for hemostasis are suture ligation or clipping of vessels. These both techniques are effective but time consuming.[3]

The use of Ultrasonic Dissector (UD) was introduced two decade ago. UD can cut the tissues and seal vessels simultaneously. Other advantages of UD over CS include; least thermal injury to the adjacent tissues, avoidance of electrical energy transmission between the two poles & avoids neuromuscular stimulation.[4] The various studies which have been carried out in European centers concluded that use of UD saves operative time. Post operative complications such as transient hypocalcaemia and recurrent laryngeal nerve injury are relatively uncommon but similar with both techniques.[5] However very few studies have been conducted in Pakistan. The purpose of this study was to compare the CS with UD and to see which technique is safer & time saving for thyroidectomy.

Methods

A prospective randomized control study was conducted at surgical Unit-II of Services Hospital, Lahore. Duration of study was two years from March 2008 to February 2010. After approval from ethical committee 100 patients with Goitre were included. These patients were divided in UD group & CS group (50 each). Patient with recurrent Goitre, malignancy & having any co-morbid features e.g; cardiac disease and Para-thyroid disease were excluded from the study. All patients were operated under general anesthesia. These patients were Euthyroid with or without medical treatment at the time of anesthesia induction & subsequent surgery. In UD group patients under went thyroidectomy with use of harmonic scalpel while in CS group patients were operated with suture ligations of vessels along with use of monopolar or bipolar cautery. All the data was collected on self designed proforma & SPSS 20 version was used for data analysis. Variable like age,

operative time, hospital stay, drainage was presented in mean and SD. Postoperative complications including hematoma / seroma formation, infection & neck stiffness was presented in percentages. P value less than 0.005 was considered significant.

Results

One hundred patients were enrolled in this study. The mean age was 30 ±17 years with dominant female gender. In UD group the mean operative time was 50.4 ± 7.41 minutes which was significantly lower than CS group (88.6±3.89 minutes). During post operative time drain output was 23.9±15 ml and 33.7 ±30.2 ml in UD and CS groups respectively (p- value 0.024). Hospital stay in UD group was 2.60±1.06 days while 5.44±2.08 days in CS group (P-Value <0.000). **(Table-1)** Post operative parathyroid complication was noted in 12% cases in group UD & 16.0% in CS group. Hematoma / seroma formation was noted in 12% patients in each group. The rate of infection was 4 % and 12 % in UD and CS groups respectively. Neck stiffness was seen in only 3 patients in UD group as compared to 7 patients in CS group. **(Table -2)**

Table-1: Comparison of two groups (operative time, drainage & hospital stay)

	UD Group	CS Group	P-value
Operative time (min)	50.4±7.41	88.6±3.89	0.00
Draom age (ml)	23.9±1.5	33.7±30.2	0.024
Hospital stay (days)	2.60±1.06	5.44±2.08	0.00

Table-2: Details of complications in both groups.

	UD Group	CS Group
Post-operative parathyroid complications	12	16
Hematoma, seroma formation	12	12
Infection	04	12
Leck stifness	03	17

Discussion

The modern surgery for thyroidectomy is developed on the basis of technique introduced by Kochar and Bleroth in the nineteenth century.[1] The focus of all the developments in basic technique was the safety by facilitating the dissection of tissues and ensuring the effective hemostasis. Traditionally dissection has been a combination of sharp and blunt dissection and people tried suture ligation or metal clips with monopolar or bipolar cautery & recently ultrasonic energy for control of hemostasis.[6] Although ultrasonic dissector was initially developed for use in laparoscopic procedures; it is well suited to thyroid surgery.[7] Its ability to simultaneously dissect and secure hemostasis ensures a clean, dry surgical field, despite the highly vascular nature of the thyroid gland. This facilitates easy identification of important local anatomy including the recurrent and superior laryngeal nerves, and the parathyroid glands. According to literature UD has benefits over other haemostatic devices in shortening the operative time and decreasing the blood loss, as compared to the conventional techniques.[7]

We found in this study the mean operative time was significantly lower in UD group (50.4±7.41 min) as compared to CS group (88.6±3.89 min). Thyroidectomy with ultrasonic dissector & conventional methods was compared by shemen in 2002, they operated in 50 minute with ultrasonic dissector while mean operative with conventional method was 80 min, these results were comparable with our study.[8] However much longer operative time was reported by Voutilainen and Haglund with both techniques i.e. (99min with UD and 134 min with conventional technique).[9] According our results drain output was 23.9±15 ml & 33.7 ±30.2 ml in UD & CS group respectively (p- value 0.024). Similar study by Grasso E, et al. showed that post operative oozing was less in UD group as compared to conventional techniques group i.e. (45±27 vs. 54±51 ml).[10] Akshaya et al showed that amount of post operative drain out was higher in both group however it was more with conventional (98.1±19.7 and 123.5±21.7 ml).[11] We found total hospital stay in UD Group was 2.60±1.06 days while it was 5.44±2.08 in CS Group (P-Value <0.000). Akshaya et al found longer hospital stay in both group, 4.6±0.8 days in Ultrasonic Dissector group and 5.8±0.8 days with conventional method.[11] Nadim khan & colleagues' findings were comparable with present study. They reported mean hospital stay 3.1+0.65 days after thyroidectomy with ultrasonic dissector.[12]

According to our results post operative hematoma / seroma formation was noted in 12% in each group. The rate of infection was 4 % and 12 % in UD and CS groups respectively. Literature showed both UD and Conventional methods have variable complications rate after thyroidectomy. Abdulameer Muhsin Aldaraji, Jeong JJ et al and Pardal-Refoyo JL reported hematoma /seroma formation in 9.52%, 2.7% and 5.13% cases respectively with conventional method.

While after UD use they found hematoma and seroma formation in 5%, 8.5% & 0.74% case respectively. [13, 14, 15] According to Yao et al, The utilization of Ultracision permits a more accurate dissection and a statistically significant reduction of intraoperative blood loss compared to the patients operated with conventional vessel ligation in thyroidectomy, no advantage in patients operated with Ligasure.[16]

Conclusion

On the basis of current study results we are able to conclude that not only the use of UD significantly decreases operative time compare to CS techniques with ties, clips, and/or electrocautery but it is also safer in terms of reducing the incidence of postoperative complications. UD use they found hematoma and seroma formation in 5%, 8.5% & 0.74% case respectively. [13, 14, 15] According to Yao et al, The utilization of Ultracision permits a more accurate dissection and a statistically significant reduction of intraoperative blood loss compared to the patients operated with conventional vessel ligation in thyroidectomy, no advantage in patients operated with Ligasure.[16]

Conclusion

On the basis of current study results we are able to conclude that not only the use of UD significantly decreases operative time compare to CS techniques with ties, clips, and/or electrocautery but it is also safer in terms of reducing the incidence of postoperative complications.

Department of General Surgery
Services Institute of Medical Sciences Lahore
www.esculapio.pk

References

1. Shuja A. History of thyroid surgery. Professional Med J. 2008 Jun;15(2):295-7.
2. Kaplan E, Angelos P, Applewhite M, Mercier F, Grogan RH. Surgery of the thyroid.
3. Yener O, Demir M, Yılmaz A, Yıgıtbaşı R, Atak T. Harmonic scalpel compared to conventional hemostasis in thyroid surgery. Indian Journal of Surgery. 2014 Feb 1;76(1):66-9.
4. Broughton D, Welling AL, Monroe EH, Pirozzi K, Schulte JB, Clymer JW. Tissue effects in vessel sealing and transection from an ultrasonic device with more intelligent control of energy delivery. Medical devices (Auckland, NZ). 2013;6:151.
5. Zakaria HM, Al Awad NA, Al Kreedes AS, Al-Mulhim AM, Al-Sharway MA, Hadi MA, Al Sayyah AA. Recurrent laryngeal nerve injury in thyroid surgery. Oman medical journal. 2011 Jan;26(1):34.
6. Hettlich BF, Cook L, London C, Fosgate GT. Comparison of harmonic blade versus traditional approach in canine patients undergoing spinal decompressive surgery for naturally occurring thoracolumbar disk extrusion. PloS one. 2017 Mar 2;12(3):e0172822.
7. Huang J, Yu Y, Wei C, Qin Q, Mo Q, Yang W. Harmonic scalpel versus electrocautery dissection in modified radical mastectomy for breast cancer: a meta-analysis. PloS one. 2015 Nov 6;10(11):e0142271.
8. Shemen L. Thyroidectomy using the harmonic scalpel: analysis of 105 consecutive cases. Otolaryngology Head and Neck Surgery. 2002 Oct;127(4):284-8.
9. Voutilainen PE, Haglund CH. Ultrasonically activated shears in thyroidectomies: a randomized trial. Annals of surgery. 2000 Mar;231(3):322.
10. Grasso E, Guastella T. The use of Ultrasonic Dissector in the Prevention of Risk in Thyroid Surgery. Clin Surg. 2016; 1. 2016;1212.
11. Upadhyay A, Gupta AK, Karigoudar A, Gupta N, Krishnegowda U, Naskar D, Durga CK. A comparative study between ultrasonic dissector versus conventional methods in achieving haemostasis in thyroid surgery. Hellenic Journal of Surgery. 2016 Nov 1;88(6):410-4.
12. Khan N, Bangash AN, Sadiq M. Thyroidectomy with ultrasonic dissector: an early experience at lady reading hospital. Journal of Postgraduate Medical Institute (Peshawar-Pakistan). 2014 Jan 14;28(1).
13. Aldaraji AM. Ultrasonic Dissection Versus Conventional Ligation Coagulation In Thyroidectomy. Basrah Journal of Surgery. 2017;23(1):66-75.
14. Jeong JJ, Kim KH, Koh YW, Nam KH, Chung WY, Park CS. Surgical completeness of total thyroidectomy using harmonic scalpel: comparison with conventional total thyroidectomy in papillary thyroid carcinoma patients. Journal of the Korean Surgical Society. 2012 Nov 1;83(5):267-73.
15. Pardal-Refoyo JL. Hemostatic systems in thyroid surgery and complications. Acta Otorrinolaringologica (English Edition). 2011 Sep 1;62(5):339-46.
16. Yao HS, Wang Q, Wang WJ, Ruan CP. Prospective clinical trials of thyroidectomy with LigaSure vs conventional vessel ligation: a systematic review and meta-analysis. Archives of Surgery. 2009 Dec 21;144(12):1167-74.

Original Article

Efficacy of Local Corticosteroid Therapy in Adult Trigger Finger Deformity at a Tertiary Care Hospital Setting

Fahad Nazir, Fatima Chaudhry and Ghulam Qadir Fayyaz

Objective: Trigger Finger also called Stenosing Flexor Tenosynovitis is common hand pathology in adulthood. Efficacy of local corticosteroid injection was investigated in adult trigger finger deformity

Methods: Seventy females and 40 males injected with 1cc local corticosteroid at the level of A1 pulley were followed for a period of 6 months and consequent symptomatic relief was classified as good, moderate and bad.

Results: Out of a total of 110 patients, 70 females and 40 males, 40 patients had triggering in thumb, 26 patients in index finger, 22 patients in middle finger, 13 patients in ring and 9 patients had triggering deformity in little finger. All had pain and triggering in the involved digit proximal to metacarpophalangeal joint. 81 patients were observed to have no more triggering and pain while 15 patients had pain without triggering and 14 patients had both triggering and pain at the end of 1st month. At 3 months the number of patients who had no pain and no triggering remained the same whereas 3 patients had additional symptoms of triggering apart from pain thus increasing the number to 17. At the end of 6 months duration 11 patients demonstrated no response to treatment and were advised surgical intervention for definite cure.

Conclusions: Injection of local corticosteroid drug mixture in treatment of trigger finger deformity is an easy, cheap and effective method and trial should be given once before definitive treatment that is surgery.

Keywords: corticosteroid, trigger finger, tertiary care hospital,

Introduction

Trigger finger is 4th leading cause of referral in hand surgery facilities.[1] The life time incidence of trigger finger is 28:100000 per year or a lifetime risk of 2.6% in the general population, but it increases to 10% in the diabetic population.[2,3] The mean age of onset of trigger finger is 58 years and women have a tendency of 2-6 times as compared to men.[4] Patients with trigger finger have discomfort while flexing the digits and restriction of movement upon extending them. Without treatment, there may be a gradual worsening of symptoms to severe pain and locking of digits in flexion.[5]

The primary goal of treatment is to alleviate discomfort during finger movements. Steroid injection is a conservative first line intervention for trigger finger according to guidelines. Surgical intervention is recommended if conservative intervention fails to relieve the symptoms.[6] In our study, we aim to investigate efficacy of local corticosteroid therapy in adult trigger finger deformity so that we be able to counsel patients precisely regarding the risk of symptom recurrence after a corticosteroid injection. As the triggering is believed to occur due to a mismatch between the A1 pulley and flexor tendons the following protocol was followed for accurate placement of corticosteroid within the tendon sheath.

The A1 pulley overlies the metacarpal neck and it marks the proximal border of the flexor tendon sheath. This border is roughly in line with the distal palmar crease in the index, middle, ring and little finger. In the thumb proximal crease was used as a surface marker for injection.

The needle was inserted on the distal palmar crease through the skin to the bone over the finger involved and then withdrawn 1cm so that the tip was now in the flexor tendon. The patient was asked to slowly flex and extend the digit. If the needle moved with the movement of digit this confirmed that the needle was in the tendon.

Then the needle was withdrawn about 1mm until it did not move with the movement of the digit anymore this time it was in the gap between the tendon and the A1 pulley. With gentle pressure the tip of the needle was passed into the flexor sheath.

Methods

Between July 2015 and June 2016, new patients diagnosed with one or more trigger fingers at Outpatient Department, Plastic Surgery Unit Services Hospital Lahore were included in this institutional review board approved, prospective study. Patients previously treated for trigger finger, pregnant women, patients younger than 18years, having multiple triggering fingers or degenerative joint disease were excluded from this study. In total 122 patients fulfilled out eligibility criteria. 12 declined participation. This resulted in a final sample of 110 patients. In total informed consent was obtained from 70(64%) women and 40(36%) men. The mean age was 58years (SD 11years).A mixture of triamcinolone, 1% lidocaine, 0.5% bupivacaine was used in a ratio of 2:1:1.1cc of this mixture was injected using insulin syringe beneath the A1 pulley of the patients deploying the previously described technique. In the post procedure period patients were advised to move their fingers actively as required. Outpatient follow up was conducted over a minimum period of six months. The patients were prospectively assessed after one month, three months and six months after which they were discharged from the study. We defined treatment failure after there had been no symptomatic relief despite repeated injections during 6 months time period. The results were classified as good, moderate and bad as in the study of Anderson. On follow up, if patient had relief from triggering the procedure was considered effective. If the patient had no symptomatic relief they were advised a 2nd steroid injection followed by another six week appointment. After the 2nd injection if the symptoms were not relieved they were offered the 3rd and final injection. If the 3rd injection also failed the patient were offered the surgical release of A1 pulley.

Results

Out of a total of 110 patients, 70 females (mean age 48 years), 40 males (mean age 53 years) comprised the study. 40 patients had triggering in thumb, 26 patients in index finger, 22 patients in middle finger, 13 patients in ring and 9 patients had triggering deformity in little finger. All had pain and triggering in the involved digit proximal to metacarpophalangeal joint. At 1 month after the injection 81 patients (56 Female, 25 Male) were observed to have no more triggering and pain while 15 patients (10 Female, 5 Male) had pain without triggering and 14 patients(4 Female,10 Male) had

Table-1: Distribution of the deformity.

Thumb	Index	Middle	Middle	Ring
40	26	22	13	09

Table-2: Findings of clinical examination on 1st month.

No pain-no triggering (Good)	Pain without triggering (Moderate)	Pain and Triggering (Bad)
81(25 Male,56 Female)	15(5 Male,10 Female)	14(10 Male, 4 Female)

Table-3: Findings of clinical examination on 3rd month.

No pain-no triggering (Good)	Pain without triggering (Moderate)	Pain and Triggering (Bad)
81(25 Male,56 Female)	12 (4 Male, 8 Female)	17 (11 Male, 6 Female)

Table-4: Findings of clinical examination on 6th month.

No pain-no triggering (Good)	Pain without triggering (Moderate)	Pain and Triggering (Bad)
81(25 Male,56 Female)	18 (7 Male, 11 Female)	11 (8 Male, 3 Female)

Table-5: Statistical analysis of response to treatment at 1st month (t-test).

		Frequency	Present	Valid Percent	Cumulative Percent
Valid	None	14	12.7	12.7	12.7
	Moderate	15	13.7	13.7	13.7
	Good	81	73.6	73.6	100
	Total	110	100	100	

Table-6: Statistical analysis of response to treatment at 3rd month (t-test).

		Frequency	Present	Valid Percent	Cumulative Percent
Valid	None	17	15.5	15.5	15.5
	Moderate	12	10.9	10.9	26.4
	Good	81	73.6	73.6	100
	Total	110	100	100	

Table-6: Statistical analysis of response to treatment at 6th month (t-test).

		Frequency	Present	Valid Percent	Cumulative Percent
Valid	None	11	10	10	10
	Moderate	18	16.4	16.4	26.4
	Good	81	73.6	73.6	100
	Total	110	100	100	

both triggering and pain at the end of 1st month. At 3 months the number of patients who had no pain and no triggering remained the same whereas 3 patients had additional symptoms of triggering apart from pain thus increasing the number to 17(6 Female, 11 Male). At the end of 6 months duration 11 patients (3 Female, 8 Male) demonstrated no response to treatment and were advised surgical intervention for definite cure. Patients with pain but no triggering were given oral anti-inflammatory drugs and advised physical therapy. The t-test was used for statistical analysis. It revealed that the positive effects of the treatment were statistically significant (p=0.01). While the difference between the 1st, 3rd and 6th month results were statistically insignificant, (p=0.28) (Tables 1 to 7).

Discussion

Trigger finger is defined as a finger that displays snapping or uneven movement during flexion and extension.[7] The etiology of trigger finger deformity is not clear. Corticosteroid injection is the definitive treatment for the newly diagnosed trigger finger.[8] Response to the initial corticosteroid injection is well studied with the percentage of symptom free patients gradually declining over first year post injection. In some studies a success rate up to 80% was reported after a single corticosteroid injection.[9] Griggs et al reported 50% relief of symptoms by local injection treatment in trigger finger deformity. They also further stated that results were more successful in non diabetic patients. Murphy et al reported good results in 64% of participants after single dose of corticosteroid compared with 20% results in placebo group. Steroid injection was their favorite non operative treatment modality. The study by Anderson et al has 61% good results with 12% bad results in their study. Peters et al reported that the combination of corticosteroid and local anesthetic yielded better results compared with use of either modality. Similarly Cyriac et al declared steroid injections to be effective and safe in trigger finger deformity with an efficacy lasting 1 year. A recent study based in Peshawar had an efficacy of 72% with no complications.[10]

All the injections were performed by a single doctor in our study under kind supervision of our Head of Department. Fortunately we did not face any complication, but many complications have been reported in the literature due to inappropriate injection. Kazuki et al reported no complication after local steroid injection of 100 patients and concluded that extra synovial placement of injection was an effective and safe method for treatment of trigger finger deformity. Diabetic patients have propensity for some fearful complications. Wangg et al reported that single dose of steroid can cause symptomatic hyperglycemia in early post injection period. Many studies have stated that local steroid injections seems to have diminishing efficacy as the difference between the 1st,3rd and 6th month results were statistically insignificant. Published literature suggested that repeat injections for trigger finger offer some benefit but are less effective than initial injections.

Several limitations are inherent to this study design. First follow up period was short i.e. 6 months. Secondly we had not taken into account the severity of disease and outcome based on severity. Lastly different factors that affect the outcome such as nature of job were overlooked. Albeit all the confounders and reservations we can safely conclude that administration of corticosteroid injection does have a role as first line treatment in patients with trigger finger and a trial of injection should be given before any surgical intervention undertake to cure the disease.

Conclusion

The study demonstrates that corticosteroid injection therapy is an accessible, cheap and easy to administer treatment option for trigger finger deformity and it should be used before undertaking surgical option for definitive treatment.

Department of Plastic Surgery
Services Institute of Medical Sciences Lahore
www.esculapio.pk

References

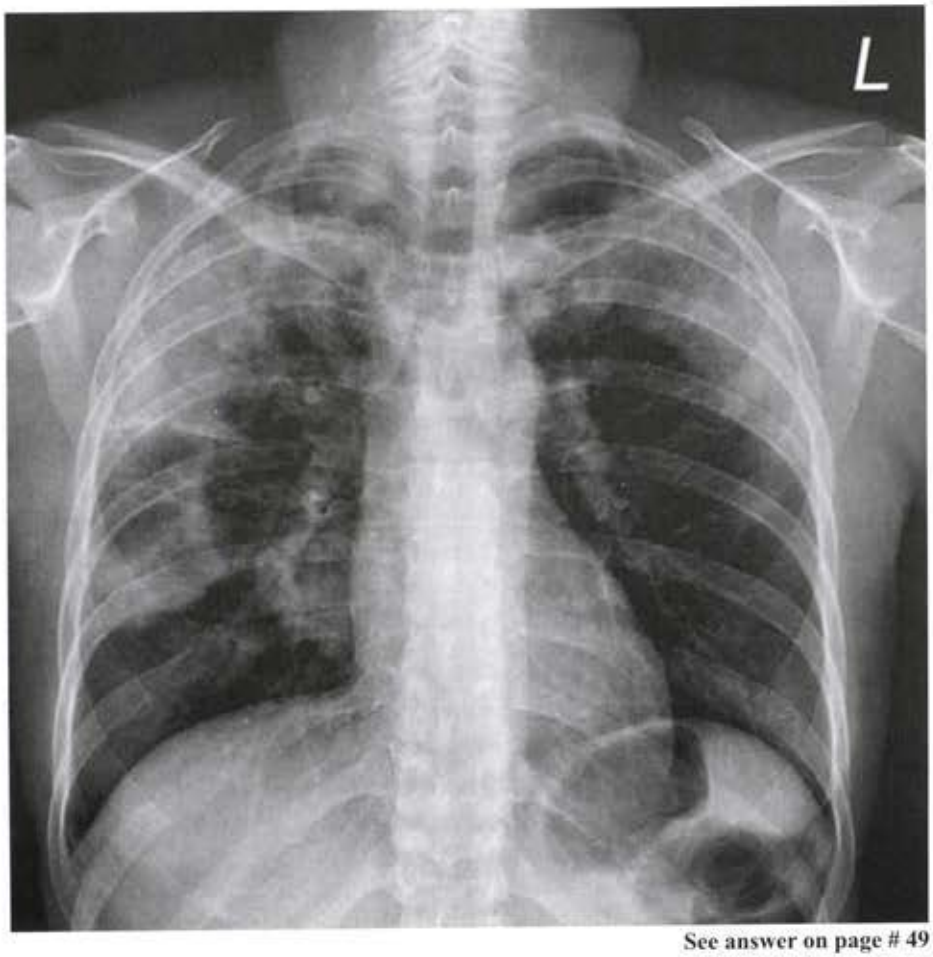
1. Kerrigan CL, Stanwix MG. Using evidence to minimize the cost of trigger finger care. Journal of Hand Surgery. 2009 Jul 1;34(6):997-1005.
2. Tung WL, Kuo LC, Lai KY, Jou IM, Sun YN, Su FC. Quantitative evidence of kinematics and functional differences in different graded trigger fingers. Clinical Biomechanics. 2010 Jul 1;25(6):535-40.
3. Akhtar S, Bradley MJ, Quinton DN, Burke FD. Management and referral for trigger finger/thumb. BMJ: British Medical Journal. 2005 Jul 2;331(7507):30.
4. Makkouk AH, Oetgen ME, Swigart CR, Dodds SD. Trigger finger: etiology, evaluation, and treatment. Current reviews in musculoskeletal medicine. 2008 Jun 1;1(2):92-6.

5. Colbourn J, Heath N, Manary S, Pacifico D. Effectiveness of splinting for the treatment of trigger finger. Journal of hand therapy. 2008 Oct 1;21(4):336-43.
6. Huisstede BM, Hoogvliet P, Coert JH, Fridén J, European Handguide Group. Multidisciplinary consensus guideline for managing trigger finger: results from the European HANDGUIDE Study. Physical therapy. 2014 Oct 1;94(10):1421-33.
7. Sato ES, Gomes dos Santos JB, Belloti JC, Albertoni WM, Faloppa F. Treatment of trigger finger: randomized clinical trial comparing the methods of corticosteroid injection, percutaneous release and open surgery. Rheumatology. 2011 Oct 28;51(1):93-9.
8. Rozental TD, Zurakowski D, Blazar PE. Trigger finger: prognostic indicators of recurrence following corticosteroid injection. JBJS. 2008 Aug 1;90(8):1665-72.
9. Carlson JC, Curtis RM. Steroid injection for flexor tenosynovitis. The Journal of hand surgery. 1984 Mar;9(2):286-7.
10. Waheed A, Sattar A, Ahmad I, Khan MA. Steroid injection in the treatment of trigger finger. Pak J Surg. 2017;33(3):208-13.

Picture Quiz

QUESTIONS

1- What does the chest radiograph show?
2- What is the differential diagnosis?
3- Which further investigations would you perform?



See answer on page # 49

Original Article

Complications of NA External Fixator and Related Factors: A Retrospective Cohort Analysis in Tibial Non-union Patients

Syed Asif Ali, Usman Zafar Dar, Tayyab Shoib, Salma Batool, Farrukh Siddique, Faridoon Siddique

Objective: To determine the complications of NA external fixator and their predictors/related factors in tibial non-union patients in a tertiary care hospital, Lahore, Pakistan.

Methods: This was retrospective cohort analysis conducted in the Department of Orthopedics, Mayo hospital, Lahore on the data of the patients who followed from July 2002 till June 2012. Patients with tibial non-union of any age groups with both open and closed fractures were included.

Results: Out of total of 144 patients, 61.8% had complications of external fixator: 44.8% (n=39) had loosening of pin, 34.5% (n=30) had loosening of clamp, 17.2% (n=15) had breaking of pin, and 3.4% (n=3) had breaking of clamp. The occurrence of the complications had statistically significant association with age groups (p=0.009), presence of skin lesion (p=0.000), bone grafting (0.031), no leg length discrepancy (p=0.000), and skin reactions to pins (p=0.000). The occurrence of the complications had no significant association with gender (p=0.440), presence of comorbid disease (p=0.728), side involved in fracture (p=1.000), and mode of reduction of fracture (p=0.074).

Conclusions: Fixator complications were seen commonly in tibial non-union patients managed with NA external fixator. Among different complications, loosening of pin was most prevalent followed by loosening of clamp, breaking of pin, and breaking of clamp. Middle age group of patients was more prone to the complications of fixator. Co-existing skin trauma and bone grafting predict the subsequent occurrence of complications of external fixator. Similarly, no leg length discrepancy and skin reactions to pins also had a positive statistical correlation with complications of fixator. However, gender, coexisting systemic diseases, site of fracture, and mode of reduction of fracture had no statistically significant association with occurrence of the complications of the fixator.

Keywords: external fixation, NA fixator, tibial non-union, complications of fixator, SPSS

Introduction

External fixation[1] is a surgical treatment used to stabilize bone and soft tissues at a distance from the operative or injury focus. In an external fixator, metal pins and clamps are placed into the bone through small incisions into the skin and muscle. The pins and clamps are attached to a bar outside the skin.[2] Tibial nonunion[3] is an arrest in the fracture repair process, where fracture still is unable to unite usually by 6-9 months post-injury. It occurs most commonly due to inadequate fracture stabilization and poor blood supply.[4] Cigarette smoking is a known risk factor.[5] In a large series, the prevalence of tibia shaft nonunion was 12%.[6] Nonunion can be classified as atrophic, hypertrophic or infected depending upon its pathophysiology.[7] External Fixators are frequently used in the management of non-union tibial fractures especially infected nonunions.[8] Naseer Awais (NA) external fixator was invented by Professor Muhammad Awais in 1980 and is common in practice in our hospitals. There are multiple complications associated with the use of external fixators, where pin track sepsis is most common one.[9,10] Our study will discuss prevalence of the different complications of NA external fixator like pin loosening, clamp loosening, pin breaking and clamp breaking, about which nationally and internationally data was scarce. Our study will also provide the predictors of these complications in tibial nonunion patients among Pakistani population.

Methods

This retrospective cohort11 study was conducted in the Department of Orthopedics, Mayo hospital, Lahore on the data of the patients from July 2002 till June 2012. Patients with tibial non-union of any age

groups with both open and closed fractures were included. The data of the patients without complete follow up was excluded. Non-union was defined by non-healing at 9 months of management of the fracture.3 The complications of the external fixation including pin loose, pin break, clamp loose and clamp break were noted till the time healing achieved or persistent nonunion was documented. The age of the patients was categorized into childhood if < 13 years, adolescence if 13-18 years, young adults if 19-44years, middle aged adults if 45-65 years, and older adults if >65 years.12,13 Gender of the patients, comorbid systemic disease like hypertension, diabetes and ischemic heart disease, side of fracture, coexisting skin trauma, mode of reduction of fracture, bone grafting, leg length discrepancy (LLD), and skin reaction to pins of fixator like erythema and purulent discharge were also noted.

Statistical analysis was completed using the Statistical Package for Social Science (SPSS), version 25. Age of the patients was the only quantitative variable, while gender, age groups, coexisting systemic disease, side of the fracture, coexisting skin trauma, mode of reduction of fracture, bone grafting, LLD, and skin reaction to pins were the qualitative variables. Frequencies and percentages were computed for qualitative variables, while mean and standard deviation was calculated for quantitative variable. The chi-square test14 was applied on the data and p-values were considered as statistically significant if < 0.05. Odds ratios15 with 95% confidence interval for predictors of complications of external fixator were also calculated.

Results

Out of total of 144 patients, 61.8% had complications of external fixator: 44.8% (n=39) had loosening of pin, 34.5% (n=30) had loosening of clamp, 17.2% (n=15) had breaking of pin, and 3.4% (n=3) had breaking of clamp **(Fig-I)**. The age of patients ranged from 2-80 years, with a mean value of 35.06 + 17.89 years. 61.9% (78 out of 126) males & 50% (9 out of 18) females suffered complications of the fixator. The association between gender and the occurrence of the complications of fixator was not statistically significant (p=0.440). Amongst different age groups, fixator complications were most prevalent in middle aged adults. 20% children, 50% adolescents, 64.3% young adults, 72.7% middle aged adults, and 50% older adults suffered complications of the fixator. The association between age groups and the occurrence of the complications of fixator was statistically significant (p=0.009). 68.4% (78 out of 114) patients who had coexisting skin trauma (i.e. open fracture) and only 30% (9 out of 30) patients without coexisting skin trauma (i.e. closed fracture) faced the complications of fixator. The association between coexisting skin trauma and the occurrence of the complications of fixator was statistically significant (p = 0.000). 77.8% (21 out of 27) in which bone grafting was performed and 56.4% (66 out of 117) patients without bone grafting faced the complications of fixator. The association between bone grafting and the occurrence of the complications of fixator was statistically significant (p=0.031). 43.5% (30 out of 69) patients with LLD and 76% (57 out of 75) patients with no LLD suffered complications of the fixator. LLD had a statistically significant negative association with the occurrence of the complications of fixator (p=0.000). 74.3% (78 out of 105) patients with skin reactions to pins of fixator and 23.1% (9 out of 39) patients with no skin reactions to pins suffered complications of the fixator. The skin reactions to pins had a statistically significant positive association with the occurrence of the complications of fixator (p=0.000). However, the associations between the complications of fixator and coexisting systemic disease (p=0.728), side involved in fracture (p=1.000), and mode of reduction (p=0.074). were statistically insignificant. **(Table 1)**

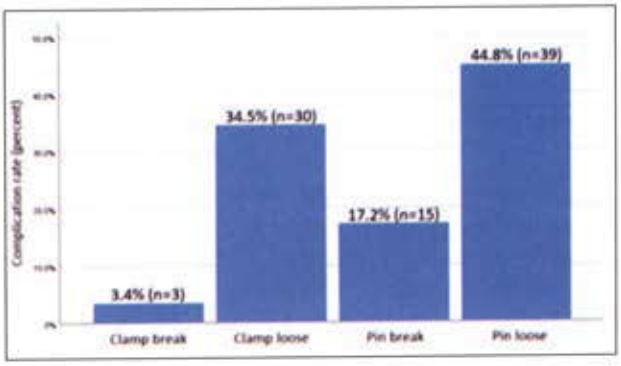


Fig-1: Complication of external fixator in non-union tibial patients (n=87/144).

Discussion

External fixation was widely used in the early part of the 20th century[16] but fell into disregard later with advent of new internal fixation devices. Its use is popular again, however there were several questions

Table-1: *Statistical correlation between Predictors and complications of external fixator in tibial nonunion patients (n = 144)*

Predictors/Factors		Complications No.	No.	Total	P-value	Odd ration with 65 confidence interval
Alternatess	Male	78 (61.9%)	48 (38.1%)	126	0.440	1.625 (0.6.3-4.38)
	Female	9 (50.0%)	9 (50.0%)	18		
Cyanosis	Childhood	3 (20.0%)	12 (80.0%)	15		
	Adolescence	53 (50.0%)	3 (50.0%)	06		
	Young adults	54 (64.3%)	30 (27.3%)	84		
	Middle age adults	24 (72.7%)	9 (27.3%)	33		
	Olders adults	3 (50.0%)	3 (50.0%)	06		
Comorbid systemic disease	Yes	33 (57.9%)	24 (42.1%)	575	0.728	0.840 (0.4425-1.661)
	No	54 (62.0%)	33 (37.9%)	87		
Side of lesion	Right	60 (60.6%)	18 (40.0%)	99	1.000	1.026 (0.499-2.107)
	Left	27 (60.0%)	18 (40.0%)	45		
Skin trauma	Yes	78 (68.4%)	36 (31.6%)	114	0.000	5.056 (2.107-12.128)
	No	9 (30.0%)	21 (70.0%)	30		
Mode of reduction	Open	66 (64.7%)	36 (35.3%)	102	0.074	1.833 (0.885-3.0799
	Closed	21 (50.0%)	21 (50.0%)	42		
Bone graft	Yes	21 (77.8%)	6 (22.2%)	27	0.031	2.705 (1.017-7.1193)
	No	66 (56.4%)	21 (43.6%)	117		
Leg lenght discreppancy	Yes	30 (43.5%)	39 (56.5%)	69	0.000	0.243 (0.119-0.495)
	No	57 (76.0%)	18 (14.0%)	75		
Skin reaction to pin	Yes	78 (74.3%)	27(25.7%)	105	0.000	(4.059-22846)
	No	9 (23.1%)	30 (76.9%)	39		

** Odd ratio can only be computed for 2 X 2 tables*

and problems with its use. International review suggests that pin loosening is a major concern in external fixation of fractures.[17] Pin loosening is usually the sequalae of the pin site infection.[18] In our study, pin loosening was the commonest complication, seen in and breaking of clamp. In our study, we divided the age of the patients in 5 groups,[12,13] and the complications of fixator were most prevalent in middle age group of patients. Such comparison was not performed ever before, so larger studies are required to validate the findings.

A fracture in which there is an open wound or break in the skin near the site of the broken bone is called an open fracture.[19] Studies shows that skin trauma increases risk of external fixators complication in tibia fracture.[20] Similarly, in our data, it was seen that co-existing skin trauma increases 5 times the risk of complications of external fixator (Odd ratio= 5.056). When, we compared the bone grafting with the occurrence of complications of external fixator, the Odd ratio with 95% Confidence interval was 2.705 (1.017-7.193). Hence, bone grafting increases the chance of the complications of external fixator approximately 2.7% in our population. This finding is of importance that the need of the grafting should be minimized to avoid the complications of the fixator. Our data also showed a positive correlation between the complications of external fixator and LLD and skin reactions to pins.

On the other hand, no correlation was seen between the complications of the fixator and multiple other factors/predictors like gender, coexisting systemic diseases, side of fracture, and mode of reduction of fracture. However, it is suggested that studies with larger data should be planned to validate all these findings.

Conclusion

Fixator complications were seen commonly in non-union tibia patients managed with NA external fixator. Among different complications, loosening of pin was most prevalent followed by loosening of clamp, breaking of pin, and breaking of clamp. Middle age group of patients was more prone to the complications of fixator. Co-existing skin trauma and bone grafting predict the subsequent occurrence of complications of external fixator. Similarly, no leg length discrepancy and skin reactions to pins also had a positive statistical correlation with complications of fixator. However, gender, coexisting systemic diseases, side of fracture, and mode of reduction of fracture had no statistically significant association with occurrence of the complications of the fixator.

Department of Orthopaedics
KEMU/Mayo Hospital, Lahore
www.esculapio.pk

References

1. Beltsios M, Savvidou O, Kovanis J, Alexandropoulos P, and Papagelopoulos P. External fixation as a primary and definitive treatment for tibial diaphyseal fractures. Strat Traum Limb Recon 2009; 4: 8187.
2. Pontarelli WR. External Fixation of Tibial Fractures. Iowa Orthop J. 1982; 2: 8088.
3. Wiss DA, Stetson WB. Tibial Nonunion: Treatment Alternatives. J Am Acad Orthop Surg. 1996; 4(5): 249257.
4. Ferreira N, Marais LC, and Aldous C. The pathogenesis of tibial non-union. SA Orthopaedic Journal Autumn 2016; 15 (1): 51 59.
5. Schmitz MA, Finnegan M, Natarajan R. Effect of smoking on tibial shaft fracture healing. Clin Orthop 1999; 8: 184 200.
6. Antonova E, Le TK, Burge R, and Mershon J. Tibia shaft fractures: costly burden of nonunions. BMC Musculoskelet Disord. 2013; 14: 42.
7. Ferreira N, Marais LC, and Aldous C. Challenges and controversies in defining and classifying tibial non-unions. SA Orthopaedic Journal Winter 2014; 13 (2): 52 56.
8. Sahu RL, and Ranjan R. Treatment of complex nonunion of the shaft of the tibia using Ilizarov technique and its functional outcome. Niger Med J. 2016; 57(2): 129133.
9. Clifford RP, Lyons TJ, Webb JK. Complications of external fixation of open fractures of the tibia. Injury 1987; 18(3): 174-6
10. Ayyaz M, Wali S, and Qadir RI. Role of external fixator in the management of type II &III open tibial fracture. JPMI 1987; 18(1): 12-17.
11. Sedgwick P. Retrospective cohort studies: advantages and disadvantages. BMJ 2014; 348: 1072.
12. Https://en.Oxforddiction- aries. com/definition/us/middle_age
13. Www.widener.edu /about/ campus-resources/wolfgram. ../life_span_chart_final.pdf
14. McHugh ML. The Chi-square test of independence. Biochem Med (Zagreb) 2013; 23(2): 143149.
15. Szumilas M. Explaining Odds Ratios. J Can Acad Child Adolesc Psychiatry 2010; 19(3): 227229.
16. Qiu S, Liu J, Liu C. Effects of external fixation technique on hospitalization time, fracture healing time and complication rate of pediatric fracture. Int J Clin Exp Med 2017;10(8):12179-12185.
17. Hyldahl C, Pearson S, Tepic S, Perren SM. Induction and prevention of pin loosening in external fixation: an in vivo study on sheep tibiae. J Orthop Trauma 1991; 5(4): 485-92.
18. Kazmers NH, Fragomen AT, and Rozbruch SR. Prevention of pin site infection in external fixation: a review of the literature. Strategies Trauma Limb Reconstr 2016; 11(2): 7585.
19. Babhulkar S, and Raza HKT. Open fractures. Indian J Orthop 2008; 42(4): 365367.
20. Elniel AR, and Giannoudis PV. Open fractures of the lower extremity: current management and clinical outcomes. Effort Open Rev 2018; 3: 316-325.

Original Article

FREQUENCY OF PLEDS IN PATIENTS WITH ACUTE STROKE

Adnan Tariq, Ayesha Aslam, Satia waheed, Ahsan Numan, M. Shahzad Hafeez and Nasir Abbas

Objective: To determine the frequency of PLEDS in patients with Acute Stroke.
Methods: This Cross sectional study was conducted in Neurology out door, Lahore General Hospital from 1stjune 2016 to 31st may 2017..
Results: The results of the current study reveal that 17.67%(n=53) cases were between 40-50 years, 24.67%(n=74) between 51-60 years, 25.66%(n=77) between 61-70 years and 32%(n=96) had >70 years of age, mean and SD was calculated as 66.78+3.65 years, 58%(n=174) were male and 42%(n=126) were female, 71%(n=213) were between 24-48 years, and 29%(n=87) were between 48-72 hours, mean+SD was calculated as 33.54+1.54 hours, while regarding frequency of PLEDS in patients with acute stroke it was recorded in 13.67%(n=41) while 86.33%(n=259) had no findings of PLEDS.
Conclusions: The results of the study conclude that the frequency of PLEDS among patients with Acute Stroke is not very high but considerable and every patient who present with acute stroke may be evaluated for PLEDS.
Keywords: PLEDS, acute stroke, frequency.

Introduction

Periodic lateralized epileptiform discharges (PLEDs) are presence of a pattern of repetitive paroxysmal slow or sharp waves, uni- or bilateral at intervals of between 0.5 to 3 seconds.[1] PLEDS mean increased seizure propensity. There has been increased frequency of seizures in patients with PLEDS in EEG.[2] A higher percentage of PLEDS was associated with higher mortality, perhaps representing greater severity of the underlying etiology. PLEDS can be found in diseases as CNS infections, Tumors and demyelination but by far the most common reaching about 26% are found in Acute Stroke.[3] PLEDS mean increased seizure propensity. There has been increased frequency of seizures in patients with PLEDS in EEG.[4]

A higher percentage of PLEDS was associated with higher mortality, perhaps representing greater severity of the underlying etiology. [5]Earliest changes of ischemia can be detected with EEG[6]. Even the CT-Scan Brain is not able to detect changes within 24 hours.Study reveals that greater number of patients with PLEDS in acute stroke is associated with poor functional outcome.[3] Patients with stroke have the highest proportion of disabilities as well as having acute complications and morbidities occurring in later life but doctors in emergency and medical wards in our setup discharge these patients early not knowing its hazards on the patients. PLEDS are a good early predictor of these complications. Early recognition of these complications and prompt and aggressive management can serve to decrease mortality and morbidity. Studies conducted internationally have almost a constant percentage regarding the presence of PLEDS reaching 26%, meanwhile only one such study that was done locally reports 0% PLEDS in post-stroke fits,[7] which as obvious is a huge difference and thus is negating its significance entirely. Before embarking on wide scale EEG for PLEDS in acute stroke patients the study of its frequency in local setting is required so that its occurrence and thus its feasibility can be established.

Methods

This was a cross sectional study, conducted in Neurology out door of Lahore General Hospital Lahore, from 1st June 2016 to 30th May 2017.The calculated sample size was 300 cases, with 5% margin of error, 95% confidence level, taking expected percentage of PLEDS in acute stroke is 26%.[3] Non probability purposive sampling technique was used. Study cases between age 40-100 were selected according to following criteria;1)Patients diagnosed as Ischemic stroke (defined as focal neurological deficit of more than 24hour duration as determined by history, clinical examination and by CT-Scan Brain).Patients with Duration of symptoms after stroke onset <24hours and >72 hours and History of previous epilepsy (defined as tendency to have recurrent convulsions) or Intracerebral bleed or Subarachnoid hemorrhage(as reported in CT-Scan)

were excluded. After ethical approval and written informed consent 300 patients presenting to neurology outdoor of General hospital Lahore, who fulfilled the inclusion and exclusion criteria were recruited. Patients' demographic information was recorded. Each patient was explained the importance and procedure of study. Data was collected with help of E.E.G tracing on the E.E.G machine which was reported in Neurology Department. Patients reported as having periodic lateralized epileptiform discharges were documented as PLEDS +ve. Data was entered in the Proforma given at the end. All the data collected through Proforma was entered in SPSS version 22 and analyzed through its statistical package. Descriptive statistics were calculated. Quantitative variables of study included age and duration of Stroke. This was presented as mean and standard deviation. Frequency and percentage of presence and absence of PLEDS was calculated and if present was presented by frequency and percentage.

Results

A total of 300 cases fulfilling the inclusion /exclusion criteria were enrolled to determine the frequency of PLEDS in patients with Acute Stroke. Age distribution of the patients was done which shows that 17.67% (n=53) cases were between 40-50 years, 24.67% (n=74) between 51-60 years, 25.66% (n=77) between 61-70 years and 32%(n=96) had >70 years of age, mean and SD was calculated as 66.78±3.65 years. Gender distribution of the patients was done which shows that 58% (n=174) were male and 42% (n=126) were female. Duration of acute stroke (in hours) was recorded which shows that 71%(n=213) were between 24-48 years, and 29%(n=87) were between 48-72 hours, mean±sd was calculated as 33.54±1.54 hours. **(Table-1)**

Table-1: Duration of acute stroke (n=300)

Duration (in hours)	No of patients	Percentage
24 - 48	213	71%
48 - 72	87	29%
Total	300	100%

Mean±SD: 33.54+1.54

Table-2: Frequency of pleds in patients with acute stroke (n=300).

PLEDS	No of patients	Percentage
Yes	41	13.67%
No	259	86.33%
Total	300	100%

Frequency of PLEDS in patients with acute stroke revealed in 13.67% (n=41) while 86.33% (n=259) had no findings of PLEDS. **(Table-2)**

Discussion

Periodic Lateralized Epileptiform Discharges (PLEDs) are usually seen in the context of destructive structural lesions of the cortex, more frequently in acute ischemic stroke and less common in tumors and meningoencephalitis, especially herpes simplex virus. Its origin and prognosis are uncertain but it is known that PLEDs are linked to epileptic seizures, including status epilepticus.[8] There is a wide variety of potential PLEDs etiologies, most of them focal lesions, of which acute ischemic stroke is the most frequent cause in all series. Although PLEDs may also appear in tumours, haemorrhages or CNS infections, this waveform is considered a quite specific EEG pattern for herpes simplex virus encephalitis,[9] but they are also related to inflammatory processes of different origins such as neurosyphilisl,[10] demyelinizing diseases,[11] neurocysticercosis,[12] influenza,[13] neuro-Behcet's disease[14] or bacterial meningoencephalitis, including Q fever.[15] We planned this study as we found that studies conducted internationally have almost a constant percentage regarding the presence of PLEDS reaching 26%, meanwhile only one such study that was done locally reports 0% PLEDS in post-stroke fits,[7] which as obvious is a huge difference and thus is negating its significance entirely. The results of the current study reveal that 17.67%(n=53) cases were between 40-50 years, 24.67%(n=74) between 51-60 years, 25.66%(n=77) between 61-70 years and 32%(n=96) had >70 years of age, mean and SD was calculated as 66.78±3.65 years, 58%(n=174) were male and 42%(n=126) were female, 71%(n=213) were between 24-48 years, and 29%(n=87) were between 48-72 hours, mean±sd was calculated as 33.54±1.54 hours, while regarding frequency of PLEDS in patients with acute stroke it was recorded in 13.67%(n=41) while 86.33%(n=259) had no findings of PLEDS. The findings of the study are nearly agreement with the studies conducted internationally i.e. 26%,[3] while in contrast with a local study,[7] the reason behind this difference is unknown. Another study by Cyril Charlin[16] evaluated the incidence and the clinical significance of periodic lateralized epileptiform discharges (PLEDs) in acute ischemic stroke and recorded overall PLEDs in 13(27.7%) patients. Though the results are in agreement with other international studies but more trials in our society are required to confirm the

findings of our study and this data may be considered as primary.

present with acute stroke may be evaluated for PLEDS.

Conclusion

The results of the study conclude that the frequency of PLEDS among patients with Acute Stroke is not very higher but considerable and every patient who

Department of Neurology
Lahore General Hospital, Lahore
www.esculapio.pk

References

1. Wieser HG, Chauvel P: Simple partial status epilepticus and epilepsiapartialis continua of Kozhevnikov. In Epilepsy. Edited by Engel J, Pedley TA. A comprehensive textbook. Philadelphia: Lippincott Williams and Wilkins; 2008:707-09.
2. Mecarelli O, Pro S, Randi F, Dispenza S, Correnti A, Pulitano P,. EEG*Patterns and Epileptic Seizures in Acute Phase Stroke. Cerebrovasc Dis 2011;31:191-98.
3. Fitzpatrick W, Lowry N. PLEDS. Clinical Correlates. The Canadian Jr of Neurological Sciences 2007;34:443-50.
4. Mecarelli O, Pro S, Randi F, Dispenza S, Correnti A, Pulitano P,. EEG Patterns and Epileptic Seizures in Acute Phase Stroke. Cerebrovasc Dis 2011;31:191-98.
5. Orta DSJ, Chiappa KH., Alejandro ZQ, Daniel JC, Andrew JC: Prognostic Implications of Periodic Epileptiform Discharges. Arch Neurol 2009;66(8):985-91.
6. Mubeen FR, Miguel AC, Gabrielle AV, Cherrie TD, Amna AF, Woojin Y,.Predictive Value of Clinical and EEG Features in the Diagnosis of Stroke and Hypoxic Ischemic Encephalopathy in Neonates with Seizures. Stroke.2009; 40:2402-07.
7. Khealani BA, Ali S, BaigSM.Post stroke seizures:Descriptive study from a tertiary care centre in Pakistan.J Pak Med Assoc2008;58:365-8.
8. Fernández FH, Fernández-Díaz E, Pardal-Fernández JM, SeguraT, García-García J. Periodic lateralized epileptiform discharges as manifestation of pneumococcal meningoencephalitis. Inter ArchMed 2011;4:23.
9. Beneto A, Gomez E, Rubio P, Sobrino R, Esparza A, Gil M. Periodical EEG pattern modifications in herpetic encephalitis treated with acyclovir. Rev Neurol 1996;24:829-32.
10. Camacho-Salas A, Martínez-Salio A, García-Morales I. Descargase-pileptiformeslateralizadas y periódicascomo forma de presentación de neurosífilis. Rev Neurol 2002;35:734-7.
11. Chabolla DR, Moore JL, Westmoreland BF. Periodic lateralized epileptiform discharges in multiple sclerosis. Electroencephalogr Clin Neuro physio1 1996;98:5-8.
12. De Carvalho-Filho P, Arruda OM, DeMelo-Souza SE. Periodic lateralized epileptiform discharges in neurocysticercosis. ArqNeuropsiquiatr 1989;47:94-9.
13. Kurita A,Furushima H, Yamada H, Inoue K. Periodic lateralized epileptiform discharges in influenza B-associated encephalopathy. Intern Med 2001;40:813-6.
14. Kihara M, Takahashi M, Mitsui Y, Tanaka H, Nishikawa S, Nakamura Y. A case of neuro-Behçet's encephalitis with pleds as distinct from herpes simplex encephalitis: a differential diagnosis. FunctNeurol 1996;11:99-103.
15. Mateos V, Salas Puig J, Leiva P, Lahoz CH. Acute meningoencephalitis caused by Coxiellaburnetii with periodic EEG complexes.Neurologia 1992;7:30-3.
16. Charlin C, Tiberge M, Calvet U, Martinez P, Larrue V. The clinical significance of periodic lateralized epileptiform discharges in acute ischemic stroke. Journal of Stroke & Cerebrovascular Diseases. 2000;9:298-302.

Original Article

BMI AND HAND GRIP FORCE: BOYS WIN THE LEAD

Ayesha Sadiqa, Hina Pasha, Farida Munawar and Nayab Fatima

Objective: To gender in young adults via PowerLab and to observe the role of BMI in connection to Hand Grip Force.

Methods: A total of 30 participants involved in the study consisting of 15 boy and 15 girls, ranging between 20 to 23 years of age. All were physically healthy and no one on any medication nor involved in any physical training program. PowerLab along with hand grip transducer as hardware and Lab tutor as software were used to measure Grip force values. For weight and height measurement Adult Weighing Scale was used for each volunteer.

Results: We found >350% high value of maximum grip force in boys as compared to girls. Mean hand grip force was 48% raised in boys than girls. Also a 70% increased hand grip force was found in boys just before fatigue. A direct relation existed between BMI and Hand Grip Force in boys. While in girls, we observed, an increase in Mean Grip Force, but a decrease in Maximum Hand Grip Force and Hand Grip Force just before fatigue with increased BMI.

Conclusions: Thus boys have got higher Hand Grip Force than girls, in terms of maximum, average and just before onset of fatigue values. The BMI showed a direct relation with Hand Grip Force in boys. Although in girls, it was in inverse relation with Hand grip force and grip force just before fatigue; but in direct relation with Mean grip force.

Keywords: hand grip force, power lab, hand grip transducer

Introduction

Hand Grip Force is devoted to unit forces with zero ultimate value applied by hand digits on any object with contact interface.[1] Hand digits exert forces mainly because of the activation of the flexor digitorum profundus and the flexor digitorum superficialis muscles, however intrinsic and extrinsic muscles too participate physiologically in the production of grip force.[2] The maximum grip force is obtained by forceful flexion of all fingers of hand with the maximum voluntary power under physiological bio-kinetic environment.[3] Muscle fatigue is termed as a motor insufficiency that leads to gradual decline in maximum force or strength of muscle and it can be quantified through force reduction of muscle.[4]

Here we aim to assess the difference of Maximum and Mean hand grip force, with respect to gender in young adults via PowerLab.

PowerLab is considered the world's first data acquisition system designed for the field of life sciences research, which provides faster results with computed analysis.[5] This advanced digital data recording technology comprised upon a hardware and software, with improved applications and efficiency in terms of various human physiological parameters including muscle activity.[6] Hand grip force was used to be measured in kilograms, pounds, milliliters of mercury and even in Newtons;[7] however on PowerLab the grip force can be quantified and analyzed in percentages.

Methods

Thirty participants involved in this study through random sampling, consisting of fifteen boys and fifteen girls, ranging in-between 20-23 year of age. All were physically healthy and no one was on any medication nor were they involved in any physical training program. Also all participants were with right hand dominance. PowerLab along with hand grip transducer as hardware was used in the study and Lab tutor as software were used to get related Grip force values.

When Volunteer was instructed to grip the transducer in his/her right fist, "Grip Force Calibration" was directly obtained on window by connecting the "Grip Force Transducer" into the main Hardware of PowerLab, as showed in Figure 1a & 1b given below. Grip Strength showed in percentage (%) on y-axis and Time in seconds on x-axis. On maximum squeezing the transducer peak grip force values was obtained. Labeling on the digital graph could also be done for the identity of the volunteer. Moreover on both axis the scales could also be adjusted. BMI values were

taken in kg/cm via "Adult weighing scale".

For more than two groups one way ANOVA (analysis of variance) was applied on the data, using SPSS version 16. Where value of alpha (∞) was considered 0.05 i.e. 95 % confidence interval was selected. Lastly analysis among different groups was expressed in terms of p-value (Probability value), for evaluation of statistical significance.

Fig-1a: MLT004/ST Grip Force Transducer

Fig-1b: Sitting position of the Subject holding Grip Force Transducer.

Results

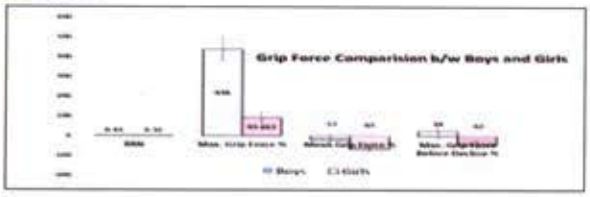


Fig-2: Bar graph showing Comparison of BMI and hand muscle grip force of the boys & the girls on Power lab (p=<0.0001).

We found a high value for maximum grip force in boys as compared to girls of same age group, >350 % increased value for boys comparing to their counterpart girls. **(Fig-2)**

The average grip force is higher in boys as compared to girls with a rise of 48% in boys, although the average values for both genders are in negative numerical, which means that average grip force is too low for hand muscles with respect to our unit of analysis. **(Fig-2)**

A 70 % rise in maximum hand grip force just before onset of fatigue, in boys as compared to girls. **(Fig-2)**

Discussion

In connection to grip force the muscular anatomy of human digits consisted of two major groups of muscles, known as intrinsic and extrinsic muscles[2]. The bellies of the intrinsic muscles lie in hand, while the bellies of extrinsic muscles are placed in forearm[8]. Previously a study conducted on Australian population used dynamometer with standardized positioning of the subjects in order to quantify hand grip strength[5]. According to another research hand grip force can be measured in terms of total static force by which hand can squeeze a dynamometer[9].

The potential contributors that act as bond among human digits included connective tissue, which provide mechanical connections between fingers[8], multi-tendon extrinsic muscles of hand and neural factors such as overlapping cortical projections in fingers[10]. All of these possessed a key role in isometric hand muscle force[10]. A static work or push against a stable resistance is stated as Isometric force[11]. Many other factors influence grip force and muscle strength is one of them, which is mainly determined by the interplay of flexors and extensors in each muscle group[8].Other factors which affect hand grip force included as age, gender, ethnicity, fatigue, time of day, nutrition, any pathology or pain, and hand dominance (right or left)[12].According to a study the dominant hand owns approximately 10% more strength than the non-dominant one, while other group of researchers argued that dominant hand carries about 12.7% more strength as compared to other[3].

Gender based analysis of grip strength has been shown higher grip force in males at all ages compared to counterpart females. While specifically analysis of hand grip force with respect to different age groups confirmed that maximum grip strength present in the fourth decade of life in both genders and then begin to decline gradually[13].

Conclusion

The boys have more hand grip force than girls in terms of maximum, average and just before fatigue onset values, measured through PowerLab. Although .the average grip force was in negative numerical, indicating that the Mean hand grip force was quite less than its maximum value. All was with satisfactory significant differences.

Department of Physiology
Shalamr Medical and Dental Hospital, Lahore

References

1. Sonne MW, Hodder JN, Wells R, Potvin JR. 2015. Force time-history affects fatigue accumulation during repetitive handgrip tasks. J ElectromyogrKinesiol, 25, 130-5.
2. Incel NA, Ceceli E, Durukan PB, Erdem HR, Yorgancioglu ZR. 2014. Enslaving in a serial chain: interactions between grip force and hand force in isometric tasks. Exp Brain Res, 232, 775-87.
3. Incel NA, Ceceli E, Durukan PB, Erdem HR, Yorgancioglu ZR. 2002. Grip strength: effect of hand dominance. Singapore Med J, 43, 234-7.
4. Enoka RM, Duchateau J. 2008. Muscle fatigue: what, why and how it influences muscle function. J Physiol, 586, 11-23.
5. Nauman Aziz, Giuseppe Simonetta, Kellie Forrester. 2006. Recent developments in data recording systems for physiology. Pak J Physiol, 2.
6. Casotti G, Rieser-Danner L, Knabb MT. 2008. Successful implementation of inquiry-based physiology laboratories in undergraduate major and nonmajor courses. AdvPhysiolEduc, 32, 286-96.
7. Schaefer LV, Bittmann FN. Are there two forms of isometric muscle action? Results of the experimental study support a distinction between a holding and a pushing isometric muscle function. BMC Sports Science, Medicine and Rehabilitation. 2017;9(1):11.
8. NCBI Website - Book: Informed Health Online. 2010. How does the hand work?Institute for Quality and Efficiency in Health Care (IQWiG).
9. Ekşioğlu M. 2016. Normative static grip strength of population of Turkey, effects of various factors and a comparison with international norms. ApplErgon, 52, 8-17.
10. Angst F, Drerup S, Werle S, Herren DB, Simmen BR, Goldhahn J, 2010. Prediction of grip and key pinch strength in 978 healthy subjects. BMC Musculoskeletal Disorders, 11, 94.
11. Schaefer LV, Bittmann FN. 2017. Are there two forms of isometric muscle action? Results of the experimental study support a distinction between a holding and a pushing isometric muscle function. BMC Sports Sci Med Rehabil, 11, 9-11.
12. Wichelhaus A, Harms C, Neumann J, Ziegler S, Kundt G, Prommersberger KJ, Mittlmeier T, Mühldorfer-Fodor M. 2018. Parameters influencing hand grip strength measured with the manugraphy system BMC MusculoskeletDisord. 19, 54.
13. Lam NW, Goh HT, Kamaruzzaman SB, Chin AV, Poi PJ, Tan MP. 2016. Normative data for hand grip strength and key pinch strength, stratified by age and gender for a multiethnic Asian population. Singapore Med J. 57, 578-584.

Original Article

Observation of Clinical Courseand Response to Conservative Management Inpatients with Hypertriglyceridemic Acute Pancreatitis Admitted to Medical Ward.

Kamran Rashid Mirza and Ambreen Kamran Mirza

Objective: To study the characteristics and clinical course of hypertriglyceridemic acute pancreatitis patients admitted under care of medical department and observed the effects of conservative management on triglyceride levels.

Methods: Patients presenting with mild to moderate acute pancreatitis having admission triglyceride levels more than 11.3mmol/l (1000 mg/dl), normal biliary anatomy and absent gall stones were included. They were closely monitored clinically as well as with serial pancreatic enzymes and triglyceride levels. Initially, the patients were started on conservative regimen including NPO, IV fluids, insulin infusion and anti-lipid medications. Plasmapheresis considered as a non-conservative intervention was not done immediately on admission, but was reserved for the cases showing lack of improvement, worsening of symptoms or lack of reduction in triglyceride levels within 24 to 48 hours of starting treatment.

Results: Twelve patients over the period of five years were studied, including nine males and three females. Diabetes turned out to be main cause of hypertriglyceridemia (nine out of 12 patients were known diabetic, and two were newly diagnosed during this admission). Patients with diabetes were found to be poorly compliant with their treatment and monitoring of blood sugar levels. All patients were either overweight or obese, BMI ranged from 27.8-35.5 Kg/m2. Four patients gave history of alcohol intake and two had hypothyroidism. Five patients were known to be dyslipidemic but none of the patients were aware of any family history of hyperlipidemia. Three patients needed plasmapheresis due to systemic complications and persistent pain whereas, the remaining patients improved with conservative management only. Triglyceride levels declined rapidly and steadily for almost all patients and average time of discharge was approximately one week.

Conclusion: Rising obesity and diabetes can lead to increase in cases of hypertriglyceridemic pancreatitis. Diagnosis can easily be missed if triglyceride levels are not checked on admission, as levels can drop rapidly due to treatment started for acute pancreatitis. Patients should be strongly emphasized for compliance to treatment of diabetes and hyperlipidemia and advised to lose weight to prevent occurrence of these cases.

words: hypertriglyceridemia, acute pancreatitis, hypertriglyceridemic pancreatitis.

Introduction

Acute pancreatitis (AP) is a common and potentially fatal medical condition.[1] Hypertriglyceridemia is frequently associated with AP, both either as a precipitant or as anepiphenomenon. While mild to moderate elevations are found in up to 47% of cases, it is the severe hypertriglyceridemia that has been described to cause AP.[2] Up to 7% of AP could be due to severe hypertriglyceridemiaand it is accepted as third most common cause after gall stones and alcoholism.[3] There is a suggestion that hypertriglyceridemic pancreatitis (HTGP) is associated with higher severity and complication rates,[4] but it is not agreed by all.[5] The increasing prevalence of hypertriglyceridemia due to the changing eating habits, sedentary lifestyle, alcohol consumption, obesity and concomitant diabetes mellitus can lead to increased frequency of the acute HTGP in future.[6] Bulk of the literature indicates that triglyceride level (TGL) of at least 11.3mmol/l (1000mg/dl) are required to cause pancreatitis.[7] Some other studies indicate requiring even higher levels.[2]

High levels of serum triglyceridecan be result of either genetic factors or secondary causes or in most cases involving both. In Frederickson Classification of hyperlipidemias types I, IV and V can lead to hypertriglyceridemia. Types I and V can by themselves lead to very high levels, whereas type IV in addition requires secondary causes to be present.[8]

Secondary causes in addition to those mentioned above also include drugs like tamoxifen, estrogens etc.[8]

It is advised to reduce TGL below5.65 mmol/l [500 mg/dl] to alleviate symptoms and prevent recurrences.[9] The standard treatment of AP includes Intravenous fluids (IVF) and nothing per oral (NPO), this also helps in reducing TGL. Multiple treatment strategies available to treat severe hypertriglyceridemiaincluding anti-lipid drugs like fibrates and omega 3 fatty acids, heparin and insulin infusions, and more aggressive methods like plasmapheresis and lipid apheresis.[10] The treatment to reduce triglycerides should be started as early as possible and usually more than one treatment options are used. Plasmapheresis is expensive, hazardous and is not available widely. Some studies have shown early use of plasmapheresis associated with better outcome.[10] American Society for Apheresis (ASFA) guidelines recommend plasmapheresis as category III grade 2C in acute HTGP.[11] The purpose of our study was to see the effects of conservative management on the clinical course and TGLof patients with acute HTGP and to reserve plasmapheresis only for those cases not showing improvement. In our hospital standard international units (mmol/l) are used. In this study units in metric system (mg/dl) are also given where necessary.

Methods

We collected twelve cases of acute HTGP from December 2012 to March 2018. The study was conducted at the Department of Medicine, Al-Adan Hospital, Kuwait. The diagnosis of AP was basis on Revised Atlanta Classification 2012.[12] The severity was judged into mild, moderately severe and severe AP also based on Revised Atlanta Classification. The inclusion criteria were age greater than 18 years, admitted to medical ward with AP of mild to moderate intensity having initial TGL greater than 11.3 mmol/l [1000mg/dl]. TGLs were done on admission for all patients presenting with AP and having normal biliary anatomy and absent gall stones on imaging. Those patients who were on any medication, probable of causing AP including GLP-1 receptor analogs and DPP-4 inhibitors were excluded. Social alcohol drinkers were included as do most studies on HTGP however patient with history of recent heavy alcohol intake were not included. Also the patients who got directly admitted to ICU were not included in the study. All the information was noted on a pre-devised Performa.

Secondary causes like diabetes, alcohol intake, hypothyroidism, and hyperlipidemia as well as drug history were looked for. Treatment taken by patient including anti-lipid and anti-diabetic medications and there compliance was noted, as well as any drugs that can cause hypertriglyceridemia like estrogens. The physical examination included BMI, search for any local or systemic complications. During the stay in the ward patients were regularly and closely monitored. Serial serum triglyceride, cholesterol, amylase and lipase levels were done alongwith CT abdomen.

As initial management all patients were put on NPO and IVF and received Fenofibrate145 mg once daily (with sips of water). Insulin infusion was planned for patients with hyperglycemia at the rate of 0.05 U/Kg/Hour. Blood sugar was monitored hourly and insulin infusion rate was titrated to maintain target blood sugar levels approximately 6.111mmol/l [110200mg/dl].Insulin infusions were continued for 48 to 72 hours depending upon the condition of the patient. Plasmapheresis was not included as initial treatment and was only to be done if there was lack of improvement, worsening of symptoms or persistently elevated triglyceride levels. Admission TGL was not considered as an indication.

Results

Nine patients were male and three females, five were Arab and seven belonged to Indian Subcontinent. All patients were of younger to middle aged group with mean age of 41.6 years [range 29 to 55 years]. All patients were either overweight or obese, the BMI ranged from 27.8 to 35.5 Kg/m^2 (average BMI; 31.2 Kg/m^2). Type 2 diabetes mellitus was major secondary factor for hypertriglyceridemia present in eleven out of twelve patients. Of these nine were known diabetics whereas two were newly discovered. All diabetic patients had uncontrolled blood sugar readings on admission and received insulin infusions. History of dyslipidemia was found in only five patients. One of these patient was known to have an attack of acute HTGP. She was on fenofibrate and was admitted this time with second attack due to poor compliance of treatment. Other four patient were prescribed statins in past, but no old lipid profile lab results were available with them. All patients confessed to poor compliance of diabetic and hyperlipidemic treatment. Surprisingly none of our patients had any idea about the history of dyslipidemia in their families. Four patients had history of alcohol intake. Only two patients were hypothyroid. All patients were admitted with chief

complaints of vomiting and abdominal pain of varying duration of few days.TGLs on admission ranged from 14.86 mmol/l [1315mg/dl] to 48.28 mmol/l[4272mg/dl] (average: 26.44 mmol/l [2339.8mg/dl]). Lipase was found to be more consistently elevated above the three times normal limit [10 patients] as compared to serum amylase (**see tables)**. Two patients had normal amylase on admission, however their CT scan were suggestive of AP thus fulfilling the revised Atlanta Classification 2012 criteria for diagnosis. Five patients were diagnosed with mild AP and remaining with moderately severe pancreatitis. CT scan was done in all patients except one, who was known case of HTGP, admitted with second attack and refused the scan. The results of CT scan revealed oedematous non-necrotizing pancreatitis in six patients and other five patients having necrotizing pancreatitis [see tables].Transient respiratory dysfunction was noted in one patient (see below), luckily none of our patients deteriorated to develop any permanent organ damage. As noted before all patients were initially put on NPO and started on IVF and fenofibrate whereas eleven patients received insulin infusion. Plasmapheresis was needed for three patients. One of them (pt. no: 1) had developed systemic complications including basal pneumonitis and bilateral pleural effusion with transient episode of desaturation which improved in ICU without need for ventilation. The other two patients [pt. no: 3& 10]had persistent pain in spite of improving TGL. Luckily all patients had rapid fall in their TGLas well as improved clinically post one session of plasmapheresis ruling out the need for any further sessions. Those patients who were managed conservatively showed a progressive drop in TGL (see chart) except one who had an increase in TGL on second day of admission [pt. no: 4], his TGL rose from 19.49 to 25.84 as he was clinically improving and his pancreatitic enzymes were reducing we continued to manage him conservatively and from day three onwards his TGL started to come down. No patient developed any complications that needed prolonged admission. Patient stay ranged from four to 9 days. Our aim was to discharge patients when TGL reach less than 5.65 mmol/l (500mg/dl), however some patients asked for earlier discharge. They were discharged with dietary advice and follow up in OPD.

Pancreatic oedema, peri-pancreatic fluid and phlegmon, particularly around pancreatic tail. CT abdomen picture of patient no: 1

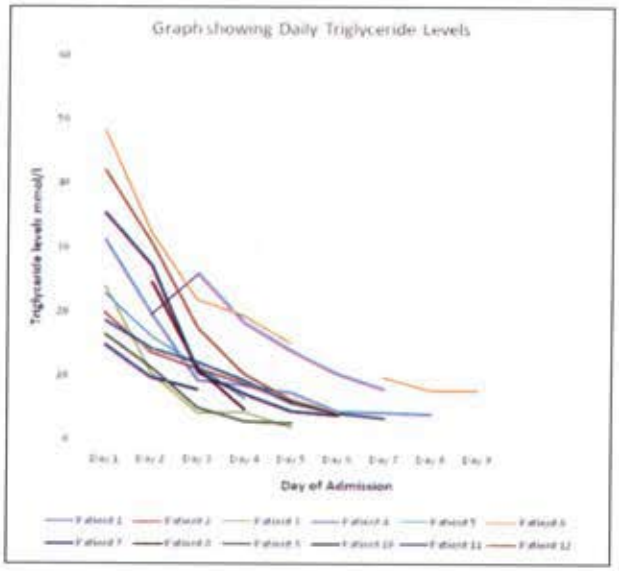


Table-1:Socio-demographic characteristics of the family.

	Patient 1	Patient 2	Patient 3	Patients 4	Patients 5	Patients 6
Age (in years)	31	49	41	35	29	39
Gender	Male	Male	Female	Male	Male	Male
Nationality	Subcontinent	Arab	Arab	Subcontinent	Subcontinent	Subcontinent
BMI [Kg/m2]	3.0.5	28.7	33.2	31.8	32.6	28.1
Alcohol intake	Yes	Yes	No	No	No	No

Diabetes	No	No	Yes	Yes, newly discovered	Yes	Yes
Hypothyroidism	No	No	Yes	No	No	No
Known case of dyslipidemia	No	No	Yes	No	No	No
CT ABD	Non-necrotizing Oedematous pancreatitis with mild free fluid	Oedematous Pancreatitis	Necrotizing pancreatitis, small necrotic foci in pancreatic head	Acute necrotizing pancreatitis, pelviabdominal collection	Oedematous non-necrotizing pancreatitis.	Necrotizing pancreatitis
Triglyceride mmol/l [mg/dl] (on admission)	31.15 [2756]	19.96 [1766]	19.49 [1724]	19.49 [1724]	22.7 [2008]	48.28 [4272]
Total cholesterol mmol/l-[md/dl] (on admission)	13.3 [513]	13.99 [540]	11.29 [436]	18.36 [709]	18.3 [706]	20.25 [782]
Amylase U/L (on admission)	180	66	485	255	613	742
Lipase U/L(on admission)	623	94.8	717.3	482	867	1216
Blood Sugar mmol/l[mg/dl] (on admission)	11.6 [209]	13.4 [241]	14.2 [256]	9.81 [176]	13.3 [239]	14.4 [260]
Plasmapheresis	Yes	No	Yes	No	No	No
Triglyceride on discharge mmol/l [mg/dl]	3.98 [35.2]	6.13 [542.5]	1.91 [169]	7.96 [7.4]	6.3 [557]	7.8 [690]

Table-2: Characteristics and lab results of the patients.

	Patient 7	Patient 8	Patient 9	Patients 10	Patients 11	Patients 12
Age (in years)	44	35	52	43	47	55
Gender	Male	Male	Emale	Female	Male	Male
Nationality	Arab	Subcontinent	Subcontinent	Arab	Subcontinent	Arab
BMI [Kg/m2]	27.8	34.1	31.7	30.9	28.6	35.3
Alcohol intake	No	Yes	No	No	Yes	No
Diabetes	Yes	Yes	Yes, newly discovered	Yes	Yes	Yes
Hypothyroidism	No	No	No	Yes	No	No
Known case of dyslipidemia	Yes	No	No	Yes	No	Yes
CT ABD	Not done refused	Oedematous pancreatitis, peripancreatitic fluid	Oedematous pancreas, no necrosis	Acute necrotizing pancreatitis Pelviabdominal, peipancreatic fluid collection	Oedematous Pancreatitis	Acute Necrotizing Pancreatitis
Triglyceride mmol/l [mg/dl] (on admission)	14.86 [1315]	24.46 [2164]	16.4 [1452]	35.4 [3133]	18..6 [1646]	42.1 [3726]
Total cholesterol mmol/l-[md/dl] (on admission)	9.43 [349]	11.22 [433]	9.7 [375]	14.2 [548]	12.4 [479]	17.4 [672]
Amylase U/L (on admission)	184	157	210	187	92	394
Lipase U/L(on admission)	702	520	411	592	107	1017
Blood Sugar mmol/l[mg/dl] (on admission)	15.5 [279]	11.1 [200]	17.2 [310]	16.7 [301]	18.4 [332]	13.9 [251]
Plasmapheresis	No	No	No	Yes	No	No
Triglyceride on discharge mmol/l [mg/dl]	4.57 [404]	2.78 [246]	2.55 [226]	3.8 336]	3.3 [292]	4.1 [363]

Discussion

Our study shows that most patients with mild to moderate HTGP can be managed conservatively with plasmapheresis reserved only for selected cases. Our study was limited by smaller number of patients and the fact that it did not include patients with severe pancreatitis who are usuallyadmitted directly to ICU. High TGL could be primary (genetic), secondary or both. We didn't have means to study the genetic defects, however searched for secondary causes of hypertriglyceridemia.Forston et al in a study of seventy five patients described poorly controlled diabetes as most common association with hypertriglyceridemic pancreatitis followed by alcohol intake.[13] Diabetes was a major risk factor in our patients too. All our patients were either obese or overweight. Alcohol intake and hypothyroidism were other secondary causes for hypertriglyceridemia. No one was taking any drug which would cause hypertriglyceridemia neither did we encounter any pregnant patient. As mentioned before minimum TGL believed to cause pancreatitis is 11.3 mmol/l (1000mg/dl) and in most cases levels are in excess of 20 mmol/l.[2]In our study the mean TGL at time of admission was 26.44 mmol/l [2339.8 mg/dl]. At these levels there is presence of

chylomicrons in blood which are large TG rich lipoproteinsand have highest capacity of carrying triglycerides in their core.[14] The exact pathogenesis of hypertrigly ceridemia induced pancreatitis is still unclear. The proposed mechanisms include hydrolysis of triglycerides in and around the pancreas by pancreatic lipase seeping out of acinar cells leads to accumulation of free fatty acids (FFA) in high concentration. These unbound free fatty acids are toxic and produce injury to acinar cell or capillariescausing inflammation. Chylomicrons induced hyperviscosity leadsto impairment of circulatory flow in capillary beds and ischemia.[8] Genetic predisposition may also play a role. In a review by John Scherer et al potential role of FFA have been further described citing multiple experimental animal and in vitro studies. FFAs cause mitochondrial damage, necrosis via inhibition of mitochondrial complexes I and V and decrease acinar ATP levels. In vitro studies that used orlistat to pharmacologically inhibit pancreatic lipases and block FFA production prevented the injury to acinar cells co-incubated with chylomicrons.[8] Hypertriglyceridemia is frequently an under recognised as a cause of AP.[15] Chylomicrons are rapidly metabolised on fasting instituted as a treatment of AP and in majority of the patients TGLwill fall within 72 hours, hence delay in consideration can lead to failure to diagnose correct etiology. Searles et al recommended to consider chylomicronemia in all patients with AP even in presence of other etiological factor.[15] Even if it is not possible to investigate hypertriglyceridemia in all patients of acute pancreatitis it is strongly recommended to do lipid profile on admission for the patients who have risk factors for hypertriglyceridemia, have normal biliary anatomy on imaging or have lipemic serum. The process of lowering TGL can be further accelerated by adding anti-lipid drugs known to cause reduction in TGL like fenofibrate which is considered as first line medication for treatment of hypertriglyceridemia[16] as well as insulin infusion. Our observations have also shown steady decline in TGL upon starting treatment. (Graph)The diagnostic criteria of AP includes at least three times elevated pancreatic enzymes. In absence of this clinicians rarely consider this diagnosis. However the levels of pancreatic enzyme levels can be spuriously low when TGL are higher than 5.65 mmol/l [500mg/dl], possibly due to interference with the assay.[8] This can be corrected with serial dilutions. Fortson et al noted elevations in serum amylase and lipase greater than 2 times normal in 54% and 67% cases respectively.[13] In our study three times above normal elevation for serum amylase was found in only four patients [33%]whereas for serum lipase in ten patients [83%].Two patients presented with normal serum amylase levels on admission. Therefore patients of HTGP may not meet this diagnostic criterionand it requires to maintain a high level of suspicion of HTGP in appropriate clinical setting and the confirmation of diagnosis should be done by imaging.

Lipoprotein lipase (LPL) is responsible for removing chylomicrons from blood.[17] Deficient LPL activity is noted in patients with hypertriglyceridemia. Insulin and heparin infusions have shown to enhance the activity of LPL. In diabetic patients insulin infusion should be used to enhance reduction in TGLas well as to maintain euglycemia. Insulin infusion have shown to be helpful even in non-diabetic patients.[17] All our patients received insulin infusion except one(pt; 1). We did not considered heparin infusion in our patients as its role is still controversial. Its effects on raising LPL levels are usually transient followed by markedly decreased LPL activity and accumulation of chylomicrons.[17] However there are studies where heparin and insulin infusions were used together successfully.[17]Direct and rapid removal of chylomicrons can be achieved by lipopheresis or plasmapheresis. Lipopheresis was not available to us. Numerous studies have documented the effectiveness of plasmapheresis in hypertriglyceridemia with[9] or without pancreatitis.[18] Plasmapheresis is an expensive treatment, not free from hazards[6] and may not be widely available. However it is very reliable methods to achieve lower TGL. A single session of plasmapheresis can lower TGL up to 70%.[19] Three of our patients received plasmapheresis. All of them were having moderately severe pancreatitis and needed just one session. However it may be noted that patient suffering from severe pancreatitis may need more than one sessions. Some algorithms[20] suggest to consider plasmapheresis if TGL above 11.3mmol /l(1000mg/dl) however in our study we have seen this is not necessary as most patients even with much higher TGLcan do quite well without it. Based on our study we suggest that its use should be individualized.

Conclusion

Number of HTGPcases may rise in future as the risk factors like diabetes and obesity are on rise. Diagnosis can easily be missed or delayed if high level of suspicion is not maintained. Patients with no clear

cause of pancreatitis on admission should have their TG levels done especially if they are obese or have diabetes. Early diagnosis and prompt treatment of hypertriglyceridemia will lead to lesser complications and improved outcome. Multiple treatment options should be used to treat hypertriglyceridemia. Plasmapheresis where available and affordable can be used on individualized basis. To prevent further attacks compliance to treatment of diabetes and hyperlipidemias should be strongly emphasized. Weight loss and adherence to healthy lifestyle needs to be encouraged and proper education provided in this regard.

Department of Medicine,
Al-Adan Hospital Kuwait
www.esculapio.pk

References

1. Lujano-Nicolás LA, Pérez-Hernández JL, Durán-Pérez EG, Serralde-Zuniga AE. Corelation among clinical, biochemical and tomographic criteria in order to evaluate the severity in acute pancreatitis. Rev Esp Enferm Dig. 2010 Jun;102(6):376-80.
2. Gan SI, Edwards AL, Symonds CJ, Beck PL. Hypertriglyceridemia-induced pancreatitis: A case-based review. World J Gastroenterol. 2006 Nov 28;12(44):7197-202.
3. Kota SK, Kota SK, Jammula S, Krishna SV, Modi KD. Hypertriglyceridemia-induced recurrent acute pancreatitis: A case-based review. Indian J Endocrinol Metab. 2012 Jan;16(1):141-3.
4. Deng HI, Xue P, Xia Q, Yang XL, Wan MH. Effect of admission hypertriglyceridemia on the episodes of severe acute pancreatitis. World J Gastroenterol. 2008 Jul 28;14(28):4558-61.
5. Balachandra S, Virlos IT, King NK, Siriwardana HP, France MW, Siriwardena AK. Hyperlipidaemia and outcome in acute pancreatitis. Int J Clin Pract. 2006 Feb;60(2):156-9.
6. Uyar S, Harmandar F, Kök M, Tas Z, Dolu S, Tokuc A et al. Management of hypertriglyceridemia induced acute pancreatitis and therapeutic plasmapheresis: Report of nine cases and review of literature. Acta Gastroenterol Belg. 2017 Jan-Mar;80(1):71-74.
7. Tran T, Lee N. Recurrent Hypertriglyceridemic Pancreatitis (HTGP); and the Use of Insulin Drip as Treatment. J La State Med Soc. 2017 Mar-Apr;169(2):55-56.
8. Scherer J, Singh VP, Pitchumoni CS, Yadav D. Issues in hypertriglyceridemic pancreatitis: an update. J Clin Gastroenterol. 2014 Mar;48(3):195-203.
9. Anderson F, Mbatha SZ, Thomson SR. The early management of pancreatitis associated with hypertriglyceridaemia. S Afr J Surg. 2011 Apr;49(2):82-4.
10. Ewald N, Kloer HU. Treatment options for severe hypertriglyceridemia (SHTG): the role of apheresis. Clin Res Cardiol Suppl. 2012 Jun;7(Suppl 1):31-5.
11. Schwartz J, Winters JL, Padmanabhan A, Balogun RA, Delaney M, Linenberger ML et al. Guidelines on the Use of Therapeutic Apheresis in Clinical Practice Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Sixth Special Issue. J Clin Apher. 2013 Jul;28(3):145-284.
12. Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG et al. Classification of acute pancreatitis--2012: revision of the Atlanta classification and definitions by international consensus. Acute Pancreatitis Classification Working Group. Gut. 2013 Jan;62(1):102-11.
13. Fortson MR, Freedman SN, Webster PD 3rd. Clinical assessment of hyperlipidemic pancreatitis. Am J Gastroentrol 1995 Dec;90(12):2134-9.
14. Brahm A, Hegele RA. Hypertriglyceridemia. Nutrients. 2013 Mar 22;5(3):981-1001.
15. Searles GE, Ooi TC. Underrecognition of chylomicronemia as a cause of acute pancreatitis. CMAJ. 1992 December 15; 147(12): 18061808.
16. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). JAMA. 2001 May 16;285(19):2486-97.
17. Kuchay MS, Farooqui KJ, Bano T, Khandelwal M, Gill H, Mithal A. Heparin and insulin in the management of hypertriglyceridemia-associated pancreatitis: case series and literature review. Arch Endocrinol Metab. 2017 Mar-Apr;61(2):198-201.
18. Wassay SAM, Dar FJ, Saleh AK, Mansoor I. Role of therapeutic plasma exchange in the treatment of severe hypertriglyceridemia: an experience. Ther Adv Endocrinol Metab. 2017 Dec;8(12):169-172.
19. Kopecky K, Moreland A, Hebert C, Colbert GB. Plasmapheresis for recurrent acute pancreatitis from hypertriglyceridemia. Proc (Bayl Univ Med Cent). 2017 Jul;30(3):358-359.
20. Tsuang W1, Navaneethan U, Ruiz L, Palascak JB, Gelrud A. Hypertriglyceridemic pancreatitis: presentation and management. Am J Gastroenterol. 2009 Apr;104(4):984-91.

Original Article

Amyand's Hernia In Children; 10 Years Single Center Experience

Asif Iqbal, Naeem Liaqat, Imdad Ahmed Zahid, Saqib Hassan, Arsalan Wasti, Sajid Hameed Dar and Fozia Bashir

Objective: To determine the presenting features and management of patients having Amyand Hernia.

Methods: This retrospective study was conducted at Paediatric Surgery Department of Services Hospital, Lahore. All the patients diagnosed as Amyand's hernia in last 10 years from January, 2007 to December, 2016 were included in the study. Their file records were reviewed and all the data was analyzed by simple descriptive statistics.

Results: During this period, a total of 3213 inguinal herniotomies were done. Of these, 27 patients had Amyand hernia and incidence was calculated as 0.8%. The mean age was found as 56.71 ± 44.24 months. Of these 27 patients, 25 patients (92.6%) were male and 2 patients (7.4%) were females. Right side was involved in 25 patients (92.6%) while 2 patients (7.4%) had left side involved. Per-operatively, normal appendix was found in 15 patients (55.5%), inflamed appendix in 9 patients (33.3%) and perforated appendix in 3 patients (11.1%). Operative procedures included high ligation herniotomy in 24 patients (88.9%) and high ligation herniotomy along with appendectomy in 3 patients (11.1%).

Conclusions: Treatment of AH is tailored according to presentation and most of the patients having inflamed appendix do not get complications if not excised.

Keywords: appendix; inguinal; hernia; amyand

Introduction

Inguinal hernia is one of the most common conditions encountered by the pediatric surgeon. Amyand's hernia (AH) is named after Claudius Amyand who was a British surgeon of French origin and first described this entity in 1735. It is defined as an inguinal hernia which contains a normal or inflamed appendix within its sac.[1,2] AH is a rare variety of inguinal hernia. Its rarity is underscored by the reported incidence of an AH which is 1% of all inguinal hernias containing a normal appendix and 0.13% of all inguinal hernias containing an inflamed appendix.[3-6] It is not possible generally to identify AH preoperatively and usually, this distinction becomes apparent during surgery.[7] This is because there are few if any clinical findings to raise suspicion of presence of an appendix within the hernia sac. As there is a deficiency of literature readily available on this rare subject, we planned to share our 10 years experience of operating on patients with AH in the form of a case series. Our series consists of 27 cases, and is among the larger case series on the subject.

Methods

This retrospective descriptive study was conducted at Paediatric Surgery Department of Services Hospital, Lahore. In this study all the patients having diagnosis of AH from 2007 to 2016 were included. The demographic details of all the patients including gender and age at presentation were noted. Also mode of admission, side of hernia, presenting complaint of the patients was noted. Preoperative findings including condition of appendix and procedure done in all patients were also noted. Results were analyzed by descriptive statistics using SPSS version 20.

Results

In our institute, a total of 3154 patients had undergone inguinal herniotomy over a period of 10 years. Among these 3154 patients, 59 patients undergone bilateral inguinal herniotomies, hence total herniotomies done were 3213, and 27 cases were of AH. The incidence of AH was calculated to be 0.84%. So a total of 27 patients were included in the study. The mean age of the patients was found to be 56.71 ± 44.24 months. Among these patients, only one patient (3.7%) was neonate and 6 patients (22.2%) were infants. Of these 27 patients, 25 patients (92.6%) were male while remaining 2 patients (7.4%) were females. Seventeen patients (63%) were admitted through outdoor department with simple complaint of inguinal swelling while 10 patients (37%) were admitted through emergency who presented with complaint of irreducibility. Of all these patients, 25 patients had right sided inguinal

hernia (92.6%) while 2 patients (7.4%) had left side involved. The most common complaints of the patients was found to be swelling at inguinal region and pain in 15 of 27 patients (55.55%), followed by complaint of only swelling without pain in 12 patients (44.44%) and vomiting along with swelling in 3 patients (11.11%). Per-operatively, 9 patients (33.3%) found having inflammed appendix and 3 patients (11.1%) had perforated appendix. Appendectomy was done in all those having perforated/gangrenous appendix while those having inflamed appendix were left as such. Post-operatively, all those having inflamed appendix did well and none of them got any complication. Per-operative and postoperative course of patients in the study is summarized in **Table-1.** In none of patients during follow up, recurrence was noted. All the data of patients is summarized in **Table 2.**

Table-1: Per-operative and Post-operative course of patients in the study.

Operative and post-operative course of the patients		
Peroperative findings:	Normal appendix	15 (55.5%)
	Inflamed appendix	9 (33.3%)
	Perforated appendix	3 (11.1%)
Surgical incision	Inguinal skin crease	225 (92.5%)
	Inguinal skin crease+ laparotomy	2 (7.5%)%
Wound infection	Yes	2 (7.5%)
	No	25 (92.5%)

Table-2: Per-operative and Post-operative detail of patients.

Age (in months)	Gender	Mode of presentation	Side	Presenting features	Per-operative findings	Surgery
02	Male	OPD	Left	Pain and swelling	Perforated appendix	Herniotomy & appendicectomy
48	Female	OPD	Right	Swelling	Normal appendix	Herniotomy
24	Male	Emergency	Right	Pain and swelling irrducibility	Inflammed appendix	Herniotomy
120	Male	OPD	Right	Swelling	Inflammed Appendix	Herniotomy
72	Male	OPD	Right	Swelling	Normal appendix	Herniotomy
108	Male	OPD	Right	Swelling	Normal appendix	Herniotomy
144	Male	Emergency	Right	Pain and swelling irreducibility	Inflammed appendix	Herniotomy
84	Male	OPD	Right	Swelling	Inflammed appendix	Herniotomy
144	Male	OPD	Right	Swelling	Normal appendix	Herniotomy
12	Male	Emergency	Right	Pain and swelling irreducibility	Normal appendix	Herniotomy
18	Male	Emergency	Right	Pain and swelling irreducibility	Normal appendix	Herniotomy
05	Male	Emergency	Right	Pain and swelling irreducibility	Normal appendix	Herniotomy
60	Male	OPD	Right	Pain, swelling and vomiting	Normal appendix	Herniotomy
36	Male	OPD	Right	Swelling	Normal appendix	Herniotomy
02	Male	OPD	Right	Swelling	Normal appendix	Herniotomy
96	Emal e	Emergency	Right	Swelling, irreducibility	Normal appendix	Herniotomy
48	Male	OPD	Right	Swelling	Normal appendix	Herniotomy
106	Male	OPD	Right	Swelling	Normal appendix	Herniotomy
60	Male	OPD	Right	Pain and swelling	Normal appendix	Herniotomy
84	Male	OPD	Right	Pain and swelling	Perforated appendix	Herniotomy and appendicectomy
48	Male	OPD	Right	Pain and swelling	Normal appendix	Herniotomy
72	Female	Emergency	Right	Pain and swelling, irreducibility	Normal appendix	Herniotomy
60	Male	OPD	Right	Pain and swelling	Normal appendix	Herniotomy
0.9	Male	Emergency	Right	Pain and swelling vomiting irreducibility	Perforated Appendix	Herniotomy and appendicectomy
2.5	Male	Emergency	Right	Pain and swelling vomiting irreducibility	Normal appendix	Herniotomy
72	Male	OPD	Left	Swelling	Normal appendix	Herniotomy
03	Male	Emergency	Right	Pain and swelling irreducibility	Inflammed appendix	Herniotomy

Discussion

In our case series we calculated the incidence rate of AH to be 0.84%. This is comparable to the incidence rate mentioned in a similar case series published by Cigsar et al. in which over 11 years out of a total of 4498 patients with inguinal hernia 1% had AH.[8] In our study the mean age of patients was 56.71 months (or 4.72 years). This is markedly different from the case series from Turkey published by CankorKmaz et al. which had a median age of just 40 days.[9] In the case series by Cigsar et al. the mean age was 16.7 months which is closer to our study.[8] In another smaller series by Okur et al. which had 21 patients the median age was 20.3 months.[10] Therefore, the children in our series were considerably older than in other similar series.

In our series one patient was a neonate while 6 were infants. Other series include infants and neonates such as the series by CIgsar et al.,[8] Cankorkmaz et al.[9] and Okur et al.[10] And there are a number of isolated case reports, however it is clear that these are even rarer cases and therefore have been separately mentioned in our study.

Among the patients we operated, 25 (92.6%) were male while only 2 (7.4%) were female. Analysis of various other case series in both children and adults revealed a similar predominance of male patients. A case series of adult patients by Sharma et al. had a total of 18 patients, and of those only one was female.[11] In the case series of Cigsar et al.[8] and Cankorkmaz et al. [9] all patients were male. These series had 12 and 46 patients of AH respectively. The one-sided gender distribution of AH is also remarked upon in a literature review conducted by D'Alia et al.[12]

Of the 27 patients with AH we have mentioned in our series 25 (92.6%) had hernias of the right side while 2 (7.4%) had hernias of the left side. It is well known that due to the normal anatomical position of the appendix on the right side, AH most commonly occurs on the ipsilateral side. However, it can occur on the left side, but this is rare.[13] Such an occurrence should arouse the suspicion of the surgeon and diagnoses such as malrotation and situs inversus should be considered. In the case series by Cigsar et al., only 2 had a left sided hernia, 7 had a bilateral hernia and the remaining were all right sided [8]. Similarly in the series of Kaymacki et al. out of 30 cases only 3 were left sided and they also did not encounter any case of bilateral hernia.[14]

We classified the presenting complaints of our patients as follows: most patients presented with pain and swelling in the inguinal region (15 patients or 55.55%), 9 patients (33.33%) had only swelling and no pain, only 3 (11.11%) patients presented with the triad of pain, swelling and vomiting which indicated obstruction. Of our 27 patients, 17 (63%) had presented in the OPD and 10 (37%) in the emergency department. All the 12 patients in the series by Cankorkmaz et al. had a preoperative diagnosis of incarceration or strangulation and underwent emergency appendicectomy.[9] Our findings were closer to those of Cigsar et al., in whose study only 9 patients had a preoperative diagnosis of incarcerated hernia, in the rest, the appendix was an incidental finding during elective hernia repairs.[8] Therefore, it can be safely said that AH has a varied presentation, and it is impossible to predict its presence on clinical grounds alone.

Appendix within the sac can be normal, inflamed or perforated. We found 15 patients (70.4%) having normal or non-inflamed appendix and in 9 patients (18.5%) had inflamed appendix while only 3 patients (11.1%) had perforated appendix. In the case series by Cigsar et al, of 46 patients with AH, 33 patients had normal appendix while 9 had inflamed appendix which is comparable without results but they found only 1patient with perforated appendix.[8] The high incidence of perforated appendix in our series suggests a potential delay in diagnosis or presentation. This presents an opportunity for further research and possibly a clinical audit.

We preformed simple herniotomy with high ligation of hernia sac in 24 patients (88.9%) while herniotomy along with appendectomy was done in 3 patients (11.1%). Various studies done at pediatric centers showed the consensus that in cases of normal appendix, herniotomy is recommended.[11,15] The management of an inflamed appendix is debatable.[16,17] In a review by Galyna Ivashchuk, authors suggested that the choice of open and laparoscopic procedure and which form of herniorrhaphy to perform is matter of intense debate among surgeons.[18] It is the subject of active research and appears to be guided more by the surgeon's preference than a uniform consensus. In cases of perforated appendix the procedure of choice is appendicectomy either through the herniotomy incision or via a separate incision.[19]

We had published a case report of our department which was a case of perforated appendix in a neonate.[20] That case has also been included in this series. We conclude on the basis of this study that treatments of AH is tailored according to presentation and most of the patients having

inflamed appendix do not get complications if not excised. However, this does not include those having gross inflammatory signs and gangrenous appendices.

Conclusion

Treatment of AH is tailored according to presentation and most of the patients having inflamed appendix do not get complications if not excised.

Department of Peads Surgery
Children Hospital, Lahore
www.esculapio.pk

References

1.Hutchinson R. Amyand's hernia. Journal of the Royal Society of Medicine. 1993;86(2):104.
2.Morales-Cardenas A, Ploneda-Valencia CF, Sainz-Escarrega VH, Hernandez-Campos AC, Navarro-Muniz E, Lopez-Lizarraga CR, et al. Amyand hernia: Case report and review of the literature. Ann Med Surg (Lond). 2015;4(2):113-5.
3.Losanoff JE, Basson MD. Amyand hernia: what lies beneath--a proposed classification scheme to determine management. Am Surg. 2007;73(12):1288-90.
4.Logan MT, Nottingham JM. Amyand's hernia: a case report of an incarcerated and perforated appendix within an inguinal hernia and review of the literature. The American Surgeon. 2001;67(7):628-9.
5.Dange A, Gireboinwad S. Case Report: a Rare Case of Amyand's Hernia Presenting in a 3-year-old Male Child. Indian J Surg. 2013;75(4):332-3.
6.Yagnik VD. Amyand hernia with appendicitis. Clin Pract. 2011;1(2):e24.
7.Burgess PL, Brockmeyer JR, Johnson EK. Amyand hernia repaired with Bio-A: a case report and review. J Surg Educ. 2011;68(1):62-6.
8.Cigsar EB, Karadag CA, Dokucu AI. Amyand's hernia: 11years of experience. Journal of pediatric surgery. 2016;51(8):1327-9.
9.Cankorkmaz L, Ozer H, Guney C, Atalar MH, Arslan MS, Koyluoglu G. Amyand's hernia in the children: a single center experience. Surgery. 2010;147(1):140-3.
10.Okur MH, Karaçay Ş, Uygun I, Topçu K, Öztürk H. Amyand's hernias in childhood (a report on 21 patients): a single-centre experience. Pediatric surgery international. 2013;29(6):571-4.
11.Sharma H, Gupta A, Shekhawat N, Memon B, Memon M. Amyand's hernia: a report of 18 consecutive patients over a 15-year period. Hernia. 2007;11(1):31-5.
12.D'Alia C, Schiavo ML, Tonante A, Taranto F, Gagliano E, Bonanno L, et al. Amyand's hernia: case report and review of the literature. Hernia. 2003;7(2):89-91.
13.Johari HG, Paydar S, Davani SZN, Eskandari S, Johari MG. Left-sided Amyand hernia. Annals of Saudi Medicine. 2009;29(4):321.
14.Kaymakci A, Akillioglu I, Akkoyun I, Guven S, Ozdemir A, Gulen S. Amyand's hernia: a series of 30 cases in children. Hernia. 2009;13(6):609-12.
15.Losanoff JE, Basson MD. Amyand hernia: what lies beneatha proposed classification scheme to determine management. The American Surgeon. 2007;73(12):1288-90.
16.Sahu D, Swain S, Wani M, Reddy PK. Amyand's hernia: Our experience in the laparoscopic era. Journal of minimal access surgery. 2015;11(2):151.
17.Kouskos E, Komaitis S, Kouskou M, Despotellis M, Sanidas G. Complicated acute appendicitis within a right inguinal hernia sac (Amyand's hernia): report of a case. Hippokratia. 2014;18(1):74.
18.Ivashchuk G, Cesmebasi A, Sorenson EP, Blaak C, Tubbs SR, Loukas M. Amyand's hernia: a review. Medical science monitor: international medical journal of experimental and clinical research. 2014;20:140.
19.Sandhu A, Liaqat N, Nayyar SI, Faryal R, Shafique S. Amyand's Hernia with Perforated Appendix in a Neonate. APSP J Case Rep. 2014;5(3):34.

Original Article

SUCCESS RATE OF PROBING AND SYRINGING AT DIFFERENT AGE GROUPS AT NISHTAR HOSPITAL MULTAN

Muhammad Anwar Chaudhary, Muhammad Imran and Syed Ahmer Hussain

Objective: To determine the efficacy of Probing and Syringing in Congenital Nasolacrimal Duct Obstruction (CNLDO) patients of various age groups.

Methods: In this study, two hundred and forty six patients of either gender and ≥ one year of age with Congenital Nasolacrimal Duct Obstruction were included in this study. Demographic details from all the patients in terms of age and gender were recorded. The probing was done under general anesthesia, in stepwise manner using Bowman's probe size 00, followed by probes size 0, then 1, 2, 3.The patients were visited at 2 weeks, and 3 and 6 months postoperatively. Successful probing was documented as complete remission of watering and discharge together with no reflux from with lacrimal sac pressure two weeks after the procedure

Results: Age range in this study was ≥ one year with mean age of 6.804 ± 5.56 years. Majority of patients according to age groups were belongs to 1-5 years125(50.8%).Frequency and percentage of patients according to gender was 102(41.46%) males and 144(58.54%) females. The overall success rate of probing was seen in 173(70.3%) patients. Success rate was significantly better in 1-5 years age group which gradually decline as age increased (p=0.000),

Conclusions: Probing and Syringing has remained the best and time-tested procedure for the treatment of congenital NLD obstruction under General Anaesthesia. The best time is between 1 to5 year of age.

Keywords: congenital nasolacrimal duct obstruction, probing, age and efficacy.

Introduction

Congenital Nasolacrimal Duct Obstruction (CNLDO) is a common problem that ophthalmologists routinely face in their practice.[1] Most of the cases are self resolving. While up to 20 % of newborns have CNLDO, only 1-6% of infants have symptomatic obstruction.[2] The majority of cases (upto 96 %), usually resolve by the age of 1 year.[3] Most commonly, this is due to the presence of a membrane at the level of the valve of Hasner, which is present at the nasal opening of the nasolacrimal duct. Less frequent causes include congenital atresia of the NLD, congenital lacrimal sac mucocele, congenital absence of valves, absence or atresia of canaliculi and puncta, and facial cleft anomalies.In cases of congenital lacrimal system obstruction, the diagnosis is usually clear cut on history and examination as child present with watering, discharge, matting of eyelashes and inferior palpebral congestion. In doubtful cases, the dye disappearance test can be conducted.

Crigler was the first to describe lacrimal sac massage.[4]This is the first line of management before probing. Conservative management by massage can be done safely upto 1 year of age; the reason being most of the cases (96 %) will resolve within the first year of life.[5]

Probing of the nasolacrimal duct system is a standard procedure in the management of congenital nasolacrimal duct obstruction.[6] However, the timing for initial probing has been a matter of controversy.[7] Any decision to probe before one year should take this high rate of spontaneous resolution into account. However, recurrent infection and discharge and the attendant lid irritation may occasionally prompt the decision to probe early, as the need for anesthesia at an early date for some other procedure.

The success of probing falls after 1 year of age. Hence in a child 1 year of age or more, it is best to recommend probing to the parents. Success ranges between 92 % 97 % if done before 1 year of age but beyond 1 year the success falls to 55 %-80 %.[8,9] Controversy exists regarding the natural course and management of CNLDO. The standard surgical procedure for children with persistent obstruction is probing of the lacrimal system under general anesthesia (GA). However, timing of probing has long been a controversial topic. The purpose of our study was to determine the efficacy of Probing and Syringing in CNLDO patients of various age groups.

Methods

This descriptive case series was conducted in indoor

Department of Ophthalmology Nishtar Hospital Multan from 01-01-2014 to 02-08-2016. Two hundred and forty six patients of either gender and ≥ one year of age with Congenital Nasolacrimal Duct Obstruction were included in this study. Patients with any secondary cause of watering eye, eye conditions such as punctal agenesis, ectopic puncta, multiple puncta, congenital ectropion, blepharitis, congenital glaucoma and conjunctivitis were excluded. The diagnosis of was based on the history of watering or discharging eye and confirmed by evidence of epiphora with or without mucopurulent discharge and regurgitation on ocular examination. Demographic details from all the patients in terms of age and gender were recorded.

The probing was done under general anesthesia, in stepwise manner using Bowman's probe size 00, followed by probes size 0, then 1, 2, 3. Probing was done through the upper punctum, and then passed through the canaliculus till the hard feel of the medial wall of the lacrimal fossa was felt. The probe was turned to enter the nasolacrimal duct (NLD), and gently advanced till resistance was felt. The probe was then advanced to overcome the obstruction. When a firm or hard resistance was encountered during probing, this was recorded as complex NLD obstruction. Patency was confirmed by irrigating flourescein stained saline, and its flow was detected by placement of pediatric size suction catheter in the nose. Following the procedure, topical antibiotic drops were continued for 2 weeks. The patients were visited at 2 weeks, and 3 and 6 months postoperatively. Successful probing was documented as complete remission of wateringand discharge together with no reflux from with lacrimal sac pressure two weeks after the procedure. Data were analyzed with statistical analysis program (SPSS version 20). Frequency and percentage was computed for qualitative variables like age groups and gender. Mean±SD was presented for quantitative variable like age. Age and gender was controlled by stratification. Post stratification chi square test was applied $p \leq 0.05$ was considered statistically significant.

Results

Age range in this study was ≥ one year with mean age of 6.804±5.56 years. Majority of patients according to age groups were belongs to 1-5 years125(50.8%) as shown in **Table-I.** Frequency and percentage of patients according to gender was 102(41.46%) males and 144(58.54%) females as shown in **Graph-I.** The overall success rate of probing was seen in 173(70.3%) patients as shown in **Table-II.**

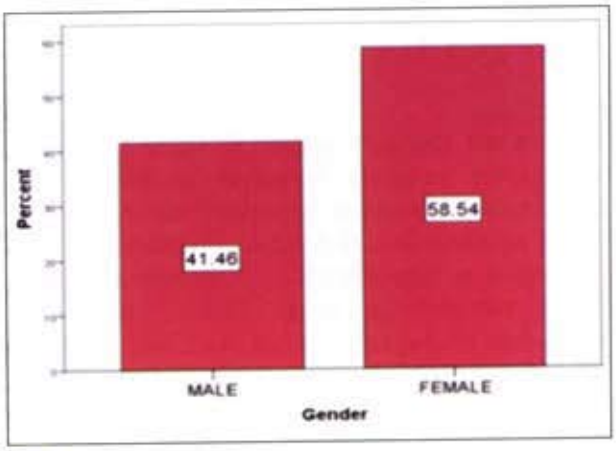


Fig-1: Frequency and percentage of patients of ocular trauma according to gender.

Table-1: Frequency and percentage of age groups in patients .

Age in (years)	No of patients	Percentage
1 - 5	128	50.8%
6 - 10	48	19.5%
11 - 15	47	19.1%
16 - 20	21	8.5%
> 20	05	02%
Total	246	100%

Table-2: Success rate.

Success Rate	No of patients	Percentage
Yes	173	70.3%
No	73	29.7%
Total	246	100%

Table-3: Stratification of success rate with respect to age groups.

Age in (years)	Success Rate Yes	No	P-value
1 - 5	115 (92%)	10 (8%)	
6 - 10	36 (75%)	12 (25%)	
11 - 15	19 (40.4%)	28 (59.6%)	0.000
16 - 20	2 (9.5%)	19 (90.5%	
> 20	1 (29%)	4 (80%)	
Total	173 (70.3%)	73 (29.7%)	

Table-4: Stratification of success rate with respect to gender.

Age in (years)	Success Rate Yes	No	P-value
Male	70 (68.6%)	32 (31.4%)	
Female	103 (71.5%)	41 (28.5%)	0.624
Total	173 (70.3%)	73 (29.7%)	

Success rate was significant better in 1-5 years age group which gradually decline as age increased (p=0.000) as shown in **Table-III.** There was no significant difference of success rate in male and female groups as shown in **Table-IV.**

Discussion

The lacrimal drainage system is formed as a depression termed lacrimal groove at approximately 6 weeks of gestational age. A solid cord of ectoderm is buried and canalization of the cord begins at approximately 3.5 months and is usually complete at birth. Failure of the canalization of the nasolacrimal duct may occur leading to epiphora. Probing and syringing is the main form of treatment. Spontaneous resolution occurs in majority of infants. Advocates of early probing suggest that early correction avoids complications such as acute dacryocystitis, recurrent dacryocystitis or canaliculitis[8] and prevents months of morbidity due toEpiphora and chronic dacryocystitis. In our study, the overall success rate was around 70.3% which is comparable to previous studies.[10-14] Our study showed a significant trend of decreasing success rates with increasing age: 92%, 75%, 40%, 9.5% and 20% at 1-5, 6-10,11-15,16-20 and >20years of age, respectively which is consistent with other studies.[14,15] A success rate of 94% was reported by Havins and Wilkins[16] for probing done in children less than 8 months compared to 56% in children age 18 months and older. Sturrock[17] and associates reported 86% success when probed under one year compared to 72% between 1 and 2 years of age and 42% for more than 2 years of age. Katowitz and Welsh[8] had a success rate of 76.4% between 13-18 months, but the curerate declined to 33.3% in children older than 24 months. Mannor[18] and colleagues found a negative correlation between the age and the success rate of probing. In contrast to these studies, El-Mansoury[19], Robb[20], and Zwaan[21] and colleagues found more than 90% success rate in late and very late probing. Robb[20] found no difference in cure rate with increasing age and noted an overall success rate of 92% varying from 88.9-96.8% at different age intervals up to and beyond 3 years of age. Honavar[22] et al. reported a success rate of 75.0% upto 4 years of age, after which it was 42.9% in children older than 4 years. Casady[23] et al. reported a success rate of 85% for probing in children, more than 18 months age.

Conclusion

Probing and Syringing has remained the best and time-tested procedure for the treatment of congenital NLD obstruction under General Anaesthesia. The best time is between 1 to5 year of age.

Department of Ophthalmology
Lahore General Hospital, Lahore

www.esculapio.pk

References

1. Dotan G, Nelson LB. Congenital nasolacrimal duct obstruction: common management policies among pediatric ophthalmologists. J Pediatr Ophthalmol Strabismus 2015; 52(1):14-9.
2. Aldahash FD, Al-Mubarak MF, Alenizi SH, Al-Faky YH. Risk factors for developing congenital nasolacrimal duct obstruction. Saudi J Ophthalmol 2014 Jan; 28(1):5860.
3. Mac-Ewen CJ, Young JDH. Epiphora during the first year of life. Eye 1991; 5:596-600.
4. Crigler LW. The treatment of congenital dacryocystitis. JAMA 1923; 81:21-24.
5. Watering eyes[internet]. Clinica London; [cited 2016 Oct 10]. Available from URL: http://www.clinicalondon.co.uk/watering-eyes-tearing-children/.
6. Mac-Ewen CJ, Young JD. Ep-iphora during the first year of life. Eye1991; 5:596600.
7. Elbakary MA, Shalaby OE. Initial late probing for congenital nasolacrimal duct obstruction, rate of success and factors associated with failure. Int J Ophthalmol Res 2015; 1(3):83-85.
8. Katowitz JA, Welsh MG. Congenital nasolacrimal duct obstruction. Ophthalmology 1987; 94:698-705.
9. Zwaan J. Treatment of congenital nasolacrimal duct obstruction before and after the age of one year. Ophthalmic Surg Lasers 1997; 28(11):932-6.
10. Kim YS, Moon SC, Yoo KW. Congenital nasolacrimal duct obstruction: irrigation or probing? Korean J Ophthalmol2000; 14:90-96.
11. Stager D, Baker JD, Frey T, Weakley DR Jr, Birch EE. Office probing of congenital nasolacrimal duct obstruction. Ophthalmic Surg1992; 23:4824.
12. Syed SH, Arif M, Sultan Mahmood M. Syringing and probing results for congenital nasolacrimal duct obstruction. APMC 2009; 3:67-70.
13. Dabir SA, Gul S, Khanzada MA, Jatoi SM. Efficacy of probing for congenital nasolacrimal duct obstruction in children uptill twenty four months of age. MedicalChannel 2009; 15:194-7.

14. Kashkouli MB, Kassaee A, Tabatabaee Z. Initial nasolacrimal duct probing in children under 5: cure rate and factors affecting success. J AAPOS 2002; 6:360-3.
15. Mannor GE, Rose GE, Frimpong-Ansah K, Ezra E. Factors affecting the success of nasolacrimal duct probing for the congenital nasolacrimal duct obstruction. Am J Ophthalmol1999; 127:616-7.
16. Havins HE, Wilkins RB. A useful alternative to silicone intubation in congenital nasolacrimal duct obstruction. Ophthalmic Surg 1983; 78:892-4.
17. Sturrock SM, MacEwen CJ, Young JD. Long-term results after probing for congenital nasolacrimal duct obstruction. Br J Ophthalmol 1994; 78:892-4.
18. Mannor GE, Rose GE, Fringpong-Ansah K, Ezra E. Factors affecting thesuccess of nasolacrimal duct probing for congenital nasolacrimal ductobstruction. Am J Ophthalmol 1999; 127:616-7.
19. El-Mansoury J, Calhoun JH, Nelson LB, Harley RD. Results of late probing for congenital nasolacrimal duct obstruction. Ophthalmology 1986; 93:1052-4.
20. Robb RM. Probing and irrigation for congenital nasolacrimal duct obstruction. Arch Ophthalmol 1986; 104:378-9.
21. Zwaan J. Treatment of congenital nasolacrimal duct obstruction before and after the age of 1 year. Ophthalmic Surg Lasers 1997; 28:932-6.
22. Honavar SG, Prakash VE, Rao GN. Outcome of probing for congenital nasolacrimal duct obstruction in older children. Am J Ophthalmol 2000; 130:42-8.
23. Casady DR, Meyer DR, Simon JW, Stasior GO, Zobal-Ratnar JL. Stepwise treatment paradigm for congenital nasolacrimal duct obstruction. OphthalPlastReconstrSurg 2006; 22:243-7.

Original Article

FIVE YEARS REVIEW OF TRENDS IN MATERNAL MORTALITY AT FATIMA MEMORIAL HOSPITAL LAHORE

Fauzia Manno Khan, Samina Khurshid, Aimen Musa,Umtal Batool and Shanza Zafar

Objective: To determine the causes and factors leading to maternal mortality with main focus on pulmonary embolism as cause of death in pregnancy

Methods: Review and Analysis of medical records of all maternal deaths occurred in FMH. Demographic characteristics including age, socioeconomicstatus, address was retrieved from record. Information regarding causes and events leading to death were gathered and results compiled.

Results: Between the year 2012-2017 there were 7856 live births and 28 maternal deaths were observed during the period of study giving a combined MMR of 356.4/100,000 live births. Leading cause of death was hemorrhage 36% followed by hypertensive diseases 18% and pulmonary embolism14% respectively. Other causes were cardiac diseases and sepsis which caused 10% and 7% deaths. Majority of deaths were observed in multigravid as 64%, unbooked and referred patients 79%.

Conclusions: MMRis still very high due to hemorrhage and hypertensive diseases which are preventable causes of death. Efforts should be made on primary, secondary and tertiary level to ensure proper system of assessment, management and referral. Pulmonary embolism is major cause of maternal death that cannot be ignored, deaths can be reduced by thromboprophylaxis and active management of the disease.

Keywords: maternalmortality, Hemorrhage, pulmonary embolism.

Introduction

Maternal mortality is an important indicator of a health and socioeconomic development of a country. According to recent report of WHO, maternal mortality has been decreased by 43 % between 1990 and 2015.[1]Despite the decline in overall maternal mortality, several developing countries including Pakistan are making significant share toward maternal mortality worldwide.[2]

Although, there has been significant investment in maternal and child health care, maternal mortality is still a major global public health concern. Current maternal mortality rate of Pakistan is 178/100,000 live births as quoted by WHO.[3] Actually, figures are alarmingly high, because of the fact that a lot of deaths are unregistered.[4]

Among direct causes of maternal mortality hemorrhage contributes the major share, second being eclampsia followed by sepsis, unsafe abortions and obstructed labour respectively[4,5,6,7] indirect causes include anemia, hepatitis and cardiac diseases.[8] several studies confer that there is a huge disparity between the mortality of developed and underdeveloped countries, [4,9,10] which is evidence of the fact that most of the deaths are preventable, however this largely depends upon the social and economic circumstances ,health care system and health facilities available in the country.

pulmnary embolism is the major cause of maternal mortality and morbidity in pregnancy, that is often under diagnosed. A high index of suspicion is needed as symptoms are nonspecific and common in pregnancy. Pregnancy increases the risk of thromboembolism six-fold which increases further during perpeurium. Pulmonary embolism in pregnancy and perpeurium kills 5 to 10 women each year in UK. Thrombosis and thromboembolism has been the leading direct cause of maternal mortality in United Kingdom since the confidential inquiries into maternal death began.[11]However, there was a significant fall in maternal mortalities after introduction of thromboprophylaxis.[12] Incidence of pulmonary embolism is believed to be less in developing world as compared to developed countries. However, no local study is available for comparison.

.

Methods

Data collected from various sources, that include in-patient and labour ward registers, medical and surgical intensive care register and hospital birth register. Every admitted patient is assigned a specific medical record number, that is used to trace files of patient that are kept in hospital record room. Patient information collected, including demographic

hospital based data we were able to determine that most of these women have risk factors for maternal thromboembolism and none of them received thromboprophylaxis. Timely identification of these risk factors and prevention through use of thromboprophylaxis[12] would have prevented some of these deaths .This is favored by the fact that reduction in maternal mortality has been observed in united kingdom after publication and implementation of the guideline about thromboprophylaxis in pregnancy.[20] According to Royal college of obstetrician and gynecologist guideline every women should be assessed for risk factors of thromboembolism in prepregnancy and early pregnancy ,risk assessment should be repeated on hospital admission , intrapartum and postpartum.

MMR in our study is slightly lower as compared to study conducted at ayub medical college recently, that was 772/100,000 for 10 years.[21] However, there is wide range of difference between maternal mortality of different regions of Pakistan. still results may be biased because of the fact that data does not represent the actual facts and figures of community because the proper system of data collection is lacking in our country.[21]

Begum et al reported 69%, 19.2% and 11.5% maternal mortality in grandmultipara, multipart and primigravida respectively.[7] While In our study death rate among the multiparous women (64%) was higher as compared to primiparous women (28%) and lowest in grandmultipara (7%).According to our study higher proportion of deaths were noted in patients who were unbooked (79%).they visited hospital facility less than two times during antenatal period .similarly higher death rate was reported among the patients who were referred(71%) as compared to patients who were already booked(29%) in the same hospital .These results closely resemble some international studies done in developing countries.[22,23]The main reason being most of the patient referred in critical and moribund condition and a lot of factors affect the outcome of the patient i.e. time of transfer from the health care facility, skills of health care provider[22] who attended the patient and condition at the time of referral.. A lot of patients who died stayed in hospital for less than 24 hours (72%) which represent most of them came in critical condition

Hospital based study does not represent the actual figures of general population as some information of study participants must eliminate in analysis and hospital mainly received complicated cases which can lead to selection bias. However, a large sample size over a period of 5 years provides us with a quick review of trends in maternal mortality.

Conclusion

Hemorrhage and hypertensive diseases are still the major causes of maternal mortality. Both are preventable. If proper antenatal and peripartum care is ensured, maternal mortality can be reduced. Deaths due to pulmonary embolism can be prevented by risk assessment and prevention in the form of thromboprophylaxis.

Department of Obstetrics and Gynecology
Fatima Memorial Hospital, Lahore
www.esculapio.pk

References

1. WHO; Global health observatory data , 2017 http://www.who.int /gho/maternal_health/mortality /maternal_mortality_text/en/
2. Maternal deaths Pakistan ranks third: expert. Available from http://www.brecorder.com/gen eralnews/ 172/1244514/. Business recorder news; October 25, 2012
3. World Health Organizatio: Maternal Mortality 2015. Available from URL: http:// www.who.int/en/
4. Jafarey SN. Maternal Mortality in Pakistan Compilation of available Data. (2002). Journal of Pakistan Medical Association; 52(12), 539-544.
5. Nisar, N., & Sohoo, N. Maternal mortality in rural community: a challenge for achieving millennium development goal. (2010). JPMA; 60: 20-24
6 .Shah N, Hossain N, Noonari M, Khan H. Maternal mortality and morbidity of unsafe abortion in a university teaching hospital of Karachi, Pakistan. (2011). JPMA; 61: 582.
7. Begum S, Nisa A, & Begum I. Analysis Of Maternal Mortality In A Tertiary Care Hospital To Determine Causes And Preventable Factors. (2003). Journal of Ayub Medical Abbottabad; 15: 2.
8. Iftikhar R. A Study of Maternal Mortality. (2009). Journal of Surgery Pakistan; 14(4): 176-178.
9. UNICEF data:monitoring the situation of children and women. available from URL:https: //data.unicef.org/topic/maternal -health/maternal-mortality/
10.Stokoe U. Determinants of maternal mortality in the developing world. (1991). Aust N Z J Obstet Gynaecol; Feb; 31 (1): 8-16.
11.guy's and st Thomas Catherine

Nelson-piercy. 2015.hand book of obstetric medicine; CRC press.

12.Royal College of Obstetricians and Gynecologists. (2009). Thrombosis and embolism during pregnancy and the puerperium, reducing the risk (Green-top 37a).

13.Ambreen A, khurshidS, A 5 year review of maternal mortality at FMH.2013; Vol 9

14.Evance I, Mbaruku G, Masanja H, Kahn K. Causes and risk factors for maternal mortality in rural Tanzania cases of Rufiji Health and Demographic Surveillance Site (HDSS). Afr J Reprod Health Sept 2013; 17(3): 119-130.

15.Yego F, Williams JS, Byles J, Nyongesa P, Aruasa W, D'Este C.A retrospective analysis of maternal and neonatal mortality at a teaching and referral hospital in Kenya. Biomed Cent Reprod Health 2013; 10: 13.

16.Stein PD, Henry JW. Clinical characteristics of patients with acute pulmonary embolism stratified according to their presenting syndromes. Chest 1997; 112:974979

17.James, A. H., Jamison, M. G., Brancazio, L. R., & Myers, E. R. (2006). Venous thromboembolism during pregnancy and the postpartum period: Incidence, risk factors, and mortality. American Journal of Obstetrics and Gynecology, 194(5), 1311.

18.Knight, M. On behalf of UKOSS. (2008). Antenatal pulmonary embolism: risk factors, management and outcomes. BJOG, 115,453461.

19.Larsen, T. B., Sorensen, H. T., Gislum, M., & Johnsen, S. P. (2007). Maternal smoking, obesity, and risk of venous thromboembolism during pregnancy and the puerperium: A population based nested case-control study. Thrombosis Research, 120(4),505-509

20.Saving Mothers' Lives. (2011). Reviewing maternal deaths to make motherhood safer: 200608. The eighth report of the confidential enquiries into maternal deaths in the United Kingdom.BJOG, 118(Suppl. 1), 1203.

21.Khan B, deebaF, NaseemS. Maternalmortality; Aten-year review of maternal mortality at tertiary care setup. Journal of Ayub Med Coll Abbottabad 2012;24(3-4)

22.Eusebious W.Maro,Neema R. Mosha. Ten years trend in maternal mortality at Kilimanjaro Christian Medical Center Tanzania, 20032012: A descriptive retrospective tertiary hospital based study Citation data: Asian Pacific Journal of Reproduction, ISSN: 2305-0500, Vol: 5,: 3; 214-220

23.Yego F, Williams JS, Byles J, Nyongesa P, Aruasa W, D'Este C.A retrospective analysis of maternal and neonatal mortality at a teaching and referral hospital in Kenya. Biomed Cent Reprod Health 2013; 10: 13

Original Article

Treatment of Pulmonary Aspergilloma- Is Surgery A Safe Option? A Review of 289 Cases at Two Centers in Pakistan

Muhammad Shoaib Nabi, Aneela Chaudhary, Dawar Mahmood Ayyaz, Muhammad Saquib Musharaf and Fariha Bashir

Objective: To determine outcome of surgery in adult Pakistani population with aspergilloma.

Methods: A total of 289 adults of both sexes with unilateral aspergilloma cavity were enrolled in this prospective study spanning 16 years carried out in Services Institute of Medical Sciences and Surgimed Hospital Lahore. Out of 289, only 102 patients were electively fit for surgery. Exclusion criteria involved any patient with extensive bilateral disease, advanced age (65+) and lack of consent. Data was collected on hard copy forms with entry and analysis done in SPSS version 23. Follow up period was of 36 months.

Results: Our study consisted of 289 patients with 102 selected for surgical intervention. The median age of the patients was 33.4. The most common presenting complaint was recurrent hemoptysis, seen in 75 patients (73.5%). The most common underlying lung pathologies predisposing to Aspergilloma were Tuberculosis (76.4%) and Bronchiectasis (14.7%). The most common co-morbidities were Hepatitis C 23.5% and Diabetes 20.5%. Out of 102 cases postoperative complications were documented in 24 (23.5%) patients of which 9(37%) patients had more than one complications.10 (9.8%) patients had prolonged air leak, 8 (7.8%) had surgical site wound infection, 8 (7.8%) had mild hemoptysis for couple of weeks, 5(4.9%) had bronchopleural fistula, 5(4.9%) had intra thoracic haemorrhage (>1500 ml blood loss), 4 (3.9%) had post resection loculated empyema and 4(3.9%) had pneumonia. Post-operative mortality was 1.96% with zero per-operative mortality. One patient died due to pulmonary embolism on 5th postoperative day and the other patient died of myocardial infarction. Follow up was for 36 months postoperatively.

Conclusions: Although surgical intervention for aspergilloma is technically difficult,scrupulous selection of patients, meticulous surgical techniques and good postoperative care can reduce mortality and morbidity and favourable outcome can be achieved.

Keywords: pulmonary aspergilloma, mycetoma, fungal infection & haemoptysis.

Introduction

The term Pulmonary Aspergilloma also known as mycetoma(fungal ball) refers to colonization of pre-existing lung cavities with the aspergillus fungus, most commonly the fumigatus species.[1] The lesion itself consists of a tangled mass of fungal hyphae, fibrin, epithelial cells, mucus, debris, and blood cell.[2,3] Aspergilloma secondary to cavitary disease is now considered a frequently encountered disease. After the formation of a fungal ball, antifungals are generally considered ineffective.[4] Tubercular lesions are the most common cause of such cavities; however, they may occur within cavities of diverse aetiologies including sarcoidosis, bronchiectasis, cysts and bullae, neoplasms, ankylosing spondylitis, granulomatosis polyangiitis (Wegener's granulomatosis), and pulmonary infarction.[5,6] Tuberculosis and bronchiectasis are common diseases in developing countries such as Pakistan. According to a study conducted in 2011, in absolute numbers Pakistan ranked 5th out of 22 high burden countries.[7] There is a paucity of literature and limited data on aspergilloma and its clinical presentations in Pakistan, possibly due to under reporting.[8]

Aspergillus fumigatus is an airborne filamentous fungus favouring a habitat of moist soil having a diameter of 2-3 micrometre.[9,10] In an immuno-competent person, it is normally eliminated by the immune and mucociliary clearance mechanisms. Hinson and colleagues have classified pulmonary aspergillosis into allergic, invasive and saprophytic infections.[1,11] The diagnosis is usually made radiographically without lung biopsy. Haemoptysis is commonly reported as the main symptom, that can be mild to moderate but at times it can be massive and life threatening. Massive haemoptysis represents one of the most challenging conditions encountered by thoracic surgeons and pulmonologists. In a few cases patients may be asymptomatic. Bleeding is usually

caused by local invasion and endotoxic or Mechanical irritation of exposed bronchial blood vessels. Symptoms like cough and dyspnoea are more likely related to underlying diseases, making a clear diagnosis difficult.[11,12] Sputum cultures for Aspergillus spp. are negative in >50% cases. Serum IgG antibodies to Aspergillus are positive in most cases, but may be negative in patients under corticosteroid therapy or in rare cases of pulmonary aspergilloma caused by species other than A. fumigatus.[13,14] Chest radiographies show intracavitary mass (fungus ball) with an air crescent (Monod sign) in about two-thirds of the cases.[15] Controversy still exists concerning the optimum management of aspergilloma. It is important to decide which patient should be offered treatment. 10% of asymptomatic cases resolve spontaneously but if patient is symptomatic and has significant morbidity in terms of hemoptysis then treatment should be offered to the patient. Clinical cases and retrospective series have reported that various oral triazoles provide suitable treatment for broncho-pulmonary aspergillosis in immunocompetent patients.[16] In inoperable cases treatment with antifungal agents can be tried. There have been inconsistent results with intracavitary, and endobronchial instillations of antifungal agents. Among antifungals, itraconazole and voriconazole have been effective. Definitive treatment for an aspergilloma is surgical resection of the diseased area. However, surgical resection of the affected lung is associated with considerable morbidity and mortality and outcome depends upon various preoperative, interoperative and postoperative factors. Depending upon the extent of disease, lobectomy, segmentectomy, pneumonectomy, or cavernostomy can be done.[17,18] Studies show that in carefully selected patients long term results of surgical treatment of aspergilloma is quite satisfactory.[19]

Methods

Between January 2002 and December 2017 289 patients were enrolled in this prospective study conducted at Services Institute of Medical Sciences and Surgimed Hospital, Lahore. Adults of both sexes and unilateral aspergilloma cavity were enrolled in the study whereas patients having extensive bilateral disease, advanced age and lack of consent were excluded. The diagnosis of aspergilloma was CT scan based. Preoperatively, Fiberoptic bronchoscopy was performed in all patients. Bronchoalveolar lavage and sputum was sent for acid fast bacilli smear, AFB, fungal and bacterial culture & sensitivity. Preoperative anaesthesia assessment was performed in all the patients. Two hundreds eighty nine aspergilloma patients were enrolled in the study but only 102 finally underwent surgery either due to loss of follow up or were declared unfit for surgery by anaesthesia department. One lung ventilation was maintained in all the patients using double lumen endobronchial tube. Posterolateral muscle sparing thoracotomy was used to enter the chest cavity through the 5th or 6th intercostal space depending on the type of resection (segmentectomy, lobectomy, pneumonectomy or any other possibility anticipated). Video-assisted thoracoscopic (VATS) wedge excision was performed in patients with eithersmall peripheral lesions or poor respiratory functional reserve. All the patients had been infected by chronic recurrent infection and destructive tuberculosis with subsequent pleural reaction and patchypleuritis. In most of cases we have to do decortication, which is a procedure by which fibrotic tissue between the visceral and parietal pleura is removed to free the lung for anatomical lung resection and enable remaining lung to expand adequately. Resected specimens were sent for histopathology, acid fast bacilli, fungal and bacterial cultures. Bleeding was considered excessive when the sum of peroperative and postoperative drainage in first 24 hours exceeded 1500ml. Air leaks was considered important if it lasted beyond 7 days. Operative deaths and deaths from all causes were included in the survival statistics. Operative death was defined as any death occurring during the first 30-day period or during the initial hospital stay. Follow up period was 36 months.

Results

Out of 102 patients 62 (61%) were male and 40 (39%) were female with median age of 33.4 years. **(Fig 1).**

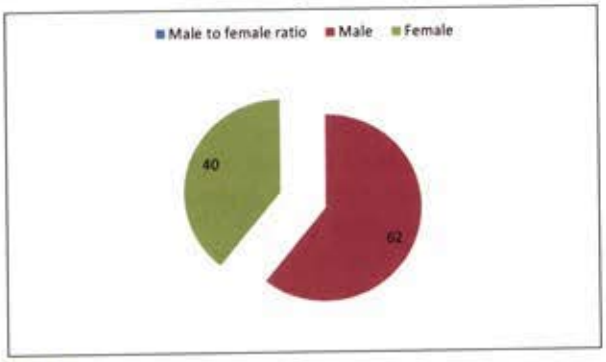


Fig-1: Male to female ratio.

Majority patients were symptomatic. Presenting complaints included recurrent hemoptysis seen in 75

(73.5%), productive cough in 15(14.7%) patients whereas 12 (11.7%) were asymptomatic **(Table-1).** In78(76.4%) cases, aspergilloma developed in tuberculosis cavity, 15(14.7%) in bronchiectasis,5 (4.9%) in bullous emphysema and 4(3.9%) developed in cavities of treated cases of lung abscess. **(Fig-2)**

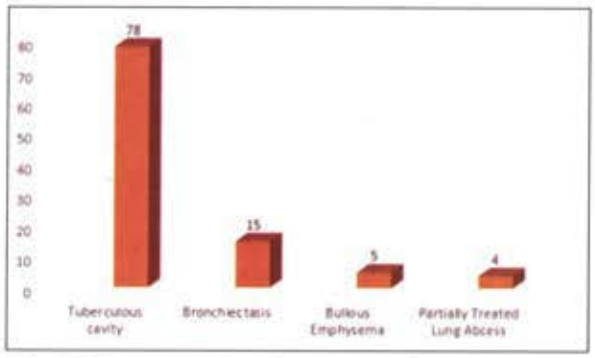


Fig-2: Factors causing formation of aspergilloma.

Sputum and BAL cultures done preoperatively were positive for aspergillus fumigatus in 3(2.9%) and 14(13.7%) cases respectively. Culture of resected lung tissue revealed growth of aspergillus fumigatus in 85.2% cases, mucormycosis in 4.9% cases and AFB culture was positive in 8.8% cases **(Table-2)**. Depending upon the cases, appropriate surgical procedures were opted and all cases were followed for 36 months postoperatively. Wedge resection was done in 6 (5.9%) whereas 67(65.7%) patients underwent lobectomy among which right upper lobectomy was performed in 33 (49%), left upper lobectomy 18(27%), left lower lobectomy 9(13.4%) cases and right lower lobectomy in 7(10.5%) cases. Bi-lobectomy (right upper and middle lobe) was performed in 9 (8.8%) patients. 15 patients (14.7%) underwent pneumonectomy among which 9 (60%) was right sided and 6(40%) were left sided. Bronchial stump was covered with pleural flap in all patient with lung resection (Fig 3). We used fibrin glue as sealant at pulmonary parenchymal suture line and broncho-vascular stumps in 29 patients. Thoracoplasty was done in 5 (4.9%) patients. Three patients underwent right apical thoracoplasty whereas 2 patients had left apical thoracoplasty **(Table 3)**.

The postoperative course was uneventful in 78 (76.4%) patients. Postoperative complications were documented in 24 (23.5%) patients of which 9(37%) patients had more than one complications. 10 (9.8%)patients had prolonged air leak, 8 (7.8%) had surgical site wound infection, 8(7.8%) had mild hemoptysis for couple of weeks, 5(4.9%) had bronchopleural fistula, 4(3.9%) had intra thoracic hemorrhage (>1500 ml blood loss), 4 (3.9%) had post resection loculated empyema and 4(3.9%) had pneumonia. Two (1.96%) patients died in our study. One patient died due to pulmonary embolism on 5th postoperative day and other patient died of myocardial infarction **(Table 4).**

Table-1: Clinical Presentation.

		n=102	Percentage
Symptoms	Hemoptiysis	75	73.5%
	• Mild moderate	15	58.8%
	• Severe	09	8.8%
	• Massive	06	5.8%
	Productive Cough	15	14.7%
	Asymptomatic	12	11.7%
	Anti HCV	24	23.5%
	Diabetes	21	20.5%
	Asthmatic	6	5.8%)

Table-2: Pathological Features of 102 Surgical Patient.s

		n=102	%Age
Preoperative sputum	**Positive for aspergillus fumigates**	**3**	**2.9**
	Positive for AFB smear	0	0
	Positive for culture	0	0
Preoperative BAL	**Positive for aspergillus fumigates**	**14**	**13.7**
	Positive for AFB smear	0	0
	Positive for culture	0	0
Postoperative llung tissue with cavity cultures	**Positive for aspergillus fumigates**	**87**	**85.2**
	Positive for smear	0	0
	Positive for culture	9	8.8
	Positive for mucomycosis	5	4.9

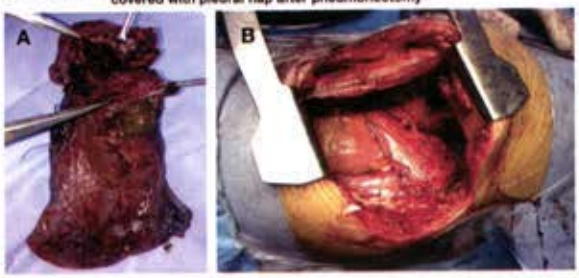
Table-3: Surgical procedures performed in 102 patients.

Procedure	**n=102**	**%Age**
Wedge resection (right upper lobe)	**06**	**5.9**
Lobectomy	67	65.7
• Right upper lobectomy	33	32
• Right lower lobectomy	**07**	**6.8**
• Left upper lobectomy	18	17.6
• Left lower lobectomy	09	8.8
Bilobectomy (right upper and middle lobes)	**09**	**8.8**
Pneumonectomy	15	14.7
• Right pneumonectomy	09	8.8
• Left pneumonectomy	06	5.8
Thoracoplasty	05	4.9
Subsequent thoraocplasty	05	4.9

Table-4: Postoperative outcome of surgical procedures.

Varibales	Wedge resection (n=4)	Lobectomy (n=66)	Lobectomy (n=66)	Pneumoectomy (n=14)	Thoracoplasty (n=9)
Hemorrhage (>1500ml	-	3	1	-	-
Penumomia	-	3	1	-	-
Prolonged air leak (> 7 days)	-	9	1	-	-
Bronchopleural fistula	-	4	-	1	-
Empyema	-	3	-	1	-
Wound infection	1	4	-	1	2
ICU stay (days)	1	3±1	3±1	2±1	4±1
Mortality	-	1	-	1	-

Fig 3: A) resected lung showing fungal material in the cavity , B) bronchial stump covered with pleural flap after pneumonectomy



Discussion

Aspergillus fumigatus, a saprophytic fungus is ubiquitously present in our environment. Mostly it colonizes a pre-existing cavity. According to World Health Organization (WHO) Global TB report 2017, Pakistan ranks 5th in 22 high burden countries with 510,000 new cases and 15,000 MDR TB cases each year.[20] According to British cooperative study patients having thick walled lung cavities for more than 7 years who were treated for tuberculosis bear higher risk for Aspergilloma.[21] In our study 78% of aspergillomas developed in residual tuberculous cavities. Preoperatively Sputum and BAL cultures for Aspergillus fumigatus were positive only in 3 (2.9%) and 14 (13.7%) cases respectively whereas postoperatively resected lung grew Aspergillus Fumigatus in 85% cases. This emphasizes the point that preoperative immunological or culture testing is not required to make diagnosis in fact sputum cultures have a low yield in detection of mould.[22] A majority of patients who are offered surgical treatment have hemoptysis for which they present to pulmonologist.[23] According to most studies, the percentage of symptomatic patients is around 80%,[23,25] which is confirmed in our study where 75% patients were symptomatic. There is no consensus on the management of pulmonary aspergilloma. Due to poor results of treatment with local and systemic antifungal agents, surgery remains the most promising option.[6] Due to risk of bleeding, surgery is mainly recommended in cases who are in good health and does not have complex disease. In our study we enrolled 289 cases but only 102 underwent surgery due to fitness issues and due to fear of surgery many patients refused to take this option and were lost to follow up. Depending upon the extent of disease, lobectomy, segmentectomy, pneumonectomy, and cavernostomy were done in our study. Standard thoracotomy and lobectomy were the preferred surgical procedures in a series of 212 patients, done by Qian-Kun et al.[26] The most commonly encountered complications listed in the literature arebleeding, prolonged air leaks and residual pneumothoraces.[27] Pleural space problems were the most common postoperative complications in our study, seen in 20 patients (19.61%). We used fibrin glue in 29 patients, which was shown to be an effective sealant for pulmonary parenchymal suture line and broncho- vascular stumps. We agree with Babatasi et al and Massard et al that thoracoplasty may be indicated subsequent to space problem after lung resection for Aspergilloma.[28,29] In our study, 5 patients had subsequent thoracoplasty for bronchopleural fistula or empyema as a second procedure. Three patients had thoracoplasty after lobectomy whereas 2 patients had pneumonectomy. The outcome after thoracoplasty was good with no post-operative mortality. In our study 5(4.9%) patients had bronchopleural fistula whereas in a previous series by Barik et al, BPF was reported between 2.5 and 15.8.[30] 10 (9.8%)patients had prolonged air leak, 8 (7.8%) had surgical site wound infection, 8(7.8%) had mild hemoptysis for a few weeks,4(3.9%)had intra thoracic haemorrhage (>1500 ml blood loss) which was managed with blood transfusions and volume replacement. 4(3.9%) had post resection loculated empyema & 4(3.9%) had pneumonia. No adjuvant anti fungal treatment was offered to the patients as there no is significant data to back up post-operative use.[31] The long term outcome in our cases remained encouraging.

Conclusions

Although surgery of aspergilloma is considered to be a technically difficult surgery with scrupulous selection of patients, good surgical skills and postope- rative care, morbidity and mortality can be reduced significantly and long term surgical outcome can be very favourable. Based on literature and on our experience, we suggest that surgery should be offered to these patients especially those who are having recurrent haemoptysis.

Department of Thoracic surgery
SIMS/ Hospital, Lahore

References

1. Hinson KF, Moon AJ, Plummer NS. Broncho-pulmonary asperg- illosis; a review and a report of eight new cases. Thorax. 1952;7(4): 317-33.
2. Riscili BP, Wood KL. Noninvasive pulmonary Aspergillus infections. Clin Chest Med. 2009;30(2):315-35, vii.
3. Passera E, Rizzi A, Robustellini M, Rossi G, Della Pona C, Massera F, et al. Pulmonary aspergilloma: clinical aspects and surgical treatment outcome. Thorac Surg Clin. 2012;22(3):345-61.
4. Jewkes J, Kay PH, Paneth M, Citron KM. Pulmonary aspergilloma: analysis of prognosis in relation to haemoptysis and survey of treatment. Thorax. 1983;38(8): 572-8.
5. Akbari JG, Varma PK, Neema PK, Menon MU, Neelakandhan KS. Clinical profile and surgical outcome for pulmonary aspergilloma: a single center experience. Ann Thorac Surg. 2005;80(3):1067-72.
6. Kim YT, Kang MC, Sung SW, Kim JH. Good long-term outcomes after surgical treatment of simple and complex pulmonary aspergilloma. Ann Thorac Surg. 2005;79(1):294-8.
7. Population Based National Tuberculosis Prevalence Survey among Adults (>15 Years) in Pakistan, 20102011. 2018.
8. Iqbal N, Irfan M, Zubairi ABS, Jabeen K, Awan S, Khan JA. Clinical manifestations and outcomes of pulmonary aspergillosis: experience from Pakistan. BMJ Open Respir Res. 32016.
9. Shah R, Vaideeswar P, Pandit SP. Pathology of pulmonary aspergillomas. Indian J Pathol Microbiol. 2008;51(3):342-5.
10. Latge JP. Aspergillus fumigatus and aspergillosis. Clin Microbiol Rev. 1999;12(2):310-50.
11. Kousha M, Tadi R, Soubani AO. Pulmonary aspergillosis: a clinical review. Eur Respir Rev. 2011;20(121):156-74.
12. Walsh TJ, Anaissie EJ, Denning DW, Herbrecht R, Kontoyiannis DP, Marr KA, et al. Treatment of aspergillosis: clinical practice guidelines of the Infectious Diseases Society of America. Clin Infect Dis. 2008;46(3):327-60.
13. Yamada H, Kohno S, Koga H, Maesaki S, Kaku M. Topical treatment of pulmonary aspergilloma by antifungals. Relationship between duration of the disease and efficacy of therapy. Chest. 1993;103(5):1421-5.
14. Rafferty P, Biggs BA, Crompton GK, Grant IW. What happens to patients with pulmonary aspergilloma? Analysis of 23 cases. Thorax. 1983;38(8):579-83.
15. Youssef C, Widlus DM. Imaging diagnosis of aspergilloma. J Community Hosp Intern Med Perspect. 22012.
16. Camuset J, Lavole A, Wislez M, Khalil A, Bellocq A, Bazelly B, et al. [Bronchopulmonary aspergillosis infections in the non-immunocompromised patient]. Rev Pneumol Clin. 2007;63(3):155-66.
17. Soubani AO, Chandrasekar PH. The clinical spectrum of pulmonary aspergillosis. Chest. 2002;121(6):1988-99.
18. Daly P, Kavanagh K. Pulmonary aspergillosis: clinical presentation, diagnosis and therapy. Br J Biomed Sci. 2001;58(3):197-205.
19. Rosenberg RS, Creviston SA, Schonfeld AJ. Invasive Aspergillosis Complicating Resection of a Pulmonary Aspergilloma in a Nonimmunocompromised Host1,2. Http://dxdoiorg/101164/arrd198212661113. 2015.
20. Organization WH. Global Tuberculosis report, Pakistan 2018 [Available from: http://www.emro.who.int/pak/programmes/stop-tuberculosis.html.
21. Aspergilloma and residual tuberculous cavities - the results of a resurvey Aspergillus & Aspergillosis Website 2018 [Available from: https:// www.aspergillus.org.uk /content / aspergilloma-and-residualtuber- culous-cavities-results-resurvey.
22. Vergidis P, Moore C, Rautemaa-Richardson R, Richardson M. High-volume Sputum Culture for the Diagnosis of Pulmonary Aspergillosis. Open Forum Infect Dis. 42017. p. S609.
23. Lee JG, Lee CY, Park IK, Kim DJ, Chang J, Kim SK, et al. Pulmonary aspergilloma: analysis of prognosis in relation to symptoms and treatment. J Thorac Cardio- vasc Surg. 2009;138(4):820-5.
24. Ahmad T, Ahmed SW, Hussain N, Rais K. Clinical profile and postoperative outcome in patients with simple and complex aspergilloma of lung. J Coll Physicians Surg Pak. 2010;20(3):190-3.
25. Ngo Nonga B, Bang GA, Jemea B, Savom E, Yone P, Mbatchou N, et al. Complex Pulmonary Aspergi- lloma: Surgical Challenges in a Third World Setting. Surg Res Pract. 2018;2018.
26. Chen QK, Jiang GN, Ding JA. Surgical treatment for pulmonary aspergilloma: a 35-year experience in the Chinese population. Interact Cardiovasc Thorac Surg. 152012. p. 77-80.
27. Daly RC, Pairolero PC, Piehler JM, Trastek VF, Payne WS, Bernatz PE. Pulmonary aspergilloma. Results of surgical treatment. J Thorac Cardiovasc Surg. 1986;92(6):981-8.
28. Massard G, Roeslin N, Wihlm JM, Dumont P, Witz JP, Morand G. Pleuropulmonary aspergilloma: clinical spectrum and results of surgical treatment. Ann Thorac Surg. 1992;54(6):1159-64.
29. Babatasi G, Massetti M, Chapelier A, Fadel E, Macchiarini P, Khayat A, et al. Surgical treatment of pulmonary aspergilloma: current outcome. J Thorac Cardiovasc Surg. 2000;119(5):906-12.
30. Brik A, Cardiothoracic Surgery Department FoM, Zagazig University, Zagazig, Egypt, Salem AM, Cardiothoracic Surgery Department FoM, Zagazig University, Zagazig, Egypt, Kamal AR, Cardiothoracic Surgery Department FoM, Zagazig University, Zagazig, Egypt, et al. Surgical outcome of pulmonary aspergilloma. European Journal of Cardio-Thoracic Surgery. 2018;34(4):882-5.
31. Benhamed L, Department of Thoracic and Vascular Surgery VH, Valenciennes, France, Woelffle D, Department of Thoracic and Vascular Surgery VH, Valenciennes, France. Adjuvant antifungal therapy after pulmonary surgery for aspergilloma: is it useful? Interactive CardioVascular and Thoracic Surgery. 2018;18(6):835-7.

Original Article

Negative Appendectomy at Tertiary Care Hospital, Lahore: A Review of Over 500 Appendectomy Cases

Anum Nadeem , Salman Hameed , Usman Ismat Butt , Barza Afzal, Waseem Hayat Khan and Muhammad Umar

Objective: To determine the incidence of negative appendicitis among patients undergoing appendectomy at our unit.

Methods: This was an observational descriptive study. We collected data of all patients presenting with acute appendicitis at Department of Surgery, Services Hospital, Lahore from 1st July 2017 to 30th June 2018.Data was analyzed.

Results: A total number of 537 cases were reviewed, spanning a period of 1 year. Out of these 237 were males and 300 were females. The incidence of alternative diagnosis was 2.6%.

Conclusions: On the basis of our results it is concluded the incidence of negative appendectomy in our population is 2.6%. Almost 80% of such cases were female. Further studies on larger scale on local population should be carried out to confirm these findings.

Keywords: negative appendectomy, tertiary care, incidence.

Introduction

Inflammation of the vermiform appendix is known as "appendicitis". Appendix is a vestigial organ. Appendicitis is the most common abdominal emergency with a lifetime risk of developing appendicitis being approximately 7%.[1] A great variation is seen in the presentation of appendicitis. Despite advances in diagnostic modalities, diagnosis of appendicitis remains essentially clinical.[2] Due to the risk of perforation and peritonitis, it remains a clinical emergency and is one of the more common causes of acute abdominal pain.The exact etiology of appendicitis remains unclear. Multiple causes have been postulated including obstruction, decreased dietary fiber, pollution and familial susceptibility.[3] Appendicitis occurs in all age groups. Appendicitis is most common in the second decade of life after which the incidence continues to decline.[4] Appendectomy for acute appendicitis is an effective, universally accepted procedure performed more than 300,000 times annually in the United States.[5] Similarly it is also one of the most common surgical case carried out in Pakistan.[6] The entity of negative appendectomy still poses a dilemma because it is associated with certain risks and unnecessary costs to both patients and the institutions. The rate of negative appendectomy varies in different studies.[7] The aim of our study was to review the case of acute appendicitis presenting to us over a 12 month period.

Methods

This was an observational descriptive study carried out in the Department of Surgery, Services Hospital, Lahore over a period of 1 year from 1st July, 2017 to 30th June, 2018. We collected data of all patients presenting with diagnosis of acute appendicitis. All the cases were evaluated and advised appendectomy after evaluation by a surgeon with minimum of 1 year experience after post graduate fellowship. Data of patients not consenting for study was not included. Patients underwent appendectomy and were admitted to our ward. Analysis of data was done. Specimens were sent for histopathological review to the Department of Pathology, Services Hospital, Lahore. An appendect- omy was considered to be negative if there were no histopathological signs of appendicular pathology.

Results

A total number of 537 cases were reviewed, spanning a period of 1 year. Out of these 237 were males and 300 were females. The incidence of negative appendectomy was 2.6%. Results are shown in tables and graphs.

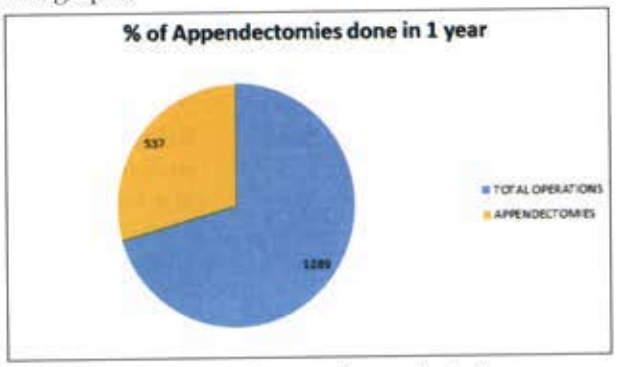


Fig-1: Percentage of appendectomies in 1 year.

Table-1: Percentage of negative appendectomies.

Appendectomies	537
Negative appendectomies	14
Percentage	2.3%

Table-2: Gender distribution of negative appendectomies.

Gender	Negative appenectomy	Percentage
Male	04	28.5%
Female	10	71.42%

Table-3: Alternative diagnosis breakdown (total 14 cases).

Alternative Diagnosis Breakdown (Total 14 cases)	Incidence	Gender breakdown Male	Female
Ruptured Ovarian Cyst	29 (4%)	0	5
Meckel's Diverticulum	14 (14%)	1	1
Mesenteric Lymphadenitis	14 (2%)	1	0
Pyo-salpinx	21 (3%)	0	3
Perforated Gallbladder	7 (1%)	0	1
Worm Bolus	7 (1%)	1	0
Meckel's Diverticulum	7 (1%)	1	0
Percentage		4 (29%)	10 (71%)

Discussion

Th first documentation of appendicitis is credited to Sir Claudius Amy in 1736 .[8] Appendectomy remains a commonly performed operation especially in the emergency setting.[9] During our study it constituted 38.8% of all cases performed. An appendectomy is considered to be negative when a normal appendix is removed following a medical workup for acute abdominal pain.It may occur as a result of other pathologies. The rate of negative appendectomy has been found to be variable in different studies. There has been a steady decrease in the incidence with improving diagnostic facilities.[10] Historically, an acceptable negative appendectomy rate (NAR)has been between 15% and 25%[11] with an even higher rate considered acceptable in women.[12]During our study we found the incidence of negative appendectomy to be 2.6%, which is comparable to the internationally documented rate which have shown a reduction from 23.0% to 1.7%.[13] 70% of the negative appendectomy were in female. And among these 80% was due to missed pathologies arising from the genitourinary tract. (Table 3) A similar trend was also noticed by other researchers.[14]

During workup of the patients we routinely carry out history, examination and basic workup including blood tests, urine examination and ultra-sound. CT scan was not routinely done in our patients. However studies have demonstrated that it may be helpful in difficult diagnosis cases where it may help to reduce the negative appendectomy rate.[13-15]

Our study has a number of shortcoming. It is a single centre study of 1 year duration. All the cases were evaluated and advised appendectomy after evaluation by a consultant surgeon. It is plausible that if a larger sample size covering the whole community were acquired the incidence would be likely higher. Furthermore we did not make use of routine CT scan during workup as it is a resource intensive investigation.

Conclusion

Negative appendectomy is still a cause of concern. It is more likely to occur in female patients. With increasing trend towards radiological studies trend is decreasing.

Department of Obstetrics and Gynecology
Fatima Memorial Hospital, Lahore

www.esculapio.pk

References

1. Petroianu A. Diagnosis of acute appendicitis. International Journal of Surgery, 2012, Volume 10, Issue 3, 115 119.
2. Sharma R ,Kasliwal DK, SharmaIndian RG. Indian J. Surg. (October 2007) 69:194197.
3. Humes DJ, Simpson J. Acute appendicitis. BMJ□: British Medical Journal. 2006;333(7567):530-534.
4. Addiss DG, Shaffer N, Fowler BS, Tauxe RV. The epidemiology of appendicitis and appendectomy in the United States. Am J Epidemiol. 1990 Nov; 132(5):910-25.
5. Paajanen H, Grönroos JM, Rautio T, Nordström P, Aarnio M, Rantanen T, et al. A Prospective randomized controlled multicenter trial comparing antibiotic therapy with appendectomy in the treatment of uncomplicated acute appendicitis (APPAC trial). BMC Surg 2013; 8: 13-3
6. Khan KI, Mahmood S, Akmal M, Waqas A. Comparison of rate of surgical wound infection, length of hospital stay and patient convenience in complicated appendicitis between primary closure and delayed primary closure. J Pak Med Assoc 2012; 62: 596-8.
7. Khairy G. Acute Appendicitis: Is Removal of a Normal Appendix Still Existing and Can We Reduce Its Rate? Saudi Journal of Gastroenterology□: Official Journal of the Saudi Gastroenterology Association.

2009; 15(3):167-170.
8. Hutchinson, R (February 1993). "Amyand's Hernia". Journal of the Royal Society of Medicine. 86 (2): 104105.
9. Joshi MK, Joshi R, Alam SE, Agarwal S, Kumar S. Negative Appendectomy: an Audit of Resident-Performed Surgery. How Can Its Incidence Be Minimized? The Indian Journal of Surgery. 2015;77(Suppl 3):913-917.
10. Seetahal SA, Bolorunduro OB, Sookdeo TC, Oyetunji TA, Greene WR, Frederick W, Cornwell EE, Chang DC, Siram SM. Negative appendectomy: a 10-year review of a nationally representative sample. Am J Surg. 2011 Apr;201(4):433-7.
11. Detmer DE, Nevers LE, Sikes ED. Regional results of acute appendicitis care. JAMA 1981;246(12):13181320.
12. Antevil J, Rivera L, Langenberg B, Brown CV. The influence of age and gender on the utility of computed tomography to diagnose acute appendicitis. Am Surg 2004;70(10):850853.
13. Raja AS , Wright C , Sodickson AD , Zane RD , Schiff GD, Hanson R , Baeyens PF and Khorasani R . Negative Appendectomy Rate in the Era of CT: An 18-year Perspective . Radiology 2010 256:2, 460-465.
14. Høydahl Ø, Kørner H, Edna T-H (2017) Preoperative Imaging in the Diagnosis of Acute Appendicitis is Associated with Low Negative Appendectomy Rate. Int J Surg Res Pract 4:060.
15. Drake FT, Florence MG, Johnson MG, Jurkovich GJ, Kwon S, et al. (2012) Progress in the diagnosis of appendicitis: A report from Washington State's Surgical Care and Outcomes Assessment Program. Ann Surg 256: 586-594.

Answer Picture Quiz

The radiograph shows bilateral, particularly right sided, peripheral air space consolidation. Consolidation is also seen posteriorly and peripherally in the right lower zone, below the level of the right hilum. The cardiac outline is normal and no pleural effusion or pneumothorax is seen.

Original Article

Association of H pylori and Morphological Changes in Mucosa of Esophagus and Gastric Antrum in Patients with Dyspepsia.

Tahira Liaquat, Eyyaz Khaleel and Tahir Bashir

Objective: To find association between H pylori and morphological changes in mucosa of oesophagus and gastric antrum in Patients having dyspepsia.

Methods: One hundred sixty nine patients presenting to outpatient department of Medical units of Lahore General Hospital and services hospital Lahore with symptoms of dyspepsia were included in the study. This study was conducted at Pathology Department of Post Graduate Medical Institute. Endoscopy of all included patients was done in the medical unit, services hospital and endoscopic biopsies from distal esophagus and gastric antrum were taken simultaneously.

Results: Out of 169 patients 31 were H. Pylori positive, 30 (96.8%) cases were with chronic inflammation, 22 (70.9%) cases with neutrophil infiltration, 21 (67.7%) case atrophic changes, 4 (12.9%) cases with metaplasia/dysplasia and 01 (3.2%) case was with malignancy.

Conclusions: Dyspeptic patients with H. pylori infection in esophageal mucosa are prone to develop morphological changes, however, histopathological changes in oesophageal and gastric mucosa of such patients are present in both H. Pylori positive and negative subjects but more in H. Pylori negative cases.

Keywords: pylori, dyspepsia, chronic inflammation, metaplasia.

Introduction

Helicobacter pylori (H. pylori), human pathogen, causes chronic gastritis and has a role in gastric and duodenal ulcer, adenocarcinoma and mucosal associated lymphoid tissue(MALT) lymphoma.[1] It is an important factor in functional dyspepsia and causes gastric carcinoma.[2] Infection with H. pylori occurs worldwide, varies greatly geographically, exceeding 90% in developing countries compared to 20% to 50% in developed countries.[3] The prevalence appears to be inversely proportional to socioeconomic status.[4]

One local study reported that H. pylori infection is 92% in cases of gastrointestinal symptoms of acid peptic disease[5] (Javed et al, 2010). There is an evidence that the disease outcome may be due to variations in infecting strains.[6] H. pylori colonization is mostly in the antral mucosa.[7] Antrum and incisura show atrophic gastritis and intestinal metaplasia with H. pylori infection.[8] The most favourable environment for bacterial colonization is esophagus.[9] Inflammation induces other changes like basal hyperplasia and dysplasia.[10] In the oesophagus of healthy patients as well as patients with reflux disease and Barrett's esophagus, H. Pylori have been detected.[11] There is paucity of literature regarding the morphological changes in H.pylori associated gastritis.[12] This study was conducted to find any association of H pylori and morphological changes in mucosa of esophagus and gastric antrum in patients having dyspepsia in local population.

Methods

169 patients presenting to outpatient department of Medical units of Lahore General Hospital and services hospital Lahore with symptoms of dyspepsia were included in the study. This study was conducted at Pathology Department of Post Graduate Medical Institute. Endoscopy of all included patients was done in the medical unit, services hospital and endoscopic biopsies from distal esophagus and gastric antrum were taken simultaneously. Biopsy was placed in jars containing 10% neutral buffered formalin solution[13]. Haematoxylin and Eosin Stain, Immunohistochemical Staining, modified Giemsa Staining were done and Inflammation, activity, H. pylori presence and other mucosal alterations were evaluated semi-quantitatively according to the Sydney system. Atrophic changes and intestinal metaplasia were also determined. Association of H pylori and morphological changes in mucosa of esophagus and gastric antrum in patients having dyspepsia was determined. The data was analyzed by using SPSS 20

(statistical package for social sciences). Quantitative variables like age and size of biopsy etc. were calculated as mean and standard deviation. Qualitative variables like gender, presenting complaint and histopathology were calculated as frequency and percentage. Data was presented in form of tables. Histopathological association with Helicobacter pylori was determined by using Chi-square test. P value of $\leq$ 0.05 was taken as significant.

Results

Out of 169 cases of dyspeptic patients, 110 (65.1%) are males and 59 (34.9%) are females. So M:F ratio is 1.9:1. Out of 169 cases, 31 (18.3%) cases are H. Pyloric positive with males and females 21 (12.4%) and 10 (5.9%) respectively and 138 cases are without H. Pylori infection with males and females 89 (52.7%) and 49 (29%) respectively. Out of 169 cases, 75 (44.4%) cases have no neutrophil infiltration activity while 94 (55.6%) cases with neutrophil activity include mild (n=61), moderate (n=25) and severe (n=8) activity. Among 94 cases with neutrophil infiltration, 72 (42.6%) cases are H. Pylori negative and 22 (13.1%) cases have H. Pylori positive. The difference between these cases is highly significant (P=0.004) statistically **(Table 4).**

Table-1: Age distribution.

Age (in years)	All subjects (n=169)	H. Pylori+ve (n=31)	H. Pylori-ve (n=138)
Mean± SD	39.9±10.8	38.1±10.1	40.4±11.0
Ranges	14 - 65	15 - 64	14 - 65
Total	169	31	138

Table-2: Gender distribution.

Gender	No of patients (n)	Percentage
Male	31	18.3%
Female	138	81.7%
Total	139	100%

Table-3: Distribution of Subjects according to H. Pylori infection.

H.Pylori Injection	No of patients (n)	Percentage
Yes	31	18.3%
No	138	81.7%
Total	139	100%

Table-4: Morphological changes.

Morphology	H.Pylori+ve Cases (n=31)	H.Pylori-ve Cases (n=138)
Neutrophil activity	22	72
Chronic inflammation	22	119
Atrophy	21	30
Metaplasia	04	35
Malignancy	01	13

Out of 169 cases, 20 (11.8%) cases have no inflammation while 149 (88.2%) cases have mild (n=84/49.7%), moderate (n=58/34.3%) and severe (n=7/4.1%) type of chronic inflammation. In 149 cases with chronic inflammation, n=30 (17.6%) cases are H. Pylori positive and n=119 (70.4%) with H. Pylori negative. The difference between these are highly significant (p=0.004) statistically. Out of 31 cases with atrophy, n=21 (67.7%) cases with atrophic changes are H pylori positive and n=30 cases are without H pylori. Out of 169 cases, n=130 (76.9%) cases have no metaplasia/dysplasia and among 39 patients with metaplasia, n=4 (2.4%) cases are H. Pylori positive and n=35 (20.7%) cases are H. Pylori negative and difference is highly significant (p=0.003) statistically. Out of 169 cases, 155 (91.7%) cases have no Malignancy while 14 (8.3%) cases are with malignancy. In 14 cases of gastro esophageal Malignancy (12 gastric, 2 esophageal), 01 (0.6%) case with gastric malignancy is H. Pylori Positive while 13 (7.7%) cases are H. Pylori negative and the difference is highly significant statistically.

Discussion

In this study, 110(65%) are males & 59(34.9%) are females and M:F ratio is 1.9:1. Regarding H. Pylori infection, 31(18.3%) cases are H. Pylori +ve and out of 31 cases, 21(12.4%) are males & 10(5.9%) are females. The number of H. pylori positive males in one study was 13 (18.6%) i.e. greater than the number of H. pylori positive women which was 9 (12.9%). This is in accordance with the data of Persson et al (2010)[14] where H. pylori positive male patients were 29% and females 26%. This research work showed n=31(18.3%) cases of positive H. pylori infection by immunostaining. Yamaoka Y et al (2006)[15] found H.pylori immunopositivity to be 68% while in the study of Afzal et al (2006)[16] this was 70%.

Chronic inflammation in our study is present in n=149(88.2%) cases. Out of 149 cases, n=30(17.6%) cases are with H. Pylori +ve infection and n=119 (70.4%) are without H. Pylori infection. Lymphocytes are not present in the normal oesophageal/gastric mucosa, so their presence in biopsies is evidence of chronic inflammation (Mackiorkowska et al 2003)[17] Nwokediuko and Okafur (2007)[18] found chronic inflammation in 66.7% patients. In this study, Neutrophil infiltration activity is present in 94(65.6%) cases while 22(23.4%) cases are H. Pylori +ve and 72 (76.6%) are with H. Pylori ve. Contreras M et al(2012)[19] showed 38(86%) cases with neutrophil infiltration activity having H. Pylori +ve.

In this study, grading of morphological variables was done according to the Upgraded Sydney System.[20] All our patients had chronic inflammatory mono-nuclear infiltrate. This was mild (grade I) in 61 (36.1%) cases, moderate (grade 2) in 25 (14.8%) cases and marked (grade 3) in 08 (4.7%). Chronic inflammation eventually progresses to atrophy of mucosal glands. The onset of atrophy is related to the duration of infection, strain of the organism, dietary factors and host immunity.[21] Atrophy in this study group is present in 51(30.2%) cases and 21(12.4%) cases are with H. Pylori +ve while 30(17.6%) without H. Pylori infection. In one study, atrophy was seen in only one (1.43%) patient whereas Parasenthi et al (2011)[22] found atrophy in 22.1% patients.

Metaplasia/ Dysplasia in our study is present in 39(23.1%) cases in which 04(2.4%) cases having H. Pylori +ve and 35(20.7%) cases are without H. pylori infection. Contreras M et al (2012)[19] Malignancy in this study is present in 14(8.3%) cases and one (0.6%) case shows malignancy with H. Pylori +ve and 13(7.7%) showed no H. Pylori infection in mucosa of esophagus of dyspeptic patients. Morphological study of the variables incorporated in the Upgraded Sydney System allows pre-cancerous changes like atrophy and intestinal metaplasia to be picked up early. Thus appropriate treatment can be instituted.[23]

Conclusion

Dyspeptic patients with H. pylori infection in esophageal mucosa are prone to develop morphological changes, however, histopathological changes in oesophageal and gastric mucosa of such patients are present in both H. Pylori positive and negative subjects but more in H. Pylori negative cases. No significant association was found among H. pylori infection, Barrett's oesophagus and oesophageal carcinoma.

Department of Medicine
Ganga Ram Hospital, Lahore
www.esculapio.pk

References

1.Shrestha S, Paudel P, Pradhan GB, Shrestha L, Bhattachan CL. Prevalence study of H. pylori infection in dyspeptic patients coming to Nepal Medical College Teaching Hospital, Jorpati, Kathmandu. Nepal Med Coll J. 2012 Sep; 14(3):229-33.

2.Mahmood S & Hamid A. 2010. Comparison between Invasive andNoninvasive Tests In Diagnosis Of Helicobacter Pylori Infection. Pak. J. Biol. Sci, 13, 509-512.

3.Frenck Jr RW, Clemens J. Helicobacter in the developing world. Microbes Infect 2003; 5:70513.

4.Domı´nguez-Bello MG, Beker B, Guelrud M, Vivas J, Peraza S, Pe´rez ME, et al. Short report: socioeconomic and seasonal variations of Helicobacter pylori infection in patients in Venezuela. Am J Trop Med Hyg 2002; 66:4951

5.Javed M, Amin K, Muhammad. 2010. Prevalence of H. Pylori. Professional Med J, 17, 431-439.

6.Nizami S Q, Bhutta Z A, Weaver L. 2005. Helicobacter Pylori Colonization In Infants In A Periurban Community In Karachi, Pakistan. J PedGastroenterol, 41, 191-194.

7.Rugge M, Mario F, Cassaro M. 2007. Pathology Of The Gastric Antrum And Body Associated With Helicobacter Pylori Infection In Non□Ulcerous Patients: Is The Bacterium A Promoter Of Intestinal Metaplasia? Histopathology, 22, 9-16.

8.Xia H H X, Kalantar J S, Talley NJ . 2000. Antral-Type Mucosa In The Gastric Incisura, Body, And Fundus (Antralization): A Link Between Helicobacter Pylori Infection And Intestinal Metaplasia&Quest. Am J Gastroenterol, 95, 114-121.

9.Herbella F A & Patti M G. 2010. Gastroesophageal Reflux Disease: From Pathophysiology To Treatment. World Jou Gastroenterology: 16, 3745.

10.Jang J, Lee S, Jung Y et al. 2003. Malgun (Clear) Cell Change In Helicobacter Pylori Gastritis Reflects Epithelial Genomic Damage And Repair. The Am Jpathol, 162, 1203-1211.

11.Pei Z, Yang I., Peek RM . 2005. Bacterial biota in reflux esophagitis and Barrett's esophagus. World J Gastroenterol 11:727783.

12.Parvez Mujawar,1 Dhiraj B. Nikumbh,2 Kishor H. Suryawanshi,3 Poonam S. Pagare,4 and Akshay Surana5. Helicobacter pylori Associated Gastritis in Northern Maharashtra, India: A Histopathological Study of Gastric Mucosal BiopsiesJ Clin Diagn Res. 2015 Jun; 9(6): EC04EC06.

13.Guenther T, Hackelsberger A, Kuester D et al. 2007. Reflux Esophagitis Or Helicobacter Infection? Diagnostic Value of The Inflammatory Pattern In Metaplastic Mucosa At The Squamocolumnar Junction. Pathology-Research And Practice, 203, 831-837.

14.Persson C, Canedo P, Machado J et al. 2010. 'Polymorphisms in inflammatory response genes and their association with gastric ca-

ncer: A Huge systematic review and meta-analyses', Am j epidemiol, 370.
15. Yamaoka, Y., Ojo, O., Fujimoto, S., Odenbreit, S., Haas, R., Gutierrez, O., El-Zimaity, H. M., Reddy, R., Arnqvist, A. and Graham, D. Y. 2006. 'Helicobacter pylori outer membrane proteins and gastroduodenal disease', Gut, 55(6), 775-781.
16. Afzal S, Ahmad M, Mubarik A. 2006. Morphological spectrum of gastic lesions-endoscopic biopsy findings. Pakistan Armed Forces medical journal,87,91-113.
17. Maciorkowska E, Kaczmarskii M, Kemona A. 2003. Comparative evaluation of gastric mucosa morphological changes in children and adults with H. pylori +ve. Ann AcademaiaeAedcae, 48:100-104.
18. Nwodiuko SC and OkafurOC. 2007. Gastric mucosa in non-ulcer dyspepsia: A histopathological study of Nigerian patiens. The Internet J Gastroenterol, ISSN:1528-8323.
19. Contreras M, Salazar V, Alexandra M. 2012. High frequency of Helicobacter pylori in the esophageal mucosa of dyspeptic patients and its possible association with histopathological alterations. Int. J Infect Dis 1016/j.ijid.Q22012.01.007.
20. Zhang YL, Lai ZS, Zhou DY. 2000. Supra angular biopsy is more reliable for atrophy recognization: analysis of 1598 cases for gastric mucosal histological examination. World J.Gastroenterol.6(6):893-897
21 .Owen DA. 2003. Gastric and Carditis.Mod.Pathol,16(4):325-341.
22. Parasenthi C, Parasenthi NL, Manikiran SS. 2011.Focus on current trends in the treatment of H. pylori infection: an update. J.Pharm. SCI.Rev. and Res. 9(2):42-51.
23. Rubio CA and Befrits R. 2004.Gastric intestinal metaplasia. J.Clin.Pathol, 57(8):894-895.

Medical News

EXERCISE MAY PREVENT HEART ATTACKS IN OTHERWISE HEALTHY PEOPLE

New research published in the European Heart Journal suggests that even people with no signs of cardiovascular disease should exercise to prevent a heart attack. Cardiorespiratory fitness can be a predictor of future problems, warn the researchers. Even fit and healthy people should exercise regularly to keep heart disease at bay. Heart disease remains the leading cause of death among men and women in the United States, responsible for the deaths of around 610,000 people each year. Coronary artery disease is the most common form of heart disease, which often results in a heart attack. However, even healthy people might be at risk of a heart attack, new research points out. Even if someone has no signs of cardiovascular problems, low cardiorespiratory fitness may predict future heart disease. For this reason, healthy individuals should exercise regularly to keep heart disease at bay.

Original Article

The Effect of Clot-Activator and Storage Time on Estimation of Free triiodothyronine T3 levels in Blood Samples

Farhana Mukhtar, Madeeha Cheema, Amina Khalid, Amtul Jamil Sami and Sumbul Mehmood

Objective: To find out the effect of clot-activator and storage time on estimation of free triodothyronine (FT3) in blood samples. .

Methods: Thirty five normal volunteers from general population were selected. Their blood samples were collected into two different types of Greigor Bio-One blood collecting tubes (BCT). Blood collecting tubes of first type were without clot activator and second type of BCT was with clot activator. Blood samples of first type of BCT were used to analyse the effect of storage time on free triodothyronine (FT3) estimation. These tubes were centrifuged and separated serum was preserved into 4 BCT without clot activator and labelled as first day, 24 hours, 48 hours and 96 hours. The serum of these tubes was estimated for FT3 at the intervals as labelled on the BCT. Free triiodothyronine estimation was done using Beckman coulter kit. To analyse the effect of clot activator on FT3 estimation, blood samples collected in BCT with clot activator were allowed to clot, serum was separated and FT3 estimation was done on the same day.

Results: Results of this study showed no statistical significance of results after 24h (p=0.256) by one way ANOVA analysis and Post Hoc test, but significant difference in values of FT3 concentration was observed after delayed analysis of 48 and 96 hours with P value(p=0.03). Paired Samples Test-BCT with and without clot activator had variation in results and significance (p =0.002) were analysed by statistical analysis.

Conclusions: This study concludes that, FT3 concentration variation was not statistically significant when it was estimated within 24 hours, but a false increase was observed after a delay of 48 to 96 hours. Samples of BCT without clot activator showed precise results of FT3 estimation when compared to the results of samples of BCT with clot activator. Therefore, BCT without clot activator should be preferred for collection of blood sample for FT3 estimation.

Keywords: Triodothyronine (FT3), thyroxine (T4), blood collecting tubes (BCT), clot activator.

Introduction

Endocrine glands secrete different types of hormones. These hormones through blood circulation reach the target organs and control their functions. The thyroid gland is also an endocrine gland which produces thyroid hormones that are classified as tyrosine derivatives.[1] Anatomically, thyroid gland consists of two lobes, lobus sinister and lobus dexter,[2] which are joined to one another by the median isthmus. In addition to that, a majority of the population (44.3%) has a pyramidal lobe, arising from isthmus or the next lobes.[3] The thyroid gland is attached to trachea via several ligaments and muscles that make it move during swallowing with the movement of trachea.[4-6] Histologically, thyroid gland is consists of epithelial cells, follicles and parafollicular cells. Epithelial cells control the T3 (triiodothyronine) and T4 (thyroxine) secretions and parafollicular cells are involved in production of calcitonin, , whereas thyroglobulin which is found in follicles (20-40 in number) helps in thyroid hormones production.[7] Spleen, kidney and liver control the 80% conversion of T4 to T3, as T3 is it's more active form (10 folds) than T4.[8-9] This conversion is done by Deiodinase enzyme followed by the release of thyroxine and triiodothyronine into the blood by protein kinase.[10] When thyroid hormone decreases in blood, TSH is released from anterior pituitary gland through feedback mechanism and binds the receptors on the thyroid follicle cells. This stimulates the production of thyroid hormones, which are released into bloodstream. In the body, only a small amount of thyroid hormones are found in free form, as FT3 (0.3%) and FT4 (0.03%). While the remaining T3 (20%) and T4 (80%) is bounded to thyroxine binding globulin, albumin and transthyretin.[11] Triidothyronine can cross the blood brain barrier via transport protein(MCT8). It is essential for neural development during fetal period of life. It is also involved in cell proliferation, growth and development of the body.[12-13]

Abnormally high production of thyroid hormones causes hyperthyroidism which may lead to thyrotoxicosis during which iodine uptake is abnormally increased. For laboratory diagnosis of thyrotoxicosis, direct measurement of FT3 is preferable. Treatment of hyperthyroidism includes anti-thyroid drugs, radioactive iodine and thyroidectomy.[14-15] In hypothyroidism, thyroid hormone synthesis is reduced that can be due to acute thyroiditis, Hashimoto's thyroiditis, radiation treatment or drugs etc. and treatment include thyroxine replacement therapy by levothyroxin[16].

Estimation of thyroid hormones in the blood samples is improved by enhancement of techniques like radioimmunoassay, IRMA, LC-MS (Liquid Chromatography-tandem Mass Spectrometry). Immunoassays have replaced the typical protein bound technique[17-18]. But still thyroid test sensitivity, stability and specificity are creating hurdles.[19]

Detection of FT3 is easy because it circulates in the blood in its free form as compared to Total T3(TT3) and Total T4 (TT4) that is bound to several proteins. Free hormone tests are developed to find thyroid hormones impact at the cellular level where antibody labelled analysis is done to get reliable results[20]. Variations of results of FT3 are found due to pre-analytical errors and endogenous materials,[21] which may be clot activator present in the BCT. Therefore, this study was conducted to determine the stability of FT3 by analysing the effect of storage time and clot-activator present in a blood sample.

Methods

Thirty five normal volunteers from general population were selected. Their blood samples were collected into two different types of Greigor Bio-One blood collecting tubes (BCT). Blood collecting tubes of first type were without clot activator and second type of BCT were with clot activator. Blood samples of first type of BCT were used to analyse the effect of storage time on free triodothyronine (FT3) estimation. These tubes were centrifuged and separated serum was preserved into 4 BCT without clot activator and labelled as first day, 24 hours, 48 hours and 96 hours. The serum of these tubes was estimated for FT3 at the intervals as labelled on the BCT. Free triodothyronine estimation was done using Beckman coulter kit. To analyse the effect of clot activator on FT3 estimation, blood samples collected in BCT with clot activator were allowed to clot, serum was separated and FT3 estimation was done on the same day. Beckman Coulter kit (REF No. IM1579) was used for determination of FT3 concentration in serum samples. The standard value of serum FT3 in pM/L is 2.5-5.8. It follows the principle of labelled antibody immunoassay (competitive).

During the procedure, 100 micro litre of control was added in a tube; calibrator 100 micro litre was added in 5 tubes, whereas 100ul of each sample was added in a separate container. Then, 400ul of tracer was introduced into each tube and mixed completely by pulse overtaxing. These tubes were then incubated for 2 hours (20°C) on shaking incubator (350rpm) followed by aspiration of each tube. Gamma (Scintillation) counter was used to count total and bound compound. From standard curve, the concentration of FT3 samples was obtained in pM.

Paired t-test, ANOVA, Post-Hoc test and correlations were performed for analysing the statistical significance of the results. IBM SPSS statistics software (version 21) was used for all statistical analysis.

Results

False increase in levels of FT3 concentration was obtained in delayed analysis, i.e. with increase in storage time. After 24 hours of delay, no statistically significant difference (p=0.256) was seen in FT3 concentration (Fig.1). Whereas, with further delay (i.e. after 48h and 96h) false increase in levels of FT3 concentration was significant (p=0.03) when analysed by one way ANOVA **(Table.1).**

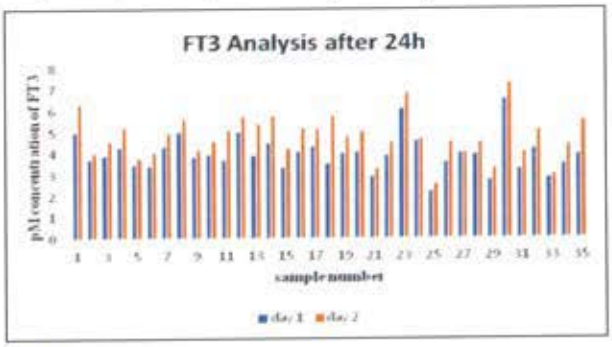


Fig-1: Showing the significance of concentration of FT3 for first day and second day (24h) of FT3 analysis. X-axis represents the no. of samples for first and second day while y-axis represents pM concentration of Ft3. It shows false increase in FT3 concentrations.

The concentration of each sample in BCT with or without clot activator was measured using the

standard technique, and the difference was observed in both the instances. The concentration of FT3 in the samples collected in BCT with clot activators were higher as compared to without clotactivators. Therefore, significant difference in the values were obtained (p =0.002) by using paired T-Test **(Table 2)**.

Significant difference in the concentration of FT3 of samples in tubes with clot activators as compared to tubes without clot activators was observed.

Table-1: Comparison of serum level of FT3 on 1st day, after 24 hours, 48 hours and 96 hours.

Parameter pM	FT3 level at 1st day Mean ± SD	FT3 level at 24 hours Mean ± SD	FT3 level at 48 hours Mean ± SD	FT3 level at 96 hours Mean ± SD
FT3 (2.5-5.8)	3.98±0.85	4.15±1.02*	4.94±1.26**	5.21±1.94**

*$p = 0.256$, **$p = 0.03$ ($p<0.05$).

Table-2: Comparison of serum level of FT3 between sample without clot activator and sample with clot activator

Parameter pM	FT3 level in sample without clot activator Mean ± SD	Ft3 level in sample without clot activator Mean ± SD	p-Value
FT3 (2.5-5.8)	4.98±1.86	6.05±1.6	0.002*

*$p<0.002$

Discussion

The thyroid gland secretes thyroid hormones into the blood stream. Thyroid hormones reach the target organs and control the functions of the body. Release of thyroid hormones T3 and T4 is controlled through TSH which is secreted by anterior pituitary gland. In the serum, concentration of FT3 in pico-moles is difficult to estimate as compared to the estimation of TT3 with conventional detection methods. Currently, radioimmunoassay kit method is used for this purpose as it is reproducible, easy to use, saves time and cost effective. In this study, the effect of storage time of sera and presence of clot activator in the BCT were analysed on the estimation of FT3 by using Beckmann Coulter Kit. It is a unique study and minimal research is available in the literature. Results of previous studies showed that prolonged storage time of sera and presence of clot activator affect the FT3 analysis.[22] In our study, insignificant increase in FT3 was observed after 24 hours of delay. Similarly, in another study, FT3 concentration increased within reference range after a delay of 24 hours.[23,24] This observation of our study confirms the results of previous studies. However, after a delay of 48 to 96 hours significant increase in FT3 was observed in our study. This false increase in FT3 was due to fibrin clot, inappropriate T3 formation or heparin interaction.[25] Analytical error in FT3 estimation was observed when clot activator coated BCT were used which is one of the causes of false increase in FT3. This research concludes that a delay of 48 to 96 hours in analysis of FT3 can significantly affect its estimation and false increase in its levels are observed. Therefore, for precise measurements BCT without clot activator should be preferred.

Conclusion

This study concludes that, FT3 concentration variation was not statistically significant when it was estimated within or after 24 hours, but a false increase in it's concentration was observed after a delay of 48 to 96hrs. Samples of BCT without clot activator showed precise results of FT3 estimation when compared to the results of samples of BCT with clot activator. Therefore, BCT without clot activator should be preferred for collection of blood sample for FT3 estimation.

Department of Biochemistry,
Sheikh Zayed Hospital, Lahore

References

1. Guyton, A.C. and Hall, J.E., (2006). "Textbook of Medical Physiology" ISBN 0-7216-0240-1.(pg:5-16,31-43).
2. Dorland' W. A. N. (2012). Illustrated medical dictionary. Elsevier Saunders. p. 1072. ISBN 978-1-4160-6257-8.
3. Williams, P., Bannister, L. H., Berry, M. M., Collins, P., Dyson, M., Dussek, J. E., & Ferguson, M. W. J. (1995). Gray's Anatomy 38th edition Churchill Livingstone
4. Yalçın, B., &Ozan, H. (2006). Detailed investigation of the relationship between the ssinferior laryngeal nerve including laryngeal branches and ligament of Berry. Journal of the American College of Surgeons, 202(2), 291-296 (2010).
5. Kamath, M. Aroon. "Are the ligaments of Berry the only reason why the thyroid moves up with deglutition?". Doctors Lounge Website. Retrieved August 24.
6. Lemaire, David (2005). "eMedicine - Thyroid anatomy". Retrieved 2008-01-19.
7. Don, F. and Ronald, J., (2002). Bloom & Fawcett's Concise Histology. New York: Arnold Publishers. pp. 257258. ISBN 0-340-80677-X.
8. Shekar-Foroosh, S., Changizi-Ashtiyani, S., Akbarpour, B., Attari, M. M., Zarei, A., &Ramazani, M.

(2012). The Effect of Alcoholic Extract of Physalisalkekengi on Serum Concentration of Thyroid Hormones in Rats. Zahedan Journal of Research in Medical Sciences, 14(5), 7-11

9.Nussey, S. S., & Whitehead, S. A. (2013). Endocrinology: an integrated approach. CRC Press.

10.Bianco, A. C., Salvatore, D., Gereben, B., Berry, M. J., & Larsen, P. R. (2002). Biochemistry, cellular and molecular biology, and physiological roles of the iodothyronineselenodeiodinases. Endocrine reviews, 23(1), 38-89.

11.Jansen, J., Friesema, E. C., Milici, C., &Visser, T. J. (2005). Thyroid hormone transporters in health and disease. Thyroid, 15(8), 757-768.

12.Zoeller, R. T. (2003). Transplacentalthyroxine and fetal brain development.Journal of Clinical Investigation, 111(7), 954.

13.Thompson, C. C., & Potter, G. B. (2000). Thyroid hormone action in neural development. Cerebral cortex, 10(10), 939-945.

14.Wallace, R. B., & Stone, M. B. (Eds.). (2003). Medicare coverage of routine screening for thyroid dysfunction. National Academies Press.

15.Daniel, K. T. (2005). The whole soy story: the dark side of America's favorite health food. New Trends Pub.

16.Negro, R., Formoso, G., Mangieri, T., Pezzarossa, A., Dazzi, D., & Hassan, H. (2013). Levothyroxine treatment in euthyroid pregnant women with autoimmune thyroid disease: effects on obstetrical complications. The Journal of Clinical Endocrinology & Metabolism.

17.Spencer, C.A., (2010). "Assay of Thyroid Hormones and Related Substances". Thyroid Disease Manager. Retrieved 5th November 2013.

18.Clarke, N. J., Zhang, Y., & Reitz, R. E. (2012). A Novel Mass SpectrometryBased Assay for the Accurate Measurement of Thyroglobulin From Patient Samples Containing Antithyroglobulin Autoantibodies. Journal of Investigative Medicine, 60(8), 1157-1163.

19.Beckett, G., &MacKenzie, F. (2007). Thyroid guidelines-are thyroid-stimulating hormone assays fit for purpose?. Annals of clinical biochemistry, 44(3), 203-208.

20.Robbins, J. (2000). Thyroid hormone transport proteins and the physiology of hormone binding. Werner &Ingbar's The Thyroid: a fundamental and clinical text. 8th ed. Philadelphia: Lippincott, Williams and Wilkins, 105-120.

21.Bowen, R. A., &Remaley, A. T. (2014). Interferences from blood collection tube components on clinical chemistry assays. Biochemiamedica, 24(1), 31-44.

22.Bowen, R. A., Sattayapiwat, A., Gounden, V., &Remaley, A. T. (2014). Blood collection tube-related alterations in analyte concentrations in quality control material and serum specimens. Clinical biochemistry, 47(3), 150-157.

23.Zhang, D. J., Elswick, R. K., Miller, W. G., & Bailey, J. L. (1998). Effect of serum-clot contact time on clinical chemistry laboratory results. Clinical chemistry, 44(6), 1325-1333.

24.Oddoze, C., Lombard, E., & Portugal, H. (2012). Stability study of 81 analytes in human whole blood, in serum and in plasma. Clinical biochemistry, 45(6), 464-469.

25.immunoassays. Clinical chemistry, 52(5), 892-893.

Original Article

Effect of Telephonic Reminder on Patient's Compliance for Follow up after Laparoscopic Cholecystectomy

Salman Hameed, Saad Ullah, Anam Nadeem, Usman Ismat Butt, Muhammad Umar and Shabbar Hussain Changazi

Objective: To assess whether phone reminders would improve patients compliance in terms of timely follow up, adherence to medical and dietary advise in patients after laparoscopic cholecystectomy.

Methods: This was a cross sectional study which was carried out in Services Hospital Lahore. A total of 100 patients who underwent laparoscopic cholecystectomy were selected and randomly allocated into two groups. Patients in group A were reminded about follow up through a telephone call and patients in group B were not contacted through telephone and turn out the patients was observed in the OPD. Chi square test was applied to compare the groups. P value less than 0.05 was considered as statistically significant. Stratification was done for age, gender and education level.

Results: Mean age of patients was 42.8 years. 64% of patients were females. Out of 50 patients, 30 (60%)adhered to the advice after in group A(after telephonic remainder) while out of 50 patients, 16 (32%)patients remained compliant to the advice in group B (no telephonic remainder). In addition younger patient were more compliant.

Conclusions: It was concluded that telephonic reminder had a statistically significant impact on the adherence of advice of doctor and young patients had a better response to the follow and to medical advice.

Keywords: laparoscopic cholecystectomy, telephonic reminder, follow up.

Introduction

It has been accepted that the ability of patients to follow the treatment plan is an essential component in increasing the efficacy of any treatment.[1] Failure on the part of the patients to follow the advice of the doctors limits the effect of the treatment. A number of studies have been undertaken in previous years to understand and enhance the adherence of the patients.[2,3] Lack of adherence has been documented to result in increased morbidity and mortality.[4,5]

Almost 30-50% patients have been reported to fail to adhere to the medical recommendations.[6-8] This may result in adverse outcome for health of the patient, lead to increased burden on healthcare system and increased expenses.[9] Adherence can be understood to the extent to which behaviors such as lifestyle modifications or diets concur with medical advice. There are often barriers to adherence that may include concerns about efficacy, fear of side effects, inconvenience, a poor doctor-patient relationship, and lack of social support, patient motivation, or incorrect education regarding proper use.[10,11] The relationship between these factors is complex and confusing.[12-14] The extent of relationship between adherence and treatment outcomes has not been yet fully explained. However, it is believed that non-adherence will lead to adverse outcome for all involved. Various studies have been done to evaluate the relationship between patient behavior and factors influencing adherence.[12-14]

The rationale of this study was to examine the impact of telephonic reminder on patients compliance in terms of timely follow up, adherence to medical and dietary advice after laparoscopic cholecystectomy.

Methods

This was a descriptive cross sectional study which was carried out at Surgical Unit 2, Services Hospital, Lahore after ethical approval from the hospital ethical committee. A total of 100 patients who were underwent laparoscopic cholecystectomy were recruited in the study. The patients were divided randomly into two groups A and B. At the time of discharge, both groups were provided with written instructions regarding medication and diet and were called for follow-up after one week (follow up at 1 week gave us good opportunity to examine the wound for infection and also most medications given after laparoscopic cholecystectomy had time period of one week). In addition, the patients of group A were also alerted with a telephonic reminder 48 hours before their planned OPD follow-up. Patients were

called once, reminded about their appointment, and counselled about their medication and diet. However, patients of group B were not reminded telephonically. Adherence/compliance (outcome) was measured by calculating the number of patients who presented to the OPDon due date, with documentation of their operation and medication and compliance to the medical and dietary advice given at discharge. Patients lacking in any of these component were termed as non-adherent. Chi square test was applied to compare the groups. P value less than 0.05 was considered as statistically significant. Stratification was done for age, gender and education level.

Results

A total of 100 patients were included in the study with 50 patients in each group. Mean age of patients was 42.8 years. In the study out of 100 patients, 64 (64%) were females. 30 out of 50 patients in group A adhered to the advice while 16 out of 50 patients in group B stick to the advice. This result was statistically significant. After stratification, age had positive correlation with adherence while education and gender had no statistically significant influence on adherence.

Table-1: Comparison between group A and group B for adherence to advice

Group	Adhered advice	Non-adherance	P-value
A- Telephonic reminder	30	20	0.047
B- No reminder	16	34	

Table-2: Stratification for gender, education and age.

	Addered to advice	Non-adhereance	P-value
Effect of Gender			
Male	26	38	0.309
Female	20	16	
Effect of education			
Below Matric level	30	139	0.352
Matric level and above	12	22	
Effect of Age (years)			
18-30	36	04	0.000
30 and above	12	01	

Discussion

Laparoscopic cholecystectomy is a commonly performed operation for gall bladder stones. Gall bladder stone is a disease which is strongly influenced by diet and sedentary lifestyle. Post-operative patients are often advised to have fat reduced diets. In the present study, younger patients were more compliant as compared to older patients. In patients with age below 30 years, 36 patients were adherent to follow up and advice while 8patients were non- adherent to advice. In age group above 30 years of age, 12 patient were adherent to advice and follow up whereas 44 patients were non-compliant. This comparison was statistically significant. These results were in contrast with the study carried out by Becker MH et al.[15] which showed that middle age patients had better compliance. Furthermore, other studies revealed that patients were more compliant in older ages especially above 60 years.[16,17]

In this study male patients seemed to be more adherent to follow up and advice as compared to females but the comparison was not statistically significant. Chen SL at al. [18] in their study showed that male patients were more adherent to therapy as compared to female patients. However, other researchers illustrated that female patients were more compliant. [17, 19] In the current study patients with education level below matriculation had greater compliant rate than patient with education above matriculation but the results were not statistically significant. In patients with education below matric 36 patients were compliant while 8 patients were non-compliant. In patients above matriculation 12 patients were adherent while 24 patients were non-adherent. These results were in concordance with study conducted byHLMBrus et al.[20] In contrary, another study showed that higher education level had improved compliance rate.[21] In the current study out of the 25 patients in Group A 60%(30) patients were adherent to follow up and medical advice where as in group B only 32%(16) patients remained adherence to follow up and to advice. This comparison was statistically significant. Similar results were also reported by other researchers.[14, 22, 23] The sample size was one of the major limitation of this study. A larger study is required to confirm the findings detected by our initial study and further elaborate the factors responsible. Furthermore, a proper system should be introduced as timely follow-up of the patients. In addition it would follow that proper patient education can lead to decreased disease burden. However, the manpower and financial support required to set up such system will need a careful thought.

Conclusion

It was concluded that telephonic reminders had a significant impact on the adherence of the patients to the advice and young patients were more adherent to the advice of doctors.

Department of Surgery
SIMS/Services Hospital, Lahore

References

1. DiMatteo MR. Enhancing patient adherence to medical recommendations. JAMA.1994; 271(1):7983.
2. Korsch BM, GozziEK, Francis V. Gaps in doctor-patient communication. 1: Doctor-patient interaction and patient satisfaction. Pediatrics. 1968;42(5):855871.
3. Davis MS. Variations in patients' compliance with doctors' advice: An empirical analysis of patterns of communication. Am J Public Health Nations Health.1968; 58(2):274288.
4. Epstein LH, Cluss PA. A behavioral medicine perspective on adherence to long-term medical regimens. J Consult Clin Psychol. 1982; 50(6):950971.
5. Vermeire E, Hearnshaw H, Van Royen P, Denekens J. Patient adherence to treatment: three decades of research. A comprehensive review. JClin Pharm Ther. 2001; 26(5):331342.
6. Sackett DL, Snow JC. The magnitude of compliance and noncompliance. In: Haynes RB, Taylor DW, Sackett DL, editors. Compliance in Health Care. Baltimore: The John Hopkins University Press; 1979:1122.
7. Lassen LC. Patient compliance in general practice. Scand J Prim Health Care.1989; 7(3):179180.
8. Griffith S. A review of the factors associated with patient compliance and the taking of prescribed medicines. Br J Gen Pract. 1990; 40(332):114116.
9. Urquhart J. Patient non-compliance with drug regimens: measurement, clinical correlates, economic impact. Eur Heart J. 1996; 17 (Suppl A):815.
10. DiMatteo MR, Hays RD, Gritz ER, et al. Patient adherence to cancer control regimens: Scale development and initial validation. Psychol Assessment. 1993;5:102112.
11. DiMatteo MR, Lepper HS, Croghan TW. Depression is a risk factor for noncompliance with medical treatment: meta-analysis of the effects of anxiety and depression on patient adherence. Arch Intern Med. 2000;160(14):21012107.
12. Haynes RB, Montague P, Oliver T, McKibbon KA, Brouwers MC, Kanani R. Interventions for helping patients to follow prescriptions for medications. Cochrane Database Syst Rev. 2000;2:CD000011.
13. Steiner A, Vetter W. Patient compliance/noncompliance, determining factors, physician-patient interaction. Schweiz Rundsch Med Prax. 1994;83 (33):889894.
14. Marinker M. From compliance to concordance: achieving shared goals in medicine taking. BMJ. 1997:314:747748.
15. Becker MH, Maiman LA. Sociobehavioural determinants of compliance with health and medical care recommendations. Med Care 1975; 13: 10-24.
16. Hadji P, Jacob L, Kostev K. Gender-and age-related treatment compliance in patients with osteoporosis in Germany. Patient preference and adherence. 2016;10:2379.
17. Farah Habib, Anisa M D. Effect of Age and Socio-Economic Status on Compliance among Type 2 Diabetic Patients. Curre Res Diabetes &Obes J. 2018; 7(3): 5 5 5 7 1 4 . DOI: 10.19080/CRDOJ.2018.07.55571.
18. Chen SL, Lee WL, Liang T, Liao IC. Factors associated with gender differences in medication adherence: a longitudinal study. Journal of advanced nursing. 2014 Sep;70(9):2031-40.
19. Manteuffel M, Williams S, Chen W, Verbrugge RR, Pittman DG, Steinkellner A. Influence of patient sex and gender on medication use, adherence, and prescribing alignment with guidelines. Journal of women's health. 2014 Feb 1;23(2):112-9.
20. Brus HL, Van De Laar MA, Taal E, RaskerJJ, Wiegman O. Effects of patient education on compliance with basic treatment regimens and health in recent onset active rheumatoid arthritis. Annals of the rheumatic diseases. 1998 Mar 1;57(3):146-51.
21. Hill J, Bird H, Johnson S. Effect of patient education on adherence to drug treatment for rheumatoid arthritis: a randomised controlled trial. Annals of the rheumatic diseases. 2001 Sep 1;60(9):869-75.
22. Sarah D FenertySD , West C , Davis SA , Kaplan SG , Feldman SR. The effect of reminder systems on patients' adherence to treatment. Dove Press Journal, Feb, 2012 ,127-36.
23. Park H, Adeyemi A, Roane T. Impact of a telephonic outreach program on medication adherence in Medicare Advantage Prescription Drug (MAPD) plan beneficiaries. Value in Health. 2015 Nov 1;18(7):A611.

Original Article

Types of Fractures Depending on Skin Involvement and Their Associations Among Tibial Nonunion Patients

Syed Asif Ali, Usman Zafar Dar, Muhammad Ali, Salma Batool, Farrukh Siddique and Faridoon Siddique

Objective: To determine the different types of skin lesion in tibial nonunion patients and associations of type of fracture (in term of open versus closed) with various predictors or cofactors, at Mayo hospital, Lahore, Pakistan.

Methods: It was retrospective analysis conducted in the Department of Orthopedics, Mayo hospital, Lahore on the data of the tibial nonunion patients of all age groups who followed from July 2002 to June 2012. Fractures were typed into open and closed depending on skin involvement. Statistical analysis was done using SPSS version 25. Independent sample T test, chi-square test of independence, and binary logistic regression were performed to ascertain the likelihood relation of open/closed fractures with different associated cofactors.

Results: Out of total of 144 patients, 79.2% had open tibial fractures while 20.8% had closed tibial fractures. Amongst open fractures, 26.3% were Gustilo type I, 31.6%) Gustilo type II, 18.4% Gustilo type IIIA, 21.1% Gustilo type IIIB, and 2.6% were Gustilo type IIIC. The mean age of the patients with open fractures was 15.11 years higher than that of patients with closed fractures ($p<0.01$). Bivariate analysis suggested that type of fracture had statistically significant association with side of lesion ($p=0.016$), anatomic location of tibial lesion ($p<0.01$), comorbid systemic diseases ($p=0.012$), and complications of external fixator ($p<0.01$). Binary logistic regression found that as compared to closed fractures, open fractures were involving 2.673 times more right side, 8.583 times more at proximal/middle location, 12 times less among patients suffering comorbid systemic diseases, 10.669 times more associated with complications of external fixator, and 11.28 times more complicated with leg length discrepancy.

Conclusions: Majority tibial nonunions were open fractures, especially Gustilo type III. Closed fractures were seen relatively among younger population. As compared to closed tibial fractures, open tibial fractures occurred significantly more in right tibia and at proximal / middle shaft location. Closed tibial fractures occurred significantly in patients with comorbid systemic diseases while open tibial fractures were more associated with subsequent complications of external fixator as well as leg length discrepancy.

Keywords: tibial nonunions, skin lesion, types, associations, SPSS.

Introduction

Tibial fractures are the most common long bone fracture and frequently involve the fibula too.[1] The incidence is the highest in young men, which is 8 per 100000 persons.[2] The most common causes are road traffic accidents and sports injuries.[3] Fracture nonunion is a common complication of tibial fracture.[4] It is defined as a fracture that has not united without additional intervention within 6-9 months.[5] Skin lesions occur frequently along fracture of tibia because of its subcutaneous location.[6] Their presence differentiates open tibial fracture[7] from closed tibial fracture.[8] The Gustilo-Anderson classification[9] categorizes the severity of open fracture into 5 types which are I, II, IIIA, IIIB, and IIIC. The classification is most precisely applied after debridement of the wound.[10] The higher the classification type number, the greater the chance of infection, need for bone graft, chance of nonunion, and chance of amputation.[11,12] The objective of our study is to determine the different types of skin lesion in tibial nonunion patients and associations of type of fracture (in term of open versus closed) with various predictors or cofactors, at Mayo hospital, Lahore, Pakistan.

Methods

This retrospective analysis was conducted in the Department of Orthopedics, Mayo hospital, Lahore on the data of the patients from July 2002 to June 2012. All the patients suffering non-union tibia of all age groups were included in this study. They were further managed using NA external fixators. The fractures were noted as open and closed fractures depending on involvement of overlying skin.[7,8] Open fractures were further categorized using Gustilo-

Anderson Classification[9] in which <1cm wound and 1-10cm wound defined type I & type II respectively. >10 cm wound with coverage available and requiring soft-tissue coverage procedure defined type IIIA and type IIIB respectively. Wound with vascular injury requiring repair defined type IIIC. Gender of the patients, side of the fracture, anatomic location of tibial lesion, comorbid diseases, healing of nonunion, leg length discrepancy, and complications of external fixator were also noted. Diabetes mellitus, ischemic heart disease, chronic pulmonary disease, chronic liver disease, and chronic renal disease were comorbid systemic diseases. Statistical analysis was completed using the Statistical Package for Social Science (SPSS), version 25. Age of the patients was only the quantitative variable, while type of fracture, gender, side of the fracture, anatomic location of tibial lesion, comorbid diseases, healing of nonunion, leg length discrepancy, and complications of external fixator were the qualitative variables. Frequencies and percentages were computed for qualitative variables, while mean and standard deviation were calculated for quantitative variables. Independent sample T test was used to compare the mean age of patients in two outcome groups (open fracture/closed fracture). Bivariate analysis was performed to find the associations with type of fracture using the chi-square test of independence.[14] All p-values were two sided and considered as statistically significant if < 0.05. The binary logistic regression was also performed to ascertain the likelihood relation of open/closed fracture with different associated cofactors. Odds ratios[15] with 95% confidence interval for various predictors or cofactors of type of fracture were also calculated.

Results

Out of total of 144 tibial non-union patients, 30 (20.8%) had closed tibial fractures and 112 (79.2%) had open tibial fractures (Picture 1). Amongst open fractures, 30 (26.3%) were Gustilo type I, 36 (31.6%) Gustilo type II, 21 (18.4%) Gustilo type IIIA, 24 (21.1%) Gustilo type IIIB, and 3 (2.6%) were Gustilo type IIIC (Picture 2). The mean age of nonunion patients with closed fracture was 23.10 ± 20.10 years and the mean age of nonunion patients with open fracture was 38.21 ± 15.91 years. The mean age of the patients with open fractures was 15.11 years higher than that of patients with closed fractures, and the difference was statistically significant ($p<0.01$) **(Table-1).** Bivariate analysis suggested that type of fracture had statistically significant association with side of lesion i.e. right or left ($p = 0.016$), anatomic location of tibial lesion ($p<0.01$), comorbid systemic diseases ($p=0.012$), and complications of external fixator ($p<0.01$). On the other hand, there was statistically insignificant association of type of fracture with gender ($p=0.212$), healing of nonunion ($p=0.714$), and occurrence of leg length discrepancy ($p = 0.412$) **(Table-2).**

A logistic regression was performed to ascertain the likelihood correlation of type of fracture with gender, age, side of the fracture, anatomic location of tibial lesion, comorbid diseases, healing of nonunion, leg length discrepancy, and complications of external fixator. The logistic regression model was statistically significant, $p<0.05$. The model explained 53.8% (Nagelkerke R^2) of the variance in groups of patients with open/ closed fractures and correctly classified 89.6% of cases. Amongst tibial nonunion patients,

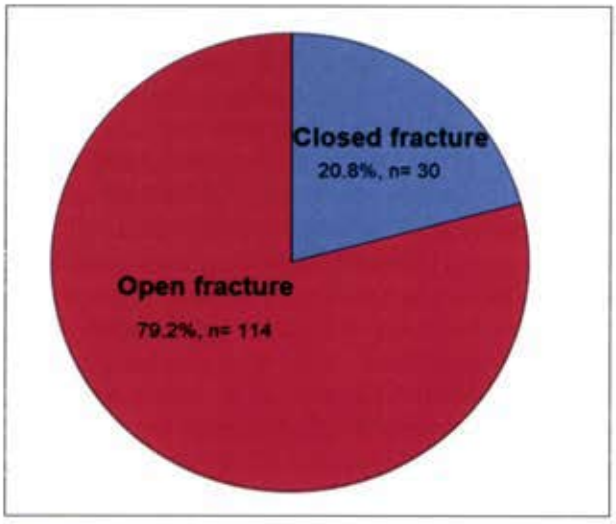


Fig-1: Distribution of tibial nonunion patients in term of skin lesion (n=144)

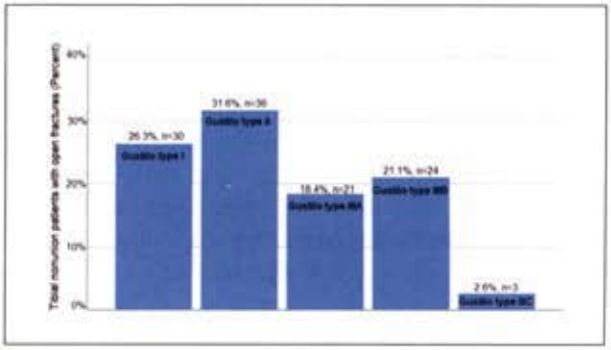


Fig-2: Distribution of open fractures according to Gustilo-Anderson classication amongst tibial nonunion patients (n=144)

open fractures involved right side 2.673 times more as compared to closed fractures, however correlation found significant during chi-square test, was actually insignificant (p=0.126) on regression analysis. Open fractures were significantly 8.583 times more at proximal/middle location as compared to closed fractures. In comparison to open fracture, closed fractures were 12 times more common among patients suffering comorbid systemic diseases. Open fracture had 10.669 times more complications of external fixator than closed fractures in our nonunion patients. Similarly, leg length discrepancy was 11.28 times more among open fracture patients as compared to closed fracture patients **(Table 3).**

Table-1: Comparison of mean age of patients suffering tibial nonunion with type of fracture (Open/Closed) (n = 144) *

Type of fractur	Mean age (years)	Standard deviation	Mean difference	P-Value	95% confidence interval
Open	38.21	15.91	15.11	<0.01	8.275 - 21.947
Closed	23.10	20.10			

**Independent sample T-test was used*

Table-2: Statistical correlation between type of fracture in term of skin lesion and multiple. Predictors/ factors in tibial nonunion patients (n = 144) *

Predictors/Fractures		Type of fracture			P-value
		Open Fracture	Closed Fracture	Total	
Gender :	Male	102 (89.5%)	24 (80%)	126 (87.5%)	0.212
	Female	12 (10.5%)	6 (20%)	18 (12.5%)	
Side of lesion:	Right	84 (73.7%)	15 (50%)	99 (68.8%)	0.016
	Left	30 (26.3%)	15 (50%)	45 (31.2%)	
Anatomic location of tibial lesion:	Proximal/middle	108 (94.7%)	21 (70%)	129 (89.6%)	<0.01
	Distal	6 (5.3%)	9 (30%)	15 (104%)	
Co-morbid systemic disease:	Yes	39 (34.2%)	18 (60%)	57 (89.6%)	0.012
	No	75 (65.8%)	12 (40%)	87 (60.4%)x	
Healing of tibial nonunions:	Achieved	105 (92.2%)	27 (90%)	132 (91.7%)	0.714
	Not-achived	9 (7.9%)	3 (10%)	12 (8.3%)	
Leg length discrepancy:	Yes	57 (50%)	12 (40%)	69 (47.9%)	0.412
	No	57 (50%)	18 (60%)	75 (52.1%)	
Complication of external fixator:	Yes	78 (68.4%)	9 (30%)	87 (60.4%)	0.01
	No	36 (31.6%)	21 (70%)	57 (39.6%)	

**Chi-square test for independence was used*

Table-3: Binary Logistic Regression Output with Co-efficient, Odds Ratio and their 95% CI.

Risk Factors	B	S.E.	Wald-statistic	P-value	Odds Ratio	95% C.I. For EXP (B) Lower	Upper
Age	-0.063	0.020	10.233	<0.01	10.939	0.903	0.976
Gender (Male/Female)	-0.407	0.892	0.209	0.648	0.665	0.116	3.822
Side of lesion (Left/Right)	0.983	0.642	2.345	0.126	2.673	0.760	9.405
Anatomic location of tibial lesion (Proximal plus middle/distal)	2.150	0.950	5.117	0.024	8.583	1.333	55.287
Comorbid systemic disease (Yes/No)	-2.428	0.771	9.922	<0.01	0.088	0.019	0.400
Healing of tibial nonunion (Achieved /Not achieved)	-0.168	1.286	0.017	10.896	.846	0.068	10.524
Leg lenth discrepancy (Yes/No)	2.423	0.755	10.288	<0.01	11.280	2.566	49.583
Complications of external fixator (Yes/No)	2.367	0.676	12.273	<0.01	10.669	2.837	40.119
Constant	-1.106	1.090	1.029	0.310	0.331		

Discussion

In a large study of 523 tibial fractures from Scotland,[16] 76.5% (n=400) were closed fractures while 23.5% (n=123) were open fractures. While in our study of tibial nonunion patients, more were open fractures (79.2%).

This is because of facts that open fractures creates higher incidence of nonunions.[4,6] Hence, among tibial nonunions, more percentages will be of open fractures. In our study, among open fractures, majority were Gustilo type-III (42.1%). Out of the type-III fractures, 50% were type-IIIB. Similarly, Court-Brown et al[16] found in their study that 59.8% were Gustilo type-III, of which 60.3% were type-IIIB. Alex De Lima Santos et al[17] found that among open fractures, all were Gustilo type-III, out of which 82% were type IIIA, 11% type IIIB, and 7% type IIIC.

Hence, our findings were in concordance with available data[16,17] which was suggestive of higher incidence of Gustilo type-III among open tibial fractures. This can be explained by facts that road traffic accident and sport-related injuries, being major etiologies, often involve high energy mechanisms resulting severe form of skin lesions in addition to tibial fractures.[18]

Secondly, type III skin lesions are more prone to nonunions[19] resulting this type in more proportion in our data. In our study, mean age of the nonunion patients with closed tibial fractures was less than that of patients with open tibial factures (23.10 ± 20.10 vs 38.21 ± 15.91 years). Similarly, in Court-Brown study,[16] average age of the patients with closed tibial fractures was less than that of patients with open factures (35.6 years vs 42.4 years).

In a 358 patients' study, Harm Hoekstra[20] compared gender with type of fracture. 64.7% open fracture and 57.5% closed fractures occurred in male. The association between gender and type of fracture was statistically insignificant (p=0.07). Similarly, the association was statistically insignificant in our study (p=0.212). In 2007, Farmanullah et al[21] found that right tibia was involved more than left tibia in tibial nonunion patients (55.17% vs 44.83%).

Our research work elaborated further and found that in tibial nonunion patients, right tibia had significantly more open fractures than closed fractures in comparison to left tibia (p=0.016). No such correlation was performed ever before.

In 2013, Antonova et al[4] found that patients with nonunion had more comorbidities (30 vs 21) than those without nonunion. Our study found that comorbid diseases were significantly more in group of nonunion patients with closed tibial fractures than those with open tibial fractures.

This can be elaborated by facts that open tibial fractures are common in young healthy athletes and travelers due to high energy impact. In patients with comorbid diseases as well as multiple problems like low bone mass and osteoporosis, low energy impact results tibial fractures usually closed one.

In our study, nonunion patients with open fracture developed significantly more complications of external fixator than those with closed fractures (p=0.000). Similarly, in tibial fractures managed with internal fixation, Prakash Doshi[22] found that incidence of infection was much more in open fractures than closed fractures (8% vs 1.6%).

Baldwin et al found that Gustilo type III fractures had a 3.5-fold and a 2.3-fold higher infection risk than types I and II, respectively.[12] In addition to all above findings, our data was also suggestive that open fractures were significantly more at proximal / middle shaft location than close fractures.

Type of fracture has no statistical association with healing of nonunion and leg length discrepancy. However vast studies with larger sample size are required to elaborate these findings.

Conclusion

Majority tibial nonunions were open fractures, especially Gustilo type III. Closed fractures were seen relatively among younger population. As compared to closed tibial fractures, open tibial fractures occurred significantly more in right tibia and at proximal/ middle shaft location.

Closed tibial fractures occurred significantly in patients with comorbid systemic diseases while open tibial fractures were more associated with subsequent complications of external fixator as well as leg length discrepancy.

Department of Orthopaedic Surgery
SIMS/Services Hospital, Lahore
www.esculapio.pk

References

1. Al-Hadithy N and Panagiotidou A. The management of open tibial shaft fractures. BMJ 2012; 345 (6348): 1 6.
2. Singer BR, McLaughlan GJ, Robinson CM, Christie J. Epidemiology of fractures in 15 000 adults. The influence of age and gender. J Bone Joint Surg Br 1998;80-B:243-8.
3. Court-Brown CM, Rimmer S, Prakash U, McQueen MM. The epidemiology of open long bone fractures. Injury 1998; 29: 529-34.
4. Antonova E, Kim Le T, Burge R, Mershon J. Tibia Shaft fracture - costly burden of nonunions. BMC Musculoskelet Disord. 2013; 14: 42.
5. Wiss DA, Stetson WB. Tibial Nonunion: Treatment Alternatives. J Am Acad Orthop Surg. 1996; 4(5): 249257.
6. Johnson B and Christie j. Open Tibial Shaft Fractures: A Review of the Literature. The Internet J Orthopedic Surgery 2007; 9 (1): 1-5.
7. Gougoulias N, Khanna A, Maffulli N. Open tibial fractures in the paediatric population: a systematic review of the literature. Br Med Bull. 2009. 91:75-85.
8. Courtney PM, Bernstein J, and Ahn J. In Brief: Closed Tibial Shaft Fractures. Clin Orthop Relat Res 2011; 469(12): 35183521.
9. Gustilo RB, Anderson JT. Prevention of infection in the treatment of one thousand and twenty-five open fractures of long bones: retrospective and prospective. J Bone Joint Surg Am 1976; 58: 453-8.
10. Gustilo RB. Interobserver agreement in the classification of open fractures of the tibia. The results of a survey of two hundred and forty-five orthopaedic surgeons. J Bone Joint Surg Am 1995; 77: 1291-2
11. Gustilo RB, Mendoza RM, Williams DN. Problems in the management of type III (severe) open fractures: a new classification of type III open fractures. J Trauma 1984; 24: 742-6.
12. Baldwin KD, Babatunde OM, Russell Huffman G, Hosalkar HS. Open fractures of the tibia in the pediatric population: a systematic review. J Child Orthop. 2009 Jun. 3(3):199-208.
13. Sedgwick P. Retrospective cohort studies: advantages and disadvantages. BMJ 2014; 348: 1072.
14. McHugh ML. The Chi-square test of independence. Biochem Med (Zagreb) 2013; 23(2): 143149.
15. Szumilas M. Explaining Odds Ratios. J Can Acad Child Adolesc Psychiatry 2010; 19(3): 227229.
16. Court-Brown CM, McBirnie J. The epidemiology of tibial fractures. J Bone Joint Surg Br. 1995; 77(3): 417-21.
17. Santos AL, Nitta CT, Boni G, Sanchez GT, Tamaoki MJS, Reis FBD. Evaluation and comparison of open and closed tibia shaft fractures in a quaternary reference center. Acta Ortop Bras 2018; 26(3): 194-197.
18. Courtney PM, Bernstein J, and Ahn J. In Brief: Closed Tibial Shaft Fractures. Clin Orthop Relat Res 2011; 469(12): 35183521.
19. Thakore RV, Francois EL, Nwosu SK, Attum B, Whiting PS, Siuta MA et al. The Gustilo-Anderson classification system as predictor of nonunion and infection in open tibia fractures. Eur J Trauma Emerg Surg 2017; 43(5): 651-656.
20. Hoekstra H, Smeets B, Metsemakers WJ, Spitz AC, and Nijs S. Economics of open tibial fractures: the pivotal role of length-of-stay and infection. Health Econ Rev. 2017; 7: 32.
21. Farmanullah, Khan MS, and Awais SM. Evaluation of management of tibial non-union defect with Ilizarov fixator. J Ayub Med Coll Abbottabad 2007; 19(3): 34-36.
22. Doshi P, Gopalan H, Sprague S, Pradhan C, Kulkarni S, and Bhandari M. Incidence of infection following internal fixation of open and closed tibia fractures in India (INFINITI): a multi-center observational cohort study. BMC Musculoskelet Disord. 2017; 18: 156.

Original Article

Education Status as a Determinant of Adherence to Treatment in HIV/AIDS Patients

Memoona Irshad, Sobia Qazi and Hassan Ali

Objective: To evaluate education status as a determinant of treatment adherence in HIV/AIDS patients.

Methods: This descriptive cross-sectional survey was conducted at Special/HIV clinic of Medical Unit IV, Services Hospital Lahore over six months from 01-06-2017 to 31-12-2017, using non-probability consecutive sampling. A total of 140 patients fulfilling the inclusion criteria were enrolled. Informed consent was obtained; demographic data and disease characteristics were recorded. Education status and adherence was assessed. SPSS version 20.0 for windows was used to analyse data and to evaluate treatment adherence.

Results: Among the 140 patients, 94(67.1%) were males and 46(42.9%) were females. Patients who completed their college education were 22(15.7%) while 37 (26.4%) were illiterate, 43 (30.7%) and 38 (27.1%) completed their primary and secondary education. The overall adherence of patients with HIV/AIDS showed that 131 (93.6%) were adherent. Data was stratified with respect to gender, age, disease duration and level of education, Chi-square (x2) test in each stratifications demonstrated absence of statistical significance (p>0.05).

Conclusions: Among these 140 patients, 131(93.6%) were adherent and only 9(6.4%) were non adherent despite the education status however there is improvement of adherence with high education Therefore key to providing best medical facility to HIV patients lies in proper guidance, counseling and to a minor extent on education status of patients.

Keywords: education status, HIV, adherence.

Introduction

The human immunodeficiency virus (HIV) and acquired immune deficiency syndrome (AIDS) have become one of the major health problems in many countries in the world. According to UNAIDS 2011, the disease is widely spread in low- and middle-income developing countries, such as South Africa, Botswana and other sub-Saharan African countries. However, the introduction of antiretroviral therapy (ART) brought dramatic changes to the lives of people.[1] The number of infected people with HIV has been estimated at around 5.63 million of a population of 46 million.[1,2] HIV/AIDS related stigma is invoked as a persistent and pernicious problem in any discussion about effective responses to the epidemic. In addition to devastating the familial, social, and economic lives of individuals, HIV positive stigma is cited as a major barrier to accessing prevention, care, and treatment services.[3-5] Despite a fair amount of progress on understanding HIV epidemiology globally, the Middle East and North Africa region is the only region where knowledge of the epidemic continues to be very limited, and subject to much controversy.[6] Substantial changes are needed to achieve a more targeted and strategic approach to investment in the response to the HIV/AIDS epidemic that will yield long-term dividends.[7] Adherence to antiretroviral medications is a primary determinant of both the effectiveness of treatment and the clinical course of HIV/AIDS.[8] Non-adherence with therapy is a significant problem, particularly when the disease process is chronic and therapeutic regimens are employed for prolonged periods. The study assessed the prevalence and variables associated with adherence with antiretroviral therapy in patients with human immunodeficiency virus infection.[9]

Knowledge and attitudes regarding HIV/AIDS and antiretroviral therapy among patients at a Nigerian treatment clinic shows the majority of respondents had good knowledge of and a positive attitude toward HIV/AIDS and ART adherence. Most (77.7%) respondents had good knowledge of HIV/AIDS while 75.2% had good knowledge of ART. Respondents with good knowledge about HIV/AIDS and a positive attitude about the disease tend to be more adherent to ART.[15]

The study conducted in Addis Ababa, Ethiopia indicate that stigma and discrimination, and poor relationship with health care provider to be associated with low adherence. Based on the finding,

keep away from stigmatization and discrimination, and enhancing good relationship need to be given attention for improving ART adherence.[16] In another study it is shown that ART adherence in resource-limited settings, where treatment is generally provided free of charge, may be contingent upon structural barriers, such as food insecurity[7,12] or geographic isolation and lack of resources to pay for transportation to clinic.[13,17]

In Pakistan, unfortunately, the education system has been described as one of the most underdeveloped in the world. Hardly 60% of children complete grades 1 to 5 at primary school.[18] The situation is even worse in rural areas due to limited resources and lack of awareness. Education results in improvement of living standards, enhances the quality of life and can provide essential opportunities for all. However in Pakistan, access to schools and colleges remains a major problem. This study however, helps us in determining the education level in patients of HIV and the whether the adherence of patient is affected by it or not. This study will also help in determining one of the many factors related to adherence and directing the resources and efforts for the betterment of the patients. This study has never been done in Pakistan and data is therefore limited from local surveys.

Methods

This cross-sectional, observational study was conducted in Special/HIV clinic of Medical Unit IV Services Hospital Lahore over six months from 01-06-2017 to 31-12-2017. Sample size of 140 with 7% margin of error and 95% confidence level calculated with WHO software sample determination and taking expected percentage of adherence i.e. 77.7 % in HIV/AIDS patients using Non-Probability Consecutive Sampling was calculated. The study was conducted on 140 patients between the ages of 18-60 years without gender discrimination on HAART/Highly Active Anti-Retroviral Therapy already registered in the HIV "Special Clinic" in Medical Unit IV Services Hospital having documented disease for six months or more informed consent was taken. Demographic details of each patient were noted. Evaluation of treatment adherence was assessed by medication dosage taken by the patient and trends in CD4 count and viral load results depending on the education status. All the data were collected in a specially designed performa (attached).

Data was entered and analyzed using SPSS v20.0. Quantitative variables like age, and duration of HIV/AIDS were expressed by using mean± SD. Qualitative variables like gender, stage of HIV/AIDS, trend of CD4 count and viral loads, adherence and education status were expressed using frequencies and percentages. Data was stratified for the age, gender and stage of HIV/AIDS to deal with effect modifiers. Post stratification Chi-Square test was applied by taking p-value ≤ 0.05 as significant.

Results

Among the 140 patients, 94(67.1%) were males and 46(42.9%) were females. 93.6% patients were adherent and 6.4% were non adherent. **Fig-I** illustrate bar charts showing frequencies according to education levels while in **Fig-II** status of adherence among these patients is shown by pie chart.

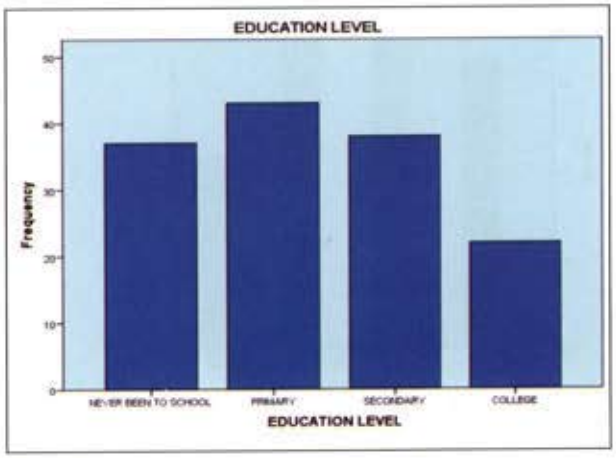


Fig-1: Education level.

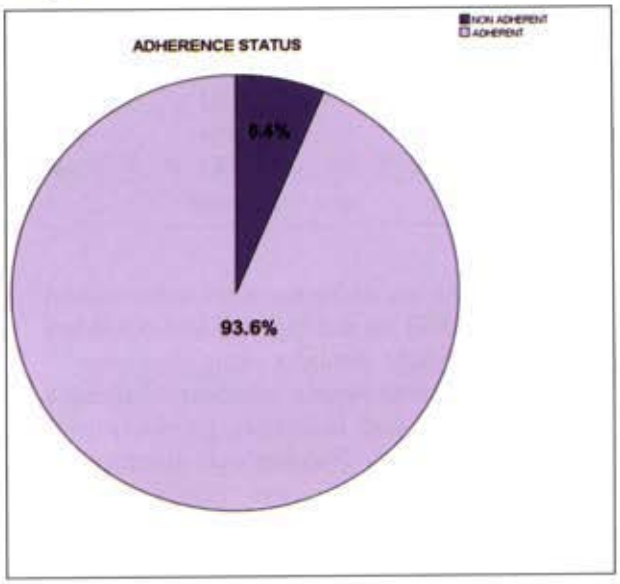


Fig-1I: Adherence status.

Table-2: Stratification of adherence with respect to education status (n=140)

		EDUCATION LEVEL					
		Illiterate	Primary	Secondary	College	Total	P-value
Adherent	Non Adherent	04	04	01	0	09	
	Adherent	33	39	37	22	131	0.241
Total	Non Adherent	37	43	38	22	140	

Adherence status in relation to different education levels is demonstrated in **Fig-III**. **Table-I** demonstrates the education status in patients while **Table-II** shows stratification of adherence with respect to education status, Chi Square test concludes there is no significant effect of adherence on education status ($p>0.05$). Chi Square test failed to show any statistical significance in both stratification groups ($p>0.05$).

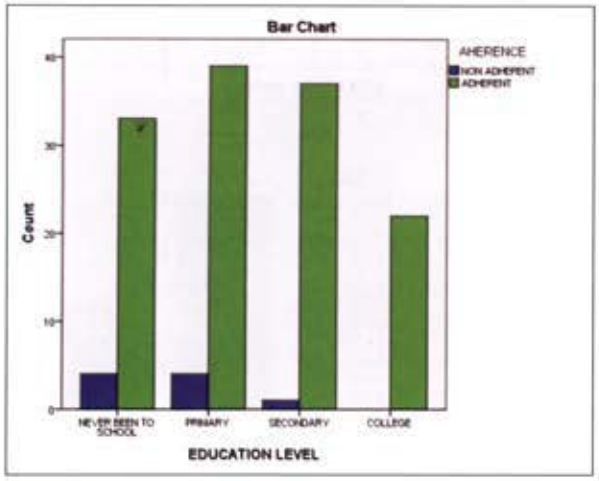


Fig-3: Education Level.

Table-1: Education status in patients (n=140).

	Frequency	Percent	Valid percent	Cumulative percent
Iliterate	37	26.4	26.4	26.4
Primary	43	30.7	30.7	57.1
Secondary	38	27.1	27.1	84.3
College	22	15.7	15.7	100.0
Total	140	100.0	100.0	

Discussion

The shift to the use of highly-active antiretroviral therapy (HAART) for treating HIV and AIDS has led to increasingly complex drug regimens.[10-12] These drug regimens present significant challenges to both patients and healthcare providers with respect to adherence.[11] Patients were stratified on basis of education status into four categories; illiterate, who were never been to school 37(26.4%); primary, who completed 1st five grades of school education 43(30.7%); secondary, completed fifth to tenth grade of school education 38(27.1%) and finally those who completed their college education and above 22(15.7%). Adherence is defined as an extent to which a person's behaviour is involved regarding medication intake, following a diet plan, and lifestyle changes, all of these in coherence with recommendations from a health care provider.

The frequency of non adherent patients in this study was 9 (6.4%) that was significantly lower than reported in study by M.A.Chesney et al. frequency was 17% at ten AATCG sites in USA.[19] The frequency of adherence in this study is significantly high 131(93.6%). We found patients with college education and above are more adherent to treatment than the ones who are illiterate or have not completed their primary and secondary education. We stratified data and calculated significance between adherence and education status, no statistical significance was found using Chi-square test. There is an increasing need for future researchers to study and analyze other factors influencing adherence of patients. We found that patients are adherent to treatment despite low education status however there is still need to educate the masses regarding the importance of adherence in HIV patients. This study has many advantages regarding the adherence of patients if there is failure of adequate adherence, antiretroviral agents would not be capable of suppressing HIV replication because of insufficient concentrations of drugs in the blood and may lead to difficulties suppressing plasma viral load [12, 13]. In addition to being associated with poor short-term viral response; poor adherence to ART accelerates development of drug-resistant HIV. Therefore, identifying and mitigating the factors that reduce adherence to combination antiretroviral agents are important for prolonged viral load suppression.[12,14]

A study published in international journal including 960 journal articles, dissertations and abstracts concluded that HIV related stigma results in poor adherence to treatment.[20] As with any study there are few limitations with this study, it was conducted in a single centre, while a multicenter study can be carried out in coming days to strengthen the data. Our study was done for 6 months period; there is room for longer studies in future.

Conclusion

This study concludes that 93.6 % (n=131) of HIV/AIDS patients were adherent. Education status plays a minor role but it does have an impact on adherence status so improving the education status definitely will improve the adherence. However there is need for identifying other factors affecting the adherence of the patients for better outcome of the disease and its progression.

Department of Medicine Unit-IV
SIMS/Services Hospital, Lahore

www.esculapio.pk

References

1. WHO, UNICEF, USAID. (2011) Progress Report 2011: Global HIV/AIDS response, Geneva.
2. Department of Health. (2009) HIV & AIDS and STI STRATEGIC PLAN FOR SOUTH AFRICA 20072011. Pretoria: Government Press.
3. Bond V, Chase E, Aggelton P. Stigma. (2002). HIV/AIDS prevention, and mother to child transmission in Zambia. Evaluation and Program Planning, 25, 242356.
4. .Chesney M, Smith A. (1999). Critical delays in testing and care: the potential role of stigma. American Behavioral Scientist, 42, 11621174.
5. Kalichman SC, Simbayi L. (2003). HIV testing attitudes, AIDS stigma, and voluntary counseling and testing in a Black township in Cape Town, South Africa. Sexually Transmitted Infections, 79, 442447.
6. Laith J. Abu-Raddad et al. (2010). Characterizing the HIV/AIDS Epidemic in the Middle East and North Africa: Time for Strategic Action.
7. Michel S. (2011, June 18). A strategic revolution in HIV and global health. The Lancet, Volume 377, Issue 9783, 1824.
8. Mark J. Atkinson, and Jeffrey J. Petrozzino. (2009, Nov 20). An Evidence-Based Review of Treatment-Related Determinants of Patients' Nonadherence to HIV Medications. AIDS Patient Care and STDs, Vol.23, No.11 . Available https://doi.org/10.1089/apc.2009.0024
9. N. Singh, C. Squier, C. Sivek , M. Wagener , M. Hong Nguyen & V. L. Yu . (2010, 27 May). Determinants of adherence with antiretroviral therapy in patients with human immunodeficiency virus: Prospective assessment with implications for enhancing adherence, AIDS Care - Psychological and Socio-Medical Aspects of AIDS/HIV, Volume 8,Issue 3, 261-270.
10. Weiser S, Wolfe W, Bangsberg D. (2003, Nov 1). Barriers to antiretroviral adherence for patients living with HIV infection and AIDS in Botswana. JAIDS Journal of Acquired Immune Deficiency Syndromes, Volume 34, Issue 3,281288.
11. Biressa S, Erku Abegaz W, Abebe M, Taye W, Belay M. (2013, Sep 2). Adherence to antiretroviral therapy and associated factors among HIV infected children in Ethiopia: Unannounced home-based pill count versus caregivers' report. BMC Paediatrics. 13:132. Available: http://dx.doi.org/10.1186/1471-2431-13-13 PubMed
12. Phelps BR, Hathcock SJ, Werdenberg J, Schultze GE.(2010,Dec 6). Experiencing antiretroviral adherence: Helping healthcare staff better understand adherence to paediatric antiretrovirals. JIAS Journel of the International AIDS Society,13(48),620638. Available: http://dx.doi.org/10.1186/1758-2652-13-48 PubMed
13. (2010). Department of Health Sou- th African Antiretroviral Guide lines. Pretoria: Government Press
14. (2005). Department of Health Monitoring and evaluation of the operational plan for comprehensive HIV/AIDS care, management and treatment for South Africa. Pretoria: Government Press.
15. Olowookere SA1, Fatiregun AA, Adewole IF. J Infect Dev Ctries, (2012, Nov 26). Knowledge and attitudes regarding HIV/AIDS and antiretroviral therapy among patients at a Nigerian treatment clinic, 6(11),809-16.
16. Mengistu Z1, Chere A. Ethiop Med J, (2012 Oct). Adherence to antiretroviral therapy and its associated factors among people living with HIV/AIDS in Addis Ababa, Ethiopia, 50(4),355-61.
17. Paterson DL, Swindells S, Mohr J, Brester M, Vergis EN, Squier C, Wagener MM, Singh N Ann Intern Med. (2000, Jul 4). Adherence to protease inhibitor therapy and outcomes in patients with HIV infection, 133(1),21-30.
18. n.d. Education System in Pakistan. Available: www.scholaro.com /pro/Countries/Pakistan/Education-System
19. M. A. Chesney et al , (June 2000). Self-reported adherence to antiretroviral medications among participants in HIV clinical trials: The AACTG Adherence Instruments, AIDS Care, Pages 255-266 .
20. Ingrid T Katz, Annemarie E Ryu, Afiachukwu G Onuegbu, Christina Psaros, Sheri D Weiser, David R Bangsberg, and Alexander C Tsai.(2013 Nov 13). Impact of HIV-related stigma on treatment adherence: systematic review and meta-synthesis, J Int AIDS Soc, 16(3Suppl 2).

Original Article

Evaluation of Result after Ahmad Glaucoma Valve Implantation in Refractory Pediatric Glaucoma: A Prospective Study

Amtul Mussawar Sami, Intzar Hussain, Muhammad Hamza Shahid, Abdul Baqi and Saba Tauqeer

Objective: To evaluate the effectiveness and complications profile of Ahmad Glaucoma Valve implantation in refractory pediatric glaucoma.

Methods: This prospective study was conducted in Eye unit 1, Services Hospital / Services Institute of Medical Sciences, Lahore from Dec 2003 to Dec 2006. Total numbers of patients were 08, between 2-6 years. Ahmad glaucoma valve was implanted in 14 eyes, bilateral cases were 12 while unilateral were 02.Inclusion criteria for Ahmad valve implantation were diameter of cornea which should be 14mm or more, IOP was more than 30mmHg in spite of full anti-glaucoma treatment and previous failed unsuccessful filtration procedures. All the children were completely evaluated in outpatient department of Services Hospital, Lahore. Qualified success was defined as IOP < 21mmHg regardless of the number of glaucoma medications. Complete success was defined as IOP < 21 mmHg without any glaucoma medication.

Results: Qualified success was noted in 7.14 % of cases while complete success was obtained in 71.43% of cases.

Conclusions: Despite of the small number of cases in this study, Ahmad Glaucoma Valve seems to be effective in primary congenital glaucoma. Success rate decline over time, considering the need for further alternative medication and surgical procedure.

Keywords: paediatric glaucoma. ahmad glaucoma valve. glaucoma drainage devices. Intra ocular pressure.

Introduction

Pediatric glaucoma is a potentially blinding disease, accounting for about 18% of blindness in blind institutions and 5% of overall pediatric blindness worldwide.[1, 2] It has heterogeneous etiologies characterized by elevated intraocular pressure (IOP). It is defined as primary when an isolated, idiopathic developmental anomaly of the anterior chamber angle exists, and secondary when aqueous outflow is impaired due to preexisting ocular or systemic disease.[3,4] In a recent study in the United States, the incidence of childhood glaucoma was 2.29 per 100,000 (or 1 per 43,575) residents younger than 20 years of age. Acquired (traumatic or surgical, drug-induced and uveitic) and secondary (e.g. SturgeWeber syndrome) forms of glaucoma were the most common, whereas congenital and juvenile glaucoma were rare.[5] Primary congenital glaucoma (PCG) is the most common type of glaucoma in infancy. The incidence of PCG in Western countries has been estimated at 1 per 10,000 to 1 per 30,200 populations.[6] As the disease has an autosomal-recessive pattern of transmission, it is reported to occur more frequently in certain ethnic and religious groups where consanguineous marriage is common.[7] The highest reported prevalence has been among individuals of Saudi Arabian racial descent.[8] Ahmed introduced the Ahmed glaucoma valve in 1993, which was pressure sensitive, unidirectional valve was designed to open when intra-ocular pressure is 8mmHg.This is highly effective in reducing the risk of early post operative hypotony compared to other drainage devices. Many studies of Ahmad valve implantation used in refractory paediatrics glaucoma show comparable results to Ahmad valve implantation in adults and implantation of other drainage devices.

The aim of this study was to evaluate the efficacy and complications of Ahmad glaucoma valve implantation in paediatric refractory glaucoma.

Methods

This prospective study was conducted in Eye unit 1, Services Hospital / Services Institute of Medical Sciences, Lahore from Dec 2003 to Dec 2009. Total numbers of patients were 08, between 2-6 years. Ahmad glaucoma valve was implanted in 14 eyes, bilateral cases were 12 while unilateral were 02. Inclusion criteria for valve implantation were

diameter of cornea which should be 14mm or more. IOP was more than 30mmHg inspite of full anti-glaucoma treatment and previous failed unsuccessful filtration procedures. All the children were completely evaluated in outpatient department of Services Hospital, Lahore including comprehensive prenatal, natal and postnatal history including systemic disease, complete pediatric evaluation, history of glaucoma surgeries and anti-glaucoma medications. All the patients underwent examination under general anesthesia to examine the anterior segment including corneal haziness, corneal diameter, depth of anterior chamber, status of lens, vitreous and retina, cupping of optic nerve head, any association of other retinal pathology, retinoscopy and record of intra ocular pressure. B-Scan was done in hazy refractive media. All the valves were implanted by one surgeon (Dr IHB).Qualified success was defined as IOP < 21mmHg regardless of the number of glaucoma medications. Complete success was defined as IOP < 21 mmHg without any glaucoma medication.

Results

Qualified success was noted in 7.14 % of cases while complete success was obtained in 71.43% of cases. Post operative complications included, post operative hyphema in 01 patient, hypotony in 01 patient, Tenon's encapsulation in 01 patient, choroid and retinal detachment in 01 patient respectively.

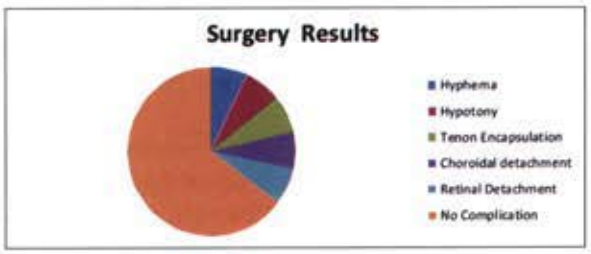


Fig-1 Results surgery.

Discussion

The management of refractory pediatric glaucoma is a difficult scenario for an ophthalmologist due to a number of anatomical and surgical features especially the technique of surgery which has limited success in pediatric glaucoma patients. There are multiple factors which have made the management of refractory pediatric glaucoma difficult. For example vigorous wound healing response, unique biochemical properties of the eye, need for multiple surgical procedures and frequent follow ups and difficulty with proper examination of patient in this age group pose significant challenges.[9] Sex incidence of our study is comparable with HK Vong et al which demonstrate male predominance. Our all patients were diagnosed cases of congenital glaucoma. While HK Yang et all[10] study shows prominent group of congenital glaucoma etiology, qualified success was observed in 75% and complete success was found 71.43%, consistent with Yang et al, Englert et al noted the high success in congenital glaucoma. They reported high success rates (92.2%) in congenital glaucoma. Our study also demonstrate a high success rate i.e. 71%, which is also consistent with Yang et al, success rate was maintained for four years our study as Yang et al.10. Infectious endopthalitis is rare complication of implant replacement in the literature, this devastating complication occurs due to consequence of erosion over an implant tube which may be portal of entry of the organism. Hypotony is one of the important complication of Ahmad glaucoma valve implantation, which was occurred in our two children this finding is similar with Vong and Englert et al.[11-12] The most detected organisms causing endophthalmitis following GDD (Glaucoma drainage devices) in children are Hemophilius inflenzae, streptococcus pneumonae or both as h.influenzae is part of normal bacterial flora.[13-15] These two devastating complications occurred in our study due to lack of post operative examination or have poor compliance. In our study over all rates of complications were lower than present reported by Yang et al.[10]

Conclusion

Despite of the small number of cases in this study Ahmad Glaucoma Valve seems to be effective in primary congenital glaucoma. Success rate decline over time, considering the need for further alternative medications and surgical procedure.

Department of Ophthalmology
SIMS/Servieces Hospital, Lahore

References

1. Gilbert, C.E., Canovas, R., Kocksch de Canovas, R., Foster, A., 1994.Causes of blindness and severe visual impairment in children in Chile. Dev. Med. Child Neurol. 36, 326333.
2. Gilbert, C.E., Rahi, J.S., Quinn, G.E., 2003. Visual impairment and blindness in children. In: Johnson, G.J., Minassian, D.C., Weale,R.A., West, S.K. (Eds.), The Epidemiology of Eye Disease, second ed., Arnold, London, pp. 260286.
3. Papadopoulos, M., Khaw, P.T., 2005. Childhood glaucoma. In:Taylor, D., Hoyt, C.S. (Eds.), Pediatric Ophthalmology and Strabismus, third ed., Elsevier Saunders, New York, pp. 458471.
4. Aponte, E.P., Diehl, N., Mohney, B.G., 2010. Incidence and clinical characteristics of childhood glaucoma: a population-based study.Arch. Ophthalmol. 128 (4), 478482.
5. Taylor, R.H., Ainsworth, J.R., Evans, A.R., Levin, A.V., 1999. The epidemiology of pediatric glaucoma: the Toronto experience. J.AAPOS 3, 308315
6. Ben-Zion, I., Bogale, A., Moore, D.B., Helveston, E.M., 2010. Bilateral primary congenital glaucoma in monozygotic twins. J.Pediatr. Ophthalmol. Strabismus 47, 124126.
7. Ben-Zion, I., Tomkins, O., Moore, D.B., Helveston, E.M., 2011.Surgical results in the management of advanced primary congenital glaucoma in a rural pediatric population. Ophthalmology 118, 231235.
8. Kipp, M.A., 2003. Childhood glaucoma. Pediatr. Clin. North Am. 50(1), 89104.deLuise, V.P., Anderson, D.R., 1983. Primary infantile glaucoma (congenital glaucoma).Surv. Ophthalmol. 28 (1), 119.
9. Miller, S.J., 1966. Genetic aspects of glaucoma. Trans. Ophthalmol. Soc. UK 86, 425434.
10. Jaafar, M., 1988. Care of the infantile glaucoma patient. In: Reinecke, R.D. (Ed.), Ophthalmology Annual. Raven Press, New York, NY
11. PARS PLANA Vong et and KH Park, Clinical outcomes after Ahmad valve implantation in refractory pediatric glaucomaeye,2009 23,1427-1435
12. Englert,J.A.FreedmanS.F,Cox,T.A 1999,The Ahmad valve in refractory glaucoma,Am .J. of ophthalmology127(1)34-42
13. Djodeyre, M.R, Peralta Calvo,j2001,,Clinical evaluation and risk factors of time to failure of Ahmad glaucoma valve implant in paedreatic patients ophthalmology108,614-620
14. Al-Torbak et al,2005:Al-Torbak and Edward,2002:Gedde et al.2001

Medical Guidlines

Massage may Provide Short-Term Improvement of Knee Osteoarthritis Symptoms

A weekly session of massage therapy may provide short-term benefits for people with osteoarthritis of the knee, including reduced pain and stiffness and improved function, according to a new NCCIH-funded study. The study, which was done at locations in North Carolina, New Jersey, and Connecticut, was published in the Journal of General Internal Medicine.

Researchers randomly assigned 222 people with knee osteoarthritis to receive whole-body Swedish massage, light touch, or usual care. Light touch involved the massage therapist gently placing his or her hands in a specified sequence on the participant's major muscle groups and joints. Usual care was the participant's typical care regimen for osteoarthritis. Participants in the massage or light touch groups received 8 weekly treatments (lasting 60 minutes each), and then were randomly assigned to receive treatment every 2 weeks or usual care to week 52. The researchers found that 8 weeks of massage provided statistically and clinically significant improvement of osteoarthritis symptoms, as assessed by a widely used questionnaire that evaluates the condition of people with arthritis. Pain, stiffness, and physical function all improved. Side effects were minimal. The researchers noted that these findings support the results of their previous research in people with knee osteoarthritis, which demonstrated the safety, feasibility, and potential efficacy of 8 weeks of massage therapy in improving pain, stiffness, timed 50-foot walk, and physical function compared to a waitlist control. However, long-term benefits were less clear; after 8 weeks of treatment, massage therapy maintained improvement but did not provide additional benefit beyond usual care. The researchers noted that the study size was relatively small, and the participants were mostly white women. The results may not be generalizable to other groups of people.

Original Article

RAPE, A MYTH OR REALITY: AN OVERVIEW OF LACK OF FINAL OUTCOME OF SEXUAL ASSAULT CASES IN LAHORE, PAKISTAN

Khalid Mahmood, Ahmad Raza Khan, Muhammad Abaidullah and Naveera Ahmed

Objective: To elucidate lapses in medicolegal cases of sexual assault victims inclusive of lack of follow up for declaration of final opinion.

Methods: Cross sectional retrospective study inclusive of volunteer female victims of sexual victimization reported in medicolegal section of Services Hospital Lahore either with police docket, court order or both. Sample size calculated according to statistical formula was 150. Data was recorded from medicolegal reports regarding rape history and examination.

Results: In 2016 cases recorded were 78 and they amounted up to 75 in 2017 with a total sample size of 153 candidates. Surprisingly out of 153 cases only 01 reported back to demonstrator medicolegal for declaration of final opinion. More than 80% of cases were advised to get urine examined along with abdominal sonography for pregnancy, but not even a single case reported back. Around 60% of victims were conscious and well oriented. 25% exhibited signs of depression and 11% were shy and confused. 3% were agitated, less than 1% reported semiconscious and disoriented. Only 10 cases out of 153 were victims of sexual coercion, with signs of fresh bleeding on genital examination. 04 cases had intact hymen.

Conclusions: What does lack of final opine in sexual violation depict? Victim drops charges, or it is break in chain of custody, it seems to be an awful waste of valuable medicolegal resources. Is there any justice pursuit or just a futile exercise for money extortion? Cases needed to be finalized for presentation in courts of law to maintain a sexual harassment free society where children and women are safe from genitive violence especially rape.

Keywords: rape, docket, court order, PFSA, final opinion.

Introduction

No age is immune to sexual violence but most vulnerable age group is the young female children traumatized by sexual predators.[1] Younger children being innocent are victimized most often by offenders who are usually an adult they trust, who might be family member or close friend of family or a neighbor.[2] This is inclusive of teenage girls who usually fall for the curiosity that comes along puberty achievement. In this scenario the offender might be the same stated perpetrator or a so called boyfriend who just seeks out sex to satisfy his sexual cravings.[3] Young housemaids who work as full time servants are among sexual abuse sufferers, exploited on terms of poverty, and mostly being underage, even if and when brought to emergency examination for sexual offence are either drugged or threatened and silenced. This early exposure not only traumatizes females physically but also scars them psychologically for rest of their lives.[4] By the time female reach adult age, this age group is responsible for consensual sex with motive being both pleasure and business.[5] Monetary targeted sexual advances last only as long as expenses are met and it is either refusal of the male to further comply with financial demands or denial of a marriage proposal that is the main causative factor for reporting a medicolegal case. Finally as the age advances the tables are turned and hunted becomes the hunter.[6] Adult women in their fourth decade, usually become the sexual predators whose main prey are the young puberty attaining curious boys, who seek out sex on experimentation basis.[7]

Ironically speaking only a fragment of the actual rape trauma victims are reported in;[8] the ulterior motives for reporting the sexual offences in the medicolegal section can be enumerated in a chronological order as monetary compensation, blackmail in to marriage, and revenge for traumatic empiricism.[9] Yet most hideous aspect without which this introduction is incomplete is business run by madams of brothel houses who lure customers into having sexual fantasies fulfilled at a price too high to be paid in form of medicolegal accusation of rape, seeking out heavy compensatory damages.[10] The frivolity of the actuality regarding coital perspicacity would only be an understatement if not backed up by lack of getting the hectic exercise of medicolegal cases being

finalized by the police, who as a documented fact never turn up with serology and DNA scanning results for conclusive documentation. Only a tip of an iceberg analogy cases end up in court rooms for trial purposes to root out this social evil.[11] The samples dispatched for serological and DNA analysis either do not make it to the concerned laboratory facility, as once admitted in the PFSA, they are eventually analyzed and reported either back to concerned police station or relevant medicolegal department, and in few occasions the prosecuting lawyer presents such evidence directly in court of law.[12] Few of these analyzed cases of which reports are dispatched to concerned police stations are never reported back to medicolegal clinic for finalization and declaration of opinion as to whether female victim was actually subjected to assault of rape. What motives play role behind this negligence by either police or effected party involved in although primarily as a victim, as to why they back out and drop charges without pursuing criminal trial.[13] They rather prefer compensatory reforms rather than to see criminal brought to justice to avoid recurrence of such devious hideous act to same or some new victim. It extremely perilous to let such offenders to continue on such a deplorable spree of despicable salacious acts.[14] These felons should be dealt with a stern hand of law and made an example out of to make society a sexual assault free community. A message should be sent to all the nefarious delinquents that malicious dereliction shall not go unpunished. This being achievable only if all law enforcers work harmoniously in collaboration, resultantly seeking justice served.[15]

Methods

This is a descriptive cross sectional study which included the volunteer female victims of sexual assault reporting in medicolegal section of Services Hospital Lahore either with police docket, court order or both. Sample size calculated according to statistical formula was 150.

A thorough detailed examination was conducted after receiving detailed informed consent from victims with age of majority and for minors consent was taken from their legal guardians. General state of mind was recorded along with assessment of clothes. Any injuries besides sexual assault infliction were observed and duly reported if present. The perineal region was examined in lithotomy position, which included inspection, palpation, digital as well as specular examination in victims subjected to sexual violence, except those who had intact hymen. Samples were collected from perineal area and from within genitilia in case of ruptured hymen whether freshly torn or old. However in case of a true virgin no sample collection was done beyond hymenal area. These samples were dispatched to PFSA via police, for serology and DNA. All ethical principals were abided in case of research on human subjects according to WMA (world medical association) of Helsinki (2008). SPSS version 20 was applied for statistic study of gathered data.

Results

Data collection was from medicolegal section, Services Hospital Lahore. Highlighted points of research were reported number of cases versus the number of cases that were eventually finally declared to be presented in court of legal equity. This was inclusive of, as to manner of presentation in emergency in relation with status of the individual, both as general demeanor as well as locus examination findings, regarding acuity of case. Sample size for this study was 150. A retrospective data collection was carried out, collecting relevant details of concerned cases. As seen in **Fig-1,** 153 cases presented with police docket and a court order, which amounts to show gravity of situation as to how hectic work up is done to get the case registered.

However on contrary as depicted in **Fig- 2,** outcome is drastically astringent. The expected finalization of registered cases should be 100% but ironically it is only 1 case out of 153 that eventually turned up in the medicolegal department for declaration of final opinion. This shows that samples collected from all 153 cases which were sent to PFSA, never made it to laboratory as if they were admitted there, reports

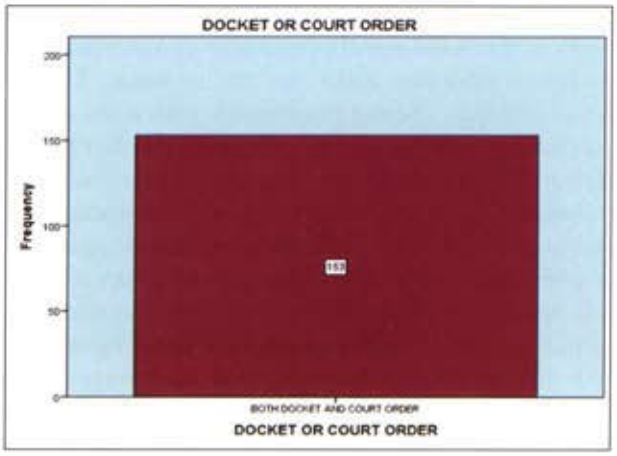


Fig-1: Docket or court order.

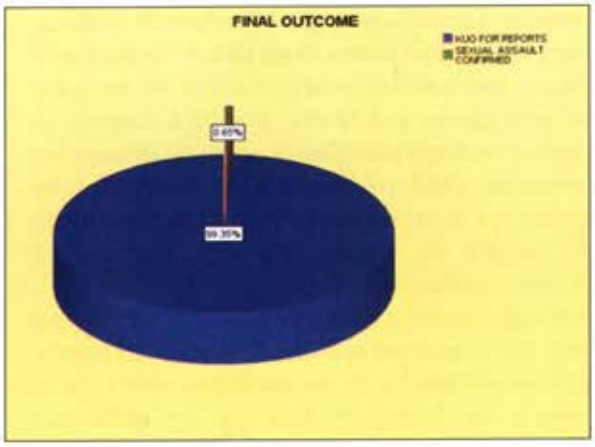


Fig-2: Final outcome.

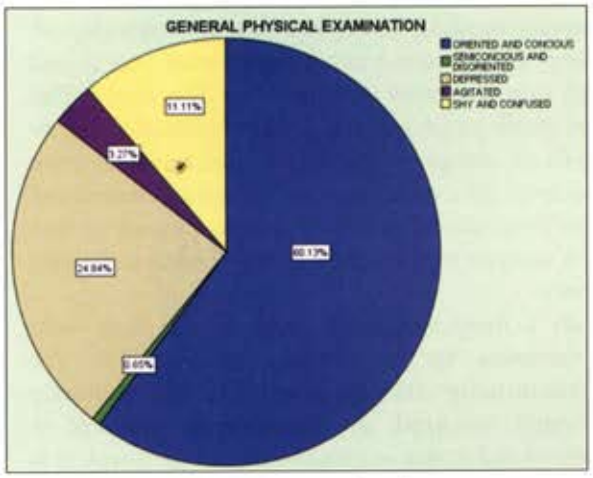


Fig-3: General physician examination.

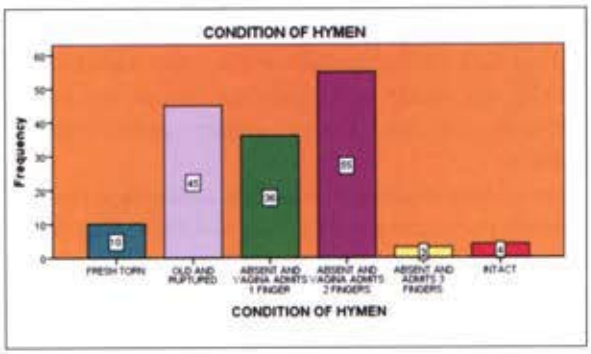


Fig-4: Condition of hymen.

Table-1: Condition of genitals.

Valid	Frequency	Percent	Valid percent	Cumulative percent
Fresh Bleeding	12	7.8	7.8	7.8
Per vaginum	03	2.0	2.0	9.8
Discharge of pus menstruating	12	7.8	7.8	17.6
Possible seminal discharge	02	1.3	1.3	19.0
No positive finding	124	81.0	81.0	100.0
Total	53	100.0	100.0	

would have made back to medicolegal department for final opinion. In Addition more than 80% of cases were referred to get urine examined for positive pregnancy and abdominopelvic ultrasound for any product of conception but no such reporting was done to forensic expert who suggested these tests **(Table-2).** General physical examination revealed more than 60% of victims were conscious and well oriented in time, place and person. 25% were depressed and 11% were shy and confused. 3% were agitated, less than 1% were semiconscious and disoriented **(Fig-3).** Furthermore 10 cases out of 153 were actual coerced sexual assault cases, backed up by information of freshly torn hymen **(Fig-4)**, along with signs of fresh bleeding on genital examination, however in more than 90% of cases hymen was absent. Only 4 cases had intact hymen. **(Table1).**

Table-2: Pregnancy related.

Valid	Frequency	Percent	Valid percent	Cumulative percent
Ultrasound and urine test for pregnancy	129	84.3	84.3	84.3
No investigation advised	24	15.7	15.7	100.0
Total	153	100.0	100.0	

Discussion

Services hospital Lahore is a tertiary care hospital with a 24 hour 7 days a week facility of healthcare inclusive of medicolegal examination. Rape cases reported in medicolegal clinic for year 2016 were 78 in number and 75 for year 2017. These cases are entertained with police docket, F.I.R. and court order, examined thoroughly with sample collection to be dispatched to Punjab Forensic Science Agency, Lahore. In addition 84% of the cases were advised analysis of urine test for pregnancy and abdominal ultrasonography. As the statistics show 153 cases were reported in medicolegal clinic, Services hospital, Lahore with all legal formalities fulfilled including police docket and court order. However irony of situation befalls under breakage of chain of custody as far as sample dispatch is concerned.[11] No advised investigation is brought back to concerned forensic specialist either. There is complete lapse in provision of serological and DNA analysis reports back to medicolegal clinic for final opinion declaration.[12] The question arises here as to whether the cases are registered as MLC, only as a ritual. What factors play role in lack of efficient working later in proceedings of the case? Primarily it is a time consuming hectic process to present the case for registration in medicolegal clinic along with complete legal

documentation inclusive of FIR, police docket, and court order from judicial magistrate, for conductance and issuance of medicolegal report. MLR is issued with samples to be dispatched for seminal and DNA analysis, which include both clothes and vaginal swabs, duly sealed signed and handed over to police. Where and why does this chain of custody break up? Whether the samples are delivered and admitted to PFSA for analytical purpose or just dumped in the store as case property. Why do the victims back out? Do they avail monetary compensation? Are they threatened or is it just a blackmail tactic for benefit extortion in one way or another. Actual rape traumatized individuals are rare, seeking justice for the heinous crime.[16] Mostly these are cases of chronic nature of which victims are of varying category, of which they may either be habitual sex worker from some brothel houses, or domestic yet unmarried women. Eventually multiparous married women, who are either willing partners in sex or their involvement is for financial reasons or they are strong-armed into such relationship.[17] This amounts for many reasons among others for cases either not to be registered to begin with and if they make it to the medicolegal department for reporting, it is a rare instance that such cases are finalized or prosecuted in courts.At times even consensual relationships have heinous outcome, either way, as male is usually in for sexual favors and female counterpart seeks out monetary compensation for the mutually consented sexual act. Either reduction in fulfilling demands or omission of funds, results in consenting sexual encounters to be reported by female, as rape in medicolegal department.[18] Yet another horrendous aspect of erotic scenario is prostitution ranging from lower strata socioeconomic status to high class illicit brothel houses run as escort services.[19] This illegal activity ends up with male being fleeced off his cash on blackmail extortion. An unspoken societal dilemma is sexual exploitation of housemaids. These are usually underage minor females who work out of their needs to support large families, living well below poverty line. These poor girls fall victim to lustrous desires of sexual predators, who not only misuse them as toilet paper but also threaten to make them jobless if they ever speak up. Most of these cases go unreported due to the reasons that either the maids are scared to lose their only source of income or threatened physically and tortured or their families are cash compensated.[20] Tragically most hideous perverse abomination regarding sexual assault ordeal is the devastating scenario of sexual predatorial vultures. These predatory monsters crave carnal covetousness by luring and enticing young children by tempting them with games and favors. Resultant outcome is emulation to despicable ghastly crime of desecrating an innocent child robbing her of innocence, by exposing her to sexual torment of rape. This might even escalate to murder for sole purpose of disclosure avoidance.[22]

Actual rape trauma victims are not reported in our society, due to multiple reasons. Shame, social stigma, fear or being forced in to reconciliation either due to influence or being hushed up by monetary compensation.[22] However unspoken abominable truth might be yet it is an inevitable to conclude that corruption in society has not only rooted itself as a monetary monster but it runs deep in morality of society. Sexual assault cases are reported only if and when compensatory measures are not met.[23] The entire medicolegal system is being exploited merely to benefit of compensation rather than to incriminate the culprit. It's a futile exercise if cases go unreported or not finalized due to non-provision of serology and DNA analysis reports from Punjab Forensic Science Agency.

Finally a most significant need of the hour only conspicuous by its absence is rape kit. An internationally standardized kit, meticulously calibrated to need of medicolegal protocol is designed and in use in most countries of world. It is about time to upgrade our forensic system for sexual assault examination and introduce an authentic systemized kit, which includes not only swab collection material but containers for urine and blood, nail picks for under nail scrapings, comb for hair collection among many other mandatory equipment.[24]

Purpose of this study is to establish a complete chain of custody sustenance so that case is followed up and an expedited justice be provided to victims and assailants be penalized. A proper message needs to be delivered to all sexual predators that exploiting weakness of victims to sexually benefit themselves shall not remain unscrupulous. Actual rape trauma victims shall be entertained in a befitting manner as to not only provision of clinical and medicolegal aid but also to face the social and moral stigma of society.[25] Law enforcers including honorable courts should inter maintain a follow up protocol for a final outcome to get offender penalized, not only preventing further victimization but also to register such criminals as sexual offenders.

Conclusion

A public awareness program is need of time for women to be empowered with knowledge of their basic rights, they are to be educated as to how and when to report any harassment with resultant causal sexual advancement.[26] Police should be trained for quick case registration and medicolegal examination.[27] Medicolegal training of the doctors is to be conducted and refresher courses to be introduced for awareness regarding examination and sample collection including clothes examination and sealing it as case property and serological swab collection.[28] Finally a prompt effective set up is to be established for maintenance of chain of custody, so that PFSA reports are duly brought back to medicolegal officers for finalization of pending cases to expedite justice. Conclusively it is emphasized that no proper kits are available for sample collection and all swabs are collected using culture sensitivity test tubes. Availability of proper kit is to be ensured by the surgeon medicolegal department for proper dispensation of the samples to PFSA.[29] It is speculated that reported cases are only tip of iceberg. Society norms are evident from results gathered from emergency medicolegal department of Forensic Medicine. Effective legal counter measures involving efficient law in corroboration with expedited judicial system for provision of accessible justice and practical application of penalty to criminals is mandatory need of time.[30] If a timely check and balance for the perverted behavior is not encountered, it shall be an unstoppable curse. A further decline in degenerate attitude of male chauvinistic world shall be a lecherous abomination, encouraged, if morally, socially and legally unchecked.

Department of Forensic Medicine
SIMS/Servieces Hopsital, Lahore
www.esculapio.pk

References

1. Salter, A., Predators: Pedophiles, rapists, and other sex offenders. 2018: Hachette UK.
2. Olson, L.N., et al., Entrapping the innocent: Toward a theory of child sexual predators' luring communication. Communication Theory, 2007. 17(3): p. 231-251.
3. Teir, R. and K. Coy, Approaches to sexual predators: Community notification and civil commitment. New Eng. J. on Crim. & Civ. Confinement, 1997. 23: p. 405.
4. Lieb, R., V. Quinsey, and L. Berliner, Sexual predators and social policy. Crime and justice, 1998. 23: p. 43-114.
5. Ranganathan, M., et al., 'It's because I like things... it's a status and he buys me airtime': exploring the role of transactional sex in young women's consumption patterns in rural South Africa (secondary fin- dings from HPTN 068). Reprod Health, 2018. 15(1): p. 102.
6. Vandiver, D.M. and G. Kercher, Offender and victim characteristics of registered female sexual offenders in Texas: A proposed typology of female sexual offenders. Sexual Abuse: A Journal of Research and Treatment, 2004. 16(2): p. 121-137.
7. Duncan, K.A., Female sexual predators: Understanding them to protect our children and youths. 2010: ABC-CLIO.
8. Acierno, R., H.S. Resnick, and D.G. Kilpatrick, Health impact of interpersonal violence 1: Prevalence rates, case identification, and risk factors for sexual assault, physical assault, and domestic violence in men and women. Behavioral Medicine, 1997. 23(2): p. 53-64.
9. Gregory, J. and S. Lees, Attrition in rape and sexual assault cases. The British Journal of Criminology, 1996. 36(1): p. 1-17.
10. O'Connell Davidson, J., Prostitution. The Blackwell Encyclopedia of Sociology, 2007.
11. Holmes, M.M., H.S. Resnick, and D. Frampton, Follow-up of sexual assault victims. American journal of obstetrics and gynecology, 1998. 179(2): p. 336-342.
12. Gray-Eurom, K., D.C. Seaberg, and R.L. Wears, The prosecution of sexual assault cases: correlation with forensic evidence. Annals of Emergency Medicine, 2002. 39(1): p. 39-46.
13. Patterson, D., The linkage between secondary victimization by law enforcement and rape case outcomes. Journal of interpersonal violence, 2011. 26(2): p. 328-347.
14. Hanson, R.K., K.E. Morton, and A.J. Harris, Sexual offender recidivism risk: What we know and what we need to know. Annals of the New York Academy of Sciences, 2003. 989(1): p. 154-166.
15. Sample, L.L. and C. Kadleck, Sex offender laws: Legislators' accounts of the need for policy. Criminal Justice Policy Review, 2008. 19(1): p. 40-62.
16. Parker, A.D. and J. Brown, Detection of deception: Statement Validity Analysis as a means of determining truthfulness or falsity of rape allegations. Legal and Criminological Psychology, 2000. 5(2): p. 237-259.
17. Shannon, K., et al., Global epidemiology of HIV among female sex workers: influence of

structural determinants. The Lancet, 2015. 385(9962): p. 55-71.
18. Cabezas, A.L., Between love and money: Sex, tourism, and citizenship in Cuba and the Dominican Republic. Signs: Journal of Women in Culture and Society, 2004. 29(4): p. 987-1015.
19. Harcourt, C. and B. Donovan, The many faces of sex work. Sexually transmitted infections, 2005. 81(3): p. 201-206.
20. Miles, G.M., "children don't do sex with adults for pleasure": Sri Lankan children's views on sex and sexual exploitation. Child abuse & neglect, 2000. 24(7): p. 995-1003.
21. Kozak, R.S., M. Gushwa, and T.J. Cadet, Victimization and Violence: An Exploration of the Relationship Between Child Sexual Abuse, Violence, and Delinquency. 2018. 27(6): p. 699-717.
22. Du Mont, J., K.-L. Miller, and T.L. Myhr, The role of "real rape" and "real victim" stereotypes in the police reporting practices of sexually assaulted women. Violence Against Women, 2003. 9(4): p. 466-486.
23. May, T., A. Harocopos, and J. Hough, For love or money: pimps and the management of sex work. 2000: Home Office, Policing and Reducing Crime Unit, Research, Development and Statistics Directorate London.
24. Luce, H., S. Schrager, and V. Gilchrist, Sexual assault of women. American family physician, 2010. 81(4): p. 489-495.
25. Foa, E.B. and B.O. Rothbaum, Treating the trauma of rape: Cognitive-behavioral therapy for PTSD. 2001: Guilford Press.
26. Craven, S., S. Brown, and E. Gilchrist, Current responses to sexual grooming: Implication for prevention. The Howard Journal of Criminal Justice, 2007. 46(1): p. 60-71.
27. Lonsway, K.A., S. Welch, and L.F. Fitzgerald, Police training in sexual assault response: Process, outcomes, and elements of change. Criminal Justice and Behavior, 2001. 28(6): p. 695-730.
28. Tozzo, P., et al., Collecting sexual assault history and forensic evidence from adult women in the emergency department: a retrospective study. BMC Health Serv Res, 2018. 18(1): p. 383.
29. Campbell, R., et al., Should rape kit testing be prioritized by victim offender relationship? Empirical comparison of forensic testing outcomes for stranger and non-stranger sexual assaults. Criminology & Public Policy, 2016. 15(2): p. 555-583.
30. Lonsway, K.A. and J. Archambault, The "justice gap" for sexual assault cases: Future directions for research and reform. Violence against women, 2012. 18(2): p. 145-168.

Original Article

To Assess the Frequency of Seizures in Patients Presenting with Recurrent Stroke

Anam Mahmood, Satia Waheed and Ali Hassan

Objective: To assess the frequency of seizures in patients with recurrent strokes.
Methods: Total 175 patients with recurrent stroke were included and were followed-up in neurological wards for 3 days. Patients were discharged and were followed-up in OPD for 15 days after stroke. Patients were advised to present in emergency in case of seizures. If fits occured within 15 days of stroke, then seizures was labeled. Data entry and analysis was done by using SPSS
Results: Seizure occurred in 16(9.1%) of the patients. Highest frequency of seizure was observed in patients in the age group 61-70 years. (62.5%) Among male and female patients frequency of seizure was same. i.e. (50%) Patients with hemorrhagic stroke had high frequency of seizure (56.3%).
Conclusions: Seizure occurred in 16(9.1%) patients. Considering the risk for seizures after certain types of cerebrovascular events might help to early identify patients for anticonvulsive treatment.
Keywords: seizures, recurrent, stroke, ischemic, hemorrhagic.

Introduction

Stroke is a major cause of disability and death worldwide, affecting 7 million people each year.[1-3] Although initial stroke events play a principal role in the outcome of stroke, recurrent stroke events are relevant to higher mortality rates and disability levels. Given these results, identifying factors that are associated with recurrent stroke is critical. Stroke recurrence is also an important factor in evaluating the quality of health care services.[3]

Survivors of stroke or transient ischemic attack who did not experience early complications have an elevated risk for recurrent stroke, death or myocardial infarction for at least 5 years following the initial stroke, suggesting that these patients require medical support to reduce their risk in the subsequent years.[4] One study reported that frequency of seizures was 4.8% in patients presenting with recurrent stroke.[5] One more study showed that 5.4% patients had acute symptomatic seizures after stroke.[6] Another study showed that 6.3% patients had acute symptomatic seizures after stroke.[7] But one study reported that the risk of seizures after recurrent stroke was 13%.[8] Rationale of this study is to assess the frequency of seizures in patients presenting with recurrent stroke. Literature showed that the frequency of seizure was low and can be considered as rare complication. But not much work has been done in this regard. Moreover, varied data has been retrieved from literature regarding the occurrence of seizures after recurrent stroke. Furthermore, there is no local study found in literature which could help us in determining the extent of problem in local population. So we want to conduct this study so that we can attain local magnitude and we can plan the strategy to prevent seizures after recurrent stroke. It was defined as presence of sudden weakness of one or more parts of body and hypodense area of brain detected on CT scan with history of previous stroke (on medical record). It was labeled if fits occurs within 15 days of recurrent stroke i.e. losing consciousness (GCS <13/15), which is followed by confusion, having uncontrollable muscle spasms and one or more of these drooling or frothing at the mouth, falling, clenching the teeth, biting the tongue or having sudden, rapid eye movements.

Methods

Descriptive case series was utilized. Patients were enrolled from Unit IV, Department of Medicine, Services Hospital, Lahore. Sample size of 175 patients was calculated with 95% confidence level, 5% margin of error and taking expected percentage of seizures i.e. 13% patients presenting with recurrent stroke Non probability consecutive sampling was done. Patients of age 40-70 years of either gender presenting with recurrent stroke (as per operational definition) were enrolled in the study. Patients with history of seizures before or after first stroke (on medical record) or previously known epileptic patients were excluded from this research. A total of

175 cases fulfilling selection criteria were enrolled in study form emergency of Department of Medicine, Services Hospital, Lahore. Informed consent was obtained. Demographic information (including name, age, gender, type of stroke and duration of previous stroke) was also recorded. Then patients were admitted as per hospital protocol and were followed-up in neurological wards for 3 days. Patients were discharged and were followed-up in OPD for 15 days after stroke. Patients were advised to present in emergency in case of seizures. If fits occurs within 15 days of stroke, then seizures was labeled (as per operational definition). All the information was collected on a specially designed performa. All the collected data was entered and analyzed into SPSS version 21. Quantitative variables like age and duration of previous stroke was presented as mean and Standard Deviation. Qualitative variables like gender, type of stroke and seizures was presented as frequency and percentage. Data was stratified for age, gender, type of stroke and duration of previous stroke to control effect modifiers. Post-stratification, chi-square test was applied to compare frequency of seizures in stratified groups. P-value≤0.05 was taken as significant.

Results

In this study, the mean age of patients was 53.17±9.06 years. **(Table-1)** Among patients 96(54.9%) were male and 79(45.1%) were females. For 73(41.7%) patients type of stroke was hemorrhagic and ischemic stroke was diagnosed in 102(58.3%) patients. **(Fig-2)** Mean duration of previous stroke was 7.58±4.12 years. Seizure occurred in 16(9.1%) patients who suffered recurrent stroke. In elderly age group (61.70 years) frequency if seizures was significantly higher as compared to other age groups i.e. 40-50 years: 18.8%, 51-60 years: 18.8% & 6-70 years: 62.5%, p-value=-0.002 .No significant difference was seen among male and female patients for frequency of seizure i.e. Male: 50% & Female: 50%, p-value=0.682.**(Fig-2)**

Patients with hemorrhagic stroke had higher frequency of seizure as compared to ischemic stroke patients i.e. Ischemic: 43.8% & Hemorrhagic: 56.3%, p-value=0.862 Seizures were more common in patients who had recurrent stroke within 1-5years (11.3%) as compared to patients who had stroke within 6-10years (9.5%) or 11-15years (6%), p-value: 0.622.

Table-1: Age of patients.

N	**175**
Mean	53.17
Standard deviation	9.06
Minimum	40
Maximum	70

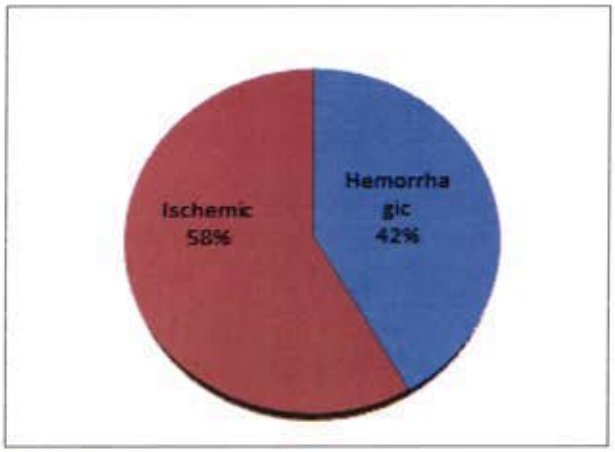


Fig-1: Type of stroke.

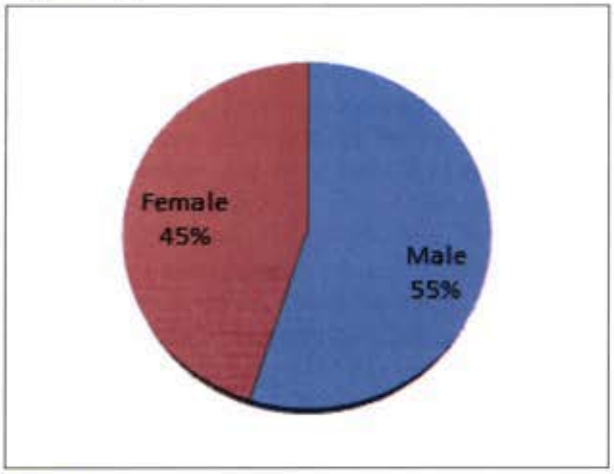


Fig-2: Seizure in relation to gender of patients.

Discussion

Although post-stroke seizures have been known for many years, many questions remain unanswered regarding this subject. Furthermore, many studies on this subject have shown different results. In this study 73(41.7%) patients suffered from hemorrhagic stroke and 102(58.3%) suffered from ischemic stroke. Seizure occurred in 16(9.1%) patients who presented with recurrent stroke. Patients who had seizure among them 7(43.8%) suffered ischemic stroke and 9(56.3%) suffered from hemorrhagic stroke.

Julian Conrad in his study reported the total prevalence of epileptic seizure as 11.6%.[9] Recently in 2017 C.

Rachel Packiaseeli and his colleague reported late onset seizure in 36% patients who presented with stroke.10.Alberti A in his study reported that frequency of seizures was 4.8% in patients presenting with recurrent stroke.5 In this study frequency of seizure was a bit higher as that of reported by Alberti A but quite lower as that of reported by Rachel Packiaseeli. E Beghi and his team members reported that the risk of seizures after recurrent stroke was 13%.[8] The rate of seizures after stroke varies widely in the literature (2.742.8%) due to different inclusion criteria, study designs, and detection modes.[11-13] Studies have reported higher risk of seizure in the first 24 hours and these tended to decrease thereafter. In the first 24 hours the risk of seizure lies in between 2.8-5.7%, [8,14,15] and suggests that during acute brain injury accumulation of intracellular calcium and sodium may result in depolarization of the trans-membrane potential and other calcium-mediated effects, which may lower the seizure threshold.[16] In this study highest frequency of seizure was seen in patients in the age group 61-70 years. (62.5%). Few studies supported the findings that younger age was associated with the development of seizures while some studies found no difference of onset of seizure regarding age.[9,11,12].On the other hand few studies have reported that post-stroke seizures are more common in the elder age group.[10,16] Aging brain undergoes degenerative and neuroplastic changes that lead to decreased excitability of the cortex. Given that the volume of cortical gray matter is higher in younger patients, it is easy to assume that these younger patients develop seizures more often. No significant difference was seen for seizure among male and female patients in this study. Similar findings were reported by Julian Conrad, Andrea Alberti and E. Beghi. Andrea Alberti reported no significant difference of seizure occurrence in ischemic and hemorrhagic stroke.[5] Similar findings were obtained in this study showing no significant difference for frequency of seizure in patients with ischemic and hemorrhagic stroke. i.e. Frequency of seizure in patients with ischemic stroke: 43.8% & Frequency of seizure in patients with hemorrhagic stroke: 56.3%, p-value=0.862.

E. Beghi in his study found that hemorrhagic transformation of cerebral infarction carried a greater risk of post stroke seizures than ischemic infarcts.[7] This provides additional evidence in support of the epileptogenic role of blood extravasation. The mechanism of seizure initiation by hemorrhage is not established. Products of blood metabolism, like hemosiderin, may cause focal cerebral irritation leading to seizures, as shown in animal models of focal epilepsy produced by iron deposition on the cerebral cortex.[17] The sequestration of hemosiderin in cortical neurons might also play a role in seizures following traumatic brain injury.

Conclusion

Findings of this study indicate that seizure occurred in 16(9.1%) patients. Frequency of seizures was highest in the elderly age group and no significant difference was seen for frequency of seizure in relation to gender and type of stroke. Considering the risk for seizures after certain types of cerebrovascular events might help to early identify patients for anticonvulsive treatment.

Department of Medicine
SIMS/Servieces Hospital, Lahore
www.esculapio.pk

References

1. Group Members Writing, Mozaffarian D, Benjamin E, Go A, Arnett D, Blaha M, et al. Heart Disease and Stroke Statistics-2016 Update: A report from the American Heart Association. Circulation 2016;133(4):e38.
2. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, et al. Executive Summary: Heart Disease and Stroke Statistics--2016 Update: A Report From the American Heart Association. Circulation 2016;133(4):447-54.
3. Wang P, Wang Y, Zhao X, Du W, Wang A, Liu G, et al. In-hospital medical complications associated with stroke recurrence after initial ischemic stroke: A prospective cohort study from the China National Stroke Registry. Medicine 2016;95(37).
4. Edwards JD. No early complications after stroke may increase long-term risk for recurrence, death. 2017 [cited 2017]; Available from: https://www. Healio.com/internal-medicine/cardiology/news/online/%7Bb9a3b074-9679-4467-935d-5a9de743fd64%7D/no-early-complications-after-stroke-may-increase-long-term-risk-for-recurrence-death.
5. Alberti A, Paciaroni M, Caso V, Venti M, Palmerini F, Agnelli G. Early seizures in patients with acute stroke: frequency, predictive

factors, and effect on clinical
L outcome. Vascular health and risk management 2008;4(3):715.
6.Giroud M, Gras P, Fayolle H, Andre N, Soichot P, Dumas R. Early seizures after acute stroke: a study of 1,640 cases. Epilepsia 1994;35(5):959-64.
7.Beghi E, D'alessandro R, Beretta S, Consoli D, Crespi V, Delaj L, et al. Incidence and predictors of acute symptomatic seizures after stroke. Neurology 2011;77(20):1785-93.
8.Burn J, Dennis M, Bamford J, Sandercock P, Wade D, Warlow C. Long-term risk of recurrent stroke after a first-ever stroke. The Oxfordshire Community Stroke Project. Stroke 1994;25(2):333-7.
9.Conrad J, Pawlowski M, Dogan M, Kovac S, Ritter MA, Evers S. Seizures after cerebrovascular events: risk factors and clinical features. Seizure 2013;22(4):275-82.
10.Packiaseeli CR, Bobby E, Radha M, Saravanan S, Murugan P, Anandan H. A Prospective Study of Seizures in Patients with Stroke. International Journal of Scientific Study 2017;5(2):94-7.
11.Burneo J, Fang J, Saposnik G, Network IotRotCS. Impact of seizures on morbidity and mortality after stroke: a Canadian multicentre cohort study. European journal of neurology 2010;17(1):52-8.
12.Misirli H, Özge A, Somay G, Erdoan N, Erkal H, Ereno□lu N. Seizure development after stroke. International journal of clinical practice 2006;60(12):1536-41.
13.Lancman ME, Golimstok A, Norscini J, Granillo R. Risk factors for developing seizures after a stroke. Epilepsia 1993;34(1):141-3.
14.Lambrakis CC, Lancman ME. The phenomenology of seizures and epilepsy after stroke. Journal of Epilepsy 1998;11(5):233-40.
15.Bladin CF, Alexandrov AV, Bellavance A, Bornstein N, Chambers B, Coté R, et al. Seizures after stroke: a prospective multicenter study. Archives of neurology 2000;57(11):1617-22.
16.Forsgren L, Beghi E, Oun A, Sillanpää M. The epidemiology of epilepsy in Europea systematic review. European journal of neurology 2005;12(4):245-53.
17.Küçükkaya B, Aker R, Yüksel M, Onat F, Yalçin AS. Low dose MK-801 protects against iron-induced oxidative changes in a rat model of focal epilepsy. Brain research 1998;788(1-2):133-6.

Original Article

To Identify the Factors that Led the Residentsto Choose Surgery as a Career

Raiha Ashfaq, Qurat-ul-Ain Shaukat and Naeem Liaquat

Objective: To identify the factors that led the residents to choose surgery as a career and to identify the factors leading to their satisfaction.

Methods: This was a cross sectional study conducted at Rawalpindi medical university over a period of 2 months from June 2017 to July2017. A specifically designed questionnaire was given to all surgical residents working in RMU teaching hospitals. The data obtained included demographic details and 24 different factors of influence were listed and there were 5 answer choices on the basis of likert scale. Data was analyzed using SPSS version 22. Response differences between different groups were analyzed using Pearson's Chi-square test.

Results: The mean age was 27.61±1.721. 62.7% were males and 37.3% were females. Most (39.2%) were 1st year residents. The most important chosen factors were I'll enjoy, surgeons look better, consultant as a role model, influence of rotation during house job, interest in general surgical procedures, best personal character fit. When comparing the responses between the four groups there were significant differences in factor rating for the following factors of influence; interest in general surgical procedures (p value0.010) and responsibilities of being a surgeon (p value 0.033).

Conclusions: This survey suggests that all the residents were satisfied with their career choice and they perceived surgery to be an enjoyable field. Majority of the residents also believed surgery as a best personal character fit. This survey also showed that there was the influence of rotation during house job in choosing surgery as a career whereas there was no role of family pressure in their career choice. We believe that this data can be helpful in overcoming the shortage of surgeons in the future.

Keywords: seizures, recurrent, stroke, ischemic, hemorrhagic

Introduction

Surgery is a branch of medicine concerned with diseases and conditions requiring or amenable to operative procedures. It is an essential part of patient care. Surgery has traditionally been a popular career choiceamong undergraduates for involvement of technical procedures, collaboration and patient care[1]. Surgery is generally perceived as an intriguing and challenging field with ample opportunities to excel.[2,5-9] A study comprising of over 2000 Canadian medical students concluded five factors that influence choice ofcareer in medical students as: social orientation, role models, prestige, medical life style and varied scope of practice.[1-5] The increased interest and enrollment of students into general surgery program was directly related with positive interactions, general surgical operative procedures and positive interactions with attending surgeons and house staff.[1,3,4] In another study, an interest in manual and technical skills, patient care, calling to field, merit of work, responsibilities and variety of tasks which are challenging were identified as factors influencing career choice.[1,3,6] There is no such study in Pakistan discussing the motivating factors for surgery residents. So we planned this study with the objective to determine the factors that motivated the residents to choose surgery as career.

Methods

This was a cross-sectional study conducted at Rawalpindi Medical University Rawalpindi (RMU) over a period of 2 months from June, 2017 to July, 2017. Study was started after approval from Institutional Research Board. All surgical residents working in RMU teaching hospitals were contacted. A 24 question anonymous survey was designed. The anonymity of residents was maintained. We excluded partially filled performas and those who had completed the training. Those who were absent or refused to fill performa due to any reason were not contacted again. After demographic details 24 different factors of influence were listed and respondents had 5 answer choices (no influence,

minor influence, intermediate influence, major influence, very strong influence) numbered 1-5 on a Likert scale. The survey was constructed and was distributed among all surgical residents by directly approaching them with the permission of surgical departments of RMU teaching hospitals. All data was analyzed using SPSS version[22].

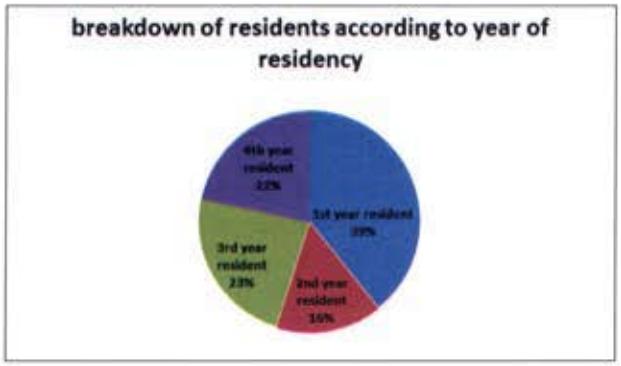


Fig-1: Breakdown of respondents.

Factors were considered high importance if respondents choose very strong influence or major influence and less important if intermediate influence, minor influence or no influence were chosen. SPSS version 22 was used for statistical analysis. Response differences between different groups were analyzed using Pearson's Chi-square test to test overall distribution of each category of response between different groups with significance established at $p<0.05$.

Results

Fifty-one anonymous responses were received. The respondents were surgical residents across all the levels of training. The mean age was 27.61±1.721years. Most of the residents (62.7%) were male. Most (39.2%) were 1st year residents (Fig. 1)When asked about time elapsed between part 1 and end of house job, 49% surgical residents had less than 6 months. Mostly (56.9%) decided to become a surgeon during MBBS, 29.4% decided during house job in general surgery, 11.85% decide after completing house job and 2% decided during childhood. All respondents (100%) showed career satisfaction. Out of 51 respondents only one resident had parents who were surgeons. All data given in **Table-1.** Across all the respondents, the most common influences chosen to be of high importance were I'll enjoy, surgeons look better, consultant as a role model, influence of rotation during house job,interest in general surgical

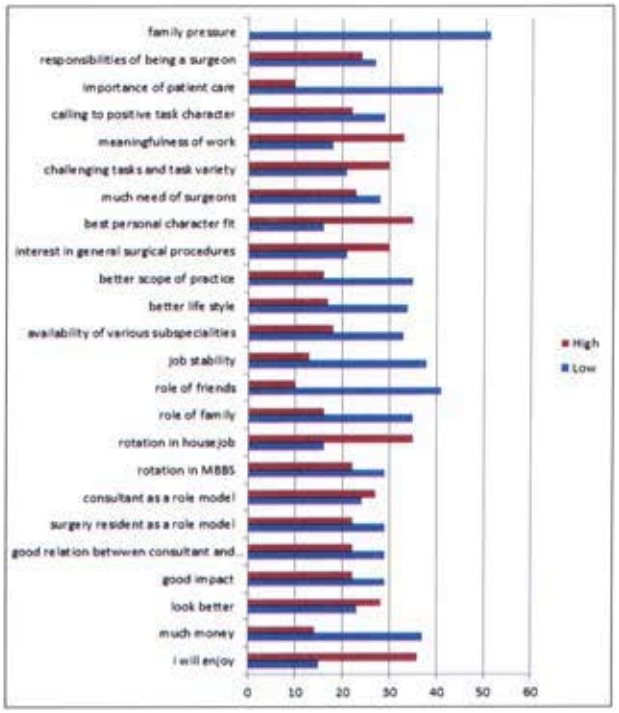


Fig-2: Factors of influence rated by level of importance by all of the respondents. Responses were considered high importance if respondents chose "very strong influence" or "major influence", and less important if "no influence", "minor influence" or intermediate influence". Comparisons were done using Pearson's Chi-Square Test. *p-value<0.05 was considered significant.

Table-1: Demographic details.

Demograhic details		
Age		27.61±1.721
Gender	Male	62.7%
	Female	37.3%
Year of residency	1st year	39.2%
	2 Year	15.7%
	3rd year	23.5%
	4th year	21.6%
Time elapsed between part -1 and house job		
	> 6 month	49.0%
	6 month-1 year	29.4%
	1st year-3 years	13.7%
	>3 years	7.8%

procedure and best personal character fit. The most common influences noted to be of low importance were family pressure, role of friends, job stability, scope of practice, much money in future and role of family.**(Fig-2).** For 1st year residents, influence of Rotation during house job was chosen as the most

Table-2: Top three most important factors rated by each of the four groups.

	Most important factor	Second most important factor	Third most important factor
1st year resident	Influence of rotation during house job	Interest in general surgery procedures	I shall enjoy surgery
2nd year resident	Best personal character fit	Influence of rotation during house job	I shall enjoy surgery
3rd year resident	I shalla enjoy surgery	Interest in general surgical procedure	Best personal character fit
4th year resident	I shall enjory surgery	Challenging tasks and task variety	Influence of rotation during house job

important factor of influence. For 2nd year residents, best personal character fit was chosen as a factor of high influence. For 3rdand 4thyear residents, the most frequently cited factor of high importance was I'll enjoy surgery. When comparing the responses between the four groups, there were significant differences in factor rating for the following factors of influence: Interest in general surgical procedures (p-value 0.010) and Responsibilities of being surgeon (p-value 0.033). (**Table-2**)

Discussion

This study highlighted the promoting factors that led the residents to choose surgery as a career. The most commonly cited factor(70.6%) among residents of all years was I'll enjoy surgery. Another factor (68.7%) commonly cited was Influence of rotation during house job while the rotation during MBBS had influenced 43.1% of respondents. When compared to another study conducted in Switzerland 13% of the respondents attributed preclinical training as a factor.[3,15,18-19] In our survey Best personal character fit was chosen by 68.6% of the respondents as a factor for choosing surgery as a career. This was consistent with two other studies which concluded that personal fit with the job was the most important influence that the students cited in planning for surgical career.[1,4] In our survey the second most common factor was the interest in general surgical procedures (58.8%). In general, surgery is considered to be an interesting and fascinating field which allows one to be passionate and involves use of combination of manual and technical skills.[3,11-19] In another study this factor was cited by 14% of the respondents as a motivational factor towards choosing surgery as a career.[3,11,14] Challenging tasks and task variety was cited by 58.8% of respondents. This was also consistent with another study which cited this factor to be the second most important motivating factor [3,16,18]. In our survey another important factor cited by the 53% of residents is consultant as a role model. This is similar to results of two other studies which attribute to be having a surgeon as a role model and mentoring an important factor in influencing students to choose surgery due to positive interactions with their role model.[1,2,5-10] Calling to field is cited by 43.1% of the respondents in our survey while in another study conducted in Switzerland this is cited by most of their respondents.[3]

Conclusion

This survey suggests that all the residents were satisfied with their career choice and they perceived surgery to be an enjoyable field. Majority of the residents also believed surgery as a best personal character fit. This survey also showed that there was the influence of rotation during house job in choosing surgery as a career whereas there was no role of family pressure in their career choice. We believe that this data can be helpful in overcoming the shortage of surgeons in the future.

Department of Peads Surgery
RMU Teaching Hospital.
www.esculapio.pk

References

1. Hossain N, Hossain T. Motivating factors and barriers towards choosing a career in general surgery: a review of the literature. Int Surg J 2015;2:121-4.
2. Lawal TA, Afolabi AO. Factors influencing the choice of surgery as a career by preregistration interns. African health sciences. 2013;13(3):814-9
3. Seelandt JC, Kaderli RM, Tschan F, Businger AP. The surgeon's perspective: promoting and discouraging factors for choosing a career in surgery as perceived by surgeons. PloS one. 2014 Jul 15;9(7):e102756.
4. Cochran A, Melby S, Neumayer LA. An Internet-based survey of factors influencing medical student selection of a general surgery

career. The American journal of surgery. 2005 Jun 30;189(6):742-6.

5. Odusanya OO, Nwawolo CC. Career aspirations of house officers in Lagos, Nigeria. Med Educ 2001; 35(5): 482-487.
6. Brownrigg JR, Khavandi K, McCollum CN. Career choices in 21st-century healthcare: Aiming for a moving target. Int J Surg 2008; 6(6): 435-436.
7. Delamothe T. Modernising Medical Careers: final report. BMJ 2008; 336(7635): 54-55.
8. Abioye IA, Ibrahim NA, Odesanya MO, Wright KO. The future of trauma care in a developing country: Interest of medical students and interns in surgery and surgical specialties. Int J Surg 2012; 10(4): 209-212.
9. Hauer KE, Durning SJ, Kernan WN, Fagan MJ, Mintz M, O'Sullivan PS, et al. Factors associated with medical students' career choicesregarding internal medicine. JAMA 2008; 300(10): 1154-1164.
10. Lefevre JH, Roupret M, Kerneis S, Karila L. Career choices of medical students: a national survey of 1780 students. Med Educ 2010; 44(6): 603-612. 7. Gelf and DV, Podnos YD, Wilson SE, Cooke J, Williams RA. Choosing general surgery: insights into career choices of current medical students. Arch Surg 2002; 137(8): 941-945; discussion 5-7.
11. Scott IM, Matejcek AN, Gowans MC, Wright BJ, Brenneis FR. Choosing a career in surgery: factors that influence Canadian medical students' interest in pursuing a surgical career. Can J Surg 2008; 51(5): 371-377.
12. Kozar RA, Anderson KD, Escobar-Chaves SL, Thiel MA, Brundage SI. Preclinical students: who are surgeons? J Surg Res 2004; 119(2): 113-116.
13. Baxter N, Cohen R, McLeod R. The impact of gender on the choice of surgery as a career. Am JSurg 1996; 172(4): 373-376.
14. Azizzadeh A, McCollum CH, Miller CC, 3rd, Holliday KM, Shilstone HC, Lucci A, Jr. Factors influencing career choice among medical students interested in surgery. CurrSurg 2003; 60(2): 210-213.
15. Yusufu LMD, Ameh EA, Wammanda RD, Odigie VI. Choice of specialty by preregistration House Officers. Nig J Surg 2004; 10(1): 8-10.
16. Griffen WO, Jr., Schwartz RW. Controllable lifestyle as a factor in choosing a medical career. Am JSurg 1990; 159(2): 189-190.
17. Lambert EM, Holmboe ES. The relationship between specialty choice and gender of U.S. medical students, 1990-2003. Acad Med 2005; 80(9): 797-802.
18. Buddeberg-Fischer B, Stamm M, Buddeberg C, Bauer G, Haemmig O, Knecht M, et al. The impact of gender and parenthood on physicians' careersprofessional and personal situation seven years after graduation. BMC Health Serv Res 2010; 10: 40.
19. Harrison RA, Gregg JL. A time for change: an exploration of attitudes toward part-timework in academia among women internists and their division chiefs. Acad Med 2009; 84(1): 80- 86. 18. work in academia among women internists and their division chiefs. Acad Med 2009; 84(1): 80- 86. 18. Park J, Philipp R, Hughes A. Do we value workPark J, Philipp R, Hughes A.

Original Article

GUILLAIN-BARRE SYNDROME, CLINICAL FEATURES AT PRESENTATION AND OUTCOME

Muhammad Azhar Shah, Mutiullah Khan, Azhar Hussain, Muhammad Latif, Ikram Ur Rahim and Zahabia Manzoor

Objective: To evaluate the frequency of clinical features of Guillain-Barre Syndrome at presentation and outcome of disease.

Methods: All patients who presented to accident and emergency department of Akhtar Saeed Trust Hospital Lahore and Farooq hospital Lahore; and were diagnosed to have Guillain-Barre Syndrome (using Brighton criteria for the diagnosis of Guillain-Barre syndrome)1 were included in the study. A total of 64 patients of Guillain-Barre Syndrome over a period of 3 years were studies. There were 37 male and 27 were female patients.

Results: Patients of adult age group with the age range from 15-73 were included in the study; and the highest incidence was in the age group 55-65 (57%). Regarding the antecedent infection, 40.6% had history of diarrhea and 26.56% had suffered from upper respiratory tract infection in the previous two to four weeks. As regards neurological features, 87.5% had acute flaccid paralysis, 53.12% had cranial nerves involvement, 73.43% had sensory deficits and 62.5% suffered from pain. Regarding autonomic dysfunction, out of 64 patients, 45.31% had tachycardia, 14.68% had bradycardia, 43.7% had paroxysmal hypertension, 17.18% had orthostatic hypotension, 17.18% had urinary bladder dysfunction, and 21.87% had diarrhea/constipation. Electromyography (EMG) was performed on all 64 patients, 3.12% had normal EMG, 43.75% were shown to have demyelinating neuropathy, 21.87% had axonal neuropathy and the results were equivocal in 31.25%. Out of 64 patients, 20.31% needed mechanical ventilation on admission and 25% needed mechanical ventilation during their stay in the hospital. After a follow up of 06 moths, 76.56% could walk independently, 15.62% patients had some disability due to their GBS and walked with some aids, while 7.81% died during their stay in the hospital.

Conclusions: Guillain-Barre Syndrome patients need careful monitoring for respiratory, autonomic and cardiovascular complications and may need ICU management in about 1/3rdof cases.

Keywords: guillain-barre syndrome.

Introduction

Guillain-Barre Syndrome (GBS) was first described by its present name by Georges Charles Guillain and Jean-Alexandre Barre[2] in 1916. The disease is still diagnosed on the basis of its clinical features supported by laboratory investigations. It is the leading cause of acute muscular paralysis in developing countries. Recently, its increased incidence was associated with zica virus infection.[6] Its subtypes include acute inflammatory demyelinating polyneuropathy (AIDP), acute motor axonal neuropathy (AMAN), acute motor-sensory axonal neuropathy (AMSAN) and Miller Fisher Syndrome. Previously studies have been performed to evaluate the subtypes and clinical presentation of GBS and their relationship to prognosis.[3,4] The presenting clinical features of GBS include acute ascending paralysis, bilateral facial palsy, diplopia, dysphagia, dysarthria, urinary retention, ophthal- moplegia, tachycardia, bradycardia, paroxysmal hypertension, orthostatic hypotension and shortness of breath on exertion. Early accurate diagnosis of Guillain-Barre Syndrome is important when specific treatment is most effective and patients need specific monitoring for respiratory, autonomic and cardiovascular complications. Brighton criteria for the diagnosis of Guillain-Barre syndrome was developed in 2009/2010 for early case detection, monitoring and treatment. In Pakistan,in most of the secondary patient care hospitals, ICU facilities are not available. So, most of the patients of GBS need to be transferred to tertiary care hospitals for management. Data from public sector hospitals in Pakistan suggests suspected rise in cases of GBS. This study was designed to emphasize the importance of early diagnosis and early referral to tertiary care

hospitals for further Management.

Methods

All patients who presented to Accident and Emergency department of Farooq hospital Lahore and Akhtar Saeed Trust Hospital Lahore with acute paralysis from August 2014 to July 2017 and were diagnosed to have GBS (using Brighton criteria for the diagnosis of Guillain-Barre Syndrome)1 were included in the study. Complete biochemical profiles were sent to the laboratory immediately which consisted of complete blood counts, blood glucose level, urea, creatinine, serum electrolytes, liver function tests, serum electrolytes, liver function tests. After their transfer to medical wards, cerebrospinal fluid analysis, Electromyography (EMG) and nerve conduction studies (NCS) were performed. MRI of brain and spinal cord was performed to exclude other possible diagnosis. The patients were monitored for respiratory complications by measuring bed side vital capacity (VC), maximal inspiratory pressure (MIP), and maximal expiratory pressure (MEP)5. Continuous cardiac and blood pressure monitoring was carried out for autonomic and cardiovascular complications associated with GBS. The patients were commenced on standard treatment of plasmapheresis or intravenous immunoglobulin. Most patients needed 6 to 10 total plasma volumes exchanged over a period of 10 to 14 days. Pain was managed by opiates and gabapentin. Deep vein thrombosis prophylaxis was provided by subcutaneous enoxaparin. Patients developing respiratory or cardiovascular complications were transferred to ICU for further management. Average length of hospital stay was between 1 to 2 months. A pre-designed Pro forma was used to collect the information about gender, age, symptoms of antecedent infection, neurological symptoms, autonomic dysfunction, mechanical ventilation on admission and during hospital stay, length of intensive care (ICU) and hospital stay, and outcome at 6 months. Data was analyzed by using SPSS version 17.

Results

A total of 64 patients of Guillain-Barre Syndrome over a period of 3 years were included in the study. Following were the salient features of the results of study. Gender as detailed in (Fig-1), 37 were male and 27 were female patients with male to female ratio of 1.4 **(Table-1)**. Patients of adult age group who suffered from Guillain-Barre Syndrome were studied and amongst them, majority were middle aged to old patients with the age range from 15-73 and the highest incidence was in the age group 55-65 (57%). Patients of paediatric age group (14 years and less) were not included in the study as they were managed in the paediatric department. As regards neurological symptoms on admission, out of 64 patients, 56 patients (87.5%) had acute flaccid paralysis, 34 patients (53.12%) had cranial nerves involvement, 47 patients (73.43%) had sensory deficits and 40 patients (62.5%) suffered from pain **(Table-2).** Regarding autonomic dysfunction, out of 64 patients, 29 patients (45.31%) had tachycardia, 03 patients (4.68%) had bradycardia, 28 patients (43.7%) had paroxysmal hypertension, 11 patients (17.18%) had orthostatic hypotension, 11 patients (17.18%) had urinary bladder dysfunction, and 14 patients (21.87%) had diarrhea/constipation **(Table-3).** Out of 64 patients, 13 patients (20.31%) needed mechanical ventilation admission and 16 patients (25%) needed mechanical ventilation during their stay in the hospital **(Table 4).** Electromyography was performed on all 64 patients, 02 patients (03.12%) had normal EMG, 28 patients (43.75%) were shown to have demyelinating neuropathy and 14 patients (21.87%) had axonal neuropathy. The results of electromyography were equivocal in 20 patients (31.25%) **(Table 5).**

After a follow up of 06 moths, 49 patients (76.56%) could walk independently, 10 patients (15.62%) had some disability due to their GBS and walked with some aids, while 05 patients (7.81%) died during their stay in the hospital **(Table 6).**

Table-1: Age and sex distribution..

		Frequency	Percentage
Gender	Male/female ration	37/27	1.4%
Age (Years)	(Years)	47(15-73)	
Antecedent infection	Diarrhea	25/64	40.6%
	Upper RTI	17/64	26.56%

Table-2: Neurological symptoms on admission.

Neurological symptoms on admission	Frequency	Percentage
Acute flaccid paralysis	56/64	87.5%
Cranial nerves involvement	34/64	53.12%
Sensory deficits	47/64	73.43%
Pain	40/64	62.5%

Table-3: Autonomic dysfunction.

Autonomic dysfunction	Frequency	Percentage
Tachycardia	29/64	45.31%
Bradycardia	3/64	04.68%
Paroxysmal hypertension	28/64	43.7%

Orthostatic hypotension	11/64	17.18%
Urinary bladder dysfunction	11/64	17.18%
Diarrhea / constipation	14/64	21.87%

Table-4: Mechanical ventilation.

Mechanical ventilation	Frequency	Percentage
Mechanical ventilation on admission	13/64	20.31%
Mechanical ventilation during the course of disease	16/64	25%

Table-5: Type of neuropathy.

Type of neuropathy	Frequency	Percentage
Normal	02/64	03.12%
Demyelination	28/64	43.75%
Axonal	14/64	21.87%
Equivocal	20/64	31.25%

Table-6: Outcome of six months.

Outcome at 6 months	Frequency	Percentage
Walking independently	49/64	76.56%
Patients with disability	10/64	15.62%
Deaths	05/64	07.81%

Discussion

A prospective cross-sectional and observational study comprising a total of 64 hospitalized patients with diagnosis of Guillain-Barre syndrome was carried out. All patients of Guillain-Barre syndrome irrespective of sex and mode of presentation were included; children below the age of 15 years usually were not included in the study as they were managed by the paediatric department. Frequency of various clinical features of Guillain-Barre Syndrome were noted; type of neuropathy according to EMG was diagnosed and the outcome in terms of discharge from the hospital or mortality was documented. The data derived from the study clearly shows that out of 64 patients studied, 37 were males and the remaining 27 were females. This male predominance is also supported by many international studies[7,8], and two other studies on Guillain-Barre syndrome recently carried out in Pakistan.[3,4]

The incidence of antecedent infection in our study was demonstrable in 67.18% of patients, 40.6% patients had history of diarrhea and 26.56% patients had history of upper respiratory tract infection in the preceding 2 to 4 weeks. The results were comparable to Shafqat et al[3] a previous study carried out in Pakistan. These results were in contrast to a few international studies[9,10] conducted in the past in which most patients reported upper respiratory tract infection as compared to diarrhea as antecedent infection. The most probable explanation for that is the far more occurrence of acute infective diarrhea in our part of the world. Regarding neurological symptoms at presentation, if we compare results of our study to the results ofFokkeet al,[12] a recently performed study in Netherlands, the frequency of acute flaccid paralysis was comparable, 87.5% versus 82.13%, cranial nerves involvement was more in patients in our study, 53.12% as compared to 36.27%. Sensory deficits were 73.43% as compared to 67.74%, and pain was present in in 62.5% of our patients as compared to 54.47% of patients in Fokkeet al.[12] If we compare our study results to Shafqatet al,[3] a study performed in Karachi, Pakistan, the acute flaccid paralysis in that study was 100% as compared to 87.5% in our study, cranial nerve involvement was 88% as compared to 53.12% and sensory deficits were present in 38%as compared to 73.43% of patients in our study.

As far as autonomic dysfunction is concerned, 21% of patients in our study had autonomic dysfunction. This prevalence of autonomic dysfunction was slightly more as compared to Anandan et al[11] a study performedin 2017 in USA, but was considerably less than Shafqatet al[3] a study performed in Pakistan in which autonomic dysfunction was 61%.

In our study, 20.31% of patients needed mechanical ventilation on admission and 25% needed the same during their stay in the hospital. Over all 45.31% patients of Guillain-Barre Syndrome needed mechanical ventilation during their course of disease, which were comparable to 55% of patients who needed mechanical ventilation as reported in Shafqatet al[3] in Karachi in 2006; but the percentage of patients who needed mechanical ventilation was higher in both thestudies conducted in Pakistan when we compare it to the world wide data of mechanical ventilation support needed for Guillain-Barre Syndrome patients. Even the percentage of patients who needed mechanical ventilationon admission in Pakistan was higher than the rest of the world. Most probably, because of poor socioeconomic conditions and the high rate of illiteracy, people seek medical advice late as compared to the developed world. The patients who have milder forms of GBS, most probably don't seek even medical advice. Regarding types of GBS on the basis of electromyography, predominant type was demyelinating (43.7%), followed by axonal (21.87%). The electromyography was normal in 3.12% of patients which does not rule out GBS.[13,1] The results were equivocal in 31.25% of patients. Although the results of our study were comparable to Shafqatet al[3] a study performed in

Karachi in 2006, but Iqbal et al[4], a recent study performed in Rawalpindi showed the dominant type of neuropathy on electromyography was axonal (74.43%), and demyelinating type was 22.72%. After a follow up of 06 months, 49 patients (76.56%) could walk independently, 10 patients (15.62%) patients had some disability due to their GBS and walked with some aids, however 05 patients (7.81%) died during their stay in the hospital. The worldwide mortality rate was 2-12%.[15]

Conclusion

Most patients of GBS in Pakistan have diarrhea as antecedent infection as compared to respiratory tract infection in the rest of the world. Acute flaccid paralysis is the commonest presentation of GBS as in the rest of the world. Cranial nerves involvement in Pakistan is higher if we compare it to GBS data worldwide. A high percentage of patients need respiratory support on admission as compared to the world. Patients need mandatory monitoring for complications of the disease during their stay in the hospital. Outcome of the disease is comparable to rest of the world if the patients are managed in a tertiary care hospital.

Department of Medicine
SIMS/ Servieces Hospital, Lahore
www.esculapio.pk

References

1.Oxford University Press © Fokke, C. et al. Brain 137, 3343 (2014). (Brighton criteria for Guillain-Barré syndrome)
2. Guillain et al., 1916
3. Shafqat S, Khealani BA, Awan F, Abedin SE. Guillain-Barré syndrome in Pakistan: similarity of demyelinating and axonal variants. Eur J Neurol. 2006 Jun;13(6):662-5.
4. Waseem Iqbal, Tahir Mukhtar Sayed, WasimWali, Nadeem Ahmed, AamirWaheed Butt, Zaheer Ahmad Gil. IS Guillain-barré Syndrome Different In Pakistan? Pak Armed Forces Med J 2018; 68 (1): 119-24
5. Lawn ND, Fletcher DD, Henderson RD, Wolter TD, Wijdicks EFM. Anticipating mechanical ventilation in Guillain-Barré syndrome. Arch Neurol. 2001;58(6):893898.
6. David W Smith, John Mackenzie, Zika virus and Guillain-Barré syndrome: another viral cause to add to the list, The Lancet, Volume 387, Issue 10027, 915 April 2016, Pages 1486-1488
7. Kushnir M; Klein C; Pollak L; Rabey JM, Evolving pattern of Guillain-Barre syndrome in a community hospital in Israel. ActaNeurol Scand. 2008; 117(5):347-50 (ISSN: 1600-0404)
8.Landaverde JM; Danovaro-Holliday MC; Trumbo SP; Pacis-Tirso CL; Ruiz-Matus C
Guillain-Barré syndrome in children aged <15 years in Latin America and the Caribbean: baseline rates in the context of the influenza A (H1N1) pandemic. J Infect Dis. 2010; 201(5):746-50 (ISSN: 1537-6613)
9.Jacobs BC, Rothbarth PH, van der Meché FG, Herbrink P, Schmitz PI, de Klerk MA, et al. The spectrum of antecedent infections in Guillain-Barré syndrome: a case-control study. Neurology. 1998 Oct. 51(4):1110-5.
10.Nelson L, Gormley R, Riddle MS, Tribble DR, Porter CK. The epidemiology of Guillain-Barré Syndrome in U.S. military personnel: a case-control study. BMC Res Notes. 2009 Aug 26. 2:171.
11.Anandan C; Khuder SA; Koffman BM. Prevalence of autonomic dysfunction in hospitalized patients with Guillain-Barré syndrome. Muscle Nerve. 2017; 56(2):331-333 (ISSN: 1097-4598).
12. Christiaan Fokke, Bianca van den Berg, Judith Drenthen, Christa Walgaard, Pieter Antoon van Doorn1 and Bart Casper Jacobs, Diagnosis of Guillain-Barre´ syndrome and validation of Brighton criteria, Brain 2014: 137; 3343.
13.Albers JW, Kelly JJ Jr. Acquired inflammatory demyelinating polyneuropathies: clinical and electrodiagnostic features. Muscle Nerve. 1989 Jun. 12(6):435-51.
14. Van den Bergh PY, Piéret F. Electrodiagnostic criteria for acute and chronic inflammatory demyelinating polyradiculoneuropathy. Muscle Nerve. 2004 Apr. 29(4):565-74.
15. Alshekhlee A, Hussain Z, Sultan B, Katirji B. Guillain-Barré syndrome: incidence and mortality rates in US hospitals. Neurology. 2008 Apr 29. 70(18):1608-13.

Original Article

Prevalence of Constipation in Healthy Population, an Observational Cross Sectional Study

Asma Sikandar, Syeda Maryam Wasif, Mohsin Zaheer, Sarwat Nazir, Aasia Noor, Nadir Zafar Khan and Ahsan Numan

Objective: To assess the prevalence of constipation in healthy population ,study was done at hospital employees and students at PGMI/Lahore General hospital , Lahore .

Methods: This was an observational cross sectional study done in sample population that includes employees and students at PGMI/Lahore general Hospital. All subjects were given set of questions which include 4 constipation related symptoms.

1 - Frequency of bowel movements on a scale of 0- 4.
2 - Difficulty or painful evacuation effort on a scale of 0-4.
3 - Assistance required to evacuate.
4 - Duration of symptoms.

Total score was 15 of which 7 was the cut off score, people reporting score 7 and above were considered as constipated while below 7 were healthy non-constipated.

Results: Total 778 healthy individuals (clinically) interviewed. The age range was between 10year to 60 years old.66% participants were female whereas 34% were male. According to set of questions 14% participants reported constipation.

Conclusions: Constipation is a common complaint but poorly defined clinical constellation, the definition of constipation is different among studies, where most studies are based on a questionnaire and may result from organic condition. Overall, prevalence of constipation in adults has been estimated as 16% worldwide which is very close to our finding of 14% of healthy population reporting constipation. Demographics of subjects of most of 14% are female and above 55 years of age.

Keywords: constipation, healthy individuals, PGMI/Lahore General Hospital .

Introduction

Constipation is a common complaint but a poorly defined clinical constellation. It is difficult to describe normal bowel function but most people evacuate between three times per day and once every three days.[1] Marginal infrequency beyond this may be attributed to poor diet and frequently responds to bulk laxatives. The definition of constipation is different among studies, where most studies are based on a questionnaire and may result from an organic condition. Overall, the average prevalence of constipation in adults has been estimated as 16% worldwide (varies between 0.7% and 79%); whereas the prevalence of 33.5% was attributed to adults aged 60 to 110 years.[2] Several prior attempts have been made to study constipation. Dross man and coworkers[3] surveyed 789 students and hospital employees and found that 18.5 percent strained at stool more than 25 percent of the time. Moreover, 4.2 percent reported to or fewer bowel movements per week. These figures were slightly higher than Thompson and Heaton[4] reported in an earlier survey. Although the survey by Dross man and colleagues queried abdominal pain, distention and incomplete evacuation, it did so in the context of diagnosis of irritable bowel syndrome rather than constipation. Much data have been published regarding psychological abnormalities in patients with constipation. One prior publication included a comparison of symptoms and type of constipation.

It has been observed clinically in patients with Parkinsonism that constipation can be present as a part of Parkinson disease. Frequency of non-motor symptoms in Parkinson's disease presenting to tertiary care Centre in Pakistan: an observational, cross-sectional study,[5] which showed that 56 percent of our population with Parkinson's disease had constipation; however, 31% had constipation before onset of disease.

Methods

This was an observational cross sectional study done in sample population that includes employees and students at PGMI/Lahore general Hospital. All subjects were given set of questions which include 4

constipation related symptoms.

1- Frequency of bowel movements on a scale of 0-4.
2- Difficulty or painful evacuation effort on a scale of 0-4.
3 - Assistance required to evacuate.
4 - Duration of symptoms.

Total score was 15 of which 7 was the cut off score, people reporting score 7 and above were considered as constipated while below 7 were healthy non-constipated. Clinically not diagnosed for any chronic disease like Diabetes, Hypertension, ischemic heart disease, cerebrovascular accidents. Both genders were included. Ages ranging from 10 60 were included. Marked abdominal pain or significant distention or cramping. Presence of any chronic medical condition that may preclude self-care laxative treatment (paraplegia, colostomy). Patients who presented with advanced severe and unstable disease like Diabetes, Mellitus, Hypertension, Ischemic heart disease). Subjects who presented with symptoms and signs of systemic medical conditions that could give rise to constipation like Hypothyroidism. Patients taking drugs that can cause constipation like opioids e.g. morphine, codeine, anti-cholinergic like atropine, trihexyphenidyl, Tricyclic antidepressants, Calcium channel blockers, anti-Parkinson drugs. Data with name, age, gender, occupational status and dietary habits were asked along designed questionnaire to fulfill all the inclusion and exclusion criteria. Questions regarding symptoms of different diseases that were mentioned in the exclusion criteria were asked. Data is analyzed by SPSS version 21 and is used to measure frequencies of responses per item. It has scoring range 1-6 that's normal, score 7 and above 7 is classified as constipated.

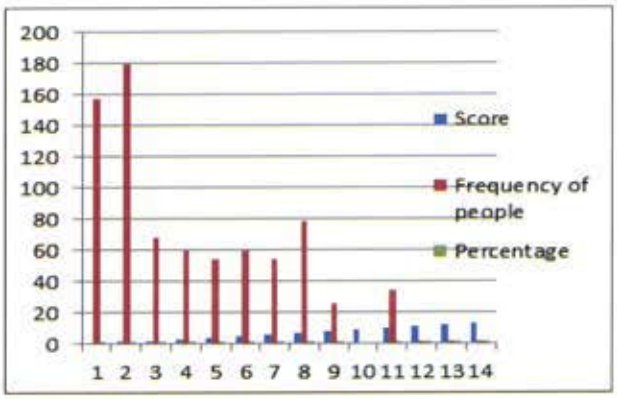
Results

Total 778 healthy individuals (clinically) interviewed. The age range was between 10-60 years old.

Sixty six percent participants were female whereas 34% were male. According to set of questions 14% participants reported constipation.

Discussion

180/778 participants reported minimal intensity and scored 2/14. Pathophysiology and current therapeutic approaches towards Chronic Constipation was studied in a research in 2016 by Sharma A. & Rao S. Later it was published in 2017 in a Pharmaco Journal. t is a common and persistent problem which is faced by a huge number of people worldwide. Term Constipation is defined as



X-axis: *no of score, y-score: number of people.*

Excessive straining, a sense of incomplete evacuation, lengthy or failed attempts to defecate, abdominal bloating or pain, hard consistency of stool and use of digital maneuvers for evacuation of stool by Sharma and colleagues.[6] As participants of current research selected any 2 of 14 constipation criteria given in questionnaire. 76% population reported symptoms of constipation but with normal and healthy severity of it. Healthy severity as scored less than cut off score 7. This showed that prevalence among healthy population is at minimal concern. Leung, Riutta, Kotecha & Rosse in 2011stated that Chronic Constipation is managed and treated by etiology and evidence-based causes. Dietary fibers, exercise and fluids are the standard advice to treat chronic constipation.[7] For treatment point of view, such people can be guided and treated easily. And most of them do not consult health practitioners but change diet or follow domestic tips to overcome them. Only 6% research participants reported maximum score and that is 13 and 14. That might have some history, genetic factor or other biological issues, but they did not report any disease or diagnosed severe medical issue. Fourteen percent of healthy population reported symptoms of constipation interpreted as "constipated", which is close to a study done in western countries, where prevalence rate was stated as between 2%-28%.[9-11] which is supported more closely by a study done in china,[12] which reported that only 14% of general population reported constipation which is exactly the same percentage observed in Pakistani population. Demographics of our study found that most of 14% are female and above 55 year, which is supported by retrieved studies evaluation where eleven studies

were retrieved; they reveal a they reveal a prevalence of constipation that varied from 2.6% to 26.9%. The most frequently cited associated factors were female gender and advanced Age, which were cited in 11 and 7 of the studies, respectively. Prevalence rates reported by the selected studies were heterogeneous.[5] higher prevalence in female gender is also supported by a systemic review done in North America[9,10] where they found that females were more likely to report FC than males, which was consistent with that in North America, Europe, and Oceania For research concerns, researchers can be interested in finding out that is there any relationship of age and gender in diagnosis, prevalence and severity of constipation.

Conclusion

Constipation is a common complaint but poorly defined clinical constellation, the definition of constipation is different among studies , where most studies are based on a questionnaire and may result from organic condition. Overall, prevalence of constipation in adults has been estimated as 16% worldwide which is very close to our finding of 14% of healthy population reporting constipation. Demographics of subjects of most of 14% are female and above 55 years of age.

Department of Neurology
Lahore General Hospital, Lahore
www.esculapio.pk

References

1.Whitehead WE, Chaussade S, Corazziari E, Kumar D. Report of an international workshop on management of constipation. Int J Gastroenterol 1991; 4:99-113.

2.Everhart JE, Ruhl CE. Burden of digestive diseases in the United States part II: lower gastrointestinal diseases. Gastroenterology 2009;136: 74154.

3.Drossman DA, Sandier RS, McKee DC, Lovitz AJ. Bowel patterns among subjects not seeking health care. Gastroenterology 1982; 83:529-34.

4.Thompson WG, Heaton KW. Functional bowel disorders in apparently healthy people. Gastroenterology 1980;79:283-8.

5.Mukhtar S, Imran R, Zaheer M, et al, Frequency of non-motor symptoms in Parkinson's disease presenting to tertiary care centre in Pakistan: an observational, cross-sectional study, BMJ Open 2018;8:e019172. doi:10.1136/bmjopen-2017-019172

6.Division of Gastroenterology and Hepatology, M. C. (2017). NCBI. Retrieved from PubMed: https://www.ncbi.nlm.nih.gov/pubmed/28185025

7.Lawrence Leung, T. R. (2011). Chronic Constipation: An Evidence-Based Review. The Journal of the American Board of Family Medicine, 436-451.

8.Journal of Wound, Ostomy and Continence Nursing , January/February 2014, Volume 41 Number 1 , p 70 - 76

9.Review Epidemiology of constipation in North America: a systematic review. Higgins PD, Johanson J.Am J Gastroenterol. 2004 Apr; 99(4):750-9.

10.A review of the literature on gender and age differences in the prevalence and characteristics of constipation in North America. McCrea GL, Miaskowski C, Stotts NA, Macera L, Varma MG, J Pain Symptom Manage. 2009 Apr; 37(4):737-45

11.Prevalence and ramifications of chronic constipation. HarrisLA ,Manag Care Interface. 2005 Aug; 18(8):23-30.

12.Gastroenterol Res Pract. 2014; 2014: 532734.