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Editorial

Prostate Enlargement and Surgery

Mohsin Masud Jan

Editor

The prostate is a walnut-sized gland located between the bladder and the penis. The prostate is just in front of the rectum. The urethra runs through the center of the prostate, from the bladder to the penis, letting urine flow out of the body. The prostate helps make some of the fluid in semen, which carries sperm from your testicles when you ejaculate.

By the time you reach age 40, your prostate might have gone from the size of a walnut to the size of an apricot. By the time you reach 60, it might be the size of a lemon. Because it surrounds part of the urethra, the enlarged prostate can squeeze that tube. This causes problems when you try to pee. Typically, you won't see these problems until you're 50 or older, but they can start earlier. You might hear a doctor or nurse call this condition benign prostatic hyperplasia, or BPH for short. Rest assured, it is not cancerous.

Who Might Get an Enlarged Prostate?

BPH is common and cannot be prevented. Age and a family history of BPH are two things that increase the chances you might get it. A few stats on that:

- Some 8 out of every 10 men eventually develop an enlarged prostate.
- About 90% of men over age of 85 will have BPH.
- About 30% of men will find their symptoms bothersome.

The signs and symptoms include:

- Your bladder doesn't empty completely after you pee
- You feel the need to go out of the blue with no sensation of build-up
- You may stop and start several times
- You have to strain to get any flow going

It's important that you see your doctor if you have early symptoms of BPH. Although rare, it can lead to serious problems such as kidney or bladder damage.

A larger prostate doesn't mean you'll have more or worse symptoms. It's different for each person. In fact, some men with very large prostates have few, if any, issues. But your doctor should be aware either way.

The main treatments are:

- lifestyle changes
- medication
- catheters
- surgery and other procedures

Lifestyle changes:

Drink fewer fizzy drinks and less alcohol, caffeine and artificial sweeteners. Drinking less in the evening
Remember to empty your bladder

Double voiding: Double voiding involves waiting a few moments after you have finished passing urine before trying to go again. It can help you empty your bladder properly. But take care not to strain or push.

Checking your medicines: Check with your doctor whether any medicines you take, such as

antidepressants or decongestants, may be making your urinary symptoms worse.

Eating more fruit and fibre. Using pads or a sheath

Bladder training: Bladder training is an exercise programme that aims to help you go for longer without peeing and hold more pee in your bladder.

Medicines: If lifestyle changes don't help or aren't suitable for you, you may be offered medicine.

Alpha-blockers: Alpha blockers relax the muscle in the prostate gland and at the base of the bladder, making it easier to pass urine. Commonly used alpha-blockers are tamsulosin and alfuzosin.

Anticholinergics: Anticholinergics relax the bladder muscle if it's overactive.

Alpha reductase inhibitors: 5-alpha reductase inhibitors shrink the prostate gland if it's enlarged. Finasteride and dutasteride are the two 5-alpha reductase inhibitors available.

Diuretics: Diuretics speed up urine production. If taken during the day, they reduce the amount of urine produced overnight.

Desmopressins: Desmopressins slow down urine production so less urine is produced at night.

Alternative treatments: Your doctor shouldn't offer you homeopathy, herbal treatments or acupuncture to treat urinary symptoms.

This is because there isn't enough reliable evidence about how well they work or how safe they are.

Herbal treatments may also cause side effects or interact with other medicines.

Catheters: If you continually have trouble peeing, a condition called chronic urine retention, you may need a catheter to drain your bladder.

A catheter is a soft tube that carries urine out of the body from the bladder. It can be passed through your penis, or through a small hole made in your tummy above the pubic bone. You may be recommended a removable catheter or a catheter that stays in your bladder for a longer period of time.

Surgery and other procedures: Most men with urinary symptoms don't need to have surgery, but it may be an option if other treatments haven't worked.

Transurethral resection of the prostate (TURP):

Open prostatectomy

Prostatic urethral lift (PUL) implants, Cystoplasty

Prostate artery embolisation, Botulinum toxin

Implanted sacral nerve root stimulation,

Urinary diversion, Water ablation

Now, keeping in mind, we might not be seeing some of these latest treatments in Pakistan for some time, we still have a lot of options over here for the successful treatment of BPH. And, that being said, most of the times lifestyle changes are more than sufficient for successful management of BPH.

Evaluation of Zinc Levels in Stroke Patients

Syed Qaiser Hussain Naqvi¹, Shamsuddin Shaikh² and Jawaaid Hussain Lighari³

ABSTRACT

Objective: To evaluate the role of Zinc in patients of stroke.

Study Design: Observational study

Place and Duration of Study: This study was conducted at the Medical Ward and Out Patient's Department of Peoples Medical College Hospital, Nawabshah from January 2016 to December 2016.

Materials and Methods: The current observational study was conducted on 200 cases comprising of 100 control cases and 100 consecutive patients suffering from stroke fulfilling the criteria. The patients were collected from medical ward and out patient's department of Peoples Medical College Hospital as well as private clinic. After taking informed consent, the demographic and clinical data were collected on a proforma designed for the study. Serum Zinc level was evaluated in all cases of both groups and results were tabulated.

Results: Out of 100 cases of stroke, 68 (68%) were male, the mean age of patients was 62 + 16 years, among these 100 cases 73 (73%) having ischemic stroke and 27 (27%) having haemorrhagic stroke. The control group consists of 100 cases of normal healthy population having serum Zinc level in normal range, comprising of 70 males and 30 females with a mean age of 58+14 years. The serum Zinc level was evaluated in all cases of stroke. In ischemic stroke group 34 (46.6%) patients, and in haemorrhagic group 9 (33.3%) cases show serum Zinc level < than 65mcg/dl. The normal serum level (reference range) considered was 65-150 mcg/dl.

Conclusion: A low Zinc level was observed in 43 (43%) of cases, among these majority belongs to ischemic stroke group, suggesting that hypozincemia is a possible contributing factor in patients of stroke.

Key Words: Serum Zinc Level, Hypozincemia, Ischemic Stroke, Hemorrhagic Stroke

Citation of articles: Naqvi SQH, Shaikh S, Lighari JH. Evaluation of Zinc Levels in Stroke Patients. Med Forum 2018;29(10):2-4.

INTRODUCTION

Stroke is a major cause of mortality worldwide especially in developed countries¹. WHO has estimated that in the year 2002, about 5.5 million peoples died because of stroke and the South East Asian countries shares about 20% of these death². The treatment of stroke is expensive³ with high mortality or with major or minor morbidity and the disease has a psychological, functional and financial impact not on the family but also on the society^{4,5}.

A reduction in the incidence of stroke is possible by prevention of various modifiable risk factors⁶. The deficiency of Zinc (Hypozincemia) is one of these modifiable risk factors resulting in stroke⁷, the Zinc deficiency results in thickening of blood vessel wall, hypertension, aneurysms, cerebrovascular accidents and other problems of cardiovascular system^{8,9}.

The hypozincemia also contributes atherosclerosis and increasing the risk of stroke^{10,11}. The integrity of the blood brain barrier is contributed by Zinc, protecting the brain from various toxic agents and hazardous foreign compounds¹², so hypozincemia results in injury to neurons and can exaggerates the injury caused by ischemia and metabolic insult¹³. It is also documented that elevated Zinc levels in blood are harmful for health and can result in neuronal death during brain ischemic injury and neuronal apoptosis^{14,15}.

MATERIALS AND METHODS

The current observational study was conducted during January 2016 to December 2016, on 200 cases comprising of 100 control cases and 100 consecutive patients suffering from stroke. The patients were collected from medical ward and out patient's department of Peoples Medical College Hospital and also private clinic. The inclusion criteria was all male and female patients of age >40 years willing for participation and had sustained stroke confirmed on CT scan. Patients having any neurological disorder, psychiatric illness, haematological disorder, history of head injury, intracranial space occupying lesion were excluded from the study. Patients on Zinc containing nutritional supplement were not recruited.

After taking informed consent, the demographic and clinical data were collected on a proforma designed for

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the study. The CT scan of brain was performed in all cases to rule out any comorbidity and to determine the type and extent of the lesion. Serum Zinc level was evaluated in all cases and results were tabulated.

RESULTS

The study was conducted on 200 cases, comprising of 100 cases as control group and 100 cases of stroke, out of which 68 (68%) were male, the mean age of patients was 62 + 16 years (Table.1), among these 100 cases 73 (73%) having ischemic stroke and 27 (27%) having haemorrhagic stroke. The control group consists of 100 cases among normal healthy population having serum Zinc level in normal range, comprising of 70 males and 30 females with a mean age of 58+14 years. The serum Zinc level was evaluated in all cases of stroke. The normal serum level (reference range) considered was 65-150 mcg/dl¹⁶. In ischemic stroke group 34 (46.6%) patients, and in haemorrhagic group 9 (33.3%) cases show serum Zinc level < than 65mcg/dl.

Table No. I: Serum Zinc Level in Study Population

Group	Total No of Cases		Age (yrs)	Male/ Female n=100	No. of Cases Having Zinc Level > 65mcg/ dl	No. of Cases Having Zinc Level < 65mcg/ dl
Control	100		58+ 14	70/30	100 (100%)	00 (00%)
Ischemic	100	73	62+ 16	68/32	39 (53.4%)	34 (46.6%)
Haemorrhagic		27			18 (66.7%)	09 (33.3%)

DISCUSSION

In this study serum Zinc level was evaluated in 100 cases of stroke patients compared with control. Among these cases of stroke majority were of ischemic attack. The mean age of these patients was 62+16, this finding was in consistent with the results of Toth et al, who describes that in the walls of cerebral vessels there is exacerbation of hypertension based production of reactive oxygen species with activation of matrix metalloproteinases (MMPs), due to this fact the blood vessels are more prone to develop high pressure induced injury¹⁷. Out of these 100 cases of stroke, hypozincemia (low serum Zinc level) was present in 43 (43%) cases that show serum Zinc level <65mcg/ dl, among these 34 belongs to ischemic group that also show poor functional status at discharge. This finding was also claimed by other workers¹⁸. In haemorrhagic stroke cases we found low Zinc serum concentration in 09 patients, which was in agreement with the study of Kardaset al, who indicated that the serum concentration

levels of Zinc and heavy metals leads to acute haemorrhagic stroke¹⁹. Alteration of Zinc level in brain may influence neurotransmission in Zinc containing glutaminergic synapses. Therefore, dietary Zinc deficiency may influence Zinc homeostasis in the brain, resulting in brain dysfunction such as stroke²⁰.

CONCLUSION

We observe low Zinc levels in 43 (43%) of cases, among these majority belongs to ischemic stroke group, suggesting that hypozincemia is a possible contributing factor in patients of stroke. Further Zinc supplements and fortified food material should be promoted to reduce the risk of stroke. This is a limited study needs further workup in support of the conclusion.

Author's Contribution:

Concept & Design of Study: Syed Qaiser Husain Naqvi
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 Data Analysis: Jawaid Hussain Lighari
 Revisiting Critically: Syed Qaiser Husain Naqvi, Shamsuddin Shaikh
 Final Approval of version: Syed Qaiser Husain Naqvi

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A Cytological Analysis of Breast Disease

Abdul Rauf and Muhammad Adnan Zaman

ABSTRACT

Objective: To study the cytological pattern of disease in females presenting with breast lumps/ swellings.

Study Design: A retrospective / descriptive study

Place and Duration of Study: This study was conducted at the Pathology Department, Nawaz Sharif Medical College, University of Gujrat from Jan 2015 to Dec 2017.

Materials and Methods: It consisted of 1046 patients having 1085 breast lumps/ swellings. Sampling was done in Aziz Bhatti Shaheed Teaching Hospital and a private hospital in Gujrat. The records of all the patients were retrieved, compiled and analyzed with respect to the types of pathology, age and various diagnostic entities.

Results: We analyzed 1085 breast lesions. More lesions were seen on left side (53.6%). Mean age of patients was 39.07 years. Most patients presented in fourth decade (27.2%), followed by third decade (24.9%). We divided the lesions into five main categories. Benign category (C2) was the largest with 56.8% of the lesions. It was followed by the malignant category (C5%) with 33.5% of the patients. The C3 and C4 categories contained 4.7% of the lesions each. C1 category contained only 0.3% of the lesions. Fibroadenoma was the commonest lesion in the benign neoplastic group. Inflammatory lesions were commonest lesion in the benign non-neoplastic group. Ductal carcinoma was the most prominent lesion in the malignant category with 69% of the cases.

Conclusion: Our findings of benign lesions being the commonest and malignant second to them is in conformity with most other studies. There are variations in the frequencies of various categories of lesions and age incidences in literature.

Key Words: FNAC Breast, Fibroadenoma, Ductal carcinoma, Proliferative breast disease, Phylloides tumor.

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INTRODUCTION

Most diseases of the breast present as lumps or swellings. Although most of these lesions are benign or non neoplastic, breast cancer is the most common cancer of the females.¹ The non-surgical methods used to evaluate the breast lesions include physical examination, mammography, USG, FNAC and core needle biopsy. The FNAC and CNB are the two main options that can provide a definitive pathological diagnosis. Various studies have been done to compare these two techniques as each of these has some advantages over the other as well as some limitations. A multidisciplinary approach like triple assessment provides a better accuracy of diagnosis than any of these modalities alone.^{2,3,4} FNAC has a high sensitivity, specificity and overall accuracy.⁵ Most patients of breast disease are females and a few are males.

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Mean age of the patients falls mostly in fourth decade.⁶ Benign lesions are found at a younger age than the malignant cases. Benign lesions are found mostly in third decade and malignant in fifth and sixth decades.⁷ More lesions are found on left side than right side and a few patients present with bilateral lesions.⁸

The breast lesions are generally divided into five cytological categories i.e. unsatisfactory, benign, atypical probably benign, suspicious of malignancy and malignant.⁹ Benign category is the largest of these categories and fibroadenoma is the most common entity in this group. Malignant lesions are mostly carcinomas and ductal carcinoma ranks first amongst these lesions.^{8,10} Other lesions that form significant proportion of cases include inflammatory lesions including pyogenic as well as granulomatous lesions, cystic/ fibrocystic lesions and benign proliferative lesions.⁸

Although FNAC has several advantages like simplicity, rapidity, cost effectiveness, least complications and high overall accuracy, the possibility of false negative as well as false positive diagnoses in a few cases should be kept in mind while interpreting a report.^{8,11}

MATERIALS AND METHODS

It is a retrospective, cross-sectional laboratory-based study of FNA cytology of breast lesions. It was carried out in the Department of Pathology, Nawaz Sharif

Medical College (NSMC), University of Gujrat, Pakistan. The procedures were performed in Aziz Bhatti Shaheed Teaching Hospital (affiliated with NSMC) and a private hospital in Gujrat. A total of 1046 female patients with complaints of breast lump/swelling underwent FNAC during three years (Jan 2015-Dec 2017).

Sampling was done using 23 G needles with 5 cc disposable syringes in most cases. In some cases, 21 G and 22 G needles with 10cc syringes were also used. Lymph nodes (axillary and cervical) were also sampled when feasible. Before allowing the patient to leave, we assessed the adequacy of aspirate by using R-O-S-E (Rapid On Site Evaluation) concept.¹² The smears were stained mostly with hematoxylin & eosin (H&E) stains. May Grunwald Giemsa and Pap stain was used in some cases. All smears were examined and reported by the author himself. We used Microsoft Excel, Minitab 14, and SPSS 24 for data analysis. The results

were presented in frequency tables/ cross-tabulations and compared with foreign and local studies.

RESULTS

There were 1046 female patients included in this study. We had 39 patients with more than one breast lesion yielding us a total of 1085 lesions. Left side contained more lesions (53.6%) than right side. Mean age of patients was 39.07 years with most patients presenting in fourth decade (27.2%), followed by third decade (24.9%). We reported the cases in five categories as per NHS/ RCPATH recommendations for FNAC breast reporting.⁹ We also tried to sub-classify the lesions into definite breast disease entities wherever possible e.g. fibroadenoma in benign (C2) category. Benign category was the largest with 56.8% of the lesions followed by malignant category with 33.5% of the patients. (Table 1).

Table No. 1: Frequency distribution of breast aspirates according to diagnostic category and age.

Diagnostic Category	Up to 20*	21-30	31-40	41-50	51-60	>60	Total (Count)	Total %
C1 Inadequate	1	2	0	0	0	0	03	0.3
C2 Benign	101	219	177	70	33	16	616	56.8
C3 APB	0	10	19	10	6	6	51	4.7
C4 SoM	0	14	15	18	3	1	51	4.7
C5 Malignant	0	25	84	104	86	65	364	33.5
Total Count	102	270	295	202	128	88	1085	100
Total %	9.4	24.9	27.2	18.6	11.8	8.1	100	100.0

*=Age in Years, APB= Atypia Probably Benign, SoM= Suspicious of Malignancy

Table No.2: Frequency distribution of lesions according to diagnosis and age.

Category	Diagnosis	Up to 20*	21-30	31-40	41-50	51-60	>60	Total Count	Total %
Inadequate		1	2	0	0	0	0	03	0.3
Benign Non Neoplastic Lesions	Inflammatory lesions	7	79	76	31	14	8	215	19.8
	Cystic lesions	2	32	27	14	4	3	82	7.6
	PD/NPD w/o atypia	10	25	21	9	9	1	75	6.9
	Others	6	16	11	4	4	2	43	4
Benign Neoplastic Lesions	Fibroadenoma	75	66	26	4	0	0	171	15.8
	Phylloides tumor	0	0	5	3	0	0	08	0.7
	Lipoma	0	0	6	5	1	1	13	1.2
	Misc. benign tumors	1	1	5	0	1	1	09	0.8
APB		0	10	19	10	6	6	51	4.7
SoM		0	14	15	18	3	1	51	4.7
Malignant Lesions	Carcinoma	0	4	20	31	21	19	95	8.8
	Ductal Ca	0	20	62	65	63	41	251	23.1
	Lobular Ca	0	0	0	0	0	1	1	0.09
	Medullary Ca	0	1	1	1	2	0	5	0.5
	Mucinous Ca	0	0	0	6	0	4	10	0.9
	Sarcoma	0	0	1	1	0	0	2	0.1
	Total Count	102	270	295	202	128	88	1085	100
	Total %	9.4	24.9	27.2	18.6	11.8	8.1	100	100.0

*=Age in Years, PD= Proliferative disease, NPD= Non Proliferative disease, Ca= Carcinoma

Table No.3: Frequency Distribution of Benign Non-neoplastic lesions according to diagnosis and age (n=415)

Categories	Diagnosis	Up to 20*	21-30	31-40	41-50	51-60	>60	Total	Total %
Inflammatory lesions (n=215, 19.8%)	Pyogenic/NOS	3	35	35	18	8	4	103	24.9
	SGI	2	19	17	4	3	2	47	11.3
	GI	2	23	24	6	3	1	59	14.2
	CGI	0	2	0	3	0	1	06	1.4
Cystic lesions (n=82, 7.6)		7	79	76	31	14	8	215	
	Simple Cyst	0	4	13	9	2	2	30	7.2
	Fibrocystic Change	0	2	2	1	0	0	05	1.2
	EIC	1	5	5	4	2	1	18	4.3
PD / Non-PD (n=6.9%)	Galactocele	1	21	7	0	0	0	29	07
		2	32	27	14	4	3	82	
PD / Non-PD (n=6.9%)	PD without Atypia	6	8	6	3	0	0	23	5.5
	NPD	4	17	15	6	9	1	52	12.5
Others. (n=43, 4%)		10	25	21	9	9	1	75	
		6	16	11	4	4	2	43	10.4
Total Count		25	152	135	58	31	14	415	100.0
Total %		6.0	36.7	32.5	14	7.4	3.4	100.0	100.0

*= Age in Years, NOS=Non-specific Inflammation, SGI= Suspicious for Granulomatous Inflammation, GI= Granulomatous Inflammation, CGI= Caseating Granulomatous Inflammation, EIC=Epidermal Inclusion Cyst, PD= Proliferative disease, NPD= Non Proliferative disease, Misc= Miscellaneous

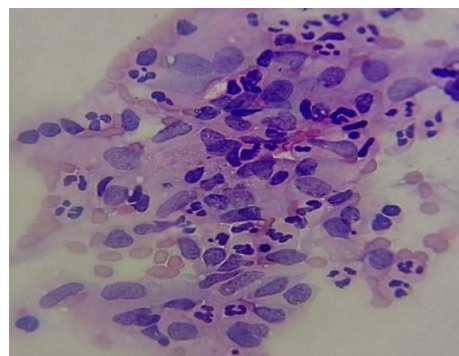


Figure No. 1: Granulomatous inflammation (H&E, X400) containing epithelioid cells and other inflammatory cells.

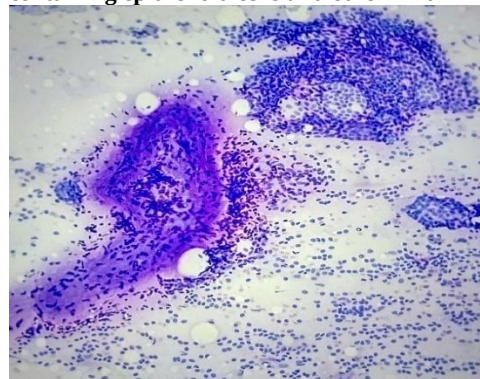


Figure No.2: Fibroadenoma (H&E, X40), showing sheets of uniform ductal cells, a myxoid stromal fragment and many bipolar naked nuclei.

Mean age of patient with benign lesions were 32.54 years. Among benign non-neoplastic lesions, most common lesions were inflammatory (Fig 1) lesions (n=215, 19.8%) followed by cystic lesions (n=82, 7.6%).

Most cases of benign non-neoplastic lesions were reported in third decade (n=152, 36.7%) followed by fourth decade (n=135, 32.5%).

However, while encountering benign neoplastic lesions, most of the cases were reported in second decade of life (76/201, 37.8%). Fibroadenoma was the most common neoplastic lesion. (Fig 2)(Table 2&3)

There were 364 cases of malignancy (Fig 3 and 4). Mean age of patient with malignant lesions was 49.84 years. Most malignant cases were found in fifth decade of life (n=104, 28.6%) followed by sixth decade (n=86, 23.6%) and fourth decade (n=84, 23.1%). The overwhelming majority of malignant cases were carcinomas (362/364) and the remaining two cases were of sarcomas (Fig 3 and 4). The most common carcinoma was ductal carcinoma (251/364, 69.1%). (Table 2)

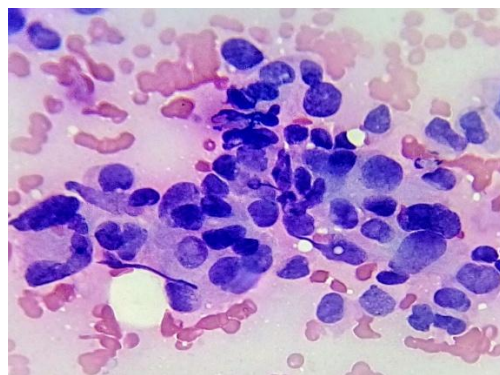


Figure No. 3 : Ductal carcinoma smear (H&E, X400) with pleomorphism and hyperchromasia.

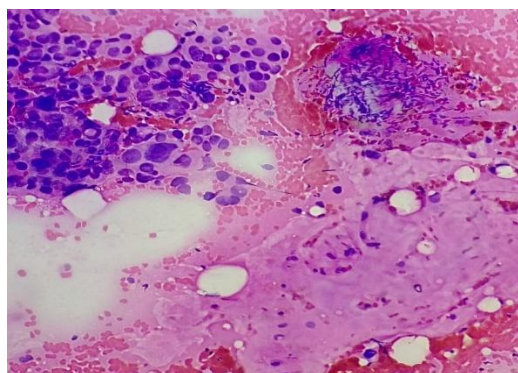


Figure No.4: Mucinous carcinoma (H&E, X400) showing thick mucinous material with cellular features of malignancy.

A total of 79 ipsilateral axillary lymph nodes were sampled. Out of these, 65 (82.3%) were proven metastatic.

DISCUSSION

Breast disease is mainly a disease of females. The study comprised 1046 female patients that contained 1085 breast lesions.

The left sided predominance of breast lesions in our study (53.6%) is in conformity with most authors while a few like Rahman has described a little majority right sided lesions.¹³

The mean age of our patients at 39.07 years is closest to the studies of Elmadhoun at 38.2 years, Hamdani at 38 and Shah at 38.1 years.^{6,10,11} The fourth decade contained highest proportion of 27.2% of lesions in our study. Shah has also reported maximum number of his cases in fourth decade while Rahman described most cases in third decade.^{10,13} Rahman has attributed this finding to the lower life expectancy in his country. The finding of benign lesions at lower age than malignant is common to our and almost all other studies.

Benign category of lesions was the largest in our study with 56.8% of the lesions, a finding similar to most studies except a few like the study of Challa who has mentioned malignant category as the largest.^{5-8,14}

There were 18.5 % (201/1085) benign neoplastic cases in our study and most of these (171/1085, 15.8%) were fibroadenomas. The frequency of fibroadenomas is our study is in concordance with Bukhari i.e. 16%.¹⁵ Our study also showed benign phylloides in 0.7 % of cases and lipoma of 1.2%. Elmadhoun showed Phylloides tumor 1.7 % and Lipoma 1.3%.¹¹

Our study found 19.8% inflammatory cases which is in concordance with Bukhari at 20%, Rahman 21.1% and Punjvani 22.5%.^{13,15,16} Our study showed granulomatous inflammation in 5.4 % cases. Punjvani showed it at 5.9%, Rahman at 6.52% and Bukhari at 2.3%.^{13,15,16} Fibrocystic disease of breast in our study is 1.2%. There is variable frequency in literature like 4.96% in

the study of Punjvani, 11.8% in the study of Rehman and 21.2% in that of Bukhari.^{13,15,16}

The malignant category was second largest in our study like most other studies. The frequency of 33.5% malignant lesions in our study is almost similar to the studies of Madubogwu (34.6%), Panjvani (31.1%) and Naz (36.9%).^{5,16,17}

Some authors have described fewer malignant cases in their studies e.g. Kamra as well as Kumari at 11.2 % each and Choudhary at even lower at 5.6%.^{18,19,20}

Mean age of our patients with malignant lesions was 49.84 years, a finding in correspondence with Naz with a mean age of 47 in her study.¹⁷ Fifth decade contained higher proportion of malignant cases than all other decades in our study (28.6%, 104). Rahman and Kujur have reported most cases in 4th decade, Shah in 5th and 6th and Kumari in 6th decade.^{10,13,19, 21}

The most common carcinoma is ductal carcinoma in our study comprising 69% of the malignancies (251/364). Our finding is in conformity with that of Yusuf at 69.9% and Madubogwu at 73.7% ductal carcinomas in their studies.^{5,23} Some studies have described a very high frequency of ductal carcinomas in their studies like Rahman at 99.6% (251/252) and Kamra at 98.1% (151/154).^{13,18}

In our study, 17.9% cases (65/364) of malignancy revealed metastatic axillary lymph node disease. There is variable frequency in literature like the studies of Rahman, Challa and Elmadhoun revealed metastatic axillary disease in 10.3% (26/252), 37.7% (170/451) and 50.8% (33/65) of the cases respectively.^{11,13,14}

CONCLUSION

The general pattern of breast pathology in our study is proportionate with majority of the studies in literature like benign category being the commonest and followed by malignant in frequency. Inflammatory lesions are commonest in benign non neoplastic and fibroadenoma in benign neoplastic category. Ductal carcinoma is the predominant malignancy. Significant variations were observed in the frequencies of fibrocystic disease and metastatic axillary disease.

Author's Contribution:

Concept & Design of Study:	Abdul Rauf
Drafting:	Muhammad Adnan Zaman
Data Analysis:	Muhammad Adnan Zaman
Revisiting Critically:	Abdul Rauf, Muhammad Adnan Zaman
Final Approval of version:	Abdul Rauf

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Frequency of G6PD Deficiency and Coombs Test Positivity in Newborn Presenting with Hyperbilirubinemia

G6PD Deficiency and Coombs Test Positivity in Newborn with Hyperbilirubinemia

Muhammad Qasim Khan¹, Subhan-ud-Din², Akhtar Ali Shah¹ and Muhammad Fazil¹

ABSTRACT

Objective: To study the prevalence of G6PD deficiency and coombs test positivity in newborn presenting with hyperbilirubinemia.

Study Design: Descriptive study.

Place and Duration of Study: This study was conducted at the Paediatric Department of Bacha Khan Medical College & Mardan Medical Complex Teaching Hospital Mardan from January 2017 to July 2018.

Materials and Methods: A total of hundred newborn with hyperbilirubinemia and fifty healthy newborns as a control group were included in the study. All the newborns were subjected to G6PD test, coombs test, Retic count, full blood count, blood groups and total, direct, indirect bilirubin level.

Results: A total of 9% Newborn with hyperbilirubinemia showed G6PD Deficiency. Mean bilirubin level was 25 ± 2.562 mg/dl, significantly elevated as compared to control group. $P < 0.00236$. Similarly 10% newborn showed coombs test positive and these were Rh incompatible. Mean bilirubin level was 26 ± 2.156 mg/dl, significantly higher as compared to control group. $P < 0.000326$. 80% Newborn had physiological jaundice. Mean bilirubin level were 13 ± 2.562 mg/dl, significantly higher than control group. $P < 0.00422$.

Conclusion: The study concluded that Newborn presenting with hyperbilirubinemia is significantly associated with high prevalence of G6PD deficiency and positive coombs test which indicates Rh-incompatibility. Therefore all the Pediatrician should have priority to screen all newborn presenting with hyperbilirubinemia for G6PD deficiency and coombs test. As these two conditions are very common in Pakistan this will early identify newborn with hyperbilirubinemia leading to serious complication like kernicterus.

Key Words: Hyperbilirubinemia, G6PD, Coombs Test, kernicterus

Citation of articles: Khan MQ, Din S, Shah SS, Fazil M. Frequency of G6PD Deficiency and Coombs Test Positivity in Newborn Presenting With Hyperbilirubinemia. Med Forum 2018;29(10):10-13.

INTRODUCTION

Neonatal hyperbilirubinemia is a common problem among neonates and in majority of neonates it is reported¹. Neonatal hyperbilirubinemia is usually reported in 60% of full term and 80% in preterm babies in the 1st week of life². Although jaundice is mostly physiological phenomenon in neonates but in 10-12% of cases they need admission³. Neonatal hyperbilirubinemia is the yellowish discoloration of skin and white part of eyes due to high bilirubin level. Other symptoms include lethargy or poor feeding. In majority of the cases there is no specific cause and jaundice is mainly physiological and this usually last for one week. But in some cases this may result from some pathological factors and includes red cell breakdown, liver disease,

infection, hypothyroidism, G6PD deficiency, autoimmune hemolytic anemia, ABO&Rh incompatibility, unsuccessful breast feedings, earlier gestational age and low birthright^{4,5}. Marked hyperbilirubinemia is associated with significant complication like kernicterus which is serious neurological disease and death⁶. However quick and accurate treatment reduce the risk of neonatal kernicterus⁷. In severe cases hyperbilirubinemia causes complication like Kernicterus, cerebral palsy and death. Therefore determining the etiology of jaundice can lead to timely prevention and treatment⁸. It is important that all the neonates with hyperbilirubinemia should be properly screened to identify the etiology. The American Academy of Pediatrics recommends. neonatal blood groups, coombs test, complete blood count, smear, G6PD level, direct and indirect bilirubin level and combination of universal screening as most effective method for identifying infants at risk of hyperbilirubinemia⁹⁻⁵.

The aim of the study is to know the prevalence of G6PD deficiency, coombs test positivity, Rh and ABO incompatibility, one of the most important causes of neonatal hyperbilirubinemia by applying G6PD deficiency test, coombs test and blood group of baby and mother in neonates presenting with hyperbilirubinemia. This study will identify neonates

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with the common etiology in Pakistan and will further guide the paediatrician to know the common causes of hyperbilirubinemia and will provide timely treatment and reduce mortality and morbidity of neonates from hyperbilirubinemia.

MATERIALS AND METHODS

The study was conducted in the Paediatric and Pathology Department of Bacha Khan Medical College and Mardan Medical Complex Teaching Hospital Mardan, for one year from December 2017 to September 2018.

Jaundiced neonates with gestational age less than 28 weeks; jaundiced neonates with weight of less than 500 gm; and babies whose mothers were hepatitis A IgM positive, HBsAg (hepatitis B surface antigen) positive, and anti-HCV (hepatitis C antibody) positive were excluded from the study.

After getting approval from the hospital ethical committee to conduct the study, data was collected of all those neonates who met inclusion criteria presenting through Out-patient department (OPD) or accident/emergency department and admitted in Paediatric and Neonatology department of Mardan Medical Complex Teaching Hospital Mardan. An informed consent was taken from parents or relatives of the neonates with hyperbilirubinemia for further evaluation. The required investigation done (as below) in the pathology department of the hospital, after taking history and doing physical examinations. All the information and other data like name, age, sex, address, date of admission, and date of discharge were entered into a parforma.

A total of 100 newborns presenting with hyperbilirubinemia, both male and female were included in the study and 50 newborns were taken as healthy individual as a control group. Patients were divided into three groups: Group A included newborn with hyperbilirubinemias with G6PD deficient group. Group B included newborns with hyperbilirubinemia with coombs positive group and group C included newborn with hyperbilirubinemia with physiological jaundice. All newborns with hyperbilirubinemia were subjected to parameters like total bilirubin, direct and indirect bilirubin level, G6PD test, coombs test, Retic count, special smear and full blood count. For this purpose samples were collected in EDTA and Gel tubes and from these samples the above investigations were performed.

G6PD tests were performed according to standard procedure by reduction test, the principle of which is: G6PD is released from lysed erythrocytes and catalyses the conversion of Glucose-6 Phosphate to 6 Phosphogluconate with conversion of NADP to NADPH and this NADPH can be detected by dye reduction test according to standard procedure. Sample when did not change colour after 60 minutes declared G6PD

deficient and sample which changed colour within 50-55 minutes were declared sufficient in G6PD.

Coombs tests were performed on all newborns with hyperbilirubinemia according to procedures as: Newborn EDTA blood taken and wash 3 times with saline. Then 5% solution prepared by adding 95 drops of saline with 5 drops of washed red blood cells of newborn, then took two drops of this washed red blood cells and mixed with two drops of coombs reagent and then centrifuged for 15 seconds, then put one drop on slide and put a cover slip on it and examined under Microscope for agglutination and declared coombs test positive when agglutination seen.

Retic count also performed on all newborns with hyperbilirubinemia according to standard procedure as take equal quantity of EDTA blood and Retic reagent in a test tube and incubate at 37°C for 10-15 minutes then prepared slide and examined for Retic counts.

Bilirubin in also performed on the sample of newborn presenting with hyperbilirubinemia (on Kit Randox) according to standard procedure. Take sample of newborn serum, then add R1 reagent 200 UI in a test tube. Then add R2 50 UI, then add R3 1ml and incubate at 37°C then after 10 minutes add 1ml R4 then analyze by Microlab 300 chemical analyzer (Merck).

Full blood counts were also performed on all these newborn for determination of Hb, TLC and Platelets by Hematology analyzer (sysmex x100 Japan). All data were subjected to statistical analysis by using Chi-square test and T-Test. Level of significance was set at p value < 0.005.

RESULTS

A total of 100 newborns with hyperbilirubinemia were included in the study. They were both males and females. All these newborns were admitted in nursery unit. In all these newborns G6PD test, Coombs test, Total bilirubin, Direct and Indirect Bilirubin, Retic counts, complete blood counts, Neonatal and Maternal blood groups with Rh antigen were performed in this study. All newborns with hyperbilirubinemia were divided into Group A, which included G6PD deficient newborns; Group B in which Coombs positive newborns were included; Group C included newborns with physiological hyperbilirubinemia and 50 newborns were included as healthy newborns. In this study newborns with Hyperbilirubinemia, 9% of newborns were G6PD deficient with mean bilirubin levels were 25 ± 2.625 mg/dl.

Direct bilirubin level were 2 ± 0.56 mg/dl and indirect bilirubin levels were 22 ± 1.25 mg/dl, which were significantly higher than the control group. $P < 0.00256$. Similarly 11% newborns, Rh incompatibility were detected in which babies were Rh positive and Mothers were Rh negative. All these newborns were presented with hyperbilirubinemia. Mean total bilirubin level, were 26 ± 2.156 mg/dl; direct bilirubin levels were

2±0.56 mg/dl and indirect bilirubin levels were 23±1.25 mg/dl in all these newborn. Hyperbilirubinemia were significantly higher as compared to control group $P < 0.00325$.

Table No.1: Frequency of G6PD deficiency, Positive Coombs and physiological jaundice in Newborn with hyperbilirubinemia

	Frequency of Parameters in Newborns with Hyperbilirubinemia	%age
Group A	Newborns with G6PD deficiency	9%
Group B	Newborns with Rh. Incompatibility	11%
Group C	Newborns with Physiological Jaundice.	80%

Table No.2: Mean Value of Total Bilirubin Direct and Indirect bilirubin levels in Newborns presenting with hyperbilirubinemia

	Newborn with G6PD Deficiency Group A	Newborns with Rh incompatibility Group B	Newborns with Physiological Jaundice Group C	Control Group
Total Bilirubin	25± 2.562 mg/dl	26± 2.156 mg/dl	13±2.562	1.5±0.32
Direct Bilirubin	2±0.56 mg/dl	2±0.56 mg/dl	2±0.56	0.5±0.12
Indirect Bilirubin	22±1.25 mg/dl	23±1.25 mg/dl	11±1.25	1±0.32

Similarly in rest of the newborns with hyperbilirubinemia no abnormality were detected and they were classified as physiological jaundice. Mean bilirubin levels were 13 ± 2.562 mg/dl. Retic counts were also performed. Retic count were comparatively higher than the control group.

DISCUSSION

The prevalence of hyperbilirubinemia is twice that of general population in males who carry the defective gene and in homozygous female. It rarely occurs in heterozygous females¹⁰. Hyperbilirubinemia is secondary to impairment of bilirubin conjugation and clearance by the liver leading to indirect hyperbilirubinemia¹¹. Neonatal hyperbilirubinemia is not harmful and most neonates get better without treatment within one to two weeks. A very high bilirubin level lead to kernicterus and may lead to serious complications like cerebral palsy, deafness or other form of brain damage¹². A lot of risk factors are responsible for hyperbilirubinemia of which G6PD deficiency, autoimmune hemolytic anemia and blood group incompatibility studied and evaluated in these newborn.

In the present study 9% newborn with hyperbilirubinemia G6PD deficiency were detected. A similar study has been conducted by Leong and reported that newborn Hyperbilirubinemia is associated with significant prevalence of G6PD deficiency¹³. Isa et al also reported in their study that G6PD deficiency is very common in neonatal hyperbilirubinemia and 42% of the newborn were detected G6PD deficient¹⁴⁻⁴⁵. G6PD deficiency is a X-linked disorder with male predominance and about 400 different types of G6PD with distinctive biochemical characteristic and about 100 various mutations have been identified¹⁶. G6PD deficiency is common worldwide and is more common in Mediterranean area, Middle East, India, China, Africa¹⁷. G6PD deficiency is an independent risk factor for hyperbilirubinemia with bilirubin level more than 18mg/dl¹⁸. The exact mechanism in which G6PD deficiency lead to hemolysis is not clear, but is suggested that G6PD converts NADP to its reduced form NADH; and reduced NADPH protects RBC from oxidative damage i.e acute hemolysis occurs when RBC exposes to oxidative stressors like infections, oxidative drugs, fava beans etc¹⁹. Neonatal occurrence of Autoimmune hemolytic anemia is very rare. Its annual incidence is one case in 80,000 live births annually. Motta et al reported one case of Autoimmune hemolytic anemia in newborn infant²⁰. ABO incompatibility is also a common condition in newborn and causes minimal hemolysis. It may cause raised level of bilirubin and anemia but is less severe than Rh hemolytic disease²¹.

In the present study 11% showed coombs positive in neonates with hyperbilirubinemia. Various studies have been conducted and showed significant prevalence of Rh incompatibility with positive coombs in neonates. Patel et al also reported in their study that newborn presenting with hyperbilirubinemia is associated with significant prevalence of Rh incompatibility²². Similarly McIntosh N et al also reported that Rh incompatibility positively associated with newborn presenting with hyperbilirubinemia²³.

CONCLUSION

The present study concluded that newborn presenting with hyperbilirubinemia is significantly associated with high prevalence of G6PD deficiency and Rh incompatibility. Therefore all the paediatrician should strictly screen all newborn presenting with hyperbilirubinemia for G6PD deficiency and Rh incompatibility. As these two risk factors are very common in our population / newborn presenting with hyperbilirubinemia; and these two investigation (G6PD test & coombs test) will timely prevent further attack of jaundice and reduce its complication like Kernicterus and further reduce mortality and morbidity from hyperbilirubinemia.

Author's Contribution:

Concept & Design of Study: Muhammad Qasim Khan
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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Anti-Hypertensive Potentiating Effects of Simvastatin on Amlodipine

Wajid Ali, Afsheen Siddiqi and Khadija Imran

Antihypertensive
Potentiating
Effects of
Simvastatin On
Amlodipine

ABSTRACT

Objective: To determine the In vivo vasodilatory effect of simvastatin (Statin) in the presence of Amlodipine (Calcium Channel Blocker).

Study Design: Experimental animal study on rats

Place and Duration of Study: This study was conducted at the Department of Pharmacology, Ayub Medical College, Abbottabad from May 2015 to June 2016

Material and Methods: Hypertension was induced in rats by giving Depomedral TM injection subcutaneously (20mg/kg) of body weight for 1 week. For antihypertensive activity single dose follow up regimen of test drugs were used. Fluctuations in systolic blood pressure (SBP) was calculated using Non Invasive Blood Pressure (NIBP) System of power lab using rat tail cuff method.

Results: Our study showed significant results for lowering of systolic blood pressure in rats receiving Amlodipine alone and then Simvastatin in the presence of Amlodipine.

Conclusion: This study demonstrates that Simvastatin and Amlodipine when used in combination have potentiating or additive vasodilatory effects resulting in lowering of systolic blood pressure.

Key Words: Simvastatin, Amlodipine, systolic blood pressure (SBP), Cardiovascular diseases (CVDs)

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INTRODUCTION

Drug-drug interaction is the change in the response of a drug due to administration of another drug, and occurs, due to simultaneous administration of two or more than two drugs¹. Drug interactions are of two types that are interactions that take place inside & outside the body. Mixing of drugs in intravenous (IV) fluid may cause chemical reactions between drugs and the constituents of IV-fluid, this can be taken as an example of interactions occurring outside body². When drugs are taken by patient and then the drugs interact inside the body of patient then such interactions are interactions inside the body. Interactions can be Pharmacokinetic or Pharmacodynamic interactions. Interactions occurring during Absorption, Distribution, Metabolism & Excretion are Pharmacokinetic interactions. Interactions between drugs having similar or antagonistic pharmacological effects and are due to either competition for the same receptor or drugs acting at a similar physiological system are Pharmacodynamic interactions. Pharmacodynamic interactions can be in the form of Addition, Synergism, Potentiation and Antagonism^{1,2}.

Cardiovascular diseases are the most prevalent cause of mortality and morbidity^{3,4}. Epidemiological and outcomes research studies shows that the current treatment strategies are not sufficient in controlling the hypertension and dyslipidemia with single drug therapy alone. This is despite the availability of well tolerated anti-hypertensives and dyslipidemics. However, there is evidence that the addition of anti-hypertensives with lipid-lowering drugs confers cardiovascular benefits^{4,5}. WHO has approved many drugs for the treatment of cardiovascular diseases. The most important of which are statins, calcium channel blockers and anti-platelet drugs³. Most commonly the statins are used for the management of hypercholesterolemia and calcium channel blockers for hypertension, in patients who are hypertensive and obese. In patients of stroke these two drugs (Simvastatin and Amlodipine) from two different groups are sometimes used together to control hypertension and hypercholesterolemia simultaneously⁶.

But the effect of this combination is still not known. However it is postulated in some research papers through conduction of experiments in animal models that statins have positive effects on the voltage gated calcium-channels, means it up-regulates the voltage gated calcium channels⁷. Recently drug study findings have proved that statins have the calcium-channel blocking effects on rabbit's jejunum^{8,9}. In this study we want to know the combined vasodilatory effects of Simvastatin (Statin) and Amlodipine (Calcium channel blockers).

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MATERIALS AND METHODS

We conducted this study in lab of Pharmacology department, Ayub Medical college, Abbottabad, from May 2016 to June 2017. Our experimental model for the study was Albino Rats. Standard laboratory diet was provided to rats in proper ventilated rooms. There were 4 groups consisting of 4 rats in each group.

1-Control group: No hypertension was induced and no drug given to this group.

2- Amlodipine group.

3- Amlodipine plus Simvastatin (EC₅₀ dose) group.

4- Amlodipine plus Simvastatin (double EC₅₀ dose) group.

In Rats of group 2, 3 & 4 hypertension was induced by injecting Depomedral TM subcutaneously (20mg/kg) of body weight for 1 week^{10,11}. Test drugs (Amlodipine & Simvastatin) were given for antihypertensive effects, via oral route using single dose phenomenon of

drugs^{12,13}. Systolic Blood pressure fluctuations (SBP) were recorded by using the Non Invasive Blood Pressure (NIBP) system of Power lab, using rat tail cuff method, on three different occasions i.e. Before hypertension induction, after hypertension induction (Pre-dose) and after test drug administration (Post-dose)^{14,15}. The observations were repeated 3-4 times for each rat and mean was calculated using Graph Pad Prism software version 6.¹⁶

RESULTS

Effects on systolic blood pressure (SBP) in hypertensive rats were observed and the data was statistically analyzed through ANOVA.

Control group: Mean baseline systolic blood pressure values were (142.16±6.33) and (14 ± 5.23) respectively at one week interval as shown in the table.

Table: Effect of drugs (test and standard) on fall in systolic blood pressure (Mean blood pressure n=4)

	Group 1		Group 2		Group 3		Group 4	
	Control group		Amlodipine group (Standard)		Amlodipine+Simvastatin (EC ₅₀ dose)		Amlodipine+Simvastatin (Double EC ₅₀ dose)	
	Initial BP	Bp after 1 week	Pre dose SBP	Post dose SBP	Pre dose SBP	Post dose SBP	Pre dose SBP	Post dose SBP
	120.2	121	203	184	185	162	191	161
	138.1	139	205	183	185	162	184	149
	135.18	136	178	173	182	165	188	162
	175.16	170	212	192	173	155	172	147
Mean SBP± SD	142.16± 6.33	141.5±5.23	199.5±7.73	183±5.7	181.25±3.2	161±2.3	183±4.54	154±5.3
*Mean↓ in SBP	No change		16.5mmHg		20.25mmHg		28.25mmHg	
	No change		100% (standard)		122.72%		171.21%	
*% fall in SBP								

*Mean Fall in SBP= Pre dose – Post dose.

$$*\% \text{ fall in the mean SBP by Amlodipine (standard)} = \frac{\text{Mean fall in SBP by Amlodipine}}{\text{Mean fall in SBP by Amlodipine}} \times 100 = \frac{16.5}{16.5} \times 100 = 100\%$$

$$* \text{ fall in mean SBP by Amlodipine+Simvastatin (EC}_{50}) = \frac{\text{Mean fall in SBP by Amlodipine+Simvastatin (EC}_{50})}{\text{Mean fall in SBP by Amlodipine}} \times 100$$

$$= \frac{20.25}{16.5} \times 100 = 122.72\%$$

$$* \text{ fall in mean SBP by Amlodipine+Simvastatin (Double EC}_{50}) = \frac{\text{Mean fall in SBP by Amlodipine+Simvastatin (Double EC}_{50})}{\text{Mean fall in SBP by Amlodipine}} \times 100$$

$$= \frac{28.25}{16.5} \times 100 = 171.21\%$$

Amlodipine group: Pre-dose mean systolic blood pressure was (199.5 ± 7.73) and post dose mean systolic blood pressure was (183 ± 5.7) with $(p=0.0011)$ as shown in table. The fall in systolic blood pressure is 16.5 mmHg. Mean fall of Systolic blood pressure by Amlodipine is taken as standard to compare all other mean falls caused by combination of simvastatin and Amlodipine. % fall by Amlodipine is taken as 100%.

Amlodipine plus Simvastatin (EC_{50}) group: Simvastatin (EC_{50}) in the presence of Amlodipine was given through oral route following single dose phenomenon. Pre-dose mean systolic blood pressure was (181.25 ± 3.2) and post-dose mean systolic blood pressure was (161 ± 2.3) with $(p=0.0038)$, the mean fall in systolic blood pressure was 22.5mmHg. % fall in mean systolic blood pressure by Amlodipine plus Simvastatin (EC_{50} dose) is 122.72%.

Amlodipine plus Simvastatin (Double EC_{50}): Simvastatin (Double EC_{50}) in the presence of Amlodipine was given through oral route following single dose phenomenon. Pre dose mean systolic blood pressure was (183 ± 4.54) and post dose systolic blood pressure after the administration of Amlodipine and Simvastatin (Double EC_{50}) was (154 ± 5.3) with $(p=0.0010)$, the mean fall in systolic blood pressure was 28.25mmHg. % fall in mean systolic blood pressure by Amlodipine plus Simvastatin (Double EC_{50}) was 171.21%.^{17,18,19}

DISCUSSION

In modern era, the practice of poly pharmacy is widely prevalent throughout the world. Clinicians use the poly pharmacy to treat most of the diseases such as cardiovascular diseases like stroke, which needs to be treated with combination of drugs like statins for hypercholesterolemia and calcium channel blockers for hypertension, but the combined effects of these drugs, still to be answered.

This in vivo study was designed to know the possible combined effects of simvastatin and Amlodipine on key physiological variables like systolic blood pressure (SBP). The Simvastatin was tested in the presence of Amlodipine, the standard calcium channel blocker that affects the vascular tone and subsequently blood pressure of test animals.

Moreover, Amlodipine alone was also tested in the same experimental animals to quantify the blood pressure lowering effects. Effects of Amlodipine alone show a mean fall in blood pressure of 16.5 mmHg, assuming Amlodipine as standard drug. While mean fall in blood pressure by Amlodipine + Simvastatin (EC_{50} and Double EC_{50} dose) are 20.25 and 28.25 mmHg respectively.

Percent falls in mean systolic blood pressure (SBP) by Amlodipine is 100% (standard), Amlodipine plus Simvastatin (EC_{50}) is 122.72 % and Amlodipine+ Simvastatin (Double EC_{50} dose) is 171.21%. So, by

comparison the greatest percent fall in mean SBP was done by Amlodipine plus Simvastatin (Double EC_{50}) then by Amlodipine+Simvastatin (EC_{50}) then by Amlodipine alone.

$171.21\% > 122.72\% > 100\%$ (Standard).

Results of our study were supported by a research work conducted by Ali N, in which it was proved that statins have calcium channel antagonistic activity⁸. Another, study conducted by Clunn GF, which shows that statins upregulates the calcium channels in vascular smooth muscles (VSM) also strongly supports our study.⁷

CONCLUSION

Based on the findings of our experimental works, it is concluded that when Simvastatin and Amlodipine are used in combination in patients suffering from hypertension and hypercholesterolemia simultaneously, then these two drugs have additive or potentiating effects on systolic blood pressure (SBP) which explicit the pharmacodynamic interactions between Amlodipine and Simvastatin.

This may sometime distort the therapeutic or pharmaceutical cure plan defined for patients who have hypercholesterolemia or are hypertensives.

Author's Contribution:

Concept & Design of Study: Wajid Ali
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Data Analysis: Afsheen Siddiqi
Revisiting Critically: Afsheen Siddiqi, Khadija Imran
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Frequency of Inter-Appointment Pain in Controlled and Uncontrolled Diabetics

Hannan Humayun Khan¹, Syed Imran Shah², Shafqat Ali Shah³ and Rizwan Ullah Afridi³

ABSTRACT

Objective: To compare the frequency of inter-appointment endodontic flare-ups in controlled diabetes mellitus patients with uncontrolled diabetic mellitus.

Study Design: Cross sectional comparative study

Place and Duration of Study: This study was conducted at the OPD of the 28th Military Dental Centre (MDC) from 01 Jan 2016 to 01 Jan 2018.

Materials and Methods: Thirty patients with controlled glucose profile and 30 uncontrolled patients were included in the study. After initiation of root canal treatment, they were recalled after the first 24 hours to assess pain.

Results: It was observed that 24(80%) uncontrolled diabetic patients exhibited evidence of symptomatic apical periodontitis because of inter-appointment pain as compared to 09(30%) controlled diabetic patients.

Conclusion: Incidence of inter-appointment pain was significantly much higher in uncontrolled diabetics as compared to controlled diabetic patients (p-value 0.00). Showing a probable relationship between inter- appointment pain and uncontrolled diabetes.

Key Words: Diabetes mellitus, symptomatic apical periodontitis, endodontic, post-operative pain

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INTRODUCTION

The core purpose of endodontic treatment is to manage pulpal and periapical diseases. This purpose is best achieved by the help of mechanical and chemical debridement of the canals for eradication of intraradicular micro-organisms.¹ In literature, various factors are considered to be contributing towards inter-appointment pain (also called “inter-appointment flare-up”). According to the American association of Endodontics, endodontic flare-up is defined as “inter-appointment pain and swelling that requires an unscheduled appointment”. The inter-appointment flare-up is characterized by symptoms of pain, swelling and difficulty in mastication of the tooth with recently performed endodontic treatment. Iatrogenic errors like ledging, perforations, missed canal, separated instrument and inadequate instrumentation and thus debridement may lead to inter-appointment flare-up.² In geriatric patients, glucose profile for diabetic patients should be obtained as the uncontrolled diabetes can adversely affect the prognosis of periradicular pathosis, thus increased incidence of flare-up.³

Cytokines’ up-regulation and growth factor’s down-regulation are considered to be the factors for altered immune cell functions, in diabetic patients. This causes rapid damage of the tissues and retarded tissue repair after inflammation.⁴ Literature also states that the incidence of symptomatic apical periodontitis is also greater when glucose profile of diabetes mellitus patient is uncontrolled. Progressive increase in apical radiolucency has also been found even after performing root canal treatment. The inter-appointment flare ups have also been reported to be high in patients with uncontrolled diabetes mellitus.⁵

Symptomatic or asymptomatic apical periodontitis is an inflammatory state caused by toxins of micro-organisms within the root canal and into the apical area⁶. Another proposed mechanism behind it is over instrumentation into the apical area during preparation. This will forcefully push infected debris to the apical site and eventually lead to inflammation. Patients either complain of severe pain that is symptomatic apical periodontitis or only in- different feeling of the tooth which is asymptomatic periapical periodontitis.⁷

MATERIALS AND METHODS

This cross sectional comparative study was carried out at the OPD of the 28th Military Dental Centre (MDC) from 01 Jan 2016 to 01 Jan 2018. Approval for this study was taken from the ethical board committee of 28th MDC. Then written signed consents were attended from the participants’. A total of 60 subjects were recruited in the study using purposive sampling technique. The subjects were divided into two groups; group A had 30 subjects in the age range of 50 – 60 years, who had controlled diabetes mellitus and

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irreversible pulpitis in posterior tooth without periapical radiolucency while group B also had 30 subjects in the same age range with uncontrolled diabetes mellitus and irreversible pulpitis without periapical radiolucency. Subjects who had taken any analgesic or antibiotic for their dental problem in the last 24 hours, teeth with periodontal involvement, and subjects with any other immunological disease or mentally or physically handicapped subjects were excluded from the study.

After the participants' were anesthetized with 2% lidocaine, first visit of endodontic treatment was started. Isolation was maintained with the help of rubber dam and Endo-Z burs (Dentsply Maillefer USA) were used for access cavity. Patency of the canals and preparation of the canal system was done with Stainless Steel manual K-files (Maillefer, Ballaigues, Switzerland). Canal flaring was done on the concept of step-back technique. During the preparation 2.5% Sodium Hypochlorite was used for irrigation of the root canals. For the removal of the smear layer Ethylene Diamine Tetra acetic acid (EDTA) was used. In the first visit of endodontic treatment initial instrumentation, preparation and confirmation of the working lengths were taken. Then Calcium Hydroxide was placed as the intra-canal medicament in all participants' with the help of K-files (Maillefer, Ballaigues, Switzerland). The visual analogue scale (VAS) was used to record the level of pain experienced by the patients after 24 hours. The scores of VAS were categorized further for the purpose of descriptions i.e. the patients reporting with score of above three were categorized to be having inter- appointment endodontic pain. While patients below the score of three on the VAS, were categorized as not having inter-appointment endodontic pain cases.

RESULTS

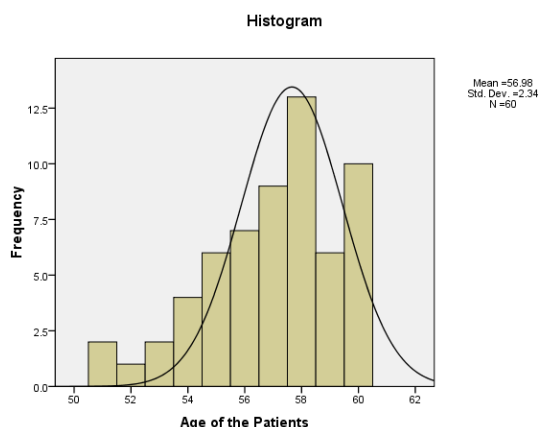


Figure No. 1: Means age of patients

A total of 60 patients participated in the study. The mean age of the patients in both the groups was 56.98 ± 2.34 years (figure 1). The mean age of patients in group A was 57.10 ± 2.264 years while that in group B was 56.87 ± 2.446 years (table 1).

A total of 33 patients presented with inter-appointment pain, in which 24(80%) patients were from group B, i.e. uncontrolled diabetic group and 09(30%) patients from the controlled group (table 2). To assess the significance of the frequency of inter-appointment pain between the two groups, Pearson chi square test was applied showing the p-value of 0.000.

Table No.1: Mean age of patients in both groups

	Group A (Controlled Diabetics)	Group B (Uncontrolled Diabetics)
Total Number of patients	30	30
Mean Age	57.10	56.87
Standard Deviation	2.264	2.446
Minimum Age	51	51
Maximum Age	60	60
Range	9	9

Table No. 2: Number of patients who developed inter-appointment pain in each group

Diabetic status of patient	Inter appointment pain developed	Inter appointment pain did not develop	Total
Controlled	9	21	30
Uncontrolled	24	6	30
Total	33	27	60

DISCUSSION

Diabetes mellitus is not only increasing in incidence here Pakistan but throughout the world it is the same scenario. The significance of controlling this metabolic disease has been highlighted multiple times for desirable medical outcomes. Also it is a known fact that if diabetes mellitus patient's glucose profile is uncontrolled the disease is a challenge for any medical or dental procedure. Again an association with the prognosis of endodontic treatment the control of glucose profile has also been established in literature. Hence it has been suggested that patients should be assessed before hand to evaluate their control of Glucose levels before starting endodontic therapy.⁴

Amongst the medically compromised patients pursuing dental treatment, diabetes is the third most prevalent condition,⁸ therefore the present study was designed to evaluate the frequency of inter appointment flare ups and apical periodontitis in patients with controlled and uncontrolled diabetes seeking endodontic treatment.

The results of the present study showed an increased frequency of inter appointment pain and apical periodontitis in the patients having uncontrolled diabetes ($p=0.000$) as compared to patients with controlled diabetes. Different studies^{9,10,11,12} have reported that there is an association between glucose

level and process of healing in periapical tissues, and the patients having uncontrolled diabetes seeking endodontic treatment have decreased ability for wound repair. A retrospective study done by Fouad et al.¹³ showed that in diabetic patients the rate of inter appointment flare-up during endodontic treatment was 8.6% and in nondiabetics it was 2.3%. The authors also concluded that the rate of inter appointment flare-ups was twice in diabetics as compared to nondiabetics. In the present study the rate of inter appointment flare ups was 80% in uncontrolled diabetics and 30% in controlled diabetics. The present study also found that the rate of inter appointment flare ups was three to four times higher in uncontrolled diabetics as compared to controlled diabetic patients. The increased frequency of interappointment flare ups in this study may be due to the inclusion of different age group patients and obtaining the data from electronic records in Fouad et al study¹³.

A study done by Nayantara,¹⁴ on comparative evaluation of interappointment flare-ups in diabetic and nondiabetic patients, had found that in diabetic group, only 5 patients out of 30 developed interappointment flare-up while in non-diabetic group only 2 patients experienced inter-appointment flare-up. While in the present study 24 patients out of 30 in uncontrolled diabetic group and 9 out of 30 in controlled diabetic group had experienced interappointment flare up. The difference between the results may be due to difference in the intracanal medicaments used and number of appointments (three visits) in which the root canal treatment was completed in the their study.

Study done by Swati et al ¹⁵ had found that the incidence of interappointment flare ups in diabetic patients was 16% while it is higher in the present study, 80% in uncontrolled diabetics and 30% in controlled diabetics. This difference in the results may be because they only included diabetic patients in their study however in the present study, we compared uncontrolled diabetic and controlled diabetic patients and secondly in their study they compared three different medicaments which may have accounted for difference in the results.

Bender et al.¹⁶ showed that patients having uncontrolled DM tends to develop periapical radiolucencies more readily during endodontic treatment while subjects having controlled DM resulted in healing of periapical lesions. Clinical and radiographic assessment of periapical lesions done by Falk et al.¹⁷ have shown higher prevalence of periapical lesions in type 1 diabetics. They noted that women having long duration DM have higher frequency of periapical lesions associated with root canal filled teeth as compared to women with short duration diabetes and without diabetes.

A multivariate analysis conducted by Fouad & Burleson¹¹ showed that there is increase prevalence of

periodontal diseases in root canal treated teeth in patients with diabetes and have higher failure rates of root canal treatment in patients having preoperative periapical lesions. An epidemiologic study carried out on population of native America by Mindiola et al,¹⁸ to figure out different factors that affects the longevity of root canal filled teeth, postulated that the longevity of root canal filled teeth is reduced by diabetes. Another study¹⁰ was conducted in a Brazilian population with type 2 diabetes to find out the prevalence apical periodontitis and endodontic treatment. 60 patients without diabetes and 30 patient with diabetes were included in the study and were assessed using panoramic and retro-alveolar radiographs. They concluded that there was higher prevalence of apical periodontitis in patients having diabetes. The results of the present study are in accordance with all the aforementioned studies.

The drawbacks of this study were that pain was only assessed for the first 24 hours after patients' appointment. Also the uncontrolled diabetic group was not further classified on the bases of blood glucose level. This would have provided an in depth relationship between inter- appointment pain and the blood glucose level of un- controlled diabetic patients.

CONCLUSION

From this comparative descriptive study, it can be concluded that the frequency of inter- appointment pain is higher in patients with uncontrolled diabetes as compared to controlled. Although there were incidence of inter-appointment pain even in the controlled DM group. The much higher incidence in the uncontrolled DM group for inter-appointment pain, points towards a probable relation between uncontrolled diabetes and inter- appointment pain during root canal treatment.

Author's Contribution:

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Impact of Educational Intervention for Improving Pharmacy Students' Knowledge of Pharmacovigilance and Adverse Drug Reactions Reporting

Students' Knowledge of Pharmacovigilance and Adverse Drug Reactions Reporting

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ABSTRACT

Objective: Impact of Educational Intervention for Improving Pharmacy Students' Knowledge of Pharmacovigilance and Adverse Drug Reactions Reporting

Study Design: Descriptive / cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Pharmacy, Lahore College of Pharmaceutical Sciences, Lahore in March 2018.

Materials and Methods: In this study, 133 pharmacy students of both genders from fourth and final year classes having studied clinical pharmacy were included.. Institutional ethical committee approval was taken and the students were required to sign the informed consent. Survey using a pre-validated multiple choice questionnaire to assess the knowledge of pharmacovigilance and ADR reporting amongst the students was used before and after an educational intervention containing a power point lecture on the subject.

Results: 123 students returned the survey forms before and after the intervention. Student's age was ranging from 18 to 25 years. There were 50 male students and 73 female students, 42 had rural and 81 had urban back ground. The majority of the parents had a graduate degree. Overall score pre lecture showed a Mean of 7.55 ± 1.812 and the score post lecture showed a Mean of 11.74 ± 2.353 with a P-value of 0.0001.

Conclusion: It is concluded that, the knowledge of pharmacovigilance and ADR reporting and awareness improved after the educational intervention. If regularly done on different forums and by different strategies this would improve the clinical practice of pharmacists by improving the ADR reporting process and culture.

Key Words: Pharmacovigilance; Adverse drug reaction; Pharmacists; Knowledge and awareness questionnaire; Educational intervention

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INTRODUCTION

Safety and Efficacy are the two outcomes followed after using a medicinal product or device. This is covered by Pharmacovigilance (PV) covering every aspect of the drug or device lifecycle. This begins during the preclinical phases I – III goes up to and beyond phase IV i.e. post marketing surveillance. This becomes the most important consideration for the healthcare. Article 21 of the constitution of the World Health Assembly requires the member states to adopt regulations concerning standards with respect to the

safety, purity and potency of biological, pharmaceutical and similar products moving in international commerce¹.

Since the disaster that occurred due to thalidomide in 1961 with use of the drug by pregnant mothers resulting in the birth of thousands of congenitally deformed infants, the first systematic international effort started to address the drug safety issues. The Sixteenth World Health Assembly (1963) adopted a resolution¹ that reaffirmed the need for early action in regard to rapid dissemination of information on adverse drug reactions and WHO technical report followed based on a consultation meeting held in 1971².

Pharmacovigilance is defined as 'the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems'. Recently, its concerns have been widened to include: herbal, traditional and complementary medicine, blood products, biological, medical devices and vaccines³⁻⁵.

Clinical trials from phase I to III give limited information to regulatory authorities about the full

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safety profile. There is a lot of responsibility on healthcare workers to keep a close eye on these issues to prevent adverse events and its increased financial burden on hospitals⁶.

With the importance pharmacovigilance has gained over the years, drug regulatory authorities have established national pharmacovigilance centers. There is a great need to improve further because of public expectations and the demands of modern public health⁷. Pakistan became an associated member many years ago and still has the same status. Recently the Pharmacy Services Directorate (which looks after Pharmacovigilance and Clinical research in Drug Regulatory Authority of Pakistan) has issued the Guidelines to be undertaken for performance of Pharmacovigilance Activities and also Med Vigilance Online Management System and is strengthening the whole process⁸.

ADR reporting is the basis of any successful pharmacovigilance system. Identifying an ADR immediately and reporting it to the concerned pharmaceutical company and the national regulatory authority is the most important step. WHO defines ADRs as 'a response to a drug which is noxious and unintended, and which occurs at doses normally used in human for the prophylaxis, diagnosis, or therapy of disease, or for the modifications of physiological function'⁹.

ADRs causes increase in mortality and morbidity and is related with increased financial loss¹⁰.

Studies have shown that optimizing knowledge, attitude and practices (KAP) with regard to PV is important in formulating strategies to encourage ADR reporting¹¹.

Literature published examining KAP towards PV and ADR reporting among pharmacists was very low. Exploring causes of underreporting, shows that lack of knowledge and unfamiliarity of the reporting system were major discouraging factors for reporting ADRs¹²⁻¹³.

MATERIALS AND METHODS

A cross-sectional descriptive study was conducted in Lahore College of Pharmaceutical Sciences. Fourth and final year students only willing to participate and having signed the informed consent were included. The questionnaire used was pre-validated and the whole process was given an approval by the college ethics review committee.

133 total students participated in the study. 66 students from fourth and 57 from final year completed and submitted the survey questionnaire. The demographic variables included characteristics like age, sex, residential status, parental educational status and usage of internet. The 16 multiple choice questions assessed the knowledge and awareness of pharmacovigilance and ADR reporting. Incorrect answer was given "0"

while the correct answer was marked "1" for calculating the mean score.

The questionnaire was repeated after an educational intervention done by giving a presentation on pharmacovigilance, its definition, importance of ADR reporting and the process being followed by the national and international bodies. The overall percentage was calculated for both the classes on their responses for pre-lecture and post-lecture survey. Descriptive statistics for continuous variable was presented as Mean $\pm$ SD and for categorical as proportion and percentage. Paired T-test was used to calculate the mean difference. Data was entered in SPSS version 24 and all statistical descriptive and analytical tests were done.

Objectives

1. To assess the knowledge and awareness regarding Pharmacovigilance and Adverse Drug Reaction Reporting amongst fourth and final year Pharmacy students.
2. To evaluate the effectiveness of an educational program for improving pharmacist knowledge of Pharmacovigilance and Adverse Drug Reaction reporting.

RESULTS

In this study 59.3% were females as compared to 40.7% males (Table 1) and 66% of participants' belonged to urban as compared to 34% from rural area. Majority of parents of the study population had done their graduation. (Table 2)

Correct response among the study participants regarding the healthcare professionals responsible for reporting ADRs in a hospital was 94 (76.4%) post-lecture as compared to 56 (45.5%) pre-lecture. Post-lecture 103(83.7%) gave the correct answer about the definition of Pharmacovigilance as compared to the pre-lecture response of 18(14.6%).

Important objective of Pharmacovigilance was correctly answered by 29(23.6%) prior to the lecture and after lecture correct response was 85(69.1%). Location of international center for ADRs monitoring was identified correctly by 85(69.1%) in post-lecture response as compared to 12(9.8%) in the initial response.

To the question on commonly used scale for assessment of causality of an ADR 114 (92.7%) were correct in their Post-lecture response as compared to 72(58.5%) pre-lecture. WHO online database for ADRs reporting was correctly marked by 96 (78%) after the lecture whereas only 27(22%) could before. Rare ADRs can be identified in the following phase of clinical trial was correctly identified by 47(38.2%) after listening to the lecture as compared to 19(15.4%) pre-lecture. Regarding the importance of reporting ADRs correct answer was identified by 110 (89.4%) in the post-lecture response group as compared to 105(85.4%) pre-lecture.

Table No.1: Gender and region demographics

Demographics	Frequency	Percentage
Male	50	40.7
Female	73	59.3
Rural	42	34.1
Urban	81	65.9

Table No.2: Parent's education level

Education Level	Father		Mother	
	Frequency	%age	Frequency	%age
PG	13	10.6	9	7.3
Primary	13	10.6	19	15.4
Matric	32	26.0	28	22.8
Secondary	8	6.5	11	8.9
Under-graduate	19	15.4	18	14.6
Graduate	38	30.9	38	30.9

About which Regulatory body is responsible for monitoring ADRs in Pakistan correct post-lecture response was 112(91.1%) as compared to pre-lecture response of 66(53.7%).

The response about which Common method is used to monitor ADRs of new drugs once they are launched was given correctly in post-lecture group by 75(61%) as compared to 47(38.2%) pre-lecture. Regarding what type of ADRs is to be reported 118 (95.9%) in the post-lecture response gave correct answer in comparison to 105(85.4%). Regarding the knowledge of ADR reporting being a Professional obligation pre-lecture response was 90(73.2%) as compared to post-lecture response 106(86.2). On the question which measures are to be taken when ADR is suspected students after the lecture responding correctly were 112(91.1%) as compared to 103(83.7%) pre-lecture . (Table 3).

Table No.3: Participant's response comparison

Characteristics	Answer	Pre-lecture response	Post-lecture response
The healthcare professionals responsible for reporting ADRs in a hospital	Incorrect	67(54.5%)	29(23.6%)
	Correct	56(45.5%)	94(76.4%)
Definition of Pharmacovigilance	Incorrect	105(85.4%)	20(16.3%)
	Correct	18(14.6%)	103(83.7%)
Important objective of Pharmacovigilance	Incorrect	94(76.4%)	38(30.9%)
	Correct	29(23.6%)	85(69.1%)
Location of international center for ADRs monitoring	Incorrect	111(90.2%)	38(30.9%)
	Correct	12(9.8%)	85(69.1%)
Commonly used scale for assessment of causality of an ADR	Incorrect	51(41.5%)	9(7.3%)
	Correct	72(58.5%)	114(92.7%)
WHO online database for ADRs reporting	Incorrect	96(78%)	27(22%)
	Correct	27(22%)	96(78%)
Rare ADRs can be identified in the following phase of clinical trial	Incorrect	104(84.6%)	76(61.8%)
	Correct	19(15.4%)	47(38.2%)
ADR and its causative drug	Incorrect	66(53.7%)	80(65%)
	Correct	57(46.3%)	43(35%)
Regarding classification of ADRs	Incorrect	18(14.6%)	13(10.6%)
	Correct	105(85.4%)	110(89.4%)
It is important to report ADRs because it leading to	Incorrect	27(22%)	18(14.6%)
	Correct	96(78%)	105(85.4%)
Regulatory body is responsible for monitoring ADRs in Pakistan	Incorrect	57(46.3%)	11(8.9%)
	Correct	66(53.7%)	112(91.1%)
Common method to monitor ADRs of new drugs once they are launched in the market	Incorrect	76(61.8%)	48(39%)
	Correct	47(38.2%)	75(61%)
Have you read any article on prevention of Adverse Drug Reaction?	Incorrect	87(70.7%)	84(68.3%)
	Correct	27(22%)	39(31.7%)
What type of ADRs to be reported?	Incorrect	18(14.6%)	5(4.1%)
	Correct	105(85.4%)	118(95.9%)
ADR reporting is a Professional obligation	Incorrect	33(26.8%)	17(13.8%)
	Correct	90(73.2%)	106(86.2)
Measures to be taken when ADR is suspected	Incorrect	20(16.3%)	11(8.9%)
	Correct	103(83.7%)	112(91.1%)

Table No.4: Comparison and correlation between responses

	Mean	Standard. Deviation	Correlation	Test Statistic (Paired T-test)	P-Value ((Paired T-test))
Overall Score (Pre)	7.55	1.812	0.41	-20.17	0.000

DISCUSSION

Safety of products being used by the doctors and dispensed by pharmacists depend on the effective pharmacovigilance system which depends on the reporting of Adverse Drug Reactions by the healthcare professionals to the regulatory authorities and individual pharmaceutical company marketing the product.

Drugs are endorsed to be marketed having adequate evidence that the product has an encouraging benefit-to-harm ratio. It is evident from systematic review that after approval of the product for general use the regulatory authorities take required action, including warnings on the label, letter to the prescribers for caution and in serious reactions withdrawal of marketing authorization depending on reported adverse drug reaction.¹⁴

Studies published from Pakistan and the region showed evidence that the knowledge, awareness and reporting of ADR is poor amongst the healthcare professionals including pharmacists¹⁵⁻¹⁷.

Most of the studies have suggested that improvement in the basic knowledge of these healthcare professionals can be achieved by reviewing and improving the curriculum is the first step and then later on continued medical education in the shape of workshops and seminars should be regularly held to support their clinical function^{18, 20}.

Our study prior to the educational intervention showed that only one third knew about the HCPs responsible for reporting, one fourth knew the definition of pharmacovigilance, one third knew of the important objective of pharmacovigilance, only few students knew of the location of international center for ADR monitoring, half of them knew of the commonly used scale for assessment of causality of an ADR, one third knew about the WHO online database for ADR reporting, only half knew about the regulatory body responsible for monitoring ADR in Pakistan, very few knew about the types of ADR to be reported and only 11% new of the measures to be taken on suspicion of an ADR. Similar results were seen on other questions asked. The results shown in our study were similar to the results reported in the literature²¹⁻²².

After the power point presentation on the subject explaining the definition and importance of PV and ADR reporting there was a significant improvement in the results of the post-KAP survey. Pharmacists who were trained regularly in their departments for PV and ADR reporting knew more the purpose of ADR forms and the system as reported in different studies^{20, 23}. Our

study also showed that educational intervention is an accepted means of improvement in knowledge of pharmacovigilance and ADR reporting. Our findings are similar to previously reported studies²⁴⁻²⁵.

CONCLUSION

ADR reporting is the main source of pharmacovigilance. Not only having information of pharmacovigilance system but actually reporting the adverse drug reactions to the regulatory authorities and the concerned manufacturer is essential. Drug Regulatory Authority of Pakistan is an Associate member of the WHO monitoring Center and has set up a system which is required to be followed. Punjab government has also established Punjab Drug Control Unit for pharmacovigilance and ADR reporting. These will also function properly if the pharmacists and HCPs have the knowledge and awareness of the system and are willing to report the adverse drug reactions. This can only be achieved if proper education on the subject is imparted during the education of healthcare professionals, but also establishing a system where constant reminders are given in shape of continuing education by workshops, seminars, newsletters and other similar programs.

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Frequency of Hepatocellular Carcinoma and Associated Factors in Patients Presenting to Mayo Hospital, Lahore

Hepatocellular Carcinoma
and Associated Factors in
Patients

Samina Qamar, Shahid Mahmood, Ahmad Hameed and Sobia Ashraf

ABSTRACT

Objective: To determine the frequency of patients having Hepatocellular Carcinoma and major causative factors associated with it, presenting to Mayo Hospital Lahore.

Study Design: Observational / cross-sectional study

Place and Duration of Study: This study was conducted at the Oncology Department of Mayo Hospital, Lahore from Jan 2017 to Dec 2017.

Materials and Methods: This study enrolled clinical data of 151/207 Hepatocellular Carcinoma patients. Their age, sex, socioeconomic status underlying co-morbidity, presence or absence of liver cirrhosis, tumor size, single/multiple tumors, tumor stage, hepatitis serologies, serum AFP levels, and portal vein thrombosis.

Results: Out of 151, 106(70%) were males and 45 (30%) were females. Mean age of presentation was 57.1 ± 8.6 years. Patients with rural background were 115 (76.2%) and urban cases were 36 (23.7%). 136 (90%) patients belonged to lower socioeconomic strata while 15 (10%) were of middle social class. 104 (69%) patients were positive for Hepatitis C virus, 27 (18%) were positive for Hepatitis B virus, 6 (4%) were infected with both viruses, 3 (2%) were alcoholic and 11(7%) patients had no known causative factor. Regarding levels of serum Alpha fetoprotein, 67 (44 %) of patients had AFP more than 400 ng/ml, 48 (32%) had AFP level between 20-400ng/ml and 36 (25%) had AFP levels below 20 ng/ml. Mean tumor size was $8.2 \text{ cm} \pm 2.9 \text{ cm}$. 3 (1.9%) patients were at Stage I, 16(10.7%) had stage II, 84 (55.7%) had stage III and 48(31.7%) of patients were at stage IV of disease., 48(32%) of patients had class A of Child classification, 71 (47%) class B, and 32(21%) had class C.

Conclusion: In our population, Hepatitis C virus is the main causative agent behind Hepatocellular Carcinoma and most of the patients present with large tumor size, multicentric tumor and portal vein thrombosis. Serum AFP levels are low in more than 50% of patients and is not reliable for detecting HCC.

We should implement effective screening programs of viral hepatitis and cirrhosis to save this precious organ and prevent the need of liver transplant.

Key Words: Cirrhosis, Hepatocellular Carcinoma, Serum AFP level, Hepatitis B and C

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INTRODUCTION

Hepatocellular carcinoma (HCC) is the most common malignancy of liver. It is second commonest cause of cancer death around the world as its incidence is $5.4\%^1$. Highest incidence is found in Asian (China, Taiwan, Korea) and Sub-Saharan African countries because of Hepatitis B virus that is transmitted to infants through vertical transmission. In Japan and Europe most important causative agent is Hepatitis C virus ². Other important causative factors of HCC are metabolic toxins like aflatoxin and alcohol, hemochromatosis, alpha1 antitrypsin deficiency and steatohepatitis.

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All these agents infect and reside in hepatocytes, disturb their structure, function and genomic material resulting in a repetitive cycle of inflammation and regeneration of hepatocytes. Hepatocytes try to overcome the damage by dividing rapidly but become dysplastic and ultimately neoplastic as they accumulate structural and numeric chromosomal abnormality resulting in genomic instability³

Developed countries like United States, HCC is relatively uncommon. Pakistan and other under-developed countries harbors great number of HCC patients. Many remain undiagnosed due to lack of proper health care facilities and unawareness to risk factors. Pakistan has 2nd highest prevalence of chronic Hepatitis C infection in the world ⁴. Approximately over 10 million people are infected with chronic Hepatitis virus in Pakistan. Hepatitis C prevalence is 6%-13% while Hepatitis B prevalence is 2-3%. According to Punjab cancer registry, it is the fifth most common cancer collectively in both genders (3.8%) and 3rd most common in men (6.6%) ⁵. Viral hepatitis and excessive alcohol consumption are the top most causes

of HCC ⁶. HCC can be treated by radioablation, chemoembolization, resection and transplant in advanced stages but has a dismal outcome ⁷.

The purpose of this study was to find out frequency of patients presenting with HCC and associated causative factors that play major role in development of carcinoma, so that we can plan proper screening methods to detect and prevent this menace. We collected data encompassing various fields like socioeconomic status and background, causative agent, stage and tumor size at presentation, cirrhotic changes, Child Pugh score (based on presence of encephalopathy, ascites, albumin, prothrombin time, bilirubin and divided into class A,B and C).

MATERIALS AND METHODS

This cross-sectional observational study enrolled clinical data base of 207 HCC patients and variables studied were age, sex, socioeconomic status (monthly income below 10,000 PKR = Low, or above =Middle class) underlying co-morbidity, presence or absence of liver cirrhosis, tumor size (Less or more than 10cm), single/multiple tumors, tumor stage, hepatitis serologies, serum AFP levels (Normal level= upto 44ng/ml), portal vein thrombosis, Child classification (Classified as A, B and C depending upon serum bilirubin, albumin, prothrombin, ascites and encephalopathy) of patients diagnosed with HCC between January 2017 till December 2017 were extracted from medical records of Oncology Department and outdoor of Mayo Hospital, Lahore with the help of participating investigators. Out of 207 patients, 151 cases fulfilled the inclusion criteria and were included in the study. All information was recorded in a predesigned proforma. All data was analyzed by SPSS 22 and descriptive statistics were used for variables. Mean and standard deviation was calculated for quantitative variables. Frequency and percentage was calculated for qualitative variables like gender, socioeconomic status, cirrhosis, stage of tumor, causes of HCC, serum AFP and portal vein thrombosis.

Inclusion Criteria: All patients presenting to Oncology department with diagnosis of HCC either biopsy proven or with radiological evidence of disease were included in the study.

Exclusion Criteria: Patients having insufficient diagnostic investigations to prove hepatic mass as HCC were excluded.

RESULTS

Total 151 patients were included in the study. Out of 151, 106(70%) were males and 45 (30%) were females. Mean age of presentation was 57.1 ± 8.6 years. Patients with rural background were 115 (76.2%) and urban cases were 36 (23.7%). 136 (90%) patients belonged to lower socioeconomic strata while 15 (10%) were of middle social class. (Table I)

According to our study 104 (69%) patients were positive for Hepatitis C virus, 27 (18%) were positive for Hepatitis B virus, 6 (4%) were infected with both viruses, 3 (2%) were alcoholic and 11(7%) patients had no known causative factor for HCC (Figure I). Analysis of child-turcotte-pugh classification, our patient population showed that 48(32%) of patients had class A, 71 (47%) class B, and 32(21%) had class C (Figure II). Levels of serum Alpha fetoprotein showed that 67 (44 %) of patients had AFP more than 400 ng/ml, 48 (32%) had AFP level between 20-400ng/ml and 36 (25%) had AFP levels below 20 ng/ml (Figure III) Mean tumor size was $8.2 \text{ cm} \pm 2.9 \text{ cm}$. Tumor size was more than 10cm in 39(25.8%) patients. Multicentric tumor was present in 97(64.2%) and Portal Vein Thrombosis was seen in 56 (37%) of patients. Regarding stage of Hepatocellular carcinoma 3 (1.9%) patients were at Stage I, 16(10.7%) had stage II, 84 (55.7%) had stage III and 48(31.7%) of patients were at stage IV of disease.

Table No.1: Demographic features of HCC.

Males	106 (70%)
Females	45 (30%)
Rural	115 (76.2%)
Urban	36 (23.7%)
Lower class	136 (90%)
Middle class	15 (10%)

Causes of Hepatocellular Carcinoma in Study subjects (n=151)

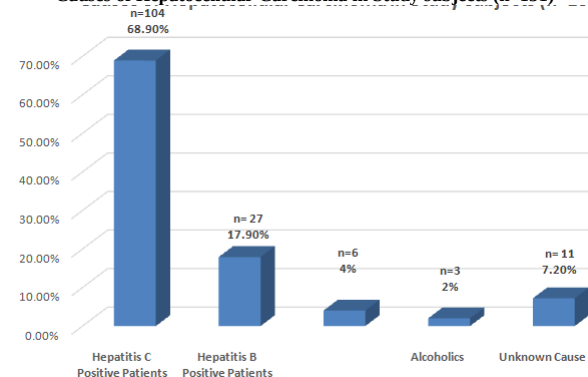


Figure No.I- Causative agent of Hepatocellular Carcinoma.

Child-Turcotte- Pugh Class at Presentation (n=151)

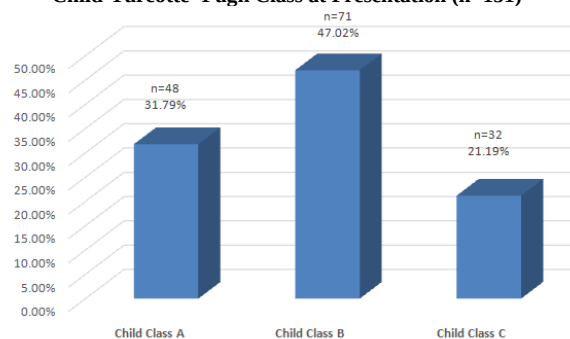


Figure No.2- Stage of cirrhosis at presentation.

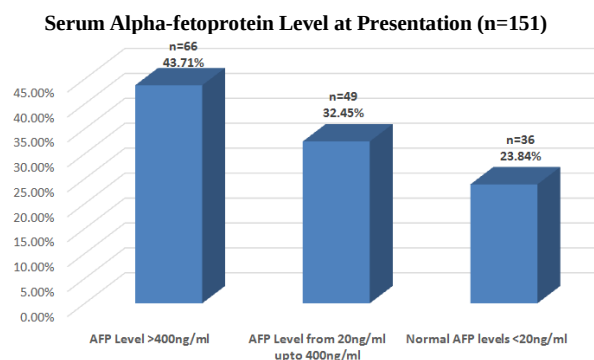


Figure No.3: Level of serum AFP (normal upto 44ng/ml).

DISCUSSION

Hepatocellular carcinoma is life threatening carcinoma with rising incidence worldwide. Despite improvement in HCC management multiple factors like lifestyle, metabolic syndrome, environmental factors, obesity, hepatitis viruses and many other are supporting its development. It is diagnosed at advanced stage and has many complications during and after treatment⁸. Males and females are affected differently from it. Zheng et al stated that estrogen /androgen signaling pathway is associated with decreased/increased transcription and replication of HBV genes that promote development of HBV infection by up/downregulating RNA transcription of viruses which in turn slows the progression of HBV induced HCC. Estrogen and androgen can also effect HBV related HCC by induction of epigenetic changes. This could be the reason behind different incidence among males and females⁹. In our study, out of 151, 106(70%) were males and 45 (30%) were females. Kao conducted multivariate analysis on HCC patients and results showed that HCC was associated with poor prognosis when accompanied by factors like age older than 65 years, Alpha fetoprotein (AFP) greater than 20 and multiple tumors¹⁰. Similarly, poor survival was seen in older patients, with advanced tumor stage and multiple tumors⁷. Kotewall's group of patients had median age of 58.5 with age range of 25-78 years¹¹. In our study, mean age of presentation was 57.1 ± 8.6 years Egyptian population also had median age of 58 years at diagnosis of HCC while African patients presented at median age of 46 years. Hepatitis C was leading cause of HCC in Egypt while Hepatitis B was major cause in African population¹². We concluded that most of our patients were from rural background 115 (76.2%) and urban cases were 36 (23.7%). 136 (90%) patients belonged to lower socioeconomic (income below 10,000 PKR/month) strata while 15 (10%) were of middle social class (income above 10,000 PKR). Similarly, in United States lower socioeconomic strata harbored more cases of HCC than higher class¹³.

AFP level more than 400ng/mL is independent risk factor for overall survival, it is still not sensitive enough

to predict the prognosis in patients with HCC diameter less than 3 cm¹⁴. Similarly, Kotewall found that AFP levels (more than 400ng/mL) were higher in HCV infected patients (78.2%) as compared to HBV infected group (67.1%)¹². We found that (67) 44 % of patients had AFP more than 400 ng/ml, 48 (32%) had AFP level between 20-400ng/ml and 36 (24%) had AFP levels below 20 ng/ml. In our patients tumor size was more than 3cm and still more than 50% of patients had AFP below 400ng/mL. We conclude that AFP is not sensitive enough to detect HCC in our population as most of them are infected with HCV.

According to our study 104 (69%) of patients were positive for Hepatitis C virus, 27(18%) were positive for Hepatitis B virus, 6 (4%) were infected with both viruses. However in United States, HCV is more common in HCC patients as compared to HBV¹⁵. Munaf A and studies in United States showed prevalence of HCV to be 66% and HBV as 34%. Patients with HCV were more likely to develop HCC at advanced age of 52 years as compared to HBV infected who developed HCC at the age of 40 years^{15,16}. A study conducted in Iran on 1654 people (healthy) with mean age of 29.1 showed HCV infection in 0.42%(7/1654) of patient population. Among them 80% were males and 20% were females. Iran has very low prevalence of hepatitis virus infection¹⁷. So our data is consistent with these observations but different from China.

In our patients tumor size was more than 10cm in 39 (25.8%) patients. Kotewall's patients had median tumor size of 2.7 cm¹². Tumor size was larger; more than 5cm in HCV group (66%) while less than 5cm in HBV group (59.3%). In our population, tumor size is much larger than seen in other studies. We found that multicentric tumor was present in 97 (64.2%) and Portal Vein Thrombosis was seen in 56 (37%) of patients. Contrastingly, Munaf states that portal vein thrombosis was seen in 8% of HCV patients and only 1% of HBV group. HCV-HCC group were more cirrhotic than HBV and had more than two times higher rate of solitary macrovascular involvement than HBV group (OR=0.245 and 2.533 respectively). Regarding stage of Hepatocellular carcinoma 3(1.9%) patients were at Stage I, 16 (10.7%) had stage II, 84 (55.7%) had stage III and 48 (31.7%) of patients were at stage IV of disease. Analysis of child-turcotte-pugh classification, our patient population showed that 32% of patients had class A, 47% class B, and 21% had class C. In West and China most patients are diagnosed with early resectable disease¹⁸. This probably is due to effective screening programs in high risk cirrhotic population which include ultrasound and serum AFP levels. While in our local population no such facility is available for cirrhotic patients and rural population is unaware of disease signs and symptoms. Lack of awareness among masses and ineffective screening leads to late disease presentation and diagnosis resulting in high morbidity and mortality due to HCC.

CONCLUSION

In our population, Hepatitis C virus is the main causative agent behind Hepatocellular Carcinoma and most of the patients present with large tumor size, multicentric tumor and portal vein thrombosis. Serum AFP levels are low in more than 50% of patients and is not reliable for detecting HCC.

We should implement effective screening programs of viral hepatitis and cirrhosis to save this precious organ and prevent the need of liver transplant.

Author's Contribution:

Concept & Design of Study: Samina Qamar
 Drafting: Shahid Mahmood
 Data Analysis: Ahmad Hameed, Sobia Ashraf
 Revisiting Critically: Samina Qamar, Shahid Mahmood
 Final Approval of version: Samina Qamar

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Vitamin B₁₂ Deficiency in Megaloblastic Anemia in Rural Population of Tando Muhammad Khan, Sindh

Inayatullah Memon and Attiya Memon

ABSTRACT

Objective: Determine the vitamin B₁₂ deficiency in megaloblastic anemia in rural population of Tando Muhammad Khan, Sindh

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Pathology Department, Indus Medical College Hospital Tando Muhammad Khan from May 2017 to Feb. 2018.

Materials and Methods: A sample of 170 cases of megaloblastic anemia (75 male and 95 female) were studied according to inclusion criteria. Volunteers were informed and asked for blood sampling. Blood samples were collected. Vitamin B₁₂ was detected by ELISA assay kit. Data was analyzed on SPSS (ver 22.0) at 95% CI (P ≤ 0.05).

Results: Mean vitamin B₁₂ deficiency was noted in both male and female subjects, however, the female subjects were having significantly low levels of 141.75±30.61 pg/ml in contrast to 201.16±36.7 pg/ml in male subjects (P=0.0001). Vitamin B₁₂ categorized as normal levels, borderline B₁₂ levels, deficient levels and severe deficiency levels were found in 40 (23.52%), 25 (14.70%), 87 (51.17%) and 18 (10.57%) respectively (P=0.0001). Total 130 (76.47%) subjects were having one or other type of vitamin B₁₂ deficiency.

Conclusion: Frequency of 76.47% of vitamin B₁₂ deficiency in megaloblastic anemia was noted in rural population of Tando Muhammad Khan, Sindh

Key Words: Vitamin B₁₂ deficiency, Megaloblastic anemia, Rural, Sindh

Citation of articles: Memon I, Memon A. Vitamin B₁₂ Deficiency in Megaloblastic Anemia in Rural Population of Tando Muhammad Khan, Sindh. Med Forum 2018;29(10):31-34.

INTRODUCTION

Megaloblastic anemia is one of macrocytic anemia characterized by large-sized red blood cells that are prone to lysis in peripheral circulation. Megaloblastic anemia is caused by delayed nuclear maturation due to deficiency of vitamin B₁₂ and folic acid.¹ Vitamin B₁₂ is also known as cobalamin. It is needed as co-enzyme for the enzymes involved in nuclear maturation. Its deficiency results in larger red blood cells (RBC). Mean corpuscular volume (MCV) is a measure of mean RBC volume and is a clinical marker of macrocytic megaloblastic anemia. MCV more than 100 femtoliter (fl) is considered as macrocytic RBC. Vitamin B₁₂ deficiency is one of cause of macrocytic megaloblastic anemia. Vitamin B₁₂ plays essential role in nuclear maturation.^{1,2} Vitamin B₁₂ forms 2 co-enzymes; the methyl-cobalamin (MC) and the S-adenosyl cobalamin (SAC). Methionine synthetase needs methyl cobalamin

as co-enzyme and catalyzes the reaction of conversion of homocysteine to methionine.¹⁻³ While the L-methylmalonyl-CoA- coenzyme A mutase requires SAC as co-enzyme; this enzyme converts methylmalonyl-CoA to succinyl-CoA. Methyl cobalamin and S-adenosyl cobalamin (SAC) act as one carbon donor for the synthesis of nucleotides of proliferating cells as red blood cells in bone marrow. This shows the essentiality of vitamin B₁₂ for nuclear maturation. Bone marrow and epithelial cells are the rapidly proliferating cells of body and vitamin B₁₂ deficiency adversely affects at the most. Diet of animal origin is the sole source of vitamin B₁₂. Vitamin B₁₂ is absorbed from gut and circulates in blood bound with its carrier proteins. Daily gut absorption approximates 5 µg. While daily body requirement of Vitamin B₁₂ is 3 µg. Human liver stores 2000-5000 µg of vitamin B₁₂ approximately and these are sufficiency for many years.³⁻⁶ The causes of vitamin B₁₂ deficiency include dietary deficiency, malabsorption syndrome and increased body demands as during pregnancy and in growing children. Causes of vitamin B₁₂ deficiency include; stomach disease, pancreatic disease, and small intestine disorders; all of these result in its malabsorption. Worm infestation is an important cause of vitamin B₁₂ deficiency as *Diphyllobothrium latum* (fish tape worm) being the cause. Megaloblastic anemia

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is a common manifestation of vitamin B₁₂ deficiency.^{4,7} True burden of Vitamin B₁₂ deficiency is not known for the developing countries, however, available studies show high burden. Search of published studies shows a few studies are available on the topic of frequency of vitamin B₁₂ deficiency.³⁻⁷ We planned a prospective cross sectional study to determine the vitamin B₁₂ deficiency in megaloblastic anemia in rural population of Tando Muhammad Khan, Sindh.

MATERIALS AND METHODS

The present cross sectional study was conducted at Indus Medical College Hospital Tando Muhammad Khan from May 2017 to Feb. 2018. Prior approval was taken from the institute's ethical review committee. A sample of 170 cases of megaloblastic anemia (75 male and 95 female) were studied according to inclusion criteria. Sample size was calculated by sampling for proportions of sample calculation. Inclusion criteria were; age 20- 40 years, both gender, MCV > 100 fl, and peripheral blood film showing hyper segmented neutrophils.⁸ Exclusion criteria were old age, normocytic and normochromic anemia, microcytic anemia and concomitant major systemic disease. Strict vegetarians, diabetics, major cardiac disorders, chronic inflammatory diseases, pulmonary tuberculosis, etc were excluded. Also the subjects taking multi vitamins were strict exclusion criteria. Medical officers and physicians were requested communicated to help in proper screening of patients and provision of complete patient's biodata. Patient's biodata, presenting problems were collected on a pre-designed clinical proforma. These were provided to the medical officers. Medical officers were requested to help in screening of patients according to the inclusion and exclusion criteria and to fill the proforma properly. Only Properly labelled blood samples were screened for study. Volunteers were asked for signing the consent form. They were informed about the objective of study. They were assured that the personal information will be confidential and there will be no harm to them and no extra financial burden. Volunteers were asked for blood sample. Prominent vein in ante cubital fossa was marked. Area was cleaned with alcohol swab. 5 ml blood was withdrawn in disposable syringe and collected in EDTA tubes. Red blood cells, hematocrit and hemoglobin were analysed on hematology analyzer (Sysmex, KX 21). Serum vitamin B₁₂ was estimated by ELISA method. Normal, borderline, deficiency and severe vitamin B₁₂ levels were defined as >240pg/ml, 170-240 pg/ml, <170 pg/ml and <100 pg/ml respectively.⁹ Data was kept confidential and consent forms were secured. Data was analyzed on SPSS (ver 22.0) at 95% CI (P ≤ 0.05). Student's t-test analysed the continuous variables (age, vitamin B12 level, etc) and Chi-square test analysed the categorical variables (gender and vitamin B12 categories).

RESULTS

Of total 170 study subjects, male and female were noted as 75 (44.17%) and 95 (55.82%) respectively (P=0.001). Female to male ratio was 1.26:1 approximately (table 1).

Table No.1: Descriptive findings of study subjects (n=170)

	Male	Female	P-value
Gender	75 (44.17%)	95 (55.82%)	0.001
Age (years)	32.95±8.43	32.35±5.73	0.17
Hemoglobin (g/dl)	13.97 ±1.45	13.06±3.13	0.0001
Hematocrit (Hct.) (%)	43.10±3.75	41.06±7.08	0.0001
RBC (million/ μ L)	4.23±0.23	4.08±0.43	0.0001
Vitamin B12 (pg/dl)	201.16±36.7	141.75±30.61	0.0001

Table No.2: Vitamin B₁₂ distribution of study subjects (n=170)

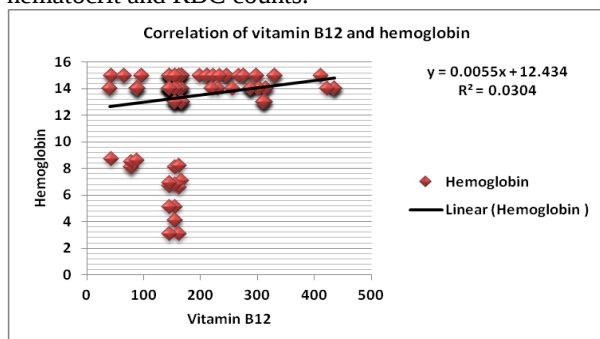
Vitamin B ₁₂ levels	Mean	SD	P-value
Normal B ₁₂ level (>240 pg/ml)	312.43	55.57	0.0001
Borderline B ₁₂ deficiency (170-240 pg/dl)	175.68	26.73	
B ₁₂ Deficiency (<170 pg/dl)	154.59	7.27	
Severe B ₁₂ deficiency (<100 pg/dl)	72.19	21.11	
Total	186.10	81.07	

Table No.3: Frequency of Vitamin B₁₂ in study subjects (n=170)

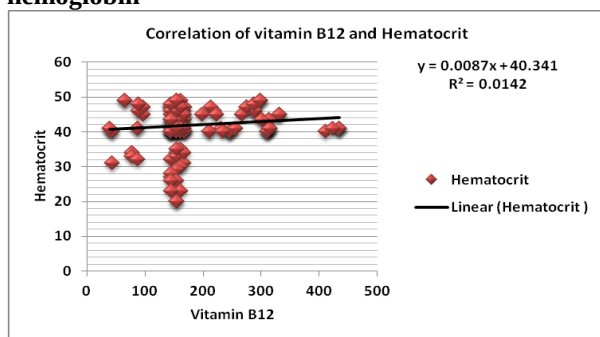
Vitamin B ₁₂ levels	No.	%	P-value
Normal B ₁₂ level (>240 pg/ml)	40	23.52	0.0001
Borderline B ₁₂ deficiency (170-240 pg/dl)	25	14.70	
B ₁₂ Deficiency (<170 pg/dl)	87	51.17	
Severe B ₁₂ deficiency (<100 pg/dl)	18	10.57	
Total	170	100	

Age (mean± SD) of male and female was 32.95±8.43 and 32.35±5.75 years respectively (P=0.17). Hemoglobin, **hematocrit** and RBC counts were low in female subjects compare to male (P<0.05) as shown in table 1. Mean vitamin B₁₂ deficiency was noted low in both male and female subjects, however, the female subjects were having significantly low levels of 141.75±30.61 pg/ml in contrast to 201.16±36.7 pg/ml in male subjects (P=0.0001). Vitamin B₁₂ categorized as

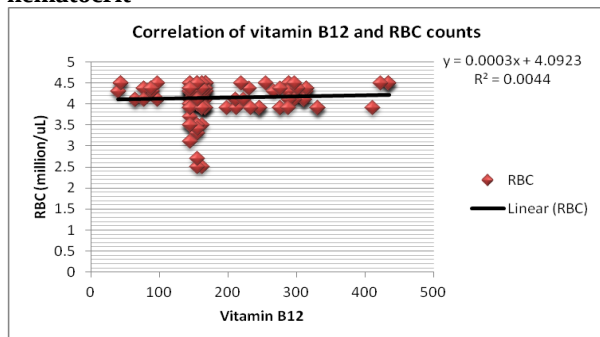
normal levels, borderline B₁₂ levels, deficient levels and severe deficiency levels were found in 40 (23.52%), 25 (14.70%), 87 (51.17%) and 18 (10.57%) respectively (P=0.0001). Total 130 (76.47%) subjects were having one or other type of vitamin B₁₂ deficiency. Graph 1-3 shows the correlation of vitamin B₁₂, hemoglobin, hematocrit and RBC counts.



Graph No.1: Correlation of vitamin B₁₂ and hemoglobin



Graph No.2: Correlation of vitamin B₁₂ and hematocrit



Graph No.3: Correlation of vitamin B₁₂ and RBC counts

DISCUSSION

The present is a small scale study reporting on the vitamin B₁₂ levels in healthy adults. Age (mean± SD) of male and female was 32.95±8.43 and 32.35±5.75 years respectively (P=0.17). Of total 170 study subjects, male and female were noted as 75 (41.17%) and 95 (55.82%) respectively (P=0.001). Female to male ratio was 1.26:1 approximately. The mean age of study subjects shows young population that is in contrast to previous studies.^{10,11} Role of Vitamin B₁₂ lies in its nucleotide

biosynthesis one carbon donation through folic acid. Both Vitamin B₁₂ and folic acid are essential for the proliferating cells in particular the bone marrow where millions of cells are proliferating each second. The bone marrow produces and supplies millions of blood cells to the peripheral circulation each moment. Thus bone marrow is affected earlier in cases of Vitamin B₁₂ deficiency. In present study, total 130 (76.47%) subjects were having one or other type of vitamin B₁₂ deficiency. A previous study¹¹ reported vitamin B₁₂ deficiency of 72.6%.¹¹ Our finding of 76.47% vitamin B₁₂ deficiency is consistent with above study. Normal, borderline deficiency, deficiency and severe vitamin B₁₂ deficiency were noted in 40 (23.52%), 25 (14.70%), 87 (51.17%) and 18 (10.57%) respectively (P=0.0001). Our findings are in agreement with previous reported studies.^{11,16-19} Vitamin B₁₂ deficiency impairs capacity of bone marrow stem cell proliferation resulting in abnormal red blood cell production that are larger than normal in size and prone to destruction in peripheral circulation resulting in anemia. Both erythroid and myeloid series of bone marrow are adversely affected by vitamin B₁₂ deficiency. Bone marrow releases immature red blood cells having large mean corpuscular volume. Also the white blood cells are abnormal showing hyper segmented polymorphs. Hypersegmented neutrophils is a reliable clinical marker of vitamin B₁₂ deficiency.^{10,11} In present study we found high frequency of vitamin B₁₂ deficiency that is prevalent in the rural population of Tando Muhammad Khan, Sindh. Most probable cause of this is the nutritional deficiency. The findings are in agreement with a previous study.¹² Vitamin B₁₂ deficiency of 76.47% of present study is consistent with a previous national study.¹³ This previous study¹³ reported frequency of deficiency of 85% and 78.5% in vegetarians and non- vegetarians respectively. A previous national study reported frequency of 65% vitamin B₁₂ deficiency, that is low and in disagreement with 76.47% noted in the present study. This discrepancy could be due to the different sample size and population. Frequency of 76.47% vitamin B₁₂ deficiency of present study is in full agreement with previous studies.¹¹⁻¹⁵ Our findings are also supported by previous studies¹⁶⁻¹⁹ that noted 76% vitamin B₁₂ deficiency. Evidence based frequency of 76.47% vitamin B₁₂ deficiency of present study is an important clinical finding and shows the prevalent vitamins deficiencies. Present study has certain limitations; first- folic acid was not estimated, second- sample size was small, third- rural population was studied, hence the results are not valid to generalize as representative of total population. However, the vitamin B₁₂ deficiency in diagnosed cases of megaloblastic anemia is important finding. The present study reports vitamin B₁₂ deficiency is prevalent in the rural population. This needs large scale studies to cover the total population of

the area for concluding proper burden of vitamin B¹² deficiency.

CONCLUSION

The present study reports frequency of 76.47% vitamin B₁₂ deficiency in megaloblastic anemia in rural population of Tando Muhammad Khan, Sindh. This shows the severity of unnoticed vitamin B₁₂ deficiency in those presenting with megaloblastic anemia. Vitamin B₁₂ screening is mandatory for those presenting with high mean corpuscular volume. Vitamin B₁₂ supplements should be given to patients for prevention of long term irreversible complications beside anemia. Further studies are recommended with large population sample.

Author's Contribution:

Concept & Design of Study: Inayatullah Memon
 Drafting: Attiya Memon
 Data Analysis: Attiya Memon
 Revisiting Critically: Inayatullah Memon,
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 Final Approval of version: Inayatullah Memon

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Role of N-Acetylcysteine in Clearance of Secretions in Mechanical Ventilated Patients

Aatir Fayyaz, Munir Ahmad and Rana Muhammad Arshad

ABSTRACT

Objective: To determine the role of nebulized N-acetylcysteine in mechanical ventilation in clearing the airway of these patients

Study Design: A Randomized Control Trial study.

Place and Duration of Study: This study was conducted at the Department of Anaesthesia and Intensive Care Unit Nishtar Medical University Hospital and Children Hospital and institute of Child Health, Multan. From January 2018 to July 2018.

Materials and Methods: In this project total 50 patients were enrolled by consecutive sampling who remained on mechanical ventilation for more than 24 hours and were between ages 15 to 80 years old. Written consent of this project was taken from relative of each patient. These patients were divided into two groups by lottery method into case and control. The case group received 2 ml of NAC 20% with 8 ml normal saline 3 times a day for 1 day. The control group only received 10 ml normal saline via their nebulizers 3 times a day at 8 AM, 2 PM, and 9 PM. Data was collected and was analyzed. SPSS 22 was used for this purpose. All numerical variables of this research such as mean FiO_2 , mean peak and plateau pressure of airway, mean blood pressure, mean age and importantly mean density of secretions were calculated. In these values t test was applied and p value was calculated. If it was less than .005, then it was considered significant. Similarly, qualitative data such as type of disease were calculated in percentage and chi square test was used to check the significance.

Results: The mean O₂ saturation of baseline, 12 hours and 24 hours of the controls was 93.84 ± 2.28 , 94.27 ± 2.33 and 94.08 ± 1.81 respectively. The mean peak airway pressure of baseline, 12 hours and 24 hours of the controls was 23.16 ± 3.49 , 25.38 ± 8.86 and 24.01 ± 4.91 respectively. The mean plateau airway pressure of baseline, 12 hours and 24 hours of the controls was 19.04 ± 7.79 , 21.37 ± 4.86 and 21.85 ± 8.93 respectively. The mean secretion density of baseline, 12 hours and 24 hours of the controls was 1.04 ± 0.024 , 1.05 ± 0.03 and 1.03 ± 0.002 respectively. While, the mean O₂ saturation of baseline, 12 hours and 24 hours of the cases was 93.08 ± 2.37 , 94.61 ± 2.56 and 94.11 ± 2.34 respectively. The mean peak airway pressure of baseline, 12 hours and 24 hours of the cases was 26.58 ± 5.81 , 23.81 ± 8.28 and 24.34 ± 6.15 respectively. The mean plateau airway pressure of baseline, 12 hours and 24 hours of the cases was 21.88 ± 78.01 , 24.88 ± 6.67 and 23.51 ± 7.55 respectively. The mean secretion density of baseline, 12 hours and 24 hours of the cases was 1.01 ± 0.021 , 1.08 ± 0.022 and 1.008 ± 0.0195 respectively. The differences were statistically insignificant. P-value ≤ 0.05 is considered as significant.

Conclusion: It is concluded from our observations that use of N-acetylcysteine in patients on mechanical ventilation is very effective in clearance of secretion and to maintain airway clear.

Key Words: N-acetylcysteine, mechanical ventilation, airway clearance, normal saline

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INTRODUCTION

Maintaining the airway hygiene and clearing the airway secretions is very essential in preventing recurrent respiratory infections and maintaining airway patency.

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Impaired clearance of the airway is one of the bigger reason of acute respiratory failure and admission in intensive care unit. In intensive care unit usually manual methods are used to facilitate airway clearance and some of them are confirmed as effective¹. Mucous plugs those are retained secretions in tracheobronchial tree are often observed in patients who are mechanically ventilated due to depressed mucociliary clearance, cough reflex and more production of sputum². The average annual relative humidity showed significant increase over the years and ranged from 58 to 71% with mean value of 64% in Indian Punjab³ which predispose patients to mucous plugs, causing severe morbidity and even mortality. Therapy with

mucolytic drugs can be used to reduce bacterial load, improve lung function, more clearance of sputum from airway and decreasing viscosity of airway. This will improve survival. Medications such as anti-DNase are expensive and locally not available. Therefore, in this situation effective and cheap methods for clearing the airway was need of the hour to reduce retention of secretions in patients with mechanically ventilated. For decades N-acetylcysteine has been used for its mucolytic properties orally. But its effects are not known if given by nebulization through endotracheal tube. It was discovered by Sheffner et al. first time the mucolytic qualities of N-acetylcysteine. After this it has been used in many situations as mucolytic drug⁴.

Mucous viscosity is reduced by N-acetylcysteine by disturbing the disulfide bonds in mucoproteins linking the proteins. After use of N-acetylcysteine may increase liquefied secretions. Patients with mechanically ventilation have reduced cough reflex so, their airway should be maintained by mechanical ventilation. N-acetylcysteine causes side effects such as vomiting, stomatitis, nausea, fever, drowsiness, clamminess, chest tightness, bronchoconstriction and rhinorrhea in some patients⁵. Significant airflow limitation is unpredictable and uncommon in asthmatic bronchitis patients or patients with bronchial asthma complicated by bronchitis⁶. In some countries of Europe N-acetylcysteine used to improve symptoms and decrease frequency of exacerbations in chronic bronchitis. Mucolytic agents are considered ineffective and are not used frequently in USA, Australia and UK⁷. Guidelines issued by British thoracic society proposed that in chronic obstructive pulmonary disease, it has no use. So due to unproven trials of these drugs and their efficacy in chronic obstructive pulmonary disease, they are not approved by British National Formulary⁸. In United States of America one multicenter randomized controlled trial showed that organic iodide can benefit in patients with chronic bronchitis⁹. In literature the use of these drugs in intensive care unit are not available. In this research N-acetylcysteine was used in nebulization form in patients who are on mechanically ventilation and was compared with normal saline in airway clearance, change in plateau airway pressure, density of secretions and peak airway pressure.

MATERIALS AND METHODS

This study and randomized controlled trial was done Department of Anaesthesia and Intensive Care Unit Nishtar Medical University Hospital and Children Hospital and institute of Child Health, Multan. From January 2018 to July 2018. In this project total 50 patients were enrolled by consecutive sampling who remained on mechanical ventilation for more than 24 hours and were between ages 15 to 80 years old. Written consent of this project was taken from relative of each patient. These patients were divided into two

groups by lottery method into case and control. The case group received 2 ml of NAC 20% with 8 ml normal saline 3 times a day for 1 day. The control group only received 10 ml normal saline via their nebulizers 3 times a day at 8 AM, 2 PM, and 9 PM. Exclusion criteria were hemodynamically unstable patients, those with tracheostomy tubes, organophosphate poisonings, and pulmonary edema. Whole proposal of this investigation was approved by institutional committee. Sample size was calculated by a reference study done by Gallon AM et al. in which weight of sputum was used after treatment in two groups by using software (www.openepi.com).

Patients who were admitted in intensive care unit and were enrolled in this study. Mucolytics were not received by both control and case. After nebulization with each agent in their respective group with designed amount and time suctioning was done and tracheal secretions were collected in calibrated container. A mucous extractor was placed between main suction container and suctioning tube and sample of secretion was obtained and its density was calculated. Density of these secretions were calculated simply by weight in grams of total secretions and dividing it to total volume of secretions in millimeter. One ml of secretion was obtained by disposable syringe and then its weight was calculated by digital scale.

In this investigation oxygen saturation, plateau pressure of airway and peak pressure of airway were recorded. Patients' blood pressure and other vitals were documented. History and other clinical examination were also documented. Personal profile was obtained. Patients were auscultated and wheezing of chest were recorded. In both groups these measurements were done at baseline and after 12 hours and 24 hours.

Data was collected and was analyzed. SPSS 22 was used for this purpose. All numerical variables of this research such as mean FiO_2 , mean peak and plateau pressure of airway, mean blood pressure, mean age and importantly mean density of secretions were calculated. In these values t test was applied and p value was calculated. If it was less than .005, then it was considered significant. Similarly, qualitative data such as type of disease were calculated in percentage and chi square test was used to check the significance.

RESULTS

Fifty patients were enrolled in this study, both genders. We further categorized the patients as case and control respectively. The mean age, blood pressure and FIO_2 (%) of controls was 45.92 ± 2.37 years, 95.7 ± 5.31 mm Hg and 46.28 ± 2.49 respectively. Gender distribution showed that there were more males than females i.e. $n=18$ (72%) and $n=7$ (28%) respectively. While, COPD, IHD, DM and mortality, in controls, was noted as $n=4$ (16%), $n=13$ (52%), $n=3$ (12%) and $n=12$ (48%) respectively. For the cases, the mean age, blood pressure and FIO_2 (%) was 57.88 ± 7.58 years, 93.5 ± 6.82 mm Hg and 47.48 ± 4.06 respectively. Gender

distribution showed that there were more males than females i.e. n=16 (64%) and n=9 (36%) respectively. While, COPD, IHD, DM and mortality, in cases, was noted as n=2 (8%), n=14 (56%), n=5 (20%) and n=14 (56%) respectively. The difference was statistically insignificant except age (p=0.000) and blood pressure (p=0.000). (Table. 1).

Table No. 1: Demographic Characteristics among the groups

Variable	Control n=25	Case n=25	P-value
Age (years)	45.92±2.37	57.88±7.58	0.000
Blood pressure (mm Hg)	95.7±5.31	93.5±6.82	0.000
FIO ₂ (%)	46.28±2.49	47.48±4.06	0.214
Gender			
Male	n=18 (72%)	n=16 (64%)	0.544
Female	n=7 (28%)	n=9 (36%)	
COPD	n=4 (16%)	n=2 (8%)	0.384
IHD	n=13 (52%)	n=14 (56%)	0.777
DM	n=3 (12%)	n=5 (20%)	0.440
Mortality	n=12 (48%)	n=14 (56%)	0.571

Table No.2: Comparison of different outcomes

Variable	Baseline	12 hours	24 hours	P-value
O ₂ saturation				
Control, n=25	93.84±2.28	94.27±2.33	94.08±1.81	0.687
Case, n=25	93.08±2.37	94.61±2.56	94.11±2.34	0.263
Peak airway pressure				
Control, n=25	23.16±3.49	25.38±8.86	24.01±4.91	0.213
Case, n=25	26.58±5.81	23.81±8.28	24.34±6.15	0.233
Plateau airway pressure				
Control, n=25	19.04±7.79	21.37±4.86	21.85±8.93	0.870
Case, n=25	21.88±78.01	24.88±6.67	23.51±7.55	0.065
Secretion density				
Control, n=25	1.04±0.024	1.05±0.03	1.03±0.002	0.180
Case, n=25	1.01±0.021	1.08±0.022	1.008±0.0195	0.192

The mean O₂ saturation of baseline, 12 hours and 24 hours of the controls was 93.84±2.28, 94.27±2.33 and 94.08±1.81 respectively. The mean peak airway pressure of baseline, 12 hours and 24 hours of the controls was 23.16±3.49, 25.38±8.86 and 24.01±4.91 respectively. The mean plateau airway pressure of baseline, 12 hours and 24 hours of the controls was 19.04±7.79, 21.37±4.86 and 21.85±8.93 respectively. The mean secretion density of baseline, 12 hours and 24 hours of the controls was 1.04±0.024, 1.05±0.03 and 1.03±0.002 respectively. While, the mean O₂ saturation

of baseline, 12 hours and 24 hours of the cases was 93.08±2.37, 94.61±2.56 and 94.11±2.34 respectively. The mean peak airway pressure of baseline, 12 hours and 24 hours of the cases was 26.58±5.81, 23.81±8.28 and 24.34±6.15 respectively. The mean plateau airway pressure of baseline, 12 hours and 24 hours of the cases was 21.88±78.01, 24.88±6.67 and 23.51±7.55 respectively. The mean secretion density of baseline, 12 hours and 24 hours of the cases was 1.01±0.021, 1.08±0.022 and 1.008±0.0195 respectively. The differences were statistically insignificant. P-value ≤ 0.05 is considered as significant. (Table. 2).

DISCUSSION

Results of this study demonstrated that in patients who are on mechanical ventilation for more than 24 hours, when nebulized with normal saline and with N-acetylcysteine in different patients, showed that both agents were almost have same effects. Density of secretions, improvement in oxygen saturation, and peak air way pressure at baseline and after 12 and 24 hours after were almost similar and there was no significant difference between these two agents. So

Personal experience was shared by Poppe in which two milliliters of N-acetylcysteine 20% was nebulized by 88 patients. Symptoms and signs were improved in these patients. A dramatic improvement was observed by mucolytic drug as compared to aerosol nebulization. It was also observed that nebulization of N-acetylcysteine induces cough for almost ten minutes¹¹. In another study done by Hirsch's investigation 20% N-acetylcysteine of about three milliliters in nebulization and 3ml of 10% N-acetylcysteine and was compared to normal saline nebulization. Results of this study demonstrated that nebulization with N-acetylcysteine was more effective in thinning the secretions and increasing its expectoration and volume than nebulization with normal saline and also 10% N-acetylcysteine was equally effective as 20% N-acetylcysteine¹². And two different studies done by Kory et al¹³ and Hirsch et al¹⁴ showed that nebulization with N-acetylcysteine with bronchodilators such as isoproterenol and racemic adrenaline were highly efficient in thinning the sputum and also it caused improvement in subjective condition due to addition of bronchodilators. In above two investigations 20% and 10% N-acetylcysteine were used and density of secretions were measured by consistometer.

Factually, viscosity and density which physical properties of fluid are different in nature and in investigation significantly decrease in respiratory secretion's density were expected but was not done. By decreasing the N-acetylcysteine amount in each dose without addition of bronchodilator in these patients did not show any significant bronchospasm due to N-acetylcysteine.

In this study oxygen saturation was not incremented as it was showed in study done by Gallon et al¹⁰. In investigation of Gallon after N-acetylcysteine

nebulization improvement was observed in oxygen saturation and there was increased expectoration of sputum, density of sputum was reduced¹⁰. In this study density of secretions and increment in saturation of oxygen was not observed significantly in both groups of patients. These results may be explained because of study design and procedure in which after 24 hours of intubation secretions in airways are not in such large amount so nebulization with normal saline and N-acetylcysteine did not cause significant impact.

In study conducted by Vargas et al. found that oxygen saturation fluctuated in values demonstrating higher values in afternoon and lower in early morning^{15,16}. In patients with multi organ failure study done by Agusti et al. found that there was decline in saturation after starting intravenous N-acetylcysteine¹⁷.

So results of this study was different from many investigations. May be it was due to limited sample size, limited time of study on each patient and also may be due to time of starting the study was early, that is it was started after 24 hours of intubation and conducted for only one day. May be larger sample size and more study time in each could have different results.

CONCLUSION

It is concluded from our observations that use of N-acetylcysteine in patients on mechanical ventilation is very effective in clearance of secretion and to maintain airway clear.

Author's Contribution:

Concept & Design of Study:	Aatir Fayyaz
Drafting:	Munir Ahmad
Data Analysis:	Rana Muhammad Arshad
Revisiting Critically:	Aatir Fayyaz, Munir Ahmad
Final Approval of version:	Aatir Fayyaz

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Role of Cerebrospinal Fluid Pleocytosis and its Biochemical Parameters in the Diagnosis of Aseptic Meningitis

Muhammad Usman Anjum¹, Mohammad Mushtaq², Syed IrfanRaza Arif³ and Arshad Wahab Shah⁴

ABSTRACT

Objective: To assess the role which CSF pleocytosis and its different biochemical parameters play in the diagnosis of aseptic meningitis,

Study Design: Prospective study

Place and Duration of Study: This study was conducted at the Frontier Medical College, Abbottabad from July 2017 to April 2018.

Materials and methods: All patients of both genders who were between the ages of 10 - 30 years and who were admitted with a suspected diagnosis of meningitis were included. All those patients who were suspected of suffering from fungal or tuberculous meningitis or who had traumatic lumbar puncture (LP) and those patients who were administered antibiotics prior to their LP were excluded. An experienced clinician made the diagnosis of meningitis considering history, physical examination as well as CSF results with significant emphasis laid on symptoms and signs of meningeal irritation (SOMI). CSF examination comprised of white blood cell count with quantification of neutrophil and lymphocyte counts, CSF protein & glucose levels and CSF Gram and ZiehlNeelsen (ZN) staining.

Results: There were 64 patients in this study. Out of which, 44 were male patients and 20 were female patients with a male to female ratio of 2.2:1. Fifty one patients, (79.69%), suffered from aseptic meningitis while 13 (20.31%) patients were suffering from bacterial meningitis. There were 51 patients who had aseptic meningitis and out of these, 37 patients were males while 14 patients were of female gender. Similarly, out of 13 patients who were diagnosed with bacterial meningitis, 07 patients were males while 06 patients were female. In patients with bacterial meningitis, white blood cell (WBC) count was distinctly higher and the predominant cell type was neutrophils while, on the other hand, lymphocytes were the chief WBC type in patients having aseptic meningitis. The mean protein levels were significantly raised in the CSF of patients who had bacterial meningitis in comparison to that of aseptic meningitis. Patients with bacterial meningitis exhibited distinctly lower levels of CSF glucose levels in comparison to those patients who had aseptic meningitis. Nearly all patients who were suffering from aseptic meningitis exhibited CSF lymphocytosis whereas 76.92% of patients who were suffering from bacterial meningitis had predominance of neutrophils.

Conclusion: Examination plays a pivotal role in the diagnosis of uncomplicated cases of meningitis. This is especially true when the CSF results were interpreted along with clinical findings in patients suffering from meningitis whether bacterial or viral. Nevertheless, advanced and more sophisticated laboratory tests should be carried out in complicated cases to make a correct and accurate diagnosis and to make a decision about the empirical drug therapy in these patients promptly

Key Words: meningitis, aseptic, CSF, pleocytosis

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INTRODUCTION

Meningitis is a serious medical disease which is associated with higher incidence of mortality.

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It is also associated with higher rate of debility especially in pediatric age group owing to permanent neurologic sequel.^{1, 2} It is estimated that more than one million cases of acute bacterial meningitis are reported annually and they primarily affect developing nations and certain geographical regions.^{3, 4} The term aseptic meningitis signifies a type of meningitis in which there is inflammation of meninges with predominance of lymphocytes in cerebrospinal fluid (CSF) and absence of bacteria.⁵ According to some, the term aseptic meningitis is considered tantamount to viral meningitis while others have a preference to call it lymphocytic meningitis.⁶ Therefore, these two terms can be used interchangeably. Clinical features and CSF findings

help to distinguish between these two types of meningitis.⁵

CSF examination is performed commonly in clinical practice. It yields invaluable information about the central nervous system (CNS), its status as well as its associated structures.⁷ Presence and type of white blood cell (WBC) in CSF, concomitant with its biochemical profile, aids in the identification of etiology well as to differentiate between different types of infections affecting the CNS as increased CSF leucocyte levels allude to an inflammatory process within CNS.⁸ Therefore, CSF examination and analysis is a vital part of workup of CNS disorders.

Bacterial meningitis constitutes a serious medical illness which needs prompt antibiotic therapy. Therefore, it is critical to distinguish it from other etiological causes of meningitis so as to make timely treatment decisions because any delay in starting drug therapy in these cases could lead to grave risk of debility and mortality.⁹ On the contrary, in patients who had aseptic meningitis, administering needless antibiotic treatment causes debility and greater economic expenditure.² Hence, timely, rapid and correct diagnosis of meningitis is crucial in such patients.¹ Therefore, this study is conducted to assess the role of CSF pleocytosis and its biochemical profile in the diagnosis of patients with aseptic meningitis.

MATERIALS AND METHODS

This was a prospective study which was conducted from July 2017 to April 2018 at Frontier Medical College, Abbottabad. All patients of both genders who were between the ages of 10 -30 years and who were admitted with a suspected diagnosis of meningitis were included. All those patients who were suspected of suffering from fungal or tuberculous meningitis or who had traumatic lumbar puncture (LP) and those patients who were administered antibiotics prior to their LP were excluded. An experienced clinician made the diagnosis of meningitis considering history, physical examination as well as CSF results with significant emphasis laid on symptoms and signs of meningeal irritation (SOMI) i.e. headache, vomiting, photophobia, seizures, changes in the level of consciousness, presence or absence of focal neurological signs and Kernig's or Brudzinski's signs. Laboratory investigations included complete blood count (CBC), blood sugar and CSF examination. CSF examination comprised of white blood cell count with quantification of neutrophil and lymphocyte counts, CSF protein & glucose levels and CSF Gram and ZiehlNeelsen (ZN) staining.

SPSS (version 22) was used to manage, quantify and analyse data. Percentages and frequencies were used to characterize categorical variables while mean $\pm$ standard deviation was used to characterize numerical variables.

Student's t-test was done for statistical significance and p-value $< .05$ taken as significant.

RESULTS

There were 64 patients in this study. Out of which, 44 were male patients and 20 were female patients with a male to female ratio of 2.2:1, Figure 1. Majority of patients had shown SOMI.

Fifty one patients, (79.69%), suffered from aseptic meningitis while 13 (20.31%) patients were suffering from bacterial meningitis, Figure 2.

Stratifying according to the gender and type of meningitis, there were 51 patients who had aseptic meningitis and out of these, 37 patients were males while 14 patients were of female gender. Similarly, out of 13 patients who were diagnosed with bacterial meningitis, 07 patients were males while 06 patients were female, Table 1.

Table No.1: Stratification of patients according to gender and type of meningitis, (n=64)

Variable	Aseptic Meningitis		Bacterial Meningitis	
	Number	%age	Number	%age
Male	37	57.82%	7	10.94%
Female	14	21.87%	6	9.37%
Total	51	79.69%	13	20.31%

Table No.2: CSF values in patients with aseptic and bacterial meningitis, (n=64)

Variable	Aseptic Meningitis		Bacterial Meningitis		P-value
	Mean $\pm$ SD	Median	Mean $\pm$ SD	Median	
WBC (cells/mm ³)	14.20 $\pm$ 51.51	02	7872 $\pm$ 17443.54	1080	0.130
Neutrophils (%)	3.04 $\pm$ 6.74	00	65.38 $\pm$ 27.95	80	0.000*
Lymphocytes (%)	96.96 $\pm$ 6.74	100	33.08 $\pm$ 25.70	20	0.000*
Glucose (mg/dL)	64.82 $\pm$ 29.18	62	31.08 $\pm$ 25.44	25	0.001*
Protein (mg/dL)	33.39 $\pm$ 12.52	30	168 $\pm$ 84.97	176	0.000*

* p-value < 0.05

As per the type of leucocytes present in the CSF examination of meningitis patients, nearly all patients who were suffering from aseptic meningitis exhibited CSF lymphocytosis whereas 76.92% of patients with bacterial meningitis had predominance of neutrophils, Table 3.

Table 2 represents the different parameters of CSF examination. Median values were also cited as there

was wide variation and skewness in the data. In patients with bacterial meningitis, white blood cell (WBC) count was distinctly higher and the predominant cell type was neutrophils while, on the other hand, lymphocytes were the chief WBC type in patients having aseptic meningitis, as shown in Table 2 & 3. Patients with bacterial meningitis exhibited distinctly lower levels of CSF glucose levels as compared to those patients who had aseptic meningitis, Table 2. The mean protein levels were significantly elevated in the CSF of patients who had bacterial meningitis in comparison to that of aseptic meningitis (p value <.05), Table 2.

Table No.3: Leucocyte differential in CSF of patients, (n=64)

Cell count	Aseptic	Bacterial
Lymphocytes > 50%	100 %, n = 51	23.08 %, n = 03
Lymphocytes < 50%	00 %, n = 0	76.92 %, n = 10

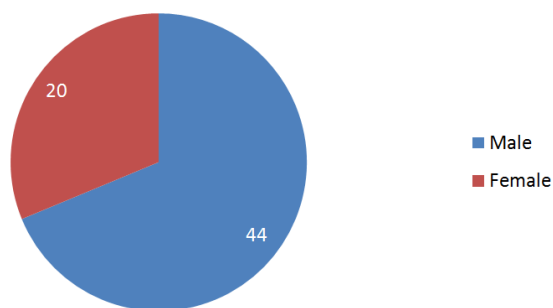


Figure No.1: Gender distribution of study patients, (n=64)

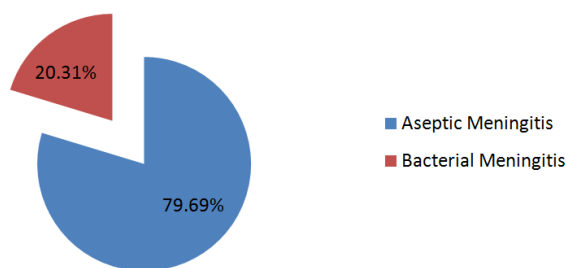


Figure No.2: Stratification of patients according to the type of meningitis, (n=64)

DISCUSSION

Meningitis is a CNS infection which is caused by a myriad of microorganisms. Amongst bacterial meningitis, the commonest bacteria causing meningitis are *N. meningitidis* and *S. pneumoniae* while amid aseptic meningitis, viruses and chiefly enteroviruses are responsible.^{2, 4, 10} Fever, vomiting, headache and neck rigidity characterizes meningitis. SOMI are frequently present in such cases.¹¹ However, CSF is required to make diagnosis and differentiate between different types of meningitis.

There was preponderance of male subjects, 68.75%, in our study. Similarly, there was a preponderance of male patients, 53%, as described by Egelund et al in their study.⁸ On the contrary, Agueda et al reported that the majority of their study subjects were females, 60.3%.² This discrepancy might be owing to the different regions in which these studies were conducted as Agueda et al performed their study in Portugal. Our study has reported the incidence of lymphocytic and bacterial meningitis to be 79.69% and 20.31% respectively. Equally, Amarilho et al stated that the frequency of aseptic and bacterial meningitis, amongst the confirmed cases of meningitis, was 89.65% and 10.35% respectively.¹² Contrarily, Abro et al reported a higher incidence of bacterial meningitis, 64.17%, as compared to aseptic meningitis, which was 35.82%.¹ Correspondingly, a higher rate of bacterial meningitis was described by Fouad et al whereas bacterial meningitis was responsible for 73.3% of cases and aseptic meningitis for 26.7%.⁴ This disparity of results among various studies could be due to variation in the place and timing of these studies as well as it might be owing to the difference in the vaccination status of the study participants.

CSF is a valuable laboratory test that aids considerably in the diagnosis and management of various CNS diseases. Presence or absence of leucocytes in CSF, their number and type has been regarded as a main criterion for the diagnosis of different CNS diseases.⁸ In this study, patients with aseptic meningitis had marked lymphocytosis while those with bacterial meningitis had discernible leukocytosis with predominant neutrophilia. Patients with bacterial meningitis had markedly raised CSF protein levels when compared with aseptic meningitis while their CSF glucose levels were characteristically lower as compared to aseptic meningitis. Our findings corroborated with other studies. Abro et al conducted their study in UAE. They have also reported a raised leucocyte count with predominance of neutrophils, elevated protein and lower glucose levels in the CSF of their patients with bacterial meningitis.¹ Equally, many other researchers have described markedly raised levels of CSF protein in patients with bacterial meningitis.^{12, 13} Likewise, many other investigators have reported neutrophilia with lower glucose levels in the CSF of patients with bacterial meningitis while predominant lymphocytosis and a normal glucose levels in patients with aseptic meningitis.^{2, 5, 8, 14, 15} We haven't performed advanced laboratory investigations e.g. polymerase chain reaction (PCR) as they were expensive laboratory procedures and concurrently being a developing state, they were only available at a very few advanced centers in our country. Aseptic meningitis can be differentiated from bacterial meningitis based on CSF analysis but this is not beyond limitations. In these patients, history and more sophisticated investigations e.g. viral culture, PCR,

considering for carcinomatous cells and fungal causes of CNS diseases like histoplasmosis, should be carried out to arrive at correct diagnosis. Likewise, other causes of aseptic meningitis e.g. malignancy, chemicals or drugs (baclofen, methotrexate, intravenous immunoglobulins), etc. should be considered while making diagnosis in such cases.^{6, 16}

CONCLUSION

CSF analysis plays a pivotal role in the diagnosis of uncomplicated cases of meningitis. This is especially true when the CSF results were interpreted along with clinical findings in patients suffering from meningitis whether bacterial or viral. Nevertheless, advanced and more sophisticated laboratory tests should be carried out in complicated cases to make a correct and accurate diagnosis and to make a decision about the empirical drug therapy in these patients promptly.

Author's Contribution:

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 Revisiting Critically: Muhammad Usman Anjum, Mohammad Mushtaq
 Final Approval of version: Muhammad Usman Anjum

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Acute Myocarditis: Clinicodemographic Features and Outcome in Children Admitted at Tertiary Care Hospital Nawabshah

Juverya Naqvi¹, Ali Akbar Siyal¹ and Tabinda Taqi²

ABSTRACT

Objective: To evaluate clinicodemographic features and outcome of acute myocarditis in children admitted at PMC hospital.

Study Design: Retrospective study

Place and Duration of Study: This study was conducted at the Department of Pediatric Medicine, Peoples University of Medical & Health Sciences, Nawabshah from January 2015 to December 2015.

Materials and Methods: We performed a retrospective study of patients aged 1 month to 16 years who were admitted PMC hospital, Nawabshah and discharged with a diagnosis of myocarditis were studied in retrospect. Clinical and demographic features and outcome were chronicled.

Results: Files of total of 37 patients with the diagnosis of myocarditis were collected and data was extracted between January 2015 and December 2015. Median age of affected children was 48 months with (35%) 13 females and (64.86%) 24 males. The primary complaint with which patient presented was respiratory distress (56%) and least common symptom was abdominal pain (5%) while the most recurrently occurring examination finding was tachycardia (68%). Averagedays in hospital were 11 days. The outcome regarding death and discharge was; 64.5% expired and rest was discharged.

Conclusion: Although Myocarditis is not a very common disease but its presentation mimics with symptoms of common diseases like RTI and our study also showed that the most common presentation was respiratory distress. Hence it is very important to look carefully at children presenting with such common symptoms but donot improve on antibiotics.

Key Words: Acute Myocarditis, Clinicodemographic Features, Children

Citation of articles: Naqvi J, Siyal AA, Taqi T. Acute Myocarditis: Clinicodemographic Features and Outcome in Children Admitted at Tertiary Care Hospital Nawabshah. Med Forum 2018;29(10):43-45.

INTRODUCTION

Myocarditis is describedas myocardial inflammation, injury or necrosis, and ultimately fibrosis. Cardiac enlargement and diminished systolic function occur as a direct result of the myocardial damage.¹ Myocarditis is linked with high morbidity and mortality². The etiology of myocarditis could be infectious as well as non-infectious, although viruses are the most common causative organisms responsible for myocarditis in all age groups. The exact incidence of myocarditis is quite problematic to assess as clinical presentations are not specific and ultimate diagnostic tests are not routinely done in all patients but estimated incidence

from various studies is 1 per 100000children³. The clinical presentation may vary in children, especially in young children. Clinical spectrum ranges from mild subclinical forms to overt heart failure. As initial presentation of myocarditis may be vague, it may mimic common pediatric problems^{4,5}. The scenario regarding outcome fluctuates from recovery to chronic disease and death⁶. The diagnostic modalities used to diagnose a case of acute myocarditis include Chest X-ray, ECG, Echocardiography, cardiac biopsy, inflammatory markers and cardiac enzymes⁷. But the diagnostic approach depends on the center where the child presents because not every center has the facilities for cardiac biopsy. As myocarditis presents with such common symptoms that a high index of suspicion is required by the attending physician to guide him/her towards the diagnosis. Various scoring systems are under study to help in clinical diagnosis of myocarditis in children but are somehow deficient in one or other area so cannot be relied upon⁸.Prognosis in case of acute myocarditis depends on the state in which the patient is received, if the patient is received in earlier stages of disease the prognosis is better, but as the condition progresses to fulminant myocarditis and

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shock the prognosis obviously becomes guarded. Regarding treatment options in pediatric myocarditis, there have been so many advances like use of ECMO and ventricular assist device in patients with fulminant myocarditis⁹. Over all acute myocarditis is a multi-faceted disease in children, and there is huge void of research in this regard, our study is just a small step taken in this huge field.

MATERIALS AND METHODS

This study was conducted at the Department of Pediatric Medicine, Peoples University of Medical & Health Sciences, Nawabshah from January 2015 to December 2015.

We performed a retrospective study of patients aged 1 month to 16 years who were admitted PMC hospital, Nawabshah and discharged with a diagnosis of myocarditis were studied in retrospect. Clinical and demographic features and outcome were recorded.

RESULTS

Records of a total of 37 patients with the diagnosis of myocarditis were appraised retrospectively between January 2015 and December 2015. Median age of patients was 48 months with (35%) 13 females and (64.86%) 24 males.

Table No.1: Presenting Complaints of Patients

S.No:	Presenting complaint	Number of Patients
1	Respiratory distress	21
2	Fever	16
3	Palpitation	5
4	Chest pain	5
5	Abdominal pain	2

Table No.2: Common Clinical Findings

S.No:	Clinical findings	Number of Patient
1	Tachycardia	26
2	Tachypnea	21
3	Fever	18
4	Low Blood Pressure	18
5	Hepatomegaly	16

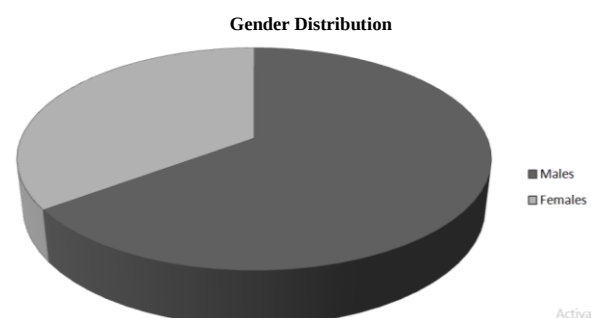


Figure No.1: Gender Distribution of Patients

The most recurrent presenting complaint observed was respiratory distress (56%) and least common symptom

was abdominal pain (5%) while the most frequently occurring examination finding was tachycardia (68%). Average Interval of the hospital stay was 11 days. The outcome regarding death and discharge was: 64.5% expired and rest was discharged.

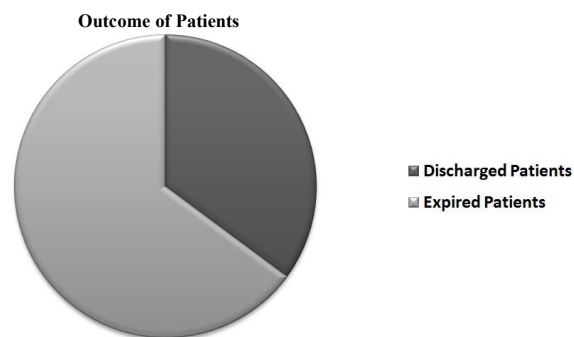


Figure No.2: Outcome of Patients

DISCUSSION

In our study we have 37 patients admitted with the diagnosis of acute Myocarditis. Myocarditis is not a common disease in pediatric population^{6, 10} but associated with high mortality even with advanced life support. Median age in our study was 48 months (4 years); in another study earlier age peak was also seen like in our study¹⁰. Male predominance is observed here, which may indicate the male child preference for seeking medical care, this matches with this study that shows 68% male patients¹¹. A contrasting gender distribution is seen in another study¹². Myocarditis presents with a wide diversity of symptoms that in most cases do not indicate an underlying cardiac problem¹³ as in our study the most frequent presenting complaint reported by parents was respiratory distress, a similar study from Canada show that most patients diagnosed later as myocarditis were initially admitted as asthma and pneumonia^{11,12}. The rest of the clinical findings are similar with other studies like this study from Taiwan which shows almost same frequency of symptoms¹⁴. All these studies including ours shows a similar array of signs and symptoms, which in most cases causes confusion in initial diagnosis of Myocarditis. The average length of stay in hospital was seen as 11 days; in reviewing the literature authors couldn't find a matching study to take reference from regarding length of stay at hospital, But in one study the average time between diagnosis and heart transplant or death is 8.4 months¹⁵. Death as final outcome was seen in majority of patients i.e. 64.5%, which show a high mortality in our set up, but this also indicates that our set up lacks ventricular support and ECMO, Sunil J et al shows that despite state of the art facilities there is still high mortality in pediatric population affected by myocarditis¹⁶, a similar study from Japan shows a high mortality in case of fulminant myocarditis but again this study is done in a highly equipped center¹⁷. Overall

there is a huge need of further studies in this regard, because myocarditis is a disease in children that presents with common sign and symptoms but outcome is worse.

CONCLUSION

Acute myocarditis in pediatric population presents with symptoms that can be mistaken for other everyday pediatric problems; respiratory presentations were most common. A high index of clinical notion for myocarditis is required. All children should undergo basic investigations if routine therapy fails.

Author's Contribution:

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 Data Analysis: Tabinda Taqi
 Revisiting Critically: Juverya Naqvi, Ali Akbar Siyal
 Final Approval of version: Juverya Naqvi

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Efficacy of Sofosbuvir and Ribavirin for Treatment of Chronic Hepatitis C Genotype 3 Treatment Naïve Non-

Cirrhrotic Patients at KGN Teaching Hospital Bannu

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Chronic Hepatitis
C Genotype 3
Treatment Naïve
Non-Cirrhrotic
Patients

ABSTRACT

Objective: to assess the efficacy of oral sofosbuvir and weight-based ribavirin treatment in non-cirrhrotic treatment-naïve patients in district Bannu, Pakistan.

Study Design: A quasi-experimental study

Place and Duration of Study: This study was conducted at the Khalifa Gul Nawaz Teaching hospital (KGNTH) Bannu from June 2016 to January 2018.

Materials and Methods: 340 patients having GT 3 which were non-cirrhrotic and treatment naïve. Non-probability consecutive sampling technique was used for sample collection. Treatment was given to all subjects with sofosbuvir (400mg)OD with weight-based ribavirin BD for a period of 24 weeks. PCR was done for follow up at the end of treatment (ETR) and at completion of week 12 of treatment in order to determine virologic response (SVR).

Results: 96.25% (n=318) of the patients had achieved negative PCR at the end of treatment. SVR 12 was achieved in 92.78% (n=306) of subjects in which 84.00% (n=260) had negative PCR. 35.55% (n=117) had Hemoglobin reductions below 10.0g/dl during the treatment course. Females population was found with a sustained virologic response a little more (p=0.003)

Conclusion: Sofosbuvir and RBV based regimen is an effective treatment option for patients in treatment naïve non-cirrhrotic GT3 patients with good tolerability and fewer side effects as compared to previous interferon-based regimens. Our results suggest the feasibility and the pertinence if including interferon-free treatment regimens in the national programme, at both provincial and national levels.

Key Words: HCV, Sofosbuvir, Genotype 3, PCR, Hepatitis C, Ribavirin

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INTRODUCTION

Hepatitis C is a persistent viral infection of the liver, if left untreated will result in major medical morbidities i.e. cirrhosis, hepatocellular carcinoma and their sequelae. Hepatitis C Virus (HCV) infection is a significant global health burden with approximately 160-180 million infected which accounts for 1% of world population. ¹Six known genotypes of hepatitis C exist, with genotype 1 predominance in USA and Europe.

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Patients who develop cirrhosis and hepatocellular carcinoma result in ~350,000 estimated deaths from these complications annually.² Pakistan is ranked second around the globe with high prevalence 4.9%.³ Pakistan is a lower middle-income country with a population of approximately 220 million. Most important risk factors for HCV transmission in Pakistan are health system-related, including a documented high frequency of therapeutic injections, reuse of syringes, and unlicensed clinics conducting high volumes of blood transfusions, dental surgeries⁴. In one study, most HCV infections in Pakistan are genotype 3 (69.1%), followed by genotypes 1 (7.1%), genotype 2 (4.2%) and genotype 4 (2.2%).^{5,6} In another study, genotype 3 accounts for around 90%.⁷ GT 3 is the second most common HCV genotype globally, accounting for 18% of all adult HCV infections. Patients with HCV GT3 infection have greater risk of developing hepatic steatosis, more rapid progression of hepatic fibrosis and cirrhosis and hepatocellular carcinoma. GT3 is less responsive to interferon-based treatment.

New direct acting anti-viral oral regimens (DAAs) have revolutionized management of chronic hepatitis C since 2011, with ease of administration and fewer serious side effects. Since the launch of DAAs, sustained virologic response was nearly 100% with exception to GT 3 which is associated with lower SVR rates⁸. Sofosbuvir and ribavirin regimen became available in Pakistan by November 2014⁹⁻¹³. Limited data was available from the clinical trials regarding the response of DAAs in GT3 patients in real-world. Based in Asian Pacific Association for the Study of Liver Disease (APASL) 2016 guidelines, recommended therapies for GT 3 include:

- 1) Sofosbuvir + weight-based Ribavirin (RBV) treatment for 24 weeks for treatment naïve patients
- 2) Sofosbuvir+ Daclatasvir for 12 weeks in patient without cirrhosis and 24 weeks with or without weight-based ribavirin with cirrhosis
- 3) Among those with treatment experienced – interferon based, Sofosbuvir+ Daclatasvir for 12 weeks in non-cirrhotic and Sofosbuvir+ Daclatasvir with weight based Ribavirin for 24 weeks with cirrhosis¹⁴

Since the introduction of DAAs, real world effectiveness results have been sporadically published with considerable heterogeneity. Bannu is the district of KP, in 2017 census had a population of 9,58,000. It is located in the southern part of Khyber Pukhtunkhwa.¹³

To gain real-world data on effectiveness in local population of Bannu, Sofosbuvir+ weight-based Ribavirin was given to all GT 3, non-cirrhotic patients for 24 weeks and studying SVR12.

MATERIALS AND METHODS

This study (quasi experimental) was conducted at Khalifa Gul Nawaz teaching hospital (KGNT) Bannu for a period of 24 months. Protocols for the use of laboratory animals were in accordance with the guidelines of the BMC ethical board. All patients with chronic HCV infection (either diagnosed with HCV in our hospital or those referred for HCV treatment from other institutions), were confirmed through baseline quantitative PCR (real time assays) followed by determination of genotype using single nucleotide polymorphism (SNP). Previous treatments for Hepatitis C was evaluated by taking proper history and going through patients documents and patients with no confirmed past exposure to any anti-HCV treatment were separated. Treatment naïve genotype 3 patients were then included in study and assessed for cirrhosis status using Child Pugh scores, ALT and hepatobiliary ultra sound study to rule out cirrhosis and hepatocellular carcinoma. Patient with age 18 years or more, having no cirrhosis or child pugh score less than 5 and genotype 3 were started on treatment with daily oral sofosbuvir 400mg and ribavirin (weight-based) for 24 weeks. A total of 340 patients got enrolled in the

study during the said duration. Patients were counselled concerning the disease, compliance with treatment and lifestyle changes including family planning. 60.00% (n=204) of patients were male while 40.00% (n=136) were female.

Inclusion criteria

- Patients having an age above or 18 years
- Male and female
- Treatment naïve
- Non-cirrhotic with child pugh <5, ultra sound study negative for cirrhosis /HCC
- GT3 mono infected patients

Exclusion criteria

- Previous anti HCV treatment experienced patients
- Acute HCV infection
- Patients with cirrhosis child pugh score >5 or hepatocellular carcinoma
- Patients with HIV/HBV co-infection
- Patients on treatment for tuberculosis and chemotherapy
- Patients eligible for treatment but not willing to undergo family planning.
- Patients below 18 years old.
- Pregnant patients and lactating mothers.”

Treatment outcomes definition

- End of treatment (ETR) response: An undetected HCV RNA by PCR at 24 weeks completion of treatment.
- Sustained Virological Response (SVR) 12: Absence of viremia 12 weeks post treatment as evidenced by a negative HCV RNA Quantitative PCR.
- Relapse: Recurrence of viremia at 12 weeks post treatment after undetected end of treatment viral load.
- Non-responder/ Treatment failure: Persistence of viremia at the end of treatment i.e. 24 weeks
- Stopped treatment: Medical decision to stop treatment either from complications of treatment or from decompensation. Patients are referred to dedicated liver centre for further management. No viral load is taken after stopping treatment.
- Lost-to-follow-up: Patients who missed follow-up consultation at least 60 days from the appointed date, despite tracing efforts. Died: Patients who died while enrolled to the programme

Treatment duration was 24 weeks. Sofosbuvir was administered orally 400mg OD. RBV was given (<75kg 1000mg and >75kg 1200 mg daily) in two divided doses. During treatment, patients were asked to come for follow-up check up every month for medications refill, clinical examination and laboratory assessment with complete blood counts, ALT, AST, assessment of compliance to family planning advice and lifestyle counseling sessions by attending physician. At the end of treatment, viral load was measured using real time

PCR assay. A second viral load was done twelve weeks after treatment completion to determine the sustained viral response (SVR).

Study Design: Open label, quasi experimental study design (single group study lacking any control group).

Variables and analysis Data from the Hepatitis C database were used to identify variables i.e. patient's name, gender, age, ID number, registration date, ultra sound abdomen, ALT, albumin, Prothromb in time, platelet count, previous HCV treatment history, genotype, pretreatment viral load, end of treatment and 12-weeks post treatment viral loads, treatment initiation, completion and SVR dates, hemoglobin (Hb) determination over the course of treatment and treatment outcomes. SPSS analysis software (version 2.2.2.183, Epi Data Association, Odense, Denmark) was used for descriptive statistics describing the study population and treatment outcomes. Relative risks with 95% confidence intervals were calculated as measures of association for factors possibly associated with pretreatment attrition and adverse outcomes

RESULTS

A total of 340 patients were enrolled with 204 male and 136 female subjects. The mean age of patients was 40 years (± 4 yrs). Baseline serum ALT was 80 IU/l (± 50.24 IU/l), mean Hemoglobin was 12.9 (± 2.10 g/dl), mean platelet count was 161216.32 per mm^3 (± 82835.01) and total leukocyte count as 6224.20 per mm^3 (± 4966.22). All patients were treatment naïve and non-cirrhotic i.e. Child Pugh class <5 and no cirrhosis on ultrasound. The results are shown in table 1.

Table 1. Parameters of the subjects studied

No of Patients (n=340)	Baseline ALT (IU/l)	Mean Hb (mg/dl)	Mean platelet Count (per mm^3)	Mean Leucocytes Count (per mm^3)
Male (n=204)	80	12.9	161216	6224
Female (n=136)				

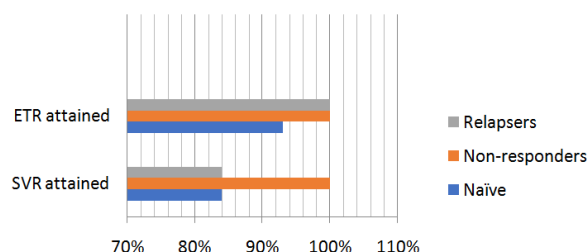


Figure No.1: Details of Patients attaining SVR, ETR and RVR

Amongst 340 patients, 10 patients got dropped out of the study. 2 females due to pregnancy and 7 patients

(male=3 and female=4) lost to follow up. In 1 female, treatment was discontinued due to development of severe anemia (which improved after stopping treatment). 318 (96.25%) patients achieved a ETR. SVR 12 was successfully achieved by 306 (92.78%) patients. The results are shown in figure 1.

Adverse effects: All 330 patients who completed treatment, anemia in 10, fatigue in 8 and headache in 12 subjects were the most common side effects which were managed with paracetamol and counselling (the effects didn't lead to discontinuation of treatment). Moderate anemia (<10 g/dl peaked at week 8) was detected in 35.55% (n=117) patients. The dose of Ribavirin was reduced as per recommendation, and patients were monitored for symptomatic anemia along with folate supplementation without discontinuation of treatment. One female patient developed progressive decline in hemoglobin during the 1st month of treatment, as a consequence of which treatment was discontinued.

DISCUSSION

The novel approach of Hepatitis C management using DAAs simple regimens with fixed dose of Sofosbuvir and weight-based Ribavirin yielded a treatment success rate of 94%. These results show how we have successfully simplified HCV management in a high-burden setting, and confirm under real world conditions the high efficacy of DAAs that has previously been reported in the controlled environment of clinical trials.¹⁶⁻¹⁹

The use of the Sofosbuvir-Ribavirin (SOF-RBV) treatment regimen in the Pakistani context is not new, given that Sofosbuvir was registered in Pakistan since November 2014.²⁰ Treatment outcomes for this setting are now coming up in different settings and regions of the country. Bannu and its surrounding districts are harbouring one of the highest burden of CHC in this province. In this study, an integrated, standard model of care for HCV was effective, with loss-to-follow-up rates at 10%. The outcomes and treatment characteristics are in line with published evidence from other settings. The new all-oral treatment regimen is highly tolerable with documented limited adverse events in clinical trials. The VALENCE study, a multicenter Phase 3 trial in Europe showed that the SOF-RBV regimen for 24 weeks in GT3 patients had an SVR12 of 85%¹⁸, we had a higher rate of SVR12 attributed to limiting the study only to non cirrhotic treatment naïve patients. Conventional management relying on an IFN-based treatment regimen over a prolonged time period¹⁰ resulted in general SVR rates of 42–93% for all genotypes, showing only moderate efficacy for the combination of pegylated IFN with Ribavirin in multiple randomized control trials.¹⁹ A real life, retrospective study done at Queen's Liver Center in Hawaii, on treatment outcomes as compared to the VALENCE study for GT3 patients on SOF-RBV

regimen for 24 weeks showed SVR rates of 81%.²¹ Two Indian studies gave initial real-life results from a treatment cohort of GT3 patients receiving 24-week of SOF-RBV, with SVR12 rates at 96% regardless of severity of disease or previous HCV treatment history.^{22,23}

Hemolytic anemia associated with Ribavirin is commonly seen in patients on a SOF-RBV regimen.^{18,20} An Hb reduction of 2.1 g/dl for a 24 week SOF-RBV treatment course for GT3 patients was observed in the VALENCE study with 6% of patients having Hb levels less than 11 g/dl at any point in the treatment.¹⁸ Our treatment cohort recorded 35% of patients developing moderate anemia with Hb less than 10g/dl at any time during the treatment course. Despite temporary discontinuation of treatment for one patient with severe anemia, SVR12 was achieved.

The following limitations were identified for this study. First, as the study reflected an interim analysis for only 24 months, only a limited sample size for treatment outcomes could be obtained. This affected analysis in terms of establishing strong associations with adverse outcomes. Secondly patients were only studied till SVR12 and therefore subsequent durability of SVR couldn't be evaluated, however we continue following these patients for the same. Third, data regarding patient's previous HCV treatment history may have been inflated, as some patients were not able to present documents evidencing past HCV medical management; however, they were still included as patients with previous HCV treatment. Strengths included the operational nature of the study, ensuring that the results likely reflect the field conditions encountered by many operational actors; and adherence to the STROBE guidelines for reporting of observational data.²¹

Our management of CHC showed good treatment outcomes. It ensured adherence to treatment through monthly follow-ups with patient support component, which likely contributed to the positive outcomes. In underserved areas of the United States the concept of task-shifting was developed, engaging mid-level healthcare practitioners in the management of CHC with DAAs with indirect supervision from a specialist: an SVR12 was achieved for 83% of GT3 patients in this treatment cohort.²² Another study involving the Extension for Community Health Outcomes (ECHO) Model engaging PHC management of CHC in New Mexico, USA by training primary care providers showed overall SVR12 rates of 58.2%.²³ Overall, the encouraging programmatic outcomes suggest that the decentralized approach can serve as a model for other stakeholders contemplating a HCV programme.

CONCLUSION

Hepatitis C management in a programmed approach using an integrated and strong follow up, using direct-

acting antivirals, produces treatment outcomes comparable to clinical trials done for Sofosbuvir-based treatment regimens.

Author's Contribution:

Concept & Design of Study: Mohammad Omar Khan, Wasim Ahmad
Drafting: Naseeb Rehman
Data Analysis: Abdul Razaq
Revisiting Critically: Abdul Razaq, Wasim Ahmad
Final Approval of version: Mohammad Omar Khan

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Frequency of Inattentive Attitude of Mothers towards Child's Milestones Among Mothers of Karachi

Tafazzul H Zaidi¹, Irfan Ashraf² and Kiran Mehtab¹

Inattentive Attitude of Mothers Towards Child's Milestones Among Mothers

ABSTRACT

Objective: To assess mother's knowledge about timely achievement of a child's milestone from birth to age 3. To assess mother's awareness about Physical, Intellectual, Social and emotional and Language development of a child.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Community Medicine, SMC, JSMU Karachi from March 2018 to August 2018.

Materials and Methods: A cross sectional study was conducted across five districts of Karachi. The districts where study was conducted included District East, West, South, North and Central Districts. The sample size of 284 mothers was drawn through non-probability purposive sampling. Data was collected through structured questionnaire. Pilot study was done to check the authenticity of questionnaire. Data was entered and analysed on statistical package for social sciences (SPSS version 20) with 95% confidence interval and 5% margin of error. P-value less than 0.005 were considered statistically significant.

Results: Out of 284 mothers, the mean age was 29.5 years ranging from 20 to 45 years. 64.8% (0.002) mothers didn't know when a child is able to roll over. 68.3% (0.022) mothers didn't know when a child starts to sit with support. 58% (0.030) mothers didn't know when a child is able to stand with support. 70.4% (0.005) mothers didn't know when a child is able to run forward. 76.8% (0.004) mothers didn't know when a child is able to recognize primary care givers. 76.1% (0.003) mothers didn't know when a child is able to pay attention to his/her own name. 62% (0.002) mothers didn't know when a child is able to feed himself/herself with finger foods. 72.2% (0.000) mothers didn't know when a child is able to indicate urge for defecation and urination. 80.3% (0.001) mothers didn't know when a child shows stranger shyness. 72.5% (0.000) mothers were unable to tell when a child is able to form a complete sentence. 57% (0.000) mothers didn't know when a child is able to say double syllable words. 56.3% (0.014) mothers didn't know when a child is able to name pictured objects.

Conclusion: The study concluded that mothers had insufficient knowledge about child's physical development and mother's awareness about child's intellectual, social and language development was extremely poor.

Key Words: Child + Development+ Milestones+ Awareness+ Attitude

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INTRODUCTION

Learning begins at birth. It's a gradual process that picks up pace as strong connection are made between neurons. Child's receptiveness to new influences and ability to learn complex things are at peak in initial stages of life.

A developmental milestone is attainment of different abilities by a child on monthly basis. A new born infant will show what appears to be random but symmetrical movement of arms and legs.

During next stage of development, which usually occurs somewhere around 6 months of age, they will begin to reach for specific objects with their arm. Somewhere around 1 year of age most children can reach for small blocks or rattle and pick them up¹ These can be evaluated with the help of standardized growth chart.

The level of awareness in mother can be influenced by maternal age, educational status and parity. Increasing mother's age was associated with improved health and development for child up to 5 years of age² And also low parity mother were independently protective from childhood death³

As problem related physical development manifest early and are easy recognizable, parental knowledge regarding physical development are fairly sound. The knowledge of physical development exceeds knowledge of cognitive, emotional and social development. Parents were aware of importance of positive experiences in influencing their child development⁴

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On the other hand, several factors on part of child can influence his development, despite the mother being competent with knowledge of milestone like physical characteristics, wellness and family nurturing methods. Exposure to biological and environmental risk factors such as chronic poverty can compromise child development leading to a loss in cognitive and developmental potential⁵

Knowledge of developmental milestones in mothers is important in relation to the development of child and early detection of any abnormality. This would help in early intervention, prompt treatment and prevent disability.

MATERIALS AND METHODS

The cross-sectional Study was conducted in five districts of Karachi. The districts included District East, West, South, North and Central Districts from March 2018- August 2018. It was non-probability purposive sampling.

Inclusion Criteria: Mothers with at least one breast feeding child.

Exclusion Criteria: Mothers who refused to take part in study. The sample size of 284 mothers was drawn through non-probability purposive sampling method. Data was collected through structured questionnaire. Pilot study was done to check the authenticity of questionnaire. Data was entered and analysed on statistical package for social sciences (SPSS version 20) with 95% confidence interval and 5% margin of error. P-value less than 0.005 were considered statistically significant.

Ethical Consideration: Informed consent was taken from mothers

RESULTS

Out of 284 mothers, the mean age was 29.5 years ranging from 20 to 45 years.

Awareness of physical development: 64.8% (0.002) mothers didn't know when a child is able to roll over. 68.3% (0.022) mothers didn't know when a child starts to sit with support. 58% (0.030) mothers didn't know when a child is able to stand with support. 70.4% (0.005) mothers didn't know when a child is able to run forward.

Awareness of social and emotional development: 76.8% (0.004) mothers didn't know when a child is able to recognize primary care givers. 76.1% (0.003) mothers didn't know when a child is able to pay attention to his/her own name. 62% (0.002) mothers didn't know when a child is able to feed himself/herself with finger foods. 72.2% (0.000) mothers didn't know when a child is able to indicate urge for defecation and urination.

Awareness of intellectual development: 80.3% (0.001) mothers didn't know when a child shows

stranger shyness. 72.5% (0.000) mothers were unable to tell when a child is able to form a complete sentence.

Awareness of language development: 57% (0.000) mothers didn't know when a child is able to say double syllable words. 56.3% (0.014) mothers didn't know when a child is able to name pictured objects.

DISCUSSION

The study assessed gaps in knowledge of mothers about a child's developmental milestones from birth to age three. Mothers were asked questions to give their opinions about age at which a normal child should begin to accomplish standard developmental milestones. The questionnaire covered four domains of child's development; physical, social and emotional, intellectual and language. The study assessed maternal knowledge of child development and whether the level of knowledge varies by content area.

Growth and development are two different entities. Growth refers to increase in physical size i.e., increase in height and weight. But developments related to the child's ability to do difficult and advanced things with the passage of time. In Paediatrics medicine, Developmental milestones are a collection of functional skills as well as physical tasks specified with a certain age range⁶ although each milestone has an age level, the actual age when a child achieved that milestone could be different from other children of the same age group. It has been observed that some children start to speak and walk at a later age as compared with other children of the same age doing that earlier.

There are many different methods to determine the growth and development of a child. Several models have been proposed that incorporate a range of factors encompassing child's physical, motor, cognitive, language, social and emotional development. Each child develops at his own pace so it's important to realize that there is wide variation in terms of what is considered "normal". A child development is broadly influenced by a wide variety of genetic, cognitive, physical, family, cultural, nutritional, educational, and environmental factors⁷

It was found in this study that majority of the mothers knew correctly when a child is able to hold his/her neck when put to sit. A child's motor skills and neck muscles are fairly weak at birth so he/she learns to hold the head by three months. Rest of the women overestimated the age for this milestone. A study done in a developing country showed that mothers believed that most developmental skills and activities should occur at later than normative ages and most mothers did not know that sight, vocalization, social smiling and overall brain development begins in the early months of life⁸ Majority of the mothers didn't know when a child gets capable to sit with support. A child begins to show willingness to sit without support on his/her own earlier if the mother sits him/her up with support of a couch/pillow in the

fourth to fifth months of life. Mothers could not tell when a child is able to distinguish family from strangers. At around seven months, a child will probably cry when he/she is in the arms of anyone else except the primary care giver which is why he/she becomes clingy.

In the beginning a child says single syllables but with time he/she learns to speak complex and meaningful sentences. Mothers didn't know at what age a child starts speaking double syllables like 'mama' & 'baba'. Maternal sensitivity is associated with early intentional communication particularly the use of communicative gestures, and also with symbolic behaviour and later comprehensive skills.⁹ A study examined a comprehensive set of predictors of preschool language performance. It was revealed that having a poor language-learning home environment was associated with children's low language scores¹⁰

Language is the foundation of communication. If hearing impairment exists from birth or occurs at a young age, speech will be affected severely. A study showed that children whose hearing losses were identified by 6 months of age demonstrated significantly better language scores than children identified after 6 months of age.¹¹ Mothers knowledge of speech milestones can indicate hearing loss or delayed language development. Therefore, it is emphasized to report any developmental delay as it may indicate any underlying disease or deficiency so it can help in early diagnosis and effective treatment. A child learns to put together short words to make a complete sentence at around the age of two. The study showed that half of the mothers didn't know the age at which a child is capable to form a complete sensible sentence. In one study it was observed that mothers' knowledge about cognitive, language, and motor abilities was stronger than their knowledge about abilities in play and social development. Across domains, mothers were more accurate at estimating the ages of abilities that emerge in the first year than those occurring during child's second and third years¹²

The study shows mothers didn't know at what age a child is able to feed him/herself with finger foods. A child between seven and eleven months old usually tries to grab food from mother and soon develops the 'pincer grasp' by ninth month that allows him/her to pick up small objects between thumb and forefinger. At this point, a mother should introduce small pieces of cooked vegetables or pea sized bites of chicken/meat to fulfill his/her nutritional requirements. In a study, majority of the children who were reported to show developmental readiness to self-feed at an earlier age (7 to 14 months) had higher intakes of energy and most nutrients than those who did not¹³

The study revealed that mothers couldn't tell the age at which a child is able to run forward which shows mother's negligence towards child's physical

development. Being able to run forward, kick a stationary ball or jump in one place by age three are some of the major physical milestone achievements. Mothers didn't know at what age a child begins to indicate an urge for defecation and urination. In a study it was found out that girls achieve nearly all toilet-training skills earlier than boys, including successful completion. Most children do not master the readiness skills until after the second birthday¹⁴

Children who do not get proper breastfeeding, are physically deprived or malnourished have increased risk of delayed achievement of developmental milestones.

A study examined maternal reports of the health and attainment of developmental milestones for breast-fed vs. formula-fed infants. The study showed smiling to be reported earlier for the infants of breast-feeding mothers. Formula-feeding mothers were quicker to introduce their infants to solid foods. Ratings of physical health were comparatively better for the breastfed than for the bottle-fed infants¹⁵ Breastfeeding also influences development of brain. A study done to investigate the association between exclusive breastfeeding and three developmental milestones related to general and fine motor skills and early language development at the age of 8 months. The proportion of infants who achieved the specific milestones increased consistently with increasing duration of breastfeeding¹⁶ Child's nutrition, healthy growth and development also depend upon financial status. Poverty and associated health, nutrition, and social factors prevent at least 200 million children in developing countries from attaining their developmental potential¹⁷ As nutrition, growth monitoring and immunization programs have dramatically increased the rates of child survival throughout the developing world there has been a ground swell of interest in going beyond survival to increase children's chances for optimal development. Past experience has shown that when developmental monitoring and stimulation programs are added to health and nutrition programs the rates of both physical and mental development may be improved¹⁸

Parental knowledge of child development has been associated with more effective parenting strategies and better child outcomes¹⁹ A survey was conducted to gauge knowledge of developmental milestones among Albertan Adults where it was found out that the majority of parents were not able to correctly answer questions related to when children under three years of age typically achieves developmental milestones. Parents were not aware of the importance of positive experiences in influencing their children's development. Mothers are the primary care givers in our society so her awareness about milestones is most important. Paediatricians should incorporate developmental surveillance at every health supervision visit.

Surveillance should involve analysing the milestones in the context of a child's history, growth, and physical examination findings to recognize those who may be at risk for developmental delay. A thorough understanding of the normal or typical sequence of development in all domains allows the clinician to formulate a correct overall impression of a child's true developmental status²⁰ Also, nutritional intervention programs had been successful in making people aware about nutritional milestones like colostrum, breastfeeding and weaning²¹ Timely achievement of milestones also depends upon the weight of an infant at birth. It has been found that low birth weight is significantly associated with delay in achieving all developmental milestones including lifting of the head, tooth eruption, sitting without support, walking without help, speech as saying words with meaning, and bedwetting cessation²² It shows that mothers should maintain healthy eating and good nutrition during pregnancy.

Mothers should be made aware about child's normal development so if any developmental delay is reported, its cause can be detected and promptly treated. The cause may be primary/hereditary or acquired, it's depends upon mothers knowledge which would help her identify the disease earlier. Mothers should also be made aware about growth charts so they can monitor their child's development at home. Growth charts used should be simple and easy to understand for the general population. This will decrease the disability and morbidity burden on the population. Government should take measures to impart milestones awareness to the expecting mothers visiting antenatal clinics. In fact, there is a need to raise awareness in both the parents by holding didactic awareness sessions and seminars in public where they can be trained by qualified instructors about normal developmental milestones²³ Primary care physicians, because they routinely see children less than 5 years of age for preventive care visits, can play a key role in the early identification of developmental delays²⁴ Precise determination of a child's milestones depends on the parent's recollection of developmental events²⁵ So it's very important to pay keen attention to each domain of child development. Such measures will decrease the disability and morbidity burden on the society. Monitoring of growth and development of children is the key to a healthy generation.

CONCLUSION

The study concluded that mothers had insufficient knowledge about child's physical development and mother's awareness about child's intellectual, social and language development was extremely poor.

Author's Contribution:

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Keratometric Values and Astigmatic Distribution in Population of South Lahore

Shahid Nazir

ABSTRACT

Objective: To assess distribution of astigmatism among individuals of South Lahore

Study Design: Cross-sectional study.

Place and Duration of Study: This study was conducted at the Central Park Medical Teaching Hospital Lahore from 1st January 2018 to 31st March 2018.

Materials and Methods: In the present study, keratometric findings of 229 patients (458 eyes) were analyzed, who were presented with refractive problems to know their refractive status. The patients belonged to different localities of South Lahore.

Results: No statistical significance was present for age; however, female gender was statistically associated with higher K readings.

Conclusion: It is concluded that there is a high prevalence of astigmatism among population of southern Lahore. Keratometric values are found higher in female population. These values should consider in planning refractive surgery.

Key Words: Kerotometry, Astigmatism, Refractive surgery

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INTRODUCTION

Astigmatism is a refractive error and an inability of cornea and lens to appropriately focus an image on the retina. It can vary from being congenital, surgically induced, contact lens induced, compounded with near sightedness or far sightedness.¹ Depending on the axis of principal meridians, it may be irregular or regular. The advanced technology has aided in precise diagnosis of astigmatism along with its proper correction. The most common method used to diagnose and measure astigmatism is keratometry.² Keratometry is a diagnostic approach used to measure anterior central corneal curvature. It is performed with a manual keratometer. This device gives an idea about the refracting power of cornea with two corneal curvature values.³

The problem of astigmatism is increasing day by day. As children have immature and developing visual system, astigmatism is highly prevalent in them. It is considered to be influenced by age. In newborns, astigmatism has been reported to be as high as 70%.⁴ Another study reports that in older children

it may decrease to 12-13 % till the age of 10 years.⁵ In another study, children with age 10 were reported to have 25 % prevalence of astigmatism.⁶ Though less prevalent than children, elder individuals also suffer from the issue of astigmatism.⁷ Keratometric values define the corneal power. Higher mean Ks may indicate the presence of higher number of Keratoconus suspects.⁸

Astigmatism is responsible for causing optical defocusing at all distances. In order to get a sharp focus, high strain is laid on ciliary muscles of the patient. This can cause asthenopia and eye-strain. Moreover, it has been reported to cause amblyopia and myopia in the patients.⁹ Thus, it is highly important to assess the distribution of astigmatism in general population to devise better strategies that can be helpful in dealing against the problem.¹⁰ The present study aims to assess the distribution of astigmatism and k values among individuals of South Lahore.

MATERIALS AND METHODS

This cross-sectional study was carried out at Central Park Medical Teaching Hospital Lahore from 1st January, 2018 to 31st March 2018. In the present study, retinoscopic findings of 229 patients was analyzed, who were presented with refractive problems to know their refractive status. All the patients were examined at Central Park Teaching Hospital from January, 2018 to March, 2018. The patients belonged to different localities of South Lahore. The patients were selected randomly on the basis of availability and

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willingness to become a part of the study. All the patients were explained about purpose of the study and consent forms were collected from each patient. Refraction was conducted on each patient objectively with the help of Helmholtz Keratometer. It is a one-time positioning device that uses adjustable image size. It is assisted with an aligning plus sign and minus sign mires. Sphero-cylindrical method of refraction was utilized to minimize movements. In order to make complete adnexal and biomicroscopic anterior segment examination, Topcon slit-lamp was used. Fundus examination was done with 90D. The children having age of 10-20 years, cyclogenic refraction was performed after 40-50 minutes with topical instillation of 1% cyclopentolate eyes drops, with interval of 5 to 10 minutes. The data was analyzed with the help of SPSS v.17. The descriptive data is represented as frequencies, percentages and mean $\pm$ SD. The Chi square test and ANOVA test was used to assess relation of K values with ages and genders.

RESULTS

According to age, out of 229 cases (458 eyes), 30.57% (n=70) were between 10-20 years, 37.55% (n=86) were between 21-40 years, 21.84% (n=50) were between 41-60 years and 10.04% (n=23) had >60 years with mean being 34.00 $\pm$ 18.02 years (Table 1). Gender distribution shows that 44.54% (n=102) were male and 55.46% (n=127) were females (Table 2). Overall mean K values of the participants were calculated as 43.93 $\pm$ 5.44 for K1R, 44.10 $\pm$ 1.57 for K2R, 44.18 $\pm$ 1.64 for K1L, and 44.16 $\pm$ 1.65 for K2L (Table 3). It was observed that there was no significant difference for any of the K-value among 4 age groups as all p-values recorded were close to 1.000 (above 0.75) after applying ANOVA test of significance (Table 4). The difference for all K-values were found significant between two genders with p-values 0.001 or less except K1R with 0.0013 and K2R with 0.0014 (Table 5). Mean astigmatic value was 0.2112 D, SD 0.1922. Central astigmatic value is 0.25 D. No significant difference is found among gender and age groups $p > 0.05$ (Table 6).

Table No.1: Age distribution

Age (years)	No.	%
10-20	70	30.57
21-40	86	37.55
41-60	50	21.84
>60	23	10.04
Mean $\pm$ SD	34.00 $\pm$ 18.02	

Table No.2: Gender distribution

Gender	No.	%
Male	102	44.54
Female	127	55.46

Table No. 3: Overall mean K values of the patients

K values	Mean $\pm$ SD
K1R	43.93 $\pm$ 5.44
K2R	44.10 $\pm$ 1.57
K1L	44.18 $\pm$ 1.64
K2L	44.16 $\pm$ 1.65

Table No.4: Stratification of K values according to age group

K values	Age (years)				P value
	10-20	21-40	41-60	>60	
K1R	43.93 $\pm$ 5.44	44.21 $\pm$ 1.58	44.33 $\pm$ 6.40	44.22 $\pm$ 1.73	0.963
K2R	45.07 $\pm$ 5.47	45.25 $\pm$ 0.02	45.25 $\pm$ 6.34	45.25 $\pm$ 0.01	0.99
K1L	43.92 $\pm$ 5.47	44.19 $\pm$ 1.57	44.44 $\pm$ 6.47	44.36 $\pm$ 1.96	0.929
K2L	43.89 $\pm$ 5.46	44.19 $\pm$ 1.64	44.40 $\pm$ 6.46	44.37 $\pm$ 1.84	0.927
KR	44.5 $\pm$ 5.45	44.73 $\pm$ 0.08	44.79 $\pm$ 6.37	44.42 $\pm$ 6.47	0.979
KL	43.91 $\pm$ 5.45	44.19 $\pm$ 1.61	44.79 $\pm$ 6.47	44.37 $\pm$ 1.9	0.75

Table 5: Stratification of K values according to gender

K value	Gender		P value
	Male	Female	
K1R	43.78 $\pm$ 1.58	44.44 $\pm$ 1.47	0.0013
K2R	43.73 $\pm$ 1.61	44.39 $\pm$ 1.47	0.0014
K1L	43.73 $\pm$ 1.70	44.53 $\pm$ 1.55	0.0002
K2L	43.71 $\pm$ 1.65	44.52 $\pm$ 1.58	0.0002
KR	43.75 $\pm$ 1.59	44.42 $\pm$ 1.47	0.0001
KL	43.72 $\pm$ 1.65	44.53 $\pm$ 1.59	0.0001

Table No.6: Comparison of TAR and TAL Keratometric Astigmatic values according to gender

Measure	Gender	N	Mean	Std. Dev.	Std. Error	Min.	Max.	ANOVA F & P value
TAR	Male	101	.2426	.19511	.01941	.00	.75	F = .221 P = .639
	Female	128	.2305	.19240	.01701	.00	.75	
	Total	229	.2358	.19327	.01277	.00	.75	
TAL	Male	101	.1906	.20046	.01995	.00	1.00	F = .075 P = .784
	Female	128	.1836	.18423	.01628	.00	1.00	
	Total	229	.1867	.19116	.01263	.00	1.00	

DISCUSSION

Refractive errors are known as the most common ocular problem, which affect all the age groups and genders. It is regarded as a public health challenge. According to WHO, 43% of visual impairments are caused by refractive errors. This has resulted in high prevalence of visual loss all over the world.² In year 2010, it was estimated that 101.2 million people have become visually impaired due to uncorrected refractive errors, whereas, 6.8 million individuals have become blind due to the same. Consequently, the economies of different nations are also affected by refractive errors. An annual loss of \$ 269 billion has been reported to result from refractive errors, worldwide.¹¹ In people with age more than 50 years, this figure has been reported to be \$ 121.4 billion. Resultantly, WHO has placed refractive errors among five highly prioritized conditions. Astigmatism is given important due to its high distribution, its influence of visual development in childhood and problem in correcting it has resulted in spectacle intolerance.¹²

Astigmatism results in optical defocus at all viewing distances. The ciliary muscles bear constant strain to obtain a sharp focus, which leads towards eye-strain and asthenopia in astigmatic individuals. Astigmatism has impact on all the ages, and genders. However, in children the effect is more pronounced due to immature and developing visual system. It is reported to be associated with myopia and amblyopia. Its detection in early years of life is important as it has high impact on normal visual development. The alternations in cornea shape can take place at once or over several years. However, after age of 15, astigmatism may not increase considerably.¹³

Shah et al⁴ estimated prevalence of different refractive errors among adults of Pakistan. According to this study, astigmatism in Pakistan is estimated to be 37%. This represents an adverse condition among residents of Pakistan. In the present study, data from South Lahore was collected, astigmatic prevalence was noted to be 64.52%. This is quite high as compared to previously reported ones. Abdullah et al¹ claimed that adults with age 30 have prevalence of 5.6% in rural population of Pakistan. This indicates a tremendous increase in prevalence of astigmatism among individuals of this age category. However, Hashemi et al¹⁰ pointed that overall prevalence of astigmatism for adults is 40.4 %. In Indonesia, prevalence for astigmatism has been noted to be 56.90 % among adults.¹⁴ Chinese population was found to have 56.35 % prevalence of astigmatism for age of 40 above years.¹⁵

The prevalence of astigmatism was found to be 66% among children of age 10-20 years. Previous studies in Pakistan have indicated that refractive errors have prevalence of 20.07% in school children of Pakistan. This figure is quite lower than the findings of present

study. In USA, prevalence of astigmatism has been noted to be 42% for children. In Iran, it was noted to be 50.2% among children with age of 5 years. On gender basis, females were found to have prevalence of 55.46% as compared to males with prevalence of 44.54%. This is in accordance with the work of Rasheed et al.¹¹

There is significant difference between mean Ks 43.57±1.57 male and 44.42±1.47 female. The higher distribution among female may show the higher prevalence of Keratoconus suspect among population. This result is consistent with the work of KhabazKhoob et al.⁸ The findings of present study have indicated that there is no statistically significant difference in astigmatism distribution among the age groups. However, higher K-means is highly associated with gender, with high statistical difference. This is in accordance with the work of Lopes et al¹⁶ and KhabazKhoob.⁸

Many immediate and long term outcomes have been related with uncorrected refractive errors in adults and children. This includes decrease in employment and educational opportunities, lost vision, poor quality of life and economic disturbances. It is important to screen the individuals with refractive errors such as astigmatism and correct it. Higher K values should consider in keratoconus classification, in refractive surgery indices and evaluation, to avoid treatment, to Keratoconus suspect and post op ecstasies.

CONCLUSION

There is a no significant difference of astigmatism distribution in different age groups. Keratometric higher values in female population should consider in defining the KC among the southern population of Lahore. These should be considered in keratorefractive indices and evaluation, to avoid treatment of keratoconus suspect and post operative ectasia

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Conflict of Interest: The study has no conflict of interest to declare by any author.

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Tissue Toxicity Threatens the Gold Standard Image of Lithium as a Mood Stabilizer Drug

Saleem Ahmed Bhutto¹, Muqem Mangi³, Azhar Ali Shah⁴, Muhammad Aslam Channa¹, and Mir Khater Ali²

ABSTRACT

Objective: To demonstrate that the lithium is generally a toxic agent to tissues of both animals and humanbeings but especially to liver and kidney.

Study Design: It is prospective, interventional, morphometric and theoretico-empirical study.

Place and Duration of Study: This study was conducted at the Basic Medical Sciences Institute, Jinnah Post Graduate Medical Centre Karachi University, Karachi, Sindh from October 2012 to March 2013.

Materials and Methods: 30 Albino rats were nursed under all necessary parameters and under the study plan were exposed to lithium carbonate with 20mg per Kg body weight per day. Under the study plan, rats were divided into two groups A and B, each group comprising of 15 rats. Group A is control group while group B is Experimental group exposed to lithium dose. Animals were killed after duration of two, six and twelve week's exposure to lithium dosage as each group was divided into three sub groups each comprising of five animals.

Results: Results of this study highlighted the fact that Lithium as the toxic metal displays significant toxic liver manifestations and disturbs the cytoarchitecture significantly along with the disturbances in the carbohydrates, protein, and fat metabolism. Alkaline phosphatase enzyme displays significant disruption therefore needs extensive evaluation for not only the hepatotoxicity but also biotoxicity and ecotoxicity.

Conclusion: conclusively inference can be made that the lithium has lost its reputation as gold-standard mood stabilizer drug but can be employed as an investigative tool in Physiology. Biochemistry, Genetics and Pharmacology but particularly in Psycho-neurology.

Key Words: Lithium, hepatotoxicity, Genotoxicity, biotoxicity, etc.

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INTRODUCTION

Human toxicity: Long-term effects on organ systems The three organ systems that may be negatively affected by lithium are the thyroid gland, kidneys and parathyroid glands.

Lithium and the kidneys: The polyuria reflects lithium's effect on the renal tubular system. Concerns that this might reflect structural irreversible damage, as opposed to simply reversibly interfering with tubular function, began with the first reports of biopsy-proven interstitial nephritis in lithium-treated patients almost 40 years ago¹. all studies examining renal morphology in lithium-treated patients have consistently found the same results: focal nephron atrophy, and interstitial fibrosis with relative preservation of glomeruli².

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This is consistent with the clinical features of lithium-associated nephropathy—obligate polyuria—but without marked decrease in filtering capacity of the kidneys as measured by eGFR and secondarily by serum creatinine. (The latter measure is less accurate than eGFR since it also reflects muscle mass which decreases with age. Thus, an older person may have substantially diminished eGFR but a relatively normal serum creatinine.) Polyuria correlates only weakly with reduced kidney function with the former rather common and the latter unusual³.

Although lithium-treated patients have, in general, a lower eGFR than those not treated, the eGFR does not correlate with time on lithium suggesting that it is not progressive within groups. However, a subgroup of lithium-treated patients does show progressive renal insufficiency. This is manifested by “creeping creatinine”⁴ with a gradual rise in serum creatinine and a decrease in creatinine clearance over years. This phenomenon occurs in approximately 20% of lithium-treated patients⁵. In one study, approximately 1/3 of lithium-treated patients had an eGFR <60 ml/min while 5% showed an eGFR of <30 ml/min^{6,7}. An even smaller subgroup of lithium-treated patients progresses towards end-stage renal disease (ESRD) and ultimately dialysis and/or renal transplantation. The prevalence of ESRD associated with lithium is difficult to estimate. One

study found the risk to be almost eightfold compared to the general population^{6,7}. In contrast, another study found risk for renal insufficiency but not ESRD⁸. While a third study found no differences in the rate of eGFR declines in lithium-treated patients vs. those treated with other psychotropic agents⁹. In the most recent study, compared to patients treated with other mood stabilizers such as valproate, olanzapine or quetiapine, lithium was associated with higher rates of chronic renal disease (eGFR <60 ml/min) but not more severe renal disease. Since lithium-associated ESRD is virtually exclusively seen in patients treated for a very long term—in one study, the average time on lithium for those with ESRD was 27 years^{6,7,10}, studies of only 10–15 years may not show the increase in ESRD. Some recent studies have suggested both lower rates of ESRD in lithium-treated patients over the last thirty years when mean therapeutic lithium levels are lower than before^{6,7} and less effect on renal function in general with lower levels¹¹.

However, the largest study of unselected: patients continued to find significant rates of renal damage and ESRD in a lithium-treated population^{6,7,10}.

Risk factors for lithium-induced nephropathy are length of treatment, age, and prior episodes of lithium toxicity^{6,12,9}. Whether the lithium regimen—once-daily vs. multiple doses—predicts differential rates of ESRD is unclear. Some evidence exists that progressive renal impairment continues even after lithium discontinuation,^{12,13}. Since the progression of renal damage is slow, if discontinuing lithium is deemed necessary, the second mood stabilizer should be added, titrated to full dose and only then should the lithium be tapered and discontinued gradually over 4–8 weeks.

Toxicity in Animals: Lithium causes multi system toxicity¹⁴. Oral administration of lithium carbonate to healthy rats strongly decreased liver glycogen content despite the simultaneous activation of glycogen synthase and the inactivation of glycogen phosphorylase. The effect seemed to be related to a decrease in glucose 6 phosphate concentration. Lithium inhibits the enzymes of glucose metabolism e.g. glucose kinase, pyruvate kinase and super oxide dismutase (SOD)^{14,15,16}.

Lithium carbonate in the dose of 150 mg /kg body weight when administered in drinking water for 30 days induces lipid peroxidation (LPO) to a significant extent that was accompanied by a marked reduction in reduced glutathione, SOD, catalase, Glutathione S-transferase (GST) and Glutathione peroxidase (GPX) activities and parallel decline in Adenosine triphosphate (ATP) in tissues. Toxicity resulted in abnormal elevation of lipids such as cholesterol, triglycerides, phospholipids and fatty acids in liver tissues^{17,18}. It impairs the DNA synthesis and DNA repair¹⁹.

The process of LPO and DNA oxidation leads to disruption of the ultra structure of the cell machinery,

diminution in the quantity of cellular ATP, reduction in the anti-oxidant systems resulting in programmed cellular

Death and necrosis: The inflammation is very wide.^{16,17} Echo toxicity and biotoxicity are also prevalent.

MATERIALS AND METHODS

Thirty albino adult rats of 90 – 120 days of age weighing about 200 – 300 grams were used for this study. Animals were obtained from the animal house of BMSI, JPMC, Karachi. These were divided into two major groups A and B each comprising 15 rats. Each major group was sub-divided into three sub-groups 1, 2 & 3 on the basis of 02 weeks, 6 weeks and 12 weeks duration of treatment respectively. Group A was control and fed on lab diet. Group B was treated with lithium in drinking water. Lithium was used in the dosage of 20 mg/kg body weight/day in water¹⁷. Each sub-group was sacrificed at the end of their corresponding duration of treatment under ether anesthesia, dissected and blood was collected through intra-cardiac puncture for serum ALP and ALT analysis. Each liver was cut into two halves. One half was fixed in buffered neutral formalin. Paraffin embedding of tissues were done after processing of the fixed tissues. 4 um thick sections were cut using rotary microtome for H&E, PAS & Gomori's calcium phosphate staining. Representative sections from the second half of liver were immediately frozen using cryostat and 10 um thick sections were cut and subjected to Oil Red O staining.

The statistical significance of the differences of various Histochemical as well as serological changes between lithium carbonate and diet treated rats from the control group were evaluated by the student T-test.

RESULTS

Results are based upon both gross and microscopic examination, the absolute and relative weights of livers were recorded and present study demonstrated that Lithium induces hepatotoxicity in animals. The dose of Lithium used in this study is similar to that used by Kolachi⁶.

Observations on absolute and relative liver weight disclosed moderately significant to significant increase in weight of liver when B group was compared to A group.

The morphological examination of haematoxylin and eosin (H&E) stained 4 um thick sections displayed dilatation and congestion of central and portal veins along with the congestion of sinusoids. There was a distortion of the wall of the central veins, plates or cords of hepatocytes seemed to be irregular and exhibited distortion. The hepatocytes were scattered in the lobules revealing vacuolation both in pericentral and periportal areas. Cytoplasm revealed mild granularity. Hepatocytes showed pyknosis of nuclei and

disintegration thereof. Kupffer cells were prominent and hypertrophied. Binucleate hepatocytes were also

seen revealing proliferation of the parenchyma. (Tables 1-4, Fig 1-4)

TableNo.1: Mean values of absolute liver weights (G).

Groups	Sub Groups	Treatment Given	Final weights at variable time intervals		
			2 weeks	6 weeks	12 weeks
A (n=15)	A1	Control (Normal Lab Diet)	8.20 ± 0.8		
	A2			8.40 ± 0.51	8.80 ± 0.37
	A3				
B (n=15)	B1	Lithium carbonate treated	12.00 ± 0.44		
	B2			14.00 ± 0.44	
	B3				15.00 ± 0.70

Statistical Analysis of mean absolute liver weight between different groups

Statistical Comparison	P Value
A1 VS B1	P<0.05**
A2 VS B2	P<0.01***
A3 VS B3	P<0.01***

Key: Non Significant*

Significant**

Moderately significant***

Highly significant****

Table No.2: Mean values of relative liver weights (G).

Groups	Sub-groups	Treatment Given	Final weights at variable time intervals		
			2 weeks	6 weeks	12 weeks
A (n=15)	A1	Control	3.30±0.32		
	A2	(Normal Lab Diet)		3.31±0.18	
	A3				3.56±0.13
B (n=15)	B1	Lithium	4.56±0.15		
	B2	Carbonate		5.30±0.17	
	B3	Treated			5.66±0.27

Statistical analysis of mean relative liver weight between A and B groups.

Statistical comparison	P value
A1 VS B1	P<0.05**
A2 VS B2	P<0.01***
A3 VS B3	P<0.01***

Key: Non Significant*

Significant**

Moderately significant***

Highly significant****

Table No.3: Glycogen Content of Hepatocytes.

Groups	Sub Groups	Treatment Given	Glycogen content in Hypatocytes at variable Time interval		
			2 weeks	6 weeks	12 weeks
A (n=15)	A1	Control (Normal Lab Diet)	N+		
	A2			N+	
	A3				N+
B (n=15)	B1	Lithium carbonate treated	+		
	B2			++	
	B3				+++

Table No.4: Distribution of the activity of alkaline phosphatase in hepatic lobules.

Groups	Sub Groups	Treatment Given	Contents of crystals (Cobalt sulphide) in Hepatic lobule at variable Time interval			Normal Mild Moderate Marked	N+ + ++ +++	Depletion
			2 weeks	6 weeks	12 weeks			
A (n=15)	A1	Control (Normal Lab Diet)	N+					
	A2			N+				
	A3				N+			
B (n=15)	B1	Lithium carbonate treated	+					
	B2			++				
	B3				+++			

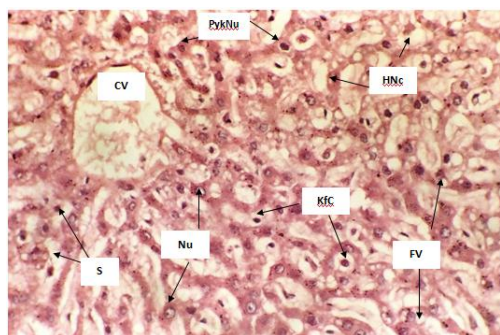


Figure No.1: Photomicrograph of H&E stained 4μm thick section of liver showing enlarged hepatocytes with large nuclei (Nu) and highly congested and dilated sinusoids (S) with disruption and distortion of lobular architecture with pyknosis of nuclei (PykNu) and cytoplasm displaying small vacuoles of microvesicular fatty change (FV), prominent Kupffer cells (KfC) in the lining of sinusoids and necrosed hepatocytes (HNC) in albino rats, after 6 weeks of lithium carbonate treatment X 1000.

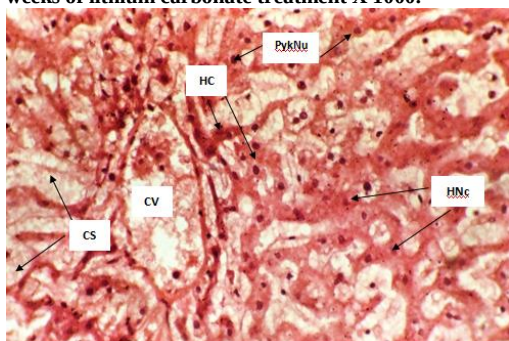


Figure No.2: Photomicrograph of H&E stained 4μm thick section of liver showing hepatic lobular architecture displaying central vein (CV) around which is depicted pyknosis of nuclei (PykNu), dilated and congested sinusoids (S) and distorted hepatic cords (HC) in the albino rats after 12 weeks of lithium carbonate treatment X 1000.

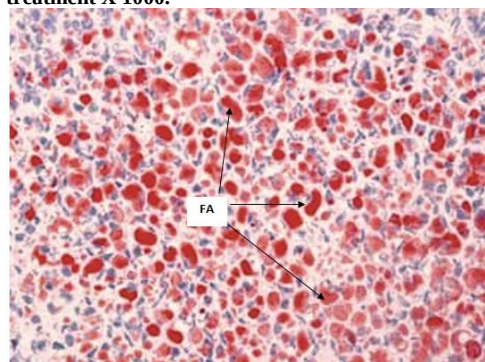


Figure No.3: Photomicrograph of oil red O stained 10μm thick frozen section of liver exhibiting densely packed fat globules (FA) in the hepatocytes of the lobular architecture in zone-II and zone-III in albino rats after 6 weeks of lithium carbonate treatment X 400.

DISCUSSION

Liver gross examination of group B animals showed significant histological alteration due to lithium toxicity. This observation correlates with the work of Sharma and^{14,16}. The augmentation in absolute and relative liver weight was due to cellular hypertrophy, hyperplasia, swelling, hydropic degeneration, increased mononuclear cell infiltration, accumulation and hypertrophy of kupffer cells, enhancement in fatty infiltration in the

form of microvesicular fatty globules and dilatation and congestion of portal and central veins which was in agreement with the suggestions of^{19,20,16}.

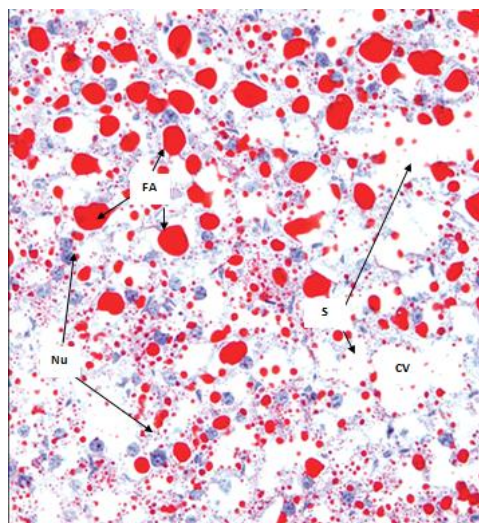


Figure No.4: Photomicrograph of oil red O and haematoxylin stained, 10μm thick frozen section of liver showing hepatic lobular cytoarchitecture displaying central vein (CV), sinusoids (S) and blue stained nuclei (Nu) of hepatocytes. It also depicts densely packed fat globules (FA) in the liver cells in all three zones in albino rats after 12 weeks of lithium carbonate treatment X 1000.

Also Group B animals demonstrated significant depletion in glycogen content in hepatocytes which was chiefly attributed by the lithium hepatotoxicity. Lithium causes disturbance of the glucose metabolism in vivo. It is also in agreement with the observations of²¹, who studied the effect of lithium on rat glucose metabolism in vivo. It also correlated with the observations of²² who reported similar type of depletion in glycogen content in hepatocytes treated with piroxicam in experimental mice.

The histochemical study of Gomori's calcium phosphate stained section of group B animals showed decreased amount of brownish black deposits of cobalt sulfide meant thereby reduced alkaline phosphatase (ALP) activity. This was due to hepatic injury which increased the permeability of cell membrane with resultant leakage of enzymes from cytoplasm to sinusoids and then into circulation with simultaneous increase in the serum hepatic ALP as described by^{19,23}. These observations match with the observations of^{14,16} who have examined liver and kidney toxicity.

CONCLUSION

Empirical outcome reveals that The Lithium is an excellent mood-stabilizer and gold-standard antisuicidal drug with very narrow therapeutic margin. But unfortunately Lithium is also widely toxic metal for all living organisms and Biosphere of planet Earth. It is toxic to both animal and human beings but predominantly to Kidney, Liver and Heart organs. It has very diverse Pharmacodynamics at various levels of biomolecular cascade systems of cellular machinery but yet its mechanisms of actions are not fully known

despite very intensive as well as extensive research over the last 70 years. Therefore conclusively inference can be made that the lithium has lost its reputation as gold-standard mood stabilizer drug but can be employed as an investigative tool in Physiology, Biochemistry, Genetics and Pharmacology but particularly in Psychoneurology.

Author's Contribution:

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Conflict of Interest: The study has no conflict of interest to declare by any author.

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Comparative Study of Hematological Parameters of Untreated Leprosy Cases and Control

Ghulam Serwar Shaikh¹, Zafar Ali Pirzado³, Ali Gul Tunio² and Viqar Sultana⁴

ABSTRACT

Objective: To evaluate the Hemoglobin, Total Leukocyte Count, Differential Leukocyte Count, Platelets, RBC Count in leprosy patients.

Study Design: A case control study

Place and Duration of Study: This study was conducted at the Department of Biochemistry, University of Karachi from March 2015 to April 2017.

Materials and Methods: A total of 110 newly diagnosed untreated leprosy patients 79 male, 31 female were taken from Marie Adelaide Leprosy Centre, Karachi. Clinical and bacterial based skin smear test for diagnostic purpose performed, 76 control samples 55 male, 21 female were taken from general population for comparison.

Results: Table 1 demonstrate that all fractions of complete blood count (CBC) were non- significant ($p > 0.05$) except hemoglobin and RBC, which were decreased significantly high ($p < 0.001$) and ($p < 0.004$) in untreated leprosy cases when compared with control group.

Conclusion: In this study hemoglobin and RBC's count were found decreased in untreated leprosy cases may be due to poor diet and inadequate nutrient intake.

Key Words: Leprosy, Total Leukocyte Count, Differential Leukocyte Count, Red Blood Cells.

Citation of articles: Shaikh GS, Pirzado ZA, Tunio AG, Sultana V. Comparative Study of Hematological Parameters of Untreated Leprosy Cases and Control. Med Forum 2018;29(10):65-67.

INTRODUCTION

Leprosy is infectious disease transmitted by droplet infection and caused by *Mycobacterium leprae*¹, it involves nerves and skin.² It is successfully treated with current treatment regimen known as multi drug therapy (MDT). This bacterium was first introduced by G.H.A Hansen in 1873 and hence it is known as Hansen's illness³. Intracellular *M. leprae* cause swelling and may destruct the cellular structures in affected individuals⁴.

Deformities may be formed in untreated leprosy patients but patient may not die due to this disease⁵. Worldwide the number of permanently disable Leprosy cases was estimated in 1995 which was 02 to 03 millions⁶. Leprosy Patients bear social, economic and mental disturbance along with physical problems^{7,8}. Females suffer these problems more as compared to male in many countries in the world^{9,10}.

In low socio economical countries leprosy may be endemic^{11,12}. In early stages the signs and symptoms may be ignored until visible disabilities have not occurred¹³. It is transmitted through nasal droplets, spitting, sneezing and coughing^{14,15}.

MATERIALS AND METHODS

A total of 110 newly diagnosed untreated leprosy patients 79 male, 31 female were taken from Marie Adelaide Leprosy Centre, Karachi. Clinical and bacterial based skin smear test for diagnostic purpose performed, control samples 55 male, 21 female were taken from general population for comparison.

CBCs including, Hb concentration, RBC count, platelets, TLC, neutrophils, lymphocytes, Eosinophils and Monocytes were analysed used automated hematology analyzer.

RESULTS

Table 1: demonstrate that all fractions of complete blood picture (CBC) were non- significant ($p > 0.05$) except hemoglobin and RBC, which was decreased significantly ($p < 0.001$) and ($p < 0.004$), where as table 2 no significant difference was observed in differential leukocyte count in untreated leprosy cases when compared with control group.

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Table No.1: Comparison of Hematological Parameters of Untreated Leprosy Cases and Control

Hematological Parameters	Leprosy Cases (Untreated) (n=110)	Controls (n=76)	P-value
	Mean $\pm$ S.D	Mean $\pm$ S.D	
Hemoglobin (g/dl)	11.0 $\pm$ 1.75 **	12.7 $\pm$ 1.07	0.001
RBC (10^6 /ul)	4.38 $\pm$ 0.45 **	4.55 $\pm$ 0.34	0.004
Platelets (10^3 /ul)	224 $\pm$ 49.8	223 $\pm$ 51.7	0.909
TLC (10^3 /ul)	7.0 $\pm$ 1.26	7.3 $\pm$ 1.04	0.136

** Statistically Significant (p<0.01)

Table No.2: Comparison of Differential Leukocyte Count of Untreated Leprosy Cases and Control

Neutrophil (%)	68.0 $\pm$ 3.56	68.0 $\pm$ 5.47	0.991
Lymphocytes (%)	27.3 $\pm$ 3.76	27.1 $\pm$ 3.63	0.803
Eosinophil's (%)	2.8 $\pm$ 0.49	2.7 $\pm$ 0.62	0.140
Monocytes (%)	1.6 $\pm$ 0.63	1.7 $\pm$ 0.58	0.943

DISCUSSION

In human body Complete blood count (CBC) is required to screen out the diagnosis of some diseases and to see various medical treatment¹⁶. Different blood counts have been used to clinical conditions since 19th century. For the estimation of CBCs an automated equipment was developed in 1950s and 1960s¹⁷. CBCs are useful to monitor whether patient need blood transfusion and plan an amount of treatment¹⁸. CBCs also includes white blood cells (WBC) count and it is broken down percentage of each type ie. neutrophils, lymphocytes, eosinophils, monocytes and immature cells¹⁹. The WBCs and its broken fractions are used to monitor different clinical conditions for diagnosis²⁰.

CONCLUSION

In this study hemoglobin and RBC's count were found decreased in untreated leprosy cases may be due to poor diet and inadequate nutrient intake.

Author's Contribution:

Concept & Design of Study: Ghulam Serwar Shaikh
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Final Approval of version: Ghulam Serwar Shaikh

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Reasons for Failure of Primary Endodontic Treatment

Khadija Jahanzeb, Syed Imran Shah, Asim Qureshi, and Fasial Pasha

ABSTRACT

Objective: The aim of this study was to evaluate the causes of primary endodontic treatment failure.

Study Design: Observational study.

Place and Duration of Study: This study was conducted at the Operative Dentistry Department of Rehmat Memorial Dental Teaching Hospital, Abbottabad (Women Medical College and Dental College) from February 2018 to July 2018.

Materials and Methods: A total of 82 patients of both genders (male and female), referred for endodontic retreatment were included in the study. The study was approved by the institutional ethical committee.

Results: Results indicated pain as the primary presenting complaint of root canal treated teeth (81%). The maximum number of failed treatments were reported in the mandibular molars (58%). Radiographic evaluation indicated underobturation (47%), missed canals (22%) and poor obturation (15%) as being the major causes of failed endodontic treatment.

Conclusion: The major factors responsible for endodontic treatment failure in this study were the defects in obturation with underobturation, poor obturation and missed canals making the highest contribution to failures.

Key Words: Endodontic Failures, Missed Canals, Poor Obturation

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INTRODUCTION

The goal of endodontic treatment is to reduce or eliminate microorganisms from the root canal space, prevent reinfection and promote healing of the periapical tissue by sealing the root canal system.^{1,2}

Generally success of RCT is considered only when there is no further need of any intervention. But it can be analyzed with reference to dentist and patient perception. For the dentist it involves absence of pain, no periapical lesion, a completely filled root canal system on a radiograph, and a well restored and functional tooth. From the patients point of view, only the absence of pain is essential for successful RCT.³ The success rate of RCT is estimated to be 90-95%.⁴ Despite this high success rate failures still occur due to lack of knowledge and non-implementation of the basic principles of endodontics.¹ Most important reason for primary endodontic failure is either the persistence of bacteria and necrotic tissue in the root canal system or recontamination because of poor seal.^{4,5} The factors which lead to bacterial persistence are improper asepsis, inadequate preparation and obturation of canals, defective coronal restorations and a number of proce-

dural errors including perforations, missed canals, ledges separated instruments, transportations.^{1,4,6-10}

A number of studies have been conducted to evaluate the causes of primary endodontic failures. According to a study undertaken in Srinagar 90.9% of patients presenting with primary endodontic failure had substandard obturation and 60.6% patients had defective coronal restoration.¹ Another study undertaken by Iqbal A, et al proposed underfilled canals (33.3%) and unobturated or missed canals (17.7%) to be the major causes of primary endodontic treatment failures.¹¹ The aim of this study is to evaluate primary endodontic failure of teeth based on clinical and radiographic findings in patients reporting to Operative Dentistry department, RMDTH, Abbottabad (Women Medical College and Dental College). This would be the first step in providing better endodontic treatment that is to identify the cause of failure and to help avoid such deficiencies in future. A few patients were excluded because of lack of conformity between the two dentists.

MATERIALS AND METHODS

This study was conducted at Rehmat Memorial Dental Teaching Hospital, Abbottabad (Women Medical College and Dental College). A total of 82 patients of both genders (male and female), referred for endodontic retreatment from the time period February 2018 to July 2018 were included in the study. The study was approved by the institutional ethical committee.

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The inclusion criteria were patients who had undergone root canal treatment and presented with complaint in the tooth and also endodontically treated asymptomatic teeth not considered suitable for prosthetic rehabilitation. The exclusion criteria included teeth that had undergone retreatment before.

Informed consent was taken from the patients. History was taken and clinical examination performed. Demographic details, the affected tooth number, and presenting complaint like pain, swelling, food impaction, fractured restoration and pus drainage were documented. Other parameters noted include time since the completion of the last treatment and the number of visits. All patients were examined by two dentists individually and the study included only those patients about whom findings of both the consultants were in conformity with each other.

Clinical examination comprised of visual inspection, response to percussion, status of the coronal restoration and the presence of crown or fixed partial denture. Radiographic evaluation included the presence or absence of radiolucent lesion, the quality of obturation, missed canals, presence of separated instrument or an indication of perforation. The quality of obturation was categorized as under obturation that is obturation or root canal filling more than 2mm short of apex. Obturation that extended pass the apex was considered over obturated and root canal filling that was not compact or had voids was considered poorly obturated. The data obtained was entered into Microsoft Excel 2007 for analysis.

RESULTS

The total patients included in the study were 82 including 46 females (56%) and 36 males (44%) as shown in (figure 1). Maximum number of patients belonged to the age group 40-49 years. Out of the teeth taken for retreatment there were 32(39%) maxillary teeth and 50(61%) mandibular teeth. Maximum number of teeth i.e. 48 teeth (58%) were mandibular molars. Second to these are the maxillary molars (12 teeth, 15%) and premolars (12 teeth, 15 %) having an equal involvement (Table 1).

According to the chief complaint, 66 patients (81%) presented with the complaint of pain. There were 8 patients (10%) who were asymptomatic and referred for retreatment for the purpose of prosthetic rehabilitation. The number of patients who presented with the complaint of defective restoration or food impaction was 6(7%). And only 2 patients (2%) presented with swelling as shown in Table 2. All cases reported were treated in multiple visits for root canal treatment. Results indicate that the maximum no of patients presented within 1 year of the previous endodontic treatment that is 40 patients (49%).

Clinical examination showed the presence of crown or fixed partial denture on only 12 cases (15%), and 70

cases (85%) showed no fixed prosthesis (table 3). Coronal restoration was found to be intact in 60 teeth (73%) and was fractured or missing in 22 teeth (27%) (Table 4). Radiographic evaluation indicated underobturation in 38 cases(47%), missed canals in 18 cases((22%), poor obturation in 12 cases(15%), overobturation in 6 cases(7%), separated instrument in 4 cases(5%) and evident perforation in 2 cases (2%) (Table 5). According to our results 60 teeth(73%) presenting with primary endodontic failure showed signs of periapical pathology on radiograph.

Table No.1: Distribution of teeth in failed root canal treatment.

	Maxillary (32)				Mandibular (50)			
	Incisor	Canine	Premolar	Molars	Incisor	Canine	Premolar	Molar
Number	4	4	12	12	0	0	2	48
Percent	5%	5%	15%	15%	0	0	2%	58%

Table No.2: Chief complaint of patients presenting with endodontic treatment failure.

Chief complaint	No. of patients	Percentage
Pain	66	81%
Swelling	2	2%
Defective restoration/ food impaction	6	7%
Prosthetic need	8	10%

Table No.3: Presence of fixed prosthesis on root treated tooth

Presence of crown	No. of patients	Percentage
Present	12	15%
Absent	70	85%

Table No.4: Status of the coronal restoration

Coronal restoration	No. of patients	Percentage
Intact	60	73%
Not intact	22	27%

Table No.5: Radiographic findings of the tooth with failed root canal treatment.

Radiographic Findings	No. of patients	Percentage
Underobturation	38	47%
Overobturation	6	7%
Missed canals	18	22%
Perforation	2	2%
Separated instrument	4	5%
Poor obturation	12	15%
Normal	2	2%

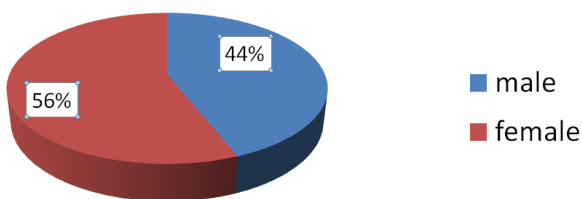


Figure No.1: Failed RCT cases

DISCUSSION

The root canals harbor bacteria and tissue debris that act as a source of infection and inflammation to the apical periodontium after irreversible pulpitis. The aim of endodontic treatment is to render the root canals bacteria and debris free by adequate cleaning and shaping of the root canals and to obliterate the canals by a dense three dimensional root canal filling.²

The results of this study indicated that the frequency of root canal failure in female patients is 56% and in males is 44%. Similar results were shown in a study by Misgar OM, et al having 43.3% males and 56.7% females presenting with primary endodontic failure.¹ This may be attributed to the fact that there are more female patients undergoing root canal treatment than male patients.¹²

The maximum number of patients (49%) reporting with primary root canal failure belonged to the age group between 40-49 years. Another study by Iqbal A, et al reported 41.11% failures in the age group between 41-50 years and explained this as being due to presence of calcified canals, uncooperative behavior, poor oral hygiene maintenance and low literacy rate.¹¹

According to the results, the maximum number of teeth presenting with root canal failure were the mandibular molars (58%), being due to the fact that mandibular first molars are the first teeth to erupt and are hence more prone to dental decay.¹³ Study by Misgar et al showed contrasting results with maxillary incisors reporting with maximum number of primary root canal failures (27%).¹

The study showed that the coronal restoration was intact in 73% of cases presenting with primary endodontic failure, indicating that defective coronal restoration may have contributed to 27% of the failure cases. Misgar OM et al reported in his study 66.6% cases with defective or missing restorations.¹ Several authors have reported that even when root fillings are satisfactory leakage of bacteria and their products along the length of the root canal is impossible to prevent.^{14,15} Hence studies have shown that sealing the coronal aspect of the tooth is of equal importance as the apical seal of the tooth for the healing of periapical tissue after root canal treatment.¹⁶

The factors considered for evaluation of the quality of root canal obturation on a radiograph are length, taper, density and homogeneity.^{17,18} The quality of obturation reflects the cleaning and shaping of the root canals.¹⁹ In

the present study the quality of obturation was found to have a significant contribution to the failure of endodontic treatment with 47% (38 cases) showing under-obturation, 7% (6 cases) showing over-obturation, 15% (12 cases) showing poor obturation and 22% (18 cases) indicated missed canals. According to a study by Hoen 65% of the teeth with failed root canal treatment exhibited poor quality obturation whereas 42% teeth had some canals which were left untreated.²⁰

The reason for flaws in obturation contributing to treatment failure is that with poor obturation of canals the apical seal is not established and contributes to failure due to microbiological persistence.²¹

Another factor in the radiographic analysis was the presence of separated instruments in 5% cases. Iqbal A et al reported similar results in his study with the presence of a separated instrument in 6.6% cases.¹¹ The influence that a separated instrument has on the prognosis of the endodontic treatment is determined by the poor filling quality due to separation and the stage of disinfection at the time of instrument separation. Causes for instrument fracture include improper use, limitations in physical properties and manufacturing faults with the most common cause being improper use in the form of overuse of instruments.²²

The limitation of this study is that in some cases multiple radiographic findings were present that may have contributed to the failed treatment. The finding that was most probable was taken into consideration. No pre-operative radiograph could be retrieved from any of the participating patients so comparison of the size of the periapical lesion could not be made. Hence all periapical lesions associated with significant abnormality of root canal filling were taken as a positive finding.

CONCLUSION

This study concludes that endodontic treatment failure is caused by multiple factors. The major factors responsible for endodontic treatment failure in this study were the defects in obturation with underobturation, poor obturation and missed canals making the highest contribution to failures. Further studies in this regard will be helpful in determining the causes and thus preventing the failure of endodontic treatment.

Author's Contribution:

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Insertion Time of the 1-Gel and LMA-C in Adult Patients under Anesthesia: A Comparison

Muhammad Shahid, Muzamil Hussain and Muhammad Omer Ajmal

ABSTRACT

Objective: To evaluate the time required for the insertion of I-gel and LMA-C in adult patients under general anesthesia.

Study Design: Randomized Control Trial

Place and Duration of Study: This study was conducted at the Anesthesia department DHQ Teaching hospital Sahiwal, from December 2016 to May 2017.

Materials and Methods: A total of 166 Patients of either sex, meeting the inclusion criteria enrolled from outpatient department. All the patients were randomly divided into two equal groups, group A and group B with 83 patients in each group. In group A, patients laryngeal mask airway was administered and inflatable cuff was inflated to 60 cm H₂O. Similarly in group B, I-gel was administered. Mean and standard deviation was calculated for qualitative variables while frequency and percentage was calculated for quantitative variables. Chi square test was applied and P value less than and equal to 0.05 was considered as significant.

Results: Gender distribution was as follows; 56.6% males in group A and 55.4% males in group B while 43.4% females in group A and 44.6% females in group B. Mean and standard deviation of age in group A and B was 38.58±1.01 and 38.71±1.13 respectively. Mean insertion time was 30.76±0.71 in group B and 34.16±0.74 in group A.

Conclusion: I-gel has significantly shorter average insertion time as compared to LMA Classic.

Key Words: Laryngeal mask airway, Anesthetized, I-GEL response, good laryngeal seal and offering similar clinical performance

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INTRODUCTION

Supraglottic airway devices are in common use for airway management in emergency and for daily life anesthesia¹. These devices are considered as advancement in the field of airway management. Advantage of supraglottic airway devices include less traumatic, easier in placement and have a role in airway protection thus making them as important devices for emergency and routine airway management². A number of supraglottic airways devices are in use currently for the airway management³.

In outpatient and elective procedures the laryngeal mask airway classic is used as supraglottic device⁴. Classic laryngeal mask airway is used in patients who are breathing spontaneously or in patients with assisted or controlled ventilation.

In some emergent cases such as in neonatal or adult resuscitation and difficult airways laryngeal mask airway classic has been reportedly used successfully⁵. Laryngeal mask airway classic has clinical usability with less pressure response and excellent laryngeal seal and has similar clinical performance. I-gel is a disposable device without inflatable cuff⁶. It is made of transparent and soft gel like thermoplastic elastomer and is latex free. It is designed in such a way that it can fit to the anatomical structures of perilaryngeal and hypopharyngeal even without the inflatable cuff. It also contains a port through which gastric tube can be passed⁷. Among the advantages of I-gel protection against aspiration, securing the airway when cardiopulmonary resuscitation is performed and protections against unanticipated difficulty in intubation. Moreover it is easier to insert and is associated with lesser tissue compression⁸.

In a study where laryngeal mask airway was compared to I-gel in terms of success rate among 60 patients suggested that laryngeal mask airway classic was more successful (95%) as compared to I-gel (93%) with P value=1.100⁹. Laryngeal mask airway classic use required less time for insertion also. As there are no local studies present regarding the comparison of these supraglottic devices in terms of ease of insertion of I-gel

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and laryngeal mask airway. Therefore in this study we are going to compare the I gel with laryngeal mask airway classic in order to assess the efficacy of the two devices and measure the time required for insertion of these supraglottic airway devices in patients under anesthesia for airway management. This will help in evaluation of the efficacy of the better device and will help in making recommendations as if to what device has easier insertion and can be used in future management of airway.

MATERIALS AND METHODS

It is a randomized control trail held in anesthesia department of District Headquarter Teaching Hospital Sahiwal from 1st December 2016 to 1st May 2017. A total of 166 patients took part in the study. Ethical approval was obtained from Hospital Ethics Committee and informed consent was taken from each patient. Patients belonging to ASA physical status of class I-II, belonging to either sex, aged in the range of 20 to 60 years, undergoing elective surgery in Nishtar Hospital Multan and requiring tracheal intubation were included in the study. Enrollment was based upon the inclusion criteria. Sample size was calculated from the reference study (9). All the patients were randomly divided into two equal groups, group A and group B with 83 patients in each group. In group A, patients laryngeal mask airway was administered and inflatable cuff was inflated to 60 cm H₂O. Similarly in group B, I-gel was administered. Optimal Jefferson's position was obtained by placing the patients in supine position and putting a 7 cm high pillow under their head. Propofol and O₂/NO₂ mixture was used to maintain the anesthesia. All the data was collected and measured by the researcher himself and data was recorded in the form of a performed performa. Computer software SPSS version 23 was used for statistical analysis of the data thus collected. Mean and standard deviation was calculated for qualitative variables while frequency and percentage was calculated for quantitative variables. Chi square test was applied and P value less than and equal to 0.05 was considered as significant.

RESULTS

Among the 166 patients who took part in this study, 83 were placed randomly in group A and 83 in group B. Group A was administered with laryngeal airway mask classic while group b was administered with i-gel. Gender distribution was as follows; 56.6% males in group A and 55.4% males in group B while 43.4% females in group A and 44.6% females in group B. Mean and standard deviation of age in group A and B was 38.58±1.01 and 38.71±1.13 respectively. Time interval of anesthesia of less than half hour was found in 90.4% of patients in group A while in 88.0% of patients in group B. Similarly duration was 1/2 hour in 9.6% of patients in group A while 12.0% in group B.

Age distribution among the two groups is shown in Table I.

Different procedures for which laryngeal airway mask classic or I-gel was used have been shown in Table II. Mean and standard deviation of insertion time in group A was 34.16±0.74 while it was 30.76±0.71 in group B. Chi square test was applied to compare the insertion time required for the two supraglottic airway devices and significant difference was found between the two groups where I-gel was associated with shorter period required for its insertion (p=0.001).

Table No.I: Age Distribution of Patients

Age (years)	group A	group B
20-29	8(9.6%)	18(22.6%)
30-39	44(53%)	32(38.6%)
40-49	19(22.9%)	19(22.9%)
50-59	12(14.5%)	14(16.9%)
Total	83(100%)	83(100%)

Table No.2:Type of procedure for which airway inserted

Procedure	No. of Patients in Group A	No. of patients in Group B
Burn Dressing	13(15.7%)	6(7.2%)
Cervical Cerclage	2(2.4%)	2(2.4%)
Dilatation and Curettage	12(14.5)	13(15.7%)
Examination under Anesthesia	20(24.1%)	32(38.6%)
Fibro adenoma	4(4.8%)	6(7.2%)
Incision and drainage	18(21.7)	20(24.1%)
Manipulation under anesthesia	8(9.6%)	2(2.4%)
Wound debridement	6(7.2%)	2(2.4%)
Total	83(100%)	83(100%)

Table No.3:Descriptive Statistics

Variables	Group A (Mean±S.D)	Group B (Mean±S.D)
Age	18.58±1.01	38.71±1.13
Height	161.78±1.13	160.81±1.13
Weight	61.06±1.14	60.81±1.13
Insertion time	34.16±0.74	30.76±0.76

DISCUSSION

In the current study comparison between the two commonly used supraglottic devices has been done i.e. laryngeal mask airway classic and I-gel. Comparison is based upon the time required for the insertion of each device in patients in need of airway management under anesthesia. I-gel is a novel airway device which is latex

free and it is disposable without inflatable cuff¹⁰. I-gel has been designed in a way that it creates separate paths for gastrointestinal tract and respiratory tract and carries a port through which gastric tube can be introduced¹¹. Some past studies have shown its efficient use for airway management for difficult intubation and resuscitation¹². Few other studies similar to the current study have been done in which I-gel has been compared to laryngeal mask airway classic¹³⁻¹⁵. Parameters of hemodynamic stability were similar in both groups such as heart rate and blood pressure. No statistically significant difference was reported by Jindal et al¹⁶ which is in accord to the results of our study.

Insertion rate of I-gel has been reported previously in a study conducted by Richez et al (17) was 97%. They also reported that insertion of I-gel was very easy to perform and was successfully administered in all patients in first attempt. In another study performed by Accot et al¹⁸ where efficacy of I-gel was assessed during general anesthesia and the results were almost similar to ours suggesting that only one attempt is required by the I-gel to get introduced in patients under general anesthesia and that duration of insertion was less than ten seconds in all cases. Similar conclusion was made by Gatward et al¹⁹.

In a study by Levitan et al¹⁰ mechanics and positioning of I-gel were studied in cadavers. They concluded that I-gel can be easily administered and can adjust to perilaryngeal anatomy despite the fact that it is devoid of inflatable cuff. Moreover ventilation was properly functioning due to sufficient positioning of the I-gel.

I-gel is superior to laryngeal mask airway in terms of safe use during cardiopulmonary resuscitation. The reason behind this advantage is the non availability of the inflatable cuff. It contains a gastric inlet and separates the gastrointestinal and respiratory tracts and prevents probable complications of gastric inflation, aspiration and regurgitation. In current study the two supraglottic devices were placed within two attempts and only simple manual maneuvers were required for their insertion²⁰. Postoperative complications are the most significant factors to be compared between the two supraglottic airway devices. But in our study the no statistically significant difference between I-gel and laryngeal mask airway classic in terms of postoperative complications. Only nausea and vomiting were the postoperative complications which were relatively higher in patients with laryngeal mask airway classic owing to the gastric insufflation. Previous literature also provides the evidence in favor of the results of this study as no major complications are associated with the use of I-gel. Aspiration is protected in I-gel and laryngeal mask airway almost equally. Sore throat, sore tongue, temporary hoarseness and hyperesthesia of tongue are few minor complications that might occur with the use of supraglottic airway devices¹⁷.

In study conducted by Accot et al¹⁸ no case with the evidence of blood stained airway device (I-gel) after its removal was reported. This result is similar to the results of our study. Moreover they reported that incidence of trauma to airway during the insertion of I-gel was very low. These findings are similar to the findings in our study. On the other hand leak pressure was significantly more among the patients who had undergone the insertion of I-gel as compared to the patients in which laryngeal mask airway was introduced. This depicts the more efficient sealing pressure with use of I-gel because it has the capability to adapt to the anatomy of supraglottic region. In this study gastric tube insertion through gastric outlet in the I-gel was 95% successful and these stats are almost similar to those reported by Richez et al¹⁷ as they reported the success rate to be 100%. By this mechanism I-gel prevents gastric insufflation and helps in decreasing the postoperative complications such as vomiting and nausea.

As far as the risk associated with laryngeal mask airway classic is concerned incomplete mask seal that results in oropharyngeal air leakage or gastric insufflation. In contrast to the findings of our study a previous study reported that I-gel was inferior to laryngeal mask airway in terms of providing better seal of esophagus²¹. On the contrary, Weiler et al²² reported that laryngeal mask airway classic was associated with higher incidence of gastric insufflation.

CONCLUSION

I-gel is superior to laryngeal mask airway classic in terms of average insertion time. However no significant difference was found between the two supraglottic airway devices in regard to any alteration in hemodynamic status or postoperative complications.

Author's Contribution:

Concept & Design of Study:	Muhammad Shahid
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Data Analysis:	Muhammad Omer Ajmal
Revisiting Critically:	Muhammad Shahid, Muzamil Hussain
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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Knowledge Attitude and Practices of Denture Wearer in the Walled City of Lahore

Faiz Rasul¹, M. Rafi Ullah Awan², Muhammad Safdar Baig³ and Hafsa Kaleem⁴

ABSTRACT

Objective: To determine knowledge, attitude and practices of the denture wearer about perception of their teeth loss, any complaints about prosthesis and hygienic practices for their denture among general population.

Study Design: Descriptive / cross-sectional study

Place and Duration of Study: This study was conducted at the Alimeran Shifa Khana, Mochi Gate Walled City Lahore from 15th October 2016 to 15th October 2017.

Materials and Methods: This study comprised of 142 partially or complete edentulous patients. A structured questionnaire was used to collect data after consent.

Results: Majority of the respondents were 47.25% in the age group 41-60 years and 54.9% were male, 52.2% respondents had 8 years or less than 8 years education. Dental caries was the major cause of teeth loss and 79.6% respondents did not ask about the cause of their teeth loss. Majority 80.3% clean their denture daily, and 33.8% put their denture in water at night. Chi square test for demographic variables and the reasons of the tooth loss statistical significant results were found with the age (p 0.001), gender (p 0.000), monthly family income (p 0.000), and with the profession (p 0.000). Similarly statistical significant variables were age (p 0.000), employed history (p 0.018), and dentist guidance to patient to remove denture and putting denture in water at night (p 0.00).

Conclusion: A proper instructions and frequent follow up of Denture wearer is recommended as per principle of prosthodontics.

Key Words: Knowledge; Attitude; Practices; Denture Oral Hygiene; General Population

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INTRODUCTION

Teeth loss increases with increasing age.¹ Dental caries and periodontal problems are the major causes of tooth loss.² Different studies also shows the lack of public awareness about the oral health.³ Particularly living either within the old walled city or from the urban and rural areas of country.⁴ The edentulous individuals are considered physically impaired⁵ as consequences of dental diseases result in poor quality of life. Conventional removable partial denture (RPD) and complete dentures (CD) are most commonly used prosthesis to restore missing teeth and resorbed alveolar ridges. Tooth loss can have problems in mastication, phonetics and esthetics. Missing teeth can be replaced by removable partial dentures (RPDs), teeth-supported

bridges, and implant supported prostheses.⁶ Acrylic RPD are associated with several complaints such as difficulty in insertion and removal, difficulty in speech, mastication, and aesthetic issues.⁷

Most of patients do not satisfy with removable dentures.⁶ One of the factors in success of complete dentures is thorough oral and denture hygiene. These instructions are most important for the denture wearers for the maintenance of the prosthesis and oral health.⁸ Such attitudes of the patient are a potential waste of their financial resource and deteriorate their health further.⁴ Patient's education and compliance both are necessary for the success of the prosthesis. Although there is practice to give instructions to the patient but some of the patients do not carefully follow the instructions.⁹

MATERIALS AND METHODS

This descriptive cross-sectional study was conducted on 142 partially or complete edentulous patients from Mochi Gate Walled City, Lahore Pakistan from 15th October 2016 to 15th October 2017. All those patients who were wearing removable partial or complete denture and data recorded from self-administrated questionnaire, data was analysed using SPSS 21 Cleaning practices and denture removal practices were computed to a single output (dependent) variable.

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RESULTS

Table No.1: Sociodemographic characteristics of denture wearer (n=142)

Demographic characteristics	No.	%
Age		
20-40	43	30.3
41-60	67	47.2
61-80	32	22.5
Gender		
Male	78	54.9
Female	64	45.1
Education		
No	35	24.6
< 8 years	42	29.6
9-10 years	38	26.8
11-12 years	11	7.7
13-14 years	8	5.6
Master or > 16 years education	8	5.6
Financial Status		
< Rs. 15000.	83	58.5
Rs. 15001-50000.	59	41.5
>50000	0	0
Profession		
Labourer	52	36.6
Unemployed	36	25.4
Employed	54	38

Table No.2: Knowledge attitude and practices of denture wearer (n=142)

Question	No.	%
Perceived reasons of tooth/teeth loss?		
Mobility	55	38.7
Khore	87	61.3
Did you ask your dentist about the reasons of your lost tooth/teeth		
Yes	29	20.4
No	113	79.6
Did you ask your dentist about the treatment of your lost tooth/teeth		
Yes	71	50.0
No	71	50.0
Do you think extraction was the only remedy of damage teeth/tooth		
Yes	74	52.1
No	68	47.9
Did your family/friend/colleague guide you to remove tooth whenever you felt pain		
Yes	75	52.8
No	67	47.2
At the time of your tooth extraction did your dentist guide you to replace your teeth/tooth		
Yes	48	33.8
No	94	66.2
Did your Dentist guide you about the different		

types of artificial teeth/tooth		
Yes	95	66.9
No	47	33.1
Do you clean your teeth with water?		
Yes	114	80.3
No	28	19.7
Do you clean your with water, tooth paste and tooth brush		
Yes	74	52.1
No	68	47.9
Do you clean your with water, soap and tooth brush		
Yes	31	21.8
No	111	78.2
With water and cleansing solutions or tablets		
Yes	5	3.5
No	137	96.5
Do you remove your denture at night?		
Yes	118	83.1
No	24	16.9
Do you put your denture in water?		
Yes	48	33.8
No	94	66.2
Did your dentist told you to put your denture in water at night		
Yes	44	30.9
No	90	63.4
Do not remember	8	5.6
Did your Dentist told you to remove your denture at night?		
Yes	44	30.9
No	83	58.5
Do not remember	15	10.6
Do you know 24 hours wearing of denture can damage to your underlying tissues in the mouth?		
Yes	49	34.5
No	93	65.5
Do you think sometimes your denture make you uncomfortable in front of peoples/ in social gatherings?		
Yes	74	52.1
No	68	47.9
Practices of Denture wearer by computing		
No	24	16.9
Yes	118	83.1

Majority of the respondents were 47.25% in the age group 41-60 years and 54.9% were male, 52.2% respondents had 8 years or less than 8 years education. Dental caries was the major cause of teeth loss and 79.6% respondents did not ask about the cause of their teeth loss. Majority 80.3% clean their denture daily, and 33.8% put their denture in water at night. Chi square test for demographic variables and the reasons of the tooth loss statistical significant results were found with the age (p 0.001), gender (p 0.000), monthly family

Table No.3: Complains with the prosthesis among denture wearer (n=142)

Question	No.	%
Complain with your artificial teeth/tooth		
Yes	121	85.2
No	21	14.8
Pain		
Yes	41	28.9
No	101	71.1
Food Impaction		
Yes	74	52.1
No	68	47.9
Halitosis		
Yes	70	49.3
No	72	50.7
Color		
Yes	53	37.3
No	89	62.7
Phonetics problems		
Yes	33	23.2
No	109	76.8
problems in shape, size of your artificial teeth		
Yes	48	33.8
No	94	66.2

Table No.4: Association of tooth loss and sociodemographic factors among denture wearer (n=142)

Education of denture wearer	Reason of tooth loss			Chi-Square test	P-Value
	Periodontal	Dental caries	Total		
Age				15.02	0.001
20-40	8	35	43		
41-60	27	40	67		
61-80	20	12	32		
Gender				27.73	0.00
Male	15	63	78		
Female	40	24	64		
Education				3.310	0.191
Illiterate	20	20	40		
Middle pass	24	42	66		
> Middle pass	12	25	36		
Income				26.954	0.00
<15000	47	36	83		
15001-50000	8	51	59		
Above 50001	0	0	0		
Profession				15.958	0.000
Labourer	16	36	52		
Unemployed	24	12	36		
Employed	15	39	54		

Table No.5: Cross tabulation between denture practices and sociodemographic variables among denture wearer (n=142)

Independent variable	Practice			Chi-Square test	P-Value
	No	Yes	Total		
Age				15.457	0.000
20-40	8	35	43		
41-60	4	63	67		
61-80	12	20	32		
Gender				0.283	0.594
Male	12	66	78		
Female	12	52	64		
Education				2.295	0.193
Illiterate	3	32	35		
Literate	21	86	107		
Income				0.803	0.370
<15000	16	67	83		
15001-50000	8	51	59		
Profession				5.592	0.018
Unemployed	20	68	88		
Employed	4	50	54		
Did your dentist told you to put your denture in water at night				12.592	0.000
No	-	44	44		
Yes	24	74	98		
Did your Dentist told you to remove your denture at night?				12.592	0.000
No	-	44	44		
Yes	24	74	98		
Do you know 24 hours wearing of denture can damage to your underlying tissues in the mouth?				.052	.820
No	12	62	74		
Yes	12	56	68		

income (p 0.000), and with the profession (p 0.000). Similarly statistical significant variables were age (p 0.000), employed history (p 0.018), and dentist guidance to patient to remove denture and putting denture in water at night (p 0.00).

DISCUSSION

Teeth loss is a public health issue, knowledge about its causation, prevention and available treatment option depends upon health seeking behaviour, regular visit to dentist and socioeconomic status of the individual.¹⁰ In the current study, major cause of tooth loss was dental caries 61.3%, and periodontal disease 38.7% whereas Hugo et al¹¹ and Takala et al¹² also reported them major determinant of teeth loss. Almost 52.8% said that family members and colleagues suggested them for extraction. Agerberg and Carisser reported that major reason of the teeth loss was health seeking behaviour.^{13, 14}

Result of another study shows that 90% denture wearer immersed their dentures in water. Around 55% said that they did not get instruction for the cleaning of denture. About 46% cleaned their denture more than two times per day, whereas 39% were found to clean twice a day and only 15% once a day. Regarding the method of cleaning denture the most common method was found to be with water 45%, with brush and water 40%, water and salt 9%, brush and paste 5%, and finally, brush and solution 1%. More than half of the patients 51% used denture cleansers; however in the current study only 3.5% cleans with denture cleansers.¹⁵

In another study, 52.8% responded cleaned oral tissue daily, 10.2% reported lack of knowledge about cleaning method and 13.2% did not remove denture at night. There was a significant gender based difference for denture cleaning method.¹⁶ Memon et al¹⁷ in Hyderabad Pakistan revealed that 62% patients received instruction from dentist about the cleaning of dentures. Most of the patients 58% were using water and tooth brush for denture cleaning as compared to this study 52.1% clean with tooth paste and brush, only 21.8% respondents clean with soap and brush. But only 10% patients were using other substances like hypochlorite and commercially available cleansing tablets whereas in this study only 3.5%. In that study 62% patients were soaking their dentures in water while in the present study only 33.8% put the denture in water remaining people said they did not told to put denture in the water. In their findings 48% denture wearer were used to wear denture at night while in our study 83.1% were used to remove denture at night. However instructions given by the dentist regarding the removal of denture and putting it in the water at night were statistically significant, p value 0.001 and 0.000 in Memon's and our study respectively.

Ahmad et al¹⁸ conducted a study in Nishter Institute of Dentistry Multan on 85 denture wearers and reported that significant association for education level (P value 0.001) and type of denture (P value 0.014). However in this study statistical significant variables were age (p 0.000), employed history (p 0.018), and dentist guidance to patient to remove denture and keeping their denture in water at night (p 0.000) when chi square test was applied between practices of denture cleanliness, removal of denture at night and sociodemographic variables. In Ahmad's study it was found that 16.5% patients did not remove their dentures before sleeping, only 14 % RPD wearer did not soak their denture at night and only 10.6% patients soaked their dentures in denture cleansing tablets/solution as a method of denture hygiene maintenance.²⁴

Azad et al¹⁹ reported that 65% participants used to clean their dentures almost once a day, majority of the patients maintained denture hygiene with water only 50% whereas many subjects cleaned it with a combination of soap and toothbrush with water 22% followed by water and cleansing tablets 8%; on the other hand in this study 80.3% respondents cleaned their teeth daily, 52.1 % cleaned with tooth paste and

brush, only 21.8% respondents cleaned with soap & brush. Only 3.5% cleaned with the cleaning solution. Shingli et al²⁰ reported 94.7% patients were used to clean their dentures with a tooth brush, 5.3% used denture brush and 3.6% used denture cleansers, however these results are different from the finding of our study.

The most common method of denture cleaning was using water and brush 61.1% in Kosuru's²¹, 58.3% in Patel et al²² and in this study 52.1%; which is more when compared with studies reported by, Dikbas²³ 3.84%, Peracini et al²⁴ 3.7%, Azadet al¹⁹ 22%, Polyzois²⁵ 10.3%, Saha et al²⁶ 47% and Apratimet al²⁷ 31.3%. Cakan et al²⁸ reported that according to the 49% dentist did not inform them about the maintenance of the denture however in the current study 58.45% patient reported similar findings. In Cakan et al²⁸ and current study brushing was the most frequent cleaning method 57.6% and 52.1% respectively. In Cakan et al²⁸ study almost 53.1% patients did not remove their dentures at night which is very high to the finding of the present study 16.9%. Aljabri et al²⁹ and Akeel³⁰ reported aesthetic as a most common problem with the RPD followed by pain, however in our study most common problem with RPD was food deposition, followed by halitosis, aesthetic, discomfort and speaking.

CONCLUSION

The dentist's professional responsibility regarding patient counselling was not satisfactory and most of the respondents had some problems with their prosthesis such as food impaction and debris under denture, alteration of its colour, difficulty in daily wear, halitosis and perceived speaking problems. Awareness among denture wearers regarding denture hygienic practices and its proper care, and other instructions regarding oral health tissue and follow-up required toward for maximum advantages of the prosthesis and its success.

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Frequency and Awareness of Cognitive Impairment in Stroke Patients of Karachi

Irfan Ashraf¹, Tafazzul H Zaidi² and Kiran Mehtab²

ABSTRACT

Objective: To assess the frequency of cognitive impairment in stroke patients. To assess the awareness of cognitive impairment in different type of stroke patients.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Department of Community Medicine, SMC, JSMU Karachi from March to August 2018.

Materials and Methods: A Cross-sectional study was conducted over the conscious diagnosed patients of stroke above 12 years of age on a sample of 100 individuals. The sample was taken through non-probability purposive sampling from the patients who visited or admitted to Jinnah Post-graduate Medical Centre, Karachi. A structured questionnaire was then developed. Pilot study was conducted to assess the authenticity of the questionnaire. Data was collected through structured questionnaire. An informed verbal consent was taken from the patients. The data was then entered and analyzed using SPSS version 20, with 95% confidence interval and 0.05 p-values were taken as statistically significant.

Results: A total of 100 patients of stroke took part in the study, out of which 70% were males and 30% were females. In Females 60.0% had unsatisfied cognition, (54%) of the patients fall in the age group of 40 to 64 Years out of which 55.6% had unsatisfied cognition, the patients who fall in the age group between 13 to 39 had satisfactory cognition indicating significant difference in the level of cognition among different age groups. In Diabetic patients 58.5% had unsatisfied cognition, patients who had multiple attacks of stroke, 55.8% had unsatisfied cognition, Patients who had stroke attack with symptom duration less than 24 Hours (TIA) 50% had unsatisfied cognition, In patients who had stroke attack with symptom duration more than 24 Hours, 50% had unsatisfied cognition. In Hypertensive and non-hypertensive patients, both had 50% unsatisfied cognition.

Conclusion: The study concluded that more than half of the patients of stroke have unsatisfied cognition (i.e., cognitively impaired). There is a need to create awareness among public about stroke and its outcomes.

Key Words: Stroke, Cognition, Impairment, Frequency, Awareness

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INTRODUCTION

Stroke, or cerebrovascular accident (CVA), which is also defined as the dysfunction of brain due to a disturbance of the cerebral blood flow, is the second most common cause of death and adult disability around the world¹. This is further classified as Ischemic Stroke, that results due to a block of blood vessel supplying any particular area², or Hemorrhagic Stroke which is due to rupture of a weakened blood vessel³. Stroke manifesting within first 24 hours is termed as Transient Ischemic Attack (TIA)⁴. These together are termed as Cerebro-Vascular Accidents (CVA).⁵

Stroke is a common, serious, and disabling global health-care problem, and rehabilitation is a major part of patient care. There are 15 million people worldwide suffering from stroke every year, about 30% of which experience residual disabilities.⁶ There is evidence to support rehabilitation in well-coordinated multidisciplinary stroke units or through provision of early supported provision of discharge teams.⁷ The risk factors for stroke can be divided into three major classes: non-modifiable (e.g. age, sex, genetic factors, etc.); modifiable (e.g. hypertension, diabetes, hyperlipidemia, atrial fibrillation, smoking, obesity, etc.); and potentially modifiable (e.g. alcohol abuse, infection)⁸. There are many complications of stroke including recurrent stroke, epileptic seizures, infections, DVT, mobility related falls, depression etc.⁹, but one of the most common and increasing known complication is cognitive impairment. The term 'Cognitive Impairment' means, 'a state of mind where a person has trouble remembering, learning new things, concentrating, or making decisions that affect their everyday life'¹⁰. Cognitive impairment may decrease an individual's quality of life, increase resource utilization,

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and result in suboptimal medical care because of difficulty following caregiver recommendations¹¹. The risk of the cognitive impairment after stroke is associated with the overlap of the frequent cerebrovascular disease and the dementia. According to the demography, the age and the education level are related to the post-stroke cognitive impairment risk. The age is the risk factor of not only the stroke but also the cognitive decline. There's evidence suggesting that the prevalence of the cognitive decline after stroke would increase exponentially as age increases after 65 years old. Patients with cognitive impairment are subjected to lower quality of life followed by a stage of dependence and worse survival¹². Patients get attendant-dependent and are not able to conduct most of their daily routines. Different areas of brain affected, leads to different fields of impairment in cognition. Communication in all its forms is often altered after a stroke, but the location of the stroke makes a difference as to what will be affected. In addition to communication problems like aphasia, a condition affecting the ability either to understand or process language, communication deficits may include decreased attention, distractibility and the inability to inhibit inappropriate behavior. Problem-solving ability is sometimes affected, usually more in survivors of right-brain strokes¹³. Post-stroke cognitive impairment occurs frequently in the patients with stroke. The prevalence of post-stroke cognitive impairment ranges from 20% to 80%, which varies for the difference between the countries, the races, and the diagnostic criteria. The risk of post-stroke cognitive impairment is related to both the demographic factors like age, education and occupation and vascular factors. The underlying mechanisms of post-stroke cognitive impairment are not known in detail. However, the neuroanatomical lesions caused by the stroke on strategic areas such as the hippocampus and the white matter lesions (WMLs), the cerebral micro bleeds (CMBs) due to the small cerebrovascular diseases and the mixed AD with stroke, alone or in combination, contribute to the pathogenesis of post-stroke cognitive impairment¹⁴.

MATERIALS AND METHODS

It was a cross-sectional study conducted at Jinnah Postgraduate Medical Centre Karachi from March to August 2018.

Sample Selection:

- Inclusion Criteria: Stroke Patients
- Exclusion Criteria: Patients less than 12 years of age

Unconscious patients of any age.

The sample size of 100 Patients was drawn through non-probability purposive sampling method from Jinnah Sindh Medical College. A structured questionnaire was developed. Data was collected on

structured questionnaire. Pilot study was done to check the authenticity of questionnaire. Data was entered and analyzed on statistical package for social sciences (SPSS version 20) with 95% confidence interval and 5% margin of error. P-value less than 0.005 was considered statistically significant.

Ethical Consideration: An informed verbal consent was taken from the patients.

RESULTS

A total of 100 diagnosed patients of stroke took part in study, out of which, 70% were males and 30% were females, 9% were in b/w 12 to 39 year age group, 54% were b/w 40 to 64 year old age group and 37% were above 65 Years of age, 54% of the patients fell in the age group of 40 to 64 Years out of which 55.6% had unsatisfied cognition. In females 60.0% had unsatisfied cognition.

Cognition in Different Age Group Patients

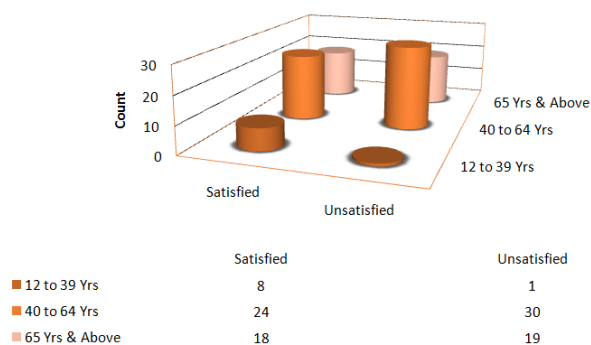


Figure No. 1: Frequency of cognition of stroke in different age groups

Cognition in Patients with Single & Multiple Attacks of Stroke

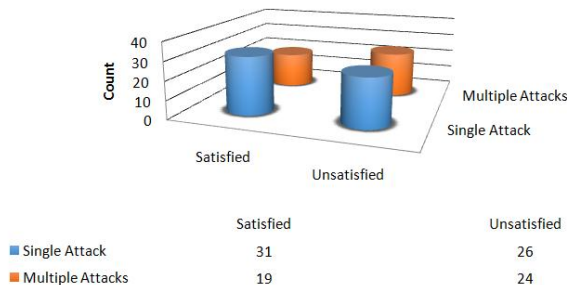


Figure No.2: Frequency of cognition with Number of Attacks

Patients who had stroke attack within 1 month, 44.8% had unsatisfied cognition while in those patients who had stroke attack before last 1 month, 57.1% had unsatisfied cognition. Patients who had single attack of stroke, 54.4% had satisfied cognition and 45.6% had unsatisfied cognition, patients who had multiple attacks of stroke, 55.8% had unsatisfied cognition. Patients who had stroke attack with symptom duration less than 24 Hours (TIA), 50% had unsatisfied cognition while in patients who had stroke attack with symptom duration

more than 24 Hours, 50% had unsatisfied cognition. In Diabetic patients, 58.5% had unsatisfied cognition, in non-diabetic patients, 44.1% had unsatisfied cognition. In Hypertensive patients, 50% had unsatisfied cognition while in non-hypertensive patients, 50% had unsatisfied cognition.

Cognition in Patients with TIA & Stroke (with symptom persistence for > 24 Hrs)

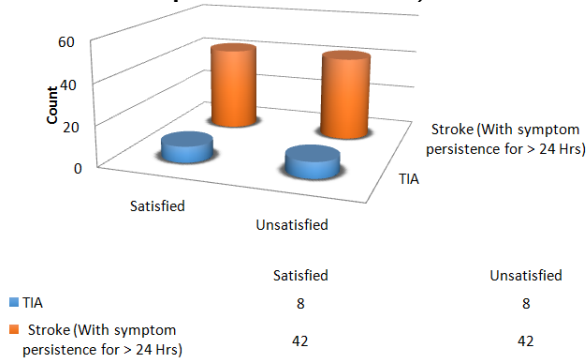


Figure No.3: Frequency of cognition with the symptoms after stroke attack?"

Cognition in Diabetic & Non-diabetic Patients

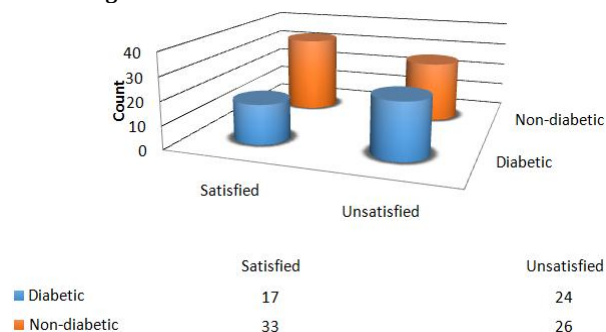


Figure No.4: Frequency of cognition of Stroke in Diabetic and Non- Diabetic patients

Cognition in Hypertensive & Non-hypertensive Patients

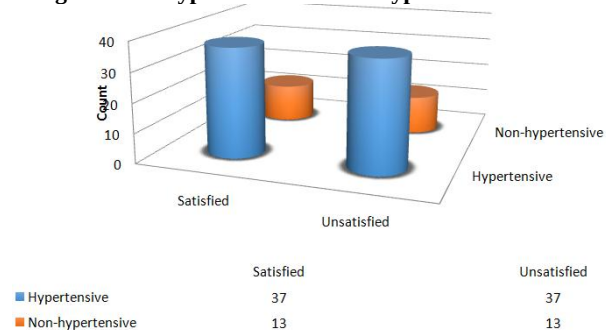


Figure No.5: Frequency of cognition of stroke with HTN Hypertension/ Non-Hypertension

DISCUSSION

Stroke is the second most common cause of cognitive impairment and dementia. The accumulation of lacunar infarcts, ischemic white matter disease and cerebral hypo-perfusion are the most common causes of cognitive impairment/dementia due to stroke that can

go unrecognized for up to 30 years, by which time there is substantial impairment.¹⁵ cardiovascular risk factors were generally more prevalent in men. Lifestyle cardiovascular risk factors were more common in the young. Prevalence of hypertension, diabetes mellitus, coronary heart disease, and, in men, also atrial fibrillation go down after the age of 70 to 80 years.¹⁶ In this study 54% of the patients fell in the age group of 40 to 64 Years out of which 44.4% had satisfied cognition while 55.6% had unsatisfied cognition and there was significant difference in the level of cognition among different age groups

Evidence reviewed here suggests that gender influences various aspects of the clinical spectrum of ischemic stroke, in terms of influencing how a patients present with ischemic stroke through to how they respond to treatment¹⁷. A total of 100 diagnosed patients of stroke were approached out of which, 70% were males and 30% were females

A stroke can produce symptoms which include altered smell, taste, hearing, or vision (total or partial), drooping of eyelid, weakness of muscles, decreased reflexes; gag, swallow, pupil reactivity to light, decreased sensation and muscle weakness of the face, balance problems and nystagmus, altered breathing and heart rate, weakness in sternocleidomastoid muscle with inability to turn head to one side, weakness in tongue (inability to stick out the tongue and/or move it from side to side), aphasia, difficulty with verbal expression, auditory comprehension, reading and/ or writing, dysarthria, altered voluntary movements, visual field defect, memory deficits, disorganized thinking, confusion, altered walking gait, altered movement coordination vertigo and or disequilibrium.¹⁸

Stroke is the second most common cause of cognitive impairment and dementia. The accumulation of lacunar infarcts, ischemic white matter disease and cerebral hypo perfusion are the most common causes of cognitive impairment/dementia due to stroke that can go unrecognized for up to 30 years, by which time there is substantial impairment. These types of stroke predominantly affect the connections between areas of cortex that associate complex types of information, the disruption of which leads to impaired cognition and function. Larger strokes are usually detected clinically and cognitive impairment is thus more likely to be detected early on. Detecting stroke early allows initiation of the appropriate treatment that can prevent or substantially delay the onset and progression of cognitive impairment/dementia.¹⁹

According To Our Study 50% of the patients had satisfied cognition while the rest 50% had unsatisfied cognition

The most common types of cognitive deficits arising from stroke are disturbances of attention, language syntax, delayed recall and executive dysfunction affecting the ability to analyze, interpret, plan, organize, and execute complex information.²⁰ Thus, an increased risk for incident stroke is associated with cognitive decline and dementia.²¹

Pakistani stroke survivors have poor outcomes in the community, mostly from preventable complications. Despite advanced disability, the principal caretakers were family rarely supported by health care personnel, highlighting the need to develop robust home care support for caregivers in these challenging resource poor settings.²²

The risk of vascular cognitive impairment and dementia as well as the rate of cognitive decline in cerebrovascular disease is highly dependent upon the control of the underlying risk factors for stroke. If left untreated, vascular cognitive impairment and dementia do decline.

CONCLUSION

The study concluded that more than half of the patients of stroke have unsatisfied cognition (i.e., cognitively impaired). There is a need to create awareness among public about stroke and its outcomes.

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Diagnosis of Active Tuberculosis with Immunochromatographic TB Test in Suspected Tuberculosis Patients

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ABSTRACT

Objective: To detect active disease in suspected cases of pulmonary and extrapulmonary TB patients we employed immunochromatographic IgG/IgM antibodies using recombinant antigen kDa 6, kDa16 and kDa 38, which has higher sensitivity and specificity.

Study Design: Prospective cohort study

Place and Duration of Study: This study was conducted at the Department of Medicine in collaboration with Radiology and Pathology Departments of Pak Red Crescent Medical and Dental College Teaching Hospital Dina Nath from March 2016 to March 2018.

Materials and Methods: A sample of Fifty four suspected TB patients with the same number of control patients were included in this study. The patients were divided in different groups as (1) 45 patients with clinical features of suspected pulmonary tuberculosis, meeting WHO criteria, (24 new and 18 old) and 3 cases of pleural tuberculosis, along with chest X-ray (CXR) had findings with suspicion of tuberculosis. (2) Nine patients with diagnosis of suspected TB lymphadenitis. (3) Forty five non-suspected TB patients with asthma, chronic obstructive pulmonary disease (COPD) and others with minor respiratory tract complaints, without constitutional symptoms but mimicking tuberculosis and having no evidence of TB findings on chest films were taken as controls. Similarly 9 controls with lymph nodes enlargement but without any suspicion of tuberculosis were taken as controls. The chest X-rays were taken in Radiology department and the laboratory investigations and ICT-TB test were performed in the pathology department of hospital.

Results: Sensitivity in newly symptomatic patients of pulmonary and extrapulmonary disease with rapid TB tests was 66% while in old healed TB cases was 16% with 100% specificity and high positive predictive values. Our focus was on finding and results in suspected cases of tuberculosis with the help of clinical features, chest x-ray findings, and confirming these with ICT-TB test.

Conclusion: Rapid TB test is helpful in early and rapid diagnosis of tuberculosis in suspected patients.

Key Words: Pulmonary and extra pulmonary tuberculosis, IgG, IgM, Chest X-ray, Recombinant antigen

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INTRODUCTION

Tuberculosis is prevalent in one third of the population of world and occurs in poor socioeconomic conditions and in immune compromised patients.^{1,2} It is active only in ten percent of cases.¹ In Pakistan active tuberculosis is prevalent in nearly 518000 patients as per WHO reports.³ TB is totally curable disease but still a major killer in infectious diseases.⁴ In pulmonary TB the disease spreads by coughing and sneezing. It usually is diagnosed by conventional methods of sputum smear positivity test which has poor specificity

and prolonged culture results although with high sensitivity.^{5,6} Chest X-rays findings in newly diagnosed cases are usually nonspecific.^{7,8}

Non availability of sputum sample is another problem in extra pulmonary TB which is prevalent in upto 15-20 percent of tuberculosis cases in Pakistan and rest of the world^{9,10} with major presentation with lymphadenopathy followed by pleural effusion and other extra pulmonary foci.^{11,12}

The immune mediated tests such as mantoux test, gamma interferon tests as quantiferon-TB gold, spot TB tests with variable sensitivities but cannot differentiate between active and latent tuberculosis.¹³⁻¹⁵ So serodiagnostic tests against specific antigens have variable sensitivities but good specificities in detection of active tuberculosis.¹⁶⁻¹⁹ Rapid ICT test for detection of serum immunoglobulin's IgG/IgM raised against 38kDa 16kDa, 6kDa antigens showed good results for rapid diagnosis of active tuberculosis, with smear positivity in national and international studies with 100 percent specificity and good sensitivity.^{20,21} In the

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present study we tried to detect active TB by ICT tuberculosis test with upto 100 percent specificity in the patients suspected to be suffering from TB with positive clinical feature of this disease and/or relevant X-ray findings in pulmonary and extrapulmonary cases.

MATERIALS AND METHODS

A prospective study with the approval of the ethical committee of the college was conducted. The patients enrolled in the study were adults 54 in number males & females from the nearby population who visited hospital in last 2 years from March 2016 to March 2018 with or without previous history of tuberculosis who meet the criteria as following.

For tuberculosis suspected patients; These forty five patients (24 fresh, 18 with previous h/o TB and three with pleural effusion in whom Tuberculosis was suspected) with either history of cough, fever & weight loss for more than 2 weeks or cough with less than 2 weeks of uncertain origin plus either bloodstained sputum, fever at night and/or weight loss in fresh or old and treated TB patients.⁵ The patients CXR were taken & only those with radiological findings of infiltration, cavitation or consolidation in 24 fresh cases and /or with findings suggestive of old tuberculosis in 18 cases that is opacities, fibrosis and mediastinal shift were included in study for pulmonary TB^{7,8}, and 3 patients with suspicion of TB with chest X-ray findings of pleural effusion. (3) The nine patients with cervical, mediastinal lymphadenopathy with symptoms of fever, loss of weight and anorexia. The cervical lymphadenitis cases have either matted or in discharging stage.

For Control patients: Forty five patients with minor respiratory problems or asthma and chronic obstructive pulmonary disease without any constitutional symptoms of tuberculosis and with normal chest X-ray were taken as controls in pulmonary cases, 2 for controls in lymphadenitis cases. The patients were selected with isolated cervical lymphadenopathy of short duration and without any constitutional symptoms of tuberculosis.

Laboratory investigations for TB IgG/IgM immune chromatographic test is based on detection of IgG and IgM raised against one or more of the three 16kDa, 6kDa, 16kDa recombinant antigens. The device has letters C (control line) M (TB IgM) test line and G (TB IgG) line. The device used is manufactured by Healgen Scientific LLC:USA. It is used in the following steps.

(1) Take fresh serum /plasma from blood as soon as possible. Stored serum may be used if kept in refrigerator at 2-8°C but should be brought at room temperature at the time of use. (2) Briefly 10 microliter of serum was added to square sample well and then 4 drops assay diluents provided in the kit was added. Interpretation of test took 15 minutes; ICT does not require special skill and equipment and (3) the results can be interpreted according to change of color of band G or M. C band must however be positive, otherwise results are wrong.

Principle underlying the ICT TB kit: The test uses a nitrocellulose membrane strip containing two lateral bands (IgG & IgM) Bands and a control band C. The M band is pre-coated with anti-human IgM antibody. The G band is pre-coated with anti-human IgG antibody and the C band is pre-coated with anti-goat antibody. The burgundy colored conjugate pad contains colloidal gold conjugated to recombinant TB specific antigens kDa38, kDa6, kDa 16. When a specimen followed by assay buffer is added to sample well IgM &/or IgG antibodies if present will bind to TB conjugates making antigen antibodies complex which will traverse through nitrocellulose membrane by capillary action. When the complex meets the corresponding immobilized antibodies (anti human IgM and /or anti human IgG) the complex is trapped forming burgundy coloured band which confirm a reactive last result and vice versa. The test contains an internal control (c band) which should exhibit a burgundy colored band of the anti-goat antibody; otherwise the test result is invalid. The data was entered and analyzed by SPSS-20.

RESULTS

Fifty four (male and female) patients in different categories as fresh pulmonary 24 in number (13 males and 11 females) lymphadenopathy cases 9 in number (2 males and 7 females), three pleural effusion (2 males and 1 female) 18 old cases (10 males and 8 females) with suspicious of relapse in age ranges shown against each group (Table 1).

Total pulmonary (fresh and extra pulmonary 24 and old 3/18) 27 positive TB cases were found. Out of these only 4 were found IgM positive (3/36 fresh positive TB cases and extra-pulmonary) and 1/18 (previously treated pulmonary tuberculosis patients), accounting for 14% total IgM positive patients). 21/36 (58 %) patients in

Table No.1: Demographic data of selected patients

Variable	No.	Male/Female	Mean age (Male/Female)	Age range (Male/Female)
Fresh cases of Pulmonary tuberculosis	24	13/11	44/35	18-60/14-100
Lymphadenopathy	09	02/07	22/21	20-30/05-33
Tuberculosis with pleural effusion	03	02/01	30/28	30/25-28
Old TB with relapse (symptomatic)	18	10/08	42/38	18-75/8-90
Total	54	27/27	36/29	18-75/8-90

Table No.2: Number of positive cases for IgM/IgG antibodies in rapid TB ICT in suspected cases

Type	Total suspected cases	Positive TB cases	TB IgM +	TB IgG +
New positive cases of respiratory tract infection + extra pulmonary tuberculosis	36	24	3 (08%)	21 (58%)
Pulmonary tuberculosis	24	13	-	13 (54%)
Extrapulmonary tuberculosis (lymph node and pleural)	12	11	3 (08%)	8 (66%)
Previously treated TB cases with symptoms	18	3	1 (5.5%)	2 (11%)

Table No.3: Total number of rapid IgM/IgG antibodies test for TB recombinant antigen positive cases with percentages sensitivity specificity positive predictive negative predictive values and confidence interval

Type	Total IgM & IgG	Sensitivity (C.I) 95%	Specificity	PPV	NPV
New cases of pulmonary tuberculosis 36	24	66% (0.56-0.77)	100%	100%	75%
Pulmonary tuberculosis 24	13	56%	100%	100%	67%
Extrapulmonary tuberculosis	11	84%	100%	100%	88%
Old cases with relapse 18	3	16% (0.1-0.17) 100%	100%	100%	54%
Total cases 54	27	50%	100%	100%	50%

fresh cases whereas 2/18 (11%) previously treated tuberculosis cases were found to be IgG positive (Table 2). Total new cases with IgM & IgG collectively show 66% sensitivity with 95% confidence interval of 0.56 to 0.77 as compared to those with previous H/O treated TB cases of 16% with confidence interval of 0.1-0.17 (Table 3).

DISCUSSION

The various tuberculosis bacilli components, consisting lipid, protein antigens have been employed in different serodignostic tests for active TB detection with different results.¹⁶⁻¹⁹ The non-specific Manteaux tests and Interferon gamma releasing assay tests cannot differentiate the active from inactive diseases.⁹⁻¹¹ The different serodiagnostic tests with various purified protein antigens alone as kDa 38 antigens¹⁶ or Lipoarabinomannan (LAM) antigens a lipid antigen¹⁴, or in combination as pathozyme myc (LAM +38kDa) with 21-46% sensitivity and pathozyme complex TB (38 kDa+16kDa) with sensitivity of 51% were employed in various studies with a specificity of 94-100%.¹³⁻¹⁵ However in a study by Selma et al²¹ reported that IgG/IgM mediated antibody responses against mycobacterial 38kDa, 16kDa, 6kDa6 in active tuberculosis with positive sputum smear in pulmonary and extrapulmonary tuberculosis IgG and IgM were 68.4% and 2.3% respectively.¹⁹ Similiarly in a study for detection of TB by Khan et.al²⁰ in Pakistan, performed on 129 cases antibody was found positive in 23/52 sputum positive 11/36 in sputum negatives 10/30 of pleural effusion and 6/16 of TB lymphadenitis case. Specificity was 100%.

The results of our present study shows the positive results with rapid IgG/IgM antibody test for TB recombinant antigens 38kDa, 16kDa, 6kDa in fresh tuberculosis suspected cases as 66% and upto 16% in healed old tuberculosis cases. So the sensitivity of these results showed 66% and 4% in fresh and old healed case respectively. As the specificity of this test is found as 100% in our study as is claimed in other studies in sputum smear positive cases.^{20,21} So our study in suspected cases of tuberculosis in detection of active tuberculosis is very encouraging as we may find the results in a large number of cases without indulging in smear positivity and long awaiting culture positive results. In our study IgM response is very poor i.e. 16% as compared to IgG response which is 66%. As it is known IgM is positive in early stages of disease, while IgG response comes later. The discrepancy found in our study may be due to quackery and deficiency of qualified doctors, so by the time the patient contacts a qualified doctor, it is already very late and we get poor IgM positivity in our cases. Another finding in our study is that the patients selected with the suspicion of relapse in old treated cases showed positivity in a very few cases (16%) which may be due to the fact that these patients have developed complications such as bronchiectasis, pulmonary abscess, and repeated nonspecific respiratory tract infections, because of previous tuberculosis, So most of the time it is difficult to diagnose tuberculosis with relapse cases clinically. However in positive cases we may declare that the patient is in relapse.

Also there are other lipid antigens such as cord factor TDM (trehalose 6, 6 dimycolate) a major part of mycobacterial cell wall is the most immunogenic

glycolipid in ELISA reported to have a sensitivity 81% and specificity of 96%²² and maybe employed in our population for early detection of tuberculosis.

CONCLUSION

The rapid test for IgM/IgG antibodies against recombinant antigen kDa38, kDa16 and kDa6 is very helpful in detection of suspected tuberculosis cases which has higher sensitivity and nearly 100% specificity. This may be used as primary test for detection of active disease. Also in sputum smear negative cases the test may be helpful in detection of disease earlier, as conventional culture test may take 4-6 weeks for results. Because of poor sensitivities of the test the patients with negative ICT TB test has limitations in suspected cases and they must be further evaluated with culture and sensitivity tests.

Author's Contribution:

Concept & Design of Study: Arif Gulzar
 Drafting: Nasir Mahmood
 Data Analysis: Fizza Muazzam
 Revisiting Critically: Arif Gulzar, Nasir Mahmood
 Final Approval of version: Arif Gulzar

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Frequency of Birth Defects in Newborns Admitted in Neonatal Unit of Pediatric Department in Tertiary Care Hospital Nawabshah, Pakistan

Ali Akbar Siyal, Naseer Ahmed Memon and Juverya Shah

ABSTRACT

Objective: To determine the frequency of birth defects in newborns presented in Neonatal unit of tertiary hospital Nawabshah.

Study Design: Observational / analytical study

Place and Duration of Study: This study was conducted at the Department of Pediatric Medicine, Peoples University of Medical & Health Sciences, Nawabshah from January 2015 to December 2017.

Materials and Methods: Total of 10388 neonates were received in neonatal unit pediatric ward of tertiary care hospital Nawabshah during study period. Files of all newborns were filtered to look for recorded birth defects. Physical defects detected by naked eye were registered; CNS, GIT and Cardiac defects were confirmed by Ultrasound and Echocardiography respectively.

Results: Out of 10388 neonates who were admitted in neonatal unit of our hospital, 519 patients were found to have birth defects (5.09%), of these babies 260 (50.09%) were males, 239 (46.05%) were females and 20 (3.85%) presented with ambiguous genitalia. Most common defects seen in our study were from CNS (17.2%), next common defect was congenital heart disease detected in (13.5%), syndromic babies like Down syndrome, Turner syndrome, Noonan syndrome and Treacher –Collin syndrome and other syndromes. Skeletal defects were talipes deformity, polydactyly, cleft lip/palate, trachea-esophageal fistula, congenital diaphragmatic hernia and miscellaneous.

Conclusion: Birth defects are quite common in our community and impose a greater burden on health care system. The most common system involved is CNS. There is an increased need for preventive measures to be implemented in pregnant women.

Key Words: Birth defects, Congenital, Spina bifida, CNS

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INTRODUCTION

A birth defect is any deformity or deviation from the normal structure/function that is present since birth; it can be a physical deformity, something that we can see in a baby with naked eyes, or other birth defects like biochemical or metabolic that may need specific tests to be detected as all of these may not be apparent at birth. Congenital birth defects may be minor or major. Minor defect is defined as structural anomaly present at birth which has slight effect on clinical function, but may have a cosmetic effect e.g. pre-auricular tag. Major malformation has a noteworthy effect on function or on

social acceptability e.g. ventricular septal defect (VSD) and cleft lip 1. Whatever the type of birth defect is there, it's sure a very stressful situation for family as in most cases parents have been expecting a normal newborn. In 2015 World Health Organization stated that around 303000 newborns die within 4 weeks of birth every year, worldwide, due to congenital anomalies². The problem with congenital anomalies/birth defects is that these are lifelong disabilities, and have a lifelong impact on baby as well as his/her family. The risk factors or causative agents have been studied extensively and are so many, but in about half of the cases no associated causative risk factors are identified². Genetic susceptibility or interfamily marriages also play a significant role in birth anomalies^{2, 3}. Incidence and prevalence of birth defects varies from population to population as well as different ethnic background has variable prevalence of birth defects⁴. In our country 6-9% of perinatal deaths are attributable to birth defects⁵. Globally the range for some birth defects like cleft lip/palate is different in different low socioeconomic regions its 82/1000 live births and in high income regions its 39.7/1000 live

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births⁶. The trend has been increasing regarding the prevalence of birth defects as new threats such as Zika virus is emerging^{7,8}. In China a surveillance system has been created to detect/identify birth defects, no such surveillance system are working in our country but there is a high need of doing that⁹. This study is conducted in hope to look at the frequency and recognize the most common varieties of birth defects in study population so that the health authorities can design the preventive strategies accordingly.

MATERIALS AND METHODS

This study was done from the period of January 2015 to December 2017, a total of 10388 neonates were admitted in neonatal unit pediatric ward of tertiary care hospital Nawabshah during study period. Files of all newborns were filtered to look for recorded birth defects. Physical defects detected by naked eye were

registered; CNS, GIT and Cardiac defects were confirmed by Ultrasound and Echocardiography respectively in the files and were taken as such.

RESULTS

Out of 10388 neonates who were admitted in neonatal unit of our hospital, 519 patients were found to have birth defects (5.09%), of these babies 260 (50.09%) were males, 239 (46.05%) were females and 20 (3.85%) presented with ambiguous genitalia (Figure 1). Most common defects seen in our study were from CNS (19.8%), next common defect was congenital heart disease detected in (18.5%), Skeletal defects like talipes deformity, polydactyly and developmental dysplasia of hip (DDH) were seen in 16.6%, syndromic presentation like Down syndrome, Turner syndrome,

Table No.1: Distribution of birth defects system wise (n=519)

S.No	System	Malformation Type	Frequency	Percentage
1	Central Nervous System	Meningomyelocele with/without hydrocephalus Microcephaly Encephalocoele Anencephaly	109 65 17 22 05	21%
2	Cardiovascular system	Acyanotic Cyanotic Complex	94 58 32 4	18.5%
3	Skeletal system	Talipes deformity Polydactyly DDH Arthrogryposis multiplex	84 44 28 08 04	16.6%
4	Syndromic babies	Down syndrome, Edward/Patau syndrome Turner syndrome/ Noonan syndrome Treacher–Collin syndrome Pierre- Robin syndrome Prune belly syndrome	68 42 11 09 03 02 01	13.2%
5	Gastrointestinal	Cleft lip/palate, Trachea-esophageal fistula, Exomphalos Imperforate anus	52 30 05 07 10	10.5%
6	Respiratory system	Choanal atresia unilateral/bilateral congenital diaphragmatic hernia Congenital sequestrations	47 17 16 14	9.0%
7	Urogenital system	Ambiguous Genitalia Bladder exstrophy	25 20 05	4.8%
8	Miscellaneous	Multi-system involvement	40	7.7%

Noonan syndrome and Teacher–Collin syndrome and other syndromes were present in (13.2%), gastrointestinal defects like cleft lip/palate, trachea-esophageal fistula, exomphalos and intestinal atresia were present in 10.5%, respiratory problems like Choanal atresia and congenital diaphragmatic hernia were seen in 9.0% and other miscellaneous defects like a combination of multiple defects were seen in 12.4% of neonates.

■ Total admissions in NICU ■ Neonates with Birth Defects

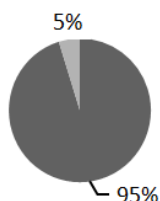


Figure No.1: Frequency of birth defects

■ Males ■ Females ■ Indeterminate

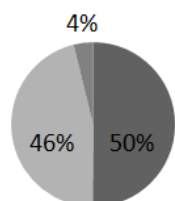


Figure No.2: Gender distribution

DISCUSSION

The frequency of birth defects in our study was 5.09%. The actual occurrence of birth defects depends on multiple factors and we know that not all newborns that have birth defects are presented to hospitals so obviously the prevalence varies among various studies even in same population and setting. The global prevalence of birth defects is 3-7% but fluctuates from country to country¹⁰. Even few studies from Pakistan show a higher prevalence than our study^{11,12,13}. Our study's frequency was comparable with a hospital based study done in Ayub Medical College and Hospital (4.23%)¹⁴. When we compare our prevalence rate to some international studies, our rate is somewhat higher compared with Prevalence from Nigeria¹⁵ which has been reported as 2.7%, Taiwan¹⁶ 4.3%, Oman¹⁶ 2.46%, Bahrain¹⁶ 2.7% and India¹⁷ 1.5%.

The gender difference in our study shows the prevalence of male babies affected with birth defects was 50% of study population and females were 46%. This gender difference is evident in other studies too^{18, 19}, but another study from Pakistan shows female predominance in their study¹³.

In our study the most commonly involved system was central nervous system followed by congenital heart defects on second place and skeletal deformities were third most common defects. When we compare this data with international studies, we see in a study from

Saudi Arabia the most common birth defect detected was also CNS related^{20,26}. Another study from Iran and India also showed CNS malformations to be on top^{21, 22} all of these support the finding of our study. But few other studies from Iran and India show some contrasting results like urogenital and musculoskeletal deformities to be the most common systems to be involved^{22, 23}. Some other Local studies^{25,26} done in Pakistan however also show some contrasting evidence from our study like they showed that most common system involved was gastrointestinal. These differences could be due to the availability of facility regarding subspecialties which are not present in our setup. This study has its limitations so it should not be considered a true representative of the whole community, as not all babies are delivered in hospital and some parents avoid seeking medical care for neonates with birth defects.

CONCLUSION

Birth defects are definitely not a rare condition in our set-up and CNS was the most commonly affected system in our study. Knowledge of incidence and pattern of birth defects will be helpful to design preventive strategies at multiple levels by healthcare providers.

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Conflict of Interest: The study has no conflict of interest to declare by any author.

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Quality of Life of Hearing Impaired Young Adults Using Hearing Aid

Hafiza Fatima Rafique¹, Saira Zaman² and Faiza Mushtaq¹

ABSTRACT

Objective: To assess the quality of life of hearing impaired young adults using hearing aid.

Study Design: Descriptive study

Place and Duration of Study: This study was conducted at the Department of ENT, Fatima Memorial Hospital College of Medicine & Dentistry, Lahore from 1st January 2018 to 30th June 2018.

Materials and Methods: Fifty individuals were collected from the “Hamza Foundation Academy for the Deaf” with “severe degree” hearing loss, all over the “age of 18 -34 years” (young adults). The patients answered the questions after the effective use of hearing aid. The questionnaire consists of “16 questions” about general quality-of-life and other aspects: physical, psychological, environmental and social relations. Questionnaire collected all objectives of study.

Results: This study shows that there were 3 (6.0%) subjects had poor quality of life, 28 (56.0%) subject had Moderate QOL and 19 (38.0%) subjects had Good Quality of Life after using hearing aid.

Conclusion: This study shows that usages of hearing aids are clearly associated with impressive improvements in the social, emotional, psychological, and physical well-being of people with severe degree hearing loss. Specifically, hearing aid usage is positively related to restore the hearing impaired person’s function in society.

Key Words: Hearing aids, Hearing loss, Quality of life

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INTRODUCTION

The World Health Organization (WHO) estimated in 2008 that over 360 million persons have disabling hearing loss which represents 5.3% of the world population. Hearing loss is an important public health concern with substantial economic and societal costs. In infants and children hearing impairment retards developmental language and educational progress. In adults, it causes difficulties in both professional and social life as well as stigmatization. Apart from consequences to the individual person, hearing loss also leads to high costs to society.¹ Hearing impairment can be caused by many factors including infections during childhood such as measles, mumps and meningitis, chronic otitis media, exposure to excessive or prolonged noise, head/neck injuries, use of ototoxic medications such as certain types of chemotherapies and antibiotics, industrial solvents, congenital abnormalities and infections and prenatal problems, certain nutritional deficiencies, genetic disorders and aging.²

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People with hearing impairment face great difficulties in their day to day life. They are less likely to be in paid work and more likely to be retired or employed part-time.³

An extensive survey found clear associations between hearing loss and feelings of loneliness, distress, depression, anxiety and summarization. Young people are more deeply affected than older people.⁴ Young people with hearing loss are more prone to a decline in psychosocial health than older hearing impaired people the risk of severe depression increased by five percent per dB of individual hearing loss. The feeling lonely was found to increase by seven percent per dB of hearing loss.

Younger people more severely affected with hearing impairment. Mild distress states are considered part of normal life and do not interfere with normal social functioning. However, elevated levels of distress with symptoms such as worry, irritability, tension, poor concentration and insomnia may force a person to give up and withdraw from major social roles, especially the occupational role. Therefore, the impact of hearing impairment in adults younger than 70 years may be greater than the impact in elderly people.⁵

Hearing, auditory perception is the ability to perceive sound by detecting vibrations, changes in the pressure of the surrounding medium through time, through an organ such as the ear. Sound may be heard through solid, liquid, or gaseous matter.⁶ In humans and other vertebrates, hearing is performed primarily by the auditory system: mechanical waves, known as vibrations are detected by the ear and transducer into

nerve impulses that are perceived by the brain (primarily in the temporal lobe).⁷

Hearing loss, deafness, hard of hearing, or hearing impairment (a term considered derogatory by many in the deaf community), is a partial or complete inability to hear. Hearing loss can be categorized by which part of the auditory system is damaged. There are three types of hearing loss. (1) conductive hearing, (2) sensori-neural hearing loss (SNHL) and (3) mixed hearing loss. Degree of hearing loss is: mild, moderate, moderately severe, severe, profound loss. We measure the different degree and type of hearing loss with the help of hearing graphs called audio gram.⁸

Treatment of severe degree hearing loss used hearing aids. A hearing aid is an electro acoustic device which is designed to amplify sound for the wearer, usually with the aim of making speech more intelligible, and to correct impaired hearing as measured by audiometry. In the United States, Hearing aids are considered medical devices and are regulated by the Food and Drug Administration (FDA).⁹ A hearing aid is a miniature amplification system. The easiest way to categories the type of hearing aid is to describe where it's worn: put simply, hearing aids can either be worn in the ear or behind the ear. Its key parts include: a microphone, an amplifier (most employ digital signal processing), a miniature loudspeaker called a receiver and a battery. These are the types of hearing aids.¹⁰ Body worn hearing aid, in-the-ear (ITE), in-the-canal (ITC), completely-in-the-canal (CIC) and behind the ear (BTE).¹¹

Hearing aids improve overall quality of life for most users. Hearing aid users enjoy better overall health than non-users. They are perceived by their families to have better cognitive functioning than non-users and to be less introverted. The most beneficial effects of hearing aids are found in the users' social lives, taking part in group activities, and family relationships.¹² Hearing impaired people with hearing aids have greater self-confidence, stronger self-image and better communicative functioning, resulting in overall higher self-esteem, than those without aids.¹³ Hearing aids help to reduce deterioration in psychological functioning as a result of hearing impairment. It can reverse social, emotional and communication dysfunctions caused by hearing impairment. They are more likely than non-users to engage in activities involving other people. Hearing aids improve most aspects of emotional life and they have greater warmth and less negativity in personal relationships than non-users.¹⁴

MATERIALS AND METHODS

This descriptive study was carried out at Department of ENT, Fatima Memorial Hospital College of Medicine & Dentistry, Lahore from 1st January 2018 to 30th June 2018. through Hamza Foundation Academy for the

Deaf" through a self design questionnaire from 50 individuals with "severe degree" hearing loss, all over the "age of 18-34 years" (young adults). The patients answered the questions after the effective use of hearing aid. The questionnaire consists of "16 questions" about general quality-of-life and other aspects: physical, psychological, environmental and social relations. The data was entered and analyzed through SPSS-20.

RESULTS

In collecting data of 50 subjects, there were 20(40.0%) male subjects and 30 (60.0%) female. Fifty hearing impaired young adults using hearing aid from 18 to 34 years age limit but the mean age was 19 to 24 years and the mean 20.88 ± 1.480 years (Table 1, Figures. 1-2).

In the collected data from 50 subjects there were 41 (82.0%) subjects using 1 (Unilateral) hearing aid and 9 (18.0%) subjects using 2 (Bilateral) hearing aids (Table 2).

Table No.1: Gender and age distribution of subjects (n=50)

Variable	No.	%age
Gender		
Male	20	40.0
Female	30	60.0
Age (19-24)		

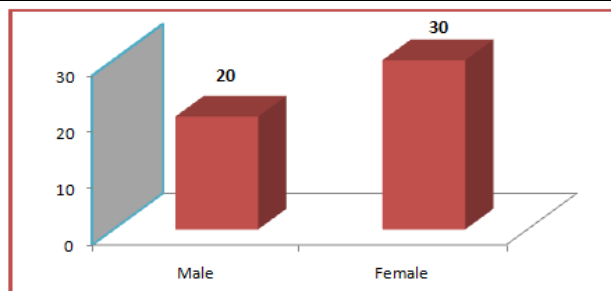


Figure No. 1: Distribution of genders

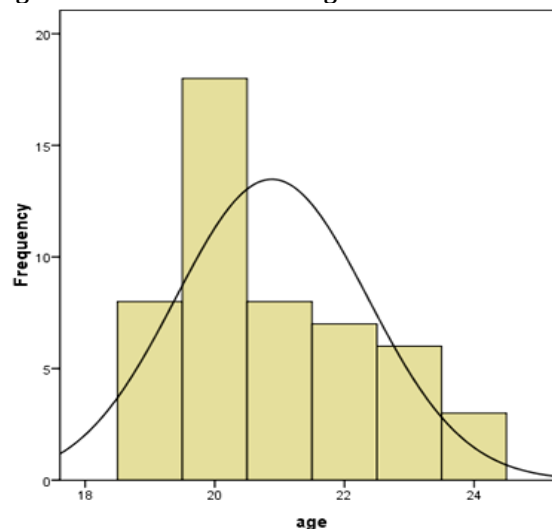


Figure No. 2: Age of the patients

In the collected data from 50 subjects there were 3 (6.0%) subjects had poor quality of life, 28 (56.0%) subject had Moderate QOL and 19 (38.0%) subjects had Good Quality of Life after using hearing aid. This study shows that usage of hearing aid improve overall quality of life of hearing impaired young adults (Table 3, Figure 3).

Table No.2: Subject using hearing aid (n=50)

Subject	No.	%
One hearing aid	41	82.0
Two hearing aids	9	18.0

Table No.3: Quality of life of hearing aid user (n=50)

Quality of life	No.	%
Poor	3	6.0
Moderate	28	56.0
Good	19	38.0

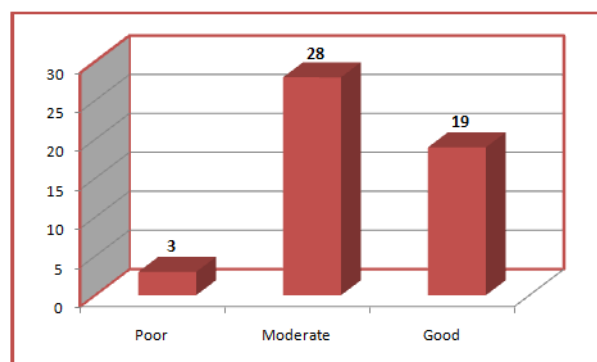


Figure No. 3: Frequency of quality of life hearing aid users

DISCUSSION

Communication is an important aspect of everyday life especially for adults. Hearing loss can impair the exchange of information and therefore reduces the quality of life. The purpose of this study was to investigate the quality of life in young adults who are hard of hearing after wearing a hearing aid.¹⁵ In 2012 a study was conducted by Mondelil, Maria Ferenda Capoanirorcia; Souza Il, Patricia Jorge Soalhei de to identify the quality of life of hearing impaired older adults after fitting hearing aid. Through the World Health Organization Quality of Life Questionnaire. They had 30 individuals all over the 60 years of age. The patients answer the WHOQOL questions after the use of hearing aid. There was a significant improvement in quality of life in general, as far as leisure activities were concerned, there were no major changes regarding the frequency of negative feelings; even after the hearing aid fitting. The use of hearing aid favored the overall quality of life of the individuals evaluated.¹⁶ While in present study we identify the quality of life of hearing impaired young adults with severe degree hearing loss after using hearing aid.

Through a self design questionnaire using COSI (Client orientation scale of improvement) scale.

In present study we collect data from 50 hearing impaired young adults all over the age of 18 to 35 years of age. The patients answer the questions after using hearing aid. It has been observed that the psycho-social problem related with hearing decreased considerably, feeling handicapped in term of hearing loss became less, and the quality of life increase.

In 2009 Soghratfaghihzadeh, Abdollah Moossavo and Saeideh Mehrkian conducted this study to investigate the quality of life in elderly people who are hard of hearing after wearing hearing aid. A questionnaire about satisfaction with hearing aid was filled by participants.

The results showed a significant improvement of quality of life after using hearing aid in all participants and betterment of their most important problem; the communication and exchange of information. In conclusion with respect to the beneficial effects of hearing aids is presbycusis.¹⁷

In present study we collected data from 50 subjects all over the age of 18 to 35 years old. This study show that there were 3 (6.0%) subjects had poor quality of life, 28 (56.0%) subject had Moderate QOL and 19 (38.0%) subjects had Good Quality of Life after using hearing aid.

This study shows us the better improvement of Quality of Life in young adults using hearing aid. In return, this study helps us to understand, to which extent their independence and function is restored in society.

CONCLUSION

The usages of hearing aids are clearly associated with impressive improvements in the social, emotional, psychological, and physical well-being of people with severe degree hearing loss. Specifically, hearing aid usage is positively related to restore the hearing impaired person's function in society.

Author's Contribution:

Concept & Design of Study:	Hafiza Fatima Rafique
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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Evaluating the Prevalence of Male Infertility in Karachi

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ABSTRACT

Objective: To analyze the prevalence of male infertility in Karachi.

Study Design: Descriptive case series

Place and Duration of Study: This study was conducted at the Civil Hospital, Karachi from 1st January 2015 to 31st December 2015.

Materials and Methods: In this study subjects were divided on age difference into three groups (Group I, 21-30 years, Group II, 31-40 years and Group III, more than 40 years). Samples were collected through masturbation, after liquefaction of sample analysis performed on light microscopy. Then, motility and morphology were performed in presence and absence of debris, agglutination and microbial contamination were noted.

Results: We found that despite of age difference young generation have more semen abnormal percentage 56% comparing to group II and near to group III (50% and 58%). Most prevalent abnormality among three groups was asthenoteratospermia. It seems that young generation in terms of abnormality is at elevated risk of infertility. This is due to environmental change, change in life style and nutritional intake of youth.

Conclusion: To overtake this alarming situation researcher must come-up with solution to cope the prevailing problem and save youth's fertility-cum-inheritance.

Key Words: Semen Parameters, Youth, Prevalence, Fecundity, Inheritance, Cope

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INTRODUCTION

A long-established semen evaluation method provides useful information about motility and morphology. However, due to variation of parameters from previous to fresh analysis and difference in performing ways among technician and laboratories, evaluation performed in this way has utility in predicting reproductive performance in an assisted reproductive setting.¹

Approximately 15% of couples attempting their first pregnancy meet with failure. Most authorities define these patients as primarily infertile if they have been unable to achieve a pregnancy after one year of unprotected intercourse. Incumbently 48.5 million infertile couples are worldwide², from which pure male factor accounts for 20-30%³ and in Pakistan male infertility is 21.91%.⁴

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A semen analysis is performed when a health practitioner thinks that a man or couple might have a fertility problem. Still routine semen evaluation is the main pillar to investigate male fertility. For semen evaluation WHO published first manual in 1980 as help hand for investigators. The recent modified manual published after the assessment of 4500 men from 14 different countries. The lower reference values for men who unable to conceive within 12 months of unprotective sex are: semen volume 1.5 per ml; total sperm count 39 million per ejaculate; sperm count per ml 15 million; 58% vitality; progressive motility 32%; total motility 40%; normal morphology 4%.⁵

Prediction of male infertility with limited power has been reported from 1980 to the presented.^{6,7} In analysis microscopic and macroscopic parameters included. Before confirmation of normal or infertile multiple analysis should be carried out due to large variation in the sperm parameters.⁸

The macroscopic parameters are such as; volume which is accurate indicator of various abnormalities, regarding the appearance absence of spermatozoa in sample gives translucent appearance and non-sperm components render opaque appearance. A sample liquifies after ejaculation within 15-30 minutes is a normal. In the absence or obstruction of seminal vesicle a sample lack secretion from seminal vesicle and failed to coagulate. Prolonged liquefaction is due to the inflammation and it cause poor prostatic secretion. Viscosity is another property consider abnormal when the length of thread exceeds 60 mm. If these cases are associated with low

sperm motility, the sperm transportation will be compromised.^{5,6}

Microscopic attributes of the seminal fluid include sperm concentration, motility, viability, morphology as well as non-sperm cellular components in the form of leukocyte concentration and immature germ cells. Among the parameters reported in a routine semen analysis, it is not yet known which one would be the most associated with fertility. While many Andrologist reports point to sperm morphology as the valuable parameter, others indicate sperm concentration and/or motility are the most valuable.⁹

In addition, a higher prevalence of primary and secondary infertility has been seen among repeated spontaneous aborters. Reports show that despite a normal fertilization rate, a higher rate of early spontaneous abortions occurred in patients with <4% morphologically normal spermatozoa as assessed by Kruger strict criteria.¹⁰ This observation indicates that the main problem with morphologically abnormal spermatozoa was not an impaired fertilization, but rather that these spermatozoa may have resulted in a higher percentage of abnormal embryos which were aborted early in gestation.

Several studies have suggested that human semen quality and fecundity have been declining during the past decades.^{11,12} Nevertheless, other works have obtained contradictory results indicating that these changes have not taken place homogeneously in the world.^{13,14} Geographical differences in semen quality also support the fact that semen quality may have declined only in some areas.^{15,16} Changes in seminal samples are recent^{17,18} and may be related to environmental or occupational pollutants, changes in lifestyles, exposure to toxins, or dietary habits.^{19,20}

MATERIALS AND METHODS

This descriptive study was carried out at Karachi City from 1st January 2015 to 31st December 2015. This study is composed of 807 subjects which came for treatment of infertility and want to know cause of their infertility at Dr. Ruth K M Pfau, Civil Hospital Karachi. Although subject number is precise as we are living in male dominant society, male is unwilling to come up for the analysis and this study will enhance awareness among the individual to come forward for the analysis and treat their defects or get treated in time. Subject were divided into three age groups such as group I, 21-30 years, group II, 31-40 years and group III, more than 40 years. Samples were collected randomly with their name, abstinence period, collection time and poured entire ejaculate in a wide mouth sterile container.

Analysis done within 1 hour of collection to limit the deleterious effects of dehydration, pH or changes in temperature on motility. After the liquefaction of the sample at 37°C whole sample mixed thoroughly by

pipetting in & out then a drop of 5-10µl poured on slides and covered with coverslip. Then slide is putted on bench top incubator to maintain 37°C temperature of the drop for the proper analysis of sample. Then microscopic study is carried out on bright field microscope of the parameters to evaluate and record the values on record register. In the end results were analyzed and concluded. All the parameters were analyzed and recorded according to the WHO criteria excepting 4% morphology, according to the analyst at IVF laboratory¹⁸ and advises caution when interpreting the new WHO reference values because they have not yet been accurately defined to discriminate fertile from infertile men that's why we retain morphology parameters as 30% as mostly IVF laboratory of Pakistan's evaluate. Samples having a major liquefaction problem, subjects under 20 years of age were also excluded from study and retain which lies under WHO criteria were included in study. All the data was analyzed by computer software SPSS 17.0.

RESULTS

The cases are assessed for the following parameters teratospermia, asthenospermia, azoospermia, Necrospermia, oligospermia and their combination were selected for the study. Objects were divided into three groups [group I (21-30 years), II (31-40 years) and III (>40 years). Apart from this, from the same study population semen parameters were compared among the age groups and research data (Table 1). In the present study we have compared different parameters among three groups to analyse a significant difference in their parameters. We found that group I has high 56 % of abnormal semen analysis compared to group II 50% and nearby to group III 58% despite of age difference.

Table No.1 Comparison of variables among the groups

Variable	Group I	Group II	Group III
Normal	46	50	42
Abnormal	56	50	58
Asthenoteratospermia	17	16	18
Oligoasthenoteratospermia	12	<1	13
Teratospermia	10	09	13
Azoospermia	08	07	09
Asthenospermia	03	08	07
Oligoasthenospermia	03	09	<1
Oligospermia	01	<1	00
Necrospermia	<1	01	00

While analysing other parameters it's found that morphology and motility in combination have no significance difference among the groups I (17%), II (16%) and III (18%). In terms of count, motility and

morphology (Oligoasthenoteratospermia) group I have significance difference with group II <1% but there is no significance difference while comparing group I 12% to group III 13%.

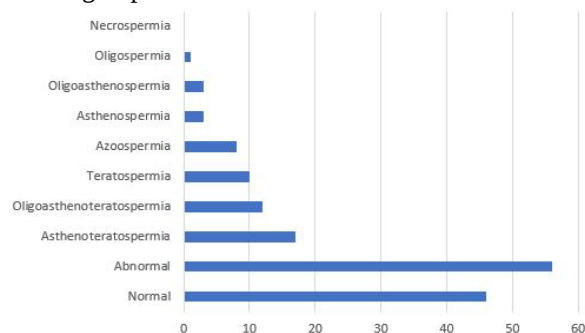


Figure No. 1: Comparison of variables among the group-I

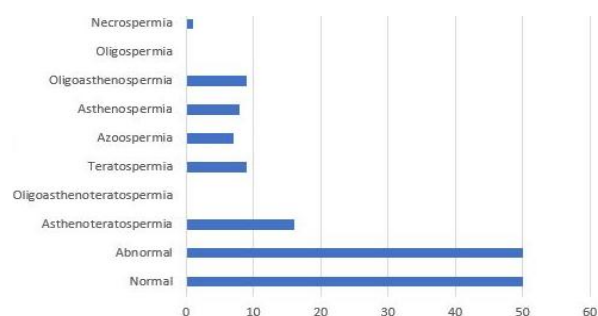


Figure No. 2: Comparison of variables among the group-II

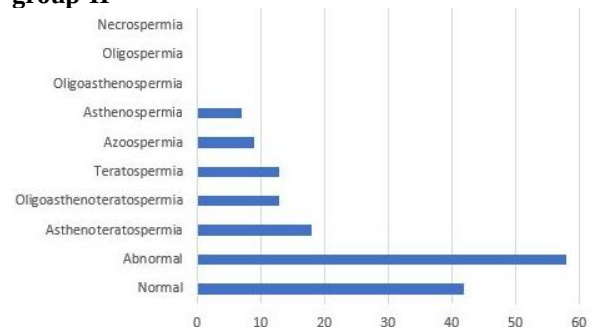


Figure No. 3: Comparison of variables among the group-III

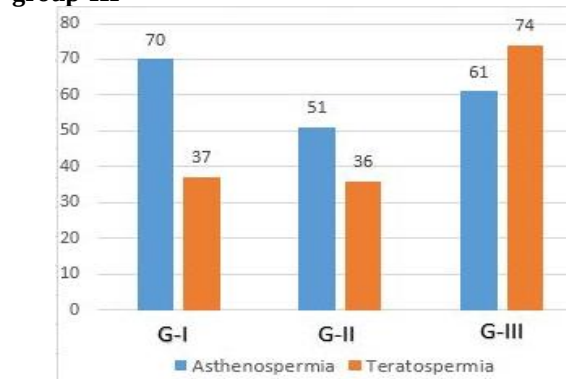


Figure No. 4: Most prevalent abnormality among the groups

By comparing motility and morphology defects, it increased as age of the subject increases. Analysing morphology, it's seem that increase in age there is increase in defects while comparison done among the groups (I-3%, II-09% and III-13%). Besides this, studying other parameter among groups we found no noticeable difference. In this study, it's found that most prevalent abnormality among the age groups (I-70%, II-51% and III-61%) is motility (Figures 1-4).

DISCUSSION

The distribution of men according to age shows most of patient's flow were between the ages of 31-40 years (48%). It is well established by the study of Merino and Carranza-Lira et al. and found in this study that only small percentage of men attending the infertility clinics are older than 40 years (10 %).

In the present study in terms of abnormality group II (50%) and III (58%) compared, and it's found that there is increase in abnormality as age increases but comparing group I (56%) to II & III there is significance difference (Figs. 1-3). There are two possibilities, first due to awareness, young generation is step forward in diagnosis to cope problem at earliest, second is that due to changing life style, nutritional intake and environmental changing young generation is badly encircled in the infertility.

While analysing different parameters it's found that morphology and motility in combination have no significant difference among the groups I (17%), II (16%) and III (18%). In terms of count, motility and morphology group I have no significance difference with group II but there is significance difference while comparing group I to group III (Figs. 1-3). And found that young generation is also severely affected by these parameters and its alarming situation for youth regarding infertility. This incumbent situation is alike study of Carlsen E. et al 1992, Swan SH 2006 and Homan et al 2007 that there is decrease in semen quality past 5 decades.

According to Nieschlag et al²¹ there is a significant decrease in sperm motility in older men but in this research, it's found that there is little bit decrease in sperm motility in older men with no prominent different among the groups (I-8%, II-8% and III-9%) of the Karachi people (Fig. 1-3).

Analysing morphology, it's seem that increase in age there is increase in defects of morphology in spermatozoa while comparison done among the groups (I-3%, II-09% and III-13%). Besides this, studying azoospermia parameter in groups (I-12%, II-07% and III-09%), there is noticeable difference (Fig. 1-3), and this Azoospermia condition also appears when Y-chromosome microdeletion occurs. It's seemed that youth is more prone to it too, researcher must study why this is happening to overcome the cause and save young's fertility.

Presently, it's found that most prevalent abnormality among the age groups (I-70%, II-51% and III-61%) is motility in combination along with the other parameters

(Fig. 1). Adding to this it seems that morphological defects increases as age increases (I-37%, II-36% and III-74%). These two are considered most important while treating male-infertility. Other parameters such as necrospemia, oligospermia and others in combination have no significance difference among the three groups.

CONCLUSION

In this research, most prevalent abnormality is asthenoteratospermia in three groups. Besides, it seems that young generation in terms of semen abnormality is at high risk of infertility. This may be due to environmental change, change in life style and nutritional intake of youth. To overtake this alarming situation researchers, must come-up with solution to cope the problem from prevailing and save youth's fertility-cum-inheritance.

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Frequency of Iron Deficiency Anemia among Children Consuming Cow's Milk

Sami ul Haq¹, Niamat Ullah² and Hazrat Bilal Khan³

ABSTRACT

Objective: To determine the frequency of iron deficiency anemia among children consuming cow's milk.

Study Design: Descriptive / cross-sectional study.

Place and Duration of Study: This study was conducted at the Pead's Deptt, PGMI, Hayatabad Medical Complex Peshawar from Jan 12, 2016 to July 11, 2016.

Materials and Methods: All children showing history of cow's milk consumption in the last at least 2 months were included in the study through OPD. Sternly exclusion criteria were followed to control confounders and biasness in the study results. Iron Deficiency Anemia (IDA) was stratified among age and gender to see the effect alterations. Post stratification was done through chi-square test keeping p-value ≤ 0.05 as significant. All results were displayed in the form of tables and graphs. Total sample size was 148 with convenience (non-probability) sampling technique.

Results: A total of 148 patients exhibiting history of cow's milk feeding were included in the study. There were 90 (60.81%) males and 58(39.19%) were females. Male to female ratio was 1.61:1. Average age of the patients was 12.26 Months ± 5.77 SD with range 2-24 months. The iron deficiency anemia in patients having history of cow's milk consumption in the last at least two months was present in 54 (36.49%) patients.

Conclusion: There is high ratio of iron deficiency anemia in this part of the world in patients using cow's milk

Key Words: Anemia, Iron Deficiency, cow's milk, Frequency.

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INTRODUCTION

Iron-deficiency anemia (IDA), defined as iron deficiency (serum ferritin $<12 \mu\text{g/L}$) with hemoglobin levels $<110 \text{ g/L}$,^{1,2} can mount a considerable load of disease in paediatrics.¹ Iron deficiency occurs when stored iron's level becomes depleted.² IDA happens if iron quantities are significantly lowered to cause anemia.³ Although children with iron deficit are commonly asymptomatic, Iron-deficiency anemia has been related in certain studies with intellectual and social delays in children.⁴ Inadequate dietary iron, iron absorption and intense exercise, along with blood loss and parasitic infestations, are some etiologies of IDA.⁵ Healthy newborn infants have a total body iron of 250 mg, which is obtained from maternal sources.⁶

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Although historically routine consumption of dairy products had a geographically limited distribution, milk consumption has become widespread among children throughout the globe, a process that has been supported, in part, by promotion of milk in school feeding programs.⁷ Infants consuming cow milk have a greater incidence of iron deficiency, because of low iron content of cow's milk, occult intestinal blood loss associated with cow's milk consumption during infancy and inhibition of non-heme iron absorption by calcium and casein.^{8,9}

Consumption of cow's milk is thought a risk factor for IDA and is advised against fore 12 months of age by the American Academy of Pediatrics, and the Centers for Disease Control and Prevention.¹⁰ In a systematic review, a study was found comparing iron- enriched formula with non-iron-enriched formula and cow's milk and the incidence of IDA was 6% vs 22% vs 43% respectively.¹¹ In another study, the prevalence of anemia among children consuming cow's milk was 45.2%.¹² In a study by Thorisdottir AV et al, the prevalence of iron deficiency was highest in the cow's milk group and lowest in the follow-on formula group.¹³

The present study is designed to determine the frequency of IDA among children consuming cow's milk. Cow's milk consumption is common in our community and involves increased risk of developing IDA. This research will give us with a regional data about the occurrence of IDA in children consuming cow's milk.

MATERIALS AND METHODS

The study was performed after approval from hospitals ethical and research committee. All children with inclusion criteria {history of cow's milk consumption in the last at least 2 months, Age group (6 months to 02 years), either gender, Quantity (cow's milk consumption of 16 to 24 ounces per day)} were included in the study through OPD. The aim and benefits of the study was explained to their guardians and a written informed consent was acquired.

All children were subjected to thorough history, followed by complete usual examination. From all the children, a 5cc of venous blood was obtained under strict aseptic practices and were sent to hospital laboratory for quantifying Hb (Hemoglobin) and Ferritin levels. All the investigations were done by same proficient hematologist.

All the above-mentioned statistics including name, age and gender were recorded in a pre-designed proforma. Strictly exclusion criteria (History of intake of iron therapy, blood transfusions & bleeding of any amount, in the last three months) were obeyed to limit confounders and bias in the study conclusions.

SPSS version 20 for windows was used to store and analyze the data. Mean + SD were computed for mathematical variables like age, Hb and Serum ferritin. Frequencies and percentages were calculated for clear-cut variables like gender and IDA. IDA was stratified among age and gender to see the effect variations. Post stratification was done through chi-square test preserving p-value ≤ 0.05 as significant. All results were presented in the form of tables and graphs.

RESULTS

A total of 148 patients presenting with history of cow's milk intake in the last at least two months were included in the study. Males were 90 (60.81%) and females were 58 (39.19%). Male : Female was 1.61:1. Fig 1.

Patient's average age was 12.26 months $\pm$ 5.77 SD with range 2-24 months. Patients were distributed age wise into 3 groups, among them frequent age category for displaying history of cow's milk ingestion was 6-15 months. There were 20 (13.5%) patients of the age ≤ 5 months, 84 (56.8%) patients were in the age span of 6-15 months and 44 (29.7%) were of age more than 16 months.

The iron deficiency anemia in patients having history of cow's milk feeding was found in 54 (36.49%) patients while 94 (63.51%) patients were found free of iron deficiency anemia. Fig 1

It is clear from data that IDA was present in most of patients having 6-15 months of age; although it was insignificant with p value=0.232. Four (20%) patients with iron deficiency anemia having age ≤ 5 months, age group 6-15 months contains 40% iron deficiency

anemia and patients having more than 10 months of age have 36.4% iron deficiency anemia. Table 1

Table No.1: Age wise distribution of iron deficiency anemia

	Iron Deficiency Anemia		Total	p-value
	Yes	No		
Age in months ≤ 5.00	4 20.0%	16 80.0%	20 100.0%	0.232
6.00 - 15.00	34 40.5%	50 59.5%	84 100.0%	
16.00+	16 36.4%	28 63.6%	44 100.0%	
Total	54 36.5%	94 63.5%	148 100.0%	

Table No.2: Gender wise distribution of iron deficiency anemia

	Iron deficiency anemia		Total	p-value
	Yes	No		
Male	35 38.9%	55 61.1%	90 100.0%	0.281
Gender Female	19 32.8%	39 67.2%	58 100.0%	
Total	54 36.5%	94 63.5%	148 100.0%	

Table No.3: Descriptive statistics for hemoglobin and ferritin

	N	Min.	Max.	Mean	STD. Deviation
Hemoglobin Level (in gm/dl)	148	8.00	13	12.25	13.68
Ferritin Level (in μ g/L)	148	9.50	14.50	13.68	3.99

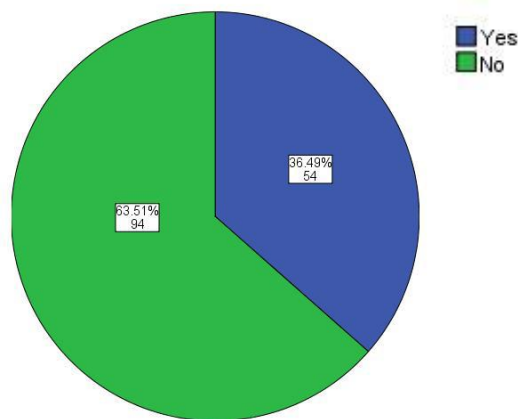


Figure No.1: Iron deficiency anemia in children consuming cow's milk

Gender wise iron deficiency anemia in patients having history of cow's milk ingestion demonstrates that gender have also no noteworthy role over them with p-value=0.281. There were 38.9% iron deficiency anemia in male and 32.8% observed in female patients. Table 2 Average hemoglobin level was 12.25 gm/dl +4.75 SD while average ferritin level was observed as 13.68 µg/L+3.99 SD. Table 3.

DISCUSSION

During gestation most of females became anemic in both developed & developing nations.

WHO reports that in developing countries from 35% to 75% (avg: 56%) & in developed countries 18% of females develop anemia in gestation.¹⁴¹ Iron deficiency is more prevalent than anemia and iron deficiency usually occurs in late stages of gestation even in females who become pregnant with comparatively satisfactory iron Depots.¹⁵

In USA, percentage of anemia have declined from twenty percent to thirty percent of children < 1 year in the 1960s and 1970s to < five percent by the mid-1980s.^{16,17} This declination in IDA incidence is due to improved iron fortified formulas, prolong period of breastfeeding, the abstention of cow's milk in infancy, and subsidized nutrition programs by government.¹⁶⁻¹⁹, the American Academy of Pediatrics (AAP) has already pointed out in 1960s, the possibility of deficiency of iron in children <1 year of age & advised a least amount of iron per day.²⁰ In infancy, anemia due to use of cow milk is also proved from early studies.^{21,22} This compelled the Committee for the usage of iron fortified formulas and cereals.²³

Changing research and recommendations have led to the present AAP strategy that cow's milk should not be used during infancy instead of breastfeeding, iron-fortified formula and beginning at the age of six months, iron fortified cereals & formulas.²³⁻²⁴

An inverse relation has been well recognized between the use of cow's milk & iron status during first 12 months of life and later in childhood.^{20,21,25-34} In toddlers, too much cow's milk use is a frequent risk factor for severe anemia.³⁵

Cow's milk contains low quantity of iron. A 240 mL of cow's milk has 0.07 mg of iron, which is merely one percent of the recommended iron per day.^{36,37} This amount of milk has 146 calories.³⁸ Majority of contributors advise 720 mL/day of milk. Toddlers dependent on milk for a large portion of their food; use a significant %age of their regular calories from low iron containing diet & so loss chances to use iron rich foods.³⁹

CONCLUSION

Iron deficiency and IDA remain to be major health issues in children. There is high proportion of iron deficiency anemia noticed in this study in patients using

cow's milk. It should be taken as serious issue. Enquiry should be done on each well-child visit about the quantity of cow's milk used & the age at which it was started. This will allow the contributor to consider additional assessment for likely iron deficiency, IDA & to encourage counseling about infant nutrition.

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Caudal Bupivacaine Alone Versus Bupivacaine with Ketamine to Compare Postoperative Analgesia

Muhammad Nasir¹, Aatir Fayyaz² and Munir Ahmad³

ABSTRACT

Objective: To compare the effectiveness of caudal bupivacaine alone and bupivacaine with ketamine in terms of duration of analgesia.

Study Design: Randomized controlled trial study

Place and Duration of study: This study was conducted at the Department Anaesthesia Bakhtawar Amin Hospital, Nishtar hospital, and Children Hospital Multan from May 2017 to May 2018.

Materials and Methods: Study was started after approval from local ethical committee a parental consent was obtained after complete information of study. Main outcome variables are duration of analgesia, pain score, and Bromage score. Data analysis was done with SPSS version 23.1. P value ≤ 0.05 was taken as statistically significant.

Results: The mean duration of analgesia and time taken to void urine after surgery of the Group A was 5.80 ± 2.71 hours and 4.45 ± 0.51 hours, respectively. While, the mean duration of analgesia and time taken to void urine after surgery of the Group B was 12.53 ± 2.51 hours and 4.52 ± 0.53 hours, respectively. Statistically significant was observed in duration of analgesia. P value 0.000.

Conclusion: Combination of Ketamine 0.5 mg/kg and bupivacaine 0.25% in a dose of 1 ml/kg prolonged the duration of postoperative analgesia to a significant range in comparison with bupivacaine 25% of 1 ml/kg alone.

Key Words: Caudal block, Spinal anesthesia, Bupivacaine, Ketamine, analgesia

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INTRODUCTION

Pain is an unpleasant feeling which is most feared symptom of an illness. Human always keep trying to terminate or conquer this unpleasant feeling in any age group¹. It is a very complicated phenomenon which cannot be described or diagnosed. It is necessary to control the pain in hospitalized patients for better outcomes or early recovery from the disease². Caudal analgesia is a most popular effective and useful regional block in these days. Caudal block is a regional analgesic technique mostly used for below diaphragmatic surgeries. It is found to be successful and effective³.

duration of action when a single injection of local anaesthetic was given, even bupivacaine which is a long

Among its disadvantages most common is short acting anaesthetic gives only 4 to 8 hours of analgesic effect^{4,5}. To overcome this short duration of action caudal catheter was inserted for repeated doses of anaesthetic agent but this method not too much popular because of high risk of infection⁶. Addition of ketamine to an anaesthetic agent enhance the duration of analgesia. Administration of epidural ketamine produce profound the analgesic effects at a level of spinal cord without any adverse effects.

Addition of preservative free drug like ketamine enhanced the time of post operative analgesic effects in patients of below diaphragm surgery⁷. Dose of ketamine caudal block is controversial, many previous studies determine the dose of ketamine but it was not justified properly. In a study Semple et al reported that 0.5mg per kg is an optimum dose of ketamine for caudal epidural blockade. This local anaesthetic effect is stimulated by N methyl D aspartate receptors antagonism also known as NMDA receptors⁸.

Use of ketamine may increase blood pressure and heart rate, because hallucinations raise intracranial and intraocular pressure and provoke acute porphyria⁹. In psychiatric patients ketamine administered with precautions, it increases the sedative effect of medicine in a dose dependent manner. Use of benzodiazepines diminishes the anti depressant role of ketamine. Other than NMDA receptors antagonism ketamine may actually on sigma receptors, muscarinic acetylcholine receptors and antagonized their effects¹⁰.

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MATERIALS AND METHODS

Study was started after approval from local ethical committeea parental consent was obtained after complete information of study. Study was completed in Department Anaesthesia Bakhtawar Amin Hospital, Nishtar hospital, and Children Hospital Multan from May 2017 to May 2018. Patients of age more than 20 years, ASA status I and II and who were selected for below diaphragm surgery were selected for study. Patients with no sensitivity or allergy to bupivacaine or ketamine or having caudal injection contraindication such as bleeding disorder, infection at the sight and vertebral column deformities were not included in study. Patients were divided into two groups A and B by lottery method. Patients in group A were given bupivacaine 2.5% with dose of 1ml per kg and in group B were given bupivacaine 0.25% with dose of 1ml per kg plus ketamine 0.5mg per kg preservative free. Bilateral IV lines of 18 G were inserted in dorsal veins of hands. Patients were kept for NPO six hours before surgery. All patients were undergone for general anaesthesia with thiopentone 5 to 6 mg per kg and inhalational N₂O, oxygen and halothane gas. Caudal injection was given before start of surgery and then surgeon was allowed to perform surgery. Patient's non invasive blood pressure, ECG, spo₂, heart rate was monitored. When surgical procedure was completed patients were shifted to recovery room and observed for one hour and then observations were done at one hour, four hours, six hours, twelve hours and 24 hours after shifting in ward. Analgesia duration was recorded by VAS core. Duration of analgesia was labeled as time between caudal injection and first analgesia requirement after surgery. Within 24 hours if analgesia was not required then duration of analgesia was noted as 24 hours. Bromage scale was used to evaluate the motor block.

Bromage scale: Complete flexion of feet and knees and able to lift legs score 0. Legs cannot be extended or lifted but flexion of knees and feet is present score 1. Flexion of knees and feet both absent score 2. Complete absence of movement in legs and feet score 3.

Data analysis was done by putting data in SPSS version 24. Mean and standard deviation were presented for quantitative data like age, duration of analgesia. Qualitative data was presented as numbers and percentages like gender. Chi square and student t-test were applied to see association among variables. Probability value ≤ 0.05 was considered as significant.

RESULTS

Eighty patients were included in this study. The patients were further analyzed into two Groups as n=40 in Group A and n=40 in Group B. The mean age, weight and duration of surgery of Group A was 3.71 ± 1.38 years, 11.42 ± 1.86 kg and 47.62 ± 3.76 minutes, respectively. Nature of surgery was observed as urethroplasty in n=16 (40%) patients, herniotomy in n=15 (37.5%) patients and orchidopexy in n=9 (22.5%) patients. While, the mean age, weight and duration of surgery of Group B was 3.50 ± 1.55 years, 11.52 ± 1.56 kg and 48.47 ± 3.01 minutes, respectively. Nature of surgery was observed as urethroplasty in n=27 (67.5%) patients, herniotomy in n=9 (22.5%) patients and orchidopexy in n=4 (10%) patients. The difference of nature of surgery among the groups was significant (0.044). (Table. I).

Table No. I: Study demographics and nature of surgery

Variables	Group A	Group B	P-value
Age (years)	3.71 ± 1.38	3.50 ± 1.55	0.544
Weight (kg)	11.42 ± 1.86	11.52 ± 1.56	0.796
Duration of surgery (minutes)	47.62 ± 3.76	48.47 ± 3.01	0.268
Nature of surgery			
Urethroplasty	n=16 (40%)	n=27 (67.5%)	0.044
Herniotomy	n=15 (37.5%)	n=9 (22.5%)	
Orchidopexy	n=9 (22.5%)	n=4 (10%)	

Table No.2: Pain Score (hourly) in both groups

Pain score (postoperative)	Groups	0	1	2	3	4/>4	P-value
1 hour	A	26(65%)	10(25%)	2 (5%)	2 (5%)	0 (0%)	0.869
	B	29(72.5%)	8 (20%)	2 (5%)	1(2.5%)	0 (0%)	
4 hour	A	26 (65%)	7 (17.5%)	2 (5%)	2 (5%)	3 (7.5%)	0.350
	B	32 (80%)	4 (10%)	2 (5%)	2 (5%)	0 (0%)	
6 hour	A	12 (30%)	7 (17.5%)	2 (5%)	2 (5%)	17(42.5%)	0.001
	B	27 (67.5%)	6 (15%)	0 (0%)	4 (10%)	3 (7.5%)	
12 hour	A	2 (5%)	1 (2.5%)	1(2.5%)	1 (2.5%)	35(87.5%)	0.020
	B	7 (17.5%)	4 (10%)	4(10%)	4 (10%)	21(52.5%)	
24 hour	A	1 (2.5%)	1 (2.5%)	0 (0%)	0 (0%)	38 (95%)	0.652
	B	2 (5%)	1 (2.5%)	1(2.5%)	1 (2.5%)	35(87.5%)	

Table No.3: Duration of motor block according to Bromage scale

Bromage scale (postoperative)	Groups	0	1	2	3	P-value
1 hour	A	25 (62.5%)	9 (22.5%)	5 (12.5%)	1 (2.5%)	0.912
	B	28 (70%)	7 (17.5%)	4 (10%)	1 (1.5%)	
4 hour	A	31 (77.5%)	4 (10%)	5 (12.5%)	0 (0%)	0.854
	B	33 (82.5%)	3 (7.5%)	4 (10%)	0 (0%)	
6 hour	A	37 (92.5%)	1 (2.5%)	1 (2.5%)	1 (2.5%)	0.562
	B	39 (97.5%)	0 (0%)	0 (0%)	1 (2.5%)	
12 hour	A	38 (95%)	1 (2.5%)	0 (0%)	0 (0%)	0.603
	B	39 (97.5%)	0 (0%)	0 (0%)	1 (2.5%)	
24 hour	A	39 (97.5%)	0 (0%)	0 (0%)	1 (2.5%)	0.314
	B	40 (100%)	0 (0%)	0 (0%)	0 (0%)	

Table No.4: Time taken to void urine after surgery

Variables	Group A	Group B	P-value
Duration of analgesia (hours)	5.80±2.71	12.53±2.51	0.000
Time taken to void urine after surgery (hours)	4.45±0.51	4.52±0.53	0.508

Pain score (postoperative) of both the groups at 1, 4, 6, 12 and 24 hours were shown in table 2. The difference was statistically significant at 6 and 12 hours, ($p=0.001$) and ($p=0.020$), respectively. Bromage scale (postoperative) of both the groups at 1, 4, 6, 12 and 24 hours were shown in table 3. The difference was not statistically significant at any of the hour among the groups.

The mean duration of analgesia and time taken to void urine after surgery of the Group A was 5.80±2.71 hours and 4.45±0.51 hours, respectively. While, the mean duration of analgesia and time taken to void urine after surgery of the Group B was 12.53±2.51 hours and 4.52±0.53 hours, respectively. Statistically significant difference was observed for duration of analgesia ($p=0.000$). (Table 4).

DISCUSSION

Study was conducted by Semple et al¹¹ on efficacy and dose of ketamine in caudal block and reported that addition of preservative free ketamine enhance the effect of 0.25% of bupivacaine when given in epidural block and optimum dose of ketamine in caudal block is 0.5mg per kg. In the study doses of bupivacaine and ketamine are similar as in our study and conclusion can be compared with our study results and conclusion. Another study was conducted by Naguib et al¹² and compared bupivacaine 0.25% alone with bupivacaine 0.2% plus 0.5mg per kg ketamine in children who were selected for inguinal herniotomy and concluded that there was not statistically significant difference between

the groups in terms of quality and duration of analgesia. In combination group only 7% patients required rescue analgesia and in other group 20% patients required rescue analgesia.

A similar study was also conducted by Cook et al¹³ and compared bupivacaine 0.25% plus 0.5mg per kg ketamine with clonidine 2microgram per kg or epinephrine 5mg per ml and concluded that ketamine group provides longer duration of post operative analgesia as compared to clonidine and epinephrine group but in our study we compared ketamine combination bupivacaine 0.25% alone but study results comparable with this study.

Another study was conducted by Martindale et al¹⁴ in 2004, he used bromage scale to assess the motor blockade and reported time of motor blockade 2.4 hours, 2 hours and 1.8 hours in bupivacaine plus ketamine group and IV ketamine group respectively. This study shows higher duration of analgesia when bupivacaine was given in caudal epidural block as compared to ketamine plus bupivacaine. Results of this study were controversial to our study results.

Kaur D et al¹⁵ conducted a similar study on children and assessed the duration of analgesia after surgery after ketamine plus bupivacaine and bupivacaine alone. He reported that addition of ketamine with bupivacaine enhances the analgesia duration in post operative time as compared to bupivacaine alone. In his study main duration of analgesia was 5.36 ± 0.98 hour in bupivacaine alone group and 10.18 ± 2.24 in combination group. P value was 0.001 which shows significance of result. This study is comparable with our study.

In a study conducted by Samad R et al¹⁶ on comparison of bupivacaine plus tramadol and bupivacaine plus ketamine and demonstrated that combination of bupivacaine plus tramadol provides longer duration of analgesia as compared to ketamine and bupivacaine. This combination also provides deep sedation. This study is comparable with our study. Singh J et al¹⁷ conducted a study on comparison of ketamine plus bupivacaine, bupivacaine plus normal saline and bupivacaine plus clonidine and demonstrated that combination of

clonidine plus bupivacaine provides longer duration of analgesia.

When we concern about the dose of ketamine in bupivacaine 0.25% Panjabi et al¹⁸ conducted a study and recommended that 0.5mg/kg is a standard dose of ketamine when added in bupivacaine for better analgesic effect and sedation of patients. He compared 0.5mg/kg ketamine with 0.25 mg/kg ketamine and side effects also limited. In a study Nasr et al¹⁹ reported that use of 0.5 mg/kg ketamine in 0.25% bupivacaine provides sufficient effect of duration of analgesia.

In a study Findlow D et al²⁰ compare the bupivacaine and combination of bupivacaine with ketamine and reported that combination of ketamine plus bupivacaine provides longer duration of analgesia about 20% greater time of analgesic effect. Results of this study are also identical to our study that for purpose of duration of analgesia combination of bupivacaine and ketamine 0.5mg/kg is an ideal choice.

CONCLUSION

Results of our study reveal that combination of Ketamine 0.5 mg/kg and bupivacaine 0.25% in a dose of 1 ml/kg prolong the duration of postoperative analgesia to a significant range in comparison with bupivacaine 25% of 1 ml/kg alone.

Author's Contribution:

Concept & Design of Study: Muhammad Nasir
 Drafting: Aatir Fayyaz
 Data Analysis: Munir Ahmad
 Revisiting Critically: Muhammad Nasir, Aatir Fayyaz
 Final Approval of version: Muhammad Nasir

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Frequency of Hepatitis B and C in Children with Hemophilia

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ABSTRACT

Objective: To determine the frequency of hepatitis B and C in children with hemophilia

Study Design: Cross Sectional Study

Place and Duration of Study: This study was conducted at the Department of Pediatric Medicine, The Children's Hospital Lahore from 03-08-2017 to 28-02-2018.

Materials and Methods: A total of 90 children aged between 6 months and 12 years with were selected after taking informed consent from parents. Bio data was entered in a predesigned structured performa. Test for hepatitis B and hepatitis C were sent. All information and test results were kept confidential. Data analysis was done using SPSS version 16.

Results: Results of our study showed that most of patients i.e. 54% were between ages of 37-72 months and all of them were male. It was also seen that most of the patients belonged to poor socio-economic status i.e. 53.3%. Regarding hepatitis prevalence, hepatitis B was present in 4 (4.4%) patients whereas hepatitis C was positive in 8 (8.9%) patients. Stratification by age, duration of disease and economic status did not reveal any significant differences.

Conclusion: Hepatitis B was found to be positive in 4.4% whereas hepatitis C was found in 8.9% of hemophilic patients.

Key Words: Hemophilia, Hepatitis B, Hepatitis C.

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INTRODUCTION

Hemophilia is an X linked hereditary bleeding disease characterized by deficiency of factor VIII (HA) or factor IX (HB) which is also known as Christmas disease^{1,2}. The clinical manifestations of hemophilia correlate with the level of factor VIII and IX. Bleeding - spontaneous or secondary to trauma or surgery- may occur at any site of the body but the most common sites are the joints(80%) whereas bleeding in the CNS is the most serious site¹⁻⁴. Treatment is with concentrated factor VIII or IX depending on the type of hemophilia although some patients may need transfusion with whole blood when they develop massive hemorrhage¹⁻⁵. Patients with hemophilia and other coagulopathies treated with multiple blood transfusions and unheated clotting factor concentrates, including factors I, VIII, and IX have a high risk of acquiring hepatitis C, hepatitis B, and other viral infections.

Although viral inactivation and the use of recombinant technologies and the administration of HBV vaccine has significantly eliminated viral transmission via blood product transfusion, still HBV, HCV and HIV infections remain important causes of morbidity and mortality in countries where these technologies are unavailable¹⁻⁷. Various studies among multi-transfused haemophilia patients demonstrated a wide range of prevalence of transfusion-transmitted infections.

Studies have found prevalence of HbsAg in hemophilia patients ranging from 0.52% to 4.9% while that of anti-HCV 8.5% to 54%¹⁻⁷. This difference in prevalence highlight the importance of local control and sociodemographics highlighting the importance of preventive strategies in these high risk patients. Furthermore, with this variation and considering that most of the studies were from database having retrospective design, it is necessary to carry out a study prospectively with proper sample size¹⁻⁷. Study by Shamsdin SA² et al showed prevalence of HbsAg and anti HCV in hemophiliacs to be 1.4% and 8.9% respectively. Study from Iraq By Alhmeed WGA³ et al found prevalence of hepatitis B & C to be 0.52% and 9.9% respectively. Another study from Iran⁴, however, found no case of hepatitis B in screened patients and 8.9% positivity for hepatitis C. In sharp contrast, another study from Iran found prevalence of hepatitis B to be 1.1% and hepatitis C to be alarmingly high 54%. The study from Sudan⁵ on 62 children found 1 patient to be positive for hepatitis B and 8 for hepatitis C. Study by Sharifi-Mood B⁶ et al showed frequency of

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hepatitis B and C to be 4.9% and 29.6% respectively. This data highlights the need for undertaking a prospective comprehensive study for determining the frequency of Hepatitis B and C among children with hemophilia as there is no local study so as to raise awareness and potentially reduce transmission in these children.

MATERIALS AND METHODS

This was a Cross Sectional Study. This study was conducted in the Department of Pediatric Medicine, The Children's Hospital Lahore. The Duration of the study was Six month (03-08-2017 to 28-02-2018). Sample size was calculated to be 90 with 95% confidence interval, 6% margin of error and 8.9%⁴ expected percentage of hepatitis C in patients with hemophilia. The Sampling technique was non probability consecutive sampling

All children of both genders with hemophilia as per operational definition aged 6 months to 12 years who had been transfused more than 2 units of blood or clotting factors upto the time they were screened were included.

Children with evidence of HbsAg or anti HCV positivity as per medical record before start of transfusions. Children born to mother positive for hepatitis B per medical record. Children who underwent any surgical intervention per medical record Children with history of hemodialysis or peritoneal dialysis as per medical record were excluded

Statistical analysis was done using Statistical Package for Social Sciences (SPSS) version 16. Qualitative data like gender, economic status, number of patients with hepatitis B and C were presented as frequencies and percentages. Quantitative data i.e., age, duration of disease were presented as means and standard deviations. Data was stratified for age, gender, economic status, duration of disease to address the effect modifier. Pot-stratification chi-square test was applied to check the significance with p value ≤ 0.05 as significant.

RESULTS

In this study, total 90 patients were included. Fifty four percent patients were between the ages of 37-72 months while 46% were between 6-36 months. Mean age of the patients was 39.40 with a standard deviation of 3.78 months. In our study, all patients were male. Regarding duration of disease, 52.2% of the patients had disease ≤ 30 months while 47.7% patients had disease > 30 months. Mean duration of disease was 32.50 $\pm$ 2.65 months.

Regarding economic status, most of the patients i.e. 53.3% had low economic status. About 36% patients belonged to mediocre families while 11.1% patients had high economic status. Hepatitis C was found in 8.9% of hemophilic patients whereas hepatitis B was found to

be positive in 4.4% of hemophilic patients. About 86% patients were having neither hepatitis B nor hepatitis C. When we stratified out data according to age of patients, duration of disease and economic status did not reveal any significant differences. P value was greater than 0.05 in all cases.

Table No. 1: Age Distribution (n=90)

Age (in months)	No. of patients	%
6-36	41	46.0%
37-72	49	54.0%
Total	90	100%

Mean $\pm$ SD: 39.40 $\pm$ 3.78 months

Table No. 2: Duration of Disease (n=90)

Duration (in months)	No. of patients	%
≥ 30 months	47	52.2%
> 30 months	43	47.7%
Total	90	100%

Mean $\pm$ SD: 32.50 $\pm$ 2.65 months

Table No. 3: Economic Status (n=90)

Economic Status	No. of patients	%
Low	48	53.3%
Middle	32	35.6%
High	10	11.1%
Total	90	100.0%

Table No. 4: Frequency of Hepatitis B & C (n=90)

Hepatitis	No. of patients	%
B	4	4.4%
C	8	8.9%
Nil	78	86.7%
Total	90	100.0%

Table No. 5: Stratification by Age (n=90)

Age Years	Hepatitis B		Hepatitis C		Total
	Yes	No	Yes	No	
6-36	2	39	3	38	41
37-72	2	47	5	44	49
P value	0.992		0.723		

Table No. 6: Stratification by duration of disease (n=90)

Duration Months	Hepatitis B		Hepatitis C		Total
	Yes	No	Yes	No	
≤ 30 months	2	45	5	42	47
> 30 months	2	41	3	40	43
P value	0.927		0.8112		

Table No. 7: Stratification by economic status(n=90)

Economic Status	Hepatitis B		Hepatitis C		Total
	Yes	No	Yes	No	
Lower	2	46	4	44	48
Middle	1	31	3	29	32
High	1	9	1	9	10
P value	0.825		0.735		

DISCUSSION

Hemophilia is an X linked hereditary bleeding disease characterized by deficiency of factor VIII or factor IX. Bleeding occurs spontaneously or secondary to some trauma or surgery. Treatment of bleeding in such patients include concentrated factor VIII or IX depending on the type of hemophilia type. Some patients may need transfusion with whole blood when they develop massive hemorrhage. Such patients with hemophilia when treated with multiple blood transfusions and unheated clotting factor concentrates have a high risk of acquiring hepatitis C, hepatitis B, and other viral infections. Although viral inactivation and the use of recombinant technologies and the administration of HBV vaccine has significantly eliminated viral transmission via blood product transfusion, still HBV, HCV and HIV infections remain important causes of morbidity and mortality in countries where these technologies are unavailable. The present study "frequency of hepatitis B and C in children with hemophilia" was conducted at Department of Pediatric Medicine, Children Hospital Lahore, to establish baseline data for hepatitis frequency in patients of hemophilia. It will also help pediatricians to reduce its transmission and severity by vaccination and early treatment.

Results of our study showed that most of patients i.e. 54% were between ages of 37-72 months and majority (90%) was of male patients. It was also seen that most of the patients belonged to poor socio-economic status i.e. 53.3%. Regarding hepatitis prevalence, hepatitis B was present in 4 (4.4%) patients whereas hepatitis C was positive in 8 (8.9%) patients. These results were comparable with the results of other studies. In a study conducted at Iran, Shamsdin SA and his colleagues showed prevalence of HbsAg and anti HCV in hemophiliacs to be 1.4% and 8.9% respectively². In another study conducted in Iraq by Alhmeed WGA et al, hepatitis B & C prevalence was found to be 0.52% and 9.9% respectively in hemophilic patients³.

Some studies showed quite surprising results. In one study conducted in Iran, it was observed that there were no hepatitis B cases screened patients. In this study, however, hepatitis C was found in 8.57% patients⁴. Similar results were also obtained in a study conducted at Sudan. In this study, a total of 62 hemophilic children participated and it was found that only 1 patient was positive for hepatitis B and 8 for hepatitis C⁵. These results were strikingly different from the results of other studies. The reason for low prevalence was age of the patients and number of transfusion of blood products. In childhood and early teens, number of transfusions is low which explains low prevalence of hepatitis B and C.

In sharp contrast to this, one study from Iran found prevalence of hepatitis B to be 1.1% and hepatitis C to

be alarmingly high 54% i.e. very high prevalence of hepatitis C among hemophiliacs⁴. Similar high prevalence results were also obtained in a study by Sharifi-Mood B et al who showed frequency of hepatitis B and C to be 4.9% and 29.6% respectively⁶. In his study, Vinelli, et al showed HBsAg positivity in 1.6% of hemophilics and anti-HBc positivity in 26.9%⁸. Surprisingly very high prevalence of hepatitis C was also observed in a study conducted in Iran by Nassiri Toosi, et al., who showed hepatitis C seropositivity in 83.3% of hemophilic patients⁹. In another study conducted by Alavian, et al., 60.2% were found to be anti-HCV Ab positive¹⁰. Similar results were also obtained by Borhany, et al., who showed HCV positivity in 54.4% and 1.73% positivity for hepatitis C¹¹. High prevalence of hepatitis C was also noted by Windyga et al., where its prevalence was 77.3% whereas HBs Ag was positive in 8.7% of them¹². These contrary results were due to number of factors. For example. Patients of all ages were included in some of these studies. With the advancing age, number of blood transfusions increases which in turn increases the risk for transmission of hepatitis B and C. Furthermore, prevalence also depends on number of transfusions. Increased requirement of blood product replacement increases transmission chances for hepatitis B and C.

Similarly, reason behind low hepatitis B prevalence as compared to hepatitis C was the introduction of hepatitis B vaccination. Hemophilic patients undergo hepatitis B vaccination, so, they have less chances of contracting hepatitis B. As no such vaccine is available for hepatitis C, so, its prevalence is high.

CONCLUSION

Hepatitis B was found to be positive in 4.4% whereas hepatitis C was found in 8.9% of hemophilic patients.

Author's Contribution:

Concept & Design of Study:	Hafiz Sajid Khan
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Revisiting Critically:	Hafiz Sajid Khan, Muhammad Obaid ur Rehamn
Final Approval of version:	Hafiz Sajid Khan

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Experience of End-to-Side and Side-to-Side Techniques of Arterio Venous Fistula Formation in End Stage Kidney Diseases

Muhammad Ali Suhail¹, Qamar Raza Brohi², Habib ur Rehman Khan Toor² and Amir Ghani¹

ABSTRACT

Objective: To determine the success rates of end-to-side and side-to-side techniques of Arterio Venous fistula formation for end stage kidney diseases.

Study Design: Descriptive study

Place and Duration of Study: This study was conducted at the Department of Urology, PUMHS, Nawabshah from March 2014 to February 2016.

Materials and Methods: Cases of end stage kidney diseases were selected from outdoor and referred cases from other health facilities on inclusion and exclusion criteria. All cases were randomly divided in two equal size groups A and B. In group A end to side technique was used and in group B side to side technique was used for arterio venous fistula (AVF) formation for hemodialysis in patients with end stage kidney diseases. All AVF was made surgically under local anesthesia at non dominant upper limb near the wrist. Success of each technique was established by determining the postoperative patency of AVF in terms of palpable thrill and flow of blood with the help of Doppler ultrasound. Data was analyzed and success rate of each technique was calculated and any difference in the results of both techniques was noted.

Results: Mean age of the patients was 44 years, SD± 7 and a range of 19 to 75 years. Male to female ratio was 5:3. In group A out of 45 cases of end to side fistula, 38 cases were found patent showing a success rate of 84%. In group B out of 45 case of side to side fistula, 36 cases were found patent showing a success rate of 80%.

Conclusion: The success rates of end to side and side to side technique of AVF are 84% and 80% respectively, reflecting no great difference between the results of these two techniques of arterio venous fistula formation for end stage kidney diseases.

Key Words: Arteriovenous Fistula, End to side Anastomosis, Side to Side Anastomosis

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INTRODUCTION

In the developed part of the world, chronic kidney diseases are the 9th leading cause of death¹. Chronic kidney diseases (CKD) encompass all degrees of long standing renal diseases whereas end stage kidney disease stands at extreme of its terminal end. In order to sustain life, end stage kidney disease requires renal replacement therapy in the form of either renal transplantation or dialysis. In 1854 Graham introduced dialysis across a semi-permeable membrane². Hass performed the first hemodialysis in human for renal failure³. Due to high cost, lack of suitable donors, shortage of well equipped health care facilities with proper teams and lack of social awareness, hemodialysis still remains a very effective tool of

management for the patients of end stage kidney diseases. At present hemodialysis and peritoneal dialysis are the two popular methods with their own indications. The economic burden of dialysis program has been increasing worldwide⁴. The purpose of dialysis treatment is to maintain human body homeostasis by removing waste material and maintaining hydration status at optimum. A certain flow of blood is required in a vein that contains arterialized blood through an established arterio venous fistulae and connected with a hemodialysis unit. Patients of end stage kidney diseases undergo dialysis usually in an indoor, outdoor and less frequently at home setup^{5, 6}. For hemodialysis a connecting channel is always needed between the dialysis unit and the patient's vascular flow. Various types of connecting routes can be established but few of them are more common including arterio-venous fistulae (AVF), synthetic graft and intravenous catheter. Among these three routes, arterio-venous fistulae AVF are most common, although all these require a minor surgical expertise⁷. Well evaluated vascular status and good collaterals are the key factors in selecting the site for surgically creating an AVF⁸. Snuff box is the most frequently

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selected chosen site for AVF⁹. Anti cubital fossa is another recommended site for establishing an AVF¹⁰. Preferably AVF are made in the non dominant upper limb by either end to side or side to side techniques between the radial artery and the cephalic vein near the wrist. Both these techniques can differ in their success rates in terms of patency and blood flow, therefore this study was conducted to determine the success rates of these two techniques of end to side or side to side Arterio-venous fistulae formation and in patients of end stage kidney diseases.

MATERIALS AND METHODS

This study was conducted from March 2014 to February 2016 at departments of urology and general surgery, Peoples University of Medical and health sciences Hospital Nawabshah. Cases of end stage kidney diseases were selected from outdoor and referred cases from other health facilities. Only those cases were selected who were the candidates for long term hemodialysis treatment and willing for surgically made arterio venous fistulae formation. All cases were underwent detailed history and clinical examination including specifically Allen test. Patients were excluded from the study on the basis of having positive Allen test, coagulopathy, malignant hypertension, severe cardiac diseases and past failure of AV fistula formation. All cases were randomly divided into two equal groups A and B. In group A all patient were underwent end to side AV fistula formation while in group B all cases underwent side to side AV fistula formation. Local anesthesia was used in all cases and informed consent was taken. In both groups AV fistulae were formed between radial artery and cephalic vein near the wrist. Post operative patency and success was checked by palpating thrill and measuring the blood flow by Doppler study in the early post operative period and then subsequently by frequent long term follow ups at least for 6 months. In the two groups AV fistulae were considered patent or successful only when both palpable thrill and a flow of blood more than 300 ml per minute were found post operatively and persist for long term at least up to six month follow up.

RESULTS

This 24 month study included 90 cases of end stage kidney diseases. Mean age of the patients was 44 years, SD± 7 and a range of 19 to 75 years. Male to female ratio was 5:3. All cases were divided randomly in two equal groups A & B, each comprising 45 cases. In group A end to side arterio venous anastomosis was made and in group B side to side arterio venous anastomosis was made. Patency of the fistulas anastomosis was established by palpating the thrill, auscultating the machinery murmur and determining the blood flow. In group A out of 45 cases of end to side fistula, 38 cases were found patent showing a success

rate of 84%. In group B out of 45 case of side to side fistula, 36 cases were found patent showing a success rate of 80%.

DISCUSSION

Our study included 90 cases of end stage kidney diseases requiring long term hemodialysis. Mean age of the cases was 44 years, that is very similar to many national and international studies^{11,12}. In the recent modern era of advancements and technologies hemodialysis still remains a very effective tool of management for the patients of end stage kidney diseases in spite of tremendous amount of progresses in the field of kidney transplantation. This is mainly due to high cost, lack of suitable donors, shortage of well equipped health care facilities with proper teams and lack of social awareness. For long term hemodialysis in the cases end stage kidney diseases a competent, durable and well functioning vascular access is always needed. Although due to the better patency and fewer complications, arterio venous fistulous access is considered superior to other two techniques of synthetic graft and double lumen tunneled cuffed catheter but still there is a need of search for even best results^{13, 14}. Present study shows success rates of 84% in end to side group of AVF and a success rate of 80% in side to side group of arterio venous fistulous anastomosis that is very much comparable to various studies¹⁵⁻¹⁸. Works of Murphy and Zeebregts show patency rate of less than 80%^{19,20}. The slightly higher rate of patency in our study could reflect the relatively smaller sample size but there is no great differences in the success rate between these two techniques end to side and side to side arterio vascular fistulous anastomosis made for hemodialysis in end stage kidney diseases.

CONCLUSION

The success rates of end to side and side to side technique of AVF are 84% and 80% respectively, reflecting there is no any great difference between the results of these two techniques of arterio venous fistula formation for end stage kidney diseases.

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An Experience of Primary Common Bile Duct Closure after Open Choledochotomy as Compared to T-Tube Closure

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ABSTRACT

Objective: To evaluate the short and long term benefits and harms of the primary closure without and with T-tube drainage after open choledochotomy.

Study Design: Prospective, comparative randomized control study

Place and Duration of Study: This study was conducted at the Surgical Unit III of Peoples University of Medical and Health Sciences for women and Jinnah Medical Center Nawabshah from June 2013 to July 2017..

Materials and Methods: Seventy patients were randomly selected for the study, 32 underwent primary common bile duct closure (Group A) and in others T-Tube (Group B) was placed. Patients demographic, intraoperative findings, postoperative stay, complications and long term follow-up data were recorded and compared.

Results: Seventy patients were randomly selected in the study. The age range of patients was 22 to 75 years. In primary closure group A (n=32) four (12.5%) males and 28 (87.5%) females. In 2 patient (6.3%) bile leakage noted which subsided without any biliary peritonitis, as compared to the T-tube group B (n=38) six male and 32 females, five patients (13.5%) resulted bile leakage. No one patient had a retained stone in both groups and no jaundice in group A but postoperative jaundice was seen in two patients (5.3%) group B because of CBD blockage. The postoperative hospital stay in group A was 4.5±1.2 days and in B was 12.5±1.5 days. The total cost of treatment in group B was Rs/60000 ± 12000 (US\$ 500 ± 100) and group A was Rs/35000±5000 (USD 200±50). Follow up time was six months.

Conclusion: The primary closure might be much effective and safe as compared to T-tube drainage after open choledochotomy and less postoperative complications.

Key Words: open choledochotomy, choledocholithiasis, primary closure, T-tube drainage

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INTRODUCTION

Cholelithiasis develops in about 03–15% of patients with gallbladder stones and literature suggests that common bile duct (CBD) stones occur in about 7–15% of patients who are undergoing cholecystectomy¹. The surgical technique to remove stones from the common bile duct (CBD) depends on anatomical characteristics, local experience, and size, location and number of stones. Most surgeons consider choledochotomy as an alternative to failed laproscopic exploration, and some use it exclusively. Commonly CBD is closed with T-tube drainage after choledochotomy, is associated with 11.3-27.5 % morbidity.

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After choledochotomy and removing of stones from the common bile duct (CBD), and placing T-tube is suggested to be a classical method since the end of the 19th century. T-tube is supposed to drain bile outside the body to avoid bile peritonitis, and supposedly a route to evaluate and remove the retained CBD stones, and to reduce the chances of CBD stricture formation. There is debate by placing T-tube that it causes bile peritonitis before and after its removal, discomfort and prolonged out-patient care^{2,5}. In addition, having bile drainage in place for at least 3 weeks causes significant discomfort in patients and delays their return to work.^{6,8} The principal treatment of open exploration of the bile duct was for several decades. The open procedure is still performed in developing countries by surgeons because of non-availability of minimally invasive techniques like ERCP⁹. Due to the lack of experienced endoscopists at secondary care hospitals most of patients need to be transferred to a tertiary centers for endoscopic diagnosis and treatment, which increases cost and patient discomfort.⁸

When it comes to laparoscopic choledochotomy, albeit recent developments in instruments, due to technical demanding of choledochotomy and prolonged operation time, mostly in putting up the T-tube and closing the

incision wound securely, there are limitations in adopting the procedure. Primary closure of the CBD after exploration is not new therefore open surgery is still a treatment of choice in many hospitals. Primary duct closure after open CBD exploration was first described by Halstead as early as 1917. Since then, the debate between primary closure and T-tube drainage continued even in the era of laparoscopic surgery. In the past few decades, numerous studies comparing primary with T-tube were published and revealed the feasibility and safety of primary closure^{9,11}. Many papers are reported by different authors, which support the direct closure of the duct immediately after exploration.^{7,9}, During surgery direct visualization with choledoscope of the CBD is possible and retained stones are not a problem in current era. In our setup, open CBD exploration is still the treatment of choice for CBD stones. In our study, we focused to compare short-term results of primary closure of CBD and T-tube drainage, and to assess the benefits of primary closure of CBD at a government and a private hospital in a developing country like Pakistan.

MATERIALS AND METHODS

This study was conducted at Surgical Unit III of Peoples University of Medical and Health Sciences for Women Nawabshah and Jinnah Medical Center Nawabshah. Seventy patients were randomly selected for the study, from June 2013 to July 2017. The patients were investigated with, complete blood counts, liver function tests, coagulation profile. The criteria for choledochotomy were (1) CBD stones were confirmed by preoperative MRCP or CT with no intrahepatic bile duct stone; (2) The diameter of CBD is more than 0.8 cm; (3) No obvious inflammatory changes of CBD are detected intraoperatively; (4) No. of stones is less than 8; (5) obstructive jaundice, (6) CBD stones suggested by ultrasound, and (7) the presence of stones in the CBD palpated during open cholecystectomy. Patients with pancreatitis, cholangitis and cholangiocarcinoma were excluded.

Prophylactic antibiotics were used at the time of induction of anaesthesia. The CBD was explored through a supraduodenal longitudinal incision. Stones were removed and patency of CBD was confirmed by flushing of saline through 8FR feeding tube. Then CBD was closed with 4/0 Vicryl continuous sutures without placing T-tube in 32 patients and T-tube in 38 patients randomly selected. A sub hepatic drain was kept in all patients. The primary closure group was discharged on average 4th postoperative day after confirming no leakage and drain was removed. T-tube cholangiography was done on the 10th postoperative day in all T-tube drained patients; T-tube was removed on 12th postoperative day, after confirmation by free flow of dye into duodenum. Comparison of postoperative complications, hospital stay and the total

cost of treatment of both groups was done. The data was analyzed in statistical program SPSS version 11.0. Fisher's exact test or the Chi-square test was used for categorical variables to calculate frequencies and percentages between the groups. The Student's t-test was used to compare the means of the continuous variables between the groups. All the parameters were calculated on 95% confidence interval. If the value of $p \leq 0.05$ it was considered statistically significant.

RESULTS

CBD was explored in 70 patients, out of which primary closure was done in 32 and T-tube was placed in 38 patients after stone removal. The mean age of group A patients was 50.0 ± 17 years (median, 49 years; range, 22–75 years) and group B patients was 43 ± 15 years (median, 41.0 years; range, 23–75 years). Four males (12.5%) and 28 females (87.5%) group A, and six males (15.7%) and 32 females (84.2%) group B (Table 1). Biliary colic was the most common presentation in both groups 22 (68.75%) and 32 (84.21%) respectively. Acute cholecystitis and jaundice were other presentations, nearly of same frequency in both groups. Twenty one patients had comorbidities like diabetes mellitus and hypertension 09 (28.12%) and 13 (34.21%) respectively in both groups. 18 patients (56.25%) in group A had concomitant cholelithiasis and 25 (65.7%) in group B has reported on ultrasonography.

LFT were compared between two groups. The level of serum glutamic pyruvic transaminase (SGPT) was significantly different between the two groups. Preoperative ultrasonography revealed the size of CBD and number of CBD stones, which was then confirmed during the operation. The mean diameter of CBD was $1.5 \text{ cm} \pm 0.47 \text{ cm}$ (median, 1.51 cm; range, 1.3–2.5 cm) in group A and $1.52 \pm 0.54 \text{ cm}$ (median, 1.49 cm; range, 0.7–2.8 cm) in group B. The maximum number of stones (46) was noted in group B (Table 1).

Thirty patients in group A did not suffer any complication. Two patients had a bile leakage that subsided on the fourth postoperative day and no biliary peritonitis. The total complication rate in group A was 6.3%

In group B, seven patients had biliary complication, (15.78%). After removal of T-tube bile leakage noted in five (13.15%) aspirated under ultrasound guidance. In these patients, the T-tube was removed on the fourteenth postoperative day. Postoperative jaundice noted in two because of a blockage T-tube. The jaundice subsided after removal of T-tube. There was no any recurrence of CBD stones up to 6 months follow up and postoperative ultrasonography was almost normal (Table 2).

The mean postoperative hospital stay in group A was 4.5 ± 1.2 days (median, 4 days; range, 3.5–6.5 days), compared to group B was 12.5 ± 1.5 (median, 14 days; range, 6–17 days). The total cost of treatment in group

B was $Rs/ = 60000 \pm 12000s \pm$ (US $\neq$ 500 $\pm$ 100) and group A was $Rs/ = 35000 \pm 5000$ (US $\neq$ 200 $\pm$ 50). The mean follow-up duration in group A was 5.5 $\pm$ 0.4

months (median, 5.0 months; range, (3–7 months) and in group B it was 5.6 $\pm$ 0.4 months (median, 6.0 months; range, (3.5–5.5 months) (Table 3).

Table No 1: Demographic Characteristics of patients Group n=70

Variable	Primary closure (A) n= 32	Median	Range Min-Max	T-tube Drain (B) n=38	Median	Range Min-Max	p value
Age years	50.0 $\pm$ 17.0	51.5	22-75 +/- 13.9	43 $\pm$ 15	41	23-75	NS
Gender							Ns
Male	4 (12.5%)			6 (15.7%)			
Female	28 (87.5%)			32 (84.2%)			
Symptoms							
Biliary colic	22 (68.75%)			32 (84.21%)			Ns
Acute cholecystitis	15 (46.87%)			15 (39.47%)			Ns
Jaundice	20 (62.5%)			26 (68.42%)			Ns
Co-morbidities	09 (28.12%)			13 (34.21%)			Ns
Preoperative LFT							
Total Bilirubin (mg%)	2.5 $\pm$ 2.01	2.0	0-5	2.1 +/- 1.85	1.0	0-8	Ns
SGPT (U/L)	150.36 $\pm$ 149.09	95.0	18-599	54.42 $\pm$ 61	36.0	7-262	0.01
Alkaline Phosphatase (U/l)	579 +/- 326.30	724.0	100.0-950	4.1 $\pm$ 2.81	492.0	135-850	Ns
Number of CBD stones	3.1 $\pm$ 1.60	2.5	2-7	46.0 $\pm$ 10	4.0	1-10	0.03
CBD Diameter (cm)	1.53 $\pm$ 0.4721	1.512.0	1.3-2.5	1.52 $\pm$ 0.5458	1.49	0.7-2.8	Ns

Results are expressed as mean +/- standard deviation, median, and range. CBD=Common Bile Duct , Ns= Not Significant

Table No 2: Postoperative Complications (n=70)

	Primary Closure (n=32)	T-tube drainage (n=38)	p value
Postoperative bile leakage	2 (6.3%)	5 (13.15%)	Ns
Jaundice	0	2 (5.3%)	Ns
Retained stones	0	0	--
Recurrence of CBD Stones	0	0	--

Results are expressed as number and percentage, CBD=Common Bile Duct, Ns= not significant

Table No. 3: Hospital Stay , cost of treatment, and follow up duration

Variable	Primary closure (n= 32)	Median	Range Min-Max	T-tube Drain n=38	Median	Range Min-Max	p value
Hospital Stay (days)	4.5 $\pm$ 1.2	4.0	3.5-6.5	12.5 $\pm$ 1.5	14.0	6-17	0.008
Cost of treatment PKR/US $\neq$	35000 $\pm$ 5000 200 $\pm$ 50.0 US $\neq$	150.5 US $\neq$	180-300 US $\neq$	60000 $\pm$ 12000 500 $\pm$ 100 US $\neq$	600 US $\neq$	300-712.5	<0.001
Followup duration months	5.5 $\pm$ 0.4	5.0	3-7	5.6 $\pm$ 0.4	6.0	3.5-5.5	NS

Results are expressed as mean +/- Standard Deviation, median and range

DISCUSSION

In the era of mini-invasive surgery, laparoscopic cholecystectomy (LC) has been the standard therapy for symptomatic gallstones. However, debate continues regarding the best treatment for managing cholecystocholedocholithiasis, and a consensus has not been reached¹². In clinical practice, three major procedures, LC + endoscopic retrograde cholangiopancreatography (ERCP) endoscopic sphincterotomy, endoscopic

papillary balloon dilation, LC+ laparoscopic transcystic common bile duct exploration were applied for treatment of cholecystocholedocholithiasis.

The role of ERCP in diagnosis of CBD stones has been replaced by MRCP, however, it is widely used to remove CBD stones in one-stage or staged procedures. EST is associated with serious short-term complications, including bleeding, post-ERCP pancreatitis (PEP), and perforation of the digestive tract. In addition, EST may increase the incidence of

long-term complications such as biliary infection due to the dysfunction of the Oddi's sphincter after the procedure^{13,14,15}. In order to preserve (at least partly) the function of the sphincter of Oddi and avoid post-EST bleeding, Now a days, open laparotomy for CBD exploration may still be the choice in some hospitals in developing countries.

Symptomatic gallstone disease is a very common indication for abdominal surgery.¹⁶, and cholecystectomy and CBD stones were removed in a single procedure with morbidity below 15% and mortality below 1%.¹⁷

We ensured the duct clearance by choledocoscopy following choledochotomy. After exploration of CBD T-tube drain has been a standard practice.²⁴ The risk of complications with use of a T-tube is higher, there are many reports of complications with T-tube.^{19,20,21}

We faced five cases of bile leakage in group B(11%), and two cases among the 32 patients (6.2%) in group A. On the other hand, in group A has no bile leakage as reported by other authors.¹⁵ There was a significant difference in postoperative stay and the total cost of treatment between two groups. The group A remained in the hospital for a shorter period where as group B remained for longer duration and there was the additional cost of postoperative cholangiography.

There have been reports of intraperitoneal leakage with subsequent biliary peritonitis.^{9,19,22} but in our study there were no major complications and mortality. This may be because we used choledochoscopy and did not probe the distal end of the CBD. The risk of biliary leakage was reduced by these measures. In developing countries, this difference in complications and expenditure has a major impact on public health. Literature⁷ suggests that early discharge and early return to work, has effect on the expenses of the patient. Other authors reported similar results^{23,24} except in Japan where the number of hospital admission days was higher.²⁵

CONCLUSION

In Developing countries like Pakistan due to deficiency of facilities and endoscopic expertise in remote areas, & in secondary care hospitals, open choledochotomy, with primary closure of the CBD rather than placing T-tube is safe and may be performed in selected patients with improved patient care. It has been concluded that, the primary closure might be much cost effective as the T-tube drainage after open choledochotomy with shorter hospital stay and less complications.

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Efficacy of CT Scan for Assessment of Headache

Muhammad Asghar Bhatti, Abdul Qayyum and Awais Hussain Shah

ABSTRACT

Objective: To determine the efficacy of CT scan for assessment of Headache.

Study Design: Prospective / cross sectional study

Place and Duration of Study: This study was conducted at the Radiology Department of RMDC Lahore from January 2018 to June 2018.

Materials and Methods: This study included 136 patients with headache. All the patients had CT scan to find out the frequency of pathologies. Data was collected on a specially designed Performa and analyzed by using SPSS.

Results: The mean age of the patients was 44.80 ± 23.25 years [range 20 – 70]. There were 58 (42.6%) female patients and 78 (57.4%) male patient in the study. CT scan could identify the lesion among 11 (8%) patients, while in rest of 125 (92%) patients; CT scan did not identify any pathology. Sinusitis was the most common pathology detected among 4 (36.4%) patients followed by stroke seen among 3 (27.2%) patients.

Conclusion: The diagnostic yield of CT scan in detecting lesion among patients with headache is low and radiation exposure is more.

Key Words: Computed tomographic neuroimaging, isolated headache, Assessment

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INTRODUCTION

Headaches is most common complaint in the primary health care se, as well as in the department of emergency, with a lifetime prevalence of headache is high as 90%.¹ This disabling symptom is estimated to be actively affecting 46% of the global adult population as a part of headache disorder, with 3-5% of the population experienced with chronic daily headache.^{2,3,4}

By comparison, the frequency of pathology presenting with headache is low. Yearly incidence of brain tumors in the US is 46 per 100,000, for subarachnoid hemorrhage (SAH), 9 per 100,000, for Arteriovenous malformations (AVMs) is about one-tenth as frequent as saccular aneurysms. Only a subset of these patients presents with isolated headache. In a retrospective review of the presentation of 111 brain tumors, headache was a symptom in 48%, equally for primary and metastatic brain tumors.^{5,6,7}

There is an emphasis on early detection of cause of headache because it may be the only initial presentation of serious illness (brain tumors)^{8,9,10,11} or may be caused by some treatable causes, which may lead to significant morbidity or mortality if treatment is delayed (chronic subdural hematoma in elderly).¹²

There is a trend of using computed tomography (CT) scan of brain as an initial diagnostic modality for evaluation of headache.^{13,14} which may be attributed to increasing numbers of brain imaging centers, increasing patient demand or fear of missing serious illness (subdural hematoma or suspected brain tumors) by physicians.^{15,16} CT scan has been found very useful in detecting the cause of headache in many disorders (82% patients yielded positive findings in HIV patients and 47 % among patients with 'thunderclap headache' when evaluated for headache).^{17,18}

Use of CT scan in evaluation of patients with isolated headache has shown a variable yield (0.4%, 1% and 2.4% in different studies) although lower than when used for other pathologies, despite a high referral rate (38%) for isolated headache.^{19,20} In most of the developing countries including Pakistan, information about usefulness of CT scan in evaluation of patients with isolated headache are lacking. Therefore, I want to conduct this study to determine that how much is the numbers of pathologies will a CT scan brain find out among the patients referred to radiology department of a teaching hospital of Pakistan. This will help us in understanding the usefulness of the technique.

MATERIALS AND METHODS

Prospective cross sectional study carried in Radiology department of RMDC Lahore from January 2018 to June 2018 including 136 patients with headache. All the patients had CT scan to find out the frequency of pathologies. Data was collected on a specially designed Performa and analyzed by using SPSS 20.

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Adding criteria:

- Gender: both male and female
- Age: 20-45 years
- Isolated headache of more than 3 months duration nor responding to treatment

Exclusion criteria:

- Previous neurosurgical procedure
- History of seizures
- Recent head trauma (less than 3 months before evaluation)
- Prior neurological abnormalities
- History of cancer
- Patients who do not gave consent for participation

RESULTS

Regarding Age: Mean age was 44.80 ± 23.25 [array 20 – 70]. There were 37 (27.2%) of 20 – 30 years, 32 (23.5%) were 31 – 40 years, 27 (19.9%) patients of age range of 41 – 50 years, 20 (14.7%) of age range of 51 – 60 years and 20 (14.7%) patients in the age range of 61 – 70 years. (Table 1)

Distribution of patients by sex: 58 (42.6%) female and 78 (57.4%) male patient in the study.

Distribution of patients by identification of pathology by CT scan heads: There were 11 (8%) patients in whom CT scan could identify the pathology, while in rest of 125 (92%) patients; T scan did not identify any pathology.

Distribution of patients by CT scan findings: There were 11 patients in whom pathology was identified by CT scan. Sinusitis was observed among 4 (36%) patients, space occupying lesions among 2 (18.2%) patients, hemorrhage among 1 (9.1%) patients, chronic subdural hematoma among 1 (9.1%) patients, stroke among 3 (27.2%) patients and none of the patients had tumor or vascular malformation. (Table 2)

Cross tabulation of patients by age with CT scan findings for detection of pathology: Hemorrhage was seen in 1 (9.1%) in age group 41 – 50 years. All of 3 (27.2%) patients with stroke were from age group 61 – 70 years. Chronic subdural hematoma was seen in 01

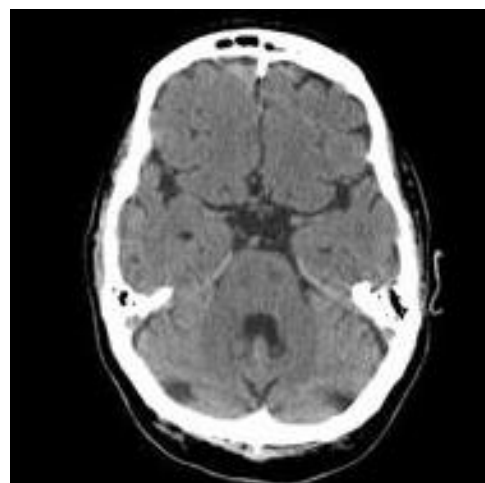
(9.1%) patient who belong to age group 61 – 70 years. (Table 3).

Table No.1: Age (n=136)

Age	No. of patients	Percentage
20 – 30	37	27.2
31 – 40	32	23.5
41 – 50	27	19.9
51 – 60	20	14.7
61 – 70	20	14.7
Mean + SD	44.80 ± 23.25	
Range	20 – 70	

Table No.2: Distribution of patients by CT scan findings (n=11)

CT scan findings for pathologies	No. of patients	Percentage
Sinusitis	4	36.4
Space occupying lesion	2	18.2
Hemorrhage	1	9.1
Chronic subdural hematoma	1	9.1
Stroke	3	27.2
Tumor	0	0
Vascular malformation: AVM/ Aneurysm	0	0

**Figure No.1: Diagram of head****Table No.3: Cross tabulation of patients by age with CT scan findings for detection of pathology (n=11)**

Age (years)	On CT scan						
	Sinusitis	Space occupying lesion	Hemorrhage	Stroke	Chronic subdural hematoma	Tumor	AVM
	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)
20 – 30	2 (18.2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
31 – 40	2 (18.2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
41 – 50	0 (0)	0 (0)	1 (9.1)	0 (0)	0 (0)	0 (0)	0 (0)
51 – 60	0 (0)	1 (9.1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
61 – 70	0 (0)	1 (9.1)	0 (0)	3 (27.2)	1 (9.1)	0 (0)	0 (0)
Total	4 (36.4)	2 (18.2)	1 (9.1)	3 (27.2)	1 (9.1)	0 (0)	0 (0)



Figure No.2: Diagram of head

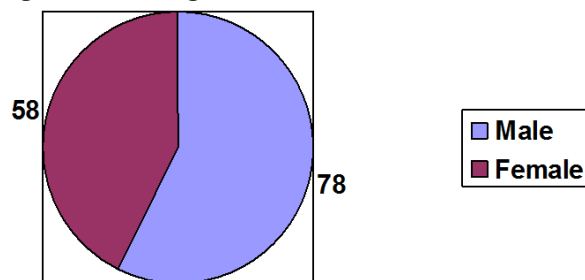


Figure No.3: Distribution of patients by sex (n=136)

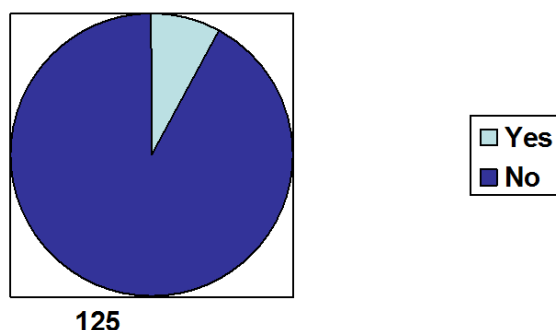


Figure No.4: Distribution of patients by identification of pathology by CT scan heads (n=136)

DISCUSSION

Headache is routinely encountered by physicians in their outdoor and emergency setting. Due to fear, or over demanding by the patients, CT scan is very frequently advised by the treating physician. Even so much advancement has been made in this technology; CT scan cannot establish the diagnosis in all cases.

In this study, we tried to determine the diagnostic yield of CT scan, and this was detected that it could establish the diagnosis among 8% patients with isolated headache. The yield of CT scan was low in our study. Sinusitis was diagnosed in 36.4% patients, followed by space occupying lesion among 18.2% patients.

The diagnostic yield of CT scan has already been discussed by many other authors in literature and there is no common consensus over it.

Patients mean age was 46 ± 10 years. So, this can be observed that in local study, there was not much difference of age group. So, this age group difference may be geographical, which needs to be evaluated.

There were 57.4% male patients in our study, while 42.6% female patients. Saberi H, et al.¹⁸ documented a female dominance with a frequency of 69% female patients in their study. Ahmad A, et al.¹⁶ also noted a female dominance in their study. There were 61% patients who were female and 39% patients were male.

The diagnostic yield of CT scan in our study was 8%. Some other studies also studied the diagnostic yield of CT scan. Saberi H, et al.^{19, 20} conducted a study on 146 patients in whom CT scan was conducted for headache. They found that CT scan yielded diagnosis in only 6% patients.

CONCLUSION

The diagnostic yield of CT scan in detecting lesion among patients with headache is low and radiation exposure is more.

Author's Contribution:

Concept & Design of Study:	Muhammad Asghar Bhatti
Drafting:	Abdul Qayyum
Data Analysis:	Awais Hussain Shah
Revisiting Critically:	Muhammad Asghar Bhatti, Abdul Qayyum
Final Approval of version:	Muhammad Asghar Bhatti

Conflict of Interest: The study has no conflict of interest to declare by any author.

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CONCLUSION

In this link write the goals of the study but avoid unqualified statements and conclusions not completely supported by data.

RECOMMENDATIONS

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