

PMDC No. IP0042

ISSN (Online) 2309-592X

ISSN (Print) 2309-3080

Volume 11, Issue 1, January-March, 2015

Esculapio

Journal of Services Institute of Medical Sciences, Lahore.



Comparison of Apoptotic Effect of Withania Coagulans in Helal, Viro and BHK Cancer Cell Lines

Effect of Aloe Vera Leaf Gel Extract on Lipid Profiles of Alloxan Induced Diabetic Rabbits

Frequency of Common Pathogens in Vaginal Discharge

Encountering Xanthogranulomatous Inflammation in a Myriad of Settings

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JOURNAL OF SERVICES INSTITUTE OF MEDICAL SCIENCES, LAHORE.

VOLUME. 11

JANUARY - MARCH 2015

ISSUE. 01

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Original Article

EFFECT OF SEASONAL VARIATIONS ON ORGAN WEIGHTS (FAT, LIVER AND GONADS) IN A MALE POIKILOTHERM VERTEBRATE, UROMASTYX HARDWICKII

Ghazala Qureshi, Samina Malik, Aalia Dilawar, Tanvir Shirvani, Usman Khurram and Ramsha Khan

Objective: *Uromastyx hardwickii*, a local lacertilian species, is widely distributed in the Indo-Pakistan subcontinent and inhabits mostly the arid regions of the country. This study has been carried out to assess the seasonal variations on fat, liver and gonads in a poikilotherm vertebrate species and to develop an experimental model for the study of lipid metabolism in higher vertebrates including mammals.

Material and Methods: This cross-sectional study was carried out on male *Uromastyx hardwickii* (n=60). On sacrificing the animals, abdominal fat pads, liver and gonads were quickly removed, cleaned and weighed.

Results: Maximal increase in fat pad weight was observed in autumn. Liver weight was significantly maximal in autumn and less in summer while testicular weights showed marked seasonality in weight and maximum increase in spring and decrease in summer.

Conclusion: Lipid metabolism in *Uromastyx hardwickii* undergoes significant alteration in relation to season. There is significant ($P < 0.05$) increase in liver weight, fat pad and testicular weight during different parts of the year.

Key words: Seasonal variation, organ weights, *uromastyx hardwickii*.

Introduction

Uromastyx hardwickii: Animals of this genus are terrestrial, preferably found in sandy places and semi-rocky areas. Poikilotherm is a Greek word meaning an animal whose body temperature fluctuates with that of environment. During colder months of the year (Nov- March), these animals become sluggish and metabolic activity declines. Abdominal fat pads enlarge before they go into hibernation and animals maintain them throughout the hibernating period.¹ Monthly changes in plasma and testicular androgen concentration of spiny tailed lizard, *Uromastix hardwickii* are correlated with changes in testicular weights and spermatogenic cycle in this species.² It has previously been shown that in cold acclimatized hamsters approximately 50% lipids from brown fat tissue are depleted during arousal. It is surmised that heat produced by the combustion of the lipid during arousal process could be the major factor for the heat needed to re-warm the animal following hibernation.³

In the oviparous lizard, *Phrynocephalus przewalski*, liver and muscle of these lizards are principal sites of lipid storage. Triacylglycerol mainly deposited in liver, while phospholipids are stored in the muscle and brain.⁴

Abdominal fat bodies and total body fat level exhibit

a seasonal cycle in many temperate and tropical lizards. Lipids stored in fat bodies are used for gonadal recrudescence and in females for ovarian development during the winter months.⁵ In study on gecko *japonicus* lizard in Taiwan, has no visible fat bodies and most lipids are stored in carcass, specially in posterior part of carcass and around posterior legs and tail. This lizard can also store lipids in the liver. Their fat bodies are utilized for reproduction and semantic maintenance during hibernation period.⁶ Hamsters when kept at increased ambient temperature increase their preference for saturated fats and this suggests that temperature dependent fatty acid choice in wide range of animals.⁷ The present study on *Uromastix hardwickii* was undertaken with the possibility of defining a convenient model for the study of lipid metabolism and fat mobilization specially in relation to seasonal and environmental changes.

Materials and Methods

This cross-sectional study was carried out on 60 male *Uromastix hardwickii*. The animals used in this study were collected from the vicinity of Bahawalpur (29°N, 24°E) in four different seasons through the course of one year and were immediately transported to the Physiology laboratory, University of Health Sciences, Lahore, under appropriate conditions. To

assess the effects of seasonal variations on organ weights (fat pad, liver and gonads), animals were divided into four groups on the basis of the time of the year of collection and the local ambient temperature during that period (**Table: 1**). Males were separated from females on the basis of snout vent length (SVL). Animals with SVL of less than 15 cm were not used in this study.

Sample Collection:

In all, 60 animals were sacrificed within 48 hrs of their arrival in the laboratory. On killing the animals fat pads, liver and gonads were quickly removed, cleaned and weighed.

Statistical Analysis:

The data was entered and analyzed using SPSS 16.0. Mean \pm SEM of each parameter was determined. One-way ANOVA was applied to observe group mean difference for more than two groups. Tukey test was applied to observe which group mean differs. p value < 0.05 was considered statistically significant.

Table-1: Ambient temperatures and seasons at the time catches were made in the field.

Group	Seasons	Average ambient Temperature (°C)
I	Spring	24
II	Summer	35
III	Autumn	26
IV	Winter	11

Table-2: Show fat pad weight, liver weight and testicular weight in different seasons of the year.

Groups	Fat Pad Weight(g)	Liver Weight(g)	Testicular Weight(g)
Mar-Apr. (Spring)	4.6 \pm 0.84	4.6 \pm 0.66	2.0 \pm 0.41
June (Summer)	2.0 \pm 0.40	3.0 \pm 0.27	0.1 \pm 0.01
Oct. (Autumn)	8.4 \pm 0.30	5.7 \pm 0.16	0.4 \pm 0.06
Jan (Winter)	5.1 \pm 0.31	4.4 \pm 0.32	0.5 \pm 0.04
Significance	P<0.05	P<0.05	P<0.05

Results

Seasonal variations: **Table-2** show fat pad weight, liver weight and testicular weight in different seasons of the year. Maximal increase in fat pad weight was observed in autumn (8.4 \pm 0.30 g) and decline trend were seen in winter (5.1 \pm 0.31g) spring (4.6 \pm 0.84g) and summer (2.0 \pm 0.40 g). Liver

weight was significantly maximal (5.7 \pm 0.16 g) in autumn and less in summer (3.0 \pm 0.27 g). Testicular weights showed marked seasonality in weight. Maximum testicular weight was observed in spring (2.0 \pm 0.41 g) and lowest in summer (0.1 \pm 0.01 g).

Discussion

At low temperatures, the strategy of metabolism in tissues of hibernators is to provide adequate nutritional ensure stores and availability of chemical energy.⁸ There were significant (p< 0.05) changes seen in fat pads during different parts of the year. This means that fat bodies were well formed in autumn, before the animals get into winter hibernation. During winter, fat pad weight showed a significant decline which continued during spring and summer when it became minimal. It has been reported in *Uromastix hardwickii*, soon after these animals came out of hibernation, their fat reserves decrease in weight.⁹ Mean liver weight was maximum in autumn and then showed significant decline till he summer season. These changes are in agreement with Xiang and Peichao who showed that lipid stored at this site can be used for semantic maintenance during hibernation period and partially for the demands of reproduction.¹⁰ In another study no change in weight of liver along with kidneys and heart has been observed in hibernating and non-hibernating animals.¹¹ In spring, mean testicular weight was highest as testes were full of sperms and then weights began to decrease in summer indicating that testis in this species undergo sudden regression and this state continues till autumn. In winter, testicular weight has been observed to steadily increase and become maximum in spring as both spermatids and sperms are present and testes along with epididymus are full of mature sperms.¹² However another study reveals that growth is low, but not arrested in *C. versicolor* lizard during winter.¹³

Conclusion

There is significant increase (p < 0.05) in liver, fat pad and testicular weight during different parts of the year. There is steady increase in the weights of different organs including liver, fat pad and gonads from spring to autumn because lipids and fats are used for survival during hibernation and reproduction.

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Case Series

COMPARISON OF APOPTOTIC EFFECT OF WITHANIA COAGULANS IN HELA 1, VIRO AND BHK CANCER CELL LINES

Sadia Qureshi, Saba Khalid, MH Qazi and Nakshab Choudhry

Objectives: Cancer is the second leading cause of death and has a complex etiology. Efforts are being made to target different components for its treatment. Developments in the field of molecular biology have led the researchers to target apoptotic pathway. This study has been designed to assess the apoptotic effect of the extract of withaniacoagulans on different cancer cell lines.

Methodology: This study was designed to check the anticancer activity of withaniacoagulans and to compare it in different cancer cell lines.

Results: The extract of withaniacoagulans proved to be equally effective in hela, vero and bhk cell lines even at concentration of 10µg/ml.

Conclusions: The extract has a potential to act as apoptotic compound. Study can be elaborated by isolating different components and assessing their role as apoptotic molecules on individual basis.

Key words: Withaniacoagulans, cancer cell lines & apoptosis

Introduction

Cancer a disease of complex etiology is one of the leading causes of death in the world and is still difficult to treat.^{1,2} The programmed cell death serves as a natural barrier to cancer development.³ Cell death can proceed by different mechanisms apoptosis being the typical route of cell demise under physiological conditions.^{4,6} Imperfections in the cell death mechanisms not only result in cancer but also ensure the pathological cell growth and proliferation which results in progression of cancer. Several mechanisms by which cancer cells escape endogenous cell death have been identified, hence identifying how cancer cells achieve selective advantage of survival. Molecules that create the barriers to cell death within tumors have been identified as suitable targets for drug discovery. The main idea is either to restore the integrity of natural pathways for cell turnover or promoting cell death or to induce the activation of the activators of endogenous cell death which are sometimes silenced in cancer cells.^{7,8} Resistance of cancers to conventional therapies has stimulated the researchers to search for novel stratagems for the cancer cell demise.^{3,4}

The goal of any therapeutic strategy should be to treat the cancer cells with limited harmful effect to the normal cell function. In existing years, the naturally occurring compounds and their synthetic analogs have attained great attention of the

researchers in the field of cancer research as they have proved to be the promising anti-cancer agents because of their non-toxic or less toxic effects and compelling anti-cancer properties. In addition to that different epidemiological studies have revealed that in individuals whose main component of food is from plant sources are a lower risk of cancer.⁹ Therefore, identifying anti-cancer compounds in plant extracts has become the major strategy to treat cancers. Nowadays almost 80% of the world's population is using plant derived medicine for the maintenance of health and treatment of diseases because of its very less side effects.¹⁰

Pakistan is very rich in plant resources specially the medicinal ones. Almost 1,000 species of medicinal plants have been reported in the Peshawar region only and 500 species of them are being used for health care practices. Moreover the medicinal plants have mammoth potential but unluckily very little is known about the actual size of production, their capabilities, their conservation status etc. and very little research is carried out in this field so far in Pakistan.¹¹

Withania Coagulans is usually found in Afghanistan, India and southern Pakistan. The common name of Withania Coagulans is panir or vegetable rennet and it belongs to Solanaceae family. Withaniacoagulans is an important medicinal herb and a number of phytochemicals have been isolated from it, which are used in different herbal pharmaceutical products. Phytochemical analysis of the hydro alcoholic

fraction of withania showed the presence of steroids, alkaloids, phenolic compounds, tannins, saponins, carbohydrates, proteins, amino acids and organic acids. The chloroform fraction showed the presence of steroids and alkaloids as main components. Pharmacological evaluation has shown the association of activities with the specific steroidal lactones known as Withanolides present in Withania. Major Withanolides present in Withaniacoagulans are Withaferin A and Withanolide A and Withanone.¹¹⁻¹³ Withanolides have proved to be potent suppressors of NF- κ B (nuclear factor kappa-light-chain-enhancer of activated B cells). This suppression is mediated through inhibition of IKK (I κ B kinase). This mechanism may account for the ability of Withanolides to suppress the expression of gene products that regulate apoptosis, proliferation, angiogenesis and invasion and hence may prove to be important anticancer agent.^{10,14,15}

Methodology

This study was designed to check the anticancer activity of withaniacoagulans and to compare it in different cancer cell lines.

Identification of plant:

Identification of the plant was done by Prof. Dr. Tahira Mughal (Prof. of Botany at Lahore College for Women University).

Extraction procedure:

The plant was dried in the shade after collection and identification. The plant material was ground to powder. Then the powder was placed in the thimble of Soxhlet and methanolic extract was collected at 60°C. The methanol was evaporated under vacuum by rotatory evaporator to get crude methanolic extract.

Stock solution:

1 gram of extract was dissolved in 1 ml of DMSO (Dimethyl sulfoxide) to prepare stock solution of 1000 μ g/ μ l then serial dilutions were made (250 μ g/ μ l, 100 μ g/ μ l, 50 μ g/ μ l, 25 μ g/ μ l, 10 μ g/ μ l).

Cell Lines: Three cell lines HeLa (developed from cervical cancer cells), Viro (developed from kidney epithelial cells) and BHK (derived from baby hamster kidney fibroblasts) were obtained from School of biological Sciences University of The Punjab and were cultured according to the standard procedure.

Reagents & apparatus: All reagents used were of analytical quality and were obtained from GIBCO Invitrogen USA. Methyltetrazolium salt (MTT salt) and DMSO were obtained from MB cell (Korea).

Haemocytometer used to count cells was by Marienfeld Germany and all plastic ware required for the experiment was procured from Oxygen life sciences, California.

HeLa, Viro and BHK cell lines were cultured at 37°C with 5% CO₂ in Dulbaco's Modified Eagle's Medium (DMEM) containing 10% heat inactivated fetal bovine serum (FBS), 2mM L- glutamate, 100 U/ml penicillin and 100 U/ml of streptomycin and cultures were split 1:3 in 25cm culture flask as follows:

1. Wash the cells twice with about 1ml PBS (phosphate buffer saline)
2. Then about 1-2 ml trypsin was added to the flask and placed at 37 C for 5-10 minutes.
3. After the cells were detached from the surface, about 1ml culture medium was added and the cells transferred to a 15ml falcon tube. Cells were transferred into the new culture flasks with fresh culture medium for future use.

Preparation of 96 wells culture plate for MTT assay:

The stock solutions were taken from the primary cultures. Three 96 wells culture plates were prepared for the performance of MTT assay to evaluate anticancer effect of WithaniaCoagulans in Hela, Viro and BHK cell lines. Cells were counted with the help of Haemocytometer. After calculation of the total number of cells, cell suspensions of desired dilutions were prepared to obtain 5 \times 10³ cells per well.

MTT Assay:

Short 96 well assay: Assay was performed in duplicates.

Preparation of Solutions:

1. MTT 5mg/ml of Phosphate Buffer Saline (PBS)
2. Extraction Buffer (SDS 20%; DMSO 50%)

Procedure:

1. 5 \times 10³ cells per well in 96 cavity plates were taken in 0.2ml of the medium (DMEM).
2. Different concentrations of withaniacoagulans extract solution were added and incubated at 370 C in the presence of 5% CO₂ for 24 hrs.
3. 0.025 ml of MTT reagent was added & was incubated for two hrs at 370 C.
4. Then the media was aspirated and the plates were dried while patting slowly on a tissue paper.
5. 1 ml of extraction buffer was added & was incubated again overnight
6. Optical density was read at 570nm in Elisa Reader.
7. Cell viability was calculated as follows

$$\text{Relative cell viability} = \frac{\text{OD at 570nm of the sample} \times 100}{\text{OD at 570 nm of Blank}}$$

Results

With aniacoagulansmethanolic extract was used in

Vero and Bhk cell lines. Extract induced apoptosis even at concentration of 10µg/µl (minimum concentration used) (see Fig:1). Fig:2 shows that the apoptotic effect of withaniacoagulans extract is comparable and same extent of apoptosis occurs in three cell lines even at very low concentration.

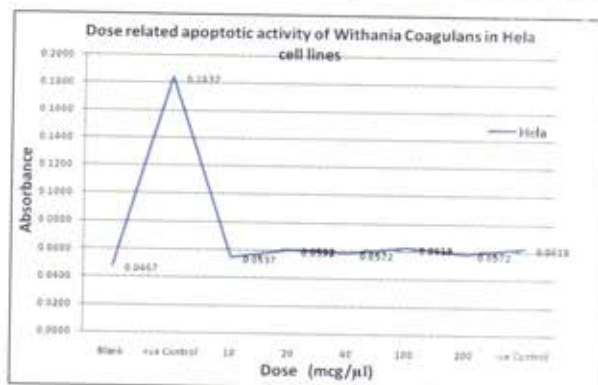


Fig-1: showing the apoptotic effect of Withania Coagulans in Hela cell lines.

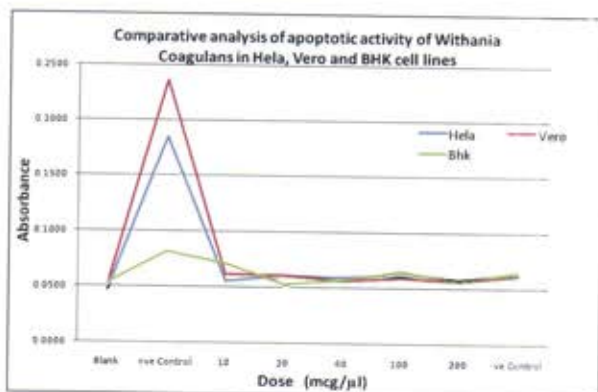


Fig-2: Showing comparison of apoptotic effect of Withania Coagulans in Hela, Vero and BHK cell lines

Discussion

Our study has proved that the active compounds in WithaniaCoagulans have apoptotic activity in human cancer cell lines even at a dose of 10µgm/µl. When a comparison was made for the apoptotic activity of WithaniaCoagulans amongst the three cell lines namely Hela, Vero and BHK, it showed that all the cell lines almost behaved the same way (see fig: 2). With positive controls they exhibited variable absorbance but when they were treated with WithaniaCoagulans extract the absorbance was markedly decreased becoming zero in Hela cell lines at a concentration of 10µgm/µl, in Vero cell lines at a concentration of 40µgm/µl and in BHK cell lines at a concentration of 20µgm/µl. Our results are comparable with studies conducted with the extracts of WithaniaSomnifera in human and with WithaniaCoagulans in animals.^{10,11,16}

Conclusion

It will prove to be very effective for the treatment of different types of cancers and can be used to design new therapy regimes targeting cell death mechanisms in cancer cells.

Limitations and Future Scope

The components of the extract should be separated out to find out the effective anti cancer compound. Moreover a study tracing the intracellular pathway to which the specific compounds of the extract target will be more conclusive.

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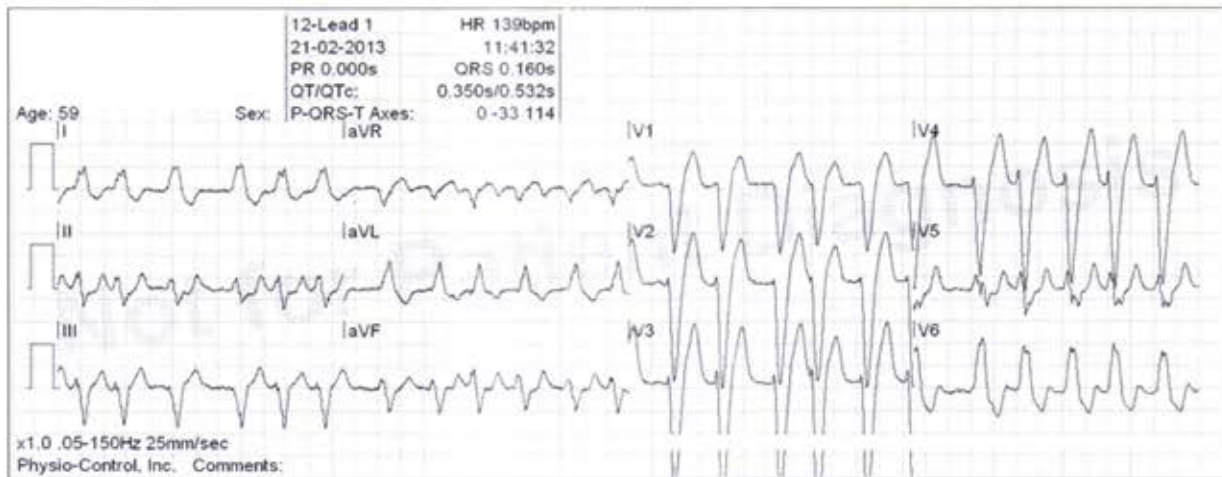
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Picture Quiz

This patient woke up 4 hours ago with shortness of breath, presyncope. What is diagnosis?



See answer on page # 31

Original Article

SURGICAL OUTCOME OF SCLERAL BUCKLING VERSUS PARS PLANA VITRECTOMY IN PRIMARY PSEUDOPHAKIC RHEGMATOGENOUS RETINAL DETACHMENT

Muhammad Naeem, Qasim Lateef, Tehmina Jahangir, Bilal Zaheer, Haroon Tayyab and Asad Aslam Khan

Objective: To evaluate anatomical and visual outcome of scleral buckling surgery versus pars plana vitrectomy in pseudophakic patients with rhegmatogenous retinal detachment.

Material and Methods: Sixty patients having rhegmatogenous retinal detachment, fulfilling inclusion and exclusion criteria were recruited for study. The patients were divided randomly in two groups of thirty patients each. In group (A) 30 patients underwent conventional scleral buckling and in group (B), 30 patients with retinal detachment had pars plana vitrectomy done. Almost all patients were having macula off, with history of decreased visual acuity ranging between one week to eight weeks. The patients with grade C proliferative vitreo-retinopathy (PVR), previous scleral buckling / vitrectomy, posterior vitreous detachment and pseudophakic with posterior capsular rupture were also excluded. After detailed preoperative assessment and surgical plan, standard scleral buckling procedure including encircling and local explants with cryo-therapy, was used to repair all primary rhegmatogenous detachments in group A. Sub-retinal fluid (SRF) drainage was performed, as needed. In group B, 20G pars plana vitrectomy was performed in all pseudophakic retinal detachments. All the per-operative and postoperative complications were recorded. The outcome measures of study were visual outcome and anatomical status of retina, after retinal re-attachment surgery. The patients were followed at least six months after surgery regarding, visual acuity, intra-ocular pressure, retinal re-attachment.

Results: Thirty eyes in group A were treated by scleral buckling and cryotherapy, while 30 eyes in group B were managed by primary pars plana vitrectomy. All retinal detachments were macula off, with grade A or B, PVR. Anatomical success rate in Scleral buckling group was 86.66 % and 13.33 % patients had re-detachment, so pars plana vitrectomy was performed. One patient was managed with intra-vitreous SF6 gas injection and 360 degree laser barrage. Anatomical success rate in pars plana vitrectomy group was 90 %, while 10 % patients were managed by second surgery. No significant complication was noted in both types of surgeries.

Conclusion: Pseudophakic rhegmatogenous retinal detachments, can be managed effectively by pars plana vitrectomy and scleral buckling, with comparable visual and anatomical outcome.

Key words: Scleral buckle, pars plana vitrectomy, pseudophakic, rhegmatogenous retinal detachment.

Introduction

Rhegmatogenous retinal detachment (RRD) can be managed by different methods, like pneumatic retinopexy, scleral buckling and pars plana vitrectomy. The decision of appropriate surgical procedure depends on many factors and also status of fellow eye. The following factors are always considered in planning a retinal re-attachment surgery like size of break, site of break, extent of detachment, retinal degenerations, associated posterior vitreous detachment and status of proliferative vitreo-retinopathy (PVR).^{1,2}

Currently, there is tendency of primary pars plana vitrectomy, in most cases of rhegmatogenous retinal detachment, especially in pseudophakic patients and

scleral buckling is favored for phakic patients. But still scleral buckle can also be used for management of pseudophakic retinal detachment. The principle of management of rhegmatogenous retinal detachment, is to identify break, seal the break, provide a tamponade either external or internal, and drainage of sub-retinal fluid either internal or external if needed. It is considered, if there is no posterior vitreous detachment, retinal re-attachment surgery can have better outcome with scleral buckling surgery. But it is an established fact that 85 % patients with rhegmatogenous retinal detachment have associated posterior vitreous detachment.^{3,4}

Pneumatic retinopexy with sulfur hexafluoride (SF6) gas tamponade is favored by some retina surgeons for

primary rhegmatogenous retinal detachment in one or two superior quadrants as outpatient procedure with good results in selected cases. Hilton and Grizzard in 1986, reported pneumatic retinopexy with successful treatment of retinal detachment case series. The main advantage of this procedure is that it can be done as an outpatient setting with even topical anesthesia. In a multicenter randomized clinical trial, a primary anatomical success rate was attained in 75% of phakic eyes and 67% in pseudophakic eyes.⁵ But pneumatic retinopexy has limitation of selected cases. Scleral buckling is considered a viable option for treatment of rhegmatogenous retinal detachment in phakic eyes because it seal the retinal break, provide tamponade with less risk of cataract formation and progression, leading to better long term anatomical and visual outcome. But some retina surgeons consider scleral buckling is not so effective for pseudophakic retinal detachment because of posterior vitreous detachment (PVD), cases with posterior capsular rupture with vitreous loss, more proliferative vitreoretinopathy (PVR). There are rapid advancements in instrumentation and techniques for vitrectomy with good anatomical and functional results. So there is growing trend of primary pars plana vitrectomy for almost all cases of rhegmatogenous retinal detachment. Many surgeons prefer to perform phacoemulsification with pars plana vitrectomy in retinal detachment patients older than 50 years, while some surgeons categorically perform vitrectomy for primary pseudophakic retinal detachment. But the retina project-report 2, showed that pars plana vitrectomy was mostly performed in pseudophakic eyes and resulted in a worse functional outcome as compared to scleral buckle.⁶

Now a days, millions of cataract surgeries being performed with implantation of intraocular lens leading to pseudophakic status of eye. Our current techniques like phacoemulsification and femtosecond laser assisted cataract surgery, are very safe and effective in cataract management. If posterior capsular rupture occur in cataract surgery, it increases risk of rhegmatogenous retinal detachment by 11%. But still after uneventful cataract surgery there is 7 % incidence of rhegmatogenous retinal detachment. There can be associated risk factors like lattice degenerations, peripheral retinal degenerations, high myopia, posterior vitreous detachment, which can increase risk of retinal detachment in uneventful cataract surgery.⁸

Rhegmatogenous retinal detachment in phakic and

pseudophakic eyes can have difference in vitreous dynamics, especially when posterior capsule is ruptured. The characteristics of retinal breaks differ in pseudophakic and phakic retinal detachments. Usually, retinal breaks are smaller and there are round holes in pseudophakic retinal detachments. It was considered, during pars plana vitrectomy, internal search of small breaks and round holes is better possible, so pseudophakic retinal detachments can be better managed with pars plana vitrectomy and risk of retinal re-detachment can be reduced. Some surgeons manage small anterior breaks with 360 encircling band, which secure even missed breaks. So encircling can be helpful to seal and secure breaks in pseudophakic retinal detachments, which favors use of scleral buckling surgery for management of pseudophakic retinal detachment.⁹

Our study was performed to evaluate how much effective scleral buckling surgery is, as compared to pars plana vitrectomy in management of primary pseudophakic rhegmatogenous retinal detachments.

Material and Methods

All the cases were recruited through retina clinic of Eye unit III, Mayo Hospital/ King Edward Medical University Lahore. Informed consent was taken to include in study. It was a prospective, comparative and consecutive cohort study conducted from 01, July 2013 to 30, September 2014. The study included sixty patients of primary pseudophakic rhegmatogenous retinal detachment. Detailed history and clinical examination was performed, with drawing of breaks and configuration of retinal detachment. Lens status of patients were categorically noted either phakic or pseudophakic. Aphakic and phakic patients were excluded. Systemic status of patients was evaluated for fitness of surgical procedure under local anesthesia.

Both male and female patients with rhegmatogenous retinal detachment were included. B Scan Ultrasonography was performed if needed. Control of diabetes mellitus was given priority. The patients having retinal detachment due to penetrating trauma, previous retinal surgery, choroidal detachment, significant cataract obscuring view of retina, proliferative vitreoretinopathy (PVR) grade C, retinovascular disorders like proliferative diabetic retinopathy (PDR), retinal vein occlusion (RVO) were excluded. The patients with combined tractional and rhegmatogenous retinal detachment were not included. Systemic diseases like diabetes mellitus and hypertension were managed.

The surgical procedures were performed by three

experienced surgeons randomly, under local anesthesia. Standard scleral buckling with cryotherapy was performed in 30 cases under microscope with help of indirect Ophthalmoscope. The procedure started with 360 degree peritomy, followed by separation of four rectus muscles. The recti were tied with silk 1/0 suture. Indirect ophthalmoscopy was performed to localize retinal break and marked on sclera with suture. Cryotherapy was done to seal the retinal break/ breaks. 360 encircling Silicon band 2.5 mm was passed under rectus muscles and anchored to sclera with 5/0 ethibond in all four quadrants and two ends of band secured by silicon sleeve in supero-temporal quadrants. Silicon tier or sponge was applied to provide indentation and external tamponade to cover breaks for retinal re-attachment. Sub retinal fluid (SRF) drainage was performed if needed like in bullous retinal detachments, old and inferior retinal detachments. Per-operative complications were noted and managed accordingly.

In group B, 20 gauge pars plana vitrectomy was performed in all cases. Internal drainage was performed and endolaser photocoagulation was applied around breaks. Fluid air oil exchange was done. Silicon oil tamponade was used in almost all cases. No significant per-operative complication encountered. All the patients were followed for six months at least, for outcome measure of this study, which were anatomical re-attachment of retina and functional outcome like best corrected visual acuity (BCVA). All the information was recorded in proforma.

Results

Sixty patients were analyzed with minimum six months of follow up in this study. In group A, the mean age was 56.7 years (range 20-65 years) and in group B, the average age was 61 years (range 20-70 years). The p value is >0.05 , statistically no difference between two groups. (Table 1)

In group A there were 18 male and 12 female patients. In group B, 14 males and 16 females were included in the study (Table 2). In Group A, all patients were treated with Standard Scleral buckling surgery with cryotherapy. Per-operative and post-operative complications were noted and managed. Pars plana vitrectomy was performed in group B, patients with pseudophakic retinal detachment. Anatomical outcome after scleral buckling in group A was comparable to pars plana vitrectomy in group B. There was attached retina after six months follow

up in 86.66 % patients in Scleral buckle group and 90 % in pars plana vitrectomy group. (Table 3)

Best corrected visual acuity was categorized in three types, $> 6/12$, 6/18 to 6/60 and $<6/60$. In Scleral buckling group, after six months 46.66 % patients, while in pars plana vitrectomy group 43.33 % patient, had better or equal to 6/12 visual acuity. (Table 4)

Retinal re-detachment was found in 13.33 % patients in scleral buckle group and 10 % patients in pseudophakic group, which were managed by pars plana vitrectomy and one patient in scleral buckle group was managed with SF 6 gas internal tamponade, followed by argon laser barrage.

Raised intraocular pressure was found in a few patients, which was effectively managed with systemic acetazolamide and topical beta blockers.

Table-1: Age distribution of patients of both groups.

Age (Years)	Group A	Group B
40-50	08	07
51-60	07	11
61-70	11	07
71-80	04	05
Total	30	30

$p > 0.05$ (Not significant)

Table-2: Sex distribution of patients in both groups.

Sex	Group A	Group B	Total
Male	18	14	32 (53.33%)
Female	12	16	28 (46.66%)
Total	30	30	60 (100%)

$p < 0.05$ (significant)

Table-3: Anatomical outcome.

	Group A (SB group)	Group B (PPV Group)
Retinal attachment	26 (86.66%)	27 (90%)
Retinal Detachment	04 (13.33%)	27 (10%)
Secondary PPV performed	03 (10%)	03 (10%)

$p < 0.05$ (significant)

Table-4: Best Corrected Visual Acuity (BCVA).

BCVA	Group A (SB group)	Group B (PPV Group)
$>6/12$	14 (46.6%)	13 (43.33%)
6/18-6/60	09 (30%)	10 (33.33%)
$<6/60$	07 (23.33%)	07 (23.33%)
Total	30 (100%)	30 (100%)

$p < 0.05$ (significant)

Discussion

Scleral buckling and pars plana vitrectomy are two main surgical techniques for management of rhegmatogenous retinal detachment. The choice of procedure is very important for successful surgical outcome and optimal visual recovery. The best strategy to surgery is to begin with simplest method of repair and to proceed more invasive surgery as needed, depending upon status of the pathology. Coexisting medical and ocular problems should be dealt to increase surgical outcome. One must consider factors affecting both anatomical and functional outcome of surgical procedure.¹¹

There are a few risk factor for retinal re-detachment after surgery like missed breaks, proliferative vitreoretinopathy. The main risk of retinal detachment in either phakic or pseudophakic eyes is proliferative vitreoretinopathy (PVR). Research proved that PVR was found 5.3% to 11.5 % in patients after pars plana vitrectomy for rhegmatogenous retinal detachment and increased probability of retinal re-attachment surgery from 13.2 % to 24.5 %. While after Scleral buckling surgery 1.9 % cases developed PVR and 7.3 % patients needed retinal re-attachment surgery.^{11,12}

Research in last 20 years, proved that anatomical outcome and optimal visual recovery in retinal detachments with macula off has improved significantly. Now a days, we can have 90% or greater successful surgical outcome and a final reattachment rate of over 95% with retinal re-attachment surgery. Attainment of central vision better than 20/50 in macula off retinal detachments increased from 42% to between 60% and 80% of patients.¹³

Pars plana vitrectomy is becoming now a days a procedure of choice in variety of vitreoretinal disorders. Modern vitrectomy equipment and techniques are developing rapidly and effectively providing excellent surgical outcome in many vitreoretinal problems, which we were unable to manage in past. Currently, there is growing tendency to manage pseudophakic retinal detachment with pars plana vitrectomy. But still some surgeons think that Scleral buckling can be an effective treatment modality for pseudophakic retinal detachment.^{14,15}

Scleral Buckling is an extra-ocular procedure as compared to pars plana vitrectomy, with less risk of complications and long term successful outcome. Although research shows there are possible complications associated with scleral buckling, which can be scleral perforation, undesired sub retinal fluid (SRF) drainage, choroidal hemorrhage, choroidal detachment, sub-retinal hemorrhage,

retinal incarceration after SRF drainage, ocular motility disorders with diplopia, anterior segment ischemia and explant exposure. But in good surgical hands, incidence of these possible risks and complications is very low. Studies comparing scleral buckling and pars plana vitrectomy revealed that in phakic patients with rhegmatogenous retinal detachment, there was no risk of cataract formation with scleral buckling, but when pars plana vitrectomy was done, patients had cataract formation. Anatomical success rate was found very similar in both techniques.¹⁶

Bernhard et al performed segmental scleral buckle in 52 eyes with primary rhegmatogenous retinal detachment, having dialysis. After one year follow up, retina was attached in 87% patients. Azad et al, conducted a randomized comparison of scleral buckling and pars plana vitrectomy in 61 phakic eyes. After six months follow up, results showed, there was attached retina in 80.6% cases in scleral buckle group and 80 % patients in vitrectomy group. It was found that anatomical success rate was similar in this study but visual outcome was compromised in pars plana vitrectomy cases due to cataract formation.^{17,18}

Oshima et al studied 63 eyes in which pars plana vitrectomy was performed. Anatomical success rate after first surgery was 92.1 % but significant complication was cataract formation in 53.8% phakic eyes, which compromised optimal visual recovery. Tewari et al found greater complications of pars plana vitrectomy as compared to scleral buckling in pseudophakic patients and suggested scleral buckling in pseudophakic retinal detachment.^{19,20,21}

Our study proved that anatomical outcome after scleral buckling and pars plana vitrectomy, is comparable. Best corrected visual acuity was found almost similar, six months postoperatively. Only 13.33 % patients with scleral buckling had re-detachment, after six months follow up, and 10% needed secondary pars plana vitrectomy. So despite growing popularity of pars plana vitrectomy, still scleral buckling surgery is effective and safe modality for primary treatment of pseudophakic rhegmatogenous retinal detachment. Scleral buckling surgery provided good anatomical outcome with optimal visual rehabilitation.²²

Conclusion

Primary pseudophakic rhegmatogenous retinal detachment, can be managed effectively by scleral buckling and pars plana vitrectomy, with comparable results.

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Original Article

BLOOD AMMONIA LEVEL PREDICTS THE PRESENCES OF ESOPHAGEAL VARICES IN PATIENTS OF LIVER CIRRHOSIS DUE TO HEPATITIS B AND C VIRUSES

Syeda Zainab, Hamid Javaid Qureshi and Syed Muhammad Rizwan Bukhari

Objective: To determine the biochemical and ultrasonographic non invasive parameters in liver cirrhotic patients due to Hepatitis B and C virus. To validate the non invasive parameters with the presence of esophageal varices using endoscopy as gold standard.

Material and Methods: Two hundred diagnosed patients were taken. Every patient underwent esophagogastroduodenoscopy (EGD) for the presence of esophageal varices. Ultrasonography was done to calculate the spleen diameter. Blood samples were taken to find the levels of blood ammonia and platelet count.

Results: On the basis of Receiver operating curve (ROC) blood ammonia level had area under the curve (AUC) 1.000 ($p < 0.001$) platelet count/spleen diameter ratio (AUC=0.008, $p < 0.001$) platelet count (AUC 0.009, $p < 0.001$) and spleen diameter had area under the curve 0.986 ($p < 0.001$). The maximum area under the curve was observed with blood ammonia (100%) as compared to other parameters.

Conclusion: It was concluded from the present study that blood ammonia level is the most reliable non invasive parameter in predicting the presence of esophageal varices as compared to other non invasive parameters.

Key words: Esophagogastroduodenoscopy, Receiver operating curve, Area under the curve.

Introduction

Liver cirrhosis is the chronic ongoing injury to the liver leading to extensive scarring and impairment in its function. Liver cirrhosis has a worldwide incidence of 5-10%.¹ The most common cause in our country is viral hepatitis as compared to alcohol in the west. Cirrhosis causes irreversible damage and is commonly accompanied by portal hypertension leading to development of esophageal varices. Esophageal varices have a mortality rate of 17-57%.² According to recent recommendation, every diagnosed liver cirrhotic patient should undergo endoscopy for the presence of esophageal varices. Endoscopy is an invasive and expensive procedure; therefore the non invasive predictors of esophageal varices need to be determined. In liver cirrhosis, platelet count is low that is thrombocytopenia. There are number of factors causing thrombocytopenia. Portal hypertension is the major cause of thrombocytopenia. In enlarged spleen, the platelets are sequestered thus reducing their mean life time leading to low palatetelet count. There is reduction in production of thrombopoietin which is required for platelet formation. Thrombocytopenia is also due to myelotoxic effect of alcohol or hepatitis viruses³. Presence of antithrombotic antibodies and thrombocytes associated immunoglobulins, which can be found in

the sera of liver cirrhotic patients⁴.

In patients with liver cirrhosis, portal hypertension leads to vascular disturbances causing congestion of the red pulp which ultimately causes splenomegaly. Normal size of spleen is 12cm pole to pole that is longitudinal diameter⁵. Ammonia is predominantly derived from protein degradation. Most of the ammonia in the blood comes from the intestine by the action of bacterial proteases, ureases and amine oxidases and also by deamination of glutamine in the small and large intestines. Portal vein carries blood from intestines to liver that's why portal vein ammonia concentration is five to ten folds higher than in systemic circulation.

In the liver hepatocytes, 85% of ammonia is converted back into urea by urea cycle which is less toxic product. The kidney is the site for ammonia removal in the form of ammonium ions in the urine. Two factors contribute to hyperammonemia in liver cirrhosis;

1. In liver cirrhosis, there is decreased mass of functioning hepatocytes, resulting in fewer opportunities for ammonia to be detoxified in the liver.
2. There is portosystemic shunting which can divert ammonia containing blood away from the liver to the systemic circulation.

Original Article

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1. In liver cirrhosis, there is decreased mass of functioning hepatocytes, resulting in fewer opportunities for ammonia to be detoxified in the liver.
2. There is portosystemic shunting which can divert ammonia containing blood away from the liver to the systemic circulation.

Table-2: Comparison of non invasive parameters among patients having no varices and varices.

Parameters	No Varices N=59 Mean±SD	Varices Present N=141 Mean±SD	P value
Blood ammonia $\mu\text{M}/1$	33.62±2.63	85.13±25.73	0.000*
Platelet count/ml	229838±67845.03	58166±41541.21	0.000*
Spleen diameter (cm)	12.73±0.49	15.40±1.56	0.000*
Platelet count/spleen diameter ratio	18087±5435.35	4020±3128.61	0.000*

*P<0.05 is considered significant

Table-3: Maximum and minimum values of non invasive parameters in patients having no varices and varices.

Blood ammonia $\mu\text{M}/1$	Platelet count/ml	Spleen diameter (cm)	Platelet count/spleen diameter ratio
No varices 29 - 40 $\mu\text{M}/1$	110000-352000/ml	12.0-13.5cm	8222.2-29090.9
Varices 41 - 140 $\mu\text{M}/1$	4400-76000	12.5-19.5cm	25120-240.4

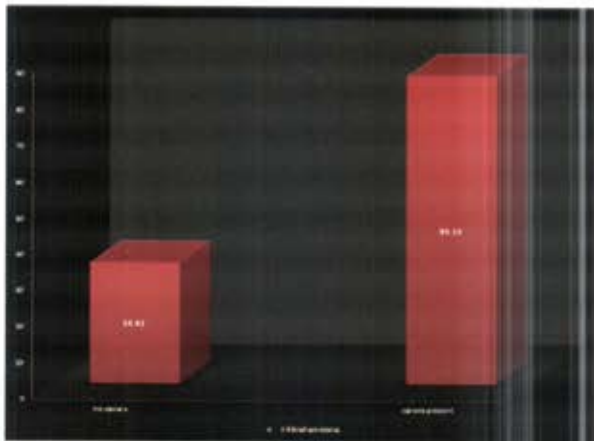


Fig-1: Comparison in the levels of blood ammonia in patients with and without varices.

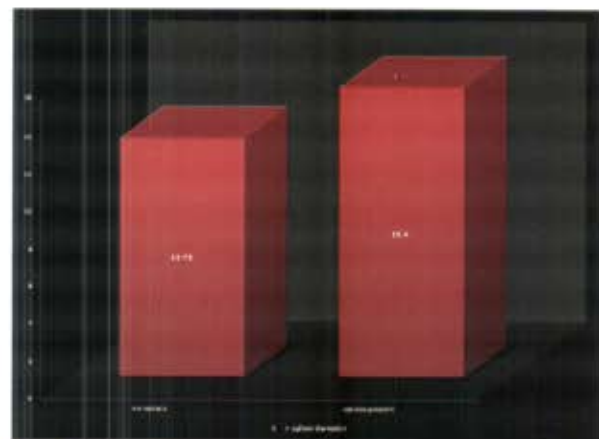


Fig-3: Comparison in the levels of spleen diameter in patients with and without varices.

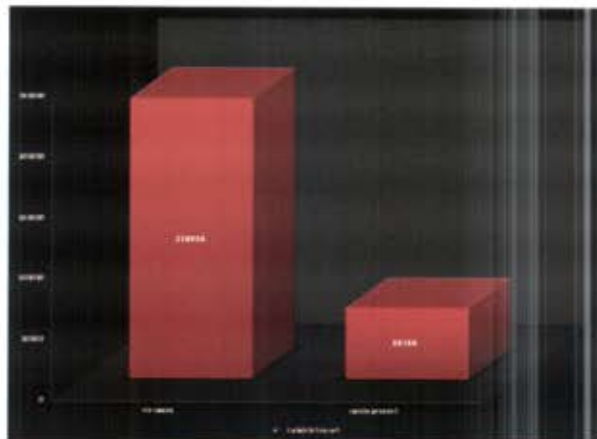


Fig-2: Comparison in the levels of platelet count in patients with and without varices.

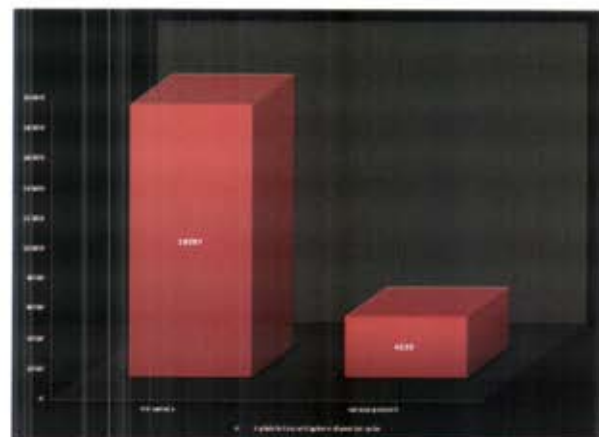
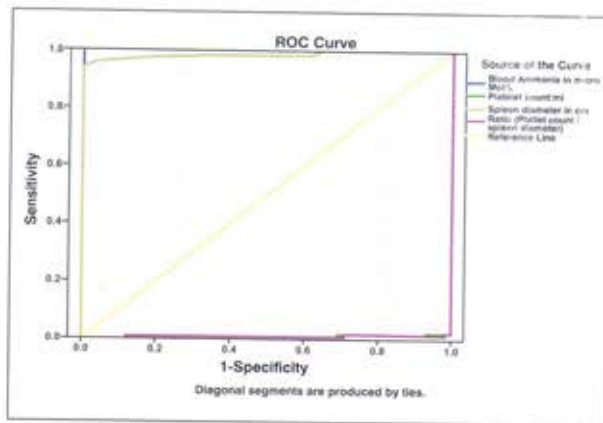


Fig-4: Comparison in the levels of platelet count/spleen diameter in patients with and without varices.



Discussion

Portal pressure increases in liver cirrhosis leading to development of varices and bleeding episodes, which may be massive and life threatening.⁶

In the present study, all those parameters which are affected by increase in portal pressure like blood ammonia, platelet count/spleen diameter ratio, platelet count and spleen diameter have been investigated. This study proved that blood ammonia level is the most sensitive and specific non invasive parameter in predicting the presence of esophageal varices in liver cirrhotic patients as compared to platelet count/spleen diameter ratio, platelet count and spleen diameter. Maximum area under the receiver operating curve i.e., 100% was observed for blood ammonia level.⁷ Various studies proved that platelet count/spleen diameter ratio as the most reliable parameter in predicting presence of varices showing maximum area under the curve receiver operating curve 8----15. The present study, didn't prove platelet count/spleen diameter ratio in detecting esophageal varices having AUROC=8%. Portal hypertension leads to splenomegaly, which is also considered to be a better predictor of esophageal varices.^{16,17,18,19} The result came out from various studies that platelet count could be used as a predictor of esophageal varices.^{20,21,22,23} Platelet count and spleen diameter are both highly interrelated because with increase spleen diameter there is greater sequestration of platelets. Also, in patients with alcoholic cirrhosis the platelet count decreases due to folate deficiency²⁴ so, the platelet count/spleen diameter is not concluded as a sensitive parameter in predicting presence and grading of esophageal varices. All the previous studies that predicted parameters other than blood ammonia didn't include hepatitis C patients.

The present study validated blood ammonia level as the most reliable parameter for predicting the

presence of esophageal varices. The other reason of concluding blood ammonia as most reliable parameter may be that in the present study most of the patients were having hepatitis C as the cause of liver cirrhosis. In HCV patients, the portal pressures are relatively stable²⁴. Blood ammonia is more related to damage in liver function as happened in progressive liver cirrhosis as compared to portal pressure so; it came out to be more reliable parameter. The source of ammonia in blood is gut, kidney and muscles. The ammonia is metabolized in the liver. As the liver dysfunction starts due to liver cirrhosis, there is development of portal hypertension and shunting of blood from the liver. As ammonia is not being metabolized, its level rises in the blood with the severity of liver damage and portal hypertension leading to development of esophageal varices. Ammonia can increase vascular tone of the vessels by causing influx of extracellular calcium through the voltage-dependent calcium channels and leading to worsen the portal hypertension.²⁵

The present study evaluated that the patients with blood ammonia level below 40 μ M/l had very less chances of having varices. This study validates that blood ammonia level is the most sensitive and specific non invasive parameter in predicting presence of esophageal varices and also prediction of medium and large varices. This validation study does mean that we are recommending to replace endoscopy with blood ammonia level but this study is pointing that when is the need of endoscopy to avoid complications and unnecessary interventions.

Conclusion

The blood ammonia has advantage over other parameters as it is very much cost effective test as compared to other non invasive parameters in predicting esophageal varices. This non invasive parameter will help to predict presence of esophageal varices very cost effectively. The cost of an endoscopy in our country is Rs 2000 5000 while the cost of blood ammonia level is Rs 200-300. Thus Rs 1800 4800 is saved when an unnecessary endoscopy is avoided. This will ease the medical, social and economic burden of the patients. It is validated from the present study that blood ammonia level is the most reliable non invasive parameter as compared to platelet count/spleen diameter ratio, platelet count and spleen diameter in predicting presence of esophageal varices.

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Original Article

EFFECT OF ALOE VERA LEAF GEL EXTRACT ON LIPID PROFILES OF ALLOXAN INDUCED DIABETIC RABBITS

Sajida Malik, Najeeba Qamar, Tehseen Ubaid and Naveed Iqbal

Objective: The study was designed to investigate the effect of aloe vera leaf gel extract on lipid profile parameters like total cholesterol, triglycerides and low density lipoproteins in alloxan induced diabetic rabbits.

Material and Methods: The rabbits were made diabetic by injecting alloxan monohydrate and divided in two groups of eight each. Group A was treated with distilled water and Group B was treated with ethanolic extract of aloe vera leaf gel for 28 days. The pre-treatment and post-treatment level of lipid profile parameters were recorded and compared. Statistical analysis was done with help of independent t-test. The effects in two experimental groups were analyzed with help of paired t-test.

Results: After 28 days of treatment the mean cholesterol level reduced to 80.9 from 97.1, the mean triglycerides reduced to 149.9 from 182.6 and mean LDL reduced to 30.8 from 35.6 mg/dl in the aloe vera group. The mean HDL levels increased to 28.2 from 24.5 mg/dl.

Conclusion: There was significant lowering of lipid profile parameters with aloe vera leaf gel extract in alloxan induced diabetic rabbits.

Key words: aloe vera, diabetes mellitus, lipid profile, rabbits.

Introduction

A type-2 diabetes has long been known as a risk factor for coronary heart disease. A conservative estimation is that it may increase the risk of fatal event by two folds. The risk is associated with increased serum levels of total cholesterol, triglycerides and low density lipoproteins.¹

Multiple anti-hyperglycemic and anti-hyperlipidemic drugs with different mechanisms of action are often required for effective treatment hyperlipidemia in type-2 diabetes patients.²

Conventional pharmacological agents used for such condition do exhibit adverse effects on long term use. Therefore, search for a harmless and clinically useful indigenous preparation which should decrease the LDL-cholesterol is warranted.³

Currently, there is a renewed interest in the plant based medicines and functional foods modulating physiological effects in the prevention and cure of type-2 diabetes and related complications. About 200 plants have been considered for their possible efficacy in the management of this condition.⁴

Aloe vera, with botanical nomenclature as aloe barbadensis miller, belongs to liliaceae family. The plant was shown to have wound healing, anti-inflammatory, anti-diabetes, antibacterial and anti-cancer properties.⁵ Furthermore, aloe vera gel reduced total cholesterol, triglycerides and LDL

levels in streptozotocin induced diabetic rats.⁶ The present study was carried out to explore the effect of aloe vera leaf gel extract on lipid profile of alloxan induced diabetic rabbits.

Materials and Methods

The study was carried out in the department of pharmacology, SIMS/PGMI Lahore. Healthy male rabbits weighing 1000 to 1700 gm were purchased from the market. The animals were acclimatized to the animal house of PGMI Lahore for 7 days prior to induction of diabetes. Green fodder, grains, plentiful of water and cereals were fed to them. All the rabbits were then made diabetic by injecting alloxan monohydrate into their ear veins.⁷ The dose of alloxan was calculated according to Puri et al.⁸ Eight day after induction of diabetes, 16 rabbits, of BSR levels > 250 mg/dl were taken in the study and divided in two groups (n=8).

Group-A, the control group, was treated with distilled water whereas, Group-B, the test group, was treated with ethanolic extract of aloe vera leaf gel. The ethanolic extract of aloe vera leaf gel was prepared in Herbal Heritage centre Department of Plant Pathology Punjab University Lahore. The mucilaginous pulp of aloe vera leaves was homogenized and filtered. The filtrate was freeze

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Dried and the end product was obtained in the form of grayish white powder. The powder was collected in colored bottles (Fig-1) and stored at room temperature.



Fig-1: Ethanolic extract of aloe vera leaf gel stored in colored bottles.

A baseline recording of lipid profile parameters including total cholesterol, triglycerides, LDL and HDL was done in both groups. After overnight fasting, 2 ml blood was collected from marginal ear veins of rabbits.⁸ The serum was separated from the samples and various lipid profile parameters were estimated in biochemistry department of PGMI Lahore.

The diabetic rabbits were then treated with their respective protocols for twenty eight days. Group-A was treated with 10 ml of distilled water daily and Group-B was treated with aloe vera gel extract in a dose of 300 mg/kg dissolved in 10 ml of distilled water. The drugs were administered through an 8 Fr nasogastric tube as a single daily dose.⁹ A second recording of biochemical parameters was done after 28 days of treatment. Pre-treatment and post-treatment values were compared in both groups. Statistical analysis was done with help of student-t test and effects in both experimental groups were analyzed with help of paired-t test.

Results:

Table-1 shows the pre-treatment and post-treatment levels of serum cholesterol, triglycerides, LDL and HDL in control group of alloxan induced diabetic rabbits treated with distilled water. In control group, there were no stastically significant changes in these parameters after 28 days.

Table-2 and figure-2 show the effect of aloe vera leaf gel extract on lipid profile parameters of alloxan

induced diabetic rabbits after 28 days of treatment. The mean levels of total cholesterol reduced from 97.1 mg/dl to 91.0 mg/dl and the change was significant. Similarly, mean triglycerides and LDL levels reduced from 182.6 mg/dl and 35.6 mg/dl to 149.9 mg/dl and 30.8 mg/dl respectively. All these changes were statistically significant. The mean HDL levels increased from 24.5 mg/dl to 28.2 mg/dl which is also stastically significant change.

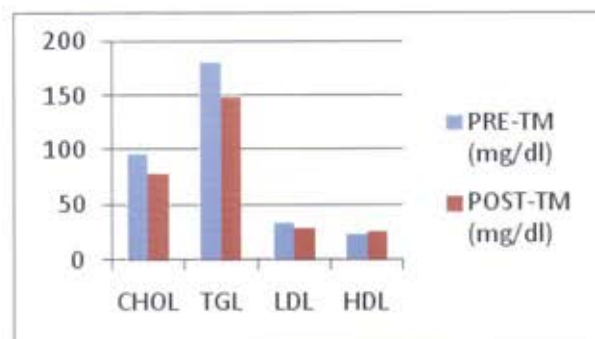


Fig-2: Bar diagram of lipid profile parameters in diabetic rabbits treated with aloe vera leaf gel extract showing a significant decrease in total cholesterol, triglycerides and LDL after 28 days. There is a beneficial increase in HDL levels.

Table-1: Lipid profile parameters in diabetic rabbits treated with distilled water.

Parameter	Pre-Tm Mean±SD	Post-Tm Mean±SD	P-Value
Cholesterol	93.1±7.5	91.04±7.6	0.411
Triglycerides	181.2±7.5	178±9.7	0.522
LDL	31.1±13.1	31.7±13.5	0.575
HDL	26.2±2.9	25.9±2.4	0.188

Table-2: Lipid profile parameters in diabetic rabbits treated with aloe vera gel extract.

Parameter	Pre-Tm Mean±SD	Post-Tm Mean±SD	P-Value
Cholesterol	97.1±7.2	80.9±6.0	0.003
Triglycerides	182.6±11.2	149.9±20.1	0.002
LDL	35.6±3.2	30.8±2.8	0.003
HDL	24.1±2.9	28.0±2.4	0.003

Discussion

Diabetes mellitus is perhaps the fastest growing metabolic disorder in the world. As the condition

exhibit a multi-factorial and heterogeneous nature, the need for search of more challenging and appropriate therapies is increasing. Traditional plant remedies have been used throughout the world for the range of diabetes complications.¹⁰ Plant extract are considered to be less toxic than synthetic agents. In previous studies, aloe vera extracts have shown a hypoglycemic effect in experimental diabetic animals. Lipid profile was also shown to be altered in these experimental animals as a result of induced diabetes.¹¹ In the present study, aloe vera extract treatment significantly decreased total cholesterol, triglycerides and LDL levels whereas the HDL levels increased. All these results suggest that aloe vera could improve lipid metabolism disorders in type-2 diabetes mellitus.

Significant lowering of total cholesterol, triglycerides and LDL and an increase in HDL levels is very much desirable biochemical state for prevention of atherosclerosis and ischemic conditions. Various studies of medicinal plants have reported a similar lipid lowering activity. Few studies about the effects of aloe vera on lipid profile metabolism are cited in literature.¹² Furthermore, the bioactives and mechanisms involved in lipid

lowering actions of aloe vera were not investigated. Few studies have been conducted on the isolation of bioactive compounds mediating the anti-hyperglycemic actions of aloe vera gel extracts. Trace elements and five phytosterols isolated from the gel were responsible for anti-hyperglycemic actions in STZ induced type-2 diabetic rat models.¹³

The bioactives and mechanisms underlying the lipid lowering effects of aloe vera gel have not been studied so far. Considering the results of the present study, further and larger clinical trials concerning the efficacy and safety of aloe vera gel extract in the treatment of patients with type-2 diabetes and associated hyperlipidemia as well as studies addressing the bioactives and mechanisms involved in anti-hyperlipidemic actions seem necessary.

Conclusion

There was significant lowering of lipid profile parameters with aloe vera leaf gel extract in alloxan induced diabetic rabbits.

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Original Article

E-HEALTH AS A COMPONENT OF SCHOOL HEALTH SERVICES IN LAHORE

Sadia Batool, Adeel Ahmed and Fatima Aleem

Objective: Facilitating health provision to masses involving internet is an emerging aspect of medical profession. This exploratory study aims to assess the adequacy of such services in schools of Lahore & form basis for further work up in this aspect.

Material and Methods: Out of 1400 schools registered with BISE, Lahore, private (43) and public (16) schools of Lahore were included in the study (purposive sampling by inclusion criteria) who had web pages (n=59); Data was collected by data extraction form through internet & descriptive analysis was done using SPSS version 17. It was a self-financed study.

Results: Our results concluded that 53% schools (n=59) had well-equipped computer laboratories; out which 40% were private & only 13% were public, however not all of them provided access to internet. 39% of the schools regularly updated their websites; 29% were private & only 10% were public. 28% of the 59 schools provided their telephone numbers which the parents can contact in case of any emergency or otherwise. 14% of the total schools had health related content available on their website. Only 3% each of both the schools displayed messages regarding health education.

Conclusion: This study implies that the provision of e-health services in the schools of Lahore is almost negligible. Internet is a rising technology in Pakistan and steps should be taken to incorporate internet based innovations in the school health policy of Pakistan.

Key words: E-health, lahore, school health, cross sectional.

Introduction

AE health is defined by WHO as, "E-health is the transfer of health resources and health care by electronic means".¹ The value of E-Health has grown substantially in the modern times when internet has turned the world into a global village and new and faster means of communication are being developed.² E-health has shown hypothesized benefits in improving better understanding of disease and prompt communication.³ Some schools provide with internet facilities and well equipped computer labs, so it was important to know the situation of E-Health in the schools, role of teachers and involvement of health care professionals in this matter. This is the first of its kind study on this subject in Pakistan as it has not been conducted previously. Our aim was to find out if E-Health is practiced in schools of Lahore, how many schools have internet connectivity and how many are active online to promote E-health.

Rationale: The E-health is very important for modern times. Our aim was to find out its prevalence in the schools because no such study has ever been conducted in Pakistan before. It is important to know the ground reality of E-Health in our country. We also wanted to know the interest of teachers and

their qualification to promote E-health and the utilization of healthcare professionals for this purpose. This is very important for planning the health policy and related strategies in the future at local, provincial and national level.

Literature Review:

E-health gives us the glimpse of modern medicine. E-health projects like "hello health", which is a Brooklyn based primary care practice is an excellent example of paper-less, web-based practice.⁴ Survey for assessment of influence of internet health information conducted by Pew Internet & American Life Project published by Elsevier in 2005 provides us with a multivariate result, with few individuals being highly aware of health usage of internet, whereas many were completely ignorant of the matter. The strongest influence to search for a health problem online was interestingly, female gender.⁵ A study conducted in 2007 in England, published by Elsevier showed people trust the information provided to them by internet so distinction between "trust" sites is important. It promotes informed choices.⁶ In 2001 A survey was conducted to find 40% of internet users use internet for health related queries 94% said it had no effect on their visits to physician, 5% admitted using internet for a prescription.⁷ A study was

conducted in 13 countries about sending messages and reminders about diseases like diabetes & asthma, and showed significant improvements in compliance with medicine taking, asthma symptoms, HbA1C, stress levels, smoking quit rates, and self-efficacy.^[9]

A study was conducted in December 2011 in colleges & universities around the world showed that although college students are highly connected to, and feel comfortable with, using the Internet to find health information, their E Health literacy skills are generally sub-par.^[9] Another study in Netherlands in 2012 states that even rural application of E health services is an emerging field which should not be undermined^[10]. Mixed findings were reported in a study conducted in 2014 in Netherlands by Maastricht University about the effectiveness of E health interventions in lifestyle to reduce smoking habits in youth^[11] However in a randomized control trial conducted in Canada in 2008, it was concluded that smoking intervention programme helped adolescents in avoiding heavy smoking^[12].

Methodology

This is a descriptive, cross-sectional study. The sampling technique followed was non probability, purposive sampling, 1400 schools of Lahore both public and private were included as two strata. Sampling unit was website of each school. The data was collected by a data extraction form through internet.

Inclusion criteria: Only the schools that had proper web addresses were included. E.g. Official website or any social media page. Descriptive analysis was done by using the software SPSS version 17.

A List was made of 127 schools after applying the inclusion criteria. (Only the schools that had web addresses were included).³

A Second list of 59 schools was made after excluding 68 non-functional/ fake/bogus web addresses.

All the 59 schools were included in the study.

Results

From a total of 59 schools, 39% of the schools regularly updated their websites; 29% were private & only 10% were public, indicating that the websites are not often used as a platform by the schools to communicate with the public in general. However, just 23.72% had any health related content available in any section of the website. 54.2% of the websites were linked to social networking sites (Facebook). 53% schools (n=59) had well-equipped computer laboratories; out which 40% were private & only

13% were public, however not all of them provided access to internet. There were discussion forums for the users and students on the website of 32.2% schools and only 10.1% of them were active. NO school had the facility to calculate BMI on their page. 28 of the 59 schools provided their telephone numbers which the parents can contact in case of any emergency or otherwise. 14% of the total schools had any type of health related content available on their website where as 6.8% gave contact information for healthcare professionals on their websites.

Discussion

E-Health literacy refers to the ability of individuals to seek, find, understand, and appraise health information from electronic resources and apply such knowledge to addressing or solving a health problem. While the current generation of school students has not appreciable access to a multitude of health information on the Internet, access alone does not ensure that students are skilled at conducting Internet searches for health information. Ensuring that school students have the knowledge and skills necessary to conduct advanced E-Health searches is an important responsibility. The information obtained in our study indicates that the provision of E-health in our education system is negligible, due to the lack of awareness, and scarcity of resources.

A systematic literature review was conducted at Department of Health Education and Behavior, University of Florida, Gainesville, FL 32611, USA, to summarize and critically evaluate the evidence from existing research on E-Health literacy levels among college students between the ages of 17 and 26 years attending various 4-year colleges and universities located around the world. It highlights similar fact that in spite of availability of internet and all type of electronic media it does not mean that today generation in schools have access to multitude of health. These results coincide with the findings in our study as our data collection clearly evaluated & focused on this aspect.

A report was published by Ray Jones PhD FFPH, Heather Skirton and Miriam McMullan in July 2006, to evaluate methods for using information and communication technologies to involve academic staff, students and patients in a common synchronous E-learning environment. Limitations in accessibility Have been demonstrated for both satellite broadcasts and videoconferencing. Having identified a feasible synchronous method we can now investigate hypothesized benefits for staff, students, and patients

Of combined e-health e-learning. An article published in American Journal of Preventive Medicine in 2007 corresponds with the results of our study, and states that interventions that feature interactive technologies need to be refined and evaluated to fully determine their⁴ potential as tools to facilitate prevention, diagnosis & treatment. These strategies are currently lying in their infancy¹³

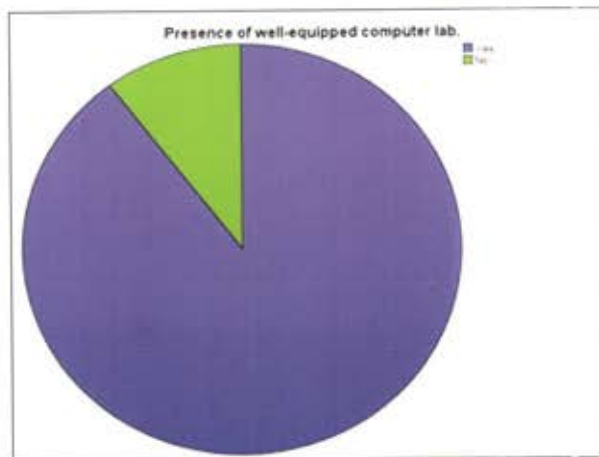


Fig-1: Presence of well equipped computer lab.

Table-1: Provision of telephone number by school in case of emergency.

	Frequency	Percentage
Yes	91.04±7.6	47.5
No	178±9.7	52.5
Total	31.7±13.5	100.0

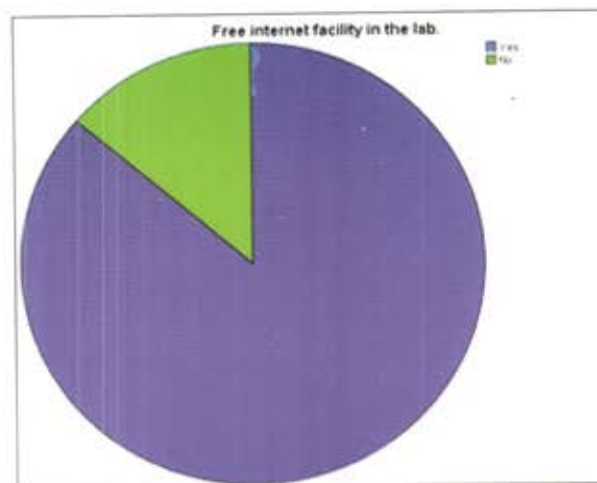


Fig-2: Free internet facility in the lab.

Conclusion

Websites were not up to date with health related issues and no particular advice by healthcare professional was given. No forums dedicated for health related queries of students. Medical reports, BMI calculators, lifestyle improvement interventions were sub-par. E-health provision is negligible in the schools of Lahore.

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Original Article

DIAGNOSTIC ACCURACY OF DOPPLER ULTRASONOGRAPHY FOR DIAGNOSING ESOPHAGEAL VARICES IN CIRRHOTIC PATIENTS

Umar Malik, Sabeen Farhan and Muhammad Arif Nadeem.

Objective: To determine the diagnostic accuracy of doppler ultrasonography for diagnosing esophageal varices in cirrhotic patients taking endoscopic findings as gold standard.

Material and Methods: One hundred and thirty five patients fulfilling inclusion criteria underwent doppler ultrasound of abdomen for esophageal varices. This was followed by upper GI endoscopy in all patients. Data was analyzed for sensitivity, specificity, positive predictive values, negative predictive values and accuracy rate of doppler ultrasonography for diagnosing esophageal varices.

Results: Frequency of esophageal varices in cirrhotic patients on endoscopy was 62.22 % (n=84). Diagnostic accuracy of doppler ultrasonography for diagnosing esophageal varices in cirrhotic patients taking endoscopy as gold standard was recorded. Results showed that 51.85% (n=70) were true positive, 2.96% (n=4) false positive, 34.81% (n=47) true negative and 10.37% (n=14) false negative. Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy rate were calculated as 83.33%, 92.16%, 94.59%, 77.05% and 86.67% respectively.

Conclusion: The diagnostic accuracy of Doppler Ultrasonography for diagnosing esophageal varices in cirrhotic patients' standard is high.

Key words: Cirrhosis, esophageal varices, diagnosis, ultrasonography, accuracy

Introduction

Liver cirrhosis (LC) is the final evolutive stage of any chronic liver disease, which is prone to multiple complications because of portal hypertension.^{1,2} Development of esophageal varices (EV) is the major complication that may occur in up to 60% of cirrhotic patients.⁶

Once esophageal varices develop, the annual risk of bleeding ranges from 10% to 30%.³ Furthermore, the mortality rate of variceal bleeding still remains as high as 20%-35% in prospective studies. Although screening endoscopy for EV is recommended for all patients with established cirrhosis, these recommendations are not a result of evidence-based data, yet has proved to be cost-effective in patients with decompensated cirrhosis, cost-effectiveness remains elusive in patients with compensated cirrhosis.^{3,4}

Early diagnosis of varices before the first bleed is essential as studies of primary prophylaxis clearly show that the risk of variceal hemorrhage can be reduced from 50% to about 15% for large EV.⁵

Color doppler ultrasonography has advantages over other techniques; it is a simple, noninvasive method, and can be used to calculate the portal vein diameter and portal pressure for diagnosis of EV.⁶

During literature search, we found a great variability in results. In one study portal vein diameter >13 mm had sensitivity of 45-50% and specificity of 100% for diagnosing EV, while another study portal vein diameter >13 mm by doppler ultrasound showed 76.5 % sensitivity and 80 % specificity for diagnosing EV.⁷ We could not find any study conducted in local population and as positive predictive value depends on prevalence of disease, we want to conduct this study to generate results in our population.

Materials and Methods

This research was conducted at Medical Unit III inpatient, Services Hospital, Lahore, Pakistan. It was a cross-sectional survey and 135 patients were enrolled. Inclusion criteria included both male and female diagnosed hepatitis B and C seropositive cirrhotic patients with ages between 20-60 years. Patients with non cirrhotic portal hypertension, hepatocellular carcinoma were excluded from the study. Informed consent was taken. Age, gender and biochemical parameters were recorded. Ultrasound examination by a single hospital radiologist was performed following the departmental protocols for EV including portal vein pressure, portal vein diameter and splenic length, and the presence

/absence of EV was recorded on the radiologist's report. This report was kept confidential until upper GI endoscopy was done. Both reports were evaluated for diagnostic accuracy of ultrasound.

Data was analyzed. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy of Doppler Ultrasound for diagnosis of EV were calculated taking endoscopy as gold standard.

Results

Age distribution of the patients showed that 43.71% (n=59) were between 20-40 years and 56.29% (n=76) between 41-60 years, and mean age was calculated as 41.22±8.63 years. (Table No. 1)

Gender distribution of the patients revealed that 57.78% (n=78) were male and 42.22 % (n=57) females. (Table No. 2)

Frequency of esophageal varices in cirrhotic patients on endoscopy was 62.22% (n=84), while 37.78% (n=51) had no varices. (Table No. 3)

Diagnostic accuracy of Doppler ultrasonography for diagnosing esophageal varices in cirrhotic patients taking endoscopy as gold standard was recorded, which showed that 51.85%(n=70) were true positive, 2.96%(n=4) false positive, 34.81%(n=47) true negative and 10.37%(n=14) false negative. Sensitivity, specificity, positive

predictive value, negative predictive value, and accuracy rate was calculated as 83.33%, 92.16%, 94.59%, 77.05% and 86.67% respectively. (Table No.4)

Table-1: Age distribution (n=135).

Age in Years	Number	Percentage
20 - 40	59	43.71
41 - 60	76	56.29
Total	135	100
Meant±sd	41.22±8.63	

Table-2: Gender distribution (n=135).

Gender	Number	Percentage
Male	78	57.78
Female	57	42.22
Total	135	100

Table-3: Frequency of esophageal varices in cirrhotic patients (on endoscopy) (n=135).

Esophageal varices	Number	Percentage
Yes	84	62.22
No	61	37.78
Total	135	100

Table-4: diagnostic accuracy of doppler ultrasonography for diagnosing esophageal varices in cirrhotic patients taking endoscopic findings as gold standard (n=135).

Doppler ultrasonography	Endoscopic Findings		Total
	Positive	Negative	
Positive	A (True positive) 70 (51.85%)	B (False positive) 4(2.96%)	a+b 74(54.81%)
Negative	C (False negative) 14 (10.37%)	D (true negative) 47 (34.81%)	c+d 61(45.19%)
Total	a + c 84 (62.22%)	b + d 51(37.78%)	135 (100%)

Sensitivity = $a / (a + c) \times 100 = 83.33\%$ / Specificity = $d / (d + b) \times 100 = 92.16\%$ / Positive predictive value = $a / (a + b) \times 100 = 94.59\%$
Negative predictive value = $d / (d + c) \times 100 = 77.05\%$ / Accuracy rate = $(a + d) / (a + d + b + c) \times 100 = 86.67\%$

Discussion

Cirrhosis represents the end stage of progressive fibrosis, which destroys normal liver tissue and produce regenerative nodules. Variceal bleeding (which is a consequence of portal hypertension) is one of the most dreaded complications of cirrhosis. The risk of variceal bleeding is 25-40% in patients with cirrhosis.^{8,9}

One of the methods of interest for gastroenterologists and radiologists is doppler ultrasound indices of spleno portal system, which shows extensive changes through cirrhosis and portal

hypertension.¹⁰

In our study, frequency of EV in cirrhotic patients on endoscopy was 62.22%(n=84), while diagnostic accuracy of Doppler ultrasonography for diagnosing esophageal varices in cirrhotic patients taking endoscopy as gold standard showed that 51.85%(n=70) were true positive, 2.96%(n=4) false positive, 34.81%(n=47) true negative and 10.37%(n=14) were false negative. Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy rate were calculated as 83.33%, 92.16%, 94.59%, 77.05% and 86.67% respectively. This is in agreement with a study, which

Revealed that EV may occur in up to 60% of cirrhotic patients.⁶

Our findings were also in agreement with a study by Arulprakash Sarangapani and Co, where Portal vein diameter >13 mm by Doppler ultrasound showed 76.5% sensitivity and 80% specificity for diagnosing EV.⁷ Our findings regarding specificity were more close with K. Khanna and workers who recorded 100%.⁸

Some other studies^{11,12} revealed that portal vein diameter more than 13 mm represent portal hypertension with a specificity of 95-100%.

Liu et al¹³ conducted a study on 383 cirrhotic patients with Child score A for diagnosing EVs with Doppler US. His results indicated that cutoff value of 3 for SPI have a sensitivity of 92%, specificity 93%, positive predictive value (PPV) of 91%, and negative predictive value (NPV) of 94% for diagnosing EVs. He concluded that this cut off had capability of diagnosing EVs in 92% of patients who did not have endoscopy, and therefore is a reliable index.¹⁴

Dib et al from France stated that although using noninvasive method for diagnosing EVs is logical and rational, but still endoscopy is the preferable and the most reliable method compared with other diagnostic methods¹⁵. Considering the facts in our study and with the help of other studies we can conclude that doppler ultrasound is a non-invasive technique, which is useful for the prediction of esophageal varices in cirrhotic patients in our population. However, our findings are primary and some other local studies on a larger scale are required to authenticate our findings.

Conclusion

We concluded that the diagnostic accuracy of Doppler Ultrasonography for diagnosing Esophageal Varices in cirrhotic patients taking endoscopic findings as gold standard is high.

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ENTHESOPHYTES ON DRIED BONES OF LOWER LIMB OF PAKISTANI POPULATION

Aliya Zahid, Muhammad Wajahat Khan and Brishna Khan

Objective: An enthesophyte is a bony spur formed at a ligament or tendon insertion into bone. It may develop in the direction of pull of the relevant tendon/ligament or in response to repetitive strain. To find out the presence of enthesophytes on dried bones of lower limb in Pakistani population

Material and Methods: Present study was conducted on dried bones of lower limb in Pakistani population in the Anatomy Departments of Allama Iqbal Medical College, Lahore and Khawaja Muhammad Safdar Medical College, Sialkot. For this purpose, 40 pelvic bones, 103 femora, 98 tibiae, and 112 fibulae were included. They were closely observed for the presence of enthesophytes. The bones with enthesophytes were photographed.

Results: Enthesophytes were found on 1 out of 40 hip bones, 2 out of 103 femora, 1 out of 98 tibia and 1 out of 112 fibulae. Enthesophyte on hip bone was present on ilium at the medial border. One of the femur shows enthesophyte inferior to lesser trochanter and other femur has enthesophyte on medial aspect of greater trochanter. On tibia, one enthesophyte was at the lower end of tibial tuberosity and second was on the posterior surface below the lateral condyle. Only one out of 112 fibulae showed enthesophyte on head of fibula.

Conclusion: Finding of enthesophytes contributes to the data of anatomical variations and to raise awareness about formation of enthesophytes. The better understanding of the localisation of enthesophytosis important in the musculoskeletal pain diagnosis so the presence of enthesophyte should be kept in mind .

Keywords: Enthesophytes, hip bone, femur, tibia, fibula, pakistani population

Introduction

Enthesophytes are bony spurs that appear as irregular outgrowths of varying size that extend from the skeleton into the soft tissue of a tendon or ligament at its enthesis.¹ The term "enthesis" describes the site of insertion of a tendon, ligament, fascia, or articular capsule into bone.² Anatomically there are four distinct zones of enthesis that include tendon substance, enthesal fibrocartilage, mineralised fibrocartilage and bone substance. The enthesis is an important structure in the cause of pain and should be taken into consideration in musculoskeletal examination.^{3,4}

Fibrocartilaginous matrix in enthesis is rich in type II collagen that enables it to bend, while its mineralized portion consists primarily of type II collagen, type X collagen and aggrecan, which give them compressive strength. Thus fibrocartilage in an enthesis accommodates the distribution of forces between the musclebone and bonebone interfaces and has tensile strength. The enthesis also minimizes stress through this functional role of fibrocartilage and enables load transfer between two distinct types of tissue (muscle and bone).⁵

An enthesopathy is usually defined as a pathological change at an enthesis. The appendicular enthesopathies may be either proliferative (e.g. enthesophytes or bone spurs) or degenerative (e.g. lytic changes, such as pitting).⁶ Enthesophytes are widely assumed to be 'traction spurs', i.e. to develop in response to high tensile forces within a tendon or ligament. It is observed that enthesophytes develop in the direction of pull of the relevant tendon or ligament and may develop in response to repetitive strain.⁷ The formation of enthesophytes can occur in many conditions including the seronegative spondyloarthritides, various endocrine disorders such as diabetes mellitus, local trauma, and calcium pyrophosphate deposition disease. The frequency increased with age, independent of gender.⁸ In addition to the "aging process" in the normal adult population, the formation of enthesophytes has been attributed to cumulative effects of mechanical loading i.e. "overuse" enthesopathies are believed to develop in response to excessive or abnormal biomechanical forces. There could be an imbalance between the anabolic and catabolic processes of bone and cartilage regulation. The presence of

Fibrocartilage at the tip of many enthesophytes suggests that endochondral ossification could play a role in their formation. Enthesophytes can form in response to repetitive strain, as in the spiking of tibial spines seen in football players.^{3,10,11}

In psoriasis, entheses are the initial site of joint inflammation in spondyloarthropathy and enthesitis most commonly localises in the lower limbs.¹² Enthesopathy is also a frequent finding in untreated coeliac disease patients.¹³ Enthesophyte formation also occurs in the absence of any clear cause. Multiple idiopathic enthesophytes are characteristic of diffuse idiopathic skeletal hyperostosis (DISH).^{14,15}

Present study was aimed to find out the incidence of enthesophytes on hip bone and long bones of lower limb in Pakistani population so the concerned clinicians have been able to advance their understanding of enthesitis disease greatly. The enthesitis is an increasingly recognised important structure in the cause of pain and should form the basis of the musculoskeletal examination. In addition, normal anatomical variants like enthesophytes can have an imaging appearance that can mimic a bone tumor so the better understanding of the localisation of enthesophytes might prevent misdiagnosis and reduces patient anxiety.

Materials and Methods

Present study was conducted in the Anatomy Departments of Allama Iqbal Medical College, Lahore and Khawaja Muhammad Safdar Medical College, Sialkot. For this purpose, 40 dried pelvic bones, 103 femora, 98 tibiae, and 112 fibulae were included irrespective of age and sex. They were closely observed for the presence of enthesophytes. The bones with enthesophytes were separated. The enthesophytes were identified and the bones were photographed.

Results

It was found that enthesophytes were found on 1 out of 40 hip bones, 2 out of 103 femora, 1 out of 98 tibia and 1 out of 112 fibulae.

Hip Bone: Enthesophyte on hip bone was present on ilium at the junction of sacropelvic surface and iliac fossa.

Femur: Two out of 103 femora showed the presence of enthesophyte. One of the femur shows enthesophyte just inferior to lesser trochanter and the other femur has enthesophyte on the inner aspect of greater trochanter.

Tibia: Two enthesophytes were present on the same

tibia, one was at the lower end of tibial tuberosity and the second was on posterior surface below the lateral condyle.

Fibula: Only one out of 112 fibulae showed enthesophyte on the head of fibula.



Fig-1: An enthesophyte projecting from the adjacent border between sacropelvic surface and iliac fossa.



Fig-2: Showing two femora with enthesophytes on greater and lesser trochanters.



Fig-3&4: Fibula showing an enthesophyte on the posterior surface of head and **Fig-4** two enthesophytes on tibia, one on tibial tuberosity and the other on posterior surface inferior to lateral condyle of tibia.

Discussion

Enthesophytes are bony outgrowths that extend from the skeleton into the soft tissue of a tendon or ligament. They become more common with increasing age and are more frequently found in males than females. Enthesophytes are comparable with the osteophytes which form around the articular surfaces

ial joints in patients with osteoarthritis. Indeed, osteophyte and enthesophyte formation are linked and that both are manifestations of skeletal response to stress. Bony spur development increases the surface area of the interface and thus could be an adaptive mechanism to increased mechanical traction¹. Since the enthesis is an increasingly recognised clinically important structure in the cause of pain, the study of enthesophytes may play an important role in diagnosing certain musculoskeletal painful conditions. Since no such study about enthesophytes is done previously in Pakistan, present study was aimed to find out presence of enthesophytes on dried bones of lower limb in Pakistani population. In a study it was found that enthesophytes were present at the greater trochanter (in gluteus tendons at their insertion) and at the tibial tuberosity (patellar tendon at its distal insertion)¹⁶, same as in present study. In another study, a survey of 39 patients with X Linked Hyperostosis (32.7 ± 19.5 years) showed the majority had evidence of enthesopathy. The predominant sites involved were the knees, ankles, pelvis, and thoracic spine. Involvement was usually bilateral for the shoulder, elbow, knee, ankle, and hand sites; and the number of sites involved increased with age.¹⁷ In a study on enthesophytes, hip joint showing enthesophyte on greater trochanter and lesser trochanter of femur, same finding as in present study. In the same study,

the iliac crest and the ischial tuberosity of hip bone have enthesophytes.¹ In present study, enthesophyte on hip bone was on the medial border between sacropelvic surface and iliac fossa. In another study, it was observed that enthesopathic abnormalities were more frequently found at the distal part of lower limbs (i.e. as patellar ligament, Achilles tendon etc) with respect to the proximal part of lower limbs (i.e. ischial tuberosity, great trochanter and insertion of adductor muscles) in 31 patients with spondylarthropathy (SpA).¹⁸

Conclusion

Finding of enthesophytes on dried bones of lower limb of Pakistani population contributes to the data of anatomical variations. Since the enthesis is an increasingly recognised clinically important structure in the cause of pain, the study of enthesophytes may play an important role in diagnosing certain musculoskeletal painful conditions. In addition, normal anatomical variants like enthesophytes can have an imaging appearance that can mimic a bone tumor so the better understanding of the localisation of enthesophytes might prevent misdiagnosis of such conditions.

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Answer: Picture Quiz

Atrial fibrillation with left bundle branch block

FREQUENCY OF COMMON PATHOGENS IN VAGINAL DISCHARGE

Nabila Abdullah, Ghazanfar Abbas and Khalid Mahmood

Objective: To determine the frequency and type of pathogens in vaginal discharge.

Material and Methods: A descriptive cross-sectional study. The out-patient department of Gynecology and Obstetrics Specialist Unit at Services Hospital, Lahore. After taking informed consent a total of 120 women of reproductive age (13 to 49 years) were included in the study by convenient sampling. After detailed history and clinical examination, two high vaginal swabs were taken and data was recorded in proforma. One swab was used immediately to prepare a wet mount with one to two drops of normal saline on a glass slide and was examined by light microscopy for motility of *Trichomonas vaginalis*. The pus cells, budding yeast cells, pseudo-hyphal and clue cells were also looked for in the same wet mount. Second swab was immediately sent to the microbiology laboratory for Gram's staining and Culture and Sensitivity. The swab was also inoculated on Sabouraud's agar and incubated at 35 °C±2 °C aerobically for 48 hours for the growth of *Candida* saprophytes. Data was analyzed through computers software SPSS.

Results: Among 120 patients who had vaginal discharge, 5.8% (n=7) were 13-20 years old, 24.2% (n=29) were 21-30 years old, 55.8% (n=67) were 31-40 years old while 14.2% (n=17) were 41-49 years old. On clinical examination, 54.2% (n=65) patients had fungal infection, 18.3% (n=22) had trichomonas and 15.8% (n=19) had bacterial vaginosis while 11.7% (n=14) patients had mixed infection. HVS microscopy / culture sensitivity, results showed, 48.3% (n=58) had fungal infection, 12.5% (n=15) had trichomonas and 25.0% (n=30) had bacterial vaginosis and 14.2% (n=17) had mixed infection.

Conclusion: Vulvovaginal candidiasis was a frequent finding in out patient departments of tertiary care hospitals of our country.

Keywords: Candidiasis, bacterial vaginosis, trichomoniasis.

Introduction

Vaginal discharge is a common gynecological condition among women of childbearing age that frequently requires care affecting about one-third of all women and half of pregnant women.¹

Vaginal discharge may be physiological or pathological. Physiological discharge comprises secretions of the Bartholin's gland and the endocervix with cells shed from the vaginal walls. These secretions are affected by hormonal changes during the menstrual cycle. Cervical ectropions, the intra uterine contraceptive device and the combined oral contraceptives may increase physiological discharge. There is a natural increase in vaginal discharge at the time of puberty, ovulation, premenstrual and during pregnancy.^{2,3}

Normal vaginal discharge is physiologic, occurs during pregnancy, sexual arousal or at specific period in the menstrual cycle. Physiologic vaginal discharge in pregnancy is colorless or white, non irritating and odorless or has mild odor and is non infective in nature with no sequelae. On the other hand, abnormal vaginal discharge is pathological, may be

green, yellow, brown or red in colour with foul smelling odor, pruritus, irritation, dysuria or dyspareunia depending on the type of infection.⁴

Symptomatic vaginal discharge is caused by inflammation due to infection of the vaginal mucosa. It occurs in 1-14% of all women in the reproductive age group and is responsible for 5-10 million OPD visits per year throughout the world.⁵ Abnormal vaginal discharge also predisposes to significant morbidity in the form of pelvic inflammatory diseases, infertility, endometriosis, cuff cellulitis, urethral syndrome, pregnancy loss, preterm labour, to enumerate a few. Most common cause of symptomatic vaginal discharge is bacterial vaginosis (33-47%), followed by candidiasis (20-40%) and trichomoniasis (8-10%).^{6,7} These three conditions account for 90% of all etiologies of abnormal vaginal discharge. Multiple infections can also coexist.⁸

A common belief is that bacterial vaginosis is the most common type of vaginal infection among women of reproductive age and accounts for at least one-third of all vulvovaginal infections. Bacterial vaginosis is not caused by a single pathogen but rather

it is a polymicrobial clinical syndrome. Common agents of bacterial vaginosis include *Gardnerella vaginalis*, *Mobiluncus*, *Bacteroides* saprophytes and *Mycobacterium hominus*.⁹

Candidiasis is mostly due to *Candida albicans* and may be associated with diabetes, pregnancy and prolonged use of antibiotics. Patient presents with vaginal discharge and pruritis. Discharge appears to be like curdled milk and deep erythema of vulva and vagina is often seen.⁹ Trichomoniasis is a sexually transmitted disease that results from infection with flagellated protozoa named as *Trichomonas vaginalis*. The prevalence of Trichomoniasis in American women is 35 million WHO estimates the world wide prevalence of Trichomoniasis to be 170 million. The discharge is thin copious and pools in the vaginal vault. On examination vaginal and vulvar erythema is noted. The strawberry cervix in trichomoniasis resulting from punctuate hemorrhage is usually observed with colposcopy.⁹ Successful management depends on accurate identification of the etiologic agent and appropriate treatment. Clinical examination and laboratory tests are usually adequate to diagnose bacterial vaginosis. Diagnosis of *Candida* vulvovaginitis and vaginitis caused by *Trichomonas* may require culture. Bacterial vaginosis is usually treated with a one-week course of metronidazole; treatment during pregnancy and the benefit of concomitant treatment of sexual partners remain points of controversy. Intravaginal application of imidazoles is the recommended initial treatment of *Candida* vulvovaginitis, although several effective alternative treatments are available. *Trichomonas* vaginitis usually responds to oral metronidazole, and treatment of sexual partners is recommended.^{10,14}

Material and Method

A It was a cross-sectional descriptive study conducted from February 2014 to January 2015 at OPD Gynecology Specialist Unit, Services Hospital Lahore. A total of 120 women of reproductive age (13 to 49 years) were included in the study. The objective of the study was to determine the frequency and type of pathogens in vaginal discharge.

Detailed history of patients was taken and every patient underwent complete clinical examination and relevant investigations. High vaginal swab culture sensitivity was done among patients then data was recorded in proforma.

Two plain cotton wool sterile vaginal swabs were

used for High Vaginal Swab (HVS) for each patient. The swabs were rubbed and rotated in posterior vaginal fornix. One swab was used immediately to prepare a wet mount with one to two drops of normal saline on a glass slide and was examined by light microscopy for motility of *Trichomonas vaginalis*. The pus cells, budding yeast cells, pseudohyphal and clue cells were also looked for in the same wet mount. Second swab was immediately sent to the microbiology laboratory for Gram's staining and Culture and Sensitivity for Bacteria. The swab was also inoculated on Sabouraud's agar and incubated at 35 °C±2 °C aerobically for 48 hours for the growth of *Candida* saprophytes. The growth was later examined for yeast cells. Infection with bacterial vaginosis and *Trichomonas vaginalis* was identified by characteristic morphology in a wet mount.

Data was analyzed through computers software SPSS version 17. Informed consent was taken from the patients and confidentiality of data was ensured.

Results

Among 120 patients who had vaginal discharge, 5.8% (n=7) were 13-20 years old, 24.2% (n=29) were 21-30 years old and majority 55.8% (n=67) was 31-40 years old while 14.2% (n=17) patients were 41-49 years old (Table-1).

According to clinical examination, 54.2% (n=65) patients had fungal infection, 18.3% (n=22) had trichomonas and 15.8% (n=19) had bacterial

Table-1: Age group of patients presenting with vaginal discharge.

Age (Years)	Frequency	Percentage
13 - 20	07	05.8%
21 - 30	29	24.2%
31- 40	67	55.8%
41 -50	17	14.2%
Total	120	100%

Table-2: Pathogens according to Clinical Examination in vaginal discharge.

Vaginal Discharge	Frequency	Percentage
Fungal (Candidiasis)	65	54.2%
Bacterial Vaginosis	19	15.8%
Trichomonas	22	18.3%
Mixed	14	11.7%
Total	120	100%

Table-3: Pathogens in HSV according to Microscopy/Culture sensitivity.

Vaginal Discharge	Frequency	Percentage
Fungal (candidiasis)	58	48.3%
Bacterial Vaginosis	30	25.0%
Trichomonas	15	12.5%
Mixed	17	14.2%
Total	120	100%

Vaginosis while 11.7% (n=14) patients had mixed infection in vaginal discharge (**Table-2**).

HVS microscopy / culture sensitivity, results showed that amongst 120 patients, 48.3% (n=58) patients had fungal infection, 25.0% (n=30) had bacterial vaginosis and 12.5% (n=15) had trichomonas, while 14.2% (n=17) patients had mixed infection, in vaginal discharge (**Table-3**).

Discussion

Vaginal discharge is a common health problem among women of reproductive age while incidence of pathogens in vaginal discharge is not exactly known in different countries of the world. This study was conducted on 120 cases and two high vaginal swabs were collected from all patients. The age of patients ranged between 13-49 years. Swabs were examined microbiologically for causative pathogens (yeast, bacteria, and *Trichomonas vaginalis*). The results of this study showed that maximum (55.8%) patients presented were in age range of 31-40 years while second highest range was 21-30 (**Table 1**).

On light microscopy of wet mount of 54.2% (n=65) showed budding yeasts, pseudohyphae while Clue cells were observed in 15.8% (n=19). *Trichomonas vaginalis* motility was seen in 18.3% (n=22) while mixed pathology was considered in 11.7% (n=14) (**Table 2**).

Culture sensitivity of 120 high vaginal swabs revealed that candidiasis 48.3% (n=58) was the most common cause of abnormal vaginal discharge followed by bacterial vaginosis 25.0% (n=30). *Trichomonas vaginalis* was found in 12.5% (n=15) and combined infections was observed in 14.2% (n=17). In 2013, Jahic M et al found that the *Candida* was the commonest organism in vaginal discharge followed by bacterial vaginosis and *Trichomoniasis* in Central Europe.¹⁵ Similarly Candidal infection 31% as reported by Trama JP in an Indian study. In

this study almost similar results were found but some previous studies done in different countries which resulted that bacterial vaginosis was the most common cause of vaginal discharge.¹⁶ Olowe OA found 36% candidiasis in vaginal discharge second to bacterial vaginosis which was 38% and trichomoniasis just 2%.¹⁷

Puri KJ in a recent study in India showed that in females with the complaint of vaginal discharge bacterial vaginosis was the highest (45%) followed by vaginal candidiasis 31% and trichomoniasis (2%).¹⁸ Similarly Samia S. Khamees found that bacterial infection was detected 75.5%.² This might be that bacterial vaginitis is the most common etiology of abnormal vaginal discharge followed by Candidal infections which was 13.12% of abnormal vaginal discharge. While combined infections were isolated from 2.6%.

Our study was conducted in a tertiary care government hospital which drains poor class of population. These patients were partially treated by general practitioners and quacks with history of multiple antibiotic courses before presentation. The presenting patients were not representative of the general population of the country and hence a different organism i.e. *Candida* was found commonest in present study. The study was also performed on limited number of cases so need of larger study with cases true representative of our country population exists.

Conclusion

Vulvovaginal candidiasis was a frequent finding in out patient departments of tertiary care hospitals of our country. All the well documented obstetrical and medical risk factors for underdeveloped world were prevailing in our local female population. All these factors were controllable with proper education, prompt treatment and with the help of media campaigns.

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FREQUENCY OF TYPE-2 DIABETES MELLITUS IN PATIENTS WITH HEPATITIS C VIRUS GENOTYPE 3a

Muhammad Azam, Muhammad Saeed uz Zaman, Muhammad Aftab, Zainab Rizwan, Tariq Suleman and Muhammad Imran

Objective: To evaluate the frequency of type-2 diabetes mellitus in patients having hepatitis C virus genotype 3(a) infection, which is the most common type of genotype in our population.

Material and Methods: A total number of 200 were enrolled from outpatient department of services hospital Lahore which is a tertiary care hospital. This was a descriptive, cross sectional survey. Both male and female patients fulfilling the inclusion and exclusion criteria were included in the study. The patients having chronic hepatitis C infection with genotype 3(a) were screened for diabetes mellitus according to the operational definition.

Results: A total number of 200 patients including 114 males and 86 females were enrolled for study. Their ages ranged from 25 to 60 years. Type 2 diabetes mellitus was found in 54.42 % (n=80) male patients and 45.58 % (n=67) female patients. Out of 200 patients having HCV genotype 3(a) infection, 147(73.5%) had diabetes mellitus.

Conclusion: We concluded that frequency of type-2 diabetes mellitus is high among patients with hepatitis C virus genotype 3(a). So it is recommended that every patient who present with hepatitis C virus genotype 3(a) infection should be screened for type-2 diabetes mellitus. Furthermore, it is also recommended that every setup should have closed surveillance of their patients in order to know the frequency of the problem.

Keywords: Hepatitis C virus, hepatitis C virus genotype 3(a), type-2 diabetes mellitus.

Introduction

Hepatitis C virus (HCV) is a major cause of chronic liver disease affecting an estimated 170 million people worldwide.¹ In Pakistan more than 10 million people are living with Hepatitis C virus, with high morbidity and mortality.² Persistent chronic liver damage eventually progresses from chronic hepatitis to cirrhosis and hepatocellular carcinoma (HCC).³ Although the main target of HCV is liver but it has been associated with diseases of other organs as well. It has been reported that 38% of patients with HCV would manifest at least one extra hepatic manifestation during the course of illness.⁵

Type 2 diabetes mellitus is a common complication of all liver diseases, independent of the etiology especially at the advanced stage. However, clinical and experimental data has suggested a direct role of HCV in the alteration of glucose metabolism.⁴ The relationship between diabetes mellitus and HCV infection has been challenging in the recent decade in the world and has been studied from several aspects.⁵ Review of literature from different parts of the world illustrates that 23% to 62% of patients with chronic HCV infection have associated diabetes mellitus especially type 2 DM. However association of type 2 diabetes mellitus with specific

genotype of HCV has been less studied.

Genotype 3 (a) is the commonest type found in HCV infected patients in our setup. Although an epidemiologic link between hepatitis C and type 2 diabetes mellitus is an established fact but there are not many studies regarding frequency of type 2 diabetes mellitus in patients having genotype 3 (a) HCV infection which is the commonest genotype in Pakistan.⁶ Therefore, this study was planned to identify type 2 diabetes mellitus in patients have HCV infection with genotype - 3(a).

Furthermore among genotypes of HCV, genotype 3 (a) has highest sustained viral response,⁷ but diabetes mellitus is known to reduce the treatment response.⁸ Therefore identification of type 2 diabetes mellitus in specific genotype infection in our population will be beneficial in planning the treatment of HCV infection.

Material and Methods

This descriptive cross sectional survey with non probability purposive sampling technique was carried out on 200 patients in medical unit-I, SIMS/Services Hospital, Lahore. With following inclusion and Inclusion criteria.

- Age between 25-60 years

- Gender: male and female
- All diagnosed cases of Hepatitis C virus, genotype 3 (a).

Exclusion criteria:

- Patient with increased BMI, i.e. ≥ 28
- Family history of diabetes mellitus (History and medical record)
- Already diagnosed patients of type 2 diabetes mellitus (History and medical record)
- Patients who are on interferon and ribavirin treatment or have already completed treatment

Operational definitions:

Type 2 Diabetes mellitus: Two fasting or two random plasma glucose levels of more than 126mg/dl and 200 mg/dl respectively

Hepatitis C Genotype 3 (a):

Hepatitis C Virus infection confirmed on Elisa method and genotype done in the hospital laboratory.

Results

A total numbers of 200 patients, fulfilling the inclusion criteria were enrolled for study to determine the frequency of type 2 diabetes mellitus in patients with hepatitis C virus, genotype 3 (a) infection. Ninety

Table-1: Age distribution of the subjects (n=200).

Age (Years)	Frequency	Percentage
25 - 40	67	33.5%
41 - 50	93	46.5%
51 - 60	40	20%
Total	200	100%
Mean and sd	43.65 \pm 3.47	

Table-2: Gender distribution of the subjects(n=200).

Gender	No. Of Patients	Percentage
Male	114	57%
Female	86	53%
Total	200	100%

Table-3: Frequency of type 2 diabetes mellitus in patients with hepatitis c virus genotype 3(a) (n=200).

Presence of Diabetes	No.of Patients	%	Male%	Female%
Yes	147	73.5%	80(54.42%)	67(45.58)
No	43	26.5%	34(64.15%)	19(35.85%)
Total	200	100%	114	86

three (46.5%) patients in our study were between the age of 41-50 years, 67 (33.5%) patients were between 25-40 years and 40 (20%) patients were between 51-60 years (Table 1). In our study 114 (57%) patients were males and 86(43%) were females (Table-2). Out of these 200 patients with Hepatitis C virus, genotype 3(a) infection, type 2 diabetes mellitus was found in 147 (73.5%) patients. Out of these 147 patients having diabetes mellitus 80 (54.42%) were males and 67(45.58%) were females (Table-3).

Discussion

Hepatitis C virus infection is linked to many extrahepatic manifestations, which include renal, dermatological, cardiac and endocrinological. Except for vasculitic essential mixed cryoglobulinemia and membranous proliferative glomerulonephritis, other manifestation are poorly linked to HCV infection.⁹

The risk of developing T2 DM increases 2-3 times in the presence of HCV infection. The frequency of T2 DM in HCV infected patients is 19-62% as compared to 3-13% in the control group.¹⁰ There is increased incidence of T2 DM in liver and kidney transplant recipients receiving kidney and liver from HCV infected persons.¹¹ Successful interferon treatment improves control of T2 DM. Moreover, T2 DM is associated with rapid progression of liver disease and development of hepatocellular carcinoma in patients infected with HCV.¹¹

We planned this study to see the frequency of T2 DM in patients infected with HCV genotype 3(a), which is the commonest type detected in Pakistan.⁶

The prevalence recorded in our study was 73.5% (n=147) with 54.42% (n=80) males and 45.58%(n=67) females. These finding are consistent with the study conducted by Muzaffar Ali shah and colleagues¹² that showed T2 DM in 84% of patients with HCV genotype 3(a) infection.

Another study done by Amarpurkar and Co-workers,¹³ HCV genotype 3 was seen in 58% of patient suffering from T2 DM.

The data regarding frequency of T2 DM in HCV genotype 3(a) is limited especially in Pakistan. However, the results of our study may be considered a start and further studies should be conducted to determine the association of T2 DM with HCV infection.

Available data has suggested that an expression of the HCV core protein induces hepatic insulin resistance through alteration in signaling in the insulin receptor substrate-1 pathway. Insulin resistance causes hyperinsulinemia. When hyperinsulinemia reaches to

the extent of no longer compensated by the B-cells, insulin secretion declines and pancreatic beta cell failure ensues.¹⁴

Both, liver being the master of metabolism and pancreases for its dual function as endocrine and exocrine gland, play pivotal role in nutrient metabolism. So, the two diseases of study share many complications in their natural course. Therefore, indentifying T2 DM in specific genotype 3(a), which is prevalent genotype in our population, is beneficial in addressing these complications in anticipation for better quality of life. Concomitant presence of T2 DM and HCV has significant implications in clinical decision making for future treatment of the patients.

Conclusions

We concluded that frequency of T2 DM is high

among patients with Hepatitis C virus genotype 3(a). So, it recommended that every patient who present with hepatitis C virus genotype 3(a) should be screened for type 2 diabetes mellitus. Since there is high frequency of T2 DM in HCV patients, it is recommended that every setup should have their own close surveillance program to know the magnitude of the problem in that population group.

This study will form the basis of future research in multiple directions of two common diseases that share many complications of disordered nutrient metabolism that may include markers of disease identification and progress.

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Case Series

ENCOUNTERING XANTHOGRANULOMATOUS INFLAMMATION IN A MYRIAD OF SETTINGS

Ambereen A Imran

Background: Xanthogranulomatous inflammation is a rare but well recognized variety of chronic inflammation seen in multiple sites. It may present as a mass lesion and mimic malignant tumors, in other cases it may be discovered as an incidental finding in tissues removed for different reasons. Xanthogranulomatous inflammation was encountered in five different cases which included two gall bladders, one kidney, one endoscopic biopsy from gastric mucosa and one collaural fistula. The demographic data as well as pathological findings are described. Although the exact etiopathogenesis of xanthogranulomatous inflammation is still debated, it is agreed that it has no pre-malignant potential. Therefore, resection is considered adequate therapy for effected patients. This makes it all the more important to recognize it in its various morphological forms, even in endoscopic biopsies, to avoid unnecessary extirpative procedures.

Key words: Xanthogranulomatous inflammation, foamy macrophages, collaural fistula, endoscopic biopsy.

Introduction

Xanthogranulomatous inflammation is a rare but well recognized variety of chronic inflammation.¹ It is described most often in kidney, gall bladder, appendix and colon, but involvement of female genital tract, breast and branchial cleft cyst have also been reported.² It may present as a mass lesion and mimic malignant tumors. Its etiopathogenesis remains obscure though infection, outflow obstruction, abscess formation and hemorrhage have been advanced as possible incriminants by different authors.^{1,3} Recognition of the entity in its various forms is important because, as stated earlier, it could be mistaken for a malignant tumor resulting in unnecessary resective surgeries.^{4,5} It was seen in five of our patients recently and the findings are being summed up in this paper.

Materials and Methods

This paper deals with five cases diagnosed with xanthogranulomatous inflammation. There were two gall bladders, one kidney, one endoscopic biopsy from gastric mucosa and one collaural fistula. All specimens were received in Pathology Department of PGMI, Lahore from Lahore General Hospital, Lahore. One of the gall bladders and the gastric biopsy had been submitted with the suspicion of a malignant growth. The demographic details as well as findings are summarized in Table. All cases were diagnosed on hematoxylin and eosin stained slides. PAS stain was employed where indicated. The microscopic findings are depicted in Fig 1-3.

All cases contained collections of foamy macrophages (Fig 1-3) with a variable admixture of giant cells, lymphocytes and plasma cells. These

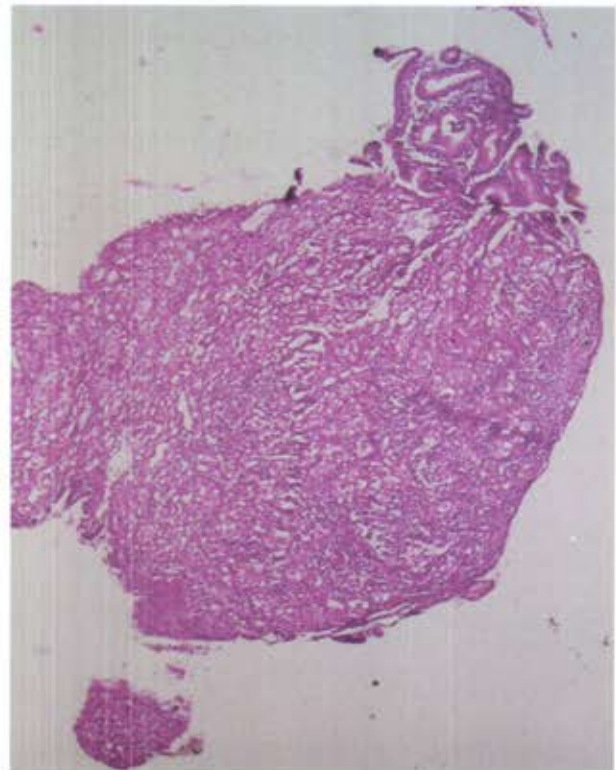


Fig-1: Photomicrograph showing endoscopic biopsy from gastric mucosa. There are sheets of foamy macrophages admixed with lymphocytes and plasma cells. (H&E, x40)

Collections replaced the native architecture to a variable degree. Cases with a short clinical history comprised mostly of rounded histiocytes with foamy to granular cytoplasm (Fig 1,2). Cases with a prolonged history showed similar cells admixed with spindle shaped cells (Fig 3). In these cases the granulomatous nature of the lesions was more obvious. They also showed adherence to and involvement of surrounding structures. The kidney and one of the gall bladders showed these changes.

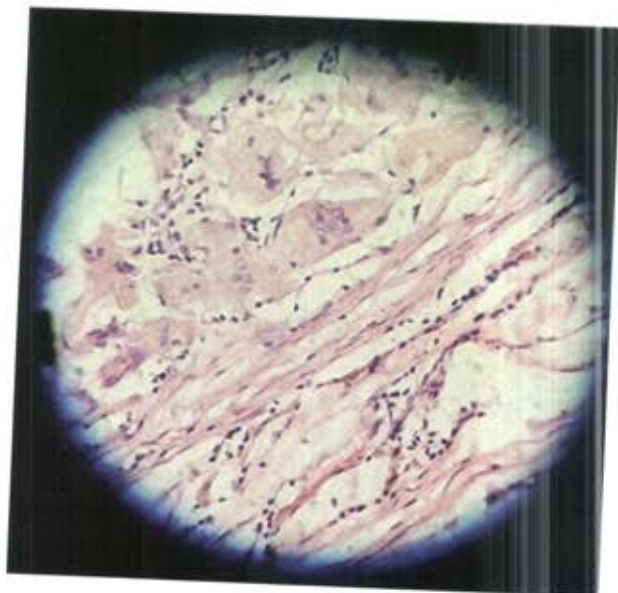


Fig-2: Photomicrograph showing the wall of collaural fistula. The lining epithelium is replaced by foamy macrophages, histiocytes with granular cytoplasm, lymphocytes, plasma cells and macrophages. (H & E, x 400)

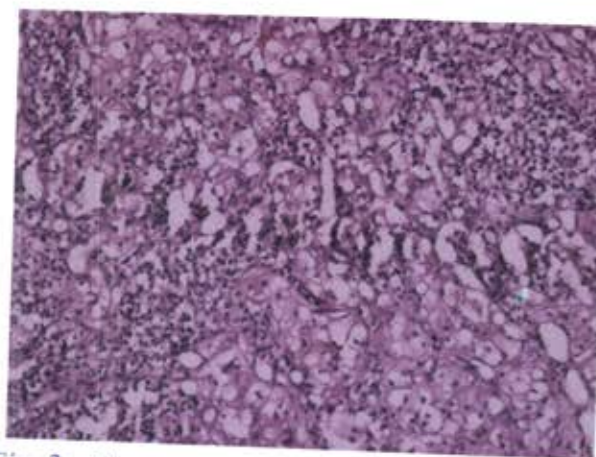


Fig-3: Photomicrograph showing xanthogranulomatous inflammation in kidney. There is an admixture of foamy macrophages with spindle cells, lymphocytes and plasma cells. (H & E, x 100)

Discussion

Xanthogranulomatous inflammation was first described by Schlagenhauser in 1916.⁴ Since then it has been reported in many different organs and tissues. Its importance stems from its ability to form a mass, a fact borne out by terms like 'inflammatory tumor of the kidney'. It has no pre malignant potential.⁷

The exact cause and pathogenesis of the entity have not been established so far. As stated above numerous factors have been considered. Of these infection and outflow obstruction are said to be the most important, though the role of mucosal breakage and leakage of contents into deeper tissues has also found favor.^{1,3,8} Several authors have described the temporal

Table-1: Table showing the demographic data and morphological findings of cases.

Organ/ Tissue	Age and Clinical gender of diagnosis the patient	Clinical Diagnosis	Gross Findings	Microscopic Findings
Gallbladder	35yr, M	Chronic cholecystitis	Thickened, ulcerated wall with yellow spots	Sheets of foamy macrophages admixed with lymphocytes, plasma cells and areas of hemorrhage. Cholesterol clefts.
Gallbladder	42yr, M	Adenocarcinoma gallbladder	Thickened, ulcerated wall with yellow spots	Foamy macrophages, spindle shaped cells, admixed with lymphocytes and plasma cells. Numerous micro abscesses and areas of hemorrhage.
Kidney	54yr, M	Chronic pyelonephritis	Scarred kidney with multiple stones	Micro abscesses, areas of hemorrhage, spindle shaped histiocytes, fibrosis, cholesterol clefts
Gastric mucosa	60yr, M	Carcinoma Stomach	Routine endoscopic biopsy	Sheets of foamy macrophages with lymphocytes and plasma cells.
Collaural Fistula	35yr, M	Collaural fistula	Multiple grey white soft tissue pieces	Foamy macrophages replacing the lining epithelium, occasional giant cells.

changes seen in cases of xanthogranulomatous inflammation. These include the gradual replacement of rounded foamy and granular histiocytes by elongated, spindle cells.⁹ This metamorphosis was seen in our cases too; those with a longer duration had a greater proportion of elongated cells and fibrosis (**Table, Fig 1-3**).

Another notable feature is the widespread tissue destruction seen around areas of xanthogranulomatous inflammation. Most authors agree that the former predates the latter, i.e., first there is tissue destruction then there is replacement by the specific components associated with xanthogranulomatous inflammation. A small subset of workers is of the opinion that the process may be self-perpetuating and once begun may continue to smolder and spread. In either case, what is undebatable is the destruction and dissolution of surrounding parenchyma and its eventual replacement by fibrous tissue.^{3,10,11} This leads to adherence to neighboring organs, difficulty in surgical excision and increased suspicion of a malignant nature (**Fig 3**). Cases are on record where xanthogranulomatous

inflammation was over-diagnosed as a malignant tumor resulting in unwarranted resections.^{3,5,8,12}

This paper is being written to highlight the fact that possibility of this lesion should be entertained in the differential diagnosis of masses from a variety of described, as well as yet undescribed, tissue sites. Since it is an inflammatory condition and has no pre-malignant potential, resection is considered adequate therapy for effected patients.^{2,8}

Conclusion

Although the exact etiopathogenesis of xanthogranulomatous inflammation is still debated, it is agreed that it has no pre-malignant potential. Therefore, resection is considered adequate therapy for effected patients. This makes it all the more important to recognize it in its various morphological forms, even in endoscopic biopsies, to avoid unnecessary extirpative procedures.

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Case Report

ISOLATED FALLOPIAN TUBE TORSION: A CASE REPORT

Naeem Liaqat, Asad Rauf, Nayyar Sultan, Ejaz Ahmad and Sajid Hameed Dar

Abstract: In children right iliac fossa pain is a common presentation and has a lot of differentials. Of the uncommon differentials, fallopian tube torsion is a rare entity. It is usually not suspected and found peroperatively. We had a 12 years old patient who presented with right iliac fossa pain and was found having isolated fallopian tube torsion. Patient underwent right salpingectomy and is doing well to date.

Key words: fallopian tube, children, pelvis, appendicitis.

Introduction

Isolated fallopian tube torsion is a rare cause of lower abdominal pain and emergency surgery in pediatric population. Its reported incidence is 1 in 1.5 million females of reproductive age, even more uncommon in adolescent age.¹ Preoperative diagnosis is very difficult. Often treatment is delayed even in the presence of modern diagnostic techniques; surgical intervention is usually required to establish the diagnosis. We report a case of twisted right fallopian tube with gangrenous distal portion in a 12 year old female.

Case Presentation

A 12 years old female presented in emergency with complaints of sudden abdominal pain in right lower quadrant, nausea, vomiting and fever. Her symptoms started 4 days ago. Her pain was sudden, colicky, non-radiating and became more severe at the day of presentation. She had a single episode of per vaginal bleeding 4 days back, which was dark red in colour and 3-5 ml in quantity. There was no history of trauma, dysuria, constipation or diarrhea. On examination she was febrile and had tenderness in right iliac fossa. Rest of general and systemic examination was unremarkable. Her laboratory investigations revealed leukocytosis with white blood count being 12000/mm.³ Ultrasonography showed a 6x2 cm right adnexal mass with mixed echogenicity, present in Right Iliac fossa. Patient was optimized and she was explored through Pfannenstiel incision. Her right fallopian tube was twisted at its distal part and was gangrenous; proximal part was edematous and inflamed. Her right ovary was slightly hyperemic while left ovary was normal looking. Gangrenous portion of fallopian tube was ligated and right sided salpingectomy was done. Post-operative period was uneventful. She was discharged on third post op day.



Fig-1: Right ovary and fallopian tube of patient showing torsion. Uterus left ovary is normal.

Discussion

Isolated fallopian tube torsion is a rare entity. Till 2014, only 45 cases are reported in pediatric population with mean age of 13.2 years. Risk factors which have been seen in adult patients include pelvic inflammatory disease, previous surgery, ectopic pregnancy, endometriosis and Para tubal cysts.² Causes for this rare entity can be classified into intrinsic, extrinsic and congenital causes. Intrinsic causes include hydrosalpinx, haematosalpinx, tubal neoplasms and prior surgery; extrinsic causes like ovarian mass, tubal adhesion trauma, uterine enlargement and venous congestion and congenital causes include incomplete distal mesosalpinx and excessive length of tube.^{3,4} Bernadus et al suggested that all of the above mentioned factors lead to mechanical blockage of the adnexal veins and lymphatics leading to pelvic congestion and local edema, which ultimately leads to enlargement of the adnexa and induces partial or complete torsion.³ Fallopian tube torsion is most often reported on right side because left sided fallopian tube is supported by sigmoid mesocolon and also right side is often explored due to suspicion of acute appendicitis.⁵ In our case it was also right side involved. Presentation is often delayed due to lack of pathognomonic symptoms. Diagnosis is usually

Confirmed on exploration. Ultrasound and CT scan can help by showing normal appearing ovaries with normal blood flow and a dilated tube with thickened, echogenic walls and internal debrinous or a convoluted echogenic mass.^{6,7} In our case it was not suspected preoperatively also and was diagnosed peroperatively.

Different treatment options are available. If it is diagnosed preoperatively, laparoscopic adnexal detorsion is the procedure of choice particularly if ischemic damages appear to be reversible, and no malignancy is suspected. Efforts should be made to preserve fertility and a complete resection is

performed only when the tissue is gangrenous or there is a tubal or ovarian neoplasm suspected.⁸

Conclusion

In conclusion although a rare cause of acute abdomen and pelvic inflammatory disease, it must be kept in mind as pelvic pathology and should be promptly treated.

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Short Communication

EBOLA VIRUS DISEASE: AN EMERGING THREAT, ARE WE SAFE?

Akbar Shoukat Ali

Ebola virus (EBOV) is one of the emerging global health care concerns, a highly virulent pathogen capable of death-dealing within days of exposure.¹ It causes a very fatal hemorrhagic fever, called Ebola virus disease. More recent events especially the 2014 outbreak have alerted the health care systems throughout the world.² The absence of treatment combined with no vaccination options, makes Ebola virus a formidable pathogen.³ Ebola viruses belong to Filovirus family, which are pleomorphic, RNA viruses.⁴ Zaire ebolavirus, Sudan ebolavirus, Reston ebolavirus, Tai Forest ebolavirus, and Bundibugyo ebolavirus are recognized species within the genus, with Zaire ebolavirus exhibiting the highest mortality rate.^{4,5} Human-to-human transmission can occur by means of immediate contact with blood or body fluids from an afflicted individual or by contact with items contaminated by the organism, especially needles and syringes.^{6,8} Bats are viewed as the regular reservoir of the Ebola disease.^{7,8} Symptomatology of Ebola virus disease can be characterized by fever, malaise, cephalgia, joint, muscle and abdominal pain.⁹ As the disease advances, patients display coagulation abnormalities, for instance, gastrointestinal bleeding and a range of hematological irregularities, such as lymphopenia and neutrophilia. The terminal stage manifests as diffuse bleeding, and hypotensive shock.^{10,11}

2014 Ebola Outbreak

The incidence of the Ebola virus disease occurred for the first time on 26th august 1976¹² in Democratic Republic of Congo.² Many outbreaks have occurred so far in Africa,¹³ with mortality rates ranging from 25% to 90% in past outbreaks, averaging 50%.⁵ As of October 5, 2014, there were 8033 identified cases of Ebola virus disease, with 3865 associated deaths in West Africa.¹⁴ It has been estimated that five new cases are being reported every hour in Sierra Leone.¹⁵ Certainly 2014 outbreak has surpassed the mortality rate from all previous outbreaks combined.¹⁶ Lack of appropriate treatment options further exacerbates the nature of disease and can increase associated morbidity and mortality.⁴ Vaccine is still under the process of development.¹⁷

Prevention

Ebola virus outbreak has already affected the health

care systems throughout the world. Though Pakistan is to date Ebola free but the danger keeps looming, indeed we need a multifaceted strategy to get ourselves prepare from any future uncertainties.¹⁸ Realizing the alarming situation, Ministry of National Health Services of Pakistan has forewarned that Ebola virus might attack Pakistan due to frequent movement of people from African countries.¹⁹ Precautions are similar to those for any other viruses such as avoidance of contact with blood and body fluids and not to handle items that may have come in contact with an infected person's blood or body fluids. In addition to that contact with bats and blood, fluids, and raw meat prepared from these animals must be avoided. Standard precautions such as protective clothing, including masks, gloves, gowns, and eye protection and proper infection control and sterilization measures should be practiced while handling patients infected with Ebola virus disease.¹⁹ Quarantine is an effective method in mitigating the spread of disease.²⁰ Moreover, movement of people from or to affected areas should be extensively monitored by higher authorities. Another strategy could be the arrangement of seminars and symposia for public awareness.

Conclusion

To date, there are no reported cases of Ebola virus disease in Pakistan but according to WHO declaration, it is a global public health emergency which demands extreme precautionary measures. Unfortunately, Pakistan lacks necessary quarantine facilities in case of any reported infection. It is noteworthy to mention here that government and health policy makers can play a key role by establishing programs or workshops aimed at facing any untoward situation associated with this emerging disease. Moreover, research is of utmost importance in this regard for better understanding of mechanisms underlying the pathogenicity of Ebola virus disease. There is no doubt disease anywhere is disease everywhere whatsoever.

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