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Original Article

Experience of Subfascial Endoscopic Perforator Surgery (SEPS) for Treating Venous Ulcers at Tertiary Care Hospital, Lahore

Fara Hassan, Muhammad Naeem Afzal, Shabbar Hussain Changazi, Muhammad Umar Warraich, Samiullah Bhatti and Ayesha Choudry

Objective: To evaluate the outcome and post-operative complications of subfascial endoscopic perforator surgery (SEPS) for treating venous ulcers and skin changes associated with chronic venous insufficiency.

Methods: This was a prospective cross sectional survey which was conducted at surgical department of Sir Ganga Ram Hospital Lahore from September 2014 to March 2017. A total of 63 subfascial endoscopic perforator ligations were performed on 63 limbs of the patients. Quantitative data was presented using mean±SD. Qualitative data was presented using frequency table and percentages. Patient follow-up was scheduled at 2 weeks, 1 month, 6months, 12 months and 24 months.

Results: Mean age of patients was 40.7 years. Male female ratio was 6:1. The most frequent symptom at presentation was pain in the leg (66.7%) and the most frequent sign was skin changes with active ulcer (61.9%). 39 patients had incompetent saphenofemoral junction with incompetent perforating veins while 24 patients had incompetent perforating veins alone. Mean operative time for the SEPS was 66.9 minutes. Average postoperative pain score was 5. Early postoperative complications included hematoma in 14.2% of patients, edema in 28.7%, surgical emphysema in 28.6%, and saphenous neuralgia in 4.76% and wound infection in 1.6% of patients. There were no early deaths, and there was no clinical evidence of thromboembolism within 1 month of the procedure. At 6 months follow up skin changes were improved in 95% of patients, active ulcers were healed in 100 % of patients and there was no recurrence of ulcers at 24 months postoperatively.

Conclusions: SEPS is minimally invasive technique for management of venous ulcers leading to early patient mobility, early return to work, better ulcer healing and no ulcer recurrence.

Keywords: subfascial endoscopic perforator surgery (SEPS), venous ulcers, post-operative complications.

Introduction

Venous stasis ulcers which is sequelae and complication of chronic venous insufficiency always required proper management ranging from life style modification, compression stockings to surgical approach. It has long been noted that incompetent perforating veins contribute to the development of chronic venous insufficiency that are complicated by skin ulcerations or liposclerroderma. For these conditions, severing of incompetent perforating veins is an effective surgical treatment. However, severing of incompetent perforating veins by open surgical approach has become less commonly performed because of the excessive invasiveness of the procedure.[1] Endoscopic ligation of perforating veins, or subfascial endoscopic perforating vein surgery (SEPS), is valuable in treatment of venous ulcer on the medial aspect of the lower leg.[2] The procedure can be performed quickly, with fewer complications and better results than with subcutaneous or subfascial open surgical exploration.[3]

Perforating vein insufficiency can lead to varicosities, various skin changes, and ulceration. These ulcers are notoriously slow to heal, and generally recur if the underlying cause of venous hypertension is not removed. Therefore the primary goal should be to relieve high venous pressure in the skin, with ligation of the insufficient perforating veins at subfascial endoscopy. Subfascial endoscopic interruption of perforating veins (SEPS) alone or combined with ablation of superficial venous reflux has emerged as a potential y useful therapeutic option in patients with severe forms of CVI, particularly CEAP clinical class 5 and 6 disease.[4] The CEAP classification (Clinical-Etiology-Anatomy-Pathophysiology) was adopted worldwide to facilitate meaningful communication about CVD and serve as a basis for more scientific analysis of management. CEAP classification includes 7 categories. Category 0:

No visible or palpable signs of venous disease;
Category-1: Reticular veins or telangiectasia;
Category-2: Visible and palpable Varicose veins;
Category-3: Venous edema without trophic changes.
Category-4: Skin changes (pigmentation, venous eczema, lipodermatosclerosis.
Category-5: Skin changes with healed ulcers;
Category -6: Skin changes with active ulcers.[5,6]
SEPS involves the introduction of endoscope into the subfascial compartment below the knee via a small medial incision. Perforating veins are clipped and divided under direct vision through the endoscope. Furthermore, randomized clinical trials have demonstrated that when SEPS is compared with open perforator vein ligation, ulcer healing and recurrence rates are similar but there is significantly less morbidity with SEPS.[7,8] Our experience with SEPS emphasizes that SEPS either alone or combined with flush ligation of greater saphenous vein (GSV) reflux aids venous ulcer healing. The objective of this study was to see the outcome and post-operative complication of subfascial endoscopic perforator surgery (SEPS) for treating venous ulcers and skin changes associated with chronic venous insufficiency.

Methods

This was a prospective cross sectional survey which was conducted at Surgical department of Sir GangaRam Hospital Lahore from September 2014 to March 2017. First patient was recruited in September 2014 and last patient was recruited in March 2017. A total of 63 patients were included in the study. Ethical approval was obtained from the Hospital ethical committee. Written informed consent was taken from all patients. A total of 63 subfascial endoscopic perforator ligations were performed on 63 limbs of the patients. Patients with previous varicose veins surgery, previous limb surgery and complex tortuous varicosities and patients with previous history of DVT were excluded from the study. Non probability purposive sampling technique was used for sample selection. Demographic, physical and vascular laboratory data collected for all patients. Clinical severity score9,10 pre operatively was 5.73. Preoperative evaluation with detailed history and physical examination including trendelenburg test along with color ultrasound scanning was performed. Data was entered and analyzed by using SPSS 20. Quantitative data was presented using mean±SD. Qualitative data was presented using frequency table and percentages. After establishing general (=27) or spinal anesthesia (n=36), the affected limb was prepared from groin to ankle in a sterile fashion. A single dose of antibiotics administered before surgery. The leg was then positioned with the knee and ankle elevated on padded stands so that the lower leg was elevated and parallel to the table, allowing unencumbered movement of instrument handles. Two incisions were placed in the upper calf. The first incision was placed 2 cm from the edge of the tibia and at least 10 cm distal to the tibial tuberosity. A 10 mm port was then placed in the initial incision, and the subfascial tunnel was expanded and maintained with CO2 insufflation to 15 mm Hg. A 10 mm scope was used for surgery. A5 mm port was then placed approximately 5cm lateral and distal to the first incision for tissue dissection and clipping. Connective tissue bridging the subfascial plane was taken down by blunt or sharp dissection.

The perforating veins were clipped with endo clip applier. The incisions were closed and the leg wrapped with an ace bandage. All patients with greater saphenous vein incompetence underwent concomitant flush ligation of GSV. Patients were followed at 2 weeks, 1 month, 3 month, 6 month and 24 month and complications like wound infection, bleeding, surgical emphysema and edema (assessed by physical examination) and recurrence of varicose veins were noted. Post-operative duplex scanning was performed at one month to determine that the perforators were ablated. In active ulcers, saline soaked daily dressing was applied postoperatively.

Results

A total of 63 subfascial endoscopic perforator ligations were performed on 63 limbs of the patients. Among them 54 were male and 9 were females. Occupation wise 12 were traffic wardens, 15 were farmers, 17 were laborers, 5 were shopkeepers, 5 electrician and all the female were house wives. Mean age of patient was 40.7 years and ranged from 27 to 65 years. The most frequent symptom at presentation was pain in the leg (66.7%) and the most frequent sign was skin changes with active ulcer (61.9%). Among them 39 had active ulcers (C6), 18 patients had healed ulcers (C 5) and 6 patients had skin changes of chronic venous insufficiency (pain, edema, lipodermat-osclerosis without ulceration) (C 4). 24 patients had incompetent saphenofemoral junction with incompetent perforating veins while 39 patients had incompetent perforating veins alone **(Table-1).** 33 patients had SEPS on the right leg and 30 on the left

leg. Mean operative time for the SEPS was 66.9 Minutes (range 50 min to 80 min). Average number of perforators clipped were 4 with 4 perforators clipped in 39 patients, 9 perforators in 6 patients and 5 perforators in 15 patients. Average postoperative pain score was 5 (measured at 6 to 8 hrs). 45 patients (pain score >5) required one dose of analgesia (intravenous toradol) within 6-8 hrs of surgery while 18 patients required additional dose of analgesic within 8-12 hrs. Early postoperative complications included hematoma in 9 patients (14.2%), edema in 15 cases (28.7%) surgical emphysema at portal site in 18 patients (28.6%), saphenous neuralgia in 3 patients (4.76%) and only 1(1.6%) patient had wound infection **(Table-2).** There were no early deaths and there was no clinical evidence of thromboembolism within 1 month of the procedure. Clinical severity score was 1.7 post operatively after 1 month of SEPS. 45 patients (71%) patients become mobile within 8-12 hrs of surgery while 18 (28.57%) patients become mobile after 24 hrs. 51 patients (85.3%) patients had early return to work within a week after surgery mean hospital stay(1.5days). At 3 month and 6 month follow up skin changes were improved in 87% and 95% of patients and active ulcers were healed in 92% and 100% of patients respectively. There was no recurrence of ulcers at 24 months postoperatively **(Table-3).**

Table-1: Preoperative evaluation of patients.

Parameters		No. of Patients (n)	%Age
Presenting Complaint	Skin changes with healed ulcers	18	28.6
	Skin chages with active venous uker pain	39	61.9
	Pain	42	66.7
CEAP Clasification	Skin Changes C4	06	9.5
	Healed ulcers C5	18	28.6
	Active ulcers C6	39	61.9
SF Function	Competent	39	61.9
	Non cometent	24	38.1
Type of procedure	SEPS+Flush ligation of GSV	24	38.1
	Seps alone	39	61.9

Table-2: Complication of surgery.

Complications	No. of Patients (n)	%Age
Pain (score >5)	18	28.6
Hematoma	09	14.3
Wound infection	01	1.6
Surgical emphysema	18	28.6
Edema	15	23.6
Saphenous nerve injury	03	4.8

Table-3: Follow up.

Parameters		No. of Patients (n)	%Age
Pain	After 2 weeks	12	28.6
	After 1 month	03	7.1
	After 3 months	01	2.4
Skin Healing	After 1 months	16	41
	After 3 months	36	92.3
	After 6 months	39	100
Skin charges improvement	After 1 months	03	14.3
	After 3 months	18	85.7
	After 6 months	20	95.2
Ulcer Recurrence	After 6 months	0	0.0
	After 12 months	0	0.0
	After 24 months	0	0.0

Discussion

The pathophysiology of CVI suggests that venous hypertension is linked to severe skin changes and ulceration. Furthermore, these changes can be favorably modified with ablation of superficial venous reflux[11,12] Our early favorable observations of rapid ulcer healing, improvement in lipodermatosclerosis, and fading of hyperpigmentation appeared directly related to correction of perforating and superficial venous reflux by aggressive surgical intervention. Although conventional open surgical techniques like stab avulsion or open ligation of perforators are effective surgical techniques but these techniques multiple incisions with greater postoperative pain and increased risk of infections. So, SEPS was the only reliable way to correct pathologic outward flow in the perforating veins when there was persistent superficial reflux or coexistent deep venous reflux.[13] This was a prospective cross sectional study which showed that skin changes were improved to near normal in 95% of patients and active ulcer was healed in all patients at 6 months follow up while there was no recurrence at 24 months follow up.

In this study 9 patients (14.2%) developed hematoma, 3 patients (4.76%) had saphenous neuralgia in and only 1(1.6%) patient had wound infection. There were no early deaths and there was no clinical evidence of thromboembolism within 1 month of the procedure. Vashist et al.,[14] in his study demonstrated hematoma in 2% of cases but no wound infection or paresthesia. However, Tenbrook et al.[15] reported wound infection in 6% of patients, hematoma 9%, neuralgia 7%, and deep venous thrombosis 1% in patients after SEPS. Kumar et al.,[16] showed wound infection in 4.7% of cases and neuralgia in 4.7% of cases after SEPS. Nelzen reported a wound complication rate of 16% in his study.[17]In this study, SEPS either alone or combined with flush ligation of GSV (great saphenous vein) as part of a comprehensive treatment plan for CVI, yielded good results in terms of ulcer healing and symptom relief. Ulcer healing was 41% after 2 weeks and 92% after 1 month and 100% after 3 months. Skin changes alone(C4)or with healed ulcers(C5) at the time of operation were improved in 95% of patients at 3 months. There was no new or recurrent ulcer formation or recurrent varices during follow-up at 3 months. Tenbrook et al.[15] reported ulcer healing in 88% of patients while other researchers reported 100% ulcer healing rate.[14,16-19] One limitation of study was that this study could have been done as randomized controlled trail by taking open surgery as a standard. So that results could have better implication and applicability. This study showed that chronic pain was present in only 2.4% of patients at a follow up of 6 months period and there was no recurrence at 24 months period follow up so it can be proposed that this minimally invasive technique is the need of the hour and more and more young surgeons should be trained and provided facilities to learn and implement this technique.

Conclusion

SEPS is minimally invasive technique for the treatment of venous ulcers leading to early patient mobility, early return to work, better ulcer healing and no ulcer recurrence.

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Original Article

The Prognosis of Surgical Site Infection Post Osteosynthesis of Long Tubular Bones

Ehsan ul Haq, Shafqat Wasim Ch. Maryam Jamill and Ali Raza Hashmi

Objective: To identify risk factors for the development of SSI post osteosynthesis of long tubular bones with diaphyseal fractures, assess them in quantitative terms to form a risk group.

Methods: Cohort retrospective-prospective study. Inclusion criteria: patients with fracture of long tubular bone (LTB) post metalosteosynthesis (MOS), duration (2011-2016), location in our department*. Exclusion criteria: death or loss of communication with the patient in less than 12 months post intervention. A retrospective analysis of data on 179 patients who underwent MOS of LTB with diaphyseal fractures was performed. Data on 144 patients who underwent MOS without surgical site infection (SSI) were compared with data of 35 patients who had SSI within one year post operation. The method of sequential analysis was applied.

Results: When studying the data on the retrospective group, a database was created that became the basis for the development of a mathematical prognosis for the development of local infectious complications in patients who underwent MOS of LTB with diaphyseal fractures. 18 criteria for the prognosis of the development of SSI were determined. Sensitivity 94.29%.

Conclusions: In the prospective study (117 cases), the established prognosis program have been tested. As a result of monitoring patients, the incidence of SSI decreased from 19.6% to 9.4%.

Keywords: long tubular bones, diaphyseal fracture, metalosteosynthesis, surgical site infection, prognosis.

Introduction

Post traumatic fractures of long bones of extremities take the leading place in trauma in the last decades. According to different authors, it varies between 16.7% to 49.8% among all musculoskeletal injuries.[1] At the same time open fractures have been found in 10 - 18% of among all fractures of the long tubular bones (LTB).[2] Local infection rate in the early post-operative period post metalosteosynthesis (MOS) of long bones is 2 - 12%, reaching 55.9% in case of open fracture of tibia/fibula.[3,4] The deep infection rate at surgical site has been observed between 1.3% - 4.0%, at the same time it has reached 22.6% in victims with open fractures of a tibia.[4,5] In recent years there were a significant amount of the publications addressed to the question of prognosis in trauma and orthopedics.[6,7] In literature data can be found concerning infection at surgical site in treatment of fractures of long bones of extremities.[8-10] At the same time, authors have no single point of view at the type and ponder ability of prognostic criteria, and data on the capacity of such a prognosis are contradictory. In this regard, the study of aspects related to the development of methods for predicting SSI post MOS of LTB can be considered an actual topic of scientific medical research. The aim of the study was to identify the risk factors for the development of SSI occurred post MOS of LTB in diaphyseal fractures, assessing them in quantitative equivalent for the formation of a risk group.

Methods

The study was carried out with permission of the Bioethics Committee. Metallosteosynthesis with diaphyseal fractures of long tubular bones at the Department of Orthopedics* (herein after referred to as «the clinic») was conducted in 2011-2016 in 347 patients. Patients were divided into two study groups: a retrospective (230 patients who underwent MOS in 2011-2014) and a prospective (117 patients who underwent MOS in 2015-2016). In retrospective group average age of patients was 56.8 ± 18,2 (from 18 to 90 years),mortality rate 2.6% (6 cases). 224 patients were discharged from the clinic. Within one year, long-term results were evaluated in 179 (79.9%) patients. In 45 (20.1%) patients 12 months post intervention the results could not be assessed due to loss of communication with them or in case of their death.` Preoperative preparation and prevention of infection at the surgical site was carried out in retrospective group as a standard procedure. In these 179 patients,

Dynamic compression plate (DCP) was performed in 90 (50.3%) cases, IM nail - in 52 (29.1%) patients. External fixator was performed in 32 cases (17.8%). In 5 (2.8%) cases, other types of MOS were used (K-Wires, cerclage, screws, etc.) (**Table-1**). Within one year after the operation, local infectious complications were detected in 35 (19.6%) cases, with a deep infection noted in 10 patients (5.6%). Both superficial and deep infection in the field of surgical intervention were considered.[11]

In retrospective group allocated 2 subgroups: I patients who had no infection in the operation area (144 patients) within 12 months after the intervention and II - patients with superficial and deep infection in the operation area (35 patients).A comparative analysis of the data on these two subgroups of the retrospective study was carried out using the method of A. Wald (1960)[12]. At the same time, both the risk factors for the infection at the operation site and their quantitative equivalent were determined. Based on these values the risk of development of infection, identified retrospectively, a model was developed for predicting the course of the postoperative period in patients after MOS of long tubular bones. To assess the diagnostic effectiveness of the model (according to the data of the retrospective group), the sensitivity (Se) and specificity (Sp) were determined, and the positive and negative predictive value of the test was assessed using the program: Medcalc.org/calc/diagnostic-test.php. Prospective group received preoperative preparation taking into account the prognosis and the developed algorithms. Clinical implementation of the prognosis of infection in the wound area after MOS of long tubular bones was performed in 117 patients from the prospective group. The method of sequential analysis allows to carry out the forecast at all stages of treatment, including an incomplete set of characteristics. According to this method, in the presence of A and B states characterized by the same symptoms, by sequentially summing the logarithms (l) of the probability of occurrence of individual symptoms in state A and the probability of their occurrence in state B, information can gradually be accumulated that allows one to differentiate with a given accuracy these states. If the value of the error in diagnosing the state A is taken as d, and for the error value when diagnosing the state B - b, then for a sum of the logarithms of the indicated ratios greater than in (l - d / b), with the established reliability level, for a sum of logarithms smaller than ln (/l-b) - state B, with the sum of the logarithms within the specified range, a conclusion is made about an uncertain estimate for a given level of reliability.

Results

85 parameters were analyzed, reflecting the patient's condition, data of his clinical status, laboratory and radiological examination. These included information about the general and local status of the patient (sex, age, concomitant pathology, body mass index, etc.), data on surgical intervention (duration of operation, amount of intra-operative blood loss, type of intervention, etc.). Separately, a number of indicators of laboratory and instrumental research were analyzed. The risk factorsused to predict infection at surgical site include parameters that have significant differences ($p<0.05$) in the study groups, as well as prognostic criteria for which the p-level error probability exceeded the generally accepted norm, but was identified the trend of manifestations of differences (at least, 1.5 times in percentage terms). However, there was an expert evaluation of other researchers, where the p-level of the analyzed risk factor was statistically confirmed. Thus, 18 prognostic criteria were selected for the program. Among them, 12 were used in the preoperative period, 4 - during the intervention and one - in the early postoperative period. As an example, we give data on the distribution of patients, taking into account the localization of the fracture, as one of the risk factors for infection at surgical site **(Table-2).**

As follows from the data of **(Table-1)**, in the group with uncomplicated course of the postoperative period of patients with fractures of the humerus was 39.6%, and among patients with the later developed at the surgical site cases of fracture of the humerus was 17.1%, i.e. 2.3 times less. The opposite situation is observed with a fracture of the tibia/fibula. Among patients with a favorable postoperative period of such observations was 24.3%, and among patients with infectious complications 40%.In statistical analysis, it is determined that the number of degrees of freedom is 3. The value of the criterion $\chi 2$ is 14.206. The critical value of $\chi 2$ at a significance level of $p <0.01$ is 11.345. The relationship between the factor and the outcome is statistically significant at a significance level of $p <0.01$. Thus, the localization of the fracture was taken into account when developing a mathematical model for the prediction of the surgical site infection. Similarly, other criteria for predicting the development of local complications were selected. After the formation of a complete list of prognostic factors, the correlation index and the coefficient of prognosis

Were calculated. The ratio index was a quotient between the frequency of occurrence of the symptom in the group of patients with a favorable course of the postoperative period and the frequency of its occurrence among patients with infections at surgical site. The coefficient of prognosis was a natural logarithm (ln) of the ratio index increased, for convenience of calculations, by a factor of 10. As a result, the prognosis factor for fracture of the humerus was "+8.5", fractures of the forearm bones "- 0.5", femur "- 3.0", shin bones "- 5.1". This allowed to draw a conclusion about the degree of increase in the risk of surgical site infection in the localization of a fracture in the lower extremity. Subsequently, all coefficients of prognosis known at the time of the examination were summarized. The result is a summary index of prognosis (PI). This parameter is determined at different stages of the study and treatment of the patient. Before the operation - 13 items, taking into account intra-operative data - 17 items, in the early postoperative - taking into account all 18 points with confidence interval from "-14" to "+14" conventional unit(c.u).

If the total IP was at the level of "+14 c.u. "and more, then, with a probability of more than 80%, a favorable course of the postoperative period was predicted, without the development of local purulent complications. With the IP parameters less than "-14 c.u.", with the same probability it was possible to expect the development of infection at surgical site. If the IP indicators were in the range of "- 14 c.u.", up to "+14 c.u." the prognosis was considered uncertain. A complete list of prognostic criteria with calculation of the prognosis for the development of local purulent complications is presented in **(Table 3).**

Table-1: Patient groups whose data were analyzed.

Option Comparisons		No of Obs in study groups (%) Retrospective (n=179)	Prospective (n=117)
Average Age		56.8±18.2	542±14.4
Sex	Male	74 (41.3)	48 (41.0)
	Female	105 (58.7)	69 (59.0)
Location	Humerus	57 (39.6)	43 (36.7)
	Radius/Ulna	28 (19.4)	16 (13.7)
	Femur	24 (16.7)	20 (17.1)
	Tibia/Fibula	35 (24.3)	36 (32.5)
Type of MOS	DCP	90 (50.3)	55 (47.1)
	IM nail	52(29.1)	39 (33.3)
	External Fixator	32 (17.8)	21 (17.9)
	Others	5 (2.8)	2 (1.7)
SSI in 12 months time		35 (19.6)	11 (9.4)
	Superficial	25 (6.8)	8 6.8)
	Deep	10 (5.6)	3 (2.6)

Table-2: Distribution of patients with fractures.

Location of Fracture	No of Obs during the post-op period Without SSI (n=144) No	%	With SSI (n=35) No	%
Humerus	57	39.6	6	17.1
Ulna/Radius	28	19.4	7	20.0
Femur	24	16.7	18	22.9
Tibial/fibula	35	24.3	14	40.0
Total	144	100.0	35	100.0

Table-3: Patient groups whose data were analyzed.

Prognostic Criteria 1		The frequency of observations (%) Without Complications 2	With SSI 3	The ratio index 4	P-level 5	Coefficient of prognosis 6
		PRE-OPERATION				
1: Sex	Male	39	51	0.765	0.044	2.2
	Female	61	49	1.245	61	-2.2
2: Age in Years	18-29	9	6	1.500	0.210	4.1
	30-44	14	14	1.000	0.500	0
	45-59	26	23	1.130	0.311	1.2
	60-74	35	34	1.029	0.411	0.3
	75-89	16	23	0.696	0.106	-3.6
3: CVS	IHD, HTN Present	40	69	0.580	0.0001	-5.4
	IHD, HTN absent	60	31	1.935		6.6

4:Digestive System	Present	19	29	0.655	0.049	-4.2
	Absent	81	71	1.141		1.3
5: Edocrine System	DM Present	13	20	0.650	0.091	-4.3
	DM Absent	87	80	1.088		0.8
6: Excretory System	Chronic pyelonephritis present	4	11	0.364	0.030	-10.1
	Chronic pyelonephritis Absent	96	89	1.079		0.8
7: Osteoporosis	Present	21	37	0.568	0.006	-5.7
	Absent	79	63	1.206		1.9
8: Kind of Fracture	Open	4	14	0.429	0.030	-8.4
	Close	94	86	1.093		0.9
9: Location of Prognosis	Humerus	40	17	2.353	0.0002	8.5
	Ulna/Radius	19	20	0.950	0.459	-0.5
	Femur	17	23	0.739	0.145	-3.0
	Tibia/Fibula	24	40	0.300	0.008	-5.1
10:Type of fracture	Transverse	33.5	23	1.453	0.058	3.7
	Spiral	24.5	20	1.225	0.199	2.0
	Communicated	38	51	0.745	0.032	-2.9
	Impacted	4	6	0.667	0.258	-4.0
11:Season of year the	Winter	45	34	1.324	0.190	2.8
Operation has been done	Spring	20	37	0.541	0.004	-6.1
	Summer	12	14.5	0.828	0.267	-1.9
	Autumn	23	14.5	1.586	0.051	4.6
12: Pre-operative length	1	40	23	1.739	0.005	5.5
Of the stay (in days)	2-3	30	37	0.811	0.148	-2.1
	4-15	12	17	0.7.6	0.159	-3.5
	16+	18	23	0.783	0.191	-2.4
13: Operation risk,	ASA 2	56	34	1.647	0.0009	5.0
	ASA3	44	66	0.667		-4.0
14: Kind of MOS	DCP	51	49	1.041	0.389	0.4
	IM nail	28	34	0.824	0.180	-1.9
	External Fixator	19	14	1.357	0.170	3.1
	Others	3	3	1.000	0.500	0
15: Queue in Operation	**I**	8	16	1.333	0.290	2.9
Theater	**II**	54	46	1.174	0.130	1.6
	III	31	34	0.912	0.325	-0.0
	After Hours	7	14	0.500	0.053	-6.9
16 Duration of surgery	Upto to 1 h.	16	11	1.455	0.151	3.8
	From 1 to 2 H.	59	49	1.204	0.078	1.9
	More than 2 h.	25	40	0.625	0.012	-4.7
17: Intra operative	Up to 500ml	83	63	1.317	0.0007	2.8
Blood Loss	500ml. To 1000ml	12	26	0.462	0.006	-7.7
	More than 100ml.	5	11	0.455	0.059	-7.9
18: Post-operative	Strict bed rest (I)	25	49	0.510	0.0002	-6.7
Regime	Mobile (II-III)	75	51	1.471		3.9

Discussion

In the recent years in literature different methods has been widely used for predicting infection after MOS of long bones. At the same time, there is no single generally accepted method. When analyzing prognostic criteria for the development of local infectious complications after surgical intervention for trauma, including fractures of long tubular bones, many authors consider the time to be the main factor since the time of injury before surgery.[13,14] Some authors believe that the incidence of infection at surgery site depends on the type of MOS. So, Ippolitov I.Y. with co- authors (2016) reported that the frequency of infectious complications (11.5%) is higher in the case of bone MOS with DCP of long tubular bones, than with IM nailing (3.1%).[15] A. Miromanov with co-authors (2017), in a study covering 163 cases of long tubular bones fractures and their infectious complications, suggest a prognosis for infection in the field of surgical intervention (including chronic posttraumatic osteomyelitis) in MI in both early and late period of traumatic disease on the basis of genetic predisposition . These authors consider the identification of the genotype-589T/T of the IL-4 gene and the -308A / A genotype of the TNFα gene as an informative indicator of the development of SSI in fractures of long bones of extremities[8] .Some experts believe that several factors contribute to the development of local purulent complications in the treatment of long tubular bones fractures: the age of the affected (over 60 years old), obesity, concomitant diseases (diabetes mellitus, decompensated pathology of cardiovascular and respiratory systems, the presence of foci of dormant infection), alimentary protein deficiency, localization fracture in the distal parts of the lower limb, dysfunction of the immune systam etc[9,10,15]. However, these authors do not report the importance of each of the listed prognostic criteria. Most of the factors described by these researchers characterize either the general condition of the patient or the organizational parameters that reflect the availability of specialized orthopedic and trauma care. The main shortcomings of these works are the following: the authors do not provide recommendations on how to apply in practice information about the presence of a particular criterion in a patient. In some studies, experts attempt to assess the risk of infection at surgical site development according to the developed scoring system that takes into account the quantitative equivalent of each risk factor and, accordingly, the total indicator that allows to distinguish among patients a risk group with respect to the development of local infectious complications. However, information about the introduction of the proposed systems and algorithms on the material of their own prospective studies is not always met. When assessing the diagnostic effectiveness of the model (according to the data of the retrospective group), it was revealed that the sensitivity (Se) was 94.29%, and specificity (Sp) 97.92%. The positive predictive value of the test was 91.67% (78.16% - 97.13%), the negative predictive value was 98.60% (94.83% - 99.63%). The method of prognosis of infection at surgical site development, proposed by us, allows to identify a risk group among patients. The results were evaluated in the prospective study group, which included 117 clinical observations. This risk was virtually assumed in 22 (18.8%) of 117 patients. All these 22 patients (from the high risk group for surgical site infection) and 31(26.5%) patients, whose risk was assessed as uncertain, conducted a set of special preventive measures (local, general and antibiotic prophylaxis). Preventive measures in general: prognosis of the development of infection at the surgical site at the stage of preoperative examination; refinement of prognosis of infection at surgical site development taking into account intra-operative data; assessment of cardiovascular system: correction of water-electrolyte balance, heart rhythm disturbances; carbohydrate metabolism disorders; intracellular homeostasis; respiratory assessment; optimization of traffic in the operating room. Local prophylaxis measures included: ultrasound of the operation zone, aspiration of hematoma formation (according to ultrasound data), control over the amount of drainage, culture of drainage and puncture material, magnetic and laser therapy in the operationarea. After the implementation of these measures, out of 22 cases with a high risk of purulent-inflammatory complications in the surgical intervention area predicted mathematically, surgical site infection was actually detected in 11 (9.4%) patients who underwent MOS operations due to a fracture of long tubular bones. In this case, deep infection at surgical site developed in 3 (2.6%) patients.

Conclusion

Thus, the use of the technique of a mathematical prognosis for the development of infection at surgical site in practice and the use of preventive measures in patients at risk have made it possible to reduce the incidence of SSI after MOS of LTB from 19.6% to 9.4%, i.e. twice. At the same time, the frequency

of deep infection also decreased by half: from 5.6% to 2.6%. Clinical introduction of the prognosis and prophylaxis program in patients of the prospective group confirms the correct choice of the risk factors for the infection in the area of operation in the MOS of LTB. The most significant criteria were those that had the maximum range between the positive and negative values of the prognosis factor: the localization of the fracture, its appearance (open or closed), the duration of the operation, and the amount of intra-operative blood loss. The frequency of fractures of LTB does not have a steady tendency to decrease. There is also a risk of developing infectious complications in the surgical treatment of patients with fractures of LTB. In this regard, it is obvious that the allocation among the affected group of high risk of SSI and the use of preventive measures allows in half the cases to prevent the development of purulent complications in the surgical intervention zone. The practical application of the proposed method for determining the index of the prognosis of infection in the area of surgical intervention in the MOS of LTB consists in the summation of the prognosis coefficients and does not require special training or equipment. The obtained data demonstrate that the use of modern organizational approaches in patients who need surgical treatment of long bone fractures allows in some cases to prevent the development of infectious complications.

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Original Article

Prevalence of Portal Hypertensive Gastropathy in Chronic Upper GI Bleeding Presenting With Iron Deficiency Anemia in Cases of Advanced Liver Cirrhosis

Muti Ullah Khan, Muhammad Azhar Shah, Azhar Hussain, Muhammad Latif, Rizwan Zafar and Ikram Rahim

Objective: To demonstrate the prevalence of portal hypertensive gastropathy in patients with advanced chronic liver disease presenting with iron deficiency anemia due to chronic upper GI bleeding.

Methods: Portal hypertensive gastropathy is a well know clinical entity that is definitely responsible for at least some cases of acute or chronic upper GI bleeding in patients with cirrhosis of liver, but the true incidence is not known. Current study was conducted to find out the incidence of PHG as a cause of chronic upper GI bleed in patients with liver cirrhosis presenting with gradual development of iron deficiency anemia and positive fecal occult blood.

Results: Of the fifty patients selected for the study 22 were males and 28 were females. Upper GI endoscopy done in these patients showed evidence of portal hypertensive gastropathy in 38 (21male; 17 female) [76 % (75%; 77% respectively)] had endoscopic evidence of PHG; while 44 (24male; 20female) [88 % (85%; 90% respectively) patients had different grades of esophageal varices and all patients with PHG also had esophageal varices.

Conclusions: PHG is a common finding among patients with chronic upper GI bleed in patients with portal hypertension due to cirrhosis of liver presenting with iron deficiency anemia.

Keywords: portal hypertensive gastropathy, cirrhosis, esophageal varices.

Introduction

Upper GI bleed, defined as bleeding above the ligament of Treitz[1] is a common cause of morbidity and mortality in patients with cirrhosis due to any cause.[2] The bleeding can be massive and exsanguinating, presenting with hematemesis and hematochezia/melena, less severe that presents with melena with rapid drop of hemoglobin, or mild and chronic presenting with gradual development of iron deficiency anemia.[3] While the leading cause of severe upper GI bleeding is bleeding esophageal or gastric fundal varices followed by peptic ulcer,[2,4,5] the cause and incidence of chronic upper GI bleed is not well understood. Gastric or duodenal erosions, gastric antral vascular ectasia (GAVE) and portal hypertensive gastropathy (PHG) are major candidates.[6] Determination of PHG as the cause of upper GI bleed may be difficult especially if no bleeding spot is visualized during endoscopy. Various studies have reported incidence of 3-60% of chronic bleeding from PHG in patients who have this lesion. The incidence of bleeding depends upon extent and severity of the lesion. Other risk factors for bleeding appear to be advanced liver disease, presence and size of esophageal varices and prior endoscopic variceal obliteration.[7] The purpose of this study was to assess the prevalence of portal hypertensive gastropathy in patients with cirrhosis of liver presenting with iron deficiency anemia due to chronic upper GI bleeding. Various criteria have been used to diagnose chronic upper GI bleeding, but the mere presence of anemia in a patient with cirrhosis may overestimate the incidence as these patients may have low hemoglobin due to other causes like hyperslenism or bone marrow suppression. Thus the criteria used in this study included a hemoglobin drop of >2 gm/dl over last six months with presence of iron deficiency anemia and a positive fecal occult blood test in patients not taking NSAIDs.[8,9]

Methods

This study was conducted in the medical department of Akhter Saeed Teaching Hospital between June 2017 and April 2018. A total of fifty patients with advanced chronic liver disease were selected for upper GI endoscopy, who presented with a gradual drop of hemoglobin of ≥2 gm/dl. over the previous six months, and a picture of iron deficiency anemia without the presence of significant leukopenia or thrombocytopenia. Stool analysis for occult blood was done to confirm chronic upper GI bleeding and patients with obvious other causes for iron deficiency anemia like those with hemorrhoids were excluded. Other exclusion criteria included use of non-steroidal

Anti-inflammatory drugs (NSAIDs), the presence of hepatic encephalopathy, bacterial peritonitis or acute upper GI bleeding, presenting with hematemesis or melena.

Results

Of the fifty patients that were included in the study 28 were females and 22 were males. Forty eight patients were positive for hepatitis C and two were having chronic active hepatitis B virus infection. Hemoglobin level ranged from 8.2 to 10.8 gm/dl (avg. 9.5±1.3) for males and 7.8 to 10.1 gm/dl (avg. 9.0±1.1) for females. Liver functions were deranged in all patients and all had positive test for fecal occult blood. During endoscopy, 38 (21male; 17 female)[76% (75%; 77% respectively)] had endoscopic evidence of PHG; while 44(24 male; 20 female) [88 % (85%; 90% respectively) patients had different grades of esophageal varices and all patients with PHG also had esophageal varices. All patients with PHG exhibited associated esophageal varices. Three patients also had small duodenal ulcers but there was no evidence of recent bleed from either of these lesions and all patients were hemodynamically stable.

Table-1: Patient characteristics.

Patients Characteristics		Findings
	Male/Female	28/22
	Age (Years)	Male: mean; 51±12
		Female: mean; 45±10
	Chronic hepatitis C	48 (96%)
	Chronic hepatitis B	02 (4%)
Hemoglobin (gm/dl):	Male	8.2 -10.8 (mean. 9.5±1.3)
	Female	7.8 - 10.1 (mean. 9.0±1.1
PGH [number (%)]:	Male	21 (75%)
	Female	17 (77%))
Varices [number (%)]:	Male	24 (85%)
	Female	20 (90%)

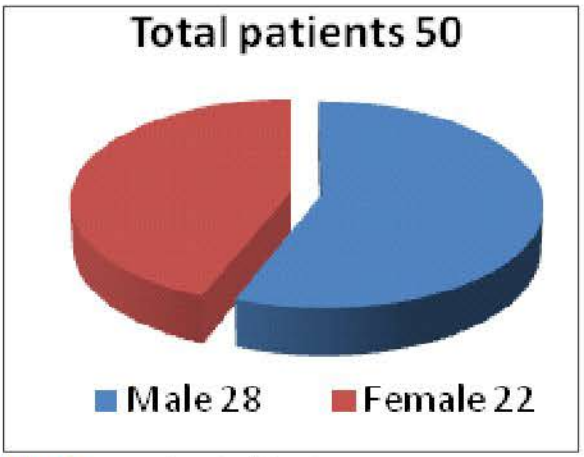

Fig-1: No. of males/females.

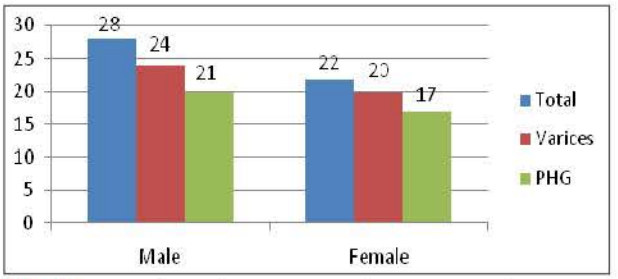

Fig-2: Number of patients with varices and PHG.

Discussion

Acute and chronic upper GI bleeding is a common life threatening condition in cases of liver cirrhosis. Most common cause of such bleeding is bleeding from esophageal or gastric antral varices.[6,10] Other possible sources of such bleeding include Gastric antral vascular ectasia (GAVE) and Portal hypertensive gastroenteropathy (PHG.[11-13] Peptic ulcers are not thought to be cirrhosis related, although 8-10% of cirrhotic patients have peptic ulcers.Gastric ulcers are known to heal more slowly and recur more frequently than in non-cirrhotic patients but majority of these ulcers are usually asymptomatic and found incidentally during upper GI endoscopy.[6,14] The true prevalence of portal hypertensive gastropathy in cirrhosis is not well known, and values ranging from 7 to 98% of patients with cirrhosis have been quoted[15]. Controversy also exists regarding incidence of acute or chronic bleeding from this lesion. Different series describe chronic bleeding from PHG as the cause of iron deficiency anemia in 3 to 60% of patients with the lesion. Acute and severe bleeding is less common (2 to 12%). This controversy is at least partly because no uniform diagnostic criteria and classification exist to diagnose and grade its severity or predict the prognosis.[16] Other causes of the controversy are different patient populations and inclusion criteria for the study. As PHG is directly related with the presence of portal hypertension, these patients also frequently have associated esophageal varices and some patients also have gastric or duodenal ulcers. In fact the presence of esophageal varices is a strong predictor for the development of PHG.[17] Obviously it is difficult to judge which lesion is responsible for the chronic bleed, unless there is clear signs of oozing from a lesion or

one type of lesion is prominently more advanced and severe. Portal hypertensive gastropathyis described as altered vascular microarchitecture with dilatation and/ or narrowing of the capillaries and veins as a result of portal hypertension. Endoscopically it is recognized as so called snakeskin like mosaic pattern of gastric mucosa, with or without red spots over it which signify more severe lesion and increased risk of bleeding.[11,12,15] Pathologically the lesion is different from that of inflammatory gastritis and the primary change is vascular ectasia. Endothelial lesions with increased capillary permeability are observed which is responsible for petechial bleeding in the gastric mucosa.[7]

The exact cause of portal hypertensive gastropathy is not well understood, but portal hypertension seems very important. There is evidence that PHG worsens after endoscopic ligation of esophageal varices[18]. While it is clear that reduction in portal pressure by shunt surgery or TIPS leads to rapid improvement in PHG, the severity of PHG has not been demonstrated to correlate with degree of portal hypertension. Definitely some other factors are also important. An apparent factor in PHG is dysregulation of gastric mucosal microcirculation leading to tissue ischemia which is responsible for bleeding and poor healing of the mucosa. Perhaps local cytokines and vascular factors also play a part.[7,19]

Portal hypertensive gastropathy can also complicate portal hypertension due to non-cirrhotic causes like extrahepatic portal venous hypertension, schistosomiasis or hepatic veno-occulsive disease, but the incidence seems to be less than in cirrhosis and is associated with less aggressive course than in cirrhosis. This is attributed to poor liver function in case of cirrhosis.[7] There is increasing evidence that portal hypertension is associated with increased incidence of gastric mucosal colonization by Helicobacter Pylori. This is especially prominent in cases with chronic liver disease or hepatocellular carcinoma due to chronic hepatitis B virus infection. But whether there is an association between this infection and development or severity of PHG is not clear.[20,21]

In our study, the vast majority of the patients had hepatitis C virus infection. All patients had altered liver function tests and all had presented with evidence of iron deficiency anemia, most likely from upper GI bleed. This was apparent from the fact that all patients included, had positive fecal occult blood test. Seventy six percent of all patients had evidence of PGH, and all of these patients had esophageal varices. This is in keeping with several observations that frequently these lesions co-exist because increased portal pressure is the most important factor for the development of both the lesions. As already mentioned, if several lesions co-exist, then there it is very difficult to judge which one of them is responsible for the bleeding, unless there is clear evidence of bleeding. This is probably the reason there is so much controversy about the incidence of bleeding from PHG.

Esophageal varices usually bleed acutely and thus PHG was the most probably the culprit lesion in this case. Other patients who didn't have PHG and they presented with gradual drop of Hb might be losing blood from other lesions like peptic ulcers (present in three of the patients). Other causes may include similar lesions in the colon and the small intestine labeled as portal hypertensive colopathy (PHC) and portal hypertensive enteropathy (PHE) respectively which are also well described lesions.[16,22] Alternatively other causes like intestinal worm infestation could have been the cause of dropping hemoglobin level in these patients.

In conclusion, portal hypertensive gastropathy is quite common finding among patients with cirrhosis especially those with evidence of chronic GI bleed and may be responsible for many of these bleeds presenting as slowly progressive iron deficiency anemia. But it is difficult to assess the exact percentage of bleeding from these lesions as other lesions which may or may not be associated with portal hypertension are also present and may be responsible. Further well planned studies are required to assess further the exact percentage of chronic bleeds from these lesions.

Conclusion

PHG is a common finding among patients with chronic upper GI bleed in patients with portal hypertension due to cirrhosis of liver presenting with iron deficiency anemia.

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Original Article

Poor Glycemic Control in Patients with Type-II Diabetes and Factors Leading to Poor Glycemic Control

Naveed-ul-Zafar, Amna Saeed, Tahir Bashir, Tahira Liaquat, Bilal Azeem Butt and Awais Abid

Objective: To determine the frequency of poor glycemic control in patients with type-II diabetes. Factors leading to poor glycemic control in patients with type II diabetes

Methods: A total of 370 patients presenting in out-patients department of Medicine, Services Hospital Lahore were recruited in the study. After informed consent, history and physical examination of all the patients was done. After overnight (minimum 8 hours) fasting, HbA1c sample was sent to the hospital laboratory. Glycemic Control of patients was recorded and possible factors affecting glycemic control like family history and low physical activities were recorded.

Results: In our study, out of 370 cases, 39.73%(n=147) were between 30-50 years of age whereas 60.27%(n=223) were between 51-70 years of age. 48.92%(n=181) were male while 51.08%(n=189) were females. Poor glycemic control was recorded in 61.08%(n=226) whereas 38.92%(n=144) had good glycemic control. Frequency of factors leading to poor glycemic control in patients with type II diabetes shows that out of 226 cases, family history was recorded in 63.72%(n=144) whereas 90.27%(n=204) had low physical activity.

Conclusions: We concluded that the frequency of poor glycemic control is higher in patients with type-II diabetes and low physical activities and family history are the major factors leading to poor glycemic control.

Keywords: Type-II diabetes, poor glycemic control, factors, low physical activity, family history

Introduction

Type 2 Diabetes Mellitus (T2DM) is a leading cause of morbidity worldwide, especially with increasing prevalence in developing countries.[1] Recent epidemiological reports indicated an increased prevalence of Type-2 diabetes in Turkey (7.2%), India (8.2%), Pakistan (11.1%), and Hawaii (20.4%). It is estimated that the developing countries will bear the brunt of diabetes epidemics in the 21st century.[2]

In 2011 the Diabetes Atlas of the International Diabetes Federation (IDF) estimated the global DM prevalence in the age group 20-79 years at 8.3%, which translates into 366.2 million people suffering from DM in 2011. The number of people living with DM is projected to reach 551.9 million by 2030. By 2030 Bangladesh is likely to emerge as the 8th highest ranking country in terms of the number of people with DM.[3] Poor and inadequate glycemic control among patients with Type 2 diabetes constitutes a major public health problem and major risk factor for the development of diabetes complications. Glycemic control remains the major therapeutic objective for prevention of target organ damage and other complications arising from diabetes.[4]

The definition of intensive glycaemic control varies among trials and guidelines. The ACCORD trial and the Veterans Affairs Diabetes Trial (VADT) used a target of glycatedhaemoglobin A1c (HbA1c) below 6.0% for intensive glycaemic control compared with a target of HbA1c below 6.5% in the Action in Diabetes and Vascular DiseasePreterax and Diamicron Modified Release Controlled Evaluation (ADVANCE) trial. The results from these trials have created a debate about the optimal choice of glycaemic target. The American Diabetes Association recommends an HbA1c level of less than 7.0% as the standard glycaemic treatment goal, whereas the International Diabetes Federation recommends a level of less than 6.5%.[5-7] A recent study[2] recorded 60% of the diabetic cases with poor glycemic control (>7HbA1c), another recent study recorded 78.6% of the cases with poor glycemic control.[8] A previous study[9] revealed that poor glycemic control was 96.4% of the cases with low physical activities. Patients with positive family history of diabetes mellitus had 24.6% poor glycemic control while those without family history was recorded in 75.4%.[10]

Physical activity is one of the important therapeutic measures to lower blood glucose in type 2 diabetes due to its synergistic action with insulin in insulin-sensitive tissues.[11] Another study on predictors of poor glycemic control in type 2 diabetics shows that female gender,

High body mass index and poor drug compliance significantly associated with poor glycemic control.[12] Patients with T2DM should perform at least 150 minutes per week of moderate to intense aerobic exercise, while resistance exercise should be performed at least three times a week, according to guidelines.[13-14] The rationale of the study is that the above studies are significantly different regarding poor glycemic control in diabetics while no recent data in our population is recorded, as we are receiving a great number of patients with poor glycemic control which needs to be recorded, the results of our study will be helpful to know the recent and exact frequency of poor glycemic control and factors affecting it. Furthermore, it will also be helpful for creating awareness regarding glycemic control in diabetics.

Methods

A total of 370 patients presenting to out patients department of Medicine, Services Hospital Lahore were recruited in the study. An informed consent of the patients was taken. History and physical examination of all the patients was taken. After overnight (minimum 8 hours) fasting, 5 ml of whole blood was collected from diabetic patients with all aseptic precautions, using a 5 cc disposable syringe at fasting without oral hypoglycemic drug or insulin as they were prescribed earlier. The sample was sent to the hospital laboratory to record HbA1c. Glycemic control (according to operational definition) of patients was recorded on the basis of HbA1c (normal value 7.5%) and factors leading to it e.g. family history and low physical activities were also recorded. The level of physical activity is monitored using the International Physical Activity Questionnaire (IPAQ) to obtain reliable conclusions and can be classified into low, moderate and high physical activity. Information was recorded on a pre-designed proforma (Annexure).

The data was entered and computed on SPSS-14. Frequency and percentages were calculated for gender, glycemic control, factors of poor glycemic control like low physical activiy and family history. chi-square test was applied for any significant difference. P-value of ≤ 0.05 was considered statistically significant.

Results

A total of 370 patients were enrolled to determine the frequency of poor glycemic control in patients with type-II diabetes and factors leading to poor glycemic control in patients with type II diabetes. Age distribution of the patients shows that 39.73% (n=147) were between 30-50 years of age whereas 60.27% (n=223) were between 51-70 years of age, mean±sd was calculated as 51.66+8.98 years. **(Table-1).** Gender distribution shows that 48.92% (n=181) were male while 51.08% (n=189) were females. **(Table-2).** Poor glycemic control was recorded in 61.08% (n=226) whereas 38.92% (n=144) had good glycemic control. **(Table-3)** Frequency of factors leading to poor glycemic control in patients with type II diabetes shows that out of 226 cases, family history was recorded in 63.72% (n=144) whereas 90.27% (n=204) had low physical activity. (**Table- 4).**

Table-1: Age distribution (n=370).

Age (Years)	No of Patients	Percentage
30-50	147	39.73%
51-70	223	60.27%
Total	370	100.0%
Mean±SD	351.66±8.98	

Table-2: Sex distribution (n=370).

Sex	No of Patients	Percentage
Male	181	48.92%
Female	189	51.08%
Total	370	100.0%

Table-3: Presence/absence of poor glycemic control (n=370).

Poor glycemic control	No of Patients	Percentage
Yes	226	61.08%
No	144	38.92%
Total	370	100.0%

Table-4: Poor glycemic control in patients with type-II diabetes and risk factors (n=226).

Factors leading to poor glycemic control	No of Patients	Percentage
Family history	144	63.72%
Low physical activity	204	90.27%

Discussion

Diabetes mellitus (DM) is a major public health problem worldwide that requires continuing medical care and ongoing patient self-management, education and support to prevent acute complications and to reduce the risk of long-term complications. American Diabetes Association (ADA) regards glycemic control as one of the important strategies for the management

of DM, and glycosylated hemoglobin (A1C) is the best measure of glycemic level over the previous 3 months. Lowering hemoglobin A1C to below or around 7% has shown to reduce microvascular complications of diabetes and if implemented soon after the diagnosis of diabetes, is associated with long-term reduction in macrovascular disease. The ADA recommends a goal of A1C less than 7% for people with DM. There is a recent study[2] which recorded 60% of the diabetic cases with poor glycemic control (>7HbA1c), findings are in agreement with this study, whereas another study recorded 78.6% of the cases with poor glycemic control.[8] These findings are slightly higher than ours. Another previous study[9] revealed that poor glycemic control was 96.4% of the cases with low physical activity. Patients with positive family history of diabetes mellitus had 24.6% poor glycemic control while those without family history was recorded in 75.4%,[10] these findings support our results. Another study[15] assessed the status of glycemic control and its contributing factors among adult patients with type 2 diabetes mellitus. They concluded that majority of patients had poor glycemic control. Patients with low level of education, being employed, on combinations of insulin and oral medication, and lower adherence to their medication, were likely to have poor glycemic control. Education and awareness creation could be a cross cutting intervention for the significant factors, however, it was not our study variable. Guidelines recommend that patients with T2DM should perform at least 150 minutes per week of moderate to intense aerobic exercise, while resistance exercise should be performed at least three times a week.[16-17] In a study, only a small percentage of patients with T2DM were doing regular physical activity and specific exercise. However, there were no statistically significant differences between patients who did not perform regular physical activity in terms of glycemic control and those who were participating in regular physical exercise. The lack of association between physical exercise and glycemic control in this study is in contrast with the findings by Empierre et al,[16] probably due to the small number of patients who were performing regular physical activity in this study. This study showed that previous data reveal significantly different magnitude regarding poor glycemic control in diabetics while no recent data in our population is recorded, as we are receiving a great number of patients with poor glycemic control which needs to be recorded, the results of our study will be helpful to know the recent and exact frequency of poor glycemic control in T2DM and factors contributing to it.

Conclusion

The frequency of poor glycemic control is higher in patients with type-II diabetes and low physical activity and family history are the major factors leading to it. It will be helpful for creating awareness regarding glycemic control in diabetics with poor glycemic control.

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Original Article

Comparison of Rifaximin with Norfloxacini in the Primary Prophylaxiso of Spontaneous Bacterial Peritonitis

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Objective: To compare the efficacy of Rifaximin vs Norfloxacin in preventing episode of spontaneous bacterial peritonitis (SBP) in patients with liver cirrhosis.

Methods: It was randomized Controlled Trial conducted at Department of Gastroenterology, Services Hospital, Lahore from 15-09-2015 to 14-03-2016. One hundred patients of both gender in the age range 18-60 with 50 patients in Rifaximin group and 50 patients in Norfloxacin group. Patients after informed consent were randomly assigned to one of the two groups and received prophylaxis for SBP with Rifaximin (1100mg/day) or Norfloxacin (400mg/day) using random tables. Patients were followed up after four weeks and outcome was efficacy in terms of prevention of episode of SBP and was assessed as per operational definition.

Results: A total of 100 patients were included in the study. The mean age of patients was 46.40(± 5.78) years with most of the patients in the age range 31-45 years. Majority of the patients in the study were male (54.0%). Mean polymorphonuclear (PMN) count was 144.4±25.8. Only 7 patients developed SBP, 4 were in Norfloxacin group and 3 were in Rifxaimin group showing efficacy of 92% and 96% respectively with no statistically significant difference(p value >0.05). Stratification of patients by Age, Gender, Duration of disease and Child Pugh score showed p value was >0.05 in all cases showing statistically insignificant difference between various subgroups.

Conclusions: The study shows that rifaximin is as effective as Norfloxacin when used for SBP prophylaxis in cirrhotic patients with ascites.

Keywords: cirrhosis, ascites, spontaneous bacterial peritonitis.

Introduction

The most common bacterial infection in patients with cirrhosis is Spontaneous Bacterial Peritonitis (SBP), ranging from 1030% of all bacterial infections in patients admitted in hospitals.[1] In the nosocomial setting the prevalence is very high ranging from 8% to 36%, however in outpatients without symptoms the prevalence is less than 3.5%.[1] The prevalence of Bacteriascites which is defined as positive culture results but no increase in the leukocyte count in the ascitic fluid is 23% in outpatients with a prevalence of up to 11% in patients admitted in hospitals.[1] The mortality for the first episode of SBP is very high ranging from 10% to 50%[1] during hospital stay. Mortality within first year after an episode of SBP has been reported to be 31% and 93%.[1-2] Bacterial translocation is implicated as the main cause of SBP.[1] Alterations in gut microbiota, increased intestinal permeability and impaired immunity have been implicated in the development of pathological Bacterial Translocation (BT) in liver cirrhosis.[2] SBP is a major complication of ascites and possibly results from a series of events, including intestinal bacterial overgrowth (IBO), BT resulting in bacteremia, endotoxemia, and colonization of mesenteric lymph nodes, and finally seeding of bacteria into the ascitic fluid (AF).[3] The high mortality associated with SBP warrants efforts aimed at prevention with administration of antibiotics to decrease the burden of gut bacteria, thus interrupting the sequence of events leading to ascitic fluid infection. One of the most commonly used medicine for primary prophylaxis of SBP is Norfloxacin; however its extensive long-term use has increased the incidence of quinolone-resistant and gram-positive SBP.[1-2] Overall, the continuous use of a single antibiotic appears not to be the optimal solution and efforts should be made to seek alternatives, which could include antibiotic cycling. The basic principle of cycling antibiotics is that bacteria acquiring resistance to the first course of treatment would remain susceptible to the second regimen, and so on. In this context, Rifaximin holds great promise as it belongs to a different antibiotic class from the antibiotics tested prospectively so far; it exerts a broad range of antimicrobial activity including Gram-positive bacteria; it appears to cause considerably less bacterial resistance.[1-2]

Studies have shown that Rifaximin reduces intestinal bacterial overgrowth, which decreases BT thus

reducing SBP potentially improving survival in cirrhotic patients.[3-6] However, there are certain limitations of available studies. All the studies done so far have used a control group which received no intervention and thus efficacy of Rifaximin cannot be compared to other antibiotics used for the purpose due to difference in patient and study settings.[3-6] In addition, the studies report wide variation in results with Vlachogiannakos J et al. reporting frequency of SBP of 4.5% vs 46% in Rifaximin vs. no antibiotic group while Hanouneh MA found that during the intervention 89% of patients on Rifaximin remained SBP free compared with 68% of those not on Rifaximin.[5,6] Moreover, Lutz P has concluded that Rifaximin does not reduce SBP occurrence in hospitalized patients even though the bacterial species causing SBP were changed by Rifaximin.[7] Fernandez *et al.* showed that Norfloxacin reduced the 1-year probability of SBP from 61% to 7% ($p<0.001$). In another study by Lontos S et al. comparing Norfloxacin with Trimethoprim/Sulfamethoxazole (TMP-SMX), they found 21.6% patients in the Norfloxacin group and 28% in the TMP-SMX group developed SBP ($P > 0.05$).[10] The rationale of present study is that there is no known direct comparison between Rifaximin and Norfloxacin comparing their efficacy in preventing SBP. In addition, there is no study on the subject from Pakistan. Therefore, a study is very much needed to compare the efficacy of Rifaximin and Norfloxacin in preventing SBP as rifaximin exerts a broad range of antimicrobial activity including Gram-positive bacteria and causes considerably less bacterial resistance with significant reduction in episodes of SBP thus improving survival in patients with SBP which carries high mortality rates.[2-4] The aim of our study was to compare the efficacy of Rifaximin vs Norfloxacin in preventing episode of SBP in patients with liver cirrhosis.

Methods

It was quasi experimental randomized controlled trial, conducted in Department of Gastroenterology, Services Hospital, Lahore from: 15-09-2015 to 14-03-2016. Sample size was estimated to be 100 patients with 50 in both Rifaximin and Norfloxacin study arm based with 80% power of test, 5% level of significance and taking and taking expected percentage of efficacy in both groups i.e., 95.5% in Rifaximin group and 78.4% in Norfloxacin group in preventing episode of SBP in patients with liver cirrhosis.[6,10]

We included patients of Liver Cirrhosis of both gender with age ranging between 18 and 60, absence of clinical signs of bacterial infections as per history and examination, no history of variceal bleeding within the 2 weeks preceding the study and no treatment with antibiotics during the last 8 weeks before inclusion.

Patients with previous episode of SBP as per medical record, patients not willing to participate in the study, those with allergy to quinolones, patients of hepatocellular carcinoma or other neoplasia and pregnant and lactating women were excluded.

After taking ethical clearance from hospital ethical committee, 100 patients in total fulfilling the inclusion and exclusion criteria, were included in the study after taking informed consent. Patients were randomly assigned to one of the two groups and received prophylaxis for primary SBP with Rifaximin (1100mg/day) or Norfloxacin (400mg/day) using random tables, Group A received Rifaximin while Group B received Norfloxacin. Bio data was entered in a predesigned structured Proforma. Patients were followed up after four weeks and data entered in the form. Outcome was efficacy in terms of prevention of episode of SBP and was assessed as depending upon whether patients developed SBP or not. Spontaneous Bacterial Peritonitis (SBP) was diagnosed if the polymorphonuclear leukocyte (PMN) cell count in the ascites exceeded 250/µl in a patient with cirrhosis. At 4 weeks, ascites tap was done and fluid was sent to laboratory for analysis for PMN count and efficacy was labelled. Statistical analysis was done using Statistical Package for Social Sciences (SPSS) version 16. Qualitative data like gender, efficacy was presented as frequencies and percentages. Quantitative data i.e., age, leukocyte count etc was presented as means and standard deviations. The efficacy in the two groups was compared by using chi square test. p value less than 0.05 was considered significant. Effect modifiers were dealt with stratifying data for age, gender, and duration of disease, Child Pugh Class which was calculated using the standard method of calculation of Child Pugh Class which includes Presence of Ascites, Hepatic Encephalopathy, Serum Bilirubin, Serum Albumin and International Normalized Ratio. Post stratification chi square test was applied. P value <0.05 was taken statistically significant.

Results

A total of 100 patients were included in the study. The mean age of patients was 46.40 ($\pm$ 5.78) years and most of the patients were in the age range 46-60 years. Majority of the patients in the study were male (54.0%). Mean PMN count of study participants was

144.4/µl (±25.8). A total of 7 patients out the 100 patients included in the study developed SBP as per the operational definition. Out of 7 patients, 4 were in Norfloxacin group and 3 was in Rifaximin group showing efficacy of 92% and 96% respectively. p value was >0.05 in all 3 cases showing statistically insignificant difference between various subgroups. Out of these 7 patients who developed SBP, between ages 18-30 years, 1 patient was in Rifaximin group while 1 in Norfloxacin group, between ages 31-45 yrs, 1 patient was in Rifaximin group and 2 patients in Norfloxacin group and between ages 46-60 yrs, 1 patient was in Rifaximin group and 1 in Norfloxacin group **(Table-1).** Of these 7 patients, 2 patients were Males in both groups and 1 was female in Rifaximin group and 2 were females in Norfloxacin group. Out of these patients, 1 patient in Rifaximin group and 2 patients in Norfloxacin group had disease duration of 0-5 years, and 2 patients in each group had disease duration of more than 5 years **(Table-2).** On the basis of Child Pugh Score, 1 patient in each group had score of 0-5, 1 patient in Rifaximin group had score of 6-10 while 2 patients in Norfloxacin group had score of 6-10 and 1 patient in each group had score 11-15 **(Table-3)**.

Table-1: Stratification with reference to age of efficacy between both groups (n=100).

Age Group (in years)	Groups	Efficacy		Total	P-value
		Yes	No		
18-30	A	1	5	6	
	B	1	5	6	0.621
	Total	2	10	12	
31-45	A	1	15	16	
	B	2	14	16	0.544
	Total	3	29	32	
46-60	A	1	29	30	
	B	1	25	24	0.918
	Total	2	24	56	

Table-2: Stratification with reference to duration of disease between both groups (n=100)

Duration of Disease	Groups	Efficacy		Total	P-value
		Yes	No		
0-5 years	A	1	22	23	
	B	2	20	22	0.53
	Total	3	42	45	
>5 years	A	2	25	27	
	B	2	26	28	0.970
	Total	4	50	55	

Table-3: Stratification with reference to child pugh score between both groups (n=100).

Child Pugh Score	Groups	Efficacy		Total	P-value
		Yes	No		
0-5	A	1	6	10	
	B	1	7	8	0.867
	Total	2	16	18	
6-10	A	1	14	15	
	B	2	16	18	0.658
	Total	3	30	33	
11-15	A	1	24	25	
	B	1	23	24	0.976
	Total	2	47	49	

Discussion

Rifaximin, a non-absorbable antibiotic, has been licensed for the prevention of relapsing Hepatic Encephalopathy (HE).[7] In addition, due to its broad intestinal antibacterial activity, it is a candidate for the prevention of SBP, which is attributed to intestinal bacterial transmigration.[1] Therefore, we prospectively studied the impact of Rifaximin co-medication on SBP in 100 patients undergoing diagnostic paracentesis in our department. Hanouneh et al. recently reported a retrospective study of 404 cirrhotic patients with HE where rifaximin effectively prevented SBP.[14] However, the authors did not compare Rifaximin to systemic absorbed antibiotic prophylaxis, which is an established clinical standard to prevent recurrent SBP. Furthermore, that study excluded all patients with a high risk for SBP. Another small case control study reported a preventive effect of rifaximin on SBP in a cohort of patients with decompensated cirrhosis.[18] However, that study only included patients who had shown a decrease in the hepatic venous pressure gradient after an initial course of Rifaximin. The authors found a 5-year cumulative survival of 61%. This is remarkable, considering that 5-year mortality in patients with decompensated liver cirrhosis has been reported to be up to 85%.[19] Taken together, these data indicate that there may be a subgroup of cirrhotic patients that benefits from Rifaximin. Rifaximin is a candidate for SBP prevention because it shows broad intestinal antibacterial activity without systemic side effects and because SBP is thought to occur from bacterial translocation. A possible explanation for episodes of SBP during Rifaximin treatment could be resistance to it. This issue is controversial and not easy

To resolve. Some studies reported a slow development and rapid disappearance of resistance to Rifaximin.[7,20,21] In contrast, more recent studies found persistently high rates of resistance in ileal E. coli and in staphylococci.[22-23] The definition of resistance to Rifaximin is difficult, since no data on the intestinal drug concentration are available to define a cut-off for minimal inhibitory concentrations. Fecal levels of Rifaximin are very high but do not necessarily reflect the intra-luminal situation in cirrhotic patients.[24,25] Another recent study did not find any impact of Rifaximin on the development of bacterial resistance in cirrhotic patients.[16] However, this study did not evaluate the effect of Rifaximin on SBP separately.

Given that immune defects are associated with liver cirrhosis and that Rifaximin lacks systemic effects, a general reduction of intestinal bacterial loads by it may suffice to significantly reduce toxin production and to prevent HE, but may not be sufficient for SBP prevention if mucosal translocation of small amounts of bacteria still occurs.[27] This hypothesis is supported by a recent study in cirrhotic patients demonstrating that Rifaximin treatment changed the pattern of metabolites produced by the intestinal bacteria rather than the quantity of bacteria.[29] In our analysis, we compared the efficacy of Rifaximin versus Norfloxacin in preventing episodes of SBP in patients with Liver Cirrhosis. In our analysis, no statistically significant differences were in the rates of SBP between patients receiving SBP prophylaxis with Rifaximin and those treated with Norfloxacin. This suggests that Rifaximin may be as safe and effective as Norfloxacin in the prevention of SBP. This has important implications given the higher cost and concerns about the development of fluoroquinolone resistance when these agents are used for long-term prophylaxis.[9,1113] The overall rates of SBP in both groups in this study were comparable to rates already reported in other studies of SBP prophylaxis. Previous studies have shown SBP prophylaxis to be cost effective when compared to a wait-and-treat approach with the greatest benefit occurring in patients with a previous episode of SBP or low ascitic protein concentration.[15,16] There has been increasing concern about the emergence of fluoroquinolone-resistant organisms in patients who receive prolonged treatment with these drugs.[1,2] Others have found a high rate of fluoroquinolone resistance amongst Gram-negative isolates causing infection.[9] An important additional concern is that a significant proportion of patients on SBP prophylaxis will subsequently go on to liver transplantation and that colonization with Norfloxacin resistant organisms may limit the antibiotic choices available to the treating clinician. Our results suggest that Rifaximin should not generally replace systemically absorbed antibiotics for SBP prophylaxis in patients at high risk for SBP and with recurrent hospitalizations. SBP is a complication of advanced liver disease and our cohort is typical for patients with advanced cirrhosis. However, it remains open whether our findings can be extrapolated to patients at low risk and with less severe liver disease. A further limitation is the fact that we did not measure Rifaximin levels in patient stool to exclude non-adherence with drug therapy. However, the observed clinical improvement of HE suggests good adherence in the studied patient cohort. In addition, the biological intestinal half time of rifaximin is several days and consequently even the omission of one or two dosages would not result in insufficient drug levels.[9,39] Future studies on the effects of rifaximin on SBP should include assessment of bacterial resistance to Rifaximin, which is complicated by the unavailability of commercially available resistance tests or standardized testing procedures with normal values.

Conclusion

In conclusion, this study suggests that Rifaximin is as effective as Norfloxacin when used for SBP prophylaxis in cirrhotic patients with ascites. The increasing concerns about the impact of fluoroquinolone-resistant organisms make this drug an attractive alternative first-line therapy for SBP prophylaxis.

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Original Article

Frequency of Intra-hepatic Factors Responsible for Portal Hypertension in Children

Riaz-ul-Haq, Muhammad Sajid, Jamal Anwar, Zahid Mehmood, Sajida Khalid and Riaz Ahmad

Objective: To determine the frequency of intra-hepatic factors responsible for portal hypertension in children.

Methods: This was a descriptive, cross-sectional Study which was conducted from 1st July 2016 to 30th June 2018 in the department of pediatric medicine, Sheikh Zayed Hospital, Rahim Yar Khan. Fourty Nine children fulfilling inclusion criteria were included and excluded if they have portal vein thrombosis on Doppler USG/CT scan and not willing for liver biopsy. Ultrasonography abdomen was done in each patient. Eye examination was done to look for KF rings if indicated. Relevant laboratory test were also done. After this liver biopsy was done in patients where other investigations were inconclusive and was sent to for histopathology for presence or absence of intra-hepatic factors responsible for portal hypertension in children.

Results: Mean age was 8.73±3.90 years. Out of the 49 patients, 27(55.10%) were male and 1.2:2 male to female ratio. In my study, intra-hepatic etiology of portal hypertension in children was cryptogenic cirrhosis 34.6.%, Wilson's disease in 32.6%, autoimmune hepatitis in 10.2%, congenital hepatic fibrosis 8.1%, biliary artesia in 8.1% and viral hepatitis in 6.1% patients.

Conclusions: This study concluded that most common intra-hepatic cause of portal hypertension in pediatric age group was cryptogenic (idiopathic) cirrhosis followed by Wilson's disease, autoimmune hepatitis , biliary artesia, congenital hepatic fibrosis, and viral hepatitis

Keywords: portal hypertension, cryptogenic cirrhosis and wilson's disease.

Introduction

The normal portal venous pressure is 7-10 mmHg and the hepatic venous pressure gradient (HVPG) is normally 1- 4 mmHg. If this portal pressure increase from 10 mmHg and if gradient is more than 4 mmHg, then it is called as portal hypertension (PH).[1,19] There are variable causes of portal hypertension. One of the clinical manifestation of PH, is upper GIT bleeding as a result of esophageal varices.[2] Portal hypertension has intrahepatic, prehepatic & post hepatic causes.[16] Our main emphasis in study was on intrahepatic causes due to their high prevalence. In a study done by Imanieh et al[3], 93.3% patients have intra-hepatic etiology while extra-hepatic causes in only 6.7% patients. Doppler ultrasonography help in diagnosis of portal hypertension as it measures increase in portal vein pressure.[4] Most patients with venous PH have intrinsic liver disease. Hematemesis resulting from esophageal varices is the most common[20] presentation in patients with PH, although some patients presents with decompensated liver disease.[17] Other supportive investigations can be ultrasonography (US) and color Doppler imaging (CDI), CT, MRI and endoscopy.[5] Accurate diagnosis is a pre-requisite for successful management. Portal hypertension and its complications remain a cause of significant morbidity and mortality. Studies have been conducted for causes and management approaches in adults have been conducted but there is a lacking data in children regarding causes and morbidity and mortality.[6] The rationale of this study was to document the frequency of intra-hepatic causes implicated in portal hypertension in pediatric age group in our local population. As intra-hepatic etiology constitutes the main bulk of portal hypertension, so this study would give us the magnitude of each intra-hepatic factor responsible for portal hypertension in pediatric age group(set of patients that fulfils operational definition of portal hypertension). The data of this study would not only add statistics of this devastating condition in our local literature but also help the clinicians to design a management protocol for these patients in order to minimize its complications as well as morbidity and mortality.

Methods

This was a descriptive, cross-sectional study conducted in the department of Pediatric Medicine, Sheikh Zayed Hospital, Rahim Yar Khan from1st July 2016 to 30th June 2018. A total 49 patients were enrolled by non-probability, consecutive sampling after fulfilling inclusion criteria (children presenting

with portal hypertension as per-operational definition of duration >3 months, age 1-15 years, both genders) and excluding the patients <1 and >15 years, patients with portal vein thrombosis (by history ,examination and doppler USG/CT scan (if required), patients not willing for liver biopsy and patients not willing for inclusion in study. After permission from the ethical review board, 49 children who were presented to department of pediatric medicine, Sheikh Zayed Hospital, Rahim Yar Khan, fulfilling the inclusion criteria were selected. After obtaining informed consent from parents of patients, serum and urine tests were sent in each patient. Ultrasonography abdomen was done in each patient for hepatobiliary system status. Eye examination was done for KF rings . After this liver biopsy was done (in patients where other test were inconclusive) and was sent for histopathology. All these reports were evaluated by consultant pediatrician for presence or absence of intra-hepatic factors responsible for portal hypertension in children as described in operational definition. A specifically designed proforma was used to document all required data. Statistical analysis was done with help of SPSS version 20.0.

Results

Age range in this study was from 1 to 15 years with mean age of 8.73±3.90 years. Majority of the patients 68 (37.78%) were between 6 to 10 years of age. Out of the 49 patients, 27 (55.10%) were male and 22 (44.89%) were females with male to female ratio of 1.2 -1. Mean disease duration was 7.39± 2.67 months. In my study, intra-hepatic etiology of portal hypertension in children found as cryptogenic cirrhosis in 17(34.6%), Wilson's disease in 16(32.6%), autoimmune hepatitis in 5(10.2%), congenital hepatic fibrosis 4 (8.1%), biliary atresia in 4 (8.1%) and viral hepatitis in 3 (6.1%) patients.

Table-1: Frequency of intra-hepatic factors responsible for portal hypertension in children.

Intra-hepatitis factors	Frequency	Percentage
Cryptogenic cirrhosis	17	34.6%
Billary atresia	04	8.1%
Wilson's disease	16	32.6%
Congenital hepatits fibrosis	04	8.1%
Autoimmune hepatis	05	10.2%
Viral hepatitis	03	6.1%

Discussion

Portal hypertension is classified based on the anatomical location into extrahepatic, and intrahepatic. Intrahepatic PH is further categorized into pre-sinusoidal, sinusoidal, and post-sinusoidal PH. Numerous vascular and hepatic diseases cause portal hypertension in pediatric age group, which has fatal complications, including symptomatic esophageal varices, pulmonary involvement, encephalopathy and ascites. To improve outcome of such children, proper preventive measures and effective management is important. This study documented the frequency of intra-hepatic factors responsible for portal hypertension in children.

In this study age was from 1-15 years with mean age of 8.73±3.90 years. Majority children (37.78%) had age 6-10 years. Intra-hepatic etiology of portal hypertension in children was found as cryptogenic cirrhosis in 17 (34.6%), Wilson's disease in 16(32.6%), autoimmune hepatitis in 5 (10.2%), congenital hepatic fibrosis 4 (8.1%), biliary atresia in 4 (8.1%) and viral hepatitis in 3 (6.1%) patients.

Western studies about pediatric portal hypertension demonstrated that 68-81 % cases were attributed to intrahepatic etiology while 9-27 % to extrahepatic factors and 5-10% to BuddChiari syndrome.[7] In one study conducted in India, extrahepatic factors were in 6876% of cases and intrahepatic factors in 2428%.[8,9] In a study done by Imanieh et al[3], a total of 45 patients included in the study, with mean age of 7.6±4.7 years. Male were 23 (51.1%) and 22 (48.8%) were females. Intra-hepatic causes (cryptogenic cirrhosis in 26.6%, biliary artesia in 24.4%, Wilson's disease in 17.7%, congenital hepatic fibrosis 6.65% and autoimmune hepatitis in 6.6 % patients) of portal hypertension in pediatric age group were found in 93.3% patients while extra-hepatic causes in only 6.7% patients.

Studies had shown the difference in etiology of portal hypertension different age groups as intrahepatic causes was more in adults and extra-hepatic etiology in pediatric age group.[10,18] One South Indian study showed that amongst the common etiological factors of portal hypertension in children were extra-hepatic portal venous blockage and then cirrhosis.[11] Bernard et al. stated that 51%of of cases were due to and 34 % because extra-hepatic venousblockage.[12] In any case, debate exists with respect to the etiology and presentation of portal hypertension in pediatric age and adult patients and it is different in various regions. In certain researches performed in the West, frequency of intrahepatic causes was more in pediatric age group.[13,14] while studies performed in India reported

That extra-hepatic etiological factors were more in frequency in children.[15]

Conclusion

This study concluded that most common intra-hepatic cause of portal hypertension in pediatric age group was cryptogenic (idiopathic) followed by Wilson's disease then autoimmune hepatitis , biliary artesia, congenital hepatic fibrosis, and viral hepatitis in a set of patients that presented with portal hypertension. So, we recommend that special attention should be given in these patients for early diagnosis, effective and proper management steps/guidelines of the these conditions for better prognosis.

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Original Article

Association of Ultrasonographic Characteristics with the Malignancy in Cold Nodules of Thyroid.

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Objective: To determine association of ultrasonographic findings with malignancy in patients with cold nodule of thyroid.

Methods: This was a observational study, conducted in Department of ENT, Jinnah Postgraduate Medical Center, Karachi. The study duration was six months, ie. from 15th April to 15th October, 2015. Patients with diagnosis of palpable nodule in thyroid gland on physical examination were enrolled. Detailed histories and physical examination was recorded. All patients underwent 99mTc-pertechnetate scintigraphy and patients with cold nodule were eligible for study after fulfilling inclusion/exclusion criteria. Thyroid ultrasonography was performed and findings such as size, shape, calcifications and echogenicity of nodule were recorded. FNA biopsy was performed under ultrasound guidance. Final diagnosis of malignancy was based on histopathologic examination. Data was analysed by SPSS and association was established between ultrasonographic characteristics and frequency of malignancy in cold nodules of thyroid gland.

Results: Out of total 188 patients of cold nodule, 17 were positive for malignancy. On analysis of association of various factors with malignancy, 04 patients of age less than 40 years while 13 of age 40 and above had malignancy (P=0.235). Ten males and 7 females had malignancy (P= 0.514). Seven patients with tumor size <2cm, while 10 patients with tumor size >2cm had malignancy (P=000). Fourteen patients with abnormal shape (irregular margins, infiltrative, microlobulated) while 03 patients without abnormal shape had malignancy (p=.036). Seven patients with calcification (microcalcifications) while 10 patients without calcification had malignancy (P=0.209). Seven patients with hypoechogenicity while 10 patients without hypoechogenicity had malignancy (P=0.533).

Conclusions: Majority of patients with malignancy are male of above 40 years of age. Tumor size above 2 cm and abnormal shape on ultrasound of thyroid gland are strongly associated with increased chances of malignancy in cold nodules of thyroid.

Keywords: thyroid malignancy, cold nodule, ultrasonography, FNA biopsy, tumor histopathology.

Introduction

A thyroid nodule is defined as a discrete lesion within the thyroid gland that is radiologically distinct from the surrounding thyroid parenchyma.[1] Thyroid nodules are frequently discovered in clinical practice, either during physical examination, but also incidentally, during various imaging procedures. [2] The prevalence of thyroid nodules in the general population goes up to 76% when evaluated with ultrasound instead of clinical examination.[3] The risk of malignancy in nodular thyroid disease varies depending on factors such as gender, age, and personal and family history. Increased suspicion is associated with male gender, age < 15 or > 45 years, nodule size > 4 cm, history of radiation exposure, and personal or family history of conditions known to be associated with thyroid cancer. [4] On thyroid scanning solitary nodules are further classified as hot, warm, or cold. Since thyroid carcinoma usually does not concentrate radioiodine as well as normal tissue, malignant thyroid nodules commonly appear as hypofunctioning or nonfunctioning areas on the radioactive iodine scan of the thyroid represented as cold nodule on isotope scanning. Therefore most malignancies are found in cold rather than in hot or functioning nodules.[5] About 80% of solitary nodules are cold, but only 4.6% prove to be malignant. Cold nodules of thyroid are extremely common but most of them are benign.[6] Ultrasound is the preferred imaging modality for thyroid nodules. A number of studies have assessed various sonographic characteristics as predictors of thyroid cancer. Ultrasonographic findings associated with an increased risk of cancer include larger nodule size, presence of calcifications, hypoechogenicity, solid composition, absence of a halo, and irregular margins. Ultrasound guided, fine

needle aspiration (FNA) biopsy is the preferred method of tissue sampling for cold nodules.[7] Its sensitivity is 6598% with a specificity of 72100%.[8] FNA biopsy, particularly when performed under ultrasound guidance, is the most cost-effective and accurate way to evaluate a thyroid nodule. Biopsy samples are evaluated histopathologically for final diagnosis.[9] Detection of a malignant thyroid nodule is an important task. Ultrasonographic findings can be significantly helpful in differentiating malignant from benign nodules of thyroid gland, even before the FNA biopsy was performed. Surgery in benign conditions is better avoided, whereas malignant lesions are successfully treated surgically. Ultrasonography can identify more suitable candidates for FNA biopsy early in the course of evaluation that will help in better management of patients presenting with cold nodule. Objective of our study was to determine association of ultrasonographic findings with malignancy in patients with cold nodule of thyroid.

Methods

The study was conducted in Department of ENT, Jinnah Postgraduate Medical Center, Karachi, during six months period, ie. from 15th April to 15th October 2015. It was an observational case series study in which a total of 188 patients were recruited in this study by non-probability consecutive sampling technique. Patients were selected from OPD and ward of department of ENT, Jinnah Postgraduate Medical Centre, Karachi. An informed consent was taken from the patient. All patients with a palpable nodule in thyroid gland on physical examination underwent a 99mTc-pertechnetate scintigraphy using a pinhole collimator. Patients with cold nodule were eligible for study after fulfilling inclusion/exclusion criteria. Thyroid ultrasonography was performed by radiologist, with special expertise in thyroid sonography. Sonographic characteristics such as size, shape, calcifications and echogenicity of nodule were recorded. FNA biopsy was performed under ultrasound guidance. Final diagnosis of malignancy was based on histopathologic examination. Frequency of malignancy was recorded. A database was developed on SPSS-17. Mean±SD was calculated for age. Frequency and percentages were calculated for gender and sonographic characters of nodule. Effect modifier were controlled through stratification of age, gender and sonographic characteristics of nodule, to see effect of these on outcome variable, by applying chi square test. Association was established between ultrasonographic findings and results of FNA biopsy/histopathological reports. P value <0.05 was taken as significant.

Results

A total of 188 patients fulfilling the inclusion criteria were included in this study. The mean±standard deviation age of study population was 47.92±9.375 years. On analysis of demographics data it was observed 65 (34.6%) were below 40 years of age & 123 (65.4%) were of age 40 years and above. Out of 188 subjects, 115 (61.2%) were male and 73 (38.8%) were female. On analysis of sonographic characteristics, 112 (59.6%) had abnormal shape. Also 56 (29.8%) had

Table-1: Frequency of malignancy in patients with cold modules, according to different parameters.

Parameters	Categories	MALIGNANCY			P-level
		Yes (17)	No (171)	Total (188)	
Age	40 years and above	13	110	123	0.2352
	Below 40 years	04	61	65	
Gender	Male	10	105	115	0.514
	Female	07	66	73	
Size of Tumour	Less than 20cm	07	147	154	0.00
	20cm and above	10	24	34	
Sape of Tumour	Abnormal (irregular margins, infiltrative microllobulated)	14	98	112	0.036
	Normal (well defined regular margins)	03	73	76	
Calcification	Non calculated	10	122	132	0.209
	Calculated (mircocalcifications)	07	49	114	
Echogenicity	Echgenic, isocchoic	10	104	114	0.533
	Hypoechgenic	07	67	74	

calcification and 74 (39.4%) had hypoechogenicity. On analysis of frequency of outcome variables, 17 (9%) had malignancy. On analysis of association of various factors with malignancy, 04 patients of age less than 40 years while 13 of age 40 and above had malignancy (P= 0.235). Ten males and 7 females had malignancy (P= 0.514). Seven patients with tumor size < 2 cm while 10 patients with tumor size >2 cm had malignancy (P=0.00). Fourteen patients with abnormal shape while 03 patients without abnormal shape had malignancy (p=0.036). Seven patients with calcification while 10 patients without calcification had malignancy (P=0.209). Seven patients with hypoechogenicity while 10 patients without hypoechogenicity had malignancy (P=0.533). Stratification with respect to age, gender and sonographic characters like size, shape, calcification, and echogenicity is mentioned in **(Table-1).**

Discussion

Several thyroid diseases may present as nodules. According to population-based studies conducted with adults in iodine sufficient areas, approximately 4 to 7% of women and 1% of men exhibit palpable thyroid nodules [10, 11]. However, the prevalence of nodules indicated by ultrasound exams is substantially higher, reaching up to 68% of the population (such high frequencies are usually found among older women than 65. Although most thyroid nodules are benign, the possibility of a malignancy must be ruled out[12, 13] It has been reported that solitary, solid and large sized nodule possesses a different clinical and pathological significance for surgical evaluation.[14, 15] In this study we analyzed frequency of malignancy in patients with cold nodule of thyroid. High resolution ultrasound is the best imaging modality for objectively detecting size, number and cellular nature of the nodules.[16] In our series ultrasound imaging single large nodule and abnormal shape have more chances of development of malignancy. Solid nodule (less than 25% of cystic component) in ultrasound image, merit further careful evaluation and eventual indication for surgical intervention. On the other hand ultrasound has not the ability to establish functional status of the nodule. Nuclear imaging is a useful modality for the functional characterization of a thyroid nodule.[17] In our series, nuclear scanning was found useful to define functional status of solitary solid nodule. Larger hot spot and image of suppressed extranodular tissue in the thyroid scintigraphy has identified hyperactive nodule, and has established the diagnosis of toxic adenoma in our 20 patients. Cold spot in the remaining 24 cases has determined hypo or inactive (functional status of the) solid nodule. Hypoactive solid nodule in nuclear scanning points out increased risk of malignancy.[18] After imaging modalities FNAC is the preferred method for preoperative pathological evaluation. As a scintigraphic feature, cold spot significantly increases the risk of malignancy in a large solid nodule. Solitary hypoactive solid nodule in our patients has supported the indication of surgical intervention. Larger size, solitary nodule, hypoechogenicity of solid elements, microcal cification, irregular shape as features of echotexture determined by ultrasound, and hypoactive nodule (cold spot) by nuclear scan have been reported as marker of high risk for malignant development.[19] The rate of 29% (10/34) of malignancy in our patients has confirmed the increased risk of malignancy in larger hypoactive nodule. Previous studies have also reported similar rates of malignancy between 16% and 30% in solitary solid nodule.[20] On the other hand the malignancy rate was 8.5% in autopsy and surgical series including solitary and multinodular goiter cases.[21] Although the number of patients is relatively small for definitive conclusion, based on our findings we have concluded that large nodule has a considerable rate among patients with cold nodular goiter in endemic area. Ultrasound objectively defines cellular architecture of the nodule, and nuclear scan its functional status. Solitary hypoactive, abnormal shape and larger nodule possess high rate of malignant change.

Conclusion

Majority of patients with malignancy are male of above 40 years of age. Tumor size above 2 cm and abnormal shape including infiltrative microlobulated irregular margins, on ultrasound of thyroid gland are strongly associated with increased chances of malignancy in cold nodules of thyroid.

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Original Article

Frequency of Nutritional Rickets Under Two Year Aged Children Admitted with Severe Pneumonia in The Department of Pediatrics, BBH, Rawalpindi

Maryam Amjad, Najaf Masood, Nadia Zaman, Madia Qamer, Shahzadi Sumbal Ghazi and Sonia Fazal

Objective: To determine the frequency of nutritional rickets in children hospitalized with severe pneumonia.

Methods: It was a cross-sectional study conducted at Department of Pediatrics, Benazir Bhutto Hospital, Rawalpindi Pakistan from 1st May 2012 to 31st October 2012.A total of 75 patients of severe pneumonia between 6 to 24months were selected according to inclusion criteria. Data was collected including admission number, age, sex, weight, consistent signs of rickets, history of breast feeding and duration of sun exposure in 24 hours. A single blood sample 5ml was collected at the same time for biochemical changes of rickets and sent to the hospital lab for analysis of serum calcium, phosphate and alkaline phosphates levels. Reports were verified by the hospital pathologist. All the data was subjected to proforma and analysed by SPSS-15.

Results: Out of 75 patients of severe pneumonia, 48(64%) were male, and 27(36%) were female. The mean age was 11.9±4.9 months and mean weight was 8.0±1.4kg. The frequency of breast feeding was 53(70.7%). The duration of sun exposure was inadequate in mostly patients 51(68%).Rickets was found in 57(76%) of patients of severe pneumonia.

Conclusions: Rickets was found in 57(76%) of patients of severe pneumonia. It is concluded that nutritional rickets is very common in children under two year of age, hospitalized with severe pneumonia.

Keywords: pneumonia, nutritional rickets, Vitamin-D.

Introduction

Childhood pneumonia is a leading cause of death, accounting for 15% of deaths worldwide in children under 5years of age.[1] In Pakistan pneumonia contributes 19% of total deaths in under 5years children.[2] According to IMNCI severe pneumonia is defined as any child with cough/fast breathing with the lower chest in drawings.[1] Bacterial pneumonia presents with high fever, chills and rapid breathing[3] while onset in viral pneumonia is slow however it worsens over time[3]. The most common typical pathogen include Streptococcus pneumonia, Haemophilus influenza and Staphylococcus aureus.[4] Clinical symptoms are crucial to diagnosis in inadequate resources settings; however, chest x-ray and laboratory investigations are confirmatory for pneumonia.[3] Diagnostic advances include the use of new radiological methods, better specimen collection, and improved microbiological tests.[5] Nutritional rickets is a public health concern in developing countries.[6] Rickets is the commonest presentation of vitamin-D deficiency.[7] Rickets is a metabolic disease of growing bones in children due to deficiency or impaired metabolism of vitamin D or calcium and may lead to fractures or deformity.[8] The prevalence of nutritional rickets in under five-years children is 15-18% in South East Asia.[9] The frequency of nutritional rickets is 2.25%in Pakistan.[10] Evaluation of nutritional rickets includes detail history, physical, laboratory, and radiological evidence.[11] The majority of cases respond to one to two doses of injectable vitamin-D (600,000 IU)i.e.stoss therapy.[10] A minimum of 400iu of vitamin-D is recommended daily to prevent vitamin D deficiency and rickets.[12]

In addition to skeletal homeostasis, vitamin-D has a physiological role.[13] In addition to Skeletal deformities, chest infection is also a complication of vitamin-D deficiency which needs focus. The rationale of this study is to highlight the importance of vitamin-D in preventing pneumonia through simple measures.

Methods

This was a cross-sectional study, conducted at Department of Pediatrics, Benazir Bhutto Hospital Rawalpindi for six months from 1st May 2012 to 31 October 2012.After approval from the ethical committee of hospital and consent from a guardian, a total of 75 children of ages between 6 to 24 months

admitted with severe pneumonia were included. Children having a history of liver or renal disease, taking isoniazid, rifampicin phenytoin, phenobarbitone, during the previous three months or on vitamin-D supplements were excluded from the study. Data was collected including admission number, age, sex, weight. Severe pneumonia was diagnosed by IMNCI classification chart for sick child age 2months to 5 years by catergeroizing any danger sign (Ask: Is he able to drink or breast feeding? Does the child vomit everything? Has the child had convulsions (fits)? Ask if more than 1 convulsion or if prolonged more than 15 minutes if yes to other. See if the child is lethargic or unconscious. Is the child convulsion now?). Any general danger sign or stridor in calm child was diagnosed as severe pneumonia. Further patients were evaluated for rickets by taking a history of breast feeding and duration of sun exposure in 24 hours along with clinical features for rickets. A single blood sample 5ml were collected at the same time for biochemical changes sent to the hospital lab. Serum calcium, phosphate and alkaline phosphatase levels were done and verified by hospital pathologists. All the findings were subjected to proforma and analysed on SPSS 15.

Results

Out of 75 children hospitalized with severe pneumonia 48(64%) were male, and 27(36%) were female. Gender distribution is represented by a bar graph in Figure 1. Mean age and weight were 11.93 months with SD of 4.979 and 8.029 kg with SD of 1.4397 respectively shown in (**Table-1).**

Table-1: Distribution of age (months) and weight (kg) in the study population.

	Age	Weight
Mean	11.93	8.029
Std. Deviation	4.979	1.4397
n:	75	75

Table-2: Frequency of breastfeeding and adequate sun exposure in the study population.

Characteristic	Options	Frequency	Percentage
Beastfeeding	Yes	53	70.7
	No	22	29.3
	Total	75	100.0
Sun Exposure	Less than 3.4 hours	51	68.0
	More than 3.4 hours	24	32.0
	Total	75	100

About two-thirds of children 53(70.7%) received breast feeding and duration of sun exposure was inadequate in most patients 51(68%) and was adequate in only 24 (32%) patients. Findings are depicted in **(Table-2)**. Rickets had a high burden and diagnosed in 57(76%) patients of severe pneumonia and absent in only18 (24%) of patients, depicted in (**Fig-2).**

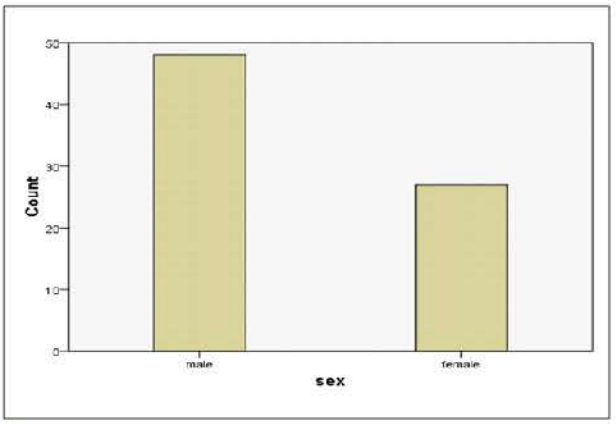

Fig-1: Gender distribution in the study population.

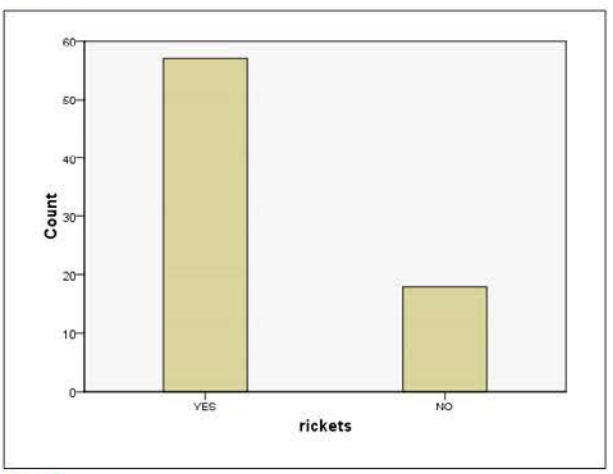

Fig-2: Frequency of nutritional rickets in the study population.

Discussion

Nutritional Rickets is among the five most common diseases of children. Rickets is not only a predictor of bone health, but it also causes other problems.[14] Over the last few years, several studies have been conducted to find out the prevalence and relationship of nutritional rickets with respiratory infections. In a study done in Karachi out of 137 patients, with severe pneumonia, 83 were male and 54 females. The frequency of nutritional rickets in children with severe pneumonia was observed in 101(74%) cases which is similar to our study. Rickets was more common in 2 to 12 months of age, i.e., 79.8% (67/84) and in those children who were breastfed (85.3% vs 40%). The

frequency was higher in those children who were not exposed to sunlight.[15] In a study, 283 infants diagnosed with nutritional rickets due to Vitamin D deficiency (67% males) that were between 6 and 14 months of age. Among the total, 70% were exclusively breastfed, and 23% were breast-fed until the age of 1 year. The most frequent clinical presentation was hypo-calcemic convulsions (34%) followed by chest infections (33%) and gastroenteritis (25%).[16] In Denmark, from 1995 to2005, the average incidence of nutritional rickets in children aged0-14.9and 0-2.9 was 2.9 and 5.8 per 100,000 per year respectively.[17] An Australian study 398 children identified with vitamin D deficiency (55% male; median age, 6.3 years). The overall incidence in children ≤15 years of age in Australia was 4.9/100 000/year. Duration of exclusive breastfeeding was inversely related to serum vitamin D levels in children less than three years of age.[18]The study was done in Qatar, and a very sun-rich area revealed that 23.9% of the studied children had nutritional rickets. The mean SD age of those with rickets (3.76 years 1.51) was slightly higher than those without rickets 3.57 years. The children with rickets spent a significantly shorter average duration (26.86 minutes 19.94) under the sun than those without rickets (30.59 minutes 15.72).[19]

In a study done in Turkey, among the causes of admission of rachitic children to the hospital, fever (66%) and coughing (62.2%) were the most frequent. Pneumonia was accompanied by rickets in 47.1% of the cases.[20] During one year in a study conducted in Turkey, 305 hospitalized children (ages between 0 to 3 years) were evaluated for clinical and biochemical markers of vitamin D deficient rickets and related factors. 21 (6.8%) were diagnosed as nutritional vitamin D deficiency and rickets. Most of the children diagnosed were under one year old (16/21, 76.2%). 14 vitamin D deficient rachitic children were admitted with infectious conditions, and most of them were respiratory tract infection.[21] In a prospective cohort study in 272 hospitalized patients with pneumonia. Hundred forty-three patients One vitamin D deficient ((53%) were<50 nmol/L), 79 patients (29%) were vitamin D insufficient (5075 nmol/L), and 50 patients (18%) were vitamin D sufficient (>75 nmol/L). Vitamin D deficiency was associated with an increased risk of ICU admission and 30-day mortality. Vitamin D status was an independent predictor of 30-day[22].

In Jordan, nutritional rickets seems to be a common problem among infants. Forty-seven infants (10.6%) out of the 443 included in the study were found to have nutritional rickets. 40 (85.1%) of the rachitic infants were admitted due to lower respiratory tract diseases compared with 30% of the control group. Rachitic infants were breastfed in 82.9%.[23] The most recent vitamin D intake guidelines by the American Academy of Pediatrics recommends that all infants, including those who are exclusively breastfed, have a minimum intake of 400IU vitamin D per day beginning as early as the first two months of life.[24] Our study focuses on the relationship between vitamin D deficiency and severe pneumonia. It highlights increasing burden of nutritional rickets in children hospitalized with pneumonia, and it should be prevented to reduce morbidity and mortality associated with pneumonia.

Conclusion

Rickets was found in 57(76%) of patients of severe pneumonia. It is concluded that nutritional rickets is very common in children under two year age hospitalized with severe pneumonia.

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Original Article

Violence Prevalence in North Lahore: Forensic Demographics

Khalid Mahmood, Fahad Saleem, Dawar Nadeem, Muhammad Javed, Ahmad Raza Khan and Muhammad Abaidullah

Objective: Demographic analysis of incidence of violence in North Lahore to objectify the prevalence of criminalistic variance categorization

Methods: It was a cohort prospective analysis throughout the year 2018, conducted in the emergency medicolegal section of Services Hospital Lahore. All cases reporting to medicolegal section were part of research project who were either accompanied by police or presented via divergent modes.

Results: Statistical perusal revealed that out of 2341 cases registered in 2018, 70% were escorted by police. 10-12% were brought by either a relative or a friend. 3% each were either self-presented cases or were rescued by 1122 to hospital.89% were either of 18 years age or more. 78% were male and 22% were female patients. 63% were subjected to a variance of physical assault.

Conclusions: Survival is a subconscious instinct which at times can make a person take extreme measures. Sometimes violence is optional at times a desperate sequalae, however at times it is such an inexplicably heinous that it requires instantaneous justice. All this categorization of deplorable immorality is to be channelized via medicolegal examination, which is mandatory participle of legal chain of custody.

Keywords: violence, medicolegal, docket, assault.

Introduction

Violent behavior is usage of physical force with intent to harm anyone in mind, body, reputation or property either individually or collectively resultant in morbidity or mortality. Violence application can be due to blunt trauma, sharp edge injury infliction, firearm weapons and in the form of sexual predation.[1]It ranges from trivial assault charges to lethal use of force and also includes sexual advances ranging from harassment to rape. Violence has only been a second nature to human beings since their origin. Being aggressive as defensive act or to embark supremacy over fellow humans comes naturally to those who believe in survival of the fittest. For centuries man has believed in law of the jungle that strongest and the fastest have the right to exist and all others should perish. In order to weed out the weak use of violence has been the trend in the human timeline.[2] Use of might by the powerful led to the creation of weapons by the weak for their defense and survival. From the initiation of the known human timeline man has evolved in many ways. One of these evolutionary steps was nomadic life style developing in sedentism. Human colonization in resourceful areas marked the era of might is right as to mightiest took charge of the place with most natural resources befitting human settlements. Primarily it was the agriculturally fertile land that was targeted, which today has been surpassed by urbanization and advanced computed technological advances. With time human desires and demands have altered but the instinctive nature to take charge has remained an undeterred factor which only enhanced sophistication in weaponry. The basic instinct of survival subconsciously drives the aggression for acquisition of power or self-perseverance.[3]

Global violence caused around more than a million deaths in 2013, with 842,000 fatalities attributed to suicidal manner and 405,000 were resultant of social violence activity. 31000 were war casualties as well as legal intercession. Among these firearm assaults was the preeminent reason of fatal outcome amounting up to 180,000 estimated numbers. Repercussions of violent deaths involve hospitalization, psychological consequences and social dilemmas for survivors who are either directly involved in the feuds or are just innocent passerby individuals who are afflicted as they happened to be on the scene of crime at the time of incidence.[4]

Violence is an avoidable variable redeemable by multitude of factors like modifiable measures to check poverty, socioeconomic status, gender bias and intake of the root cause of all social evil, alcohol. Strategic planning needs to be chalked out for effective

prophylaxis of violence by improving the social attitudes individually as well as in a collective form.[5]
Trauma has been categorized by World Health Organization, as self-inflicted, social evils and mass disaster whether it be war or an act of terrorism, which can be further sub-classified as physical, sex oriented and psychological. Yet another way to portray illegal activity is either through use of a weapon or a reactionary hostility.[6]
Medicolegal way to systemize the barbarity variables can be narrated as use of blunt force, sharp edge infliction whether incised or stab wound, firearm weapon usage, rape, sodomy, unnatural sexual offences, burns, poisoning, and alcohol intoxication.[7] This is a check and balance system to maintain societal law and order, as apprehension of being indicted in an offence is more of a prophylactic maneuver than being actually subjected to punishment. It is a general consideration that fear of punishment is more of a deterrent factor in commission of crime rather than actually being subjected to punishment.[8] Legal diversification is prevalent universally but all the legal frameworks are programmed to a common goal of rectification of malevolence. The best way to scrutinize the remedial steps is to have statistical substantiation. It not only elaborates on the prevalence of insidious nature of crime but also dissects out the efficacy of restorative counteractant legal procedures.
The contemporaneous inquisition collates vehemence preponderance during 2018. It is a narrative description of medicolegal cases per se reported in as police investigation or on magisterial inquisition. Primarily 13 allocated police stations of Lahore district were targeted for inquisitor purposes but any life-threatening situation were delved with to accommodate and facilitate law and order situation.

Method

Medicolegal section of Forensic Medicine and Toxicology is based in the emergency department of Services Hospital Lahore. Cases were followed up as they reported in medicolegal office of emergency unit Services Hospital Lahore, during the year 2018. It is an emergency facility run 24 hours a day 7 days a week. By and large bulk of cases reported were from 13 allocated Police Stations, by the Government of Punjab. Most of reported cases were brought in by Police along with a Police Docket or a Court Order for medicolegal examination of the injured. The rest either reported with implied consent of getting themselves examined for the injuries procured during fight or homicidal manner of infliction.

Results

A total figure of 2341 cases were reported during the year 2018. 1651 of these cases were brought in by Police along with Authority letter, for the medicolegal examiner, requesting to examine, either the injured or the accused assailant, which amounted to about 70% of the total turnover. 3% each were either brought in by rescue 1122 or were the patients themselves who reported in the emergency. Besides this statistical turnover 243 individuals were brought in by relatives with multifaceted accusations. 4.6% of cases did not follow up in the sense that they never came back to recollect even initial examination report let aside to get it finally declared after expert opinion or radiological feedback. **(Fig-1)** 89.3 % (2090/2341) cases reporting in the medicolegal clinic were of the age of majority and the remaining 251 (10.7%) were minors either brought in by relatives or police or both (6%). **(Fig-2)** 1834 of 2341 recorded cases were of male gender while remaining 21.7% were female. **(Fig-3)**

Table-1: radiological feedback.

Brought by	Frequency	Percent	Valid Percent
Police /Docket	1651	70.5	70.5
Self	73	3.1	3.1
1122 Rescue	83	3.5	3.5
Passer by	1	.0	.0
Relatives	243	10.4	10.4
Fariends	42	1.8	1.8
Police + Relatives	140	6.01	6.0
No follow up/ non-issued	108	4.6	4.6
Total	2341	1000.0	100.0

Table-2: radiological feedback.

Age	Frequency	Percent	Valid Percent
Major (=18 years)	2090	89.3	89.3
Minor (< 16/18 years)	251	10.7	10.7
Total	2341	100.0	100.0

Table-3: radiological feedback.

Sex	Frequency	Percent	Valid Percent
Male	1834	78.3	78.3
Female	507	21.7	21.7
Total	2341	100.0	100.0

Of these issued medicolegal reports 53.1 % were during the spring and summer season whereas during fall and winter season 42.3% cases were registered. 108 of the total cases were not followed up either by victim or by the police. Among this annual promulgation of cases the diurnal variation was also observed with 48.6% of inscribed incidence during night duty hours followed by 22.9% and 23.9% notarization during morning and evening timings of duty roster. Area engaged in high criminalistic activity was sorted out to be cantonment section of North Lahore subdivided further into north and south cantonment police stations. Collectively 555 cases were adumbrated from cantonment followed by Ghaziabad police station where 282 complaints were lodged. Defence, Gulberg and Ichra filed 233, 220 and 185 cases each. Relatively low number of incidences occurred in jurisdiction of Sarwar Road, Shadman and Race Course police stations enumerating from 0.8% to 2.2% and 4% respectively. **(Fig.4)**

Table-4: radiological feedback.

Area/Police Station	Frequency	Percent	Valid Percent
Shadman	51	2.2	2.2
Mustafaabad	159	6.8	6.8
Race Course	93	4.0	4.4
Sarwar Road	19	.8	.8
Guldasht Town	104	4.4	4.4
Miscellaneous	209	8.9	8.9
No follow up/non-issued	108	4.6	4.6
Gulberg+Ghalib market	220	9.4	9.4
Defence A B	233	10.0	10.0
Ghazi abad	282	12.0	12.0
Millat Park	118	5.0	5.0
Ichra	185	7.9	7.9
North cantt	333	14.2	14.2
South Cantt	222	9.5	9.5
Lyton Road	.5	.2	.2
Total	2341	100.0	100.0

Analytical categorization docketed the crimes as physical assault being the top of classification with 63% (1474/2341) of total declared cases. Domestic violence was the next most reported incidence with 323 cases out of 2341. This was succeeded by heinous criminality of sexual predation with 219 penned down activity. However, in 2018 only 180 cases were brought in by police for medicolegal examination of individuals with alcohol intake. **(Fig.5)**

Table-5: radiological feedback.

History		Frequency	Percent	Valid Percent
Valid	Physical Assualt	1474	63.0	63.0
	Self-infected	9	.4	.4
	Unnatural sexual effence	3	.1	.1
	Rape with minor	33	1.4	1.4
	Sodomy with minor	36	1.5	1.5
	Male accused of rape	45	1.9	1.9
	Male accused of sodomy	15	.6	.6
	Domestic violence	323	13.8	13.8
	Road Traffic Accident	103	4.4	4.4
	Sodomy with adult	37	1.6	1.6
	Rape with adult	50	2.1	2.1
	Alcohol intake	180	7.7	7.7
	Poisoning	12	.5	.5
	Dacoity	6	.3	.3
	Abduction	15	.3	.6
	Total	2341	100.0	100.0

Discussion

The main objectivity of this exercise for requisition of data regarding violence was to assess the prevalence of crime in the north segment of the city and what remedial steps can be maneuvered to rectify such law and order situations. Further elucidation was meticulously catalogued into type of crime ranging from trivial rouginess to ferocious crimes. This study not only highlighted occurrence of such heinous crimes but also introduces as to how to educate the masses to discipline their behavior as well as encourage them to inform about any illicit felonious transgressions. Year 2018 was targeted for this malfeasance scrutiny. Variables for the study purposes included age, gender, area of incidence, history and the procedural steps of divulgence with forensic specialty. Research based anatomization has explicitly annotated that fear of punishment is the prime deterrent factor rather than the actual penalty sentence carried out against the accused. Consequently, an impartial effective law and order scenario is more convincing efficacious machination for execution of discipline in the societal norms. As commination implementation against one perpetrator is a relatively less effectual directive in contrast to a practical intimidation. Public

awareness needs a mapped-out solution which ought to put an end to illegal ventures.[9] Statistical perusal revealed that out of 2341 cases registered in 2018, 70% (1651) were brought in by police who were either the victims or the accused. 89% (2090) were of age of majority and among these 78% (1834) were of male gender. 63% (1474) had a presenting complaint of being subject to a variance of physical assault. Besides these facts and figures 10-12% were accompanied by either a relative or a friend. 3% each, walked in emergency either on their own or were rescue deliverance to hospital. Of all the 2341 individuals 10.7% (251) were minors out of which 3% were subjected to sexual odious monstrosity with yet remaining minors were victimized physically in one way or another by blunt means, sharp edge weapons besides sexual predation.[10] North and South Cantonment Police stations were conspicuous due to high malefacere demographics of 14.2% (333) and 9.5% (222) reciprocally. This crime rate was closely followed by Police Station Ghaziabad enumerated by 12% (282) turnover in the medicolegal office. Least notoriety was observed in Lytton Road, Sarwar Road and Shadman Police Stations as per medicolegal record depicted by 0.2%, 0.8% and 2.2% outcome reports. Remaining strength of police stations had a range of cases between 5-8% brought in by the police, rescue or were reported by self-representation. Although this limited study does not cover the entire scope and capture the veritable in every aspect but in the least, it portrays tip of the iceberg, pointing out the locale of the hub. What circumstances give rise to such situations where either people choose to adopt collateral routes for necessity fulfilment or are actual offenders by disease of mind or they do crime just because it the easy way out or crave a curiosity or vent out frustrations.[11] What protocols are to channelized in order to improve society norms. How are these individuals handled during the police investigation procedure and what is the outcome when the cases finally make it to the judicial system? These are the queries for a further data mining. Role of forensic expert is to establishment of presentable documentary facts to the court of law for prosecution. Case declaration and issuancewas at a mentionable percentage of 95.4% with only 108 cases that remained without any follow up. This entire exercise of apprehended offenders for consequential culmination in furtherance of justice is the targeted denouncement, to discourage deplorable felonious activities in the society.

Conclusions

Survival is a subconscious instinct which at times can make a person take extreme measures. Sometimes violence is optional at times a desperate sequalae, however at times it is such an inexplicably heinous that it requires instantaneous justice. All this categorization of deplorable immorality is to be channelized via medicolegal examination, which is mandatory participle of legal chain of custody.

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Original Article

Protective Effects of Moringa Oleifera Leaves Extract on Bisphenol A Induced Changes in the Proximal Convoluted Tubules of The Kidneys of Adult Albino Rats

Rabia Ejaz, Arooj Nawaz, Fozia Farzana, Mariam Ashraf, Sharjeel Ilyas and Shagufta Nasreen,

Objective: To determine the effects of Moringa oleifera leaves extract on Bisphenol A induced changes in the PCT diameters and PCT cell vacuolization in the kidneys of adult albino rats.

Methods: Thirty adult albino Wistar rats of any gender, weighing (160-180g) were acquired from National Institute of Health, Islamabad. 30 rats were randomly divided into 3 equal groups as A, B and C, so that each group had 10 rats. Group A rats received standard rat feed and 1ml/kg of distilled water via oral gavage only. Group B received BPA at dose of 50mg/kg/day. Group C received BPA at dose of 50mg/kg/day, followed by MoLE at dose of 500mg/kg/day. All animals were sacrificed at the end of 8 weeks. The kidneys were dissected out and processed further for H&E staining and oculo micrometry was done to measure the PCT diameter and observe the PCT cell vacuolizations.

Results: The increase in diameters of PCT and PCT cell vacuolization, that was seen in group B upon giving BPA only was prevented in the animals of group C that was given MoLE with BPA.

Conclusions: Moringa oleifera leaves extract prevents BPA induced increase in the PCT diameters and PCT cells vacuolizations in the kidneys of adult albino rats.

Keywords: bisphenol a, moringa oleifera leaves extract, albino rats, proximal convoluted tubules.

Introduction

Human beings are constantly being exposed to Bisphenol A [BPA, 2, 2-bis (hydroxyphenyl) propane.[1] It contains phenolic rings and is an environmental toxin.[2] This compound is used to prepare epoxy resins (e.g., inner linings of metallic cans) and polycarbonate plastics and also in the form of non-polymer additive to various plastics. It is also present in drinking water. It is a constituent of infants and water bottles, kitchen ware, food containers and dental materials.[3] BPA causes oxidative stress and has injurious effects on kidneys, liver, and reproductive system.[4]

According to the studies on rodents, NOAEL for BPA is stated to be 5mg/kg and a lethal dose (LD50) is considered as 3.25 g/kg in rats.[5] In both, rats and humans, BPA is absorbed from gastrointestinal tract and conjugated in liver enzymatically to a glucuronide form which is excreted in urine.[6] Moringa oleifera is a valueable tropical tree which is being used as human medicine, food and also in oil production. It is known to be 'Sohanjana' in Pakistan and is grown widely all over the country. Moringa oleifera is commonly and widely found in India, Pakistan, Asia, Africa and Arabia.[7] Leaves of this tree are antihyperglycemic, hypocholesterolemic, antitumor agent, antioxidant.[8]

Methods

Experimental study was conducted at the animal house and histology lab of PGMI, Lahore. 30 adult albino rats of either sex, weighing 160 180gms were obtained from the National Institute of Health (NIH), Islamabad. Rats were provided with food and water ad libitum. Male and female rats were kept separately in iron cages under optimum temperature (24±2°C) and 12 hours light/dark cycle. Following acclimatization for a period of one week experiment was started. Each rat was weighed at start and end of experiment. Rats were divided into 3 groups comprising of 10 rats in each group **(Table-1).**

Table-1: Showing detail of the animal groups and experimental Intervention.

Group n=10	Administration	Week of scrifice	Intervention and dosage
Control B		End of 8 weeks	2ml/kg distilled water only ad libitum
Experimental C	Orally		BPA 50 mg/kg suppended in distilled water
Experimental			BPA 50 mg/kg+MOLE 500mg/kg dissolved in distilled water

Therapeutic Agents

BPA: Daejung Company, Korea.

Preparation of Moringa Oleifera Leaves Extract:[9]

Fresh Mo Leaves were procured from botanical gardens of the University of Punjab. Leaves were washed, shadow dried for 2 weeks to prevent direct

sunlight, to prevent them from damage. Leaves were ground to powder and carried to PCSIR lab complex Lahore for further processing.

Tissue Sampling: The kidneys of sacrificed rats were dissected out for detailed morphological and histological observation. For histological examination, the tissues was fixed in neutral buffer 10% formaldehyde solution and processed to make paraffin embedded blocks. Slides were stained with standard procedures of Hematoxylin and Eosin.

Mirometery of kidneys was done to determine diameters of proximal convoluted tubules.

For each slide, proximal tubules were observed in five randomly selected different fields. From each field, the diameters of three proximal tubules were determined at magnification of 40X. Tubules with clear boundaries were selected. At the end, mean size was calculated.

Results:

Diameter of PCT: One way ANOVA test was applied to compare the diameter of PCT among groups. It was found that the mean diameter of PCT in all groups were significantly different (p-value < 0.001) **(Table-2, Fig-1).** For multiple comparisons, post hoc Tukey test was used which showed that diameter of PCT in group B was significantly higher as compared to group A and C. However, no significant difference was found in the diameter of PCT among groups A and C **(Table - 3).**

PCT Cell Vacuolization: Fisher's exact test showed that there was an association between cell vacuolization of PCT and groups **(Table-4, Fig-2).** Cell vacuolization of PCT in rats of control group A was absent (Fig. 3 A). In group B, cell vacuolization was present in all rats. While in group C, only in 2 (20.0%) rats cell vacuolization was present in PCT **(Fig-3B and 3C).**

Table-2: Comparison of diameter of PCT among groups using one way ANOVA.

Parameters	Group-A	Group-B	Group-C	P-value
Diamter PCT(µm)	34.75±3.97	45.51±5.08	37.30±3.26	<0.001*

Table-3: Pair wise comparison of diameter of PCT among groups

Multiple Comparison					
	Groups-I	Groups-J	Mean difference (I-J)	Std. Error	P-value
Diameter of PCT	A	B	-10.7600	1.8652	0.000*
		C	-2.5500	1.8652	0.372
	B	C	8.2100	1.8652	0.000

**p value ≤ 0.05 is considered statistically significant*

Table-4: Distribution of PCT cell vacuolization among groups: (Fisher's exact test).

Cell Vacuolization	Group-A	Group-B	Group-C	P-value
Present	0 (0.0%)	10 (1001%)	2 (20.0%)	<0.001*
Absent	10 (100.0%)	0 (0.0%)	8 (80.0%)	

**p value ≤ 0.05 is considered statistically significant*

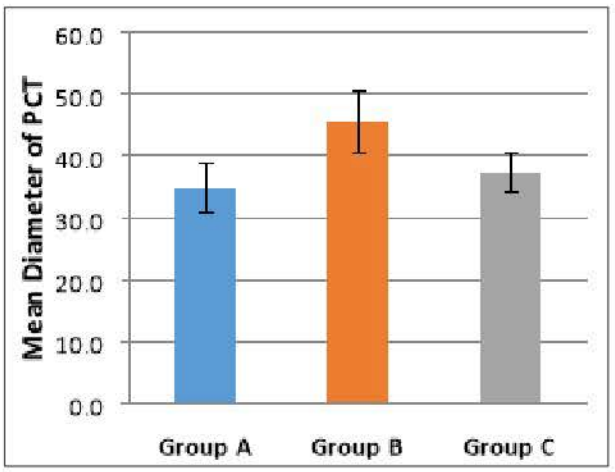

Fig-1: Bar chart showing comparison of diameter of PCT among groups.

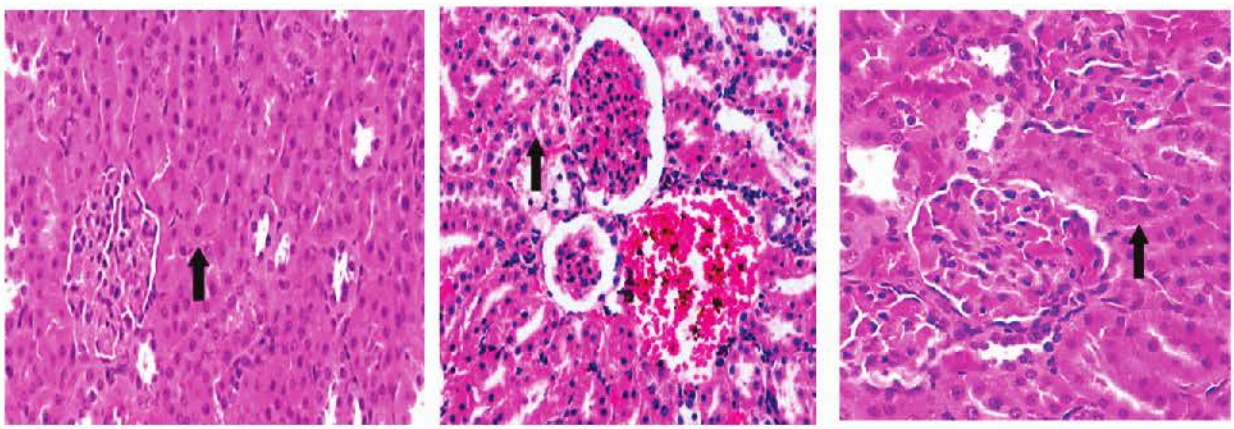

Figure 2: bar chart showing distribution of pct cell vacuolization among groups.

Discussion

The diameters of proximal convoluted tubules were measured and compared among groups in this study. The statistical analysis showed that these PCT diameters of control (34.75±3.97µm) and experimental groups receiving *Mo* along with BPA (37.30±3.26µm) were nearly similar while that in experimental group receiving only BPA, were markedly increased (45.51±5.08µm). Similarly, the results of experimentation done by Helal et al[10] and Hassan et al[11] also showed an increase in PCT diameter upon giving BPA to experimental rats. This increase in tubular diameter might be explained because of increase in tubular cell sizes due to BPA and later on degeneration of tubular cells. This might have occurred due to accumulation of BPA metabolites and inability of the rat kidneys to eliminate them causing necrosis and degeneration of renal tubules.[9,11] Similarly, dilated renal tubules were observed by Ahmed et al.[7]

On the other hand, a study conducted by Anibese et al[12] on nephro protective effects of *Mo* on potassium bromate induced kidney damage illustrated normal kidney architecture of animals that were given *Mo* which supports the present study. The proposed mechanism of *Mo* to prevent nephrotoxicity might be due to its antioxidant properties.[13] The seeds of *Moringa* contains many antioxidants like tocopherols, vitamins C, E and polyphenols possessing radical trapping ability.[14] Presence or absence of vacuolization of proximal tubular epithelial cells was noted in this study, in the kidneys of each rat in both experimental groups B (BPA alone) and C (BPA+*Mo*). It was found that all of the rats in group B had proximal tubular cellular vacuolization indicating the active inflammatory process. While, only two of the experimental rats in group C had vacuolization present in their kidneys. Whereas, proximal tubular cell vacuolization was not found in any of the rat in control group A. Vacuolization in renal tubules after BPA administration was also present in the study done by Helal et al.[10] Korkmaz et al[15] and Ola-Davies et al.[16] Cause behind this vacuolization as a marker of kidney injury probably is the oxidative stress induced by ROS produced in mitochondria and microsomes of renal tubular cells which damage the nucleic acids, proteins and lipids.[16]

Conclusion

Moringa oleifera leaves extract prevents BPA induced increase in the PCT diameters and PCT cells vacuolizations in the kidneys of adult albino rats.

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Original Article

Relationship of ABO Blood Groups with Body Mass Index and Hypertension in Medical Students

Mamoona Shabir, Syed Muhammad Shahnawaz Gardezi, Resham Sajjad Ghuman, Syeda Zainab, Rida Fatima and Sadia Sajjad

Objective: To find out the relationship of hypertension (HTN), ABO blood groups and body mass index (BMI) in medical students of Continental Medical college, Lahore.

Methods: This is a prospective study done in department of Physiology. Total participants were 300. ABO blood group was determined by antigen- antibody reaction. Blood pressure (BP) was measured two times by standard mercury sphygmomanometer and mean was calculated. Height and weight of students were measured to calculate BMI.

Results: In total 164(55%) were females and 136(45%) were males and mean age was 19 ± 0.75 years (17-23 years). Most prevalent students were of blood group B i.e.101 (34%). Maximum obese students (≥30 BMI) were belonging to blood group B i.e 18 (6%) and minimum number of obese students were of blood group AB i.e 4(1%). Blood group B has maximum prehypertensive (52 or 16.2%) and stage1 hypertensive students (3 or 16.2%) and blood group AB have minimum prehypertensive(7 or 2%) and no stage-1 hypertensive students.

Conclusions: Blood group-B students were most prevalent and more prone to high BMI and prehypertension in given population.

Keywords: ABO, hypertension, Body mass index.

Introduction

The ABO blood group system was discovered by the Austrian scientist Karl Landsteiner in 1900.[1] Its regulation is under the control of ABO gene expression.[2] Genes for ABO antigens are located on chromosome number 9. The major blood groups of ABO system are A, AB, B and O. The A and B antigens are oligosaccharide, expressed on erythrocytes, platelets, vascular endothelium and tissue cells.[3] Several epidemiological studies have reported that the distribution of different ABO blood groups vary markedly among the populations of different geographical areas reflecting racial differences.[4] Since the discovery of the ABO system, its significance regarding evolution, paternity dispute and genetic study, as predictor of national suicide rate, are all well documented by pastresearches.[1,5] The blood group systems are of interest to recent researchers of modern medicine due to its linkage with various diseases.[6]

BMI is a measure of excess body weight. It is useful for assessing aspects of health in children and adults. Based on the World Health Organization (WHO) classification of BMI, an individual may be clinically considered obese, overweight, normal, or underweight. BMI pattern of distribution differs within and between different populations globally; changing trends in BMI of individual populations are known and linked to changes in socioeconomic status.[7] Obesity and overweight are known to be harmful to health[8], and many studies have demonstrated the association of increased BMI and risk of development of certain diseases. Excess body weight is believed to accentuate the risk of numerous diseases and clinical disorders, such as coronary heart disease, strokes, cancers, type 2 diabetes mellitus, HTN, asthma, liver disease, psychopathological conditions[9] and allergic diseases.[10]

BMI is a modifiable risk factor that can be assessed in time. Moreover blood groups being non modifiable risk factor, should be identified as which of them is more prone to developing obesity, so that young adults can be accordingly counselled for the lifestyle modifications and thus be prevented from major diseases associated with increased BMI.

HTN is a condition of sustained increase in BP. In recent years, it is a major health problem in the world, without any early specific sign and symptoms, so most of the people have HTN without knowing it.[11, 12] According to Joint National Committee (JNC) 8, systolic blood pressure (SBP) 90-119 mmHg and diastolic blood pressure(DBP) 60-79 mmHg is normal BP. HTN is a condition where SBP is more than 120 mmHg and DBP is more than 80 mmHg.[13] JNC 7 defined prehypertension as SBP ranging from 120139 mmHg and DBP ranging from 8089 mmHg. Whereas, stage-1 HTN is defined as SBP ranging from 140-159 and DBP ranging from 90-99mmHg.[14]

Although ABO blood group, HTN and BMI have individually been appraised as risk factors for certain illnesses, few studies have shown that a particular ABO blood antigen potentially predisposes to higher BMI or HTN, while others couldn't found a relationship between these factors.[15, 16] Therefore, we conducted a study in medical students to find out frequency of different blood groups in the study population. Also to find out which blood group is more prone to high BMI or HTN so that the high risk population should be counselled about dietary and lifestyle modification at a younger age.

Methods

This is a prospective study carried out in 300 medical students in the department of Physiology, continental medical college, Lahore. Sampling was done by Non-Probability, Purposive technique. Written informed consent was taken from subjects, complete history and general physical examination was done. The BP was measured by mercury sphygmomanometer for two times and mean was calculated for accuracy. The Cases with HTN were excluded. Height in meters (m) and weight in kilograms (kg) were measured by weight scale and a measuring tape, respectively. The formula, weight in kg divided by height in meter square, was used to calculate the BMI of students and unit is kg/m2. According to WHO "Asian Criteria" for BMI cut off point are; less than 18.5kg/m2 is underweight,18.5-22.9kg/m2 is normal, 23-24.9 kg/m2 is overweight, 25-29.9 kg/m2 is pre-obese and ≥30kg/m2 obese (30-40 kg/m2 type-I obese, 40.1-50kg/m2 type-II obese and more than 50 kg/m2 is type 3 or super obese). ABO blood group was determined by antigen- antibody reaction in Physiology Lab. Collected data was compiled and analyzed by using Statistical Package of Social Science (SPSS) software version-20. Data was presented in the form of frequencies and percentages. Frequencies of both group was compared by Fischer's exact test and p-value of <0.05 was considered to be highly significant.

Results

Total 300 students were enrolled in the study. The overall mean age was 19±0.75 years (17-23 years). In total 164(55%) were females and 136(45%) were males as shown in (**Fig-1**). The distribution of phenotype frequencies and percentages for the A, B, AB, O, were 78(26%), 101(33.7%), 23(7.6%) and 98(32.7%), respectively. **(Table-1)**

Recording of BMI shows 180(60%) of total 300 students were with normal BMI whereas, 39(13%) were underweight, 43 (14.3%) were overweight and 38(12.7%) were obese. Most of the normal BMI students were belonging to Blood group A (n=59 or 19.7%), blood group O students were the most underweight (n=22or7.3%), most overweight and obese students were under the group B (n=18or6%) and (n=17or5.7%) respectively. Students of blood group AB shows least value for BMI.

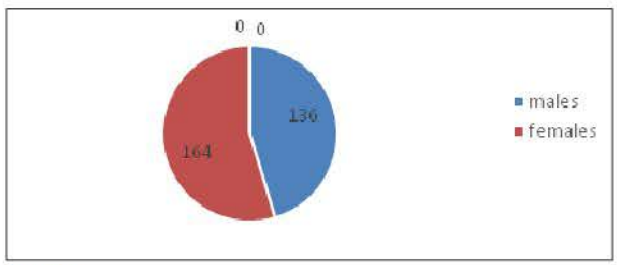
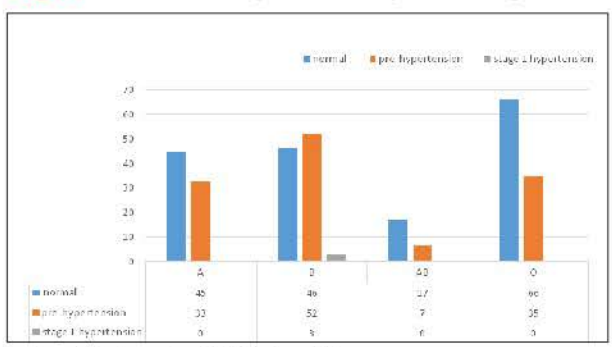


Fig-1: Distribution of gender among our study poulation.



p-value = 0.01 when compared by Fischer's exact test

Fig-2: Distribution of blood pressure among different blood groups.

Table-1: Distribution of different blood group phenotypes among our study population.

Blood Group	Male n (%)	Female n (%)	Total n (%)
A	35 (11.7%)	43 (14.3%)	78 (26%)
B	44 (14.7%)	57 (19%)	101 (33.7%)
AB	8 (2.6%)	15 (5%)	23 (7.6%)
O	49 (16.3%)	49 16.3%)	98 (32.7%)
Total	136 (45%)	164 (55%)	300 (100%)

Table-2: Distribution of BMI (kg/m2) among different blood phenotypes.

Blood Group	Under Weight n (%)	Normal n (%)	Over Weight n (%)	Obese n (%)	Total n (%)
A	9 (3%)	59 (19.7%)	5 (1.7%)	5 (1.7%)	78 (26%)
B	8 (2.7%)	58 (19.3%)	18 (6%)	17(5.7%)	101 (33.7%)
AB	0 (0%)	15 (5%)	4 (1.3%)	4 (1.3%)	23 (7.6%)
O	22 (73%)	48 16%)	16 (5.3%)	12 (4%)	98 (32.7%)
Total	39 (13%)	180 (60%)	43 (14.3%)	38 (12.7%)	300 (100%)

p-value = 0.01 when compared by Fischer's exact test

So, tendency of obesity was maximum in B and minimum in AB blood group **(Table-2).** Blood group O has the maximum students with normal blood pressure, Blood group B has maximum prehypertensive 52(16.2%) and stage1 hypertensive students 3(16.2%) and students with blood group AB have minimum prehypertensive and no stage 1 hypertensive student **(Fig-2).**

Discussion

Common blood group among our participants was B (34%), followed by blood group O (33%), A (26%) and AB (8%). Similar findings were also reported by research studies done at Punjab and Sindh[17,18] but Khyber Pakhtoonkhwa (KPK) shows more common blood group A followed by O, B and AB.[19] Our research concluded that the blood group B has more tendency to develop HTN and obesity followed by blood group O, A and AB. Whereas AB blood group has least chance of getting HTN and obesity. Similar results were seen by a research conducted at Kathmandu showing that Maximum obesity (≥30) and prehypertension was found in students with blood group B about 4(1.17%) and 55(16.2%) respectively whereas no obese student found and minimum evidence of prehpertension was found in blood group AB.[15] Other study done by Sadiq H and colleagues, at dental institution of Greater Noida, India also showed similar result as our study showing Blood group B more susceptible to HTN.[20] Chuemere and his colleagues found that postmenopausal women with blood group O and B, were more susceptible to developing HTN, obesity and diabetes together with coexistence of prehypertension, pre-diabetes and obesity, this coexistence does exist in our study also.[21]

Contrary to our study, Kaur M, at India do find a prevalence of HTN in blood group B and O but was not significant statistically ($p>0.05$) and hence they concluded that there is no correlation of developing HTN with a particular blood group.[16] Similarly, Alwasaidi TA at Saudi Arabia came to know that men are more obese than women and blood group O participant were more obese than other groups but didn't find any statistically significant difference between the prevalence of obesity or high BMI and ABO blood groups.[22]

Conclusion

We concluded from our research that Blood group B being the most prevalent group, is more prone to HTN and high BMI. The blood group AB has shown least tendency for high BMI and HTN.

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Original Article

A Study to Compare The Efficacy of Non-invasive Predictors of Esophageal Varices in Patients with Portal Hypertension

Bilal Rafique Malik, Syed Mehmood ul Hassan, Yasir Ali, Umair Asghar, Abdul Qadir and Rana M. Tayyab

Objective: To study the predictive power and compare the various noninvasive investigative parameters for detection of esophageal varices in patients with Portal Hypertension as compared to invasive parameter.

Methods: Fifty consecutive patients meeting the inclusion and exclusion criteria were enrolled in the study. All patient were subjected to complete blood count, Liver function tests, total serum proteins, albumin and globulin levels, coagulation profile (APTT, PT, INR)HbsAg, anti HCV antibodies and abdominal ultrasonography to assess the spleen longitudinal diameter of spleen and portal vein diameter and upper gastrointestinal endoscopic examination. Elastography was determined using Fibroscan. Patients were assessed with Child Turcotte Pugh (CTP) score and the esophageal varices were graded using Westaby's Classification.

Results: Predominant age group was 51-60 years. Males were the most common to present with EV. Majority of patients were Hepatitis C antibodies positive and they were the most common cause for PHT. 48% had severe thrombocytopenia of count less than twenty thousand. 56% had spleen size of less than 130mm. 4% did not have EV, 26% had Grade-I varices, 34% had Grade-II varices and 36% had Grade-III varices. Higher Fibroscan score is associated with larger varices. (p-value -0.001). Low platelet count was seen in Grade-III varices. When the Right lobe diameter albumin ratio was high the varices were also larger. Patients who had large grade-III varices also had a low Platelet / spleen ratio with a mean of 190. (p-value -0.002)

Conclusions: Overall the non-invasive parameters had a significant ability to predict and estimate grade of varices and severity of PHT.

Keywords: portal hypertension (PHT), transient elastography, esophageal varices (EV).

Introduction

Portal hypertension is defined as a pathologic increase in the portal venous pressure gradient between the portal vein and the inferior vena cava.[1] Esophageal varices (EV) have been the troublesome complications of Portal Hypertension. The common and frequent cause of morbidity & mortality is variceal bleeding which is seen in around 30-50% of the patients. EV can be confirmed endoscopy. Esophageal varices are formed only when the Hepatic vein pressure gradient (HVPG) exceeds 10 mm Hg and bleeding occurs usually when the HVPG exceeds 12 mm Hg.[3] However not all patients who have a HVPG greater than 12 mm Hg bleed. In order to reduce the burden of endoscopy, as the prevalence of EV bleeding has increased, studies have been done frequently to identify modalities to identify or predict EV noninvasively. Studies have evaluated the parameters of PHT as predictors of the presence of EV either directly or indirectly. They are splenomegaly, Thrombocytopenia and a poor Child pugh score.[4-6] In patients with CLD the presence of thrombocytopenia may be due to several other factors like the reduced lifetime of platelets, low thrombopoietin release or can also be due the myelotoxic effects of either alcohol or the hepatitis viruses. However the splenomegaly in cirrhotic patients is mainly due to PHT. Likewise studies have demonstrated the platelet count/spleen diameter ratio as a parameter predicting EV by linking thrombocytopenia to the size of spleen and Right lobe diameter/albumin ratio has also been used in the studies to predict EV.[7] The recent noninvasive technique that has been used is transient elastography or Fibroscan that measures the liver stiffness or hepatic parenchymal elasticity using ultrasound elastic waves. Many studies have proved that Fibroscan is a useful and reliable method to the assess fibrosis of the liver parenchyma. Moreover PHT is due to liver fibrosis as proved in many studies of the cases with fibrosis. Thus it can also be used a method to assess PHT and can also be used to predict the EV.[8]

EV, most of the time is asymptomatic and this can be diagnosed easily with many noninvasive parameters. In a country where there is increased caseload & higher

financial constraint, there is a need for a reliable and reproducible non-invasive predictor which can be used.

Methods

This cross-sectional study was conducted at East medical ward, Mayo hospital Lahore from March 2019 to august 2019. Patients of either gender aged between 25-65 years who were diagnosed as case of Portal hypertension clinical, biochemical, radiological and endoscopies were included. Patients with HIV, Liver metastasis, Hepatocellular carcinoma, history of prior treatment for PHT in form of surgery or EVL and pregnancy were excluded. Ethical approval was sought from the institutional review forum and written informed consent taken in each case prior to commencing the study. All patient were subjected to complete blood count, activated partial thromboplastin time ,prothrombin time and INR, Liver function tests [serum bilirubin, alkaline phosphatase (ALP), alanine transaminase (ALT), aspartate transaminase (AST)], total serum proteins, albumin and globulin levels, coagulation profile [APTT, PT, INR] serum electrolytes and blood urea, serum creatinine, random blood sugar, HbsAg, anti HCV and abdominal ultrasonography to assess the spleen longitudinal diameter and portal vein diameter and upper gastrointestinal endoscopic examination. Fibro-elastography was determined using FibroScan. Patients were assessed with Child Turcotte Pugh (CTP) score and the esophageal varices were graded using Westaby's Classification.

Westaby classification[9] (taken as it is)!

Grade-I: Varices appearing as slight protrusion above mucosa, which can be depressed with insufflations.

Grade-II: Varices occupying <50% of the lumen.

Grade-III: Varices occupying >50% of the lumen and which are very close to each other with confluent appearance.

Data was analyzed using SPSS version 21.0. Numerical values were reported using mean and standard deviation or median. Categorical values are reported using number and percentages. ANOVA was used to compare the mean scores. A p value of < 0.05 was taken as statistically significant.

Results

50 patients took part in the study with males accounting for 72% of the study population. Majority of the subjects were between the age group 51 to 60 years (44%) followed by the age group 41 to 50 years (36%), very few were below the age of 40 years (4%). Viral Hepatitis including hepatitis B and C were the commonest cause of portal hypertension (22% and 64% respectively). Rest of the causes included non cirrhotic portal hypertension, alcoholism and other cryptogenic causes. Predominantly the patients had thrombocytopenia and the mean was around 35,061 and the mean hemoglobin was 10.11g/dL. Around 56% of the patients had splenomegaly of more than 130 mm. Right lobe diameter was measured and most of the patients (around-70%) had a diameter of more than 140mm.Majority of the patients about 46% had a right lobe diameter albumin ratio between 6 -10 followed by 4-6 , very few found (6%) in the group 2-4 .Majority of the patients had a CTP score of C , around 68 % , very few had a score of A. 36 % of the study group had grade-III EV, followed by 34% of patients with grade II. Only 2 patients did not have EV.

Patients with grade-III varices had mean Fibroscan score of 62.43 and grade-II varices had a mean score of 44.77. The mean score of grade I varices is around 38.34.The relationship with Fibroscan and EV was significant as the p-value is around 0.001. When Fibroscan was compared with CTP score the p value was significant 0.003. The mean score for CTP C is 51.96, CTP B is 43.58 and CTP 30.2 (p-value 0.003).Patients with grade-III varices had mean Right lobe / albumin ratio of 7.61 and grade II varices had a mean ratio of 7.4. The mean score of grade I varices is around 6.03. The relationship with Right lobe/ albumin ratio and EV was significant as the p value is around 0.05. When Right lobe/albumin ratio was compared with CTP score the p value was significant 0.003. The mean score for CTP C is 7.49, CTP B is 5.64 and CTP 4.56. Patients with grade III varices had mean Platelet/spleen ratio of 190 and grade-II varices had a mean ratio of 253. The mean score of grade I varices is around 289. The relationship with platelet/spleen ratio and EV was significant as the p value is around 0.002. When platelet/pleen ratio was compared with CTP score the p value was significant 0.001. The mean ratio for CTP C is 169.3, CTP B is 421.8 and CTP 649.2. Patients with grade-III varices had mean Platelet count of 28411 and grade-II varices had a mean count of 31705. The mean score of grade I varices is around 38076.The relationship with platelet count and EV was significant as the p value is around 0.017. When platelet count was compared with CTP score the p value was significant 0.001. The mean count for CTP C is 23212, CTP B is 55000 and CTP 79000. **(Table-1 and 2)**

Table-1: Comparing varices grade with various non invasive markers of predicting esophageal varices.

Varixces Grade	Bibroscan score	Right lobe/ albumin ration	Platelet/ spleen ratio	Platelet count
Zero	25.45±1.34	3.8±0.15	858±189	100500±41719
One	38.34±3.7	6.03±2.2	289±249	38076±36518
Two	44.77±7.0	7.4±1.7	253±250	31705±29546
Three	62.43±6.95	7.6±2.2	190±143	28411±20633
p-value	0.001	0.05	0.002	0.017

Table-2: Comparing CTP score with various non invasive markers of predicting esophageal varices

C T P Score	Bibroscan score	Right lobe/ albumin ration	Platelet/ spleen ratio	Platelet count
A	30.2±8.28	4.56±1.27	649.2±386.3	79000±47507
B	43.58±10.21	5.64±0.98	421.8±255.5	55000±32812
C	51.96±11.93	7.4±1.7	169.3±156.9	23212±19617
p-value	0.003	0.003	0.001	0.001

Discussion

Fifty patients participated in the study. Overall the non-invasive parameters had a significant ability to predict and also identify the estimated grading of variceal size. Commonest age group involved was people aged between 51-60 years and the majority (about 4/5ths) were men. These findings are consistent with previous similar studies.

Authors	Predominant age group
Waleed K. Al-Hamoudi et al[10]	57.2 ± 15.3
Alempijevic et al[11]	55.14±7.71
El Makarem et al[12]	51.09 ± 5.1
Borro, et al[13]	62
Montasser et al[14]	53.9 ± 8.3
Bulat et al[15]	52.32 ± 13.60
Cherian et al[5]	42

The most frequent etiology was hepatitis C (64%) followed by hepatitis B (22%), alcoholism and other cryptogenic causes. This can be attributed to the alarmingly high prevalence rates of hepatitis C in Pakistan (6.8%).[16] Invariably the study population had thrombocytopenia which was similar to other studies. Thrombocytopenia also had significant relationship between the CTP score and grading of varices. The p value was 0.001 and 0.017 respectively.

Authors	Platelet count and EV
Waleed K. Al-Hamoudi et al[10]	p value -0.004
El Makarem et al[12]	p value - 0.001
Borro, et al[13]	p value-0.0001
Cherian et al[5]	p value - 0.003
Present study	p value - 0.017

Only Alempijevic et al[11] reported the relation between platelet count EV grade as statistically insignificant. (p value-0.987) Patients who had large EV grade III varices also had a low Platelet / spleen ratio with a mean of 190. This was similar to other studies and the p values were as follows: Borro, et al 0.0001 Bulat et al 0.01 Cherian et al 0.001 and Present study 0.002. However El Makarem et al[12] found the relationship as statistically insignificant. (p value-0.739). Bulat et al[15] demonstrated a significant relation between the presence of EV and right lobe diameter/serum albumin ratio (p-value<0.01) whereas in the present study similar results were observed with significant p value of around 0.05. In the study those patients with grade-III varices had mean Fibroscan score of 62.43 and grade-II varices had a mean score of 44.77. The mean score of grade-I varices is around 38.34.The relationship with Fibroscan and EV was significant as the p value is around 0.001. The results suggest that the increased liver stiffness has a direct correlation with severity of PHT. Moreover, When Fibroscan was compared with CTP score the p value was significant 0.003. Waleed K. Al-Hamoudi et al[10] showed that Fibroscan had a positive correlation when compared to the grade of EV (γ=0.747, p<0.001). The correlation coefficient for the present study was r=0.523 implying that fibroscan score had a strong positive correlation with grade of EV.

Conclusion

This study has study has revealed that the newer parameter transient elastography or Fibroscan is far more better predictor of presence of varices and also the size of varices when compared to other parameters. However the study has also reiterated the fact that older and often used non-invasive parameters like platelet count / spleen diameter ratio and platelet count are also much better when compared to the Right lobe diameter / albumin ratio. These parameters can be used in situations where the invasive endoscopic examination is not possible due to non-availability or contraindicated. Patients who satisfy the criteria can be started on early treatment with prophylactic beta-blocker therapy. These parameters can also be used to identify those patients who may have larger varices which needs an endoscopic intervention. This can avoid the overburden cases requiring endoscopy.

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Original Article

Obstructive Sleep Apnea in patients with Metabolic syndrome - A hospital Based Cross-Sectional Survey

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Objective: To determine frequency of OSA amongst patients with Metabolic Syndrome.
Methods: This was a hospital based cross-sectional study done in adult patients with MS who visited Lahore General Hospital from march 2019 to August 2019. Patients meeting the criteria for metabolic syndrome according to the new IDF definition3 (as described earlier) were screened for symptoms of OSA. Patients with end organ disease, hypothyroidism, critical illness and neoplasms were excluded from the study. Epworth sleepiness scale (ESS) questionnaire was used to evaluate EDS. Patients with symptoms indicative of OSA and ESS score of more than 10 underwent a limited sleep study with three channels recording nasal airflow measurement, chest movement and pulse oximetry. AHI > 5/Hr was considered positive for OSA. The limited PSG data was analysed and a diagnosis of OSA was made if the Apnea-Hypopnea index was >5 per hour. Further, OSA was graded as mild, moderate or severe as follows: AHI 5-15/hr: MILD OSA AHI 15-30/hr: MODERATE OSA AHI>30/hr: SEVERE OSA.
Results: Mean age of patients with OSA in our study was 55±9 years. OSA was found in 35 (37%) patients screened with ESS score>10. Twenty one out of 53 (39.6%) males and 14 out of 41 (34.1%) females had OSA. Even though the number of males was more than females in OSA group, there was no statistically significant difference between both gendes (p=0.37). Body mass index and Neck circumference were found to be significantly higher in OSA group compared with Non OSA group. Other parameters like Age, systolic and diastolic BP were not found to be significantly associated with OSA.
Conclusions: The study showed that there is a very high prevalence of OSA among patients with MS compared to that in the general population thus mandating the need for screening MS patients for undiagnosed OSA,
Keywords: obstructive sleep apnea (OSA), polysomnography, excessive daytime sleepiness (EDS), apnea-hypopnea index (AHI), metabolic syndrome (MS)

Introduction

Metabolic syndrome is becoming a matter of significant public health concern worldwide.[1] Insulin resistance plays a key role in the pathogenesis of metabolic syndrome.[2] According to the new IDF definition[3], for a person to be defined as having the metabolic syndrome they must have: (taken as it from IDF Guidelines)"Central obesity (defined as waist circumference with ethnicity specific values) plus any two of the following four factors; Recent evidence favors the notion of relation between OSA and the metabolic syndrome, which is reflective of poor cardiovascular outcomes.[4]

Obstructive sleep apnea(OSA), also known as Obstructive sleep apnea/hypopnea syndrome (OSAHS) is a sleep disorder characterized by recurrent upper airway collapse and obstruction during sleep associated with recurrent oxygen desaturation and arousals from sleep. OSA leads to symptoms such as snoring, witnessed apneas, excessive daytime sleepiness and road traffic accidents due to sleepiness. It is also associated with an increased risk of cardiovascular disease, hypertension, insulin resistance and cerebrovascular disease.[5]

Raised triglycerides:	≥150mg/dL (1.7mmol/L) or specific treatment for this lipid abnormality.
Reduced HDL cholesterol:	<40mg/dL (1.03mmol/L) in males, <50mg/dL (1.29mmol/L) in females, or specific treatment for this lipid abnormality.
Raised blood pressure:	systolic BP≥130 or diastolic BP≥85mmHg, or treatment of previously diagnosed hypertension.
Raised fasting plasma glucose:	(FPG)≥100mg/dL (5.6mmol/L), or previously diagnose type-II diabetes. If above 5.6mmol/L or 100mg/dL, OGTT is strongly recommended but is not necessary to define presence of the syndrome.

**If BMI is >30kg/m², central obesity can be assumed and waist circumference does not need to be measured.*

OSA is a fairly common condition, but often goes unrecognized. It is estimated that about 80% of cases are not diagnosed.[6] In the western population the prevalence of OSA in the middle-aged (30 to 60 years) is 4% in men and 2% in women.[7] However, very little literature [3] is available about the prevalence of OSA in south asian population. A study done in Delhi estimated the prevalence of OSA and OSAHS in an Indian study population to be 13.7% and 3.6% respectively.[9] A recent Pakistani study by Taj et al [10] reported 24.9% of the study population snoring with males snoring twice as much as females. Although loud snoring is seen in all patients with OSA, not all snorers have OSA. Understanding the differences between patients with OSA and simple snorers is important to explain the mechanisms responsible for upper airway obstruction rather than those between OSA and normal non-snorers. Polysomnography is considered to be the gold standard for diagnosis of OSA, estimation of its severity and measurement of treatment response. Sleep Labs are scarce in the country with only very few centres offering polysomnography. This study was conducted with the principal objective of determining prevalence of OSA among patients with MS.

Methods

This was a hospital based cross-sectional study done in adult patients with MS who visited Lahore General Hospital from march 2019 to August 2019 . Patients meeting the criteria for metabolic syndrome according to the new IDF definition[3] (as described earlier) were screened for symptoms of OSA. Patients with end organ disease, hypothyroidism, critical illness and neoplasms were excluded from the study. Epworth sleepiness scale (ESS) questionnaire was used to evaluate EDS. Patients with symptoms indicative of OSA and ESS score of more than 10 underwent a limited sleep study with three channels recording nasal airflow measurement, chest movement and pulse oximetry. AHI > 5/Hr was considered positive for OSA.The limited PSG data was analysed and a diagnosis of OSA was made if the Apnea-Hypopnea index was >5 per hour. Further, OSA was graded as mild, moderate or severe as follows: AHI 5-15/hr: MILD OSA AHI 15-30/hr: MODERATE OSA AHI>30/hr: SEVERE OSA. Data was analyzed using SPSS version 21.0. T test was used to compare means and Chi-square test was used to determine the association between the metabolic syndrome components and OSA. P value of <0.05 was taken as statistically significant.

Results

The mean age of patients with OSA in our study was 55±9 years. A total of 94 patients were included in this study, out of which there were 53 (56.4%) male and 41 (43.6%) female patients. The mean BMI was 31.3kg/m^2, mean waist circumference was 101cm and 48 (51%) of patients were obese. Diabetes was positive in83 (88.6%) patients, hyperlipidemia in 67 (71.3%) and hypertension in 63 (65.1%) patients. Other major comorbidities like ischemic heart disease was present in 30 (31.9%) and cerebrovascular disease in 4 (4.3%).
The symptoms of OSA among subjects were intrusive snoring, excessive daytime sleepiness and witnessed apneas. Other symptoms reported in relation to nocturnal sleep were difficulty in falling asleep in 27(28.7%), difficulty in maintaining sleep in 24(25.5%), nightmares in 7(7.4%) and limb jerking in 5(5.3%) patients. On upper airway assessment obvious nasal deformities or nasal polyps were not present. Receding jaw was present in 6 (6.4%) , and mallampati grade: 3 (3.2%) patients had grade 1, 40 (42.6%) had grade 2, 44 (46.8%) had grade 3 and 7 (7.4%) had grade 4 All those patients with clinical features suggestive of OSA and ESS > 10 underwent an overnight sleep study (limited Polysomnography) to confirm the diagnosis. It was found that 35 (37%) out of the 94 patients screened had a history suggestive of OSA and scored >10 on ESS. Hence they were subjected to an overnight sleep study. The mean AHI in these patients was 31.7/hour and Oxygen Desaturation Index (ODI) was 32.2/hour. The severity of OSA has been depicted in **(Fig-1).** Thus, there was a high pretest clinical probability of OSA in 35(37%) of patients; however 32 (91.4%) had PSG evidence of OSA; the remaining 3(8.6%) had a normal sleep study. Since the latter sub-group of 3 patients had a strong clinical history suggestive of OSA, ESS score of>10 and reported poor quality sleep on the night of the sleep study the, they were considered as mild OSA for statistical analysis. Twenty one out of 53 (39.6%) males and 14 out of 41 (34.1%) females had OSA. Even though the number of males was more than females in OSA group, there was no statistically significant difference with respect to gender between the OSA and Non-OSA groups (p=0.37). Body mass index and Neck circumference were found to be significantly higher in OSA group compared with Non OSA group. Other parameters like Age, systolic and diastolic BP were insignificant in patients with or without OSA. **Table-1**

As mentioned earlier, 67 (73.4%) of patients in this study were snorers. Other major symptoms were excessive daytime sleepiness in 46 (48.9%) and witnessed apneas in 16(17%) patients. Statistical analysis was performed to determine the correlation between these symptoms and the presence of OSA. Among patients who were snorers, 35(50.7%) had OSA. Besides, OSA was significantly higher in patients with EDS and witnessed apneas.

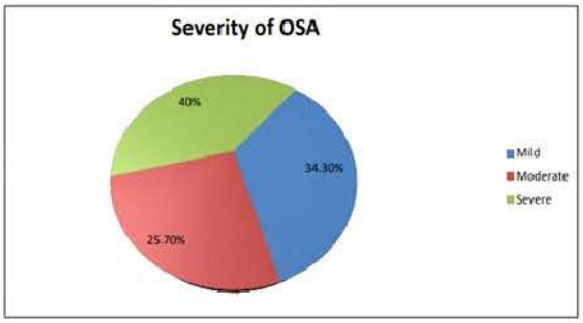

Fig-1: Severity of OSA in patients with MS and OSA.

Table-1: Comparing MS parameters between OSA and Non OSA groups.

Parameters	OSA	No OSA	P-value
Systolic BP (mmHg)	134.9±15.3	136.41±14.0	2.5
Diastolic BP (mmHg)	86.80±5.9	85.56±6.3	1.02
BMI (kg/m^2)	34.5617±6.1	29.4880±4.8	0.00
Waist circumference (cm)	1.3.37±8.5	99.93±8.9	1.4
Neck circumference (cm)	37.41±2.3	41.60±3.2	0.00

Table-2: Individual components of MS and OSA.

Individual components of MS	Total No of N	OSA	No OSA	p-value
Diabetes Mellitus	83	31 (37.3%)	52 (62.7%)	0.613
Hypertension	65	22 (33.8%)	43 (66.2%)	0.304
Hyperlipidemia	67	26 (38.8%)	41 (61.2%)	0.400

Discussion

Our study has demonstrated there is a high prevalence of OSA in patients with MS. It has been hypothesized that OSA itself may be a part of the spectrum of metabolic syndrome (Syndrome Z). Our study is unique and different from other studies for being a hospital based prevalence study of OSA in patients with metabolic syndrome. The prevalence of OSA was found to be as high as 37.2%, which is very high when compared with that reported in the general population in Pakistani as well as Western literature.[10,12-13]

Coughlin and Gruber et al reported a nine-fold and six-fold risk respectively, for independent association between OSA and metabolic syndrome.[11,14] Likewise, a study amongst Chinese subjects showed OSA subjects were at a five-fold risk of having the metabolic syndrome[15] and there was a positive correlation between AHI and the number of metabolic components present. Sharma et al conducted a community based study in South Delhi in 2010 and reported that MS and OSA (syndrome Z) in 19.9% of the population studied.[16]

Our study, being a hospital based study wherein nearly one third of patients had already developed end organ damage as a result of MS could have had metabolic derangements for a longer duration. This could have perpetuated a vicious cycle wherein the occurrence and severity of OSA among these patients could have been higher than that in the general population with MS. Due to the small sample size, it was not possible to sub-group patients on the basis of duration of various components of MS and assess the odds of having OSA or target organ damage. A larger study would be required to address this question. In our study, all patients were obese and it was found that increasing grades of obesity correlated well with presence of OSA. A higher waist circumference was noted in OSA when compared to the Non OSA group. Similarly, there was a statistically significant increased BMI in OSA group than in the Non OSA group. This observation was in concordance with many other studies which showed that obesity/BMI is one of strongest risk factors for OSA. Peppard et al[17] for instance showed that a 10% change in body weight was associated with a parallel change of approximately 30% in the apneahypopnea index (AHI), the major index of sleep apnea severity. Measurement of neck circumference (NC) is a part of the physical examination of patients suspected of having sleep apnea. The mean neck circumference in OSA patients in our study was higher than that of the non OSA group and the difference was statistically significant. Neck circumference > 16 inches in females and >17 inches in males amounts to an increased risk as it tends to make the retropharyngeal space shallow.[18] People with increased neck circumference have too much adipose tissue around the upper airway making it hard for the lumen of the pharynx to stay patent during sleep. In our study patients, snoring was commonest symptom of OSA followed by EDS and witnessed apneas. There was a significant difference between the OSA and Non OSA group in the incidence of these symptoms. Frequency of OSA among snorers was 50.7%, that among patients with EDS was 71.7% and it

was 81.2% in patients with witnessed apneas. Studies have shown that habitual snoring affects up to 50% of men and up to 30% of women in the general population. This goes largely unaddressed by medical providers due to decreased awareness regarding the issue. Snoring is also an important symptom for monitoring in long term management of OSA, because its recurrence after OSA treatment may signal a need to re-evaluate the therapy. According to Young et al.[7] (Wisconsin Sleep Cohort Study), habitual snoring occurs in 36% in adults and in more than 70% in subjects with an AHI of 5 or higher. Snoring is probably the most common complaint precipitating a referral to a sleep clinic. Excessive daytime sleepiness and witnessed apneas have been reported to be good predictors of OSA.[19] In our study, Epworth sleepiness scale (ESS) was used as a screening tool in patients presenting with symptoms suggestive of OSA. ESS is a simple, self-administered questionnaire which assesses daytime functioning including concentration levels, work performance and sleepiness. In patients with obstructive sleep apnea syndrome ESS scores were significantly higher.[19] In our study, 35(37.2%) patients had ESS score >10 and with other symptoms suggestive of OSA they underwent overnight sleep study and were proven to have OSA. Thus, the usefulness of ESS as a screening tool for OSA with almost no false positivity and good specificity has been reiterated in our study. Thus, symptoms, a high index of clinical suspicion and associated risk factors of OSA, along with an ESS score of >10 should guide further workup.

In our study population with metabolic syndrome most common component diseases were diabetes mellitus, dyslipidemia and hypertension in that order. The conclusions obtained from the analysis were that the incidence of OSA was higher in MS patients in comparison with general population. However, there was no particular group or co-morbidity that had a statistically significant association or predisposition to OSA in particular. Patients with diabetes had 37.3% prevalence of OSA, hypertension was associated with OSA in 33.8% and 38.8% had OSA among the patients with dyslipidemia. The diagnosis of OSA should always be considered in high risk patients with refractory heart failure, resistant hypertension, nocturnal cardiac ischemia and nocturnal arrhythmia. Treating sleep apnea can reduce the morbidity associated with these disease and help achieve better clinical outcomes. Significant association was seen between OSA and presence of diabetes mellitus and hypertension in the study by Udwadia et al[20] among urban Indian population.

Conclusion

The present study has demonstrated that there is a very high prevalence of OSA among patients with MS compared to that in the general population. Although a bigger study would have enabled derivation of the odds of developing OSA with MS or vice versa, there is convincing evidence from the present study to mandate screening for undiagnosed OSA in all patients with MS.

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Original Article

In Situ Fusion Versus Reduction in Lumbar Degenerative Spondylolisthesis Surgery in Pakistani Population

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Objective: To compare in situ fusion versus addition of slippery reduction in the surgical treatment of lumbar degenerative spondylolisthesis among patients who presented at neurosurgery department of DHQ teaching hospital, Gujranwala

Methods: The patients who underwent LDS surgery from Jan 2015 to Jan 2018 at DHQ Teaching hospital, Gujranwala were retrospectively analysed. The patients with slip grade I and II, and with more than two years follow up were included, while those with associated comorbidities like diabetes mellitus, severe hip or knee osteoarthrosis, autoimmune disease, or underlying malignancy were excluded. Those patients whose surgery included decompression, in situ fusion, pedicular screw and instrumentation were labelled as group A, while group B included those patients who underwent routine surgery added with slippery reduction. In formations collected included patient's gender, age, follow up period duration, level of involvement by spondylolisthesis, radiologic fusion at 12months and at end of follow up, post-operative adverse events of wound infection, neurologic injury, post-operative CSF leak, and implant failure. Statistical analysis was done using SPSS Version 25.Independent sample T test and Chi-square test for independence were used for quantitative and qualitative variables respectively to determine their significant association with type of surgery. The p values were statistically significant if < 0.05

Results: Out of 68 patients, 63.2% were female, and 63.2% had L4-L5 level involvement. Both cohorts i.e. in situ fusion group and slippery reduction group had similar ages of the patients (57.36 + 12.82 years vs 58.62 + 11.61 years, p=0.68), gender distribution (p=0.605), and post-operative follow up duration (p=0.067).95.2% of group A and 76.9% of group B patients had no post-surgical complications. One patient of group A and three of group B had superficial post-operative wound infection. Two patients in group B had neurologic injury (17.6%). One group A patient had post-operative CSF leak while one group B patient suffered screw break. The fusion rates at 12 months and end follow up were excellent and comparable in both groups. Fusion rate at 12 months was 76.2% in group A and 80.8% in group B (p=0.769) while fusion rate at end follow up was 88.1% in group A and 92.3% in group B (p=0.700). Slippery reduction group had significantly more post-operative complication rate than in situ fusion group (23.1% in group B vs 4.8% in group A, p=0.047). No post-surgical mortality occurred in our patients.

Conclusions: L4-L5 is the commonest level involved in lumbar degenerative spondylolisthesis in our population. The radiological outcome is excellent with both in situ fusion and slippery reduction surgery protocols. Addition of time-consuming step of slippery reduction is un-necessary as it does not increase the yield significantly, rather post-operative complications are more than in situ fusion group. Prospective studies with large sample size are proposed to validate these precious findings.

Keywords: Lumbar degenerative spondylolisthesis, LDS surgery, In situ fusion, Slippery reduction,

Introduction

Lumbar degenerative spondylolisthesis (LDS) is the slippage of one lumbar vertebra over the other due to degenerative sequela in the absence of problem with pars interarticularis.[1] Increasing age, female gender, increased BMI, hysterectomy and multiparity are the predictive factors for LDS.[2,3] It is the most prevalent among older females espacially those over the age of 50 years.[4] L4-L5 is the commonest level of vertebra involved in LDS.[5] Majority of the patients with LDS respond well to non-surgical treatments[6] including rest, analgesics, and physical therapy. In refractory cases unresponsive to more than three months of conservative treatment, progressive neurological deficit or sphincteric involvement or rest pain, intervention may be

Necessary.[7,8] Surgery principles include neural decompression, intervertebral fusion and screw-rod instrumentation.[9,10] In situ fusion or addition of slippery reduction is a point controversy and there are no consensus about superiority of one modality over other in guidelines. Multiple meta-analyses[1,11-13] indicate that addition of slippery reduction is not associated with increased clinical benfits compared to in situ fusion. These majority literature findings were from Western studies, local researches about such comparisons are scarce. Therefore, the objective of this study was to compare in situ fusion versus addition of slippery reduction in the surgical treatment of lumbar degenerative spondylolisthesis among patients who presented at neurosurgery department of DHQ teaching hospital, Gujranwala.

Methods

The patients who underwent LDS surgery from Jan 2015 to Jan 2018at the Department of Neurosurgery, DHQ Teaching hospital, Gujranwala were retrospectively analysed. The patients with slip grade I and II, and with more than two years follow up were included, while those with associated comorbidities like diabetes mellitus, severe hip or knee osteoarthrosis, autoimmune disease, or underlying malignancy were excluded. Those patients whose surgery included decompression, in situ fusion, pedicular screw and instrumentation were labelled as group A, while group B included those patients who underwent routine surgery added with slippery reduction. Information collected from both cohorts included patient's gender, age, follow up period duration, level of involvement by spondylolisthesis, radiologic fusion at 12months and at end of follow up, post-operative adverse events of wound infection, neurologic injury manifested as foot drop and sphincter loss, post-operative CSF leak, and post-operative implant failure (screw mal-positioning or screw breakage). Postoperative imagings were obtained at 1-, 6-, 12-months and at end of follow-upfor lucent area around the work portion and for issues with hardware (loose or broken screws). Adequate lucency i.e. upto 70-80% was seen around screws on radiographs defined the union. All findings were recorded in a structured performa. Statistical Package for Social Science (SPSS), version 25 was used. Means with standard deviations were computed of quantitative variables, and frequencies-percentages for qualitative variables. Chi-square test for independence andIndependent sample T test were used for qualitative and quantitative variables respectively to determine their significant association with type of surgery i.e. plan to include in situ fusion or addition of slippery reduction. The p values were taken statistically significant if < 0.05.

Results

Out of 68 patients with lumbar degenerative spondylolisthesis patients, 25 (36.8%) were male while 43 (63.2%) were female. The level of vertebral involvement was as follow: L4-L5 (43 cases, 63.2%), L5-S1 (18 cases, 26.5%) and L3-L4 (7 cases, 10.3%) **(Fig-1)**. All these 68 patients had slip grade I or II. 42 patients underwent surgical treatment with in situ fusion (group A) while 26 patients underwent routine surgery plus slippery reduction (group B). Both cohorts had similar ages of the patients (57.36±12.82 years vs 58.62±11.61 years, p=0.68), gender distribution (33.3%male and 66.7% female in group A vs 42.3% male and 57.7% female in group B, p=0.605), and post-operative follow up duration (29.57±3.85 months vs 31.23±3.05 months, p=0.067) **(Table 1&2)**. 95.2% of group A and 76.9% of group B patients had no post-surgical complications. One patient of group A and three of group B had superficial post-operative wound infection, all four were diabetic and responded well to diabetic control, antibiotics, and wound care. Two patients in group B with slippery reduction had neurologic injury (17.6%), one manifested with foot drop and second with both urinary and anal sphincters loss. One group A patient had post-operative CSF leak while one group B patient suffered post-operative implant failure manifested as screw break **(Fig-2)**. The fusion/union rates at 12 months and end follow up were excellent and comparable in both groups. Fusion rate at 12 months was 76.2% in group A and 80.8% in group B (p=0.769).

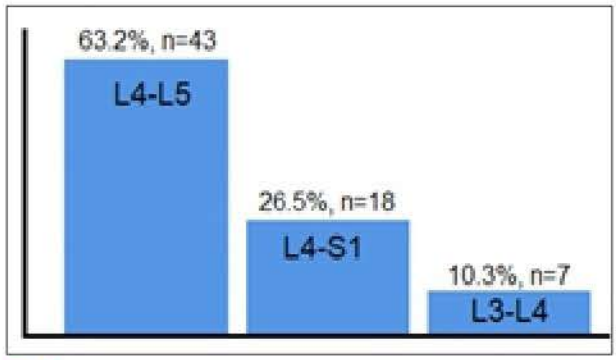

Fig-1: Level of vertebral involvement of lumber degenerative spondylolisthesis (n=68).

while fusion rate at end follow up was 88.1% in group A and 92.3% in group B (p=0.700). Slippery reduction group had significantly more post-operative complication rate than in situ fusion group (23.1% in group B vs 4.8% in group A, p=0.047) **(Table-2).** No post-surgical mortality occurred in our patients.

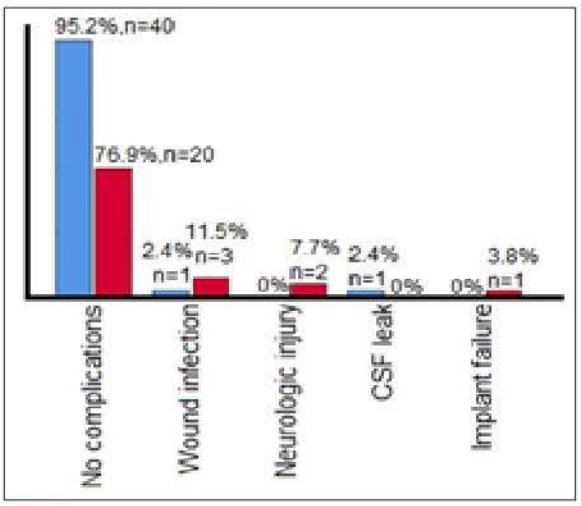

Fig-2: Various complication of surgery of lumber degenerative complication of spondylolisthesis (n=68).

Discussion

Lumbar degenerative spondylolisthesis (LDS) is a common problem worldwide, usually in old aged females. M Tahir and colleagues[14] conducted a study on 104 LDS patients in Karachi, Pakistan, where the mean age of the surgery candidates was 144±10.49 years. However, in our study, the mean age was 57.84 ± 2.3 years. Nancy E.Epstein[15] from USA concluded that LDS predominantly involve L4-L5 level and female gender is affected more at a ratio of 2 : 1 .

In our study, among LDS patients who got surgical treatment, 63.2% were female and in a similar percentage of the patients, the level of vertebral involvement was L4-L5. Guoxin Fan et al[16] found radiographic fusion rate 85.71% and 91.67% in two LDS surgery groups i.e. in situ fusion and slippery reduction groups respectively. There was no statistical superiority of one group over other (p=0.835). In a second research,[17] similar results were found with fusion rates of 81.08% versus 92.68% in in situ fusion and slippery reduction cohorts respectively (p=0.110). In our study, the fusion rates were excellent after LDS surgery, in both in situ fusion and slippery reduction cohorts. These were 88.1% and 92.3% respectively at the end of follow up by the patients and the association between two cohorts was Statistically insignificant (p=0.700).The findings showed concoderance to avaiable international data. Meta-analyses by Weteng Si[18] and Farad Omidi-Kashani[13] also found insignificant difference in fusion rates as well as complication rates between two groups.

Table-1: Comparison of quantitative variables with type of surgical treatment of lumbar degenerative spondylolisthesis(n = 68) *

Quantitative Variables	Type of Suergery		Mean Difference	P-Value
	In situ fusion Group (mean± SD)	Reduction Group (mean ±SD)		
Age of patients (years)	57.36±12.82	58.62±11.61	-1.26	0.685
Follow-up duration (months)	29.57±3.85	31.23±3.05	-1.66	0.067

**Independent sample T-test was used*

Table-2: Comparison of quantitative variables with type of surgical treatment of lumbar degenerative spondylolisthesis(n = 68) *

Predictors / Factors		Type of Suergery		Total	P-Value
		In situ fusion Group (mean± SD)	Reduction Group (mean ±SD)		
Gender	Male	14 (33.3%)	11 (42.3%)	25 (36.8&)	0.605
	Female	28 (66.7%)	15 (47.7%)	43 (83.2%)	
Fusion at 12 months	Yes	32 (76.2%)	21 (80.8%)	53 (77.9%)	0.769
	No	10 (23.8%)	5 (19.2%)	15 (22.1%)	
Fusion at end of follow up	Yes	37 (88.1%)	24 (92.3%)	61 (89.7%)	0.700
	No	5 (11.9%)	2 (7.7%)	7 (10.3%)	
Post-op complications	Yes	2 (4.8%)	6 (23.1%)	8 (11.8%)	0.047
	No	40 (95.2%)	20 (76.9%)	60 (88.2%)	

**Chi-square test for independence was used*

However in our study, slippery reduction group suffered significantly more complications than in situ fusion group (23.1% vs 4.8%, p=0.047). In a study of 45 patients who underwent LDS surgery, Farad Omidi-Kashani[17] found wound infection in two patients and post-operative screw breakage in one patients. In 154 LDS patients who underwent surgery involving in situ fusion in China,[19] 11.7% was the prevalence rate of adjacent segment disease (ASD).The rate of durotomy resulting CSF leak in LDS surgery was 1.77% among patients at Hayatabad Medical Complex, Peshawar, Pakistan.[20] Alexander T.Nixan[21] found post-surgical neurologic deficit rate of 1.2% among studied population size of 340 patients. In our study, among 42 patients who underwent LDS surgery involving in situ fusion protocol, only two had complications: One had wound infection and other one had post-operative CSF leak. Among 26 patients cohort who underwent LDS surgery with added step of slippery reduction, 6 had complications: three had wound infections, one had screw breakage and two had neurological injury, one manifested as sphincter loss and other with foot drop. The additional step of slippery reduction to LDS surgery had a similar outcome as that of in situ fusion group with a more risk of post-operative complications in our population.

Conclusion

L4-L5 is the commonest level involved in lumbar degenerative spondylolisthesis in our population. The radiological outcome is excellent with both in situ fusion and slippery reduction surgery protocols. Addition of time-consuming step of slippery reduction is un-necessary as it does not increase the yield significantly, rather post-operative complications are more than in situ fusion group. Prospective studies with large sample size are proposed to validate these precious findings.

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Original Article

Validation Study of Non-invasive Parameters in Grading Esophageal Varices

Syeda Zainab, Syed Rizwan Bukhari, Humera Ehsan Wyne, Yumna Fatima, Naila Masood Riaz and Farah Rehman

Objective: To start prophylactic measures in patients with large esophageal varices. In this study, we aimed at identifying non-endoscopic parameters that could predict the presence and grades of esophageal varices.

Methods: Two hundred patients were recruited for this study. Upper GI endoscopy was done and patients were divided into four groups on the basis of size of varices. Portal vein diameter and right hepatic lobe diameter was checked by ultrasonography. Serum albumin was checked through spectrophotometer. The data was entered and analysed using SPSS 17.0. Mean ± SD was given for normally distributed quantitative variables. Frequencies and percentages were given for qualitative variables.

Results: Statistically significant difference was observed in portal vein diameter of patients among varices that is, patients having small varices, medium varices and large sized varices $p<0.01$. (13.65±1.10mm Vs. 14.04±1.62mm Vs 15.68±2.15mm) remarkable difference was observed in right hepatic lobe diameter/ albumin ratio of patients among varices that is, patients having small varices, medium varices and large sized varices $p<0.01$ (5.37±0.53 Vs 6.15±0.61 Vs 10.96±4.38).

Conclusions: The port bal vein diameter and right liver lobe diameter/serum albumin ratio might be considered a significant predictor for the presence and grading of esophageal varices.

Keywords: esophageal varices, right hepatic lobe diameter, portal vein diameter.

Introduction

Liver cirrhosis is associated with a number of life threatening complications and portal hypertension is one of them. It leads to formation of Porto-systemic collaterals. Esophageal varices is one of the most relevant collaterals because their rupture leads to life-threatening variceal bleeding.[1] sixty to 80 percent of patients with cirrhosis of liver are associated with esophageal varices and 25-30% of them have got risk of bleeding. Despite improvement in diagnosis and therapy, mortality from acute variceal bleeding may still reach up to 20%.[2] According to the Baveno VI expanding consensus in portal hypertension recommended that all cirrhotic patients who are compensated with no varices in screening endoscopy should undergo surveillance endoscopy once in 2 years if there is ongoing liver injury otherwise once in 3 years.[3] Also, the patients with compensated cirrhosis with small varices at screening endoscopy should undergo surveillance endoscopy every year if there is ongoing liver injury otherwise once in 2 years.[4]

However, this approach has two major limitations. Endoscopy is an invasive procedure and secondly the cost effectiveness of this approach is also questionable.[5] Despite the advantages of endoscopy, it is still an unpleasant and expensive invasive method. It also carries the risk of bleeding due to manipulation.[6] Also, it may contribute to bacterial infections in patients with liver cirrhosis due to associated disruption of the natural barriers.[7]

Only 30-40% of patients with compensated cirrhosis are found to have gastroesophageal varices on screening endoscopy.[8] Ultrasound findings in portal system (portal vein size) could predict both the presence of varices and risk of variceal bleeding. It can be used for diagnosis as well as long-term clinical monitoring of patients with portal hypertension. Plestina et al concluded in their study that portal vein size on ultrasound is independently associated with bleeding esophageal varices. It may therefore be more cost effective and noninvasive method to routinely screen patients at high risk for the presence of varices, so as to reduce the increasing burden and procedure costs of endoscopy units.[9]

Right hepatic lobe diameter/albumin ratio was compared with platelet count/spleen diameter ratio in selected 94 cirrhotic patients and it was concluded that Right hepatic lobe diameter/albumin ratio was more accurate non-invasive parameter in predicting and grading esophageal varices.[10] Pakistan is an under developing country with many socioeconomic

problems. The incidence of mortality from variceal bleeding is very high in Pakistan. Moreover, endoscopy is not available in every hospital. Therefore, the purpose of this study is to find out easily approachable and cost-effective method of screening patients at risk of bleeding and give them proper treatment.

Methods

It was a cross sectional study conducted in the Department of Physiology, UHS, Lahore from March 2010 to October 2010. Two hundred patients with hepatic cirrhosis were recruited from Gastro-enterology Department, Sheikh Zayed Hospital, Lahore through convenient sampling. Irrespective of the cause of liver cirrhosis, diagnosed patients were selected having an age range of 20-60 years. Detailed history was taken and a clinical examination was performed according to the following inclusion and exclusion criteria. Subjects selected were; the diagnosed patients having any cause of liver cirrhosis, 20-60 years of age. Patients having the following conditions were excluded; on history and evidence of active bleed, band ligation, transjugular intrahepatic portosystemic stent shunt and sclerotherapy. Use of β-blockers and diuretics. Hepatocellular carcinoma and portal vein thrombosis. Esophageal ulcer and gastric ulcer. Splenomegaly due to causes other than cirrhosis. Thrombocytopenia due to causes other than cirrhosis. . Causes of high ammonia level other than cirrhosis. All patients were subjected to endoscopy using upper GI Gastroscope GIF. E3 Olympusr, after an overnight fast of 12hours. On the endoscopic findings, four groups were formed; group I patients with no varices, group II with small varices, group III with medium varices and group IV with large varices. Ultra-sonographic examination was performed to determine the following parameters: Portal vein diameter at the level of porta hepatic. Right hepatic lobe diameter along the mid clavicular line. Estimation of serum albumin, the serum albumin level was done using spectrophotometer by Randox kit. The data was entered and analysed using SPSS 17.0. Mean±SD was given for normally distributed quantitative variables. Frequencies and percentages were given for qualitative variables.

Results

Demographic details of the subjects **m**ales were more affected by the disease. Most patient were of 46 years of age. They belong to child Pugh's class A as shown in **(Table-1)** Right hepatic lobe diameter/ albumin ratio**.** The mean ± SD of right hepatic lobe diameter/ albumin ratio in patients with no varices were 4.88 ± 0.34. The mean±SD of patients having small sized varices were 5.37±0.53. The mean±SD of patients having medium varices were 6.15±0.61. The mean±SD of patients having large varices were 10.96± 4.38. Significant difference was observed in of right hepatic lobe diameter/ albumin ratio of patients having no varices and presence of varices p-value 0.01. (4.88 ±0.34 Vs 7.35±3.30) Remarkable difference was observed in right hepatic lobe diameter/ albumin ratio of patients among varices that is, patients having small varices, The mean ± SD of portal vein diameter in patients with no varices were 13.07±0.86mm. The mean ±SD of patients having small sized varices were 13.65±1.10mm. The mean±SD of patients having medium varices were 14.04±1.62mm. The mean±SD of patients having large varices were 15.68± 2.15mm.Significant difference was observed in portal vein diameter of patients having no varices and presence of varices p-value 0.01. Remarkable difference was observed in portal vein diameter of patients among varices that is, patients having small varices, medium varices and large sized varices p-value 0.01. (13.65±1.10mm Vs 14.04±1.62mm Vs 15.68± 2.15mm) **(Fig-2)** Validation of non-invasive parameters in predicting and grading esophageal varices. The receiver operating curve (ROC curve) for the four parameters were compared. The maximum area under the curve was observed with right hepatic lobe diameter/albumin ratio for small, medium and large sized varices as shown in **(Table-2).**

Table-1: Baseline characteristics of the liver cirrhotic patients.

Characteristics of Pt.	Liver cirrhotic patients n)=200 mean±SD	
Sex	Male	121 (60.5%)
	Female	79 (38.5%)
Age (Years)		46.79±7.59
Duration of disease (months)		31.18± 29.72
Etiology	HCV	182 (91%)
	HBV	10 (5%)
	HBV, HCV	6 (3%)
	Alcoholic	2 (1%)
Child Pugh class		
	A	89 (44.5%)
	B	71 (35.5%)
	C	40 (20%)

Esophageal varices		
	No varices	59
	Varices present	141
	Small varices	30
	Medium Varices	71
	Large Varices	40

Table-2: Validation of non-invasive parameters in predicting and grading esophagealesophageal varices by ROC curve analysis.

Parameters	Small sized varices	Medium sized varices	Large sized varices
Rt. Hepatic lobe diameter	0.68 (68%)	0.661 (66%)	0.74 (74%)
	p=0.000	p-0.005	p-0.000
Serum albumin	0.008 (8%)	0.34 (34%)	0.31 (31%)
	p=0.000	P-0.006	p-0.000
Portal vein diameter	0.74 (74%)	0.41 (41%)	0058 (58%)
	p=0.000	P-0.137	P-0.048
Rt. Heptic lobe diameter/albumin ratio	0.94 (94%)	0.88 (88%)	0.97 (97%)
	p=0.000	p-0.005	p-0.000

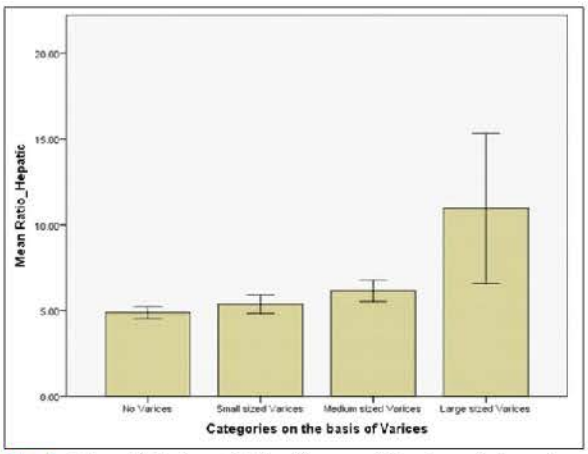

Fig-1: Mean Right hepatic lobe diameter/albumin ratio in various categories of esophageal varices.

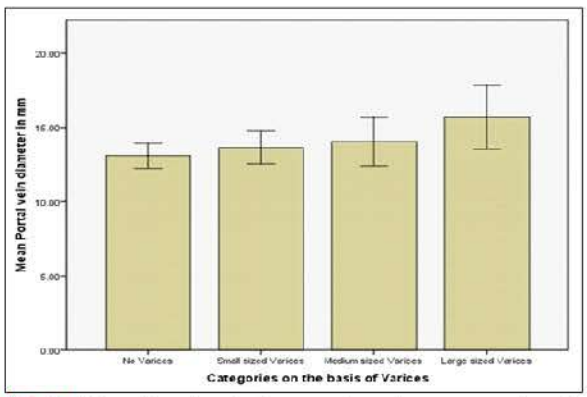

Fig-2: Mean Portal vein diameter in various categories of esophagea varices.

Discussion

Portal hypertension is a common complication of hepatic cirrhosis. Cirrhotic patients with portal hypertension develop esophageal varices and have a very high risk of variceal bleeding. Incidence of esophageal varices in patients with liver cirrhosis is approximately 90%. Therefore, regular control and evaluation of esophageal varices is necessary. Endoscopy is an invasive and costly diagnostic procedure. It was concluded from different studies that 100 screening endoscopies need to be done to prevent 1-2 cases of variceal bleeding.[10] No doubt endoscopy is the gold standard in detecting esophageal varices. But it is an invasive and expensive procedure. Many studies attempt to identify non-invasive factors predicting the presence and the grade of esophageal varices.[11] Several Studies have shown that multiple parameters can be a predictors for the presence of esophageal varices like splenomegaly,[12] ascites,[13] spidernaevi[14] Child's grade,[14,15] platelet count,[13-15] prothrombintime/activity, portal vein diameter,[16] platelet count/ spleen diameter ratio,[11,12] serum albumin[11] and serum bilirubin .[12]

Monitoring of portal vein size by ultrasonography offers an easy, normally available, non-invasive yet reliable and cost-effective way to evaluate the patients with cirrhosis for the risk of variceal bleeding. It can be used for diagnosis as well as clinical monitoring of patients with portal hypertension, which is very important for the follow-up of these patients. When portal vein diameter of patients with varices and no varices was compared it showed statistically significant difference (p-value<0.001). These results are in line with studies conducted by Prihartini et al [17] and Goyal N et al[18] who have reported in their study portal vein diameter is an effective noninvasive predictor for esophageal varices. By simple and non-invaisve ultrasonography these patients can be offered for optimal measures to prevent them from bleeding esophageal varices. In this study, statistically significant difference (p-value < 0.01) was found in right hepatic lobe/ serum albumin level ratio (4.88±0.34 Vs 7.35±3.30). Similar results have been proposed by Adel AM and George SR.[19] Also when non-invasive markers were compared by ROC curve maximum area was covered by right hepatic lobe/serum albumin ratio(94%). This is due to the fact Hypoalbuminemia in cirrhosis is multi-factorial and may be due to reduced production (liver parenchyma replaced by fibrous tissue), or increased loss through gut (portalgastro- pathy/enteropathy) all related to Portal hypertension.[20] Pakistan is an under developing country facing many socioeconomic problems.

The cost of an endoscopy in our country is Rs. 2000-5000, while the cost of ultrasonography or blood examination 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 disease. Moreover, we can also save the patient from an invasive procedure.

Conclusion

The portal vein diameter and right liver lobe diameter/serum albumin ratio might be considered a significant predictor for the presence and grading of esophageal varices. Increased portal vein diameter, decreased right lobe diameter and hypoalbuminemia were significantly associated with the presence of varices.

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Original Article

Correlation of Clinical and Microscopic Diagnosis in Hysterectomy Specimens

Kanwal Babar, Navid Qureshi, Athar Ali, Hamna Salahuddin , Hadia Rana and Irum Yousaf

Objective: To study the correlation between preoperative clinical diagnosis and histopa thological diagnosis of hysterectomy specimens.

Methods: It is a descriptive study of total 169 cases from August 2017 to August 2019. The study is conducted at Pathology Department CPMC Central Park Medical College, Lahore.

Results: The total number of hysterectomy specimens were 169. The age range is from 11 years to 80 years, mean age being 43.5 years, the commonest age group was between 41-50 years. Out of 169 cases, in 115 cases clinical diagnosis and microscopic findings were the same, while in 35 cases microscopic diagnosis were different and in 19 cases clinical history was not provided. The commonest clinical diagnosis and microscopic finding was UV prolapse in 69 cases, while other cases reveal different lesions.

Conclusions: Clinicopathological correlation of hysterectomy specimens were seen in majority of cases (115 cases 68.8 %) and 54 cases (31.2%) reveal different results. Besides clinical diagnosis many incidental findings were also reported in these hysterectomy specimens, making histopathology as a gold standard for the diagnosis of different pathologies.

Keywords: hysterectomy, uterovaginal prolapse, DUB-dysfunctional uterine bleeding, leiomyoma.

Introduction

In the female reproductive system, uterus is the most important organ as it responds to monthly cyclical changes and also the site for the development of fetus.[1] Among the gynecological procedures, hysterectomy is the commonest surgical procedure.[2] In England, in the year 1929, Charles Clay performed the first total hysterectomy procedure.[3]

The uterus can be removed by many routes, through vaginal, abdominal and laproscopically. It may be accompanied by unilateral or bilateral salpingo-opherectomy.[4] There are many clinical indications for hysterectomy, for example, fibroids, utero-vaginal prolapse, dysfunctional uterine bleeding, adenomyosis, PID and malignancies.[5]

To this date hysterectomy remains the best choice of treatment of different gynaecological disorders, though there are many options available.[6] Hysterectomies are usually performed when weightage of removal is more than keeping this organ in the body, especially the symptoms are disabling and medical treatment is of no help.[7]

In our study, we compared the histopathological findings with the clinical diagnosis of gynaecologists. The aim is to do comparison between the clinical diagnosis and findings on microscopic examination and to see the incidental findings in these specimens.

Methods

It is a descriptive study of total 169 cases from August 2017 to August 2019, conducted at Pathology Department Central Park Medical College, Lahore. All hysterectomy specimens with or without salpingo-opherectomy were included. Specimens of tubal ligation, myomectomy and oophorectomy specimens were excluded from the study. Specimens were received in 10 % neutral buffered formalin, in a plastic container labelled with patient's name, hospital number, hospital requisition form, containing all the information. Specimens were given a lab number, bivalved and left in formalin for overnight fixation. After fixation, gross examination of the hysterectomy specimen was performed and appropriate sections were taken in plastic cassettes and tissue processing was done. After that paraffin blocks were made. On a microtome, 3-4µm thin sections were cut, taken on glass slides, dewaxed and stained by H & E method. The sections were examined by using Olympus multihead microscope. The microscopic findings were recorded and information was analyzed.

Results

A total of 169 cases were received in the Department of Pathology, CPMC Central Park Medical College, from August 2017 to August 2019. The age distribution is shown in the following bar-graph.

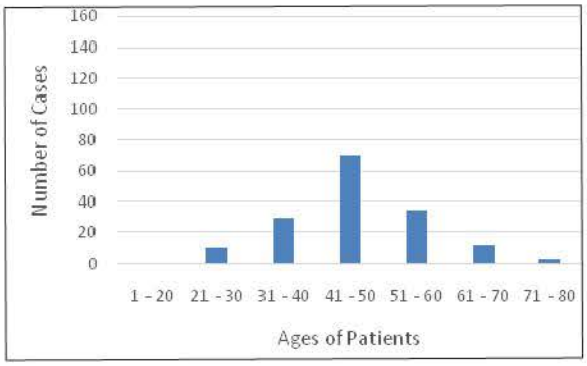

Fig-1: ?

The total 169 hysterectomy specimens were removed by different procedures. The total abdominal hysterectomies were 53, TAH with bilateral salpingoopherectomy were 28, TAH with unilateral salpingoopherectomy were 19 and 69 were vaginal Hysterectomies. The endometrium of these hysterectomy specimens showed different types of lesions shown in **(Table-1).** Out of 169 cases, 82 cases show no significant histological changes within the myometrium, however 50 specimens show leiomyomas, 35 cases show adenomyosis and 2 cases shows more than 50% invasion by invasive carcinoma. Out of total 169 cases, in 47cases bilateral or unilateral adenexa were also received. The following lesions were seen in the adenexa as shown in **(Table-2).** These 169 hysterectomies were removed because of different clinical indications. The most commonest were UV prolapsed seen in 69 cases, followed by DUB in 31 cases, fibroid in 19 cases, placenta previa in 11 cases, 9 cases of ovarian mass, 3 cases with clinical indication of ca endometrium, 2 with endometrial polyp and single case of placenta percreta, adenomyosis, endometrial hyperplasia, CP child hysterectomy, emergency cause and endometriosis. 19 cases were received without any clinical indication. Out of 169 cases, 115 cases showed same microscopic findings as suspected clinically. The correlation of pre-operative diagnosis and microscopic examination is shown in **(Table-3).** However in remaining 54 cases, 31 cases were of DUB, 1 case of CP child, 1 case with clinical diagnosis of CA endometrium, 1 was of emergency hysterectomy, 1 with endometriosis and 19 cases were received without any clinical history. In all these cases the clinical findings and microscopic diagnosis are not the same. These are given in **(Table-4).** These 31 clinically diagnosed DUB cases show, secretory phase in 3 cases, hormonal induced changes in 3, adenomyosis in 12, leiomyoma in 10, follicular cysts in 2 and endometrial polyp in 1 case. Clinically diagnosed case of endometriosis showed, simple endometrial hyperplasia and clinically CA endometrium showed complex hyperplasia. The CP child hysterectomy showed normal secretory phase and emergency hysterectomy showed decidualized endometrium. 19 hysterectomy cases with no clinical history showed different microscopic lesions.

Table-1: Microscopic lesions in endometriosis of hysterectomy specimens.

Lesion	Number	Percentage
Atrophic endometrium	54	31.9%
Secretory phase	48	28.4%
Autolyzed enodmetrium	13	7.6%
Gravid uterus	11	6.5%
Proliferative phase	11	6.5%
Hormoal effect	10	5.9%
Endomtrial polyp	07	4.8%
Endometritis	05	2.9%
Endometrial carcinoma	03	1.7%
Granulomatous endometritis	02	1.1%
Complex hyperplasia	02	1.1%
Simple hperplasia	02	1.1%
Placenta percreta	01	0.50%

Table-2: Microscopic changes seen in the Adenexa.

Lesion	Number of Lesions	Percentage
Unremarkable	15	31.91%
Follicular Cyst	09	19.10%
Paratubal Cysts	07	14.82%
Luteal Cyst	07	14.82%
Granulosa Cell Tumor	02	4.26%
Mucinous Cyst Adenoma	02	4.26%
Serous Cyst adeno CA	01	2.12%
Serous Cyst adenoma	01	2.12%
Granulomatous Salpingitis	01	2.12%
Ovary Involoved byEndometrial CA	01	2.12%
Endomtriosis	01	2.12%

Table-3: Pre-operative/clinical diagnosis and histopathological confirmation:

Lesion	Number of cases confirmed by microscopic examination
UV Prolapse (n=69)	69
Fibroid/leiomyoma (n=19)	19
Gravid uterus (n=11)	11
Ovarian mass (n=9)	09
Endometrial polyp (n=2)	02
CA Endometrial Polyp (n=2)	02
Endometrial hyperplasia (n=1)	01
Ademoyosis (n=1)	01
Placenta percreta (n=1)	01

Table-4: Microscopic diagnosis inconsistent with clinical findings:

Clinical Diagnosis	Number of cases
DUB	31
Edometriosis	01
CA endometrium	01
CP Child	01
Emergency hysterectomy	01
No clinical history	19

Discussion

Hysterectomies are universally performed as a major surgical procedure to resolve different gynaecological disorders.[8] In our study, the total number of cases were 169. The age range is from 11 years to 80 years, mean age being 43.5 years, which is comparable to the age range in the study done by Guptaet al.[9] The youngest patient was a CP child 11 years old, in which hysterectomy was done as the child is incapable of looking after herself. The oldest patient was 78 years old and operated for UV prolapse. The commonest age group was between 41 50 years, which is comparable with other studies[10,11] as most of the pathologies are seen in this age group. In this study 10 cases were seen in the younger age group between 21 30 years due to hysterectomy of gravid uterus. In our part of the world, many pregnant females do not consult for antenatal care due to poor resources and lack of awareness, as compared to western world leading to increased numberof hysterectomies of gravid uterus.[12] This study shows that the vaginal hysterectomy (69 cases -40.8 %) was the commonest surgical procedure for the removal of uterus as the clinical indication of UV prolapse was commonest in our study, followed by total abdominal hysterectomy (53 cases 31.5%), same operated procedures were reported by Mishra A et al [1], in their study. As mentioned by Iftikhar R[13] in his study, the vaginal hysterectomy is done especially if the disease is confined to uterus and uterine size is less than 12 weeks. While in many other studies done by Tiwana K et al and Pandey D et al[14,15] the abdominal hysterectomy was the commonest procedure in gynecological surgeries. The atrophic endometrium was the frequent finding seen in the endometrium of hysterectomy specimens in our study (54 cases 31.9%), followed by secretory phase endometrium (48 cases 28.4%). These results were same as seen by Rupali et al in his study[16]. Endometrial carcinoma was seen in only 3 cases, which is quite similar to study done by Harshal A P et al.[6]

The myometrium is unremarkable in 82 cases (48.5%), followed by leiomyomas 50 cases (29.5%), and adenomyosis 35 cases (20.9%). These results are comparable to the study done by Harshal A P et al[6] and Nazneen R et al.[17] Out of total 169 hysterectomy cases, in our study, 28 cases were with bilateral salpingo-opherectomy and 19 cases had unilateral salpingo-opherectomy. The most common lesion in the adenexa was follicular cysts seen in 9 cases. The granulosa cell tumor was present in 2 cases and Serous Cyst Adenocarcinoma was present in 1 case. Our findings are quite similar to findings seen by Parveen S &Tayyab S in their study.[10] Chronic cervicitis was seen in 161 cases out of 169 cases, showing that cervical infections are very common. Ghousia Rahim et al[11] had similar findings that chronic cervicitis was the commonest histopathological finding in their study.

In this study the commonest clinical indication as well as microscopic diagnosis for hysterectomy was uterovaginal prolapse, seen in 69 cases (40.8%) out of 169 hysterectomy specimens. The similar result was seen by DeeptiV[18] in their study in which UV prolapse was the most common finding. In many studies DUB was the commonest clinical indication for hysterectomy followed by fibroid[19,20], but in our study the commonest was UV prolapse due to unsupervised home deliveries by untrained dias (midwife).In 9 cases the clinical indication was ovarian mass, which is quite similar to the study done by Subrataet al.[21]

While doing correlation in our study, between clinical and microscopic findings, the results were same in most of the cases, (115 cases). Clinically diagnosed 69 cases of UV prolapse, 19 cases of leiomyoma, 11 cases of gravid uterus, 9 cases of ovarian mass,2 cases of endometrial polyp, 2 cases of endometrial CA, 1 case of endometrial hyperplasia, 1 case of adenomyosis and

1 case of placenta percreta, reveal the similar findings on microscopic examination. The findings of correlation of this study were quite similar to the findings done by Mishraet al.[1] The clinical and microscopic findings were not consistant in 54 cases. Out of these, 19 cases were received without any clinical history and variable microscopic lesions were seen in these cases. The remaining commonest clinical indication was DUB (31 cases), as it is a clinical term and different pathologies were seen in these cases. 1 case of CP child, 1 case with clinical diagnosis of CA endometrium, 1 was of emergency hysterectomy and 1 with endometriosis, show different microscopic lesions. In our study, clinicopath ological correlation of hysterectomy specimens were seen in 115 cases and 54 cases reveal different results. In 68.8 % of cases the clinical diagnosis and histopathological findings were the same while in 35 cases (20.0%), microscopic diagnosis was not the same as clinical diagnosis and in 19 cases (11.2%) no clinical history was provided. Besides clinical diagnosis many incidental findings were also reported in these hysterectomy specimens, making histopathology as a gold standard for the diagnosis of different pathologies.[1]

Conclusion

Clinicopathological correlation of hysterectomy specimens were seen in majority of cases (115 cases 68.8 %) and 54 cases (31.2%) reveal different results. Besides clinical diagnosis many incidental findings were also reported in these hysterectomy specimens, making histopathology as a gold standard for the diagnosis of different pathologies.

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Original Article

Effect Of Aloe Vera Gel On Monosodium Glutamate Induced Histological Changes In The Corora Lutea of Rat

Hina Majid, Muhammad Suhail, Javaid Iqbal and Tayyaba Muzaffar

Objective: To evaluate the possible protective effect of Aloe vera gel on reproductive toxicity induced by MSG in female albino rats.

Methods: Thirty six female Wistar albino rats were randomly divided into three groups. Group A was the control group, it was given distilled water. The experimental group B was given with 200 mg/kg b.w. of MSG dissolved in 1.5 ml of distilled water for 2 weeks by gastric intubation. While the experimental group C was co-administered with 400 mg/kg b.w. of Aloe vera gel extract along with 200 mg/kg b.w. MSG dissolved in 1.5 ml of distilled water by gastric intubation for 2 weeks. The rats were dissected and their ovaries were removed. Light microscopic examination was done to study the histological changes in the corpora lutea.

Results: Fisher's exact test showed that there was an association between corpora lutea (p-value<0.05).The corpora lutea in group B were relatively decreased in size. Four (33.3%) of the corpora lutea in the experimental group B had congested blood vessels, the cells appeared vacuolatedwith presence of inflammatory infiltrate and there was extravasation of blood. While, the corpora lutea of group C were normal and comparable to those observed in control group A.

Conclusions: Aloe vera gel co-administered with MSG has protective effects on the copor-alutea.

Keywords: Monosodium glutamate, food additive, oxidative stress, ovaries, Aloe vera, corpora lutea.

Introduction

Monosodium glutamate is a crystalline white salt of glutamate.[1] It is commonly used as a food additive to enhance the palatability.[2] Researches have reported various harmful effects of MSG on different organs of the body including brain, retina, heart, lungs, intestines, liver, kidneys and gonads.[3-6] When taken orally, glutamate gets absorbed by the small intestine and enters the circulation.[7] Later, the glutamate binds to the NMDA (N-Methyl D-Aspartate) receptors present on different organs including ovaries. This binding of L-glutamate to the NMDA receptor opens the calcium channels leading to an influx of the calcium ions. This influx activates enzymes including phospholipase and protein kinase, which cause degradation of proteins and membranes.[8] The degradation process results in a release of reactive oxygen species causing oxidative stress.[9]Oxidative stress and its subsequent organ toxicity can be prevented by antioxidants.[10] Aloe vera is a green, perennial plant that belongs to Liliaceae family.[11] The plant has been used for its medicinal potentials for centuries.[12] Aloe vera gel is a rich assortment of phenols, flavanoids, polysaccharides, vitamins, enzymes, and minerals.[13,14] The plant gel has anti-inflammatory, antifungal, antibacterial, antiviral, antidiabetic, and antioxidant properties.[15-17] The aim of the present study was to evaluate the effects of Aloe vera gel on the histologic changes induced by MSG in the corpora lutea of rat.

Methods

It was an experimental study, a randomized control trial conducted in the anatomy department of Shaikh Zayed Postgraduate Medical Institute (SZPGMI), Lahore. The study protocol was accepted by research board and ethical committee of SZPGMI. Monosodium glutamate of analytical grade was purchased from Sigma. Aloe vera plants were procured from a local nursery. A stock solution was prepared by dissolving monosodium glutamate in distilled water. Fresh Aloe vera leaves were collected from the healthy plants. The leaves were rinsed with tap water, dissected longitudinally and the fleshy mucilaginous pulp was scraped out. The pulp was homogenized with ethanol 96 % and distilled water. The solution was filtrated and evaporated under a rotatory evaporator at PCSIR laboratory**(Fig-1)** 36 healthy female Wistaralbino rats weighing between 150-200 g were used for the experiment. The rats were housed in well ventilated laboratory cages with 12 hours day/night cycle. They were given commercial poultry feed and water ad

libitum. After one week of acclimatization, the rats were divided randomly into three groups of 12 rats each. Group A (Control): The rats of this group were given 1.5 ml of distilled water, for 2 weeks by gastric intubation. Group B (Experimental): The rats were treated with monosodium glutamate 200 mg/kg body weight 18 dissolved in 1.5 ml of distilled water, by gastric intubation for two weeks. Group C (Experimental): Rats of this group were treated with 400mg/kg body weight of Aloe Vera gel extract19 along with 200 mg /kg body weight of monosodium glutamate dissolved in 1.5 ml of distilled water, by gastric intubation, for two weeks.

Fig-1: Steps showing the preparation of Aloe vera gel.

On the last day of experiment, 24 hours after the last dose all the rats were euthanized and dissected. Ovaries of all the rats were removed, fixed in 10% buffered formaldehyde for 24 hours, processed and then embedded in paraffin wax. Serial sections of thickness 5 microns were made, mounted on glass slides, stained with haematoxylin and eosin (H&E) and studied under light microscope. Photo-micrographs of the results were obtained using digital research photographic microscope.

The data was entered and analyzed by using Statistical Package for SPSS version 20. Shapiro-Wilk's test was applied to check the normality of variables. Data was normally distributed. The corpus lutea of all groups were described using frequency and percentage. Comparison among groups was made by using Fisher's exact test. A p-value ≤ 0.05 was considered significant.

Results

The corpora lutea of the control group A were located in the peripheral zone of the ovarian cortex. The granulosa lutein cells were large polyhedral cells with central round shaped nuclei. These nuclei exhibited a single darkly stained nucleolus. A copious amount of pink stained cytoplasm surrounded the nuclei. Small capillaries and venules were seen scattered throughout the corpus lutea. Towards the periphery of the corpus lutea smaller polygonal theca lutein cells with relatively dark staining rounded nuclei were observed. The blood vessels were normal and there was no extravasation of blood seen in the corpora lutea of control group A **(Fig-2).**

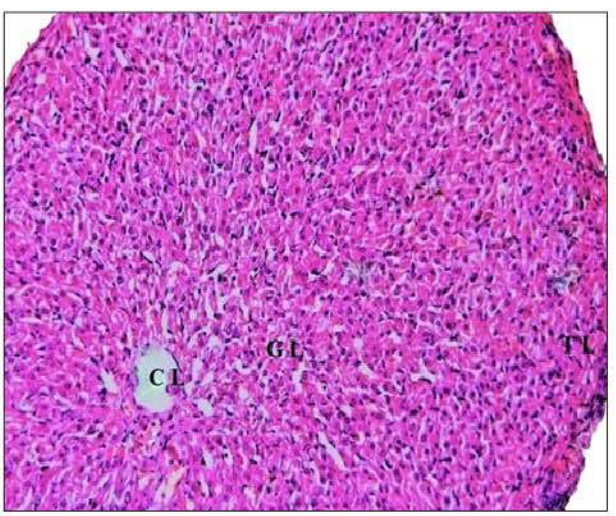

Fig-2: Photomicrograph of ovary of female albino rat of control group A showing normal Corpus Luteum (CL), with Theca Lutein (TL), and Granulosa Lutein (GL) (H &E, 100X).

The corpora lutea in the experimental group B were relatively decreased in size when compared to the corpora lutea of the control group A. Four (33.3%) of the corpora lutea in the experimental group B had congested blood vessels, the cells appeared vacuolated, with presence of inflammatory infiltrate and there was extravasation of blood in their corpora lutea **(Fig-3).** The corpora lutea of the experimental group C were also normal and comparable to the corpora lutea observed in the control group A **(Fig-4)**. Fisher's exact test showed that there was an association between corpus lutea and groups (p-value < 0.05) **(Table-1).**

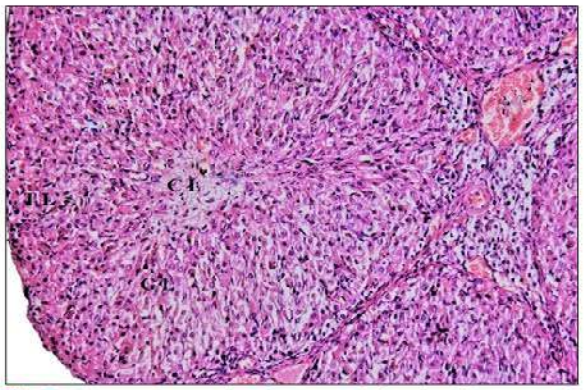

Fig-3: Photomicrograph of ovary of female albino rat of experimental group B showing Corpus Luteum (CL), Theca Lutein (TL), Granulosa Lutein (GL) with extravasation of blood in the Corpus Luteum (H&E, 100X).

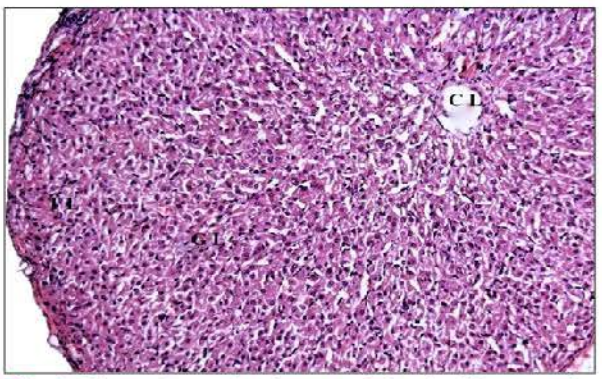

Fig-4: Photomicrograph of ovary of female albino rat of experimental group Cshowing normal Corpus Luteum (CL), with Theca Lutein (TL),ranulosa Lutein (GL) (H&E, 100X).

Table-1: Distribution of appearance of corpus lutea among groups.

Corpus luteum	Group-A n=(%)	Group-B n=(%)	Group-C n=(%)	P-Value
Normal	12 (100.0%)	8 (66.7%)	12 (100.0)	<0.005*
Abnormal	0	4 (33.3%)	0	

**p value ≤ 0.05 is considered statistically significant*

Discussion

Corpus luteum is a glandular structure comprising granulosa and theca interna cell remains of the graffian follicle after it undergoes ovulation. It is thus an indicator of ovulation. Granulosa cells undergo hypertrophy and forms granulosa lutein cells making about 80% of the corpus luteum. Theca lutein constitute the rest 20% of the corpus luteum.[20] The study proved that there was statistically significant difference between the corpus lutea of the three groups (p- value < 0.05). The corpora lutea in MSG treated group were congested, relatively decreased in size, showed areas of extravasation of blood and presence of inflammatory cells. Oladipo et al, demonstrated that the ovaries of MSG treated group had numerous atretic follicles with complete absence of the corpora lutea.[18] A study suggested that FSH levels did not change in the MSG treated females, however, there was a decline in the LH levels. The decrease in the LH concentration may produce a decrease in size and atrophy of the corpus luteum.[6] Vascular congestion results from defective intrinsic antioxidant defenses, rendering the cell more susceptible to oxidative stresses. If the free radicals are not neutralized by endogenous or exogenous antioxidant molecules, then lipid peroxidation of the cell membrane occurs, leading to damage of the cell membrane protein and capillary endothelium.[21] Hildeman et al, proposed that the excessive generation of free radicals damage the polyunsaturated fatty acids in the biomembranes and accelerates apoptosis by reducing the expression of Bcl-2 protein.[22] Kumbhare et al, noticed lymphocytic infiltration in rats treated with MSG. They suggested that chemotaxis of leucocytes towards the site of injury is the body's response to counteract any harmful insults.[23] The present study revealed normal corpora lutea with no congestion in group C. This coincides with the study by Yadav et al, who suggested that Aloe vera gel significantly accelerates healing. They found that levels of malondialdehyde, a product of lipid peroxidation was remarkably decreased by the Aloe vera, advocating that the gel reduced the oxidative stress.[24] The studies done on male mice and rats also prompted the promising role of Aloe vera on reproduction by proving significant rise in serum testosterone, FSH and LH levels associated with increase in number of mature healthy gonadal cells.[25,26] Aloe ver agel is rich phyto constituents having strong antioxidant properties including phenols, flavonoids, vitamin C and E, zinc and selenium.[27,28] These antioxidants protects against oxidative stress damage induced on corpora lutea by MSG. Thus, the current study proved that Aloe vera gel when co-administered with MSG minimized the toxic effects on the corpora lutea in rat ovaries.

Conclusion

The current research proved that MSG has a harmful impact on the corpora lutea. This should be kept in minds by young females of reproductive age group while consuming MSG added foods as it may be an underlying cause of infertility. Aloe vera gel, on the other hand when consumed with MSG reverts its harmful effects on the corpora lutea.

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Original Article

Serum Luric Acid a Marker of Poor Outcome in Obese Women with Preecampsia

Mudasar Zia, Adina Shamsi, Mohammad Shoaib and Fariha Nazneen

Objective: To find out the abnormalities of serum uric acid in obese preeclamptic women and to measure its clinical importance.

Methods: Study was conducted with 40 obese women presenting with severe preeclampsia to the Obstetric Unit of the Lahore General Hospital Lahore. Study duration was May 2017-Oct 2017. Thirty gestation-matched normotensive subjects were taken as controls. Levels of serum uric acid, blood urea and serum creatinine were estimated by Auto analyzer using standard kits. BMI was calculated by formula.

Results: Levels of BMI in preeclamptic women were non-significantly increased in comparison to control. Levels of serum uric acid, blood urea and serum creatinine were increased in women with preeclampsia, but were only significantly observed in case of serum uric acid in comparison with controls.

Conclusions: Increased level of serum uric acid in preeclampsia is associated with increased risk of complication.

Keywords: serum uric acid, BMI, preeclampsia.

Introduction

Preeclampsia/ pregnancy induce hypertension is a multisystem syndrome, develops in initial stage of pregnancy involving vascular endothelium and placenta.[1] Preeclampsia is induced by rapid increase in blood pressure (systolic ≥140/ diastolic 90 mm Hg) and increase level of protein in urine (> 300mg/24h) after 20th gestation weeks.[2] Disorder of hypertension affects 2-3 % of pregnant women.[3] Preeclampsia is the cause of morbidity and mortality in pregnant women and may be related with disorder of different organs described by renal, cardiopulmonary, neurologic and hepatic complications.[4] The fetus has adverse perinatal consequences including intrauterine growth retardation, preterm birth, and intrauterine death.[5]

Oxidative stress, placental ischemia, angiogenic imbalance and an inflammatory reaction may play a part in pathogenesis of problem. Hyperuricemia is a main condition found in preeclampsia with increased levels of circulatory uric acid at 10th gestational week and it is usually related with kidney dysfunction, tissue injury and oxidative stress. Therefore it may be a predictor of complications in women with preeclampsia.[6,7]

It is proposed that in preeclamptic women, hyperuricemia is mainly due to reduced GFR and this decreased GFR may be a result of endothelial dysfunction.[5] Many studies reported a direct relationship of raised serum uric acid with adverse fetal and maternal outcomes.[8] However, some studies found that increased uric acid may have an influential role in the pathogenesis of the fetal and maternal outcomes.[9,10]

It is demonstrated that altered invasion of trophoblast in placenta results in the formation of ischemic metabolites. These metabolites may cause vas oconstriction in glomeruli, with an outcome of decreased glomerular filtration rate in reduced GFR and raised the levels of uric acid.[11] Raised levels of uric acid may be considered as an early predictor of renal damage and may cause 10-15% fetal death in preeclamptic women.[12,13] Serum uric acid along with serum creatinine has an important role in preeclampsia. The elevation of these biochemical parameters are mainly due to reduced urinary clearance and raised reabsorption.[9] However, it is reported that level of blood urea and serum creatinine in women with preeclampsia may not change and are similar to the levels observed in women without pregnancy, due to reduced renal plasma flow and GFR.[14]

Excess gain of weight during the period of pregnancy is related to insulin resistance and systemic inflammation which may result inendothelial dysfunction, thrombotic response, maternal morbidity and mortality.[15] Because of the noteworthy discrepancies on the role of uric acid as a predictor of preeclampsia and fetal growth retardation, study was tried to find out the relationship of uric acid with BMI in obese women, Hence, there is a need to find the early

Hence, there is a need to find the early marker of preeclampsia and avoid the complications, developing in both baby and mother. A cross sectional study was planned to find that whether serum uric acid alone or in combination with some other biomarkers may have a role in developing preeclampsia.

Method

Study was directed with 40 consented obese women presenting with severe preeclampsia to the Obstetric Unit of the Lahore General Hospital Lahore. Study duration was May 2017-Oct 2017. Thirty gestation-matched normotensive subjects were taken as controls. Levels serum uric acid, blood urea and serum creatinine were estimated by Auto analyzer (Humastar 200) using standard kits. BMI was calculated by formula.

BMI= (Weight in Kg)/(Height in Meters)2

Diagnostic criteria for preeclampsia blood pressure 140 / 90 mmHg measured in two sittings with 300 or > 300 mg protein in urine sample collected in 24 hrs. Women with liver, cardiac and renal dysfunction, past history of hypertension were excluded from study. Study was approve by Ethical Committee of Research Institute. Data was entered in SPSS 20. Levels of uric acid, blood urea and serum creatinine were presented as mean±SD. Variation in the values of BMI and levels of blood urea, serum creatinine, serum uric acid of preeclamptic women were compared with the normal controls using student 't' test. Values of $P< 0.05$ is considered significant.

Results

Comparison of the levels of uric acid , blood urea and serum creatinine of obese preeclamptic women was done with controls. Levels of BMI were non-significantly increased in pre-eclamptic women in comparison to control with p value of 0.98. Levels of serum uric acid and blood urea were increased significantly in preeclamptic women with p-values of 0.008 and 0.001 respectively.

Table-1: Comparison of the levels of uric acid, blood urea and serum creatinine of obese pre-eclamptic women with controls.

Variables	Women with Pre-eclampsia (40 cases)	Controls (30 cases)	P-Value
BMI (kg/m2)	27.42±1.70	3.68±0.67	0.98
Serum Uric acid (mg/dl)	6.46±1.89*	3.68±0.67	0.008
Blood Urea (mg/dl)	33.52±6.38	23.59±3.56	0.001
Serum creatinine	1.01±0.17	0.62±0.20	0.415

*P<0.05= Significant

Serum creatinine was non-significantly changed with p value of 0.415 in comparison with controls.

Discussion

Elevated level of serum uric acid in women with hypertension showed the risk of development of preeclampsia, as well as preterm infants[1]. In most women with preeclampsia, renal plasma flow and glomerular filtration rate are at most only modestly decreased as a consequence of increased afferent arteriolar resistance and/or reduced ultra-filtration coefficient.[10] We observednon significantly increased values of BMI in preeclamptic women in comparison to control. It is demonstrated that obesity during the period of pregnancy or before pregnancy may be related tohyperinsulinism, endothelial dysfunction, systemic inflammation, proteinuria, hypertension, responses. These damaging effects on different organs increase mortality in women.[14] However a significant positive relation was observed between increased BMI progressions of preeclampsia.[16] According to our study a significant increased level of serum uric acid was observed in women with preeclampsia. Increased level of serum uric acid suggested that it is due to the decreased renal clearance. It is proposed that decreased GFR leads to reduced filtration of uric acid, and reduced plasma volume may help to increase the reabsorption of sodium via renal tubule.[10,17] Significant correlation was observed between maternal serum uric acid, disease severity and maternal outcome. [8] An experimental study proved that uric acid may deteriorate the trophoblast invasion and it also contributes in the pathogenesis of preeclampsia by encouraging oxidative stress, inflammation and dysfunction of endothelium. Therefore increase level of serum uric acid may be a risk forecaster for the development of preeclampsia.[18] A study found that serum uric acid in preeclamptic mother is an imperative predictor of small birth weight of her fetus.[19] We observed that the levels of blood urea were significantly increased while serum creatinine was insignificantly increased in women with preeclampsia, in comparison with controls. However, a study observed a significant elevated level of serum creatinine levels women with preeclampsia[17]. Positive correlation markers of renal function (uric acid, urea, and creatinine) suggest that state of preeclampsia is probably related with progression of renal problem.[20] Data of a study suggested that combination of increase level of serum uric acid along with dysfunction of renal parameters and proteinuria

in mother is strongly increased the risk of progression of eclamptic crises.[10]

Conclusion

Increased level of serum uric acid in preeclampsia may increase the risk of complications. However there is a need of study on larger number of patients to explain the clinical usefulness of uric acid in predicting the progression to preeclampsia in obese women.

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Original Article

Psychosocial Factors and Mental Health Disorders Among Patients in Punjab Institute of Mental Health : does Religion and Social Support Help?

Qurrat ul Ain Naqvi, Afshan Shahid, Dawar Nadeem Aslam Dar, Vareesha Haider and Kanwal Manzoor

Objective: To determine frequency and associated risk factors of mental health disorders in patients attending Pakistan Institute of Mental Health, Lahore (PIMH).

Methods: A cross-sectional study conducted at Punjab Institute of Mental Health. 209 patients with mental disorders aged 18 and above were included in the study through non probability convenient sampling after informed consent. A structured questionnaire was used to obtain data. Data was analyzed using SPSS version 25. Mean and standard deviation was calculated for quantitative variables. Frequencies and percentages were calculated for qualitative variables. Chi square was applied and p value ≤ 0.05 was considered significant.

Results: The mean age was 35.8±13.9 years. Among all respondents 29.7% patients were diagnosed with mood disorders, 27.8 % with schizophrenia and acute psychotic disorder,17.2% with substance related disorders, 11% with neurotic disorders and 14.4% with non psychiatric disorders. Psychosocial factors associated with mental factors were being ever married (p= 0.03), living below poverty line(p=0.00), being literate (p=0.00)and being unemployed(p=0.01), use of recreational drugs(p=0.00), being abused or neglected as a child(p=0.00), experience of a negative event in previous event(p= 0.04), inclination towards religion(p=0.02) and availability of someone for emotional(p=0.00) help were psychosocial factors associated with mental illness. Behavioral factors like being a habitual drinker(p=0.04), being smoker and not being physically active (p=0.04) were found to be associated with mental disorders. Medical factors associated with mental disorders were having positive past history of mental disorders(p=0.01) and having physical disability (p=0.03).

Conclusions: Findings from this study identified the psychosocial risk factors, socioeconomic, medical, behavioral factors of mental disorders and frequency of patients with different types of mental disorders in PIMH. Religious meditation, sharing problems with friends and family, social network groups with patients having same mental health problems can be helpful along with the treatment of these mental disorders. Further studies are needed to understand causal relationship of mental disorders to support policy makers in decision making.

Keywords: mental disorders, mood disorders, schizophrenia, recreational drugs, smoking.

Introduction

Mental health is a state where one is functioning at a satisfactory level of emotional and behavioral adjustment. Mental health includes subjective well-being, perceived self efficacy, autonomy, competence and self-actualization of one's potential. Mental illness refers to all mental disorders characterized by alterations in thinking, mood, or behavior leading to impaired functioning.[1] Mental disorders affect 450 million people worldwide.[2] Mental health disorders constitute about 14% of the global burden of disease.[3]340 million people worldwide are suffering from depressive disorder and 140 million from alcohol dependence.[4] According to WHO one person attempts suicide every 40 seconds. In Pakistan the situation is equally bleak. The prevalence of mental disorders is 27%. Depression and sleep related problems are the most common mental disorders among our population. The prevalence of depression is 6%, schizophrenia 1.5 % and epilepsy 1.5%.[4]However there are chances that this number is an underestimation of the current situation as mental disorders are associated with many social taboos and myths and are under-reported. There has been a rapid increase in mental disorder prevalence in past years due to poverty, unemployment and political unstability.[5] Mental disorders are associated with age,sex, marital status, unemployment, lack of social support, co-morbidity, educational status income and family structure.[6,7] Spirituality and meditation have been found to be protective for mental health.[8]

Considering the disease burden of mental illness in Pakistan, very limited resources are available to cope with the situation. Only 0.4% of the health budget is spent on mental health.[9]Pakistan is in lack of large mental hospitals. Currently only five mental hospitals.

Currently only five mental hospitals are working in the country. Among these the Punjab Institute of Mental Health, Lahore is a large mental health facility available to cater general population. This study is based at the out-patient department of Punjab Institute of Mental Health Lahore. We aim to assess the disease distribution and frequency and disease load along with associated risk factors coming to the above mentioned hospital. Thus contributing to the protection, promotion and restoration of mental health, as mental health is fundamental to one's ability to think, emote and live a healthy and productive life.

Methods

A cross-sectional study was carried out on 209 patients attending the OPD of Punjab Institute of Mental Health, Lahore. Interviews were conducted and questionnaires filled by the researchers. Sample size was calculated taking confidence level at 95%, anticipated population 65% and relative precision at0.10.Non-probability convenient sampling was done. Patients aged 18 years and above and diagnosed by psychiatrist and accompanied by attendants were included in the study. Informed consent was taken from the patients and the attendants. Patients with education of primary level or above were considered as literate. Patients with daily income of more than two dollars were considered to be living above poverty line. Patients doing physical activity of 30 min at least 5 times a week were considered as physically active. Household size of 7 was taken as reference as it is the average household size in Pakistan. SPSS version 25 was used for data analysis. Mean and standard deviation was calculated for quantitative variables. Frequency and percentage was calculated for qualitative variables. Chi square test was applied and p-value of 0.05 or less was taken as significant.

Results

The mean age and standard deviation of the study participants was 35.9±13.9 years. Majority of the patients were male 66%, 34% were female.58.4% were from Lahore and 42.6 % were outsiders. Majority of the patients 63.6% have been ever married and 36.4 % were unmarried. A large majority 94.7% were Muslims and 5.3% were non-Muslims. Only 12.9% participants were living above poverty line and 87.1 % were living below poverty line. 63.2% patients had a household of 7 persons or less and rest of them i.e. 36.8% lived in a household of more than 7 persons. 35.9% were literate and 64.1 % illiterate.34.4% patients were employed or retired from job, 44.5% were unemployed or housewife,3.8% were students and 17.2% patients were unable to work due to their mental illness. Two-third 74.6% of the employed population was satisfied with their job and 25.4% were unsatisfied. Out of 209 total patients included in the study 62(29.7%) were diagnosed with mood disorders, 58(27.8%) with schizophrenia and acute psychotic disorders, 36(17.2%) with substance related disorders,23(11%)with neurotic disorders and 30 (14.4%) with non-psychiatric disorders. Among these patients majority 76.6% had family history of mental illness,26.8% used recreational drugs, 35.4% were habitual drinkers, 35.4% were smokers, 5.3% had physical disability,53.6% were physically active, 44% had experienced a negative event in life, 16.7% were suffering from a chronic disease and 15.8% had history of mental illness. Regarding inclination towards religion, 1.9% had very strong inclinition, 22% had strong inclination, 31.6% had moderate inclination, 18.2% had weak inclination and 26.3% had no inclination towards religion.51.7% of the patients were socially active and 50.7% patients had someone available in the form of family or friends for social support. The sociodemographic factors associated with mental illness were being ever married (p=0.03), living below poverty line(p=0.00), being literate (p=0.00)and being unemployed(p=0.01).

Table-1: Sociodemographic profile of patients attending PIMH (n=209).

Variable		Frequency	Percentage
Age	Less than 36 years	120	57.4%
	Less than 36 years	89	42.6%
Gender	Male	138	6.6%
	Female	71	34%
Marital status	Single	76	36.4%
	Ever married	133	63.6%
Income	Above poverty line	27	12.9%
	Below poverty line	182	87.1%
Educational status	Illiterate	75	35.9%
	Literate	134	64.1%
Occupational status	Employed or retired (ever employed)	72	34.4%
	Student	93	44.5%
	Unemployed / housewife	08	3.8%
	Unable to work	36	17.2%
House hold Size	>7 members	132	6.32%
	< members	77	36.8%

Among medical factors, positive past history of mental disorders (p=0.01) and having physical disability (p=0.03) were associated with having a mental disorder. Behavioral factors associated with mental disorder were use of recreational drugs (p=0.00), being a habitual drinker (p=0.04) and smoker and not being physically active. Being abused or neglected as a child (p=0.00), experience of a negative event in previous event (p=0.04), inclination towards religion (p=0.02) and availability of someone for emotional (p=0.00) help were psychosocial factors associated with mental illness.

Discussion

The mean age of the patients was 35.8 ±13.9 years. Among all respondents 29.7% patients were diagnosed with mood disorders, 27.8 % with schizophrenia and acute psychotic disorder, 17.2% with substance related disorders, 11% with neurotic disorders and 14.4% with non psychiatric disorders. Despite the increasing burden of mental disorders, Pakistan is deficient in studies exploring mental disorders and their associated factors. The pattern of mental illnesses and their association with risk factors in this study is similar to most of other researches.[10]

Most of the study participants in this study were male 66% this is in contrast to the general population structure in our country where females are slightly more than males. The reason being that females are less privileged in our culture and have less access to the health care facilities. This finding is similar to that in another study done in Lahore where majority of the

Table-2: Risk factors associated with mental disorders in patients attending PIMH (n=209)

Variable		Mood disorders p-value	Schizophrenia & acute psychotic disorders p-valure	Neurotic Disorders p-value	Substance related disorders p-value	Non psychiatric Disorders p-value
Sociodemographic factors	Age	0.66	0.93	0.72	0.54	0.62
	Gender	0.19	0.44	0.14	0.60	0.60
	Marital Status	0.28	0.03	0.45	0.73	0.65
	Income	0.65	0.12	0.19	0.37	0.00
	Religion	0.62	1.64	0.44	0.12	0.16
	Education	0.94	0.26	0.00	0.24	0.02
	Occupation	0.72	0.03	0.99	0.01	0.14
	Job satisfaction	0.21	0.91	0.24	0.67	0.08
	Type of employment	0.66	0.82	0.08	0.85	0.07
	House hold size 7 or less	0.79	0.19	0.81	0.78	0.09
Medical Factors	Family history of mental illness	0.21	0.55	0.49	0.12	0.98
	Suffering from a chronic disease	0.33	0.31	0.61	0.98	0.60
	Physical disability	0.86	0.03	0.83	0.69	0.16
	Previous history of mental illness	0.25	0.67	0.01	0.73	0.38
Behavioral fctors	Use of recreational drugs	0.13	0.01	0.00	0.27	0.36
	Habitual drinking	0.04	0.58	0.16	0.26	0.38
	Smocking	0.74	0.55	0.02	0.38	0.79
	Level of physical activity	0.39	0.86	0.46	0.53	0.04
Psychosocial factors	Abuse or neglect as a child	0.01	0.86	0.98	0.00	0.09
	Experience of any negative event	0.83	0.22	0.16	0.24	0.04
	Social activeness	0.99	0.86	0.95	0.18	0.17

respondents were males.[7] This health care facility is one of its own type in Punjab, despite its exclusive nature the majority of patients utilizing this facility belonged to Lahore. It is because that the access to health care facilities is difficult for people coming from peripheries and their health beliefs regarding mental disorders do not compel them to seek medical advice.

A great majority of the patients;76 %were living below poverty line. This corresponds to the economic status of our country. Similar findings were reported in a study conducted in Istanbul, Turkey another developing country like ours.[11] Almost half of the patients had poor social support system. In country like ours, where social systems are disintegrating owing to industrialization and urbanization, this finding is a depict of the current scenario.

Among the associated factors, living below poverty line was significantly associated with mental disease(non- psychiatric). Low level of income was also found significantly associated with mental illness in urban Tanzania.[12] Low income has also been declared significant risk factor in a population based study conducted in US.[13] Unemployment was found to be significantly associated with mental illness (neurotic type). Same association is found in a study conducted in Bosnia and Herzegovenia an under-developed country with a large chunk of unemployed population.[14] Low income poses new stressors in life related to survival, shelter, food, social position and self-esteem making individual at risk of developing mental disorders. Related to aforementioned factors; physical disability is also associated with mental disorders (schzopherenia and acute psychotic disorder). With the advent of bio-psycho-social model of health, physical health and mental health are proven to be intricately linked. In China, physical disability was found to be associated with physical disability causing motor limitations and physical disability occurring in old age.[15] This can be partly explained by social exclusion, social isolation, lack of social participation, loneliness and monetary disadvantages that comes with physical disability.

Among personal habits, smoking use of recreational drugs and habitual drinking were found to be significant risk factors for mental illnesses (mood disorders, schzopherenia, acute psychotic disorders, neurotic and non psychiatric disorders). A survey conducted in USA has reported smoking to be significantly associated with mental disease prevalence and onset.[15] Alcohol was found significantly associated with mental illness especially mood disorders in a study conducted in Ohio.[17] It can be explained by the expected alcohol's depressant effect on brain and a constellation of symptoms of alcoholism and mood disorders. Similarly, drug addiction was found significantly associated with mental disorders in Netherlands.[18] The protective effect of physical activity was found to be present only for non-psychotic illness which is contrary to the study done at Oxford university where physical activity and exercise was found to be protective for anxiety and mood disorders.[19]

No association was found between family history of mental disorder with mental illnesses. This is opposite to the findings of international literature where family history is associated with increased risk of developing bipolar disorder and also with severity of mental disorders.[20,21]

This in contrast can be explained because of our social norms and taboos associated with mental disorders people hesitate to disclose family history of mental disorders, hence it is under-reported. Our findings suggest that abuse or neglect as a child in a person leads to substance abuse disorder later in life. This is exactly the same as reported by Choi NG and colleagues, adverse childhood experience poses a threat to mental health in later life leading to substance abuse.[22] Lack of social support was found to be only associated with non psychotic disorders. However, social support systems were found to be protective for mental health in a study conducted in UK.[18] Social support provides physical and psychological advantages to people in distress. Perceived social support can inhibit the adverse physiological complications of diseases and increase self-care among older people.

In a country like our where social support is taken for granted, it is likely that it might be under-reported by the respondents. This can lead to aforementioned finding. Inclination towards religion was found to be protective against mental disorders. This finding is in line with the study done in Bhutan where spiritualism was found to be associated with mental health.[23] Believers easily tolerate stressors, strains and difficulties in life.

Religion is associated with well-being. Religion helps by explaining the situations, gives a sense of empowerment and provides personal identification.[24] Most of these studies are mostly done on Christian populations. However findings of these studies can be generalized on Muslim population as the two religions share many common beliefs.

Conclusion

Findings from this study identified the psychosocial risk factors, socioeconomic, medical, behavioral factors of mental disorders and frequency of patients with different types of mental disorders in PIMH. Religious meditation, sharing problems with friends and family, social network groups with patients having same mental health problems can be helpful along with the treatment of these mental disorders.

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Original Article

To Evaluate the Diagnostic Accuracy of Ultrasound with Computed Tomographic Guided Peripheral Lung Biopsy (A Descriptive Analytical Study)

Asif Hanif, Salman Ayyaz, Afshan Qureshi, Affaf Javaid, Farah Ayyaz and M. Saqib Saeed

Objective: To evaluate the diagnostic accuracy of Ultrasound with Computed Tomographic guided peripheral lung biopsy.

Methods: This descriptive analytical study was conducted in the Institute of TB and Chest medicine, KEMU/King Edward Medical University Lahore during the period of April 2018 to April 2019. 30 patients with normal coagulation profile were selected 15 patients were biopsied by CT and 15 were biopsied by USG guidance by a trained radiologist. Trucut semi-automated 18G biopsy needle was used in CT guided as well as USG guided peripherally located lung mass biopsy measuring more than 10 mm in size.

Results: After the diagnosis of mass lesion was made by CT chest with i.v contrast, 15 patients were biopsied by CT guidance and 14 were proved to be positive out of which 7 were adenocarcinomas , 4 were non small cell carcinomas not specified and 3 were benign tumours. Whereas in 15 USG guided biopsies, 11 turned out to be positive out of which 6 were adenocarcinomas, 3 were squamous cell carcinomas, 1 was mesothelioma and 1 was infectious (tuberculous). Figure 1 statistical evaluation. The sensitivity of CT guided biopsy was 98% and specificity was 99% whereas sensitivity of USG guided biopsy was 90% and specificity was 96%. (Fig-2 sensitivity and specificity). In all USG guided biopsies time taken was less than 30 minutes and time taken by CT guided biopsy was more than 30 minutes. Pneumothorax was observed in 2 patients in CT guided biopsies whereas no complication observed in USG guided biopsies.

Conclusions: TUS guided peripherally located abutting mass lesions more than 10 mm in size is very much comparable with CT guided biopsies of the lesions in terms of reliability accuracy and complications.

Keywords: USG, CT scan, TUS, Trucut needle biopsy.

Introduction

With the advent of lung cancer screening, diagnosing peripherally located, small sized lesions, which are either pleural based or abutting chest wall, gain paramount importance which is challenging, keeping in view relatively low yield of both flexible bronchoscopy and sputum cytology.[1] Here comes the role of imaging-guided percutaneous transthoracic biopsy which not only helps in diagnosing, staging, and differentiating primary cancers from metastatic, infective and inflammatory lesions but also in genetic and immunologic testing of cancer mutations.[2-5]

Computed Tomography (CT) is most commonly employed imaging guided technique for percutaneous tranthoracic biopsies, being more impeccable as far as needle trajectory and lesion displacement with respiratory movements are concerned, but these are the perks of recently introduced CT fluoroscopy as conventional CT is devoid of these capabilities.[6,7] However, both expose patients to large amounts of ionizing radiation and are unable to provide real-time multiplanar monitoring of procedure.[8,9] However CT fluoroscopic guided biopsies vs chest biopsies using multislice CT biopsy mode show dramatically lower CT dose index levels in CTF guided biopsy mode with relatively same diagnostic yield in both groups and higher number of post procedure pneumothoraces in multislice CT biopsy mode. Transthoracic Ultrasound (TUS) has been proven to be of great help for diagnosing and managing lesions involving pleural cavity such as pneumothorax and pleural effusion as US waves are unable to penetrate aerated lung tissue.[10-12]

However it has now been used increasingly for imaging guided transthoracic biopsies for masses abutting chest wall and pleural and subpleural pulmonary nodules.[13,14]

This modality is relatively inexpensive, easily available at bedside, portable, free from hazards of exposure to ionizing radiation and provides real-time guidance.[15,16]

The aim of this study was to retrospectively compare the outcomes of CT and TUS guidance for percutaneous transthoracic biopsies.

Methods

This descriptive analytical was conducted in the Institute of TB & Chest Medicine, KEMU/King Edward Medical University Lahore during the period of April 2018 to April 2019 after taking permission of Ethical Committee. The inclusion criteria includes:

1. Age between 35 to 80 years.
2. Either sex.
3. Peripherally located mass lesion without intervening aerated lung on CT chest.
4. Clinically stable patient.

5 mass lesion more than 10mm in size and exclusion criteria was 1 critically unwell patient 2 pregnancy. 3 lesions centrally located and close to big vessels. 4 lesion less than 10mm in size. 30 patients with normal coagulation profile were selected. 15 patients were biopsied under ultrasound guidance while other 15 patients were biopsied under CT guidance. Under aseptic measures, we localized the lesion on USG and measured its depth. After local anesthesia injection, geotek trucut semi-automated 18G biopsy needle is directed perpendicularly into the lesion under ultrasound guidance and multiple samples (6-8) taken at different depths and were preserved in biopsy jars filled with formalin and sent for histopathology. Post procedure ultrasound was done to rule out pneumothorax, which was later confirmed on chest x-ray.

Results

All statistical analysis was done with SPSS. After the diagnosis of mass lesion was made by CT chest with I.V contrast. Out of 30 patients, 15 patients were biopsied by CT guidance and 14 were proved to be positive out of which 7 were adenocarcinomas, 4 were non-small cell carcinomas not specified and 3 were benign tumours. Whereas in USG guided biopsies of 15 patients, 11 turned out to be positive out of which 6 were adenocarcinomas, 3 were squamous cell ca, 1 was mesothelioma and 1 was infectious (tuberculous). **(Fig-1)** statistical evaluation. The sensitivity of CT guided biopsy was 98% and specificity was 99% whereas sensitivity of USG guided biopsy was 90% and specificity was 96% by either modality. **(Fig-2)** sensitivity and specificity).In all USG guided biopsies time taken was less than 30 minutes and time taken by CT guided biopsy was more than 30 minutes. Pneumothorax was observed in 2 patients in CT guided biopsies whereas no complication observed in USG guided biopsies.

CT showing soft tissue density enhancing mass lesion abutting the chest wall on the right side.

Same patient or USG showing mixed echogenicity mass lesion with internal necrotic areas.

CT showing mixed density enhancing mass abutting right lateral chest wall.

Same patient showing hypoechoic mass lesion with air in it.

CT showing mixed density rounded enhancing mass abutting right lateral chest wall.

On USG same soft tissue mass which is hypoechoic.

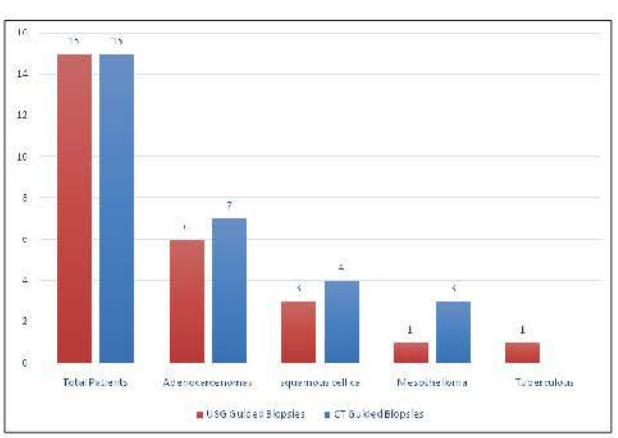

Fig-1: Statistical Evaluation of CT and USG Guided Biopsies.

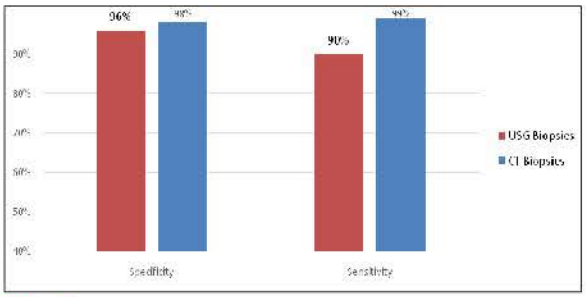

Fig-2: Sensitivity and Sensitivity of CT and USG Guided Biopsies

Discussion

While deciding which image guidance has to be preferred for peripheral lung and pleural biopsies, selecting safest, most feasible and effective method should be a priority. In our study, we compared the diagnostic yield of thoracic US with CT-guided trucut biopsies for lesions more than 10mm.30 patients were recruited. Out of 15 patients who underwent US- guided biopsy,11 turned out to be positive. Among other 15 patients who were biopsied under CT-guidance,14 turned out to be positive. Hence, sensitivity and specificity of CT-guided biopsy was 98% and 99% respectively whereas sensitivity and specificity of US-guided biopsy was 90% and 96%respectively. Our results were in agreement with a study conducted by Lichtenstein et al. (2004)[13] which showed 90% sensitivity and 98% sensitivity of TUS however Diacon et al. (2004)[14] showed lower diagnostic yield than our study stating it to be 85.5% for US-guided procedures. Similarly Liao et al. (2000)[16] showed diagnostic accuracy for malignant lesions reaching 92% with US-guided biopsy. Another study conducted by Khan RA[17] revealed sensitivity and specificity of 95.80% and 90% with US-guided biopsy procedures. Khosla R (2009)[18] did US-guided fine needle aspiration biopsy and established diagnosis in 89.5 % of patients in first attempt, disease being malignant in nature.Pneumothorax was most commonly occurring complication of CT-guided trucut biopsy with a reported frequency between 2.8% to 60%.[8,9,19,20] In our study the complication rate with pneumothorax was 6% in CT guided biopsy (over all 15%) which is comparable and fits within the range. Interaparenchymal hemorrhage is another know event which in our series did not occur in a single case. In the light of our study outcomes, we can suggest that TUS modality is an effective, feasible and affordable tool, in the expert hands, for the peripherally located abutting chest lesions. In our centre we are using it frequently and safely in the evaluation of such lesions. Although these data are compelling, small sample size is a limitation of our study, so we suggest a larger randomized trial to confirm our findings.

In conclusion, we found that, in expert hands, US-guidance is an effective, reliable, feasible, safer and more affordable modality for biopsing pleural as well as peripheral lung lesions abutting the chest wall as compared to CT-guidance, especially when the lesion size is more than 10mm. It is especially useful in primary and secondary health care where CT scan is not readily available at all setups.

Conclusion

TUS guided peripherally located abutting mass lesions more than 10 mm in size is very much comparable with CT guided biopsies of the lesions in terms of reliability accuracy and complications.

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Original Article

Effects of Aspartame on Relative Tissue Weight Index and Venous Drainage in Mice Liver

Shakeela Nazir, Attya Shahid, Nazia Siddique, Fatima Qaiser, Muhammad Amin and Ashiq Hussain

Objective: To determine the effects of increasing dose of aspartame on liver weight index, hepatic sinusoids, central& portal veins in mice liver.

Methods: Sixty albino mice were divided equally in four groups A,B,C and D (15 animals in each).Group "A" was the control group and the groups "B", "C" and "D" were experimental groups. All animals of experimental groups "B", "C" and "D" were given aspartame solution, through oral route, as 100, 250 and 500mg/kg/ body wt. respectively, once daily for 9 weeks. Control animals were given same amount of distilled water through oral route. Animals were sacrificed and dissected, liver was removed and weighed. Its microscopic as well as macroscopic examination was carried out to note any discernable abnormality.

Results: Aspartame reduced body weight, provoked statistical significant increase in liver weight index with increased dose in albino mice. Congestion and dilation changes were seen in sinusoids, portal and hepatic veins with increased dose and duration.

Conclusions: Aspartame is frequently used for weight reduction but with caution because excessive use leads to hepatic damage.

Keywords: aspartame, body weight index, liver weight index, hepatic sinusoids, portal vein, hepatic vein.

Introduction

Artificial sweeteners are taking special attention among food additives because it reduces sugar consumption and caloric intake.[1] They are also of primary importance as part of nutritional guidance for diabetes.[2] Aspartame is a commonly used non-caloric artificial sweeteners, which is a white, odorless, crystalline powder with molecular weight of 294.3 Daltons. It is the second most commonly used synthetic sweetener of low caloric value (4 kilocaloric/gram) with sweetening power 180-200 times greater than that of sucrose or table sugar.[3] It is frequently used in foods, medications, and beverages, notably carbonated and powdered soft drinks.[4] It has been found that aspartame is used in nearly 500 pharmaceutical products like sugar-free cough syrups, multivitamins, and 6000 food products including diet soft drinks, yogurt, candies, desserts, chewing gums, ice-creams and as a table top sweetener.[3,5] Aspartame Information Center estimated that more than 200 million people worldwide consumed aspartame and its consumption is increasing day by day.[6] The solubility of aspartame in water is dependent on pH and temperature, the maximum solubility is reached at pH 2.2 (20 mg/ml at 25°C) and the minimum solubility at pH 5.2 is 13.5 mg/ml at 25°C. In solution, when stored at temperatures ranging from 30 to 80°C, aspartame is progressively degraded into diketopiperazine.[7] It is therefore not usable in foods heated at higher temperature (cooking, sterilization etc.) At room temperature its stability is good at pH values of between 3.4 and 5 and maximum at pH 4.3. At pH below 3.4 the dipeptide is hydrolyzed and at a pH greater than 5, cyclization occurs with the formation of diketopiperazine. Diketopiperazine is a degradation product of aspartame which has no sweetening properties. The safety of aspartame has been assessed and recognized by a number of other national and international organizations including the Joint Expert Committee of Food Additives (JECFA) of FAO/WHO and, at EU level, by the Scientific Committee on Food. It was authorized by Directive 94/35/EC of the European Parliament and of the Council on sweeteners for use in foodstuffs (adopted on 30 June 1994) and its use is permitted in more than 90 countries.[8] The Acceptable Daily Intake (ADI) of aspartame for humans was established by FAO/WHO Joint Expert Committee on Food Additives (JECFA), Scientific Committee for Food (SCF), and Committee on Toxicity (COT) as 40 mg/kg/body wt./day and by FDA was 50 mg/kg/body wt./day.[5] The oral LD_{50} of aspartame in rats and mice was reported to be more than 10 g/kg/day. (RTECS, 2007 and 2010).Although its consumption is considered to be safe in acceptable daily intake ranges which were set by the United States

Food and Drugs Administration and other regulatory agencies, there are lots of controversies regarding its safety nowadays.[9] It may have unfavorable effect on health including glucose intolerance and failure to cause weight reduction.[10]

Method

Sixty albino mice of both sex 5-8 weeks old, weighing from 18-32 grams were procured from animal house of Veterinary Research Institute (VRI), Lahore. All the animals were examined thoroughly before the commencement of the experiment. Mice were housed in iron cages in animal house of Post Graduate Medical Institute, Lahore, under controlled conditions of temperature (25 ± 1 degree centigrade), humidity (70%) and light and dark cycles of 12 hours. They were fed on standard mouse diet and fresh tap water ad libitum.

After acclimatization of one week, weight of each animal was taken before the commencement of experiment. The mice were randomly distributed into 4 groups A, B, C and D, each comprised of 15 animals. Group "A" is labeled as control group and groups "B", "C" & "D" are labeled as experimental groups. Animals were placed in their respective cages which were labeled by tags.

Aspartame of Searle Pharmaceutical Company was used in this research in powder form. Aspartame solution was prepared by dissolving aspartame in distilled water. The dose of aspartame was calculated on individual basis for each mice according to the body weight. The oral recommended human therapeutic dose (HTD) of Aspartame is 20 mg/kg/body wt. Oral Acceptable Daily Intake (ADI) of Aspartame is 40-50 mg/kg/body wt and LD-50 is 4-5 g/kg/wt.Now due to five times increased metabolic rate in albino mice, the dose calculated was 100 (HTD X 5), 250 (ADI X 5) and 500 mg/kg/body weight. All experimental animals of groups "B", "C" and "D" were given aspartame solution, through oral route, as 100, 250 and 500mg/kg/ body wt. respectively, once daily for 9 weeks. Control animals were given same amount of distilled water through oral route.

During experimental period, all the animals were weighed on weekly basis, before and after sacrificing. Animals were sacrificed at the end of 9 weeks, 24 hours after administering the last dose of aspartame. Animals were sacrificed by anesthetizing them with chloroform. Animals were dissected, liver was removed and weighed. Its macroscopic examination was carried out to note any discernable abnormality.

Qualitative parameters

1. Sinusoidal congestion
2. Portal triad congestion
3. Central vein congestion

Quantitative parameters

Relative tissue weight index was calculated by the following formula. The data was entered and analyzed using SPSS 17.0 (Statistical Package for Social Sciences). Body weight of adult mice before and after dissection (g), liver weight and relative tissue weight index were described by mean±S.D. One-way ANOVA was applied to observe mean differences between and within groups. The difference was regarded statistically significant if P-value was <0.05. The qualitative data was analyzed statistically by Pearson's Chi square test.

Results

Qualitatively the central vein, portal triad and hepatic sinusoids in control group "A" didn't show any change while in experimental groups "B", "C" & "D" these structures were found to be significantly congested as these are dilated and filled with erythrocytes after 9 weeks of treatment **(Fig-1).** Animals in control group A showed a continuous statistically significant gain in body weight. While those in experimental groups (B, C & D) showed negative growth rate in body weight with increasing dose of aspartame **(Fig-2).** Decrease in weight gain %age in animals of groups C and D treated for 9 weeks give statistically significant results ($p<0.05$) with mean values of 48.16±13 & 45.9±30.8 respectively when compared with control group 74.92±18.4 **(Table-1).** While animals of group B treated with lowest dose give decrease in weight but statistically insignificant results ($p>0.05$) with mean values of 64.42±23.23 when compared with control groups. It showed that with increased dose of aspartame, animal body weight was decreased.

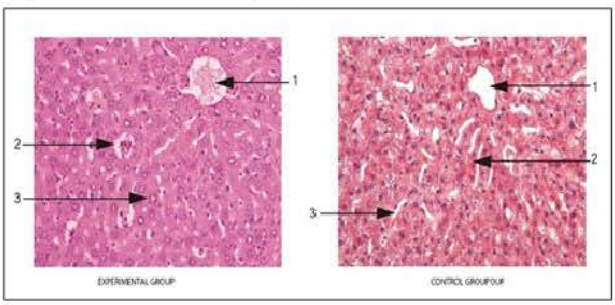

Fig-1: Photomicrograph showing normal hepatic lobule and congestion of central vein of liver, portal triad and hepatic sinusoids in experimental groups of albino mice.

Table-1: Changes in the body weight of Albino mice after oral administration of increasing doses of aspartame for 9 weeks.

Duration of Treatment	Animal weight in (gm) a start	Group A Control	Group B Control	Group C Control	Group D Control
9 Weeks	At Start	20.45±1.52	22±4.6	23.27±2.05	21±4.23
	At End	35.54±1.63	35.27±3.29	34.27±1.85	29.64±3.17
	Weight Gain %	74.92±18.43	64.42±23.23	48.16±13.1	45.9±3.85
P-Value			>0.05	<0.05	<0.05

Table-2: Changes in the liver weight, body weight and relative tissue weight index of Albino mice after oral administration of \ increasing doses of aspartame for 9 weeks.

Parameters	A Contol	B 100mg/kg	C 250mg/kg	D 500 mg/kg
Body weight (gm)	35.54±1.63	35.27±3.29	34.27±1.85	29.64±3.17
Liver weight (gm)	1.92±0.11	21.5±0.1	2.27±0.17	2.18±0.41
RTWI (%)	5.39±0.13	6.1±0.32	6.61±0.3	7.3±0.8
P-Value		P<0.000	P<0.000	P<0.000

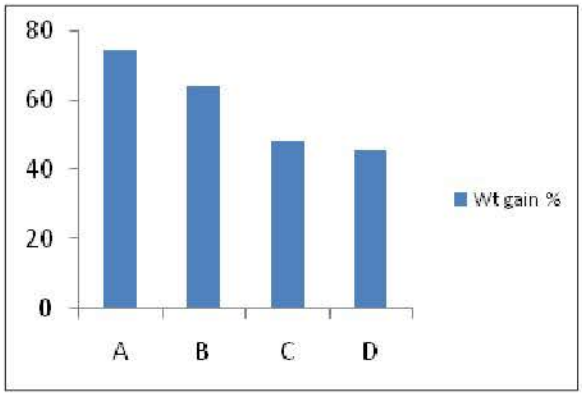

Fig-2: Effect of aspartame on mean weight gain % in different groups of albino mice.

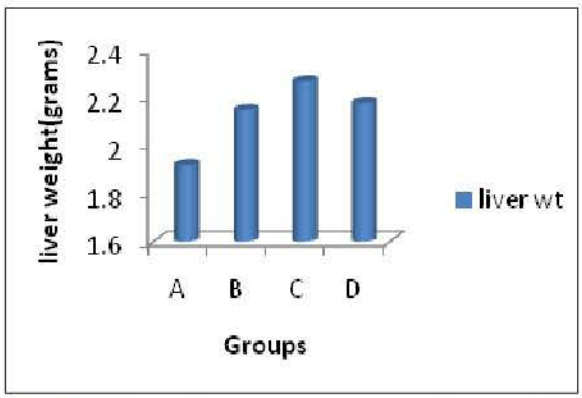

Fig-3: Effect of aspartame on mean liver weight (grams) in groups of albino mice.

The mean values of liver weight in groups A, B C and D were 1.92±0.11, 2.15±0.1, 2.27±0.17 and 2.18±0.41 respectively. These values showed statistically significant increase in liver weight when treated with increased dose of aspartame. The mean values of relative tissue weight index (RTWI) at the end of experiment showed considerable significant statistical increase (P<0.000) when compared between and within groups. The mean values of RTWI in groups A, B, C and D were 5.39±0.13, 6.1±0.32, 6.61±0.3 & 7.3±0.8 respectively **(Table 2).** Values are expressed as mean±standard deviation. For statistical significance experimental groups have been compared between groups and within groups. Values are expressed as mean ± standard deviation.

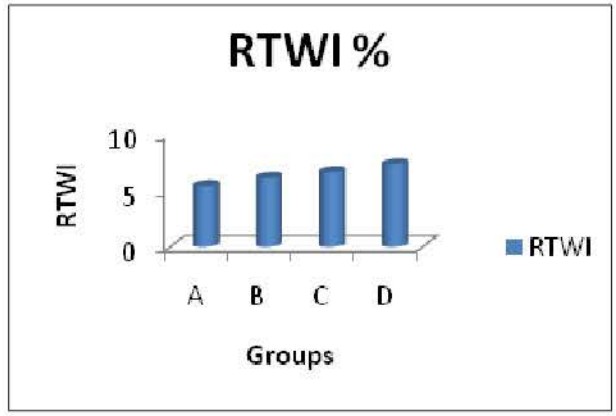

Fig-4: Effect of aspartame on mean values of relative tissue weight index (%) in different groups of albino mice.

Discussion

Sensitivity of people about general health has increased, that is why, to prevent caloric intake people are using artificial sweeteners. Several previous studies

revealed that the use of artificial sweeteners may entail some hazards to the users. Aspartame is one of the widely consumed artificial sweetener and most of the people are unaware about the consumption of the amount of aspartame they consume through various products. An important question is whether chronic uncontrolled consumption of aspartame is safe to humans or not. The present study highlights the effects of aspartame on body and liver weights in a dose of 500 mg/kg/BW after 9 weeks of consumption.[11] It was found in this study that aspartame induced statistical significant reduction in body weight when compared with control groups of mice. These results were consistent with the study conducted by Abdallah (2002), who reported a significant reduction in body weight of rats after oral administration of aspartame with a dose of 100 mg/kg/body weight for 14 weeks. He attributed this weight loss to reduce food consumption per day.[12] Blundell & Hill (1986) and Rolls (1991) also concluded that aspartame may lead to a reduction of food intake. This reduction in the appetite was responsible for the decrease in body weight. A decrease in the body weight in treated animals might be due to stress caused by elevated levels of phenylalanine, decreased level of norepinephrine and thus suppressing the appetite of the treated animals and decreasing their body weight due to lower energy intake. In another study, Blackburn et al., (1997) undertook a randomized, controlled trial in 163 obese women, to investigate the effect of aspartame during 16-week weight loss and one-year maintenance program. It was concluded that aspartame facilitate reduction and also maintenance of reduced body weight. Study by Raben (2002), provide evidence that supplementation with non-nutritive sweeteners like aspartame prevent intake of extra calories and thus prevent weight gain.[13] Likewise, De La Huntyet al., 2006, concluded that intense sweeteners are not appetite suppressants. Their ultimate effects only depend on their integration within a reduced energy diet. From above discussion it was not confirmed that aspartame reduced body weight either due to low caloric intake or by suppressing the appetite center due to its toxic metabolites effects.[14] Although body weight was decreasing but liver weight and relative tissue weight index were increasing. According to Robbins et al (2004) increase in liver weight and enlargement of liver may be associated with accumulation of fat in hepatocytes (fatty change). Mild fatty change may not affect the gross appearance. With progressive accumulation the organ enlarges, mostly this extreme enlargement is seen in alcoholics. Increase in liver weight may be due to acutely developing congestion. These reasons of liver enlargement were alarming sign of hepatic disease, indicated that aspartame is hepatotoxic. Further researches are required to evaluate the effects of aspartame in other tissues due to its toxic metabolites.

Conclusion

The present study demonstrated the reduction in body weight after 9 weeks' administration of aspartame in three different doses. Significant decrease in weight gain %age indicates that aspartame can be used in weight loss programme but with caution. But statistical significant increase in liver weight and relative tissue weight index indicating hepatic damage so excessive use of aspartame should be discouraged.

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Original Article

Attenuation of Hemodynamic Responses to Tracheal Intubation: Fentanyl Vs Lignocaine

Sana Siddiq, Saadia Khaleeq, Zulqarnain Butt, Tayyiba Wasim, Maqsood Ali and Kiran Riaz Khan

Objective: To compare mean hemodynamic response between fentanyl and lignocaine group after tracheal intubation under general anesthesia.

Methods: This randomized controlled trial study was carried out at Department of Anesthesiology, Jinnah Hospital, Lahore over a period of six months from 2nd June to 2nd December 2017. A total of 110 patients requiring GA with endotracheal intubation were included in this study. They were divided in two equal groups, Group F (Fentanyl) and group T (Lignocaine). Each group comprised 55 patients. Hemodynamic parameters were measured at baseline, before giving any premedication drug, then measured 1 minute after administration of premedication drug. Then Hemodynamic responses was measured soon after intubation, and then for every minute till 3 minute post intubation.

Results: Mean Heart rate during the time between groups was not significant till 23 minutes while at 3 minutes mean HR was significantly high in group T than group F (p=0.0005). Mean systolic blood pressure at 2 and 3 minute, was significantly high in group T as compare to group F. mean arial pressure was also significant between groups at 1,2 and 3 minutes.

Conclusions: It is evident that both lignocaine and fentanyl in are effective in attenuating the hemodynamic responses to tracheal intubation like heart rate and blood pressure.

Keywords: hemodynamic response, fentanyl, lignocaine, tracheal intubation, general anesthesia.

Introduction

Stress response under anesthesia has been universally recognized phenomenon, which may be in the form of endocrine or autonomic disturbance.[1] Translaryngeal intubation of the trachea stimulates laryngeal and tracheal sensory receptors, resulting in marked increase in the elaboration of sympathetic amines (adrenaline and noradrenaline). This sympathetic stimulation results in tachycardia and elevation in blood pressure. In normotensive patients, this rise is approximately 20 to 25 mm Hg; it is much greater in hypertensive patients.[2] These changes are the maximum at 1 minute after intubation and last for 5-10 mins.[1] A number of drugs have been used to reduce presser response.[3] Pretreatment medications are typically administered 2-3 minutes prior to induction and paralysis. These medications can be remembered by using the mnemonic LOAD (ie, Lidocaine, Opioid analgesic, Atropine, Defasciculating agents).[4] Fentanyl is an opioid analgesic with an analgesic potency of approximately 80 times that of morphine. The addition of fentanly to the thiopental used for induction has been advocated as a method of lessening the hypertensive response to intubation.[5] Lidocaine hydrochloride, an amino ethylamine local anesthetic and class IB antidysrhythmic drug, is acceptable for attenuation for the cardiovasucular response to intubation and also diminishes cough reflexes, dysrhythmias, and increase in intracranial and intraocular pressure.[6] Previous studies have shown that mean systolic blood pressure, 1 minute after tracheal intubation with in fentanyl and lignocaine group was 124.8+3. 10 and 128+5.06 respectively.[7] As the control of blood pressure and heart rate is of utmost importance in preventing the detrimental outcomes in patients with hypertension, IHD and intracranial HTN, there is a need for a safe and effective drug to attenuate the cvs responses to intubation. No randomized control trials regarding these two drugs i.e. fentanyl and lignocaine are available locally and need more research to justify their use in attenuation of mean hemodynamic response to tracheal intubation. The result of present study will helps us determine a better premedication drug among these two and use of that in future will improve quality of anesthesia for patients undergoing tracheal intubation under general anesthesia.

Methods

This randomized controlled trial study was carried out at Department of Anesthesiology Jinnah Hospital

Lahore over a period of six months from 2nd June to 2nd December 2017. A total of 110 patients requiring GA with endotracheal intubation were included in this study. They were divided in two equal groups, Group F (Fentanyl) and group T (Lignocaine). Each group comprised 55 patients. Patients ages between 18 and 65 years, physical status classification l and II, mallampatti class I and II and scheduled for elective surgery, requiring GA with endotracheal intubation were included. Those patients who have severe co-morbidities, full stomach, ASA class III and above, known allergy to drug, expected difficult intubation and airway abnormalities were excluded from the study. Inside operating room, after applying routine non-invasive monitors (blood pressure monitor, pulse oximeter, ECG monitors) IV assess was secured and the infusion of normal saline 0.9% 5ml/kg/hr was started. At minute zero, study drug fentanyl 2 microgram/kg or lignocaine 1.5 mg/kg as per group was injected over 20 seconds. Then the patient was oxygenated with 100% oxygen. At minute 3, IV thiopental Na 5mg/kg was administered in incremental doses until loss of eyelash reflex occurred. This was followed by injection atracurium 0.15 mg/kg over 20 seconds. Patient ventilated with oxygen and volatile anesthetic agent i.e isoflurane upto 5 minutes. Then at minute 5, patients were intubated. Tube was fixed and secured, after minute 10 only, surgery will be allowed to commence. Hemodynamic parameters HR, SBP, DBP and MAP will be measured at baseline, before giving any premedication drug, then measured 1 mintue after administration of predmedication drug. Then Hemodynamic responses was measuered soon after intubation, and then for every minute till 3 minte post intubation. The data was analyzed in SPSS-16. Student T test was applied to compare mean HR in both groups taking p value less then 0.05 as significance.

Results

There were 63 (57.3%) male and 47 (72.7%) female. Mean heart rate during time between groups was not significant till 2 minutes while at 3 minutes mean HR was significantly high in group T than group F (p=0.0005). Mean systolic blood pressure was not significant between groups at BL, zero, and 1 minute while at 2 and 3 minute, it was significantly high in group T as compare to group F. Mean diastolic BP was also observed significant at 1 , 2 and 3 minutes. Mean arterial pressure was also significant between groups at 1 2 and 3 minutes **(Tables 1-4).**

Table-1: Comparison of mean heart rate between groups.

Time	Group F (n=55)	Group T (n=55)	P-Value
Baseline	84.85±7.62	84.85±7.62	0.81
After drug administration	83.98±8.28	83.98±8.28	0.31
0 min	87.49±7.96	87.49±7.96	0.69
0 min	85.82±8.25	85.82±8.25	0.85
1 min	84.65±8.14	84.65±8.14	0.35
2 min	95.38±15.47	95.38±15.47	0.0005
3 min	84.85±7.62	84.85±7.62	0.81

Table-2: Comparison of systolic blood pressure between groups.

Time	Group F (n=55)	Group T (n=55)	P-Value
Baseline	121.27±8.29	122.00±6.66	0.61
After drug administration	119.31±12.14	122.00±10.89	0.22
0 min	121.38±9.60	122.65±10.14	0.50
0 min	116.93±9.58	118.45±9.45	0.41
1 min	117.91±10.40	123.62±10.84	0.006
2 min	124.00±1074	13047±11.84	0.003
3 min	121.27±8.29	122.00±6.66	0.61

Table-3: Comparison of diastolic blood pressure between groups.

Time	Group F (n=55)	Group T (n=55)	P-Value
Baseline	81.67±6.41	82.45±7.19	0.054
After drug administration	75.22±6.67	75.47±7.41	0.85
0 min	72.76±8.00	73.09±7.63	0.82
0 min	67.02±9.03	74.82±9.07	0.03
1 min	67.15±7.45	74.96±10.31	0.0005
2 min	76.04±7.175	84.89±9.66	0.0005
3 min	81.67±6.41	82.45±7.19	0.054

Table-4: Comparison of mean arterial pressure between groups.

Time	Group F (n=55)	Group T (n=55)	P-Value
Baseline	90.80±9.18	93.51±9.54	0.13
After drug administration	84.35±9.34	85.49±10.17	0.28
0 min	78.65±9.17	81.40±12.17	0.18
0 min	79.51±8.73	83.45±9.57	0.029
1 min	79.24±8.73	84.71±9.44	0.002
2 min	81.40±9.87	85.44±9.84	0.03
3 min	90.80±9.18	93.51±9.54	0.13

Discussion

Endotracheal intubation and laryngoscopy is associated with rise in blood pressure, heart rate and cardiac dysarrythmias.[6] These above mentioned effects may be short lived but they may have adverse effects in high risk patients like, those with cardiovascular diseases increased intracranial pressure or anomalies of cerebral vessels.[7,8]

Fentanyl acts at opioid receptors and predominantly acts on u receptors.[9,10] Fentanly brings haemo-dynamic stability during preoperative period by its action on cardiovascular and autonomic regulatory areas. It decreases sympathetic tone and increases parasympathetic tone. Fentanyl inhibits pituitary adrenal response directly or indirectly via hypothalamus. It attenuates the response at 2ug/kg IV given before laryngoscopy and intubation. Ooptimal time of administration is 5 minutes before laryngoscopy and intubation.[11,12]

Lignocaine blocks the sodium channels in the cell membranes of the heart and reduces the rate of the rise of the action potential and hence the conduction velocity above all the His Purkinje system and in the artial and ventricular musculature.

Some studies note a response of intravenous lignocaine in blunting rises in pulse, blood pressure, intracranial and intraocular pressure. Studies have discussed the possible mechanisms to account for these observation with IV lignocaine. These include a direct myocardial depressant effect a peripheral vasodilating effect and finally an effect on synaptic transmission.[13] A review on "Prophylactic lidocaine of 1.5 mg/ kg given intravenously 3 minutes before intubation is optimal. No studies document any harmful effects of prophylactic lidocaine given preintubation.[14,15] In this study the average age of the women was 29.45±9.62 years (range:18-60). In Gupta and Tank (1) study mean age of patients was 31.3±2.38. Mean Hear rate during the time between groups was not significant till 2 minutes while at 3 minutes mean HR was significantly high in group T than group F (p=0.0005) in present study. Wilson et al.,[16,17] showed that irrespective of the timing of administration of injection of lignocaine 2,3 or 4 minutes beofe tracheal intubation, there was a significant increase in heart rate of 21-26% in all groups. Mollick et al.[18,19] observed that intravenous lignocaine with pethidine did attenuate the sympathetic response to laryngoscopy and endotracheal intubation which came down to base line before 5 mintue after intubation. But the group of patients which was treated only with lignocaine, their sympathetic response did not come down to base line at 5 minute after laryngoscopy and endotracheal intubation. Similar to our observation Bachofen M[2] too reported that fentanyl showed a significant pressure-lowering action persisting over the whole observation period in all patients while no significant effect of lidocaine on the pressure response could be observed. Gupta and Tank[20,3] showed that fentanly in bolus dose of 2 ug/kg before induction of anesthesia are effective in attenuating the hemodynamci responses to laryngoscopy and endotracheal intubation like heart rate and rate pressure product.

Low doses of fentanyl were employed because a large dose was lead to muscular rididity, bradycarddia, nausea and vomiting. Large doses may also cause postoperative respiratory depression; especially in surgery with short duration of less than 1 hour.[12,13] McClain et al., reported apnoeic episodes in four out of seven patients who received 3.2-6.5 ug/kg fentanyl.

In present study mean systolic blood pressure was not significant between groups at BL, zero and 1 minute while at 2 and 3 minute, it was significantly high in group T as compare to group F. Mean diastolic BP was also observed significant at 1, 2 and 3 minutes. Mean Arial pressure was also significant between groups at 1 2 and 3 minutes. Malde and Sarode[21] concluded that "given 5 minutes prior to intubation, lignocaine (1.5 mg/kg) and fentanyl (2 ug/kg) both attenuated the rise in pulse rate, though fentanly was better". Kobayashi also reported intubation conditions were better in the fentanyl group than in the lignocaine group.

Conclusion

From the present study it is evident that both lignocaine and fentanyl in are effective in attenuating the hemodynamic responses to tracheal intubation like heart rate and blood pressure. Fentanyl 2 microgram/kg i.v. bolus provides a consistent, reliable and effective attenuation as compared to lignocaine. It is advisable and safe to use fentanly in patients who are prone to have exaggerated responses of cardiovascular system during intbation.

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Original Article

Nocturnal Sound Intensity Levels in the Gulberg Area of Lahore and Their Possible Effects on Sleep And Resulting Health Hazards

Shiraz Aslam, Sumira Qambar Bokhari, Qambar M. Bokhari, Farooq T. Khan, Tariq Shaikh and Shahid H. Warris

Objective: To ascertain the night time noise pollution levels in specific areas in Lahore which can lead to sleeping disorders and other health issues.

Methods: A professional sound pressure meter was used to measure noise levels in specified areas in a residential area of Lahore at the time which is considered as the hour for rest and sleep.

Results: The three areas of Gulberg, Lahore which were monitored were found to have unacceptable night time sound intensity levels (average 43.9dBA). These levels, according to standards issued by international organizations can lead to health issues if not reduced.

Conclusions: It is important to check the present night time noise levels and to try to bring them down for a quiet night's sleep. If the sleep patterns are disturbed by a constant or even an occasional loud noise, this can lead to behavioral, psychological and pathological problems in the sleep deprived person.

Keywords: noise, transportation, sleep initiation and maintenance disorders.

Introduction

It is paramount that for a quiet and restful sleep there is darkness, a comfortable room temperature and most important of all- silence. Dwellings near busy areas such as airports often complain of irregular sleeping patterns. This of course leads to ailments like headaches and a 'nervous stomach'. It is known that an occasional noise breaking the silence is found to be more annoying than a continuous sound in the background. It is seen that low frequency sounds (60Hz) are more disturbing at night especially which may have a major component in traffic noise. This lies within the chest resonance frequency as well (30-90 Hz). These are also the most difficult to insulate against as well. It's like a heavy dumper, filled up above its allowance with a heavy load like stones or rocks pulled by a huge engine and broad tires on weak asphalt will produce a low frequency sound. More the intensity at this frequency more will be the annoyance level. If the speed of the dumper truck is increased twofold there will an increase of about 10 dB in the maximum noise level. It is interesting to note that an increase of only 3 dB will result in 1.23 times increase in loudness in volume and will 'double' the sound intensity.[1] The decibel is the logarithmic unit used to measure the sound level. Thus, it is common sense to try to live away from a busy road in order to lower the intensity of sound one is exposed to. Double glazing the windows will have the same effect. Therefore, if the source of sound is 5metres from the window and producing the noise at 80dB, then because of double glazed windows the sound is reduced to 50dB inside the room. This is an appreciable attenuation in the intensity of sound. Because the dB scale is a logarithmic scale, this 30dB decrease in the sound value means that the sound intensity is decreased by a factor of 1000 by double glazing a window which is equivalent to a decrease in perception of sound on the other side of the window by a factor of eight. This attenuation in the noise level is a huge noise benefit.[2-4] The 'dBA' is a measure of sound pressure level in decibels as indicated by a sound level meter which complies with British Standard BS EN 61672-1:2013 Electro-acoustics Sound Level Meters Part-I Specifications".[5,6] Research has shown that thin layer porous asphalt can reduce noise from passenger vehicles by between 3-4dB compared to non-porous surfaces. Also reducing the speed of a heavy dumper truck from 90 to 60 Km/h can reduce the sound pressure level by 4dB.[7]

Methods

The device used was NEDA 1604 IEC 6F22 (Universal supplies LTD). This is a professional sound pressure meter with a special wind or breeze filter. The 'A' weighted sound pressure levels were measured. The day and time of the week selection was random. Time slots from 12 to 1am and 2 to 3am were separately written on a piece of paper and folded so as not to be visible and someone was asked to retrieve one paper blindly from a bowel. A similar exercise was done for the selection of the day of the week for the monitoring. Saturdays and Sundays were excluded as

major working days were preferred to be measured for annoyance levels. Noise intensity was measured at 2AM in the morning from three blocks or areas of Gulberg in Lahore (Main Gulberg, Gulberg-2, and Gulberg-3). Five readings were taken from each block. These readings were at different roads of the particular Gulberg area. The selection of the roads was random. An (arbitrary) duration of 3 minutes was decided for the final reading to be taken at each spot. It was made sure that the monitoring vehicle was switched off. The highest sound intensity level during those 3 minutes was recorded. The results were tabulated.

Results

In the present study **(Table-1)**, the overall average in all areas of Gulberg came out to be 43.9 dBA. The noisiest of the Gulberg areas was the Gulberg-2 area, while the quietest was the Main Gulberg area. According to the European standards steering group any noise level above 42dB can result in 'environmental insomnia'. There is a difference of almost 2dB which is basically an increase in loudness by a factor of 1.26 (Acoustic Ratio of 44/42). This 2dB difference will be difficult to detect and for all intents and purposes an assumption can be established that the values obtained in Gulberg in Lahore are quite similar to levels found to be at the threshold over which 'environmental insomnia' can set in. However, a slight increase over this level, (with a difference of 3dB) will double the sound pressure level. Thus it is understandable how things start to get worse if we add electricity generator noises from even a few houses in this locality. This might be the reason why the sound intensity levels are a little elevated in the Gulberg area 2, as the houses are large and might have big generators as well. The Gulberg-II area also has in it the main commercial area, the Main Market nearby which is busy through the night. However, in the Gulberg area 3, the Gulberg main Boulevard is nearby and can be the reason why the sound pressure level is a bit high there. It was also noted during the measurement of the noise levels in Gulberg 3, site 5 (Hali Road), that passage of heavily laden dumper trucks (with construction material) raised the noise levels occasionally to 84dBA at a distance of 5 meters. Similarly, a car horn could raise the noise level to 88dBA. Whereas, these levels especially at Main Gulberg, Lahore might be acceptable for big houses where, presumably the bedrooms are located at an appreciable distance from the front gates with intervening walls of other rooms but if there is a room located 10 meters or so from the road where these occasional dumpers pass then it is understandable how one can end up having a broken night's sleep with chronic health issues setting in gradually.

Table-1: Measurements at different sites of three areas of Gulberg in Lahore at 2AM.

Time of readings, 2am	Site in Gulberg Areas mentiond	DBA	Average at the three individual areas (dBA)
Area 1 main Gulberg, Lahore	Site 1	44	
	Site 2	41.6	
	Site 3	42	
	Site 4	46	
	Site 5	41.7	**43.06 (Area-I)**
Area 2 Gulberg-II, Lahore	Site 1	41.7	
	Site 2	43	
	Site 3	48	
	Site 4	53	
	Site 5	42	**45.54 (Area 2)**
Area 3 Gulberg-III Lahore	Site 1	42.5	
	Site 2	41.5	
	Site 3	45.1	
	Site 4	44.5	
	Site 5	42.6	**43.24 (Area 3)**
Average of Total		43.9	

Discussion

The WHO Regional Office for Europe' established a Steering Group and a Guideline Development Group (GDG) who were tasked to recommend the noise guidelines for Europe. Survey results held in the Netherlands reported that the main source of sleep disturbance during the night was from road traffic rather than air, rail or construction noises. The GDG found out that the night time noise level due to traffic should be reduced below 45dB level. In their research they observed that traffic noise above this level resulted in adverse effects on the sleep pattern of the residents. About 3% of residents included in their studies were highly sleep-disturbed at a noise level of 45.4 dB. It is observed that three groups are most vulnerable when it comes to sleep disturbance, namely the children and the elderly. The third group, are the workers on a shift basis. Their sleep patterns are already disturbed and so feel the effects of sleep

pattern of the residents. About 3% of residents included in their studies were highly sleep-disturbed at a noise level of 45.4 dB. It is observed that three groups are most vulnerable when it comes to sleep disturbance, namely the children and the elderly. The third group, are the workers on a shift basis. Their sleep patterns are already disturbed and so feel the effects of sleep deprivation more. Shift work disorder is a circadian rhythm sleep disorder. [8]

The European steering group also found out that the residents started to get sleep pattern alterations at a noise level above 35dB. This resulted in alterations in stages of sleep and people often complained of a broken sleep in the mornings. If the traffic noise was above 40 dB, then people reported taking sleeping pills. Anything above 42dB, effects of clinical 'environmental insomnia' crept in, where environmental chemicals or toxins make it difficult for the person to get down to sleep. [9]

Environmental noise disturbs sleep and thus there is a separate category of sleep disturbances created by competent authorities responsible for classifying sleep disorders. According to the American Academy of Sleep Medicine, environmental sleep disorder is a "sleep disturbance due to a disturbing environmental factor that causes a complaint of either insomnia or daytime fatigue and somnolence. Secondary deficits may result, including deficits in concentration, attention, and cognitive performance; reduced vigilance, daytime fatigue, malaise, depressed mood and irritability." The elderly patients are more severely affected. [10] The diagnostic criteria for environmental insomnia which is classified under 'other insomnias' consists of sleeplessness, fatigue during the day, which is caused by an environmental factor whose physical properties cause sleep disturbance which is not attributable to any other sleep disorder. [11]

Insomnia due to traffic noise may produce a number of bad effects on the body including, behavioral or psychiatric changes as well as clinically evident organic diseases like hypertension, obesity, heart problems and pre mature mortality.

An interesting experiment by researchers in USA in 2004, allocated 10 participants to a sleepless group where they were not allowed to sleep for 88 continuous hours while the other group of 10 were allowed (randomly) to sleep for 8.2 h (control) or 4.2 h (partial sleep deprivation) only. C reactive protein was recorded on a regular basis. CRP was seen to be elevated in the total or partial sleep loss group. This is a known marker for inflammation and is a significant predictor of cardiovascular morbidity. [12]

A further group of US researchers reported in the Lancet (1999), that the effects of sleep deprivation on the body were found to be similar to age related endocrine (thyrotropin function) or carbohydrate effects (carbohydrate metabolism), but in addition, these effects may be more pronounced in the elderly group. [13] The European centre for environment and health, reports that a hormone called Leptin is also decreased during sleep deprivation. This regulated energy hemostasis and fluctuates in relation to sleep. A decrease in Leptin will increase appetite and weight gain and will ultimately lead to obesity.

Another aspect of the human physiology that sleep deprivation strongly affects is the hypophysis-pituitary axis. This axis is affected by external stress to the body or the mind. Thus, with prolonged stress, in the shape of chronically disturbed sleep, there might be increased cortisol levels which can predispose the human to cardiovascular diseases. [14] Researchers have reported that the amygdala detects danger signals the fastest in the brain and thus even normal but occasional sharp sounds like the airplane over head or the siren of an ambulance or a sudden mobile ring at night during sleep might be seen as 'danger signals' and result in the release of stress hormones. An elevated level of these stress hormones over prolonged periods can give rise to cardiovascular disease especially if the daytime immission level exceeds 65 dB (A. [15]

Stress reactions are common in people who don't get good night's sleep and can lead to cardiovascular events. It is also suggested that the immune system might be suppressed as well in sleep deprived people. In a socio-acoustic survey by Hatfield et al, in 2002, sleep deprivation, sleep cycle and the immune response had a strong association with noise exposure.

Van Kempen, et al, looked at a meta-analysis of 61 studies and concluded that there was an association between road traffic noise and the *prevalence* of ischemic heart disease (IHD). [16] Hearing loss is possible if the ear is exposed to sounds above 87 decibels for daily or weekly personal noise exposure for at least 8 hours a day. [17] The GDG in Europe considered that noise exposure level beyond 80 dB during 40 years of working a 40 hour work week can give rise to permanent hearing impairment.

A lack of proper night's sleep can have numerous effects on the body. A single night's bad sleep pattern can make the person sleepy the next morning but can impair the concentration span as well, but these effects will be short term as long as the sleep disturbance was transient.

for adults lack of sleep can lead to psychological disturbances ranging from a bad mood the next morning to a serious motor car accident due to a lack of concentration at the wheel. At the workplace, the person may not be able to perform as well as he or she could have, had they had a good night's sleep.

Children can be affected just as bad not being able to focus and concentrate on studies well leading to poor performance in the class room and in their exams. If this pattern of a lack of sleep is a prolonged one then, it can lead to major psychiatric diseases like anxiety, depression, schizophrenia, bipolar disorder, and attention deficit hyperactivity disorder (ADHD). Solace from sleeplessness of a victim might be sought in mind altering drugs. Drug addiction thus is a serious consequence of long term sleep disturbance.[18] Children with ADHD, have a major problem with sleep disturbances (25-50% of the children) and similarly, people with sleep problems end up with anxiety disorders 27% of the time, and are result with depression 69% of the time. It is well documented that (50% to 80%) of general psychiatric patients have chronic sleep problems.[19]

A cohort of people where interviewed twice in 1987-88 and then in 1990 regarding sleep disturbances and it was found that sleep disturbances and depression were commonly found together in people. Insomniacs were thus more prone to getting depression.[20]

Conclusion

For People living on the side lines of Data Darbar and the Ravi Road, where the noise intensity measured in an earlier study (by the present author) was found to be 90 dB, it is understandable how the noise can be an issue with the dwellers inside. The people living on even the first floor, 10 to 12 feet above ground level, can be in the line of the sound pressure wave, unhindered by people, cars or even trees. There is no concept of double glazing the window at these sites as well. It will be interesting to conduct another study on the views of these dwellers living on the first floor and if they have become used to the noise and has adaptation masked the outside sounds. It is imperative that a 'noise map' of Lahore be plotted in order to firstly, have information about the scale of the noise problem and secondly, to organize and plan acceptable noise levels on Lahore roads especially during the night time.

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