ISSN-0301-035X(Print)
2219-1607(Online)

Bangladesh Medical Journal

Official Organ of Bangladesh Medical Association

Vol. 46 No. 2 May 2017

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Diabetes Prevention Program Research Group.

Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance. Hypertension. 2002;40(5):679-86
No author given:
21st century heart solution may have a sting in the tail. BMJ. 2002;325(7357):184

Volume with supplement:
Geraud G, Spierings EL, Keywood C. Tolerability and safety of frovatriptan with short- and long-term use for treatment of migraine and in comparison with sumatriptan. Headache. 2002;42 Suppl 2:S93-9.

Issue with supplement:
Glauser TA. Integrating clinical trial data into clinical practice. Neurology. 2002;58(12 Suppl 7):S6-12.
Article published electronically ahead of the print version:
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Original Article

Factors Affecting the Success Rate of Renal Stone Treatment by Extracorporeal Shock Wave Lithotripsy

Haque AHMA[1], Islam MW[2], Kallol HK[3], Babul MSA[4], Rahman MH[5]

Abstract

ESWL is one of the treatment modalities for kidney stones smaller than 2 cm. However, not all ESWL treatments are successful. The success rate has been reported to be between 50% to 87%, depending on various factors. This study was conducted to evaluate Factors affecting the success rate of renal stone treatment by extracorporeal shock wave lithotripsy (ESWL). The study was carried out for a period of one year where total 96 patients with single or multiple radio-opaque renal stones treated with ESWL monotherapy using Stortz Modulith SLX-F2 lithotriptor were included. The results of treatment were evaluated after 3 months of follow-up. Treatment success was defined as complete clearance of the stones or presence of clinically insignificant residual fragments (<4mm). The results of treatment were correlated with the patient characteristics (age, sex, body mass index) and stone features (size, site, number & radio density). At 3-months follow-up, the overall success rate was 76%. Among them, repeated ESWL sessions were required in 19 patients (53.9%). Post-ESWL complications were recorded in 8 patients (12.5%). Four factors had statistically significant impact on the success rate, namely stone site, size (the largest diameter of the stone), stone number, BMI (body mass index) of the patient. The success rate is highest for stones located in the upper calyx (26/26; 100%) and lowest for those located in lower calyx (15/20; 75%) (p=0.019). Stone with a largest diameter of <15mm are associated with a success rate of 93.6% (59/63), compared to 75.82% (25/33) for those with a diameter of >15mm (p=0.01). The success rate is also higher for single stone (76/84; 90.5%) than multiple stones (8/12; 66.7%) (p=0.02). Patients with lower BMI (<24) have a better success than higher BMI (>25) (p=0.001).Other factor including age, sex and stone radio density compared to ipsilateral 12th rib have no significant impact on the success rate. The success rate for ESWL for the treatment of renal stones can be predicted by stone size, location, number, and patient BMI.

Key words : Eswl, eswl for renal stone,renal stone, renal stone treatment, nonoperative treatment of renal stone, success rate of eswl.

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INTRODUCTION:

Urolithiasis is a problem that has confronted by clinicians since the time of Hippocrates and the prevalence of urolithiasis is approximately 4 to 15 percent in general population and the estimated lifetime risk of developing a kidney stone is about 12 percent for white males. Approximately 50 percent of patient with urinary calculi have a recurrence within 10 years. 1

Renal stones are common approximately 50% of patient between the ages of 30 to 50 years. The male-female ratio is 4:3. Calculi smaller than 0.5 cm, pass spontaneously unless they are impacted. Any surgical intervention carries risk of complication and needless intervention should be avoided. Small renal calculi may cause symptoms by obstructing a calyx or acting as a focus for secondary infection. However most can be safely observed until they pass. 2

The development of endourological and extracorporeal lithotripsy techniques led to an increasing number of options for the management of renal calculi. Each of the methods available needs to be evaluated in term of its stone clearance rate, potential morbidity and cost effectiveness. Extracorporeal shock wave lithotripsy (ESWL) is an effective, well established method for treatment of renal calculi. 3,4

Chaussy et al was the first to report the clinical application of shock wave lithotripsy in the management of kidney stones and then the management of nephrolithiasis has undergone a complete revolution. 5 For most renal stone smaller than

20mm, ESWL is the most effective primary treatment modality. ESWL is effective in all calyceal locations which are less than 20mm. The success rate of ESWL has been depending on stone size, stone location, stone number, renal morphology, congenital anomalies and stone composition. 4

Stone radio density, a useful parameter for predicting outcome of ESWL for stone ≤20mm. Mina suggests that for stones <20mm within renal pelvis, the value of radiographic appearance of a stone alone in determining treatment outcome on the doli machine is somewhat limited. 6 There seems to be tendency for a worse outcome for stone 11to 20mm that have a radio density greater than 12th rib. 7

Treatment outcome after lithotripsy depends on several factors. The type of lithotriptor, stone characteristics (number, size, composition and location), patient characteristics and renal anatomy and function are important factors for determining treatment characteristics and outcome. Although the role of shock wave lithotripsy for management of lower pole nephrolithiasis has been questioned in some studies, Overall stone free rates after ESWL vary from 50% to 87%, depending on many factors affecting the overall success rate. 1, 8 On the other hand, shock wave lithotripsy is not without complications and renal trauma from treatment in time may lead to hypertension and renal insufficiency. Factors associated with increased renal damage due to shock wave lithotripsy include high shock wave number & energy. 9

Materials and method

This hospital based prospective study was conducted on the patients with renal stone (≤ 20 mm), in OPD basis in the department of Urology, NIKDU, Dhaka from July 2015 to June 2016. All patients were evaluated by detailed history, physical examination and some investigations. Urinalysis, urine culture and sensitivity, complete blood count (CBC), blood urea nitrogen (BUN), serum Creatinine, coagulation profile and plain X-Ray KUB region, ultrasonography of KUB region, IVU or Non contrast CT Scan of KUB region were done. Patient with documented urinary tract infection were treated with appropriate antibiotic before surgery. Inclusion criteria were patients with renal stones attended at the outpatient department as well as admitted in NIKDU-who are selected for ESWL; Age ≥18 years irrespective of sex and BMI; Size of stone will be >5mm or ≤ 20mm (largest diameter of stone) irrespective of site, laterality, number (single or multiple) and stone composition. Exclusion criteria were age <18 years; patient with ureteric stricture, coagulopathy, nonfunctioning kidney and congenital anomalies of kidney and urinary tract; stone size >20mm; recurrent stones; physical disfigurement eg. Kyphosis, Scoliosis, Lordosis; Spina bifida and spinal cord injury; pregnant women. Patients, selected for ESWL according to inclusion and exclusion criteria, underwent ESWL using the MODULITH SLX-F2 (STORZ, Switzerland). All the patients were nothing per oral from morning and were given intravenous fluid with diclofenac sodium suppository 30 minutes before ESWL. In a single session, maximum of 3000 shock waves were given. Repeated sessions of ESWL were given for an incomplete fragmented calculus after 3 weeks, highest upto 3 sessions.

The patients were termed as ESWL failure when no fragmentation or incomplete fragmentation found after three sessions. Patients were evaluated for stone clearance, time to stone clearance, number of ESWL sessions, pain intensity, incidence of steinstrasse, and any side effects at 1, 2, and 3 months. Visual analogue scale was used to measure the pain intensity.

Treatment success was defined as a complete stone clearance or clinically presence of insignificant residual fragments (CIRFs) (Stone Size < 5mm). Failure was defined as presence of significant residual fragment (SRFs) after 3rd month.

Statistical analysis was done with the data of all 96 patients from the master data sheet. The success rate was correlated with characteristics of the patients and stone feature with chi square test by using SPSS program version 22. A p value <0.05 was considered statistically significant.

Results

At 3 months follow-up of 96 cases complete stone free were observed in 68 patients (70.8%), clinically insignificant residual fragments (CIRFs) were observed in patients 16(16.7%) & significant residual fragments (SRFs) were observed in 12 patients (12.5%).

Table-I: Distribution of the study patients by stone clearance rate (n=96)

Parameters	No of patients	Percentage (%)
		Success
70.8	68	Stone-free
16.7	16	CIRFs
		Failure
12.5	12	SRFs
100.0	96	Total

At 3 months follow-up, number of overall success were 84(87.5%) and number of failure were 12(12.5%) shown in Fig-1. Among 96 cases, 45 patients (46.9%) needed single sessions of ESWL for success. Repeated treatment was needed in 51 patients (53.1%). Among the re-treatment group 28 patients (54.9%) needed two and/or three sessions of ESWL to ensure success. The mean number of shocks per patient was 4883±2382. The mean voltage was 5.76±0.68kv. Among the failure group 2 patients were with open surgery and rest of them were referred to an urologist for post-ESWL auxiliary procedure. Among the 96 cases, post-ESWL complications were encountered in 12 patients (12.5%).

Fig-1: Bar diagram of overall success & failure after 3rd month. Success 86 (87.5%), failure 12 (12.5%).

The mean (±SD)age of 96 patients was 38.6±10.28 years (ranging from 19 to 60). The number of patients with age ≤ 40 years were 52 (54.2%), among them number of success were 46 (88.5%) & age >40 years were 45 (45.8%), among them number of success were 38(86.3%). P value was >0.05, that was not statistically significant.

Among 96 cases, males were 53(55.2%), among them number of success rate were 47(88.8%). The series also includes 43 females (44.8%), among them number of success were 37(86.0%). P value was >0.05 that was not statistically significant.

Among the 96 patients mean height of the patients was 1.56 m (1.56±0.073). Minimum height was 1.40 meter and maximum was 1.70 meter. The mean weight of the patient was 57.45 kg (57.35+6.8). The minimum weight was 42 kg & maximum was 70 kg. The mean BMI of 96 patients was 23.27 ± 1.68 (ranging from 19.78 to 26.22). The number of patient BMI <24 (ranging from 19 to 24) were 67 (69.8%), among them number of success were 65(97.0%) & patient BMI >24 (ranging from 24 to 27) were 29(30.2%), among them number of success were 19(65.5%). So the success rate decreased from 97.0% to 65.5% for patient BMI (19 - 24) to (>24 - 27) respectively. P value was <0.001, that was statistically significant.

Table II: BMI (kg/m2) and stone features in correlation with success rate (n=96)

% success rate	No. of success Rate	%	No. of pts	BMI (kg/m2)	P-value
97.0	65	69.8	67	<19 (19.0-24.0)	<0.001
65.5	19	30.2	29	24(24.01-27)	

The mean stone size of 96 patients was 14.21 mm (14.21± 4.61). The smallest stone size was 6 mm & largest stone size 20mm. The sizes of the stones were divided into two groups. In one group the no. of stones <15mm (ranging >4mm to 15mm) were 63 (65.6%), among them no. of success were 59 (93.6%) and another group the no. of stones size >15mm (ranging 16rnm to 20mm) were 33(34.4%), among them no. of success were 25(75.8%). So in this study, the success rate for stones <15mm was 93.6%, while it was 75.8% for stone >15mm (p=0.011). That was statistically highly significant.

Table III: Stone size and stone features in correlation with success rate (n=96)

% success rate	No. of success Rate	%	No. of pts	Stone size	P-value
93.6	59	65.6	63	≤ 15 mm (>4-15)	0.011*
75.8	25	34.4	33	> 15 mm (16-20)	

The series included the number of stones in the upper calyx were 26 (27.3%), middle calyx were 28(29.2%), lower calyx were 20(20.8%) & renal pelvis were 22(22.9%), where the number of success were 26(100%), 22(78.6%), 15(75.0%) & 21(95.5%) respectively. Success rate was decreased from 100% to 95.5% for upper calyx and renal pelvis, respectively. It was also decreased from 78.6% to 75.0% for stones middle calyx and lower calyx, respectively (p=.019). That was statistically significant.

Table IV: Stone site and stone features in correlation with success rate (n=96)

% success rate	No. of success Rate	%	No. of pts	Stone site	P-value
100.0	26	27.3	26	Upper calyx	0.019
78.6	22	29.2	28	Middle calyx	
75.0	15	20.8	20	Lower calyx	
95.5	21	22.9	22	Renal pelvis	

Patients with single stone were 84(87.5%), among them number of success were 76(90.5%). On the other hand, patients with multiple stones were 12(12.5%), among them number of success were 08(66.7%) (p=0.020). That was statistically significant.

The number of stones with radiodensity <12m rib were 56(59.3%), equal to 12th rib were 22(22.9%) & >12ih rib were 18(18.8%), among them number of success were 52(92.9%), 18(81.8%) & 17(77.8%) respectively. Here success rate was gradually increasing with decreasing the radiodensity. But p value was >0.05 that was not statistically significant.

In 96 cases, post-ESWL complications were encountered in 12 patients (12.5%), Among them, 6 patients (6.3) were severe pain, 4 patients (4.2%) were massive haematuria & pain. Two patients (2.1%) were ureteric obstruction along with haematuria and pain.

Table V. Distribution of the study patients by post ESWL complication (n=96)

Percentages (%)	No. of patients	Complications
6.3	6	Severe pain
4.2	4	Massive haematuria & severe pain
2.1	2	Ureteric obstruction, massive
87.5	84	No complications
100.0	96	Total

All the complications were managed conservatively according to standard protocol. No complications were encountered in 84 patients (87.5%).

Discussion:

At 3-months follow-up, the overall success rate was 87.5%. This result was matching with some similar previous studies that reported stone free rates were 75-85% for treatment of renal stones by ESWL. 1, 4, 10 This study examined only four factors that had a significant impact on the success rate namely stone size, site, number of stone & BMI of the patient. Other factors like age, sex & radiodensity had no significant impact on the success rate.

In this study, stone size was a significant predictor of ESWL outcome. The success rate for stones <15mm was 93.6%, while it was 75.8% for stone for >15mm (p=0.011). AI-Ansari et al. did a prospective study under 427 patients with single or multiple stones (<30mm) underwent ESWL monotherapy using SL20 lithotriptor. 4 At 3-months follow-up, the overall success rate was 78%. There 10 prognostic factors were studied, 5 had a significant impact on the success rate namely renal morphology, congenital anomalies, stone size, stone site and number stone treated stones, other factors including age, sex, nationality, stone nature and ureteric stenting had no significant impact on the success rate.

In this study, as in others stone size had a significant predictive impact as factor of ESWL outcome. 3, 4, 5, 11 In another study, Lalak et al. evaluated the outcome of ESWL of 500 renal calculi using the dornier compact delta lithotripter. 10 Here the authors found the overall stone free rate was 66%, while <10mm in size was 76% at 6 months follow-up. For 10-20mm stones, the success rate was 66%, while the rate for stones >20mm in size was 47%. Here the authors did not recommend ESWL as primary therapy for stones >20mm in size. 10

In the present study, the success for stones located in the renal pelvis, upper, middle and lower calyces were 95.50%, 100%, 78.6% & 75.0% respectively (p=0.019). This finding was supported by similar previous studies, where for upper and lower calyceal stones free rate ranges from 90% to 70% respectively, whereas that for lower calyceal and multiple site stones ranges from 70% to 50% respectively. All the studies had shown that better stone clearance rate were in the renal pelvis, upper, & middle calyx than stone in lower calyx. 1, 4, 8, 12

In this study, the success rate for stones located in the lower calyx was 75%. This result is in agreement with a study done by Chen who evaluated the impact of radiological anatomy as predictive factors of lower calyceal stone after ESWL. 13 Here 112 patients with a solitary lower calyceal stone measuring 20mm or less in size were enrolled in that retrospective study. Pretreatment IVU was reviewed for measuring the anatomical predictors, such as lower pole infundibular length (IL), infundibular width (IW) and infundibulopelvic angle (IPA), while the stone location and size were determined on plain abdominal X-ray. All treated with Siemens Lithostar Plus lithotriptor and were followed-up for 3-months. Three months after ESWL, only 49(43.7%) patients were stone free. Under multivariate analysis with logistic regression, smaller stone size (10mm or less, p=0.005) and greater IW (4mm or more, 0.029) were significant favorable predictors for better stone clearance. The authors concluded, in addition to the influence of stone size, lower pole anatomy especially IW, had a significant impact on stone clearance for lower calyceal stone after ESWL, that was similar with other studies. 14, 15

In the present study, stone number had a significant impact on stone clearance by ESWL. The success rate for single stone was 90.5 & 66.7% for multiple stones. This result is similar to that of Abdel Khalek et al., where the authors did a studied 2954 patients with single or multiple radiopaque renal stones (<30mm) underwent ESWL monotherapy. The results of treatment were evaluated after 3 months of follow up. By a multivariate regression model analysis the authors

found that success rate was lower in multiple renal stones than single stone. 1

In the present study, stone radiodensity alone was not a useful parameter for outcome of Extracorporeal Shock Wave Lithotripsy. This finding was supported by Mina et al. The authors studied 211 patients with solitary renal pelvic stones <2cm by Dornier Doli 50 Lithotriptor. The radiodensity was compared to ipsilateral 12th rib. Following after 3 months follow-up they declared that there was no co-relation between stone radiodensity and stone composition. For stone <10mm within renal pelvis, the SFRs were similar (71-74%) regardless of stone radiodensity. For stone between 11 to 20mm, the SFR was 60%, if the stone had a radiodensity >12th rib compared to a SFR of 71%, if the stone radiodensity was <12th rib. However, these differences in SRFs were not statistically significant. 6 In this study, we also had shown that, success rate was gradually decreasing with increasing the radiodensity of stone, but it was not statistically significant (p=0.128).

In the present study, success rate was significantly higher (86%) in patients with BMI 19 to 24 compared to BMI 24 to 27 (57%). This result was also matching with Ackermann et al. who stated that BMI influences the outcome of ESWL. They found that body mass index (BMI) and stone number were the only significant predictors. The authors stated that the best chance of success for ESWL was found in patients with BMI 20 to 28. 16 But Robert et al. found patients with a BMI >25 had a worse outcome after ESWL that matched with present study. 17

6. Conclusion

The overall success rate of ESWL using Stortz Modulith SLX-F2 Lithotriptor for treatment of renal stones was 87.5%. The success rate gradually decreased in relation to increasing the size of the stone. But it was higher in the upper calyx pelvis and middle calyx than in the lower calyx and multiple sites of kidney. Success rate was higher for patient BMI <24. Repeated sessions were needed in 53.1% and overall complication rate was 12.5%. Factors that significantly affected the success rate included stone size, stone location, multiple stones and patients BMI.

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Obituary news January-17

BMA would like to express deep condolence on deaths of the following notable physicians in recent past:

SL.No	Name	Age	Name of District	Date of Death
1	Dr. M. Moazzem Hossain	68	Dhaka, Ex- Vice President of BMA	23/9/2016
2	Dr. Abdur Rashid	99	Dhaka	24/9/2016
3	Dr. A.H.M. Manzurul Islam	49	Rangpur	25/9/2016
4	Dr. A.K.M. Mahbubur Rahman	62	Secretary, BMA Election Commission-2016-2017.	30/9/2016
5	Dr. Abdullah Al Mamun (Omit)	27	Sirajgonj	06/10/2016
6	Dr. Md. Babar Ali	52	Naogaon	14/10/2016
7	Prof.(Dr.) M. R. Khan	88	BMA Life Member -1402898 Dhaka City House # 27 (Old-125), Road # 3, Dhanmondi R/A, Dhaka-1205.	05/11/2016
8	Prof.(Dr.) M. A. Quashem	95	House # 27 (Old-125), Road # 3, Dhanmondi R/A, Dhaka-1205. Phone : 01711525423	05/11/2016
9	Dr. Lutfor Rahman	73	Ex-Vice President, Bangladesh Aomelig Jalokati Dist.	07/11/2016
10	Dr. Modan Mohan Roy	85	Senior Doctor of Lalmonirhat District.	15/11/2016
11	Language Fighter Dr. Abdul Mutaleb Khan	86	Sirajgonj	27/11/2016
12	Dr. Razib Kumar Roy	33	Bagerhat	01/12/2016
13	Alhaj Dr. Matlubor Rahma Chowdhury	82	Nilphamari	10/12/1620
14	Freedom Fighter Dr. Azahar Hossain	66	Naogaon	14/01/2017
15	Freedom Fighter Dr. Hanif Uddin	87	NilPhamari	14/01/2017
16	Dr.Golam Mushtakim Mison			22/01/2017

May Allah bless the departed souls. Our heartiest commiseration to the deceased's family, our prayers are with them during this difficult moment of their life.

GPO registration number, Dhaka-1725 Vol. 46 No. 2 May 2017

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* সংক্রমণের হার কমানোর জন্য হাত ধোয়াসহ সকল সাধারণ স্বাস্থ্যবিধি মেনে চলতে হবে।

Original Article

Microbiological Study of Chronic Suppurative Otitis Media

Shumi RN[1], Siddiqe A[2], Akter A[3]

Abstract

Chronic suppurative otitis media (CSOM) is a prevailing and notorious infection in developing countries causing serious local damage and threatening complications. The purpose of the present study was determine the microbiological profile of isolates from discharge in CSOM. This study was conducted at out-patient department of ENT at Rajshahi Medical College Hospital, Rajshahi from January 2014 to December 2014. Samples were taken from 185 patients (both male and female) in all age groups suffering from chronic suppurative otitis media. Their Gram staining, culture, and biochemical tests were carried out to identify the organisms. It showed the predominance by staphylococcus aereus (29.13%), followed by Psedomonas Aeruginosa (22.83%), Streptococcus Pyogen (14.96%), E. Coli (9.44%), Proteus Mirabilis (6.29%), Klebsiella Pneumonia (4.72%).

Key Words: Chronic suppurative otitis media.microbiological study,all age groups.

INTRODUCTION:

Otitis media is the infection of the middle ear including eustachian tube when get blocked with fluid1 mucus, pus and bacteria can also pool behind the ear drum, causing pressure and pain. In a severe ear infection; pressure may build up and cause the ear drum to rupture. Pus and blood may drain out; in most cases ear drum heals on its own. Otitis media is of three types such as acute purulent otitis media, otitis media with effusion and chronic supportive otitis media.

Ear infections usually start with cold. They are most common in infant and young children with a peak incidence between 4-7 years old. Otitis media is common in infant and young children due to horizontal eustachian tubes are narrower than adult. Otitis media is a common community health disorders of children in all developing countries like Bangladesh which causes significant impact in speech, cognative, educational and psychological development. Patient of otitis media present with pain or discomfort, coughing, nasal congestion, fever, irritability, sleeplessness, sore throat and ear discharge. Fever, vertigo and otalgia should prompt urgent referral to intratemporal or intracranial complications. Hearing loss is common in the affected ear. About 60% of cases of otitis media is caused by bacteria, occasionally by fungi and viruses.1 The bacteria most commonly causing otitis media are Psedomonas aeruginosa causing 20%-40%, Staphylococcus Aureus is 20%-30%, Streptococcus spp. is 10%-20% and other bacteria include Klebsiella spp., Proteus spp., E coli etc.4

Fungal infections of the middle ear are common where there is bacterial infection is present, moist environment helps fungal growth. The most commonly found fungi are Candida species and Aspergillus species.5

In a study from India, fungus was found in 15% of cases, out of which 60% were Candida species and 40% were Aspergillus species. In another study from Singapore, fungus accounted for 8.8% of the total isolates, out of which Aspergillus species was found in 33.3% followed by Candida species 22.2%.6 Rhinovirus is a common virus that causes sore throat and plays a leading role in the development of ear infections by other bacteria. Other viruses, such as respiratory syncytial virus and influenza virus may also be responsible for child hood ear infections.

MATERIALS AND METHODS

This descriptive study carried on Department of Microbiology and Department of ENT at Rajshahi Medical College Hospital from January 2014 to December 2014.

A total 185 Samples were collected by sterile swab stick .After the external ear canal was rinsed with sterile saline, exudates were collected with sterile swab sticks and were immediately processed. A smear was prepared from the swab and stained by Gram stain. The swabs were cultured on Blood agar media, Mac Conkey's agar media, Chocolate agar plate and Sabouraud's dextrose agar media. The plates were incubated overnight at 37°C. The growth of organisms were characterized by colony morphology and Gram's staining from the culture plates.

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RESULTS

Table-I: Distribution of ages in culture positive cases. (n=127)

Age (Years)	Number of culture positive cases
<10	56(44.09)
11-20	36(28.35)
21-30	16(12.59)
31-40	13(10.24)
41-50	3(2.36)
51-60	2(1.58)
>60	1(0.78)
Total	127(100)

The culture samples of the 127 out of 185 patients were positive, yielding 103 bacteria. Fungi were isolated in 11 patients and 13 were mixed growth of both bacteria and fungus. Staphyliccocci Aureus 29.13% were the most prevalent microorganism isolated followed by p. aeruginosa 22.83% , St.pyogen 14.96%, E. coli 9.44%, p. mirabilis 6.29%, K. pneumonia 4.72% and St. pneumonae were 1.57%. Among 11.03% fungal isolates, as fumigatous were 6.29% and C. Albicans were 4.72%.

Table-II: Bacterial and fungal isolates in culture positive cases. (n=127)

Organism **Bacteria**	Single growth	Mixed growth	Total
Staphylococcus aureus	34(26.77)	3(2.36)	37(29.13)
Pseudomonas aeruginosa	26(20.47)	3(2.36)	29(22.83)
Streptococcus pyogen	17(13.38)	2(1.57)	19(14.96)
E.coli	10(7.87)	2(1.57)	12(9.44)
Proteus mirabillis	8(6.29)	0(0.0)	8(6.29)
Klebsilla pneumoniae	6(4.72)	0(0.0)	6(4.72)
Streptococcus pneumonae	2(1.57)	0(00)	2(1.57)
Fungus			
Aspergillas fumigatous	6(4.72)	2(1.57)	8(6.29)
Candida albicans	5(3.93)	1(0.78)	6(4.72)
Total	114(89.76)	13(10.24)	127(100)

Out of 127 culture positive cases 55.11% were male and 44.88% were female, most of the cases were from age group less 10 years and 66.93% cases were detected from rural area and 43.07% were urban areas.

DISCUSSION:

Chronic suppurative otitis media is frequently encountered in tropical and subtropical areas.7 Diagnosis of this diseases in often based solely on the clinical symptoms. Children less than 5 years and more prone to Otitis media due to shorter and more horizonatal Eustachian tube, lower immunity and better adherence of bacteria to epithelial cells than adults. In this study, aural swab are one of the most frequently request for culture and antimicrobial susceptibility tests.

Chronic supportive otitis media is a major public- health problem and persistent diseases with great risk of complications. CSOM is an important cause of preventable hearing loss particularly in the developing world2 and it may have long- term effects on early communication, language development, auditory processing, educational process, and physiological and cognitive development. Early microbiological diagnosis ensures prompt and effective treatment to avoid such complications.

In our study, males were more commonly affected than females which are nearly similar with the study of kumar et al 9 in which males were 61.73%, 53.92% and female were 38.26%, 45.23% respectively.

In our study most prevalent in the age groups of less than 10 years and 11-20 years which is comparable to study of Adoga et al.10 High prevalence of CSOM in children may be attributed to the fact that they are more prone to upper respiratory tract infections. In the present study, the most common bacterial isolates were St. aereus (29.13%), P.aeruginosa (22.83%), St. pyogen (14.96%), E. coli (9.44%), P. mirabilis (6.29%), K. pneumonia (4.72%), As. Fumigatous (6.29%) and C. albicans (4.72%) which is similar to studies performed by Haider and Roa et al.11 Otitis media is not an un common disease, encountered by ENT surgeon.12 Diagnosis of this disease is usually done by clinical symptoms. But in many cases only clinical symptoms cannot

give the real diagnosis. This results in treatment failure and complications such as irreversible destruction of middle ear, facial palsy, intra and extra cranial complications. For this accurate diagnosis or detection of pathogens are essential.

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Original Article

Incidence of Central Diabetes Insipidus among the Patients Undergoing Pituitary Tumor Surgery Through Trans-sphenoidal Approach

Ialam KMT[1], Alam S[2], Amin R[3], Deb-nath H[4], Hossain M[5] , Khan AH[1], Hossain ATMM[2], Barua KK[3]

Abstract

This study was carried out to find out the incidence of central diabetes insipidus (DI) among the patients undergoing pituitary tumor surgery through trans-sphenoidal approach either endoscopic or microsurgical for the first time. Patients with central (Neurogenic) diabetes insipidus prior to surgery, comorbidities like diabetes mellitus, kidney diseases, electrolyte imbalance, recurrent cases were excluded from this study. Patients were followed up to 7th postoperative day by recording and analyzing findings of postoperative serum electrolytes, urinary specific gravity, hourly urinary volume for establishing diabetes insipidus. 76.9% and 23.1% of patients developed diabetes insipidus those who underwent pituitary tumor surgery by trans-sphenoidal endoscopic approach and microsurgical approach respectively. 70% and 30% of patients did not develop diabetes insipidus those who underwent pituitary tumor surgery by trans-sphenoidal endoscopic and microsurgical approach respectively. There was no significant deference between the approaches were found. Fisher exact test was done and p-value was 0.712. Prediction of DI help us in pre-operative counseling and post-operative management of the patients as well as to reduce complications related morbidity after pituitary tumor surgery.

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Key Words: Diabetes insipidus, Trans-sphenoidal approach, pituitary tumor.

INTRODUCTION

The pituitary gland is a remarkable organ that is located at the base of the brain at the center of the skull base. The gland controls an array of endocrine functions important for human growth and metabolism. The most common pituitary- related pathologies that are surgically treated are pituitary tumors (mostly adenomas) and pituitary apoplexy. The classic indications for surgical treatment include visual loss from progressive mass effect, hormonal control in hyper functioning adenomas, failure of medical therapy, and necessity for a tissue diagnosis. Transcranial approaches to the sella for treating pituitary pathologies have been in existence since the late 19th century. In the early 1 900s, Hirsch descried a trans nasal approach to the sella turcica that was refined by Gushing, who standardized the trans labial, transseptal, Trans-sphenoidal approach to the pituitary gland. Recently, given the technologic enhancements in endoscopic visualization and instrumentation, the endo-nasal endoscopic Trans-sphenoidal approach has gained popularity for addressing pathology of the pituitary gland1. Diabetes insipidus (DI) is a common complication following pituitary surgery. This condition can be transient or permanent and the signs and symptoms of this disorder can be mimicked by the normal postoperative course2.

There are two subtypes of DI: nephrogenic and central (neurogenic). Nephrogenic DI occurs when there is an inadequate response to AVP in the renal tubules, leading to an inability to concentrate urine; this can be caused by certain drugs, hypercalcemia, and primary kidney diseases3. Central (neurogenic) diabetes insipidus (DI) is a significant postoperative complication of pituitary tumor resection. Disturbance of the posterior pituitary, pituitary stalk, or neurons originating in the Paraventricular or supraoptic hypothalamic nuclei during pituitary tumor resection may lead to transient or permanent imbalance of anti-diuretic hormone regulated water homeostasis. Clinical manifestations consist of polydipsia and uncontrolled excretion of dilute urine, which, if not treated, lead to elevated serum sodium and serum osmolality4.

Most cases of DI after pituitary surgery have been reported as transient, resolving within the first few days postoperatively. Nevertheless, studies report permanent DI ranging from 0.5% which constitutes a noteworthy risk5. The overall incidence of any postoperative (transient or permanent) DI in trans-sphenoidal pituitary surgery series has been reported to range from 1.6 to 3 1%6,7,8. Recently, Nemergut et al. reported their large series of patients undergoing non-endoscopic Trans-sphenoidal pituitary microsurgery9.

Polyuria is common after trans-sphenoidal surgery; however, it is not always due to DI. These should be considered and excluded before treatment of DI is initiated. Acromegalic patients have been known to have increased urinary output following resection of the pituitary microadenoma due to diuresis of excess fluid in the soft tissues. Nevertheless, polyuria remains a hallmark of DI. As such, accurate measurement of urine output is critical. When DI is suspected, additional tests are needed to confirm the diagnosis including measurement of urine specific gravity, urineand serum osmolality, and serum sodium. A diagnosis of DI is contingent upon the presence of polyuria and polydipsia in conjunction with specific laboratory abnormalities2.

Unfortunately, there are a wide range of measurements that have been used to establish a diagnosis of DI in the literature. For example, various authors have reported different thresholds of elevated urine output that should raise suspicion for DI such as >250-500ml/hr for 3 consecutive hours and 2.5- 18 L/day. Urine specific gravity <1.005 is often used as a diagnostic parameter of DI11. Urine osmolality <300 mOsm/Kg and serum osmolality >300 mOsm/kg are also thought to be diagnostic of DI. In addition, one should be suspicious of DI when serum sodium increases to levels >140-145 mequ/L10,11.

Transient DI is commonly seen after Trans-sphenoidal pituitary surgery. With a transnasal microsurgical approach, the rate of transient DI has been reported between 1.6 and 45.6%11. The incidence of temporary DI following a transnasal endoscopic approach has been reported between 2.5 and 15.2%12. Similar studies have shown that the rate of DI is roughly the same between transnasal microscopic resection and transnasal endoscopic resection13.

However, a recent meta-analysis by Goudakos et al. found that postsurgical DI was less frequent in those who underwent endoscopic surgery compared to those who had microsurgical resection (15% vs. 28%, p= 0.03)2.

Diabetes insipidus is a common but usually transient complication following pituitary surgery. In rare instances of massive damage to AVP-producing magnocellular neurons of the hypothalamus, a permanent lack of endogenous vasopressin ensues. While certain factors appear to carry a higher risk for postoperative DI, it is important to monitor all postsurgical patients closely in an intensive care setting and to treat DI when appropriate. Other causes of postoperative polyuria must be ruled out, so as to avoid unnecessary pharmacotherapy. Meticulous surgical technique and careful preservation of the critical neurovascular structures in the hypothalamic-pituitary axis are essential in averting postsurgical DI2.

MATERIALS AND METHODS

This cross sectional type of observational study was carried out in the department of Neurosurgery, Bangabandhu Sheikh Mujib Medical University July, 2013 to June, 2014 on 33 consecutive patients with age ranged from 24 to 70 years. Among 33 Patients, 20 ware male. All the consecutive patients who underwent surgical intervention for pituitary tumor for the first time through Trans-sphenoidal approached either endoscopic or microsurgical were included in this study. Patients with central (Neurogenic) diabetes insipidus prior to surgery, co-morbidities like diabetes mellitus, kidney diseases, electrolytes imbalance, recurrent cases were excluded from this study. All patients were evaluated by detailed history, thorough general and neurological examination. Patients were followed up to 7th postoperative day. Findings of postoperative serum electrolytes, urinary specific gravity and hourly urinary volume were recorded and analyzed for establishing diabetes insipidus. Data collection sheet was used to collect necessary information. Informed written consent was taken from each participant or guardian before data collection. Data was processed by utilizing IBM SPSS statistical program (Version 17.0). Results were described in frequencies or percentage. Statistical comparison was done using fisher exact test, and chi-square test. P-value ≤.05 was considered statistically significant.

RESULTS

The age range was from 24 to 70 years. Mean age of the patients was 40.5 1±10.58 years. Maximum patients (73.4%) were in between 21 to 50 years. Most patients were male with a male female ratio was 1.53:1. Among 33 patients 57.6% had normal level of serum sodium ion concentration and 42.4% of the patient had hypernatremia in postoperative period. 23.1% developed diabetes insipidus were <30 years of age, 38.5% of patients were between

31-40 years age group and 38.5% of patients were >40 years age group. The patients who did not develop diabetes insipidus 15.0% were <30 years age group, 50.0% of patients were between 31-40 years age group and>40 age group of patients were 35.0%. 39.5% of male and 60.5% of female developed diabetes insipidus. Among the patients who did not develop diabetes insipidus 75.0% of patients were male and 25% of patients were female. Most of the patients (92.9%) having Na+ concentration >145 mmol/L had DI.

36.4% of patients had tumor size (maximum diameter in coronal or sagittal plan of MRI) were <30mm and in 63.6% of patient's tumor size were. >3Omm. The range of tumor diameter was between 15mm and 50 mm. (Table-I)

Table I: Distribution of patients according to pre-operative image finding (diameter of tumor) (n=33)

Tumor diameter (mm)	N(%)	Mean ±SD	Mim-Max
<30	12(36.4)	21.91±4.10	15-25
>30	21(63.6)	35.28±5.36	30-50
Total	33(100.00)	30.42±8.15	15-50

Table II shows that resection through Trans-sphenoidal endoscopic rout was done on 72.7% of patients. 27.3% of patients underwent surgery through Trans-sphenoidal microsurgical approach.

Table II: Distribution of patients according to operative procedure (n=33)

Pre-operative image finding	Frequency	Percentage
Trans-sphenoidal endoscopic	24	72.7%
Trans-sphenoidal microsurgical Approach	9	27.3
Total	33	100.0

Table III shows that among 33 patients 57.6% had normal level of serum sodium ion concentration and 42.4% of the patient had hypernatremia in postoperative period.

Table III: Distribution of patients according to increased and normal Na+ concentration (n=33)

Normal Na+ concentration	Frequency	Percentage
<145	19	57.6%
>145	14	42.4
Total	33	100.0

33.4% cases developed diabetes insipidus in postoperative period and 60.6% case did not develop diabetes insipidus. (Table IV)

Table IV: Distribution of patients according to development of diabetes insipidus (Dl) (n=33).

Development of DI	Frequency	Percentage
Absent	20	60.6
Present	13	39.4
Total	33	100.0

Table V shows that among the patients who developed diabetes insipidus (n=13) of them 76.9% developed in first postoperative day and 23.0% developed in the second post-operative day.

Table V: Distribution of patients according to postoperative day of development of diabetes insipidus (Dl) (n=13).

Postoperative Day of development of DI	Frequency	Percentage
First	10	76.9
Second	3	23.00

Among <30 mm tumor diameter group 30.8% of patients developed diabetes insipidus and 40.0% of patients did not develop diabetes insipidus. Among >30 mm tumor diameter group 69.2% of patients developed diabetes insipidus and 60.0% of patients did not develop diabetes insipidus.

Table VI: Development of diabetes insipidus (DI) in tumor size groups (n=33).

Tumor (mm)	Diabetes insipidus (Dl)		
	Present n(%)	Absent n (%)	
P value			
<30	4 (30.8)	8 (40.0)	
>30	9 (69.2)	12 (60.0)	
Total	13 (100.0)	20 (100.0)	(100.0)
		0.590	

There was no significant deference between the two groups and p-value was 0.590. (Table VI).

Table VII: Development of diabetes insipidus (DI) in operative procedures

Tumor (mm)		Diabetes insipidus (Dl)	
		Present n(%)	Absent n (%)
P value			
Trans-sphenoidal Approach	Endoscopic	10 (76.9)	14(70.00)
Trans-sphenoidal Approach	Microsurgical	3(23.1)	6(30.0)
Total	13 (100.0)	20 (100.0)	0.712

76.9% of patients developed diabetes insipidus and 70.0% of patients did not develop diabetes insipidus those who underwent pituitary tumor surgery by trans-sphenoidal endoscopic approach; 23.1% of patients developed diabetes insipidus and 30.0% of patients did not develop diabetes insipidus those who underwent pituitary tumor surgery by trans-sphenoidal microsurgical approach. There was no significant deference between the approaches were found. Fisher exact test was done and p-value was 0.712. (Table VII)

DISCUSSION

Incidence of DI in postoperative patients in our study is 39.4% which is similar to other study and DI occurred in 86.3% of the affected patient on the second postoperative day11. It was found that 71.2% of the patients manifested DI within 24 hours of undergoing surgical intervention14. In our study we found that 76.9% of the patients developed DI on the first postoperative day and 23.0% of the patients developed DI on the second postoperative day. Our observation is in agreement with reports of postoperative DI generally occurring within 24 hours of the surgical procedure.

The mean age of our study population was 40.51 years (SD±10.58 years) which is similar to other study were mean age at the time of surgery was 40.114.

Adams JR. et al. included total 59 patients with DI. Of them 16 were men and 43 were women14. They found that 27.1% of men and 72.9% of women had postoperative DI. We found 39.5% men and 60.5% women had postoperative DI which is nearly similar to the finding above.

It was found that DI is commonly seen after trans-sphenoidal pituitary surgery. With transnasal microsurgical approach the rate of development of DI ranges between 1.6% and 45.6%. In our study 23.1% of patients develop DI who underwent trans-sphenoidal microsurgical approach for surgical removal of pituitary macroadenoma which was within range according to above studies11

It was found that the incidence of DI following a transnasal endoscopic approach between 2.5% and

15.2%. In our observation we found that 76.9% of the patients developed DI who underwent pituitary tumor resection by trans-sphenoidal endoscopic approach. Our incidence of DI is much more than that of Jho HD'S findings12.

It was shown that the relationship between elevated serum sodium levels (>145mmol/L) within the first five days postoperatively and the incidence of overall postoperative DI4. They found that the development of hypernatremia within five days postoperatively was strongly associated with postoperative DI (transient or permanent) (p=<O.0001). Of the 14 patients who had a serum sodium level >145mmol/L within the first five days postoperatively, all 14 met criteria for DI. In our study among the 33 patients 14 of them developed hypernatremia (serum sodium level >145mmol/L) within first two days postoperatively and 13 of them met the criteria for DI. So, in our study we also found that there was a strong association between postoperative hypernatremia with DI. But hypernatremia of another patient due to over infusion of sodium containing fluid.

Incidence of development of serum sodium imbalance in both male and female is equal and the ratio is 1.1:0.915. Previous study also found no impact of gender on the incidence of postoperative DI7. In our study there was association between gender and postoperative DI (p=O.O35) which does not correspond with the study of the above mentioned investigator.

Some authors have shown that DI is more common after the resection of macroadenoma. The circumstance is likely to be caused by the more aggressive gland and stalk manipulation required during resection as well as changes in sellar and suprasellar anatomy in patients with macroadenoma9.

It was found in their that among the patients who had a pituitary adenoma and no preoperative DI, 69.4% had macroadenomas. Microadenomas were found in 30.6% of patients9. Diabetes insipidus was more likely to be diagnosed in patients with microadenomas (21.6% developed postoperative DI) than with macroadenomas (14.3% developed postoperative DI) (p=0.O49). They found that adenoma size had no impact on the development of persistent DI. In our study all the 33 patients had

macroadenoma. Among them 63.6% had tumor diameter >30mm and 36.4% had tumor diameter <30mm. In >30mm tumor diameter group 69.2% developed postoperative DI and <30mm tumor diameter group 38.8% developed postoperative DI (p=0.59O). It was statistically insignificant. So, we could predict that large tumor sizehas no impact on the development DI. But we could not compare with microadenomas because in the perspective of our country we only found macroadenomas.

Trans-sphenoidal surgery, include more than 95% of the surgical indications in the sellar area and approximately 96% of all pituitary adenomas (Jho et al., 2012). However, a recent meta-analysis by Goudakos et al. found that postsurgical DI was less frequent in those who underwent endoscopic surgery compared to those who had microsurgical resection (15% vs. 28%, p =0.03)17. In our study approach did not influence much the postoperative diabetes insipidus (p=O.0712) which does not correspond with meta-analysis of Goudakos et al16 .

Limitation of the study were duration was short, limited number of patients, surgical procedures were performed by different surgeons, we could not find the incidence of postoperative DI in relation to the extent of tumor resection due to unavailability of postoperative imaging. So it remained unpredicted.

Early prediction of this notorious complication is essential for post-operative management of the patient. This will help us in preoperative counseling and postoperative management of the patients as well as to reduce complications related morbidity after the pituitary tumor surgery. Practitioners should prevent the overtreatment of polyuria with desmopressin, especially in patients who can keep up with urinary loses through oral fluid intake. Excessive desmopressin treatment can result in hyponatremia and significant morbidity.

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Original Article

Sero-prevalence of Transfusion Transmissible Infections Among Voluntary Blood Donors of Khulna Medical College Hospital.

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Abstract

Transfusion transmitted infections (TTI) are a great concern of safety for patients. Blood transfusion is a lifesaving procedure but always caries a potential risk of infections. The present study was designed to evaluate the prevalence of infectious disease markers and frequency in males and females of various age groups among healthy blood donors. A retrospective review of donor record over a period of 2 years between 2015 to2016 was done at the department of transfusion medicine Khulna medical college Hospital, Khulna, Bangladesh.Among the total 37,266 donors,358(0.96%) donors were infected and therefore not suitable for blood donations.HBV was found to be the most frequent infection with a total frequency of 0.72% followed by TP (0.20%), HCV (0.03%) and HIV (0.01%). None of the blood samples showed positivity for malarial parasite.Majority of the seropositive donors, (47.96%) were in the age group of 26 to 35 years followed by 29.47% in 18 to 25 years' age group.

Key Words: Transfusion Transmitted infection(TTI), Seroprevalence, Voluntary donors.

INTRODUCTION

Transfusion medicine has a great public health importance worldwide. Blood transfusion has been used since 1930 for various indications and the demand for blood and its components is likely to increase in the future 1. In Bangladesh blood transfusion service was started in 1950 at the Dhaka Medical College Hospital. The importance of ensuring blood safety as well as the adequacy of the national blood supply is highlighted due to the emergence of HIV in the 1980. The following screening tests were performed in the blood transfusion centers: HBsAg, Syphilis, Malarial Parasite, Anti-HCV, Anti-HIV. To ensure safety, adequacy, accessibility and efficiency of blood supply at all levels, the Bangladesh Government has passed 'Safe Blood Transfusion Law 2002' in the Parliament and 'Safe Blood Transfusion Rules 2008'2. The magnitude of the TTIs varies from country to country depending on the incidence of these infections in that particular population. Majority of the problems are due to the prevalence of asymptomatic carriers in the society, as well as blood donations during the window period of infections 3,4. These unsafe blood transfusions are very costly from both human and economic points of view.Hence, implementation of effective donor selection criteria and quality of screening tests are important and critical in preventing transmission of these infections. Screening for TTIs also gives clue about the prevalence of these infections in healthy populations and is the greatest challenges to transfusion medicine in developing countries5. This study was undertaken to see the sero-prevalence of TTI among healthy blood donors at Khulna Medical College Hospital.

MATERIALS AND METHODS

This retrospective study was conducted among healthy blood donors at transfusion medicine department of Khulna Medical College Hospital over a period of two years between January 2015 to December 2016. The study population constituted voluntary donors and most of the cases relatives of thepatients. Voluntary blood donors are those who donate blood without remuneration. During these period, total 37,266 subjects of both sexes, different age groups and from different nearby districts of Khulna were screened. Donors were selected by taking history, clinical examination and following strict donor selection criteria to eliminate professional donors. All the samples were screened for HBsAg, HCV, HIV 1 and 2, Syphilis and malaria parasite by rapid immunochromatographic (ICT) assay (EXCEL).

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All the positive samples were repeated 3 times before labeling as seropositive and respective blood units were discarded. All data were analyzed by MS-EXCEL 2016.

RESULTS

In the present study, a total of 37,266 units of blood were collected from the volunteer blood donors at Khulna medical college hospital, Khulna during the year 2015 and 2016. Of these, 35,081 (94.14%) were males and 2,185(5.86%) were females which shows predominance of males as compared to females for the two studied years (Table I).

Table I. Yearly gender wise distribution of blood donors in the present study year total samples tested males and females (n= 37,266).

Year	Total sample tested	Males	Females
2015	18,179	17,177 (94.49%)	1,002(5.51%)
2016	19,087	17,904(93.80%)	1183(6.20%)
Total	37,266	35,081(94.14%)	2,185(5.86%)

None of the blood samples showed positivity for malarial parasite. HBV and TP were the most prevalent infections throughout the study period. Among the seropositive donors, 184 (47.96%) were in the age group of 26 to 35 years followed by 109 (29.47%) in 18 to 25 years' age group (Table-III).

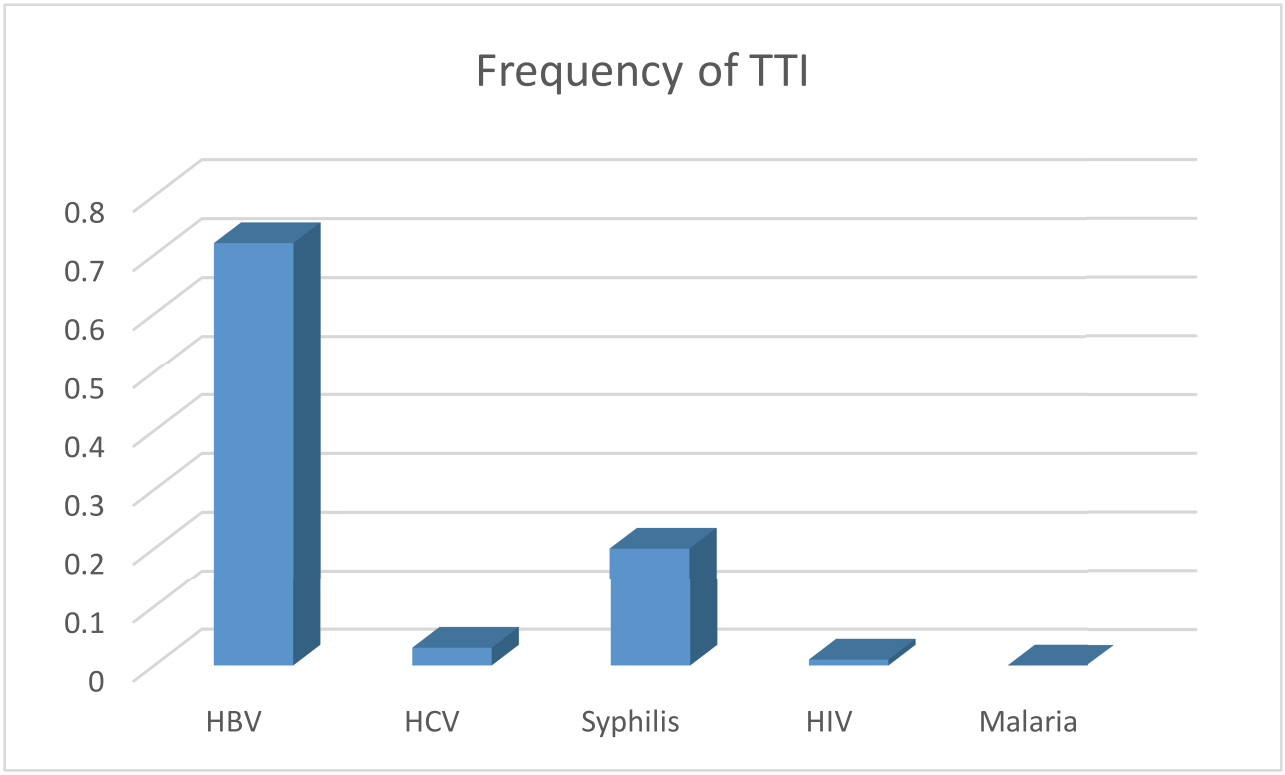

Figure-1: Frequency of transfusion transmissible infections (n= 37,266).

Among the total 37,266 donors, 36,908 (99.04%) were found healthy and safe for transfusion while the remaining 358(0.96%) donors were infected and therefore not suitable for blood donations. During the study period, HBV was found to be the most frequent infection among blood donors with a total frequency of 0.72% followed by TP (0.20%), HCV (0.03%) and HIV (0.01%) as shown in (TableII)

Table II. Prevalence of HBV, HIV, HCV and Syphilis among blood donors in the present study (n= 37,266).

Year	Sample tested	Positive samples(%)	HBV(%)	HCV(%)	SYPHILIS(%)	HIV(%)
2015	18179	197(1.08%)	142(0.78%)	9(0.05%)	46(0.25%)	0
2016	19,083	161(0.84%)	127(0.66%)	2(0.01%)	30(0.16%)	2(0.01%)
Total	37,266	358(0.96%)	269(0.72%)	11(0.03%)	76(0.20%)	2(0.01%)

Table III. Prevalence of transfusion transmitted infections among different age groups (n= 37,266).

Age(Years)	18-25(%)	26-35(%)	36-45(%)	46-55(%)	Total
HBV	83(30.86)	146(54.28)	28(10.40)	12(4.46)	269
HCV	3(27.28)	5(45.45)	2(18.18)	1(9.09)	11
SYPHILIS	23(30.26)	32(42.10)	16(21.05)	5(6.58)	76
HIV	0	1(50)	1(50)	0	2
Total	109(29.47)	184(47.96)	44(24.90)	18(6.71)	358

DISCUSSION

Transfusion transmitted diseases have an increased significance worldwide because they contribute towards the spread of infectious diseases to the population while proper screening of donors can considerably reduce the possibility of transmission .6 In the developing countries, along with various other factors, poor socioeconomic conditions favor the prevalence of infectious diseases among population such as Hepatitis B, Hepatitis C and HIV. The present study was aimed to determine the frequency of HBV, HCV, HIV, TP and MP among blood units donated at Khulna Medical College Hospital, Khulna during the study period spanning from January2015 to December, 2016.

The majority of the donors in the present study were males (94.14%) with a small percentage (5.86%) of female donors (Table 1). This is comparable to the studies done by Prakash et al5. Pahuja et al.7, Karmakar PR et al.8 and Shrestha AC et al.9 noting more than 90% of the male donors. Similarly, male dominated donor pool was reported by the studies done in South-East Nigeria by Okacha10 and in Tanzania by Matee11. They also recorded the higher prevalence of all TTIs in male donors than females. In contrast, a study in China showed higher rate of female donors (44.5%) which was attributed to increased knowledge regarding the blood donation12.

The prevalence of HBV, HCV, syphilis and HIV in the present study was 0.72%, 0.03%, 0.2% and 0.01% respectively (Table II). In Bangladesh, a study was conducted by Ara F et.al13showed prevalence of HBV, HCV, HIV, and syphilis were 0.009, 0.0004, 0.0001 and 0.0001% respectively which is low in comparison with present study. Another study was conducted byAra F et .al14the Prevalence of hepatitis B virus (HBV), HCV, and syphilis were 1.20, 0.68 and 0.34% respectively which is similar to present study.

Another study was conducted in Bangladesh by Saha SK et .al15 the Prevalence of hepatitis B virus (HBV), HCV, HIV and syphilis were 2.19%, 0.25% ,0.06% and 0.15%.

At Mysuru, India, a study was conducted by Prakash P et.al16reported the prevalence of HBV, HCV, syphilis and HIV was 0.96%, 0.13%, 0.15% and 0.26%, respectively.

The overall seroprevalence of TTIs in the present study was 0.96% which is comparable to the study done in Mangalore, Karnataka by Lathamani et al. reporting TTIs of 0.82%17.

Howerver, the seroprevalence in thepresent study is low when compared to the studies done by Chaurasia et al. and Karmakar et al. noting 2.5% and 2.79% respectively18,19. High prevalence rate of 15.9% and 20.09% was observed in African countries of Tanzania and Nigeria20,21. This variation in magnitude of TTIs from country to country depends on loads in that particular population. This could also be due to study site lacking sensitive donor screening program, public awareness and education so that infected persons can self-select themselves and opt out from donating blood due to problem of asymptotic carriers, window period, and false negative tests19.

In the present study, the seropositivity was high (47.96%) among the age group of 26-35 years and a small fraction 6.71% were in the age category of 46 - 55 years. The 18-25

years age group showed the second highest clustering of TTIs with 29.47% positive rates (Table III).

In India, a study was conducted the seropositivity was high (43.35%) among the age group of 26-35 years and a small fraction 10.80% were in the age category of 46 - 55 years. The 18-25 years' age group showed the second highest clustering of TTIs with 27.60% positive rates5.

In our country, majority of the donors belongs to 18-35 age group. Among them seropositivity is high in 25-35 years. From this study, it may be suggested that if we recruitedmore donors form younger age group (18-25 yrs.) and counselled them about route of transmission of STI and vaccinated them in seronegative donors of HBV, reduce the significant rise of TTI among them, who ultimately comprise 26-35 years' age group in near future.

The sero-prevalence of TTIs in the present study was highest for HBV infection (0.72%). A study was conducted by Ara F et.al13, atNational Institute of Neurosciences (NINS) and Hospital in Dhaka, Bangladesh,the prevalence of HBsAg was 1.196%. In Bangladesh another study was conducted by Saha SK et al15the prevalence of HBV was 2.19%. In India, comparable sero-prevalence of HBsAg was noted by Prakashet al (0.99%) 5, Giri et al. (1.09%) 1 and Chattoraj et al. (0.99%)21.

In our study, seropositivity of HCV and HIV was low (0.03% and 0.01% respectively). This value was much lower than other studies conducted in Bangladesh 2,14,15. In India, the seroprevalence of HCV is relatively high in comparison to our study1, 5,21. The worldwide prevalence ofhepatitis C virus infection is estimated by the World Health Organization (WHO) to be approximately 3% corresponding to 130–150 million infected persons22. The highest prevalence(28%) of HCV has been reported in Egypt22.

The seropositivity for syphilis in the present study was 0.20% which is second highest in this study. A study conducted by Saha K et.al.in Bangladesh, the reactivity of VDRL varied from 0.09 to 0.23%. Another study done by Ara F et.al.the VDRL reactivity was 0.341%14.

Similar findings were noted by Prokash et.al.(0.15%)16 and Karmarkar et al. (0.23%)19.

The World Health Organization estimated that approximately 6 million new cases of syphilis are reported each year in the world.23 So, the reason for high prevalence of syphilis in our study might be due to more numbers of replacement donors and improved detection methods.

Syphilis is detected in significantly high number among healthy donors. So most sensitive methods should be adopted to screen syphilis. More studies are needed to find the prevalence of syphilis in public sector hospitals.

In the present study there was no positive cases found for malarial parasite.Malaria is estimated to be directly responsible for around one million deaths annually worldwide26. The number of malaria cases in Bangladesh fluctuates seasonally. The majority of these cases occur in the thirteen districts close to and/or bordering India and Myanmar. These thirteen districts, out of the 64 administrative districts of Bangladesh, are recognized as malaria endemic. Ninety-eight percent of the malaria case reports come from these thirteen districts. Three out of these thirteen districts, Bandarban, Khagrachari and Rangamati, collectively known as the Chittagong Hill Tracts (CHT) districts, report the highest incidence of malaria within the country24. Khulna is not enlisted of these thirteen districts for malaria.

Zero prevalence rates for malaria amongthe donor set in this study may be due to the fact that infection with malarial parasite results in development of fever and weakness.Because of the prominent signs and symptoms majority of the infected persons will not visit the blood donation Centre and even if theycome, will be readily excluded by medical fitness examination and counselling3.In Bangladesh two study reported by Ara F et al. and Saha SK et al. have also not found any of the donors positive for malaria13,15.

The greatest threat to the safety of the blood supply is the donation of blood by seronegative donors during the infectious window period when the donors are undergoing seroconversion. Such people represent new, or incident infections. Although new techniques of testing will bring us closer to the goal of zero risk, it is unlikely that any test or combination of tests will be 100percent effective in detecting window-period infections. It is also important to recognize that new, direct viral-detection tests will supplement existing screening assays rather than replace them25. A considerable portion of this improvement is due to the introduction of nucleic acid testing (NAT), rather than relying solely on measuring pathogen-specific humoral immune responses in the donor. This will decrease the window period and hence decrease the incidence of TTI. But the cost-effectiveness of NAT is poor. The NAT has added benefits but its high financial cost is of concern, especially in economically restricted countries18. Currently, no technology exists to completely detect all window period

donations. No matter how sensitive NAT becomes, we will never be able to completely close the exposure-to-seroconversion window period. The general public and media might believe that with the advancement in testing technologies zero risk blood products are currently available. This generalization is far from reality as judged by our current experience with new testing methodologies18.

Serosurveys are one of the primary methods to determine the prevalence of TTIs because blood safety in very important especially in patients requiring regular blood transfusion such as those with sickle cell disease especially thalassemia, haematological malignanacies, and dialysis patients. Various studies have shown that high rate of transfusion transmissible viral infections in such high risk patients. Hence, the assessment helps in determining the safety of blood products and also gives an idea of the epidemiology of these diseases in the community.

There is a need for increased awareness for safe blood which can be obtained by motivating young donors. Also, implementation of strict donor selection criteria, use of sensitive screening tests and establishment of strict guidelines for bloodtransfusion are highly recommended to reduce the incidence of TTI and ensure the safety ofblood for recipient.

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Review Article

Liquid biopsy: A new era in the management of cancer patients

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Abstract

Cancer is associated with multiple genetic mutations and analysis of these is increasingly used for management. Mainly histopathological examination of biopsy specimen is used for decision but sometimes biopsy specimen cannot be available due to invasive nature of surgical procedures and inaccessible tumour site. Tumour cells release circulating free DNA (cfDNA) in blood. This can help to detect genetic aberration. A liquid biopsy can provide information from blood samples or body fluids and it is non-invasive. It can help to screen, diagnose and treatment in a personalized way and also detect mutations over time.

INTRODUCTION

The term liquid biopsy was first used to refer to the diagnosis and characterization of solid tumours by harvesting and analyzing circulating tumour cells (CTC) from the blood and same techniques were used like haematoxillin and eosin (H & E) staining, immune-histochemistry (IHC) and gene sequencing to detect mutation as for regular biopsies. More recently, the term has been extended to the detection of the tumour nuclear material in the blood. So liquid biopsy can be defined as, "the analysis of blood and blood products to detect and analyze cells or nuclear material derived from a tumour." However, now-a-days the term liquid biopsy again broadened to the analysis of body fluids like cerebrospinal fluids (CSF), amniotic fluid for detection of the presence of the cells or nuclear material for detection of pathological conditions. Molecular diagnostics is increasingly impacting a number of areas of cancer care delivery including diagnosis, prognosis, in predicting response to treatment and monitoring. Disease-specific molecular biomarkers represent the abnormalities in genetic or epigenetic pathways those control cellular proliferation, differentiation or death.

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Biopsies have been used for diagnosis of diseases for 1000 years1. But malignant tumours are heterogenous. In a study by Gerlinger et al2 it was found that there is extensive intratumoural and intertumoural variation in biopsy specimen taken from both primary and metastatic sites. There is also biasness in single-biopsy as it reflect single snap-shot of a tumour. So multiple biopsies are needed from the primary and the metastatic sites for a therapeutic decision after considering the genomic landscape of the tumour. But multiple or serial biopsies are often impractical due to discomfort of the patient, clinical risk, surgical complications and economic burden. In addition, some tumours may not be accessible for biopsy. Moreover, biopsy can inform the genotype at that particular time-point. But malignant tumours are very dynamic and change their dominant mutation pattern over time or may acquire new mutation especially after treatment. These issues are particularly important to identify when targeted therapies are prescribed to the patient. It was found in a study that approximately 50% of non-small-cell lung cancer (NSCLC) patients become resistant to tyrosine kinase inhibitors (TKI) through an EFGF T790M mutation3,4. But only <5% NSCLC patients had this mutation detectable in primary biopsy5. In another study, it has been shown that 38% of colorectal cancers with wild-type KRAS developed mutation after anti EGFR (epidermal growth factor receptor) therapy as rapidly as six months after therapy6. All these limitations lead to the detection of a specific therapeutic biomarker at an early stage of the disease for a successful treatment outcome. Liquid biopsy for detecting and studying circulating free DNA (cfDNA) and RNA was the first step to overcome the limitations of the tissue biopsy. Specific detection of tumour derived cfDNA or circulating tumour DNA (ctDNA) help to assess tumour burden, treatment response and also to identify the subpopulation of cells that are resistant to treatment7,8. Now with the very sophisticated techniques the heterogenous landscape of the tumour can be detected using a blood sample9.

HOW TO DETECT ctDNA

There are two mechanisms by which DNA can enter into the

circulation- passive and active. In passive mechanism the apoptotic and necrotic cells release nuclear and mitochondrial DNA into the circulation during cellular destruction and the ineffective clearance of cfDNA by the phagocytes lead to the accumulation in the blood10,11. In another mechanism, tumour cells release DNA actively in the blood12,13,14,15. At present, most common procedure requires 3 millilitre of blood or 1 ml of plasma or serum and the preparation should be completed within 4-5 hours of blood collection. For plasma preparation, blood is collected in a tube treated with an anticoagulant preferably EDTA (ethylenediaminetetraacetic acid) and cells are then removed by centrifugation16. Serum is collected after clotting of the blood17. The circulating DNA is extracted from the plasma or serum with commercially available kits and analyzed. cfDNA may be of tumour tissue or non-tumour tissue origin. A proportion of cfDNA is derived directly from the tumour (ctDNA) and the fraction is quantified18-23. There is direct correlation between tumour burden and the quantity of ctDNA released21. Techniques are available for the detection and reliable monitoring of tumour-associated genetic aberration, including somatic mutations, loss of heterozygosity (LOH) and chromosomal aberrations in the blood24,25,26. The fraction of ctDNA can range from 0.01% and 93%. The genetic material is sometimes in the form of micro RNAs (miRNAs) which have prognostic significance in a variety of cancers and can be used as biomarkers. But ctDNA carrying cancer specific mutation is the most specific circulating biomarker. As the fraction of ctDNA is very low in the circulation (<0.1%), it may not be detected even with highly developed technologies. Circulating tumour cells (CTC) are even less desirable for liquid biopsies because it present in the circulation when disease is already in the metastatic stage and CTCs are about hundred times less frequent than DNAs. FDA approved the CellSearch CTC test requires sample processing within 96 hours of collection of blood and it is a platform for CTC numeration. A positive test (more than five detected CTCs for metastatic breast and prostate cancer and more than three CTCs for metastatic colorectal cancer per 7.5 ml of blood) is associated with decreased progression-free survival (PFS) and decreased overall survival (OS) in these patients28-32.

CIRCULATING FREE DNA (cfDNA)

cfDNA can enter into the circulation after necrosis or apoptosis of a cell. Late stage cancer patients have high cfDNA level in the plasma but most of them are from non-tumour cells. The advantages of cfDNA is that it can be analyzed from bio-banked biofluids, such as frozen plasma. The median half-life of cfDNA in circulation ranges from 15 minutes to few hours. The total concentration of cfDNA in the blood of the cancer patients varies considerably with tumour specific mutations ranging from undetectable (less than one copy per 5 ml of plasma) to over hundred thousand copies of mutations per ml of plasma33.Exercise increases cfDNA level 10 fold and other pre analytical variables such as blood collection and extraction protocols affect the amount and size of cfDNA fragments in a samples34,35. Delay in the blood processing, blood storage temperature, agitation of the sample and shipment also can cause release of wild-type cfDNA from the lysed nucleated cells and affect the allelic frequency36. Plasma is preferred over the serum for cfDNA detection37.

EXOSOMES

The exosomes study has developed in the last few years in various areas of research. Exosomes are actively released vesicles (carrying RNA, DNA, proteins) and can function as inter-cellular messengers. They are particularly interesting as biomarkers since they are stable carriers of genetic materials and proteins of their cell of origin. Tumour exosomes can stimulate tumour cells growth, suppress the immune response and induce angiogenesis38,39. It also involved in the metastatic process40,41. Tumour cells actively release exosome tens of thousands of vesicles per day resulting in hundreds of billions vesicles per ml of plasma42.They contain highly stable packages of RNA from their cell of origin43 and can be isolated from bio-fluid samples and stored for many years in the freezers38,44 and help in the diagnosis. DNA associated with exosomes can be used to detect gene amplification and mutation45,46,47.

CLINICAL APPLICATION

Assessment of prognosis

Prognosis of any particular disease specially in malignant tumour depends on a number of factors. Clinicians use different tools to identify these factors like clinical examination, staging by imaging and biopsy, histopathological and biomolecular characterization of different tumours. Liquid biopsy is particularly helpful when a biopsy is not available or genetic analysis of archived tumour sample is not possible48,49. Studies have shown that there is statistically significant correlation between the disease stage and the presence of tumour-associated genetic aberrations like mutation in TP53, KRAS and APC for breast, ovarian, pancreatic, colorectal and oral squamous cell carcinoma. In breast cancer, tumour-associated genetic aberration like TP53 mutation or loss of heterozygosity

(LOH) correlated with both overall survival (OS) and disease free survival (DFS)50,51. Liquid biopsy has a limited role in assessing the prognosis of the disease in the early stage resectable tumours where tissue is available for analysis. But in the unresectable, advanced stage of the disease liquid biopsy is very important for assessing the prognostic information. In a multivariate analysis, KRAS mutation present in the plasma of 246 patients with advanced-stage NSCLC was shown to predict poor prognosis in patients receiving first line chemotherapy52. KRAS mutation in the circulation also have been assessed in a cohort of 44 patients with pancreatic cancer to determine the prognosis, it was shown that KRAS mutation was associated with significantly reduced probability of survival compared to those patients without KRAS mutation (17% versus 41% at six months and 0% versus 24% at twelve months in KRAS mutant and wild type respectively)53. Neuroblastoma is another special case where amplification of MYC-related oncogene (MYCN) has been identified as genetic hallmark of aggressive disease and also provide important information for treatment decision.Liquid biopsy can accurately detect MYCN amplification in the serum of stage III and IV neuroblastoma with a sensitivity and specificity of 75-85% and 100% respectively54,55.

Detection of recurrence

A very important clinical application of liquid biopsy is the early detection of relapse of the disease after potentially curative treatment. In follow-up, patients are assessed clinically by history, physical examination and some investigations like imaging studies and blood reports. It was found that, by monitoring of tumour-specific genetic aberrations (including APC, KRAS, TP53) in the plasma of patients with colorectal cancer, it was possible to detect recurrence with almost 100% sensitivity and specificity56. In breast, lung and oral squamous-cell carcinoma, there is a consistent relationship between disease recurrence and the reappearance of certain tumour aberration(KRAS,TP53,APC)57,58,59,60. Another important aspect of liquid biopsy is to identify dormant disease more commonly in breast cancer, melanoma, NHL (non-hodgkin lymphoma), renal cancer which are not detected by standard method61. But the sensitivity of detecting single tumour-specific genetic aberration in serum or plasma is very variable, particularly in the setting of low tumour burden57. Next generation sequencing (NGS) technology might offer the opportunity of increased sensitivity.

Difficult-to-diagnose cancers

Sometimes there are difficulties in diagnosing diseases when patients present with metastatic disease or very advanced stage of the disease or deep pelvic masses62,63. In a study targeted deep sequencing of cancer-related genes (TP53, KRAS, PIK3CA) was carried out in cfDNA in a patient with synchronous bowel and ovarian cancer to detect the origin of the metastasis63. In these types of cases, liquid biopsy can help to assess ctDNA or cfDNA and unnecessary delay for starting treatment can be avoided.

Prediction of response to treatment

Now-a-days a number of novel targeted agents are available for treatment. For example, gefitinib for EGFR mutation in NSCLC, vemurafenib for BRAF mutation in melanoma, cetuximab or panitumumab in KRAS mutation in colorectal cancer, crizitinib for AIK rearrangement for NSCLC64,65,66. Studying of testing genetic alterations are increasing as there are a number of targeted agents are on their way. Sometimes molecular tests are performed on archived tumour tissue that may not reflect the current genomic landscape of the tumour. Even it was also found in a study that patients with metastatic breast cancer acquired a HER-2 positive status on disease recurrence despite being previously classified as HER-2 negative by tissue biopsy67. So obviously, liquid biopsy has a considerable impact on the treatment of these recurrent cases. Detection of high levels of KRAS mutant alleles in the plasma is a clear indicator of response to treatment with third line cetuximab and irinotecan in metastatic colorectal cancer68. It was found that, when mutated KRAS level in the plasma <75, 42% had disease control whereas >75% plasma level of mutated KRAS, there was no response to the treatment. So, level of mutated KRAS in the plasma is a strong indicator of poor outcome of the disease and treatment response.

Prediction of acquired resistance

Targeted therapies are novel agents act as magic bullets. But unfortunately, the development of secondary or acquired resistance is a common outcome of the majority of the patients treated with these targeted agents. So, every patient who becomes resistant to a particular therapy should undergo a tissue biopsy and molecular analysis (including NGS) and it should be compared with the tissue collected pretherapy. Archived tissue sample might not be representative of genetic landscape of the disease at the time of acquired resistance owing to clonal divergence. So, the detection of the emergence of the resistant clone by the presence of tumour-associated genetic aberrations in the blood, can identify treatment resistance up to ten months before radiological methods. This rapid detection will allow

the clinician to halt the expensive and toxic treatment in patients unlikely to continue responding and start alternate therapies. For example, the acquisition of the T790M substitution in the membrane receptor EGFR conferring resistance to gefitinib and crizotinib in NSCLC and third generation inhibitors have shown activity in the presence of this mutation69. So, liquid biopsy can provide a novel paradigm for the study of clonal evolution in human cancers under the pressure of the targeted therapies and the disease can be challenged with novel drugs or drug combinations long before relapse is detected clinically or radiologically70,71,72.

Although liquid biopsy has a great ability to open a new paradigm in diagnostics and therapeutics still it has some limitations. There are three major limitations to liquid biopsy application in general- high cost, the requirement for high quality DNA and extensive data analysis by a dedicated bioinformatician. Another point of consideration is how tumour markers should be selected, that is whether multiple mutational panels should be adopted or personalized panels based on the sequences of the cancer of an individual. Logistic consideration to run a facility for tracking and monitoring of tumour-associated genetic aberrations in the blood is also an issue. For the patients, there is an obvious and clear advantage to liquid biopsy in comparison to conventional surgical methods. In most of the studies, actionable mutations are detected in bio-fluids that make only a fraction of the capability of liquid biopsy in enabling personalized medicine. DNA mutation can inform only some aspects of the disease, so, RNA expression in bio-fluids can give more information. Cancer is a complex and dynamic disease. To provide personalized medicine to these patients, reliable and robust non-invasive tools for diagnosis, patient stratification and monitoring treatment response are mandatory. Liquid biopsy has the potential to add value to the care of cancer patients.

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Original Article

Predisposing Factors and Surgical Management of Obstructive Sleep Apnoea in Children

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Abstract

Obstructive sleep apnoea (OSA) is a condition characterized by episodic partial or complete obstruction of the upper airway during sleep. This cause apnoea or cessation of breathing. During sleep, muscles around the airway relax causing the throat and upper airway to narrow. This leads to snoring, but it can also lead to the airway being blocked. Trying to breathe against a blocked airway causes oxygen levels to fall and carbon dioxide to rise. This cross-sectional study was conducted in Department of ENT, Dhaka Shishu (Children) Hospital and Dhaka Medical College Hospital from April to September'2015. The purpose of the study was to prevent significant morbidity and enhancement of child growth. One hundred children of OSA were studied by detail history and clinical examination. All children whose parents consulted their ENT surgeon in Dhaka Shishu(Children) Hospital and DMCH for snoring or laboured breathing during sleep (nocturnal sweating particularly in the nuchal area, unusual sleeping positions, restless sleep, awakening and excessive movements, intercostals recession and dry mouth) were included in the study. More common predisposing conditions for OSA were obesity and Craniofacial anomalies which were 34% and 27% respectively. In present study most of the children (73%) were managed by Adenotonsillectomy and 27% children were manage by Adenoidectomy. Outcome data have demonstrated that surgical therapy can be successful in the treatment of OSA.

Key Words: Obstructive sleep apnoea, enlarged adenoid or enlarge adenoid and tonsil

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INTRODUCTION

Obstructive sleep apnoea (OSA) is one of the most common causes of sleep-disordered breathing (SDB) in children. It is associated with significant morbidity, potentially impacting on long-term neurocognitive and behavioural development, as well as cardiovascular outcomes and metabolic homeostasis.1 The prevalence of OSA has been estimated to be 14% of men and 5% of women, in a population-based study utilizing an apnoea and hypopnoea index (AHI) cutoff of ≥ 5 events/h (hypopnoeas associated with 4% oxygen desaturations) combined with clinical symptoms to define OSA.2 The prevalence of OSA is substantially higher than this estimate, for example, in patients being evaluated for bariatric surgery (estimated range of 70% to 80%)3 or in patients who have had a transient ischemic attack or stroke (estimated range of 60% to 70%).4 Other disease-specific populations found to have increased rates of OSA include, but are not limited to, patients with coronary artery disease, congestive heart failure, arrhythmias, refractory hypertension, type 2 diabetes, and polycystic ovarian disease.5,6 Obstructive sleep apnea (OSA) is a problem that affects your child's breathing during sleep. An obstruction is a blockage of airflow into the lungs. Apnoea means a pause in breathing for at least 10 seconds. Six seconds or less may be pathological in children. A child (or adult) with obstructive sleep apnea has times during sleep when air cannot flow normally into the lungs.7 The immediate consequences of obstructive sleep apnoea syndrome (OSAS) in children include behavioral disturbance and learning deficits, pulmonary hypertension, as well as compromised somatic growth. However, if not treated promptly and early in the course of the disease, OSAS may also impose long term adverse effects on neurocognitive and cardiovascular function, thereby providing a strong rationale for effective treatment of this condition.8 Obstructive sleep apnoea (OSA) in children has emerged not only as a relatively prevalent condition but also as a disease that imposes a large array of morbidities, some of which may have long-term implications, well into adulthood.9 The major consequences of paediatric OSA involve neurobehavioral, cardiovascular, and endocrine and metabolic systems. The underlying pathophysiological mechanisms of OSA-induced end-organ injury are now being unrevealed, and clearly involve oxidative pathways.9 Children with enlarged adenoid and tonsil should be referred for tonsillectomy and

adenoidectomy. This successfully treats OSA in 80-90% of children. Children at high risk of postoperative respiratory complications after adenotonsillectomy should have their surgery in centres with expertise in paediatric anaesthesia and paediatric intensive care facilities.10 Children who are overweight (obese) would benefit from an exercise and weight management program. Children with chronic nasal allergy may trial a mix of different medical treatments including topical steroid sprays. Children with persisting OSA despite other treatments can be treated with continuous positive airways pressure (CPAP).10

MATERIALS AND METHODS

This observational type of cross-sectional study was conducted department of ENT, Dhaka Shishu (Children) Hospital and Dhaka Medical College Hospital among 100 patients during April to September'2015. All patients with OSA of both sexs and children were included . Mentally Ill patients patients , adult patients were excluded from this study. The purpose of the study to prevent significant morbidity and enhancement of child growth. 100 children of OSA were studied by detail history, clinical examination. This 100 children whose parents consulted their or ENT surgeon in Dhaka Shishu(Children) Hospital and DMCH for snoring or laboured breathing during sleep (nocturnal sweating particularly in the nuchal area, unusual sleeping positions, restless sleep, awakening and excessive movements, intercostals recession and dry mouth) were included in the study. All children had enlarged adenoid or enlarge adenoid and tonsil, which were confirmed by ENT examination. This was also confirmed in all cases by lateral radiography of the nasopharynx and flexible nasoendoscopy. After collection of data, data were edited by meticulous checking and rechecking. SPSS (statistical Package for Social Science) version 23.0 package program was used for analysis of these data. The statistics used to analyze the data were descriptive statistics and tests done were students't' test and $\chi 2$ test. Level of significance was set at 0.05 and $p<0.05$ was considered significant.

RESULTS

Data were obtained from 100 patients, at the time of the diagnostic sleep study, 32 (32%) patients were less than 5 year, (40%) were aged 6–10 years, (19%) were aged 11–15 years, and (9%) were aged 16–19 years (Table-I). Regarding sex distribution (62%) boys and (38%) girls (Table II). More common predisposing conditions for OSA were obesity and Craniofacial anomalies which were 34% and 27% respectively (Table-IV). In present study most of the children (73%) managed by Adenotonsillectomy and 27% children manage by Adenoidectomy (Table-V).

Table I: Distribution of the study patients by age (n=100)

Age (in year)	Number of patients	Percentage
≤5	32	32.0
6-10	40	40.0
11-15	19	19.0
16-18	09	09.0

Table II: Distribution of the study patients according to sex (n=100)

Sex	Number of patients	Percentage
Male	62	62.0
Female	38	38.0

Table III: Distribution of the study patients according to obstructive sleep apnea syndrome (n=100)

Obstructive sleep apnea syndrome	Mean±SD
Total sleep time (min)	370±53
Sleep latenth (min)	16.2±14.0
Awake time after sleep onset (min)	38.0±36.1
No. of rapid eye movement periods	4.1±1.2
Rapid eye movement sleep (% of total sleep)	20.5±5.8
Sleep efficiency (%)	87.1±8.9
Arousals per hour of sleep	2.5±0.5
Awakenings per hour of sleep	0.8±0.5
Movements per hour during sleep	16.9±12.9
Breathing during sleep obstructive AHI	12.1±7.8
Sp02 while awake	98.6±1.8
Lowest Sp02 (%)	78.4±13.9`
Peak end-tidal C02 (mmHg)	56.8±9.7

Table IV: Predisposing conditions for OSA in 100 children

Predisposing conditions	Number of patients	Percentage
Obesity	34	34
Craniofacial anomalies	27	27
Idiopathic	13	13
Sickle cell disease	03	03
Glycogen storage disorder	04	04
Trisomy	03	03
Neuromuscular disease	05	05
Retrognathia and cerebral palsy	10	10
Malformation	04	04
Pharyngeal flap surgery	05	05
Other*	05	05

*Tracheomalacia after tracheal reconstruction in child who had tracheostomy because of laryngeal papillornatosis.

Table V: Surgical management of the study children (n=100)

Surgical treatment	Number	Percentage
Adenotonsillectomy	73	73
Adenoidectomy	27	27
Total	100	100

DISCUSSION

The UpToDate series implies that obstructive symptoms and signs frequently persist after adenoidectomy alone for treatment of OSA, and that many children who undergo adenoidectomy are not spared tonsillectomy,11-13 although a comparison between these two surgical approaches in regards to long-term resolution of OSA symptoms has never been performed. Gov-Ari et al. showed that patients undergoing adenoidectomy for upper airway obstruction are likely to be at an increased risk of subsequent tonsillectomy when compared with those who undergo adenoidectomy for other indications. Young age, female sex, and large tonsil size may further increase the risk for subsequent tonsillectomy.14

In present study showed that data were obtained from 100 patients, (62%) boys and (38%) girls. At the time of the diagnostic sleep study, 32 (32%) patients were less than 5 year, (40%) were aged 6–10 years, (19%) were aged 11–15 years, and (9%) were aged 16–19 years. Mitchell study observed that the mean age was 6.3 (range, 3.0-14.0) years.15 Tang et al. study revealed that the mean time interval between PSG and telephone interview was 3.6 ± 1.33 years. The mean age of the cohort was 3.38 ± 2.61 years at PSG and 7 ± 3.03 at follow-up evaluation.16

In current study observed that more common predisposing conditions for OSA were obesity and Craniofacial anomalies which were 34% and 27% respectively. Trosman et al studied 19 of the 62 patients were obese, while 15 had a craniofacial syndrome or hypotonia.17 Andersen et al. study observed that OSA was significantly more likely to persist in obese children after adenotonsillectomy.18 The prevalence of persistent OSA ranged from 33 to 76% in obese children and from 15 to 37% in non-obese children depending on the definition of OSA, the degree of obesity and the age of the study population. The few studies that investigated the effect of weight loss found that OSA improved significantly after intervention and that the prevalence of persistent OSA varied between 10 and 38%.18 In present study most of the children (73%) managed by Adenotonsillectomy and 27% children manage by Adenoidectomy. In study of Trosman et al observed that Adenotonsillectomy leads to a significant improvement in apnea-hypopnea index.17 on follow-up polysomnography over an observational approach, especially in non-obese, non-syndromic children. Mitchell RB15 study observed that the mean total OSA-18 score and the mean scores for all domains showed significant improvement after surgery (P < .001). Adenotonsillectomy for OSA results in a dramatic improvement in respiratory parameters as measured by polysomnography in the majority of healthy children. Quality of life also improves significantly after adenotonsillectomy for OSA in children. Similar observation was found Tang et al. study revealed that Adenotonsillectomy was performed in 394 children (76.5%) and adenoidectomy in 121 (23.5%).16 this study suggests that the indiscriminant approach to perform adenotonsillectomy for all children with OSA who undergo surgery may not be justified. We propose that subjective, long-term outcomes of adenoidectomy are comparable to those of adenotonsillectomy in non-obese children under 7 years old with moderate OSA and small tonsils.

CONCLUSION

Surgical therapy is an alternative in patients who are intolerant of conservative treatments. Outcome data have demonstrated that surgical therapy can be successful in the treatment of OSA. A careful evaluation of location and cause of airway abnormality and proper selection of patients can result in improved clinical outcome, the patients' quality of life, and general health with minimal complications.

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Original Article

Aetiological Evaluation of Patients with Meningitis in a Tertiary Care Hospital of Bangladesh

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Abstract

Meningitis is a global health problem as mortality is high and a large proportion of survivors suffered from significant morbidity. The physicians are facing this challenge of emergency identification of this clinical syndrome, establishing its etiology and its prompt treatment not only to ensure survival but also to prevent long term sequelae in these patients. Poor outcomes caused by bacterial meningitis due to delays in diagnosis and treatment. In Bangladesh, the epidemiological study regarding meningitis in adults is rare. Rapid & easily available as well as specific test or means are also not in our hand. The aim of this study was to evaluate the aetiology of patient with meningitis in tertiary care hospital of Bangladesh. The main objective was to evaluate the aetiology of meningitis of patients admitted in medical wards of a tertiary care hospital. The study was a descriptive type of observational study. The study was carried out in the Department of Medicine, Dhaka Medical College Hospital, a tertiary level hospital of Bangladesh from first July 2013 to thirty first December 2013. A total 50 patients were enrolled with Meningitis, diagnosed on clinical, biochemical, other investigational background , fulfilling the inclusion and exclusion criteria.Patients having feature of meningitis was enrolled in the study after getting informed written consent from patient or attendant. Detail demographic data were collected from the informant was recorded in structured case report form. Clinical examination and relevant investigation with CSF study were done. Routine follow up of the patient was done. Data analysis was conducted with SPSS software. Among the 50 patient the mostly affected groups were below 40 years of age comprising 66%. The mean(±SD) age was 33.04 ±18 years. There was an overall male preponderance with a male to female ratio 1.63:1 (N=31 vs N=19). The highest number of patients were presented with fever (100%), headache (98%) and altered mental status (88%). Among all 50 cases of meningitis 27(54%) were diagnosed as pyogenic, 9 (18%) were tuberculous meningitis and 14(28%) were viral . Out of 27 pyogenic meningitis cases 19 (70.37%) developed convulsion, out of 9 tuberculous meningitis 3 (33.33%) developed convulsion and 11 (78.57%) out of 14 viral cases had convulsion, that is convulsion was more common in viral cases. Sixteen male patients (51.61%) and 11 female patients (57.89%) had pyogenic meningitis, 5 male patients (16.12%) and 4 female patients (21.05%) had tuberculous meningitis. On the other hand, 10 (32.25%) male and 4 (21.05%) female had viral meningitis. P value was 0.369, So the male and female difference was not statistically significant. Diagnosis was made on the basis of clinical findings and CSF study. Pyogenic were more common than viral cases and tubercular meningitis. Meningitis is foremost causes of morbidity and mortality. It is recommended that provision of proper health care support, Proper and rapid detection and others investigation facilities reduce the disability. In the interim, this study provides data that can inform public health strategies directed at assessing and reducing meningitis severity and meningitis events.

Key Words: Meningitis, Aetiology, CSF study

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INTRODUCTION

Meningitis is an acute inflammation of the protective membranes covering the brain and spinal cord, known collectively as the meninges.1 The inflammation may be caused by infection with viruses, bacteria, or other microorganisms, and less commonly by certain drugs.2 Meningitis can be life-threatening because of the inflammation's proximity to the brain and spinal cord; therefore, the condition is classified as a medical emergency.

Although meningitis is a notifiable disease in many countries, the exact incidence rate is unknown.3 As of 2010 it is estimated that it resulted in 420,000 deaths. Bacterial meningitis occurs in about 3 people per 100,000 annually in

Western countries. Population-wide studies have shown that viral meningitis is more common, at 10.9 per 100,000, and occurs more often in the summer. In Brazil, the rate at 45.8 per 100,000 annually.4 Sub-Saharan Africa has been plagued by large epidemics of meningococcal meningitis for over a century, leading to it being labeled the "meningitis belt".5 In Bangladesh major etiological factors revealed that 18% are meningococcal, 3% pneumococcal, and 3%Hib infection. Twenty percent of patients with Hib meningitis are older than 15 years. Case-fatality ratios 10% for N. meningitid is, 22% for S. pneumoniae, and 24% for Hib. Bacterial meningitis from vaccine-preventable pathogens causes significant morbidity and mortality in Bangladesh in adults and children.6

Epidemics typically occur in the dry season (December to June), and an epidemic wave can last two to three years, dying out during the intervening rainy seasons. These cases are predominantly caused by meningococci.4 The largest epidemic ever recorded in history swept across the entire region in 1996 to 1997, causing over 250,000 cases and 25,000 deaths. Several factors have been associated with the development of epidemics in the meningitis belt. They include: medical conditions (immunological susceptibility of the population), demographic conditions (travel and large population displacements), socioeconomic conditions (overcrowding and poor living conditions), climatic conditions (drought and dust storms), and concurrent infections (acute respiratory infections).7,8

The infection may trigger sepsis, a systemic inflammatory response syndrome of falling blood pressure, fast heart rate, high or abnormally low temperature, and rapid breathing. Very low blood pressure may occur at an early stage, especially but not exclusively in meningococcal meningitis; this may lead to insufficient blood supply to other organs. Disseminated intravascular coagulation, the excessive activation of blood clotting, may obstruct blood flow to organs and paradoxically increase the bleeding risk. Gangrene of limbs can occur in meningococcal disease.1

The brain tissue may swell, pressure inside the skull may increase and the swollen brain may herniated through the skull base. This may be noticed by a decreasing level of consciousness, loss of the pupillary light reflex, and abnormal posturing. The inflammation of the brain tissue may also obstruct the normal flow of CSF around the brain (hydrocephalus).9 Seizures may occur for various reasons; in children, seizures are common in the early stages of meningitis (in 30% of cases) and do not necessarily indicate an underlying cause. Seizures may result from increased pressure and from areas of inflammation in the brain tissue. Focal seizures, persistent seizures, late-onset seizures indicate a poorer long-term outcome.1

Meningitis can lead to serious long-term consequences such as deafness, epilepsy, hydrocephalus and cognitive deficits, especially if not treated quickly. Some forms of meningitis (such as those associated with meningococci, Haemophilus influenzae type B, pneumococci or mumps virus infections) may be prevented by immunization.1,9

Untreated, delay treated, bacterial meningitis is almost always fatal. Viral meningitis, in contrast, tends to resolve spontaneously and is rarely fatal. With treatment, mortality from bacterial meningitis depends on the age of the person and the underlying cause. Of newborns, 20–30% may die from an episode of bacterial meningitis. This risk is much lower in older children, whose mortality is about 2%, but rises again to about 19–37% in adults. Risk of death is predicted by various factors apart from age, such as the pathogen and the time it takes for the pathogen to be cleared from the cerebrospinal fluid,1 the severity of the generalized illness, a decreased level of consciousness or an abnormally low count of white blood cells in the CSF. Meningitis caused byH. influenzae and meningococci has a better prognosis than cases caused by group B streptococci, coliforms and S. pneumonia. In adults, too, meningococcal meningitis has a lower mortality (3–7%) than pneumococcal disease.9

Management of bacterial meningitis involves several crucial questions regarding the optimal timing of therapy. First, given that the diagnosis of bacterial meningitis can be definitively made only by CSF analysis, does early antibiotic administration before LP affect culture results and thereby compromise targeted therapy? Second, does the performance of diagnostic testing such as computed tomography (CT) and LP significantly delay antibiotic therapy? Lastly, does delayed therapy produce worse clinical outcomes? In a retrospective pediatric study, results confirmed previous suspicions that early antibiotics do, in fact, reduce culture yields: Parenteral antibiotics can complete sterilization of meningococcus in the CSF within 2 hours of therapy and pneumococcus within 4 hours.10 However, if the patient's clinical presentation mandates a head CT prior to LP, an average of 6 hours lapses between presentation and parenteral antibiotics.

One of the greatest fears passed down in emergency medicine dogma is the risk of brain herniation upon sudden release of increased intracranial pressure from LP. The true incidence of this devastating complication is unknown and is based mostly on retrospective observational data. 11

Regardless, neuro-imaging should be obtained prior to LP in patients with abnormal neurological exams. The Infectious Disease Society of America (IDSA) recommends obtaining a head CT prior to LP for patients who meet any of these criteria: immunocompromised state, history of CNS disease (mass lesion, stroke, or focal infection), new-onset seizure within 1 week of presentation, papilledema, abnormal level of consciousness, or focal neurologic deficit.11

MATERIALS AND METHODS

The study was a descriptive type of observational study. The study was carried out in the Department of Medicine, Dhaka Medical College Hospital, a tertiary level hospital of Bangladesh from first July 2013 to thirty first December 2013. A total 50 patients were enrolled with Meningitis, diagnosed on clinical, biochemical, other investigational background , fulfilling the inclusion and exclusion criteria. The inclusion criterias were hospital admitted patients in medical wards with fever, headache, and vomiting, meningeal irritation, e.g. neck rigidity, positive Kerning's sign and/or positive Brudzinskis sign,a dult patients of both genders (twelve years and above).

And the exclusion criterias were patients who refuse lumbar puncture or die before doing lumbar puncture,patients of encephalopathy due to metabolic and endocrine causes,patients who have recent head trauma, immune compromised, known malignant lesions, Central nervous system neoplasm Critically ill patient or patient refused to give consent or not able to do CT-scan will be excluded from the study, withdrawal of informed consent. Patients having feature of meningitis was enrolled in the study after getting informed written consent from patient or attendant. Detail demographic data were collected from the informant was recorded in structured case report form. Clinical examination and relevant investigation with CSF study were done. Routine follow up of the patient was done. Data analysis was conducted with SPSS software

RESULTS

In this series, the maximum numbers of patients were between 13-20 years of age group, 22(44%). Then 21-30 years of age 8 (16%)(Table 1) .Out of 50 cases 31 (62%) were male and 19 (38%) were female and male to female ratio was 1.63:1. Maximum numbers of male and female patients were in age group between 13-20 years. It is about 48.38 % and 36.84 % respectively. Patients came from both urban and rural areas with urban (66 %) preponderance. (Table-1)

Table 1: Age distribution of patient. (n=50)

Age (years)	Number of patients	Percentage (%)	Mean ± SD
13-20	22	44	33.04±18.08
21-30	8	16	
31-40	3	6	
41-50	3	6	
51-60	6	12	
>60	8	16	

Among the patients the poor class 22(44%) comprising the major percentage of the meningitis patients, which is followed by middle class 19(38 %) and remaining are upper class 9(18%). (Figure 1)

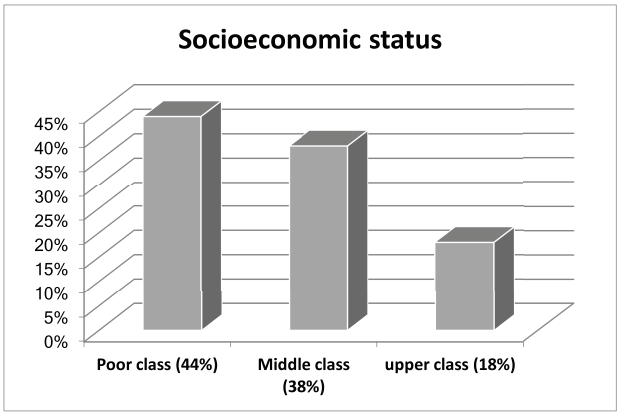

Figure- 1: Socioeconomic status.

In this series, the maximum number of patients 50 (100%) faced their crisis with acute onset fever, and then 49 (98%) of cases presented with headache, then altered mental status 44 (88%) of cases . About 50% patients (25) were Lethargic and 32% patients were comatose. The difference was statistically not significant (P>0.05).In this series, the maximum number of patients 50 (100%) presented with neck rigidity, and then kernig's sign 43 (86%), abnormal pupil 62% and extensor plantar response 40% of patient.(Table-2)

Table- 2: Distribution of patients according to symptoms and signs of meningitis. (n=50)

Presentation	Number of patients	Percentage (%)
Fever	50	100%
Altered mental status	44	88%
Headache	49	98%
New onset seizure	11	22%
Vomiting	31	62%
Restlessness	29	58%
Photophobia	21	42%
Neck rigidity	50	100%
Kernig's sign	43	86%
Abnormal pupil	30	60%
Extensor plantar response	20	40%

Among the 50 cases of meningitis 27(54%) cases were diagnosed as pyogenic meningitis. Out of 31 male patient 16 (51.61%) had pyogenic, 5(16.12%) tuberculous and 10 (32.25%) had viral causes. In case of female 11 (57.89%) had pyogenic, 4 (21.05%) tuberculous and 4 (21.05%) had viral meningitis. The difference was statistically not significant (P>0.05).(Table-3)

Table- 3: Distribution of cases according to aetiological factors. (n=50)

Type of meningitis	Number of patients		Total
	Male (n= 31)	Female(n= 19)	
Pyogenic meningitis	16 (51.61%)	11 (57.89%)	27 (58%)
Tuberculous meningitis	5 (16.12%)	4 (21.05%)	9 (18%)
Viral meningitis	10 (32.25%)	4(21.05%)	14 (28%)

The convulsions were less common in viral cases 11 (22%) cases compared to pyogenic meningitis which was 38%. The difference was statistically not significant (P>0.05).(Table-4)

Table-4: Association with seizure/convulsion. (n=50)

Type of meningitis	Convulsion present	Convulsion Absent	P value
Pyogenic	19	8	0.242
Tuberculous meningitis	3	6	
Viral meningitis	11	3	
Total	33	17	

DISCUSSION:

Our study design raises a number of important methodological issues, including patient selection, sample size and the prospective identification of case according to clinical and pathological evaluation, all of which may exert a powerful influence on the results. These issues may be particularly relevant for observational studies that use aetiology, risk, complication as an outcome measure, in which sources of bias may be sufficiently large to either obscure a real difference in rates or create an apparent one. Using our results and previous studies as examples, we shall address these issues in turn.

Most of the published studies on meningitis have focused on individual problems in isolation, such as causes or clinical manifestation e.g. seizures, acute onset fever, neck rigidity or feature of meningeal irritation. These studies have used a range of different designs; furthermore, methods of patient selection, diagnostic criteria, timing, and duration of follow-up vary considerably between studies, and therefore it is hardly surprising that the reported frequencies of specific complications in these studies also varied.

Infection of the central nervous system is a medical emergency. Fifty consecutive cases (age above 12 years) were recruited. The mostly affected groups were below 40 years of age comprising 66%. 22 cases (44%) were in 13-20 years age group and also there was a small rise in elderly patients (8 cases, 16% above 60 years of age). Mean age was 33.04 (±18.08 SD) years which correlates with another study done in India where mean age was 32.54 ± 13.32 years (range from 15-70 years) of which 56% were male and 44% were female.12 In a hospital based prospective study 13 done in Bangladesh (2003-2005) for etiology of bacterial meningitis 66% adult patients were in 15-36 years age group. In AMES surveillance14 study in Bangladesh from 2007 to 2009 mean age of Japanese encephalitis patients was 31 years ranging from 1 month to 85 years and mean age of total AMES patients was 18 years. There was an overall male preponderance with a male to female ratio 1.63:1 (N=31 vs N=19). This finding has similarity with a prospective clinical study published in Arch Neurol Journal in 1993.15

In this series13 maximum patients were presented with fever (100%), headache (98%) and altered mental status (88%). Out of 50 cases 11(22%) patients developed new onset seizure and 30 (60%) developed signs of meningeal irritation. 25 patients (50%) were lethargic and 16 (32%) cases were comatose. Female were more comatose (36.84%) compared to male (29%). It correlates with hospital based prospective study of Bangladesh. In a nation wide study done in Netherlands to determine clinical features and prognostic factors in adult with community acquired acute meningitis from October 1998 to April 2002, 95% patients had at least two of four symptoms of headache, fever, neck stiffness and altered mental status.16

Out of 27 pyogenic meningitis cases 19 (70.37%) developed convulsion, out of 9 tuberculous meningitis 3 (33.33%) developed convulsion and 11 (78.57%) out of 14 viral cases had convulsion, that is convulsion was more common in viral casesStudy showed clinical presentation of mental status among the meningitis patient. Out of 14 viral meningitis cases 6(42.85%) were comatose state, 10 (37.03%) pyogenic cases were comatose and there is no coma in tuberculous meningitis. That is unconsciousness was more common in viral group. This finding correlates with another study.18

Among all 50 cases of meningitis 27(54) were diagnosed as pyogenic, 9 (18%) were tuberculous meningitis and 14(28%) were found viral aetiology. 16 male patients (51.61%) and 11 female patients (57.89%) had pyogenic meningitis, 5 male patients (16.12%) and 4 female patients

(21.05%) had tuberculous meningitis. On the other hand, 10 (32.25%) male and 4 (21.05%) female had viral meningitis. P value was 0.369, So the male and female difference was not statistically significant. Diagnosis was made on the basis of clinical findings and CSF study (Cytology, biochemistry, Latex agglutination test). Pyogenic were more common than viral cases.

Among the 50 cases of meningitis patient, 26 (52%) cases were undernutritional condition. In case of pyogenic meningitis 13 (48.14%) cases are undernourished, in tuberculous 7(78%) patient and in viral meningitis 6(42.85%) patients are undernourished. Colour of CSF was turbid in maximum pyogenic meningitis patients and clear nearly in all viral cases. In this series CSF glucose concentration was very low 32.8 mg/dl and protein concentration was high 197.6 mg/dl in case of pyogenic cases. In viral cases glucose and protein were normal. This findings correlates with hospital based study of Bangladesh.13 In a study of CSF analysis- acute bacterial versus viral meningitis done in Dubi, United Arab Amirat from 2005-07, CSF Glucose was found to be very low in bacterial than viral meningitis where mean CSF glucose concentration was 26.50 mg/dl (±21.56) Vs 67.00 (±18.96) mg/dl.19

CSF cell counts were very high (average >4200/mm3) in case of pyogenic meningitis of which most were neutrophils (87%) but in cases of tuberculour meningitis cell counts were very low (average 223/mm3) of which most were lymphocyts (76%). This finding correlates with the findings of maximum authorities.20

Study shows that in 55.55% of the tuberculous and 51.85% of pyogenic meningitis cases duration of hospital stay was between 1 – 2 weeks duration. Hospital stay for more than two weeks was proportionately much higher in tuberculous type (44.44%) compared to pyogenic (25.92%) and viral/aseptic type (7.14%). Total 5 (10%) patients expired out of 50. Total 16 patients were comatose and 4 (25%) of them died. On the other hand normal and confused patients were 9 with out any death. Out of 25 lethargic patients 1 (4%) expired. So death was high in unconscious patients. Mortality was high in viral cases 21.43% compared to pyogenic (7.40%) cases. These findings correlate with other studies. In another study mortality rate in untreated HSE is around 70%, 40% to 70% in Nipah virus encephalitis.27

Gradual communication of the truth within the context of continued support and encouragement almost always leads to enhanced hope. Breaking bad news generally causes distress to both the patient and his/her family. In this issue we obtain the response from the attendance by consultation, counseling, open question and elicit the feelings, emotion and concern. We found that only 14% of attendance carries clear idea regarding the disease, but majority of patient attendance lack of concept about the disease, its management and prognosis on future time.

CONCLUSION:

With this shortcoming this study is designed that may help us to understand the Clinoco-pathological issue of meningitis with management and influence us to better concern to control the disease thereby rescuing some people from long term disability and or death and preventing the burden of the family and the country.

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Original Article

Elevated Level of Plasma B-Type Natriuretic Peptide (BNP) as a Prognostic Marker in Patients with Acute Coronary Syndrome.

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Abstract

Acute coronary syndrome (ACS), a life-threatening manifestation of coronary artery disease, ranges from unstable angina (UA) to acute myocardial infarction (AMI). To reduce the morbidity and mortality resulting from acute coronary syndrome, we should have to find out some predictor or prognostic indicator. A prognostic indicator should be available at the time of initial patient's evaluation, in order to maximize the potential benefits of early risk assessment. This study designed to evaluate plasma BNP as a prognostic tool in patients with acute coronary syndrome. A prognostic cohort study was carried out with 90 (ninety) acute coronary syndrome patients on the basis of their clinical and laboratory criteria with age range of 30 to 90 years in the department of biochemistry, BSMMU, in collaboration with department of cardiology, NICVD, BSMMU and BIRDEM. Plasma BNP concentrations were measured on enrollment and then grouping of the study subjects were done on the basis of their empirical cut off value of plasma BNP concentration. All the patients were free from heart failure, renal disease, thyroid disease and hepatic disorder. Main outcomes were mortality, morbidity and survival after hospital discharge with or without any disability. All the subjects were categorized into two and to see the significance between two groups in relation to age and sex Unpaired –t test and Chi square test were done. Finally, Binary logistic regression was done. Among 90 acute coronary syndromes patients, there were 74(82.2%) male and 16(17.8%) female with mean age of the study population 51.8 years and the age range of 30 t0 90 years. Among enrolled patients, 24 (26.7%) were NSTEMI and 66 (73.3%) were STEMI that includes 29 (32.2%) anterior MI, 21 (23.3%) inferior MI, 16 (17.8%) other varieties of MI. All the study subjects were grouped into two on the basis of empirical cut off value of plasma BNP 640pg/ml on enrollment. Group I with plasma BNP level less than 640pg/ml includes 57 (63.3%) subjects and group II with plasma BNP more than 640pg/ml includes 33 (36.7%) subjects. Among group I (n=57) good recovery, morbidity and mortality found to be in 41(71.9%), 15(26.3%) and 1(1.8%) patients and those in group II (n=33) found in 6(18.2%), 19(57.6%) and 8(24.2%) patients respectively. Keeping the group I in reference category binary logistic regression analysis done, showing odds ratio 11.5 with p- value 0.000. The odds ratio 11.5 indicates that there is 11.5 times higher chance of getting bad outcome in ACS patients having higher plasma BNP concentrations.

Keyword: BNP, Acute Coronary Syndrome.

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Introduction

Coronary heart disease is the leading cause of mortality & morbidity worldwide affecting millions of peoples in both developed & developing countries.1 It has been observed that prevalence of CHD is higher in South Asians, with the highest rates among Bangladeshi & Pakistani origin.2 Acute coronary syndrome (ACS) encompass a continuum of cardiac ischemic event ranging from unstable angina with no evidence of biochemical necrosis to non ST elevation myocardial infarction (NSTEMI) and ST elevation myocardial infarction (STEMI).3 The usual approach to the treatment of an acute coronary event involves the institution of early aggressive therapeutic strategies aimed at limiting the amount of myocardial injury & preventing complication. Prioritization of the bare necessity in this context in order to select high risk group for comprehensive therapy which is the only way to reduce the morbidity & mortality of ACS.4 So primary challenge is the early & specific diagnosis of ACS with identification of high risk group that helps to initiate appropriate therapy without delay. Traditional serum markers of myocardial injury (cardiac enzyme troponin & myoglobin) in ACS reflect only the sequel of inflammatory milieu & plaque rupture. In contrast to the injury markers, newly identified serum substances have drawn attention for their ability to portend

acute coronary events & their outcomes. New biomarkers, like natriuretic peptide may provide additional pathophysiological insight & add to the strategy for comprehensive assessment.5

B-type natriuretic peptide is a 32 amino acid neurohormone released from ventricular myocardium predominantly in response to increased ventricular wall stores, ventricular dilatation & pressure overload.6BNP was originally identified in the extract of porcine brain. It is subsequently found that BNP is synthesized in brain but there is considerably more BNP in the cardiac ventricles. The diverse action of BNP includes arterial and venous vasodilatation, natriuresis, diueresis, inhibition of the rennin-angiotensin-aldosteron system, and inhibition of the sympathetic nerve activity7.

BNP have been shown to aid in the diagnosis of heart failure & to correlate with LV dilatation, remodeling, dysfunction & the mortality among patient presenting with Acute MI.8 After Acute MI, BNP concentration rises rapidly during the first 24 hours and then tends to stabilize.9 There is an association between BNP and the short and long term risk of death across the spectrum of ACS including patients without myocardial necrosis or clinical evidence of heart failure.10 Plasma BNP concentration measured between one to four days after a transmural infarction provides prognostic information that is independent of the left ventricular ejection fraction and other important baseline variables.11The association between BNP and long term risk of death in ACS is independent of cardiac function, renal function, the troponin I level, electrocardiographic changes and other known risk predictors.12

After acute MI, raised concentration of BNP identifies patients at risk for adverse ventricular remodeling, left ventricular dysfunction, heart failure and death independent of age, history of heart failure and left ventricular ejection fraction. Even in patients with unstable angina and no evidence of myocardial necrosis or heart failure, raised concentration of plasma BNP are associated with an increased risk of death.13 BNP is an independent marker for risk stratification in ACS patients. So, elevated level of plasma BNP in ACS patient is serious enough to warrant the follow up examination.

The magnitude of risk relationship of ACS with BNP found to be greater than that with most currently available cardiac markers. Therefore, we want to evaluate the prognostic implications of plasma BNP, a cardiac neurohormone across the entire spectrum of ACS. BNP provides a convenient and noninvasive means to gain insight into the underlying consequences of ACS and thereby may identify high risk target cases for timely specific therapeutic intervention. Since BNP has the potential to improve substantially the outcome in patients with ACS by facilitating its risk assessment and timely clinical decision making process at its very outset , so we have decided to evaluate the prognostic value of plasma BNP in patients with ACS.

Material & Method:

The present cohort study was conducted in the Dept. of Biochemistry, BSMMU, NICVD & BIRDEM, Dhaka, Bangladesh during the period from January 2009 to December 2009. A total of 90 diagnosed acute coronary syndrome (ACS) patients free from heart failure, renal disease, thyroid disorder and hepatic disorder were enrolled from the cardiology emergency department of BSMMU, NICVD and BIRDEM. After measurement of plasma BNP concentration, subjects were categorized into two groups. Those having BNP concentration <640 pg/ml were included in Group-I and those having plasma BNP concentration >640 pg/ml were included in Group II. All patients were treated and managed identically by conventional standard management protocol during their hospital stay and even after their discharge. After discharge all patients were followed up periodically in every month up to 6 months. During hospital stay and their follow up period patients were assessed clinically for any kind of clinical outcomes (good recovery, recurrent ACS, heart failure, cardiogenic shock, stroke, and cardiovascular death.) In every visit patient was evaluated on the basis of clinical assessment, ECG, Echocardiogram, CAG, cardiac markers according to the merit individual case. At the end of follow up patients clinical outcome were evaluated on the perspective of their baseline plasma BNP concentration. All data were recorded systematically in a preformed data collection sheet. Statistical analysis was performed by using Windows SPSS 13.0 version.Unpaired t- test and Chi-square test was done to see significance between two groups in relation to age and sex. The correlation between two groups with other baseline variables was assessed by Chi square test. To evaluate the association of plasma BNP with clinical outcome, chi-square test and Fissure exact test were done. Finally, Binary logistic regression was done to evaluate prediction of the risk of adverse clinical outcome (end point) based on the baseline plasma BNP concentration.

Results:

In a prognostic cohort study, 90 diagnosed ACS patients were enrolled in the study on the basis of their clinical and laboratory diagnostic criteria. At the outset, plasma BNP concentration of all patients was measured and then followed up. Out of 90 ACS patients 74 (82.2%) were male and 16 (17.8%) were female with the mean age of 51.8 years and the age range of 30 to 90 years (Table I).

Table I: Age and sex distribution of study subjects (n=90):

Sex		Age (yrs.)	
Male	Female	Mean	Range
74	16	51.8	30 – 90
(82.2%)	(17.8%)		

Among the enrolled patients, 24 (26.7%) were non-ST-elevation myocardial infarction (NSTEMI) and 66 (73.3%) were ST-elevation myocardial infarction (STEMI). STEMI includes 29 (32.2%) anterior MI, 21(23.3%) inferior MI, and 16 (17.8%) other varieties of MI e.g. anterior-inferior MI, posterior MI, right ventricular MI. (Table II).

Table II: Clinical types of study subjects (n=90):

NSTEMI (24)	STEMI (66)		
	Anterior MI	Inferior MI	Others
24	29	21	16
(26.7%)	(32.2%)	(23.3%)	(17.8%)

Table III shows the comparison of the two groups with respect to the baseline characteristics and clinical types of ACS. With respect to hypertension, diabetes and smoking status two groups found identical but with respect to types of ACS, STEMI found to be more in group II and NSTEMI were more in group I.

Table III: Distribution of baseline characteristics and clinical types of ACS between two groups (n=90):

Characteristics	Group I (n=57)		Group II (n=33)		x^2 Value	P Value
	Frequency	Percentage	Frequency	Percentage		
NSTEMI	22	38.6	2	6.0	11.314	0.001
STEMI	35	61.4	31	94.0		
Hypertensive	24	42.1	15	45.5	0.095	0.757
Normotensive	33	57.9	18	54.5		
Diabetic	20	35.1	13	39.4	0.167	0.683
Nondiabetic	37	65.9	20	60.6		
Smokers	39	68.4	22	66.7	0.029	0.864
Nonsmokers	18	31.6	11	33.3		

Baseline plasma BNP concentration was also associated with the dichotomous clinical outcome (good outcome and bad outcome) of study subjects. In group I (n=57) good outcome and bad outcome found in 41 (71.9%) and 16 (28.1%) patients and those in group II (n=33) found in 6 (18.2%) and 27 (81.8%) patients respectively. Chi- square test was done to assess the association of baseline plasma BNP concentration with the clinical outcome of the study subjects. In group II patients having high baseline plasma BNP concentration significantly less good outcome but significantly high bad outcome found compared to those in group I patients having low plasma BNP concentration. (Table IV).

Table IV: Association of plasma BNP concentration with the clinical outcome (good and bad outcome) of the study subjects (n=90).

Group	Good outcome		Bad outcome		X^2 Value	P Value
	(n)	(%)	(n)	(%)		
Group I (57)	41	71.9	16	28.1	24.199	0.000
Group II (33)	6	18.2	27	81.8		

Table V shows the binary logistic regression analysis of plasma BNP concentration of study subjects with respect to good and bad outcome. Keeping the group I in reference category, it is found significant for group II (p- 0.000) with the odds ratio 11.5. The odds ratio of 11.5 indicates that there is 11.5 times higher chance of getting bad outcome in ACS subjects having higher plasma BNP concentration (group II) than those having low baseline plasma BNP concentration (group I) .

Table V: Logistic regression analysis of plasma BNP concentration with respect to clinical outcomes of study subjects

Parameter	Regression Coefficient	Standard Error	P - Value	Odds ratio Exp (B)	Regression Coefficient
Group II Outcome	2.4	0.5	0.000	11.5	2.4
Group I Outcome	Reference Category				1

- Mortality: Death of patients during study period as a consequence of acute coronary syndrome.
- Morbidity: Development of re-angina, re-infarction, arrhythmias, heart failure, cardiogenic shock and stroke during study period.
- Good outcome: Recovery after conservative treatment or after any intervention without developing complications like morbidity and mortality during study period.
- Bad outcome: After conservative treatment or any intervention, patient developed morbidity and mortality during study period.

Discussion:

In this prognostic cohort study, 90 diagnosed acute coronary syndrome (ACS) patients free from heart failure, renal disease, thyroid disorder and hepatic disorder were enrolled from the cardiology emergency department of BSMMU, NICVD and BIRDEM. Among 90 patients, 74 (82.2%) patients were male and 16 (17.8%) patients were female with the mean age of 51.8 years and age range of 30-90 years. Higher bad clinical outcomes in group II compared to group I indicates that the increasing baseline plasma BNP concentration is associated with worsening clinical outcome. In line with this study, many studies abroad have demonstrated BNP as a predictor of adverse outcome in ACS while others have refuted an association. This result was consistent with the several studies. Suzuki et al, (2004) found that the survival rate was significantly higher in patients with plasma BNP concentration <180pg/ml than those with plasma BNP concentration >180 pg/ml. Cox proportional hazard ratio analysis showed baseline plasma BNP as an independent predictor of death in ACS patients14. Kuklinska et al, in their study concluded that median plasma BNP value was higher in patients with adverse clinical outcomes (p<0.001). Patients with plasma BNP concentration >99.2pg/ml were significantly at higher risk of adverse clinical outcome. Logistic regression analysis showed that the plasma BNP concentration >99.2 pg/ml was the strongest predictor of adverse outcome.15 Foody (2006) found that after adjustment of multiple risk factors, patients with plasma BNP level >80 pg/ml had significantly greater risk for death when measured at baseline.16 In consistent with this findings He B et al, (2006) in their study demonstrated the prognostic value of plasma BNP and C-reactive protein in patients with ACS undergoing percutaneous coronary intervention. They found that both plasma BNP and CRP were good predictors for early mortality and major adverse cardiac events but CRP had lost its predictive value after introduction of plasma BNP into the model, while BNP was still an independent predictor for mortality and major adverse cardiac events.17 Mega et al, (2004) in their study demonstrated that after adjustment of other clinical predictors including age, heart failure, HTN, heart rate, anterior MI, patients with baseline plasma BNP level >80pg/ml was associated with a seven-fold higher mortality risk (Odds ratio 7.2, p=0.001). Patients with plasma BNP level >80pg/ml were also more likely to have impaired coronary flow (p=0.049).18 A study done by Ang et al, (2009) found that after adjustment of other predictors, baseline plasma BNP levels > 80pg/ml was associated with subsequent cardiovascular events (Relative risk, 2.63, 95% CI, 1.34-5.19).19 Sun, Wang and Zhang, (2006) demonstrated the plasma BNP as an important predictor of

cardiac death in Chinese patients with ACS. In their study mean plasma BNP concentration in the non-survival group was significantly higher than that of the survival group. Multivariate logistic regression analysis incorporating age, sex, HTN, DM, left ventricular ejection fraction, Troponin-I and therapeutic regimens indicated that plasma BNP was an independent predictor of cardiac death in Chinese patients with odds ratio of 21.19.20

Through binary logistic regression analysis of plasma BNP concentration with respect to their good and bad clinical outcome keeping the group I in reference category, presentstudy have shown the odds ratio 11.5 for group II (p-0.000) indicating 11.5 times higher chance of getting bad outcome in ACS subjects in group II having higher plasma BNP concentration than those in group I having low plasma BNP concentration. This result was consistent with several other studies.7,21,22 In a study Morrow et al (2005) demonstrated that after adjustment of other clinical predictors like age, sex, renal function, hypertension, diabetes and prior heart failure; a baseline plasma BNP >80pg/ml was associated with a 2-fold higher long term risk of death (Adjusted hazard ratio 2.1).7 De Lemos et al, (2001) stated that the association of plasma BNP with clinical outcome remained significant in subgroups of patients who had STEMI, NSTEMI.21 In another study Morrow, de Lemos and Sabatine, (2003) showed that an elevated plasma BNP level >80pg/ml at presentation identifies patients with non ST elevation ACS who are at five-fold risk of developing new congestive heart failure or death (p<0.0001) independent of other clinical predictors.22 It can be concluded from this study that higher baseline plasma BNP concentration is associated with more adverse clinical outcomes in ACS patients. Since the baseline plasma BNP concentration at the onset of event shows incremental prognostic value, so plasma BNP can be used clinically as a biomarker of prognosis in ACS patients.

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Original Article

Risk Factors of Burst Abdomen in Emergency Laparotomy

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Abstract

Burst Abdomen is a preventable condition in which many risk factors play their role and lead to life threatening complications. This study was carried out to find out various risk factors of burst abdomen following emergency laparotomy, to find out the high risk group of patients for burst abdomen, to determine the predictors of burst abdomen, to prevent the rate of burst abdomen & find out morbidity and mortality of burst abdomen. This cross sectional study was done among 100 cases of burst abdomen occurring in Sir Salimullah Medical College & Mitford Hospital, Dhaka and Dhaka Medical college,Dhaka during the period of July,2011 to December,2011. The patients were admitted for various surgical problems and underwent emergency laparotomy. Burst abdomen was taken into account. Another group of 100 patients who undergone emergency laparotomy but did not develop burst abdomen were also taken into account to make a comparison with the burst group. Patients who undergone elective laparotomy,paediatric age group,patients undergone exploration through mini laparotomy or transverse incision,patients with pregnancy were excluded from the study populations.Patients were assessed by history taking, examination and appropriate investigation before surgery and observed post operatively for any complication. The results were prepared on 100 patients underwent emergency laparotomy in SSMCMH & DMCH.

Burst abdomen following emergency laparotomy results from multifactorial causes. The main outcome measure found significant as the risk factors of burst abdomen in this study were peritonitis (95%),anaemia (26%),malnutrition (18%), in the preoperative period; inadequate peritoneal toileting and faulty surgical techniques in the per operative period; and wound infection (62%) , postoperative cough (28%), abdominal distension (22%). The result also shows that the rate of burst abdomen is still very high in SSMCMH & DMCH and most of them occur in operations done by trainee surgeons (86%) and in those patients who has 3 or more of the risk factors (44%). We hope this study will arouse awareness and concern about this problem, so that more active steps will be taken for its prevention by identifying the high risk groups. This will certainly reduce the incidence of burst abdomen.

Key Words: Burst abdomen, Emergency laparotomy, Risk factors.

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INTRODUCTION

Burst abdomen is a serious post-operative complications in case of abdominal surgery as it carries substantial morbidity and mortality, increases the cost and hospital stay of the patient. Many patients in Bangladesh have poor nutritional status and presentation of patients with peritonitis is often delayed in the emergency. This causes more common problems of wound dehiscence. Estimates of the incidence vary between 0.5 to 6% in different studies.(1) Burst abdomen is a multifactorial problem conditioned by local and systemic as well as pre-operative, per-operative and post-operative risk factors. The mortality with this burst abdomen has been computed by different authorities as 10-44%.(7) When there is extensive suppuration of the wound, the prognosis is very grave.(6) Good knowledge of the risk factors responsible for wound infection is mandatory for prophylaxis on the part of surgeon's technique & OT instrument supplying authority. Many of the emergency operations are usually done by junior / trainee doctors. This may make the problem of burst abdomen more common and graver in our country.Patients identified as being high risk may be benefited from close observation and early intervention. If the risk factors can be predicted earlier, their numbers can be decreased and the incidence of burst abdomen will be lowered significantly.

Post-operative period of a patient after emergency laparotomy may be hazardous due to burst abdomen followed by prolonged hospital stay, increased morbidity and even death. This sort of morbidity and mortality can be reduced by increasing awareness and concern about this problem and accordingly taking more active steps for its prevention by identifying the high risk groups.

MATERIALS AND METHODS

This cross sectional study was done among 100 cases of burst abdomen occurring in Sir Salimullah Medical College & Mitford Hospital, Dhaka and Dhaka Medical college, Dhaka during the period of July, 2011 to December,2011. The purpose of the study was to find out the risk factors of burst abdomen in emergency laparotomy. The patients were admitted for various surgical problems and underwent emergency laparotomy. Burst abdomen was taken into account. Another group of 100 patients who undergone emergency laparotomy but did not develop burst abdomen were also taken into account to make a comparison with the burst group.

The case notes of the patients including age, sex of the patient, were also studied to obtain the information regarding initial complaints of the patients for admission and findings of general examination with special reference to history of COPD / bronchial asthma, nutritional status, anaemia, peritonitis, diabetes mellitus, obesity, jaundice and history of tuberculosis, exposure to radiation, use of steroids, cytotoxic drug, immunosuppressive drugs. Co-morbid factors like anaemia, diabetes mellitus, malnutrition etc. were corrected where possible.

Relevant investigations which are required for all cases were carried out; such as blood for Hb%, Serum creatinine, fasting blood glucose level, serum total protein and serum bilirubin, serum electrolytes, X-ray Chest and plain X-ray of abdomen etc. before operation.

The statistical significance of these clinical variables was determined by chi-square analysis. The 95 % confidence interval (CI) was used to assess the significance of the differences between the groups. P <0.05 was considered significant. The results have been arranged in a tabulated form, A comparison has been shown in the tables with the burst cases and the patients who undergone emergency laparotomy but did not develop burst abdomen. Burst cases are designated as Group A and the patients who did not develop burst abdomen are designated as Group B. S.

RESULTS

The results were prepared on 100 patients underwent emergency laparotomy in SSMCMH & DMCH. Burst abdomen following emergency laparotomy results from multifactorial causes. The main outcome measure found significant as the risk factors of burst abdomen in this study were peritonitis (95%),anaemia (26%),malnutrition (18%), in the preoperative period; inadequate peritoneal toileting and faulty surgical techniques in the per operative period; and wound infection (62%) , postoperative cough (28%), abdominal distension (22%). The result also shows that the rate of burst abdomen is still very high in SSMCMH & DMCH and most of them occur in operations done by trainee surgeons (86%) and in those patients who has 3 or more of the risk factors (44%).

Table I: General Risk Factors of Burst Abdomen (n=100)

Factors	Group A (Patients who developed burst abdomen)		Group B (Patients who did not develop burst abdomen)		P Value
	No. of Cases (n=100)	%	No. of Cases (n=100)	%	
Malnutrition	18	18	8	08	<0.001 (S)
Diabetes Mellitus	10	10	4	04	
Malignancy	4	04	2	02	
Jaundice	4	04	2	02	
Uraemia	4	04	1	01	
Steroid Therapy	6	06	1	01	
Obesity	8	08	4	04	
COPD / Asthma	12	12	6	06	
Peritonitis	95	95	90	90	
Tuberculosis	6	06	05	05	
No risk Factors	5	05	10	10	

S= Significant, P value reached from Chi square test

Table I shows that peritonitis during admission was present in 95 % cases of burst abdomen compared to 90 % cases in the patients who did not develop burst abdomen. Anaemia was the next important co-morbid factor. It was present in 26 % cases of burst abdomen but in 12 % cases in Group B. Similarly malnutrition, obesity, jaundice, diabetes mellitus, asthma/COPD were found to play role in Group A than Group B. The differences were statistically significant.

Table II: Surgical skill of the operating surgeons (n=100)

Grade Of Surgeons	Group A (Patients who developed burst abdomen)		Group B (Patients who did not develop burst abdomen)		P Value
	n	%	n	%	
Experts(Consultant & above)	14	14	36	36	<0.02 s
Trainees	86	86	64	64	

S=Significant, P value reached from Chi square test

Table –II shows the comparison of the experience of surgeons in relation of burst abdomen. In Group A,most of the burst abdomen occurred in the hand of trainee doctors (86%) and less (14%) seen in the hand of Expert Surgeons compared to Group B. The difference was statistically significant ($p < 0.02$).

Table III: Factors in Post-operative Period(n=100)

Factors	Group A (Patients who developed burst abdomen)		Group B (Patients who did not develop burst abdomen)		P Value
	n=100	%	n=100	%	
Wound infection	62	62	06	06	<0.001 (S)
Postoperative cough	28	28	12	12	
Abdominal Distension	22	22	04	04	
Vomiting	14	14	06	06	
Bowel leakage	06	06	00	00	
No Factors	02	02	72	72	

S= Significant, P value reached from Chi square test

Table III shows that wound infection was the most frequent factor in the postoperative period and was present in 62% cases of burst abdomen which is very much higher than the group who did not develop burst abdomen.The next frequent factor was postoperative cough. Abdominal distension was present in 22 % cases of burst abdomen compared to only 4 % cases in Group B.Postoperative vomiting played role in 14 % cases of burst abdomen. The differences in between Group A and Group B were statistically significant.

Fig I: Postoperative Day of Burst Abdomen scale.

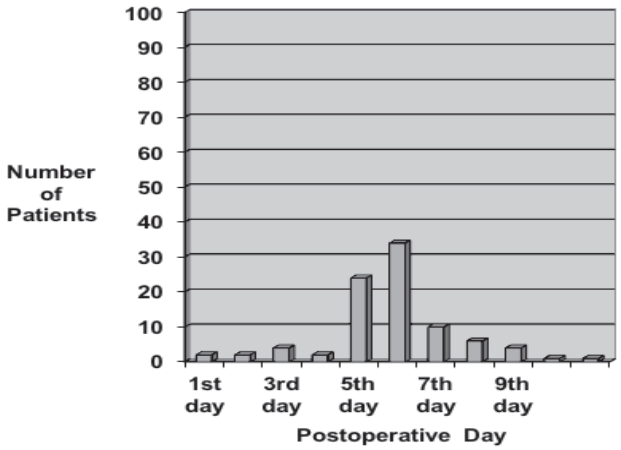

Fig-I: shows that the rate of burst abdomen is highest on 6th postoperative day (34 % cases). Maximum of the burst abdomen occurred between the 5th – 8th postoperative day.

DISCUSSION

In spite of advancement in surgical techniques, facilities for modern equipments and personal experiences, burst abdomen still play an important role in postoperative morbidity and mortality. Incidence of burst abdomen varies with underlying general condition, the type of operation and the presenting pathology.The peak incidences are between 6th and 8th Postoperative days.

Various factors are also involved in wound healing and in the process of burst abdomen; these predisposing factors that causes wound disruption have been studied extensively. They are classified as preoperative general causes, operative or local cause, and postoperative causes. In this series, I tried to identify factor or combination of factors that are responsible for burst abdomen.

Burst abdomen can occur in any age group. The age distribution in my series is 13 years to 70 years with peak incidence in patients at or above 50 years (30%) cases. This correlates with the observation of Hermosa JR, et al. They found in their series 24% cases.15 Pollock AV et al found in their series 20 % cases.16 Burst abdomen is more in old age group because of atherosclerotic change of blood vessels wall results in less tissue perfusion and also they are more prone to infection due to decreased immunity. Next higher incidence was in the 40-49 years age group (24%). This may be due to higher rate of admission of this age group in the surgical unit of this hospital.

Peritonitis during admission in the hospital was present in 95 % cases of burst abdomen which was 90 % in non-dehisced cases. Normally, in case of emergency laparotomy all patients have peritonitis. But, in my study, there are some cases those were diagnosed as acute appendicitis preoperatively but peroperatively those cases were diagnosed as caecal growth, ileocaecal TB, ruptured ectopic pregnancy, meckel's divertculitis with severe adhesions and stricture,congenital bands and adhesions etc. and so, decisions of emergency laparotomy were made. Peritonitis causes bacteraemia and leads to bone marrow suppression and even renal failure, respiratory failure and multisystem failure. All these complications may lead to postoperative wound infection and poor wound healing leading to burst abdomen.

In my series, anaemia was associated with burst abdomen in 26% as compared to only 14% cases in Group B. In their study Hermosa JR et al found that anaemia was associated with 24% cases. 15 Barbhuyan MA in his series found anaemia with wound dehiscence in 26% cases.8 Anaemia contributes wound dehiscence by producing hypoxic effect at healing area.

In the present study malnutrition is found in 18 % cases. It is quite similar to previous study done by Irvin T et al found in their series malnutrition 18% cases.18 Malnutrition contributed to dehiscence by the defective synthesis of collagen, ground substance at the site of wound healing.

Diabetes mellitus was found in 10 % cases. In the series by Barbhuyan MA diabetes was present in 8 % cases.8 Diabetes mellitus causes microangiopathy, atherosclerosis and increased susceptibility to infection and thus causes wound dehiscence as well as burst abdomen.

Jaundice was present in 4 % cases of burst abdomen in comparison to 2 % cases in the non-dehisced cases. This is dissimilar to the study done by Pollock AV et al . They found in their series jaundice in 11 % cases.16 Irvin et al found in their series in 14.6% cases.18 This dissimilarity may be due to my study limitation, a small number of cases selected for study done by me but on the other hand they have done their study on a large number of patients.

In this study, 6 % cases had history of steroid intake for bronchial asthma and previously diagnosed tuberculosis. This is supported by Busti AJ et al. In their series 8 % patients took corticosteroids.19

Obesity was present in 8 % cases of my study. In a study, Pollock AV et al found obesity in 11% of cases 16 and in study done by Bucknall T et al obesity was found in 15% cases. 17

Faulty surgical technique is one of the important local factors for burst abdomen. In my series most of the burst abdomen occurred in the hand of trainee doctors (86 % cases) and lesser percentage in operarions done by Expert surgeons(14 % Cases) in comparison to 36% cases done by experts and 64% done by trainee in Group B. In the study done by Barbhuyan A in his series trainee doctors are 52% cases and professor 14 % cases.8 Bucknall T et al found in their series wound dehiscence in the hand of trainee doctors 50.75% cases and in the hand of experienced doctors 4.25% cases.17

In my study, in the burst group where incisions was closed in by continuous running suture 66% was burst whereas in Group B where incision was closed by continuous running suture in 42 %. Continuous running suturing technique led to more burst abdomen than the group where wound was closed by continuous interlocking suture (34%). Pollock AV et al found in their series 64% cases in continuous technique and 3.5% cases in interrupted suture

technique.16

The result of the study shows that appearance of burst abdomen is highest in sixth post-operative day (34% cases). Hadded V shown that the largest number of wound dehiscence becomes clinically evident on the 6-10th postoperative day.20 In my study most of the burst abdomen occurred also at fifth to ninth postoperative day and most of were in the 6th postoperative day(34%). 26% cases occurred in the 5th post-operative day.

I observed that in most of the patients with complete wound dehiscence (44%) had 4 or more risk factors. No single factor can said to be responsible in causing burst abdomen.

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Original Article

Effect of Verapamil Adjuvant with Local Anaesthetic Mixtures in Supraclavicular Brachial Plexus Block

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Abstract

Among the various approaches to block brachial plexus , supraclavicular approach offers a high success rate for elbow, forearm and hand surgery . Various adjuvant drugs have been used with local anesthetics in order to decrease the time of onset and prolong the duration and quality of regional blocks. So efforts were made to combine the adjuvant with local anesthetics to improve patient and surgeon satisfaction. In this randomized study we tried to see the effect of verapamil in brachial plexus block as an adjuvant with local anaesthetic .This randomized study wasconducted in Anaesthesiology department of ShaheedZiaurRahman Medical College Hospital after approved by the ethical review board of this hospital.The study subject were divided into two groups (Group A=only local anaesthetics&Group B=local anaesthetics with Verapamil) , 30 IN numbers in each group. Group-A patients was administered 15ml of 1% lignocaine with 15 ml of bupivacaine 0.25% while in Group-B patients was administered injection verapamil 3.5 ml (3.5 mg) in addition to the above mixture. In this study mean onset time of sensory block was 11.53 ± 1.4 minutes in group - A and 7.12 ± 1.68 minutes in group – B which is not statistically significant (p value = 0.057). The mean onset time of motor block in group A was 15.26 ± 1.96 min, and in group B was 11.58 ± 2.68 min and this difference isstatistically significant (p value=0.000152). Duration of motor block was 96.30 min and 115.08 min in group A and Group B respectively. Sensory block was 157.26 min and 188.0 min in group A and Group B respectively. Regarding the heart rate, no significant difference was detected between the groups at the time of preanesthesia and at the 5 min after anaesthesia. Compared with group B patients, group A patients shows slight but statistically significant increased heart rate at the 10 min (80, 92 beat/min respectively) after brachial plexus block. At 30 minute after, mean systolic BP was 97.9±4.7 mmHg in group A and 84.3±5.0 mmHg in group B. At 45 minute after, mean systolic blood pressure was 94.6±15.6 mmHg and 84.3±5.0 mmHg in group A and group B respectively. At 60 minutes after, mean systolic blood pressure was 59.6±6.0 mmHg in group A and 61.2±9.4 mmHg in group B. At 15, 30 and 45 minute difference was statistically significant (p<0.05) between two groups. In conclusion, the study revealed that verapamil can be used as an adjuvant to decrease the onset time of sensory and motor blocks of bupivacaine in supraclavicular block. Moreover, verapamil doses in regional blocks did not show any hemodynamic side effects.

Key Words: Brachial plexus block, Supraclavicular block, Verapamil

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INTRODUCTION

Peripheral nerve blocks are gaining widespread popularity for perioperative pain management because of their specific advantages over general anesthesia and central neuraxial anesthesia. To select an appropriate local anesthetic drug for a specific clinical situation, one should be familiar with the clinical pharmacology of the local anesthetic drugs and adjuvants. Brachial plexus blockade is the cornerstone of the regional anesthesia practice of most anesthesiologists now-a-day1.

Supraclavicular block is performed at the level of divisions of the brachial plexus. It has a rapid onset and deep level of block making it desirable for surgeries below the mid-humerus. The complications associated with this procedure are dependent on the level of block. However, the complications are few and infrequent in experienced hands, making it

a popular procedure3. In recent years it has gained popularity with addition of various adjuncts to local anaesthetic solution in an attempt to increase its efficacy and duration.

Local anaesthetics alone provide analgesia for not more than 4-8 hours. Increasing the duration of local anesthetic action is often desirable because it prolongs surgical anesthesia and analgesia. Different additives have been used to prolong regional blockade. Vasoconstrictors can be used to vasoconstrict vessels, thereby reducing vascular absorption of the local anesthetics4-7. Others drugs like calcium blocker, opioids, alpha2 adrenergic agonist, sodium bicarbonate, neostigmine, adrenaline, ketamine etc. are used as adjuvant to local anesthetics to lower doses of each agent and enhance analgesic efficacy while reducing the incidence of adverse reactions.

Verapamil is a calcium channel blocker. It can also block slow Na+- K+ channels in cardiac muscles and vessels. Besides that, verapamil can block fast channels similar to the process of local anesthetics8. Regarding the obvious role of calcium ion in pain formation, calcium channel blockers emerged as adjuvant for analgesia and anesthesia. The aim of the study was to assess the effects of verapamil on supraclvicular brachial nerve block regarding its consequences on the onset of sensory and motor block and duration of analgesia and also the effects on hemodynamic alterations.

MATERIALS AND METHODS

This randomized control study was conducted in Anaesthesiology department of Shaheed Ziaur Rahman Medical College Hospital after approved by the ethical review board of this hospital and also written informed consent obtained from all patients. Patients undergoing upper limb surgery with ASA physical status I, II and age between 18 to 60 years were included in this study except those with severe cardiorespiratory, renal, hepatic diseases, chronic neurological disease of upper limb, with coagulopathy, any contraindication to calcium channel blockers, history of drug abuse or history with local anesthetics toxicity. Study subject were divided into two groups (Group A=only local anaesthetics&Group B=local anaesthetics with Verapamil) randomly, 30 numbers in each group. After arrival to the operating theatre all patient's received Lactated Ringer's solution, infused at 10ml/kg/h over 30 min before anaesthesia . Base line parameters like BP, Pulse, oxygen saturation, ECG and axillary temperature were recorded before anesthesia. Group-A patients was administered 15ml of 1% lignocaine with 15 ml of bupivacaine 0.25% while in Group-B patients was administered injection verapamil 3.5 ml (3.5 mg) in addition to the above mixture. Total volume was made 40 ml by adding distilled water in both the groups. About 2 cm above the midclavicular point just lateral to subclavian artery pulsation, a 22 gauge 1.5 inch needle was introduced caudally and medially and when paraesthesia encountered 40 ml of local anaesthetics with or without verapamil injected. Pulse, BP, ECG was monitored in every 5 minutes up to 30 minutes of block. Onset of motor block was considered as time from injection to the inability of the patient to move his/her hands or fingers then block was assessed by Bromage scale upto 30 minutes in 5 minutes interval.Onset of sensory block was considered as dull sensation on any dermatomes tested by icepack, pin prick sensation. The duration of sensory blockade, defined as the time between onset of sensory block and return of dull pain and VAS<3, was assessed every 30 minutes postoperatively. The duration of motor block was assessed every 30 minutes till the ability of the patient to move his/her fingers. When the patient first requested for analgesics, the time of administration of the analgesics, number of doses and the VAS score noted. Any occurrence of side-effect also noted and managed accordingly. All data analysis was done by using SPSS version 6.

RESULTS

Table I: Demographic Data and ASA status.

	Group-A	Group-B	P Value
Age in years (mean ± S.D)	36.2±6.13	34.7±8.53	
Gender	21/9	18/12	0.621
Height (mean ± S.D)	162±4.13	160±6.69	
ASA status	19/11	18/12	0.790

A Total of 60 patients were studied to determine whether addition of varapamil to local anaesthetics increases the quality of bracheal plexus block. While studying the distribution of cases by age, gender and ASA physical status no significant differences were found between groups (Table I).

Table II: Time to onset of sensory and motor block (n=60)

	Group-A	Group-B	P Value
Time of Sensory onset in minutes	11.53 ± 1.40 min	7.12 ± 1.68 min	0.057
Time of motor onset in minutes	15.26 ± 1.96 min	11.58 ± 2.68 min	0.000152

In this study mean onset time of sensory block was 11.53 ± 1.4 minutes in group - A and 7.12 ± 1.68 minutes in group – B which is not statistically significant (p value = 0.057). The mean onset time of motor block in group A was 15.26 ± 1.96 min, and in group B was 11.58 ± 2.68 min and this difference is statistically significant (p value=0.000152).Table II).

Table III: Trends of mean arterial pressure (MAP) between groups with respect to time (n=60)

Time point after block	Mean arterial pressure -MAP (mmHg)		P-value
	Group U (n=30)	Group B (n=30)	
Preanaesthesia	69.60±11.6	68.93±9.1	0.883
5 min AS	73.45±8.2	67.90±9.5	0.0001
10 min AS	75.40±7.9	70.25±10.2	0.0001
15 min AS	76.92±8.1	69.18±9.5	0.0001
20 min AS	76.31±8.6	68.73±9.1	0.0001
30 min AS	75.57±10.2	69.18±7.5	0.0001
45 min AS	71.05±9.3	64.46±11.4	0.035
60 min AS	59.55±6.8	60.52±7.1	0.486

There was no significant difference between the groups as regards Preanaesthesia MAP (p=0.883), but after induction of anesthesia significant decrease in MAP was seen in all groups compared with basal MAP. At the 15th minute MAP was statistically significant (p=0.0001), After 45 minute, mean blood pressure was 71.05±6.8 mmHg in group A and 64.46±9.4 mmHg in group B, which statistically significant (p=0.035) between two groups but follow up after 60 minute mean BP stabilized to similar in both group, which was statistically not significant (p=0.486) between two groups. (Table-III).

Table IV: Occurrence of complication

Complications	Frequency of occurrence	
	Group A (n=30)	Group B (n=30)
Nausea, Vomiting	2	0
Dyspnoea	3	3
Hypotension	0	7
Bradycardia	1	4

No significant complication was observed in both group, but in group-A patient experienced vomiting, three patients noticed respiratory discomfort. In the B-group, seven patients had respiratory discomfort; hypotension and four of them experienced hypotension (Table IV)

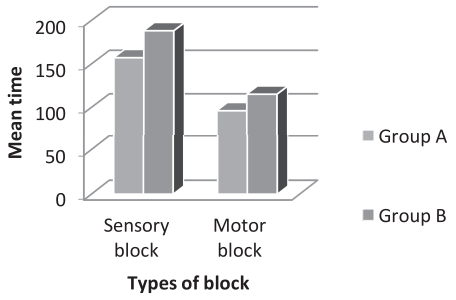

Fig 1: Mean duration (min) of motor and sensory block (n=60)

Table IV: Occurrence of complication

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Hypotension	0	7
Bradycardia	1	4

The duration of motor block was 96.30 min. and 115.08 min. in group A and Group B respectively. Sensory block was 157.26 min. and 188.0 min. in group A and Group B respectively (Figure:1).

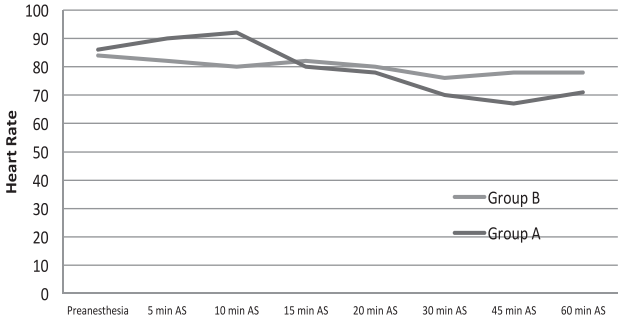

Fig 1: Mean duration (min) of motor and sensory block (n=60)

Regarding the heart rate, no significant difference was detected between the groups at the time of preanesthesia and 5 min after anaesthesia(Fig:2).

DISCUSSION

For upper limb orthopedic surgeries supraclavicular block is a very good form of regional anaesthesia for not only surgery but also to control the postoperative pain. Supraclavicular block attack the nerve fibers at the level of the trunks. Three trunks of the brachial plexus supplies the sensory, motor and sympathetic fibers to the upper limb, which contained in a very small, compact but easily accessible and relatively superficial area. So it's possible to have prompt and profound form of upper limb block with this approach.

In this way calcium channel blockers potentiate the analgesic effect of local anesthetics and acts primarily by means of vasodilatation and reduction of peripheral vascular resistance.11

In many studies calcium channel blockers along with local anesthetics been used. Nowycky et al. reported that there is three distinct types of calcium channels in sensory neurons namely, the L, T, and N types. Of these, the L and N types of channels have a strong role in regulating neurotransmitter

release from neurons.12 The antinociceptive effects of N type channels are more than L type channel and N type channel blockers were not clinically suitable for use because of their severe neurotoxicity. Hara et al.13 showed that the L-type channel blockers verapamil and diltiazem produced both somatic and visceral pain relief in a dose-dependent manner, suggesting the relevance of L-type channel blockers in pain management. Iwasaki et al.12 showed that local sensory block produced by lidocaine injection at the tail base was potentiated by verapamil, diltiazem, and nicardipine in a dose-dependent manner in rats. Moreover, intrathecal verapamil alone did not produce motor or sensory block. However, in combination with lidocaine or tetracaine, the block produced was more potent and of longer duration than that produced by the local anesthetic alone in rats.14 Brachial plexus administration of verapamil 2.5 mg increased the duration of surgical anesthesia by~90 min when added to lidocaine with epinephrine axillary block .15

In this study demographic profile and ASA status of patients which was statistically insignificant between two groups, was quite similar with other research investigations, and provided us the stable podium to evenly compare the results obtained.16

In this present study, Heart rate was comparable between groups. The mean BP had some significant variations at 15th and 45th minute but after 60th minute returned to base line, which are not comparable with other study, although it is well known that the systemic administration of calcium channel blockers cause myocardial depression leading to hypotension and bradycardia. This controversy may be due to the pharmacokinetic interaction of different drug solutions, such as changing pH and the temperature at injection site.17

In present study the onset of motor block and duration of sensory and motor block was statistically significant between groups. Mosaffa et al. also have the same effects but using 2 doses of verapamil with bupivacaine in supraclavicular brachial plexus block. They concluded that verapamil (both 2.5 mg and 5 mg) decreased the onset of sensory and motor block and increased the duration of analgesia19 Messeha and Eldeen studied role of nimodipine, a calcium channel blocker when added to lignocaine in brachial plexus block and found prolongation of sensory blockade.20

This study was not without limitation. The limitations of the studies were as follows:

• Small sample size of the study population.

• It was a single center study. Only patients admitted in SZMCH hospital were taken for the study. So this will not reflect the overall picture of the country. A large scale study needs to be conducted to reach to a definitive conclusion

• Others limitation were short duration of study and limited investigation facility.

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Original Article

Comparison of Test Validity of Magnetic Resonance Imaging in the Diagnosis of Different Grades of Astrocytoma

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Abstract

Accurate detection of astrocytomas is very difficult. The purpose of the present study was to evaluate the usefulness of MRI in detection of intracranial astrocytoma. This cross-sectional study was conducted at the Department of Radiology and Imaging with the collaboration of Department of Neurosurgery and Department of Pathology at Sir Salimullah Medical College (SSMC & MH), Dhaka from January 2013 to December 2013 for a period of one year. All the clinically suspected and CT scan diagnosed cases of intracranial astrocytoma patients of any age of both sexes were included as study population. All cases having no contraindication for MRI underwent MR examination. MR imaging was obtained with 0.5 Tesla machine (SIEMENS). The postoperative resected tissues were examined histopathological in the respective department. Then the collected reports were compared with findings of MRI. The sample size of the present study was 48 astrocytoma patients. The highest sensitivity was found in grade III astrocytoma (90.5%) followed by grade II (85.7%) grade IV (75.0%) and grade I (60.0%). The highest specificity was found in grade I astrocytoma (97.7%) followed by Grade III (96.3%), grade IV (92.5%) and grade II (91.5%). The highest accuracy was found in both grade I astrocytoma (93.7%) and grade III (93.7%) followed by grade II (92.5%) and grade IV (89.6%). In the conclusion, MRI is an effective tool for the diagnosis of astrocytoma. MRI has a high diagnostic validity for the detection of different grades of astrocytoma.

Key Words: Magnetic Resonance Imaging; astrocytoma; validity test.

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INTRODUCTION

Brain tumors account for 85.0% to 90.0% of all primary central nervous system (CNS) tumors1. Plain radiograph was previously used in the past to detect intracranial tumour. Cerebral angiography and pneumocephalography were also done; however, none of which was conclusive2. With the advent of CT and MRI there is revolutionary change in the detection of intracranial tumour. MRI scan has made a significant impact on the differential diagnosis of intracranial tumours3.

Compared with CT, MRI offers greater contrast resolution, including greater sensitivity for the detection of subacute and chronic haemorrhage in association with tumours and other lesions of brain4. MRI lacks ionizing radiation. Delineation of posterior cranial fossa soft tissue anatomy is better visualized with MRI than CT as because MRI lacks beam-hardening artefact5. Accuracy of lesion localization on MRI is enhanced by its direct multiplanar capability6. MRI provides important information regarding contrast material enhancement, peritumoural oedema, distant tumour foci, haemorrhage, necrosis, mass effect and so on, which are all helpful in characterizing tumour aggressiveness and hence tumour grade7. In this context this present study was undertaken to evaluate the usefulness of MRI in detection of intracranial astrocytoma.

METHODOLOGY

This study was designed as cross sectional study which was carried out in the Department of Radiology and Imaging with the collaboration of Department of Neurosurgery and Department of Pathology at Sir Salimullah Medical College (SSMC & MH), Dhaka from January 2013 to December 2013 for a period of one (1) year. A total number of 48 astrocytoma patients were evaluated by purposive sampling technique. Patients who were clinically suspected and CT scan diagnosed cases of intracranial astrocytomas referred to Radiology and Imaging department of Dhaka Medical college Hospital (DMCH) either from OPD or from indoor of DMCH for MRI of brain were included in this study.

Prior to the commencement of this study, the research protocol was approved by the ethical committee (Local Ethical committee) of SSMC. All cases having no contraindication for MRI underwent MR examination. Patients were asked for or checked for any metallic or harmful. MR imaging was obtained with 0.3 Tesla machine (HITACHI). T1W image in axial, sagittal and coronal plane were obtained using short TR (500-800ms) and short TE (14-20ms). T2W image in axial and coronal plane were obtained using long TR (3500-4500ms) and long TE (80ms). FLAIR images were also taken. Contrast MRI studies using intravenous Gd-DTPA (Magnevist, 0.1 mmol/Kg) with axial, coronal and sagittal T1W scan were performed in all cases. The average time of examination was 45 minutes but ranges from 30-90 minutes. Slice thickness was 5-6 mm with a field of view 230x230 mm and pictures matrix was 256x256 or 192x256. The postoperative resected tissues were examined histopathological in the respective department. MRI scan findings were compared with histopathological reports. Then the collected reports were compared with findings of MRI. Data were collected using a preformed data collection sheet. Base line information was collected from the patient after exploration of different complaints and sign and symptoms. All information regarding clinical features and histopathological results were recorded in a data collection sheet. Statistical analysis was performed by using window based computer software devised with Statistical Packages for Social Sciences (SPSS-17), 95% confidence limit was taken.

RESULTS

Table 1: Comparison of MRI findings with Histopathological Findings during Diagnosis of Grade I Astrocytoma (n=48)

MRI Diagnosis	Histopathological Diagnosis		Total
	Positive	Negative	
Test Positive	3	1	4
Test Negative	2	42	44
Total	**5**	**43**	**48**

Table 1 shows the comparison of MRI findings with Histopathological Findings during diagnosis of Grade I Astrocytoma. Both histopathological and MRI positive astrocytoma case is found in 3 cases which indicate true positive. Again, both histopathological and MRI negative astrocytoma case is found in 42 cases which indicate true negative. Histopathological positive but MRI negative case is found in 2 cases which is known as false negative. Histopathological negative but MRI positive case is found in 1 case which is known as false positive.

Table 2: Comparison of MRI findings with Histopathological Findings during diagnosis of Grade II Astrocytoma (n=48)

MRI Diagnosis	Histopathological Diagnosis		Total
	Positive	Negative	
Test Positive	12	3	15
Test Negative	2	31	33
Total	**14**	**34**	**48**

Table 2 shows the comparison of MRI findings with Histopathological Findings during diagnosis of Grade II Astrocytoma. Both histopathological and MRI positive astrocytoma case is found in 12 cases which indicate true positive. Again, both histopathological and MRI negative astrocytoma case is found in 31 cases which indicate true negative. Histopathological positive but MRI negative case is found in 2 cases which is known as false negative. Histopathological negative but MRI positive case is found in 3 case which is known as false positive.

Table 3: Comparison of MRI findings with Histopathological Findings during diagnosis of Grade III Astrocytoma (n=48)

MRI Diagnosis	Histopathological Diagnosis		Total
	Positive	Negative	
Test Positive	19	1	20
Test Negative	2	26	28
Total	**21**	**27**	**48**

Table 3 shows the comparison of MRI findings with Histopathological Findings during diagnosis of Grade III Astrocytoma. Both histopathological and MRI positive astrocytoma case is found in 19 cases which indicate true positive. Again, both histopathological and MRI negative astrocytoma case is found in 26 cases which indicate true negative. Histopathological positive but MRI negative case is found in 2 cases which is known as false negative. Histopathological negative but MRI positive case is found in 1 case which is known as false positive.

Table 4: Comparison of MRI findings with Histopathological Findings during diagnosis of Grade IV Astrocytoma (n=48)

MRI Diagnosis	Histopathological Diagnosis		Total
	Positive	Negative	
Test Positive	6	3	9
Test Negative	2	37	39
Total	**8**	**40**	**48**

Table 4 shows the comparison of MRI findings with Histopathological Findings during diagnosis of Grade IV Astrocytoma. Both histopathological and MRI positive astrocytoma case is found in 6 cases which indicate true positive. Again, both histopathological and MRI negative astrocytoma case is found in 37 cases which indicate true negative. Histopathological positive but MRI negative case is found in 2 cases which is known as false negative. Histopathological negative but MRI positive case is found in 3 cases which is known as false positive.

Table 5: Validity of MRI during diagnosis of Different Grades of Astrocytoma

Validity	Different Grades (95% CI)			
	Grade I	Grade II	Grade III	Grade IV
Sensitivity	60.0%(46.1-73.9%)	85.7% (56.1-97.2%)	90.5%(68.2-98.3%)	75.0%(62.7-87.2%)
Specificity	97.7%(93.5-101.9%)	91.2% (75.2-97.2%)	96.3%(79.1-99.8%)	92.5%(85.5-99.9%)
PPV	75.0%(62.7-87.2%)	80.0%(51.4-94.7%)	95.0%(73.0-99.7%)	66.7%(53.4-80.0%)
NPV	95.4%(89.5-101.3%)	93.9%(78.4-98.9%)	92.9%(75.0-98.7%)	94.9%(88.7-01.1%)
Accuracy	93.7%(86.8-100.6%)	90.0%(81.5-98.49%)	93.7%(86.8-100.6%)	89.6%(81.0-98.2%)

*PPV= Positive Predictive Value; NPV= Negative Predictive value

The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of MRI for the diagnosis of astrocytoma grade I were 60.0%(95% CI 46.1-73.9%), 97.7% (95% CI 93.5-101.9%), 75.0% (95% CI 62.7-87.2%), 95.4%(95% CI 89.5-101.3%) and 93.7%(95% CI 86.8-100.6%) respectively. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of MRI for the diagnosis of astrocytoma grade II were 85.7% (95% CI 56.1-97.2%), 91.2% (95% CI 75.2-97.2%), 80.0% (95% CI 51.4-94.7%), 93.9% (95% CI 78.4-98.9%) and 90.0% (95% CI 81.5-98.49%) respectively. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of MRI for the diagnosis of astrocytoma grade IIII were 90.5% (95% CI 68.2-98.3), 96.3% (95% CI 79.1-99.8%), 95.0% (95% CI 73.0-99.7%), 92.9% (95% CI 75.0-98.7%) and 93.7% (95% CI 86.8-100.6%) respectively. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of MRI for the diagnosis of astrocytoma grade IV were 75.0% (95% CI 62.7-87.2%), 97.7% (95% CI 85.5-99.9%), 75.0% (95% CI 53.4-80.0%), 95.4% (95% CI 88.7-101.1%) and 93.7%(95% CI 81.0-98.2%) respectively. The highest sensitivity was found in grade III astrocytoma (90.5%) followed by grade II (85.7%), grade IV (75.0%) and grade I (60.0%). The highest specificity was found in grade I astrocytoma (97.7%) followed by grade III (96.3%), grade IV (92.5%) and grade II (91.5%). The highest Accuracy was found in grade I astrocytoma (93.7%) and grade III (93.7%) followed by grade II (92.5%) and grade IV (89.6%) (Table 5).

DISCUSSION

The comparison of MRI findings with histopathological findings during diagnosis of Grade I Astrocytoma is recorded. Both histopathological and MRI positive astrocytoma case is found in 3 cases which indicate true positive. Again, both histopathological and MRI negative astrocytoma case is found in 42 cases which indicate true negative. Histopathological positive but MRI negative case is found in 2 cases which is known as false negative. Histopathological negative but MRI positive case is found in 1 case which is known as false positive. The validity of MRI during diagnosis of Grade I astrocytoma is recorded. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of MRI for the diagnosis of astrocytoma grade I are 60.0% (95% CI 46.1-73.9%), 97.7% (95% CI 93.5-101.9%), 75.0% (95% CI 62.7-87.2%), 95.4% (95% CI 89.5-101.3%) and 93.7% (95% CI 86.8-100.6%) respectively. The comparison of MRI findings with histopathological findings during diagnosis of Grade II astrocytoma is recorded. Both histopathological and MRI positive astrocytoma case is found in 12 cases which indicate true positive. Again, both histopathological and MRI negative astrocytoma case is found in 31 cases which indicate true negative. Histopathological positive but MRI negative case is found in 2 cases which is known as false negative. Histopathological negative but MRI positive case is found in 3 case which is known as false positive. The validity of MRI during diagnosis of Grade II astrocytoma is recorded. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of MRI for the diagnosis of astrocytoma grade II are 85.7% (95% CI 56.1-97.2%), 91.2% (95% CI 75.2-97.2%), 80.0% (95% CI 51.4-94.7%), 93.9% (95% CI 78.4-98.9%) and 90.0% (95% CI 81.5-98.49%) respectively. Similar findings are reported by Chishty et al7 and have mentioned that sensitivity of MRI in detection of low grade gliomas is 100.0%.

The comparison of MRI findings with histopathological findings during diagnosis of Grade III astrocytoma is recorded. Both histopathological and MRI positive astrocytoma case is found in 19 cases which indicate true positive. Again, both histopathological and MRI negative astrocytoma case is found in 26 cases which indicate true negative. Histopathological positive but MRI negative case is found in 2 cases which is known as false negative. Histopathological negative but MRI positive case is found in 1 case which is known as false positive. The validity of MRI during diagnosis of Grade III astrocytoma is recorded. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of MRI for the diagnosis of astrocytoma grade IIII are 90.5% (95% CI 68.2-98.3), 96.3% (95% CI 79.1-99.8%), 95.0% (95% CI 73.0-99.7%), 92.9% (95% CI 75.0-98.7%) and 93.7% (95% CI 86.8-100.6%) respectively. Similarly Chishty et al7 has reported that sensitivity of MRI for the detection of grade III is 95% which are close to the results of present study.

The comparison of MRI findings with histopathological findings during diagnosis of Grade IV astrocytoma is recorded. Both histopathological and MRI positive astrocytoma case is found in 6 cases which indicate true positive. Again, both histopathological and MRI negative astrocytoma case is found in 37 cases which indicate true negative. Histopathological positive but MRI negative case is found in 2 cases which is known as false negative. Histopathological negative but MRI positive case is found in 3 cases which is known as false positive. The validity of MRI during diagnosis of Grade IV astrocytoma is recorded. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of MRI for the diagnosis of astrocytoma grade IV are 75.0% (95% CI 62.7-87.2%), 97.7% (95% CI 85.5-99.9%), 75.0% (95% CI 53.4-80.0%), 95.4% (95% CI 88.7-101.1%) and 93.7% (95% CI 81.0-98.2%) respectively. Similar to the present study Law et al8 observed that PPV and NPV of MRI for determination of a high grade glioma were 86.1% and 44.1% respectively which is consistent with the present study.

Comparison of sensitivity of MRI for the diagnosis of different grade of astrocytoma is analyzed. The highest sensitivity was found in grade III astrocytoma (90.5%) followed by Grade II (85.7%) grade IV (75.0%) and grade I (60.0%). It is interesting that during comparison this result shows that sensitivity of the MRI for the detection of astrocytoma is decreased after increasing of grade of the tumour. Similar to the present findings Ellika et al9 has reported that sensitivity is 85.7% for different grading of astrocytomas with conventional MRI which is very close to the results of present study.

The comparison of specificity of MRI for the diagnosis of different grade of astrocytoma is recorded. The highest specificity was found in grade I astrocytoma (97.7%) followed by Grade III (96.3%), grade IV (92.5%) and grade II (91.5%). These findings are clearly shown that the specificity of MRI for the detection of astrocytoma is very high and all are more than 90.0% which is very useful during diagnosis of astrocytoma. Law et al8 found sensitivity of glioma grading ranging from 55.1% to 83.3%. Ellika et al9 found that sensitivity for different grading of astrocytoma is 60.0% which is similar to the present study. Law et al8 observed specificity of MRI in the diagnosis of high grade gliomas was 65% and in Riemann et al10 series it was 80.0% in diagnosing low grade gliomas which is consistent with the present study. During diagnosis the specificity is very important for the detection of the disease state11-12.

The comparison of accuracy of MRI for the diagnosis of different grade of astrocytoma is analyzed. The highest accuracy was found in both grade I astrocytoma (93.7%) and grade III (93.7%) followed by grade II (92.5%) and grade IV (89.6%). Accuracy of MRI for the detection of astrocytoma is very much effective and in all grade of tumor it is more than or equal to 90.0%. This indicates that MRI is very much useful for the detection of different grades of astrocytoma. Similar to this result Chishty et al7 found 94.0% accuracy of preoperative MRI grading of intracranial astrocytomas. Again Riemann et al10 found 88.0% accuracy of contrast enhanced MRI for detecting intracranial astrocytomas which is very consistent with the present study. From the results of present study as well as the findings obtained by others like Riemann et al10, Ellika et al9 and Chishty et al7, it is conceivable that MRI scan is a highly accurate and sensitive modality in the evaluation of intracranial astrocytomas.

CONCLUSION

In conclusion, the findings of this study permit to conclude that MRI is an effective tool for the diagnosis of different grades of astrocytoma. Sensitivity, specificity and accuracy of MRI for the diagnosis of astrocytoma are high in different grades of astrocytoma. Nationwide further large scale study should be carried out.

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Case Report

Pigmented Villonodular Synovitis Treated as Spondyloarthritis for Four Years: A Case Report

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Abstract

Pigmented villonodular synovitis (PVNS) is a rare disorder where abnormal synovial proliferation and insidious swelling are the characteristic features. As insidious joint swelling has many common causes and PVNS is rare entity, so that it may be missed or under evaluated. Here inconclusive biopsy findings at an early stage and features resembling spondyloarthritis (SpA) delayed the diagnosis. A 28-year-old young man presented with insidious swelling of knee. Here repeated aspiration and synovial fluid analysis with routine serological and radiological examination were inconclusive. Then he was labeled and treated as spondyloarthritis (SpA) for four years without improvement. After four years of sufferings he admitted here and reached the diagnosis of PVNS with the help of MRI and synovial biopsy. Sometimes rare disease diagnosis is complicated by the absence of typical features and inconclusive reports. Common differentials may mimic the diagnosis and rare disease may loss the attention. Here PVNS was treated as SpA for four years before being diagnosed.

INTRODUCTION

Pigmented villonodular synovitis (PVNS) is a proliferative benign disease that involves joints, tendon sheaths 1 and bursae.2 PVNS can be localized and diffuse type.3 Jaffe HL, Lichtenstein L, Sutro CJ first reported PVNS in 1941.2, 4, 5 PVNS looks like frond or leaf, brownish synovial proliferation with mononuclear stromal cell infiltration, presence of hemosiderin laden macrophages, foam cells and giant cells. 6 Knee 7, 8 is the commonest followed by shoulder, hand and hip involvement 9, 10 and is usually monoarticular and can be polyarticular.11 In a study among 20 to 50 years of age, both extra and intra-articular PVNS was found 9.2 and 1.8 per million consecutively.8 Mean diagnostic delay of PVNS was eighteen months 4 in one study and fifty four months in another study.12 Here diagnostic delay was four years. Before diagnosing PVNS, JIA, Septic arthritis, bacterial synovitis, rheumatoid arthritis, heamophilia, TB, heamangioma and other causes of heamartrhosis need to be excluded.12-15

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CASE REPORT

A 28-year-old male presented with swelling of right knee joint 4-year back. Insidious swelling with nonspecific mild pain & discomfort was his presenting feature. He did not give any history of trauma, preceding diarrhea or dysentery, family history of psoriasis and did not have any previous and present psoriatic skin and nail changes. The swelling gradually increased and discomfort increased overtime during walking and daily activities. Swelling was diffuse and boggy with normal overlying skin. All other examination findings were normal. Repeated aspiration of reddish synovial fluid was re-accumulate within a few weeks again. Her CBC, ESR, urine R/E, chest X-ray P/A view, X-ray pelvis A/P view, C reactive protein was normal 3.48 (<6mg/l), Anti CCP was 12.8 U/ml (<25 U/l), Synovial fluid analysis was done 4 times before admission but nothing was significant except plenty of RBC. Synovial protein was 41 gm/L, glucose 4.5 mmol/L, Color- red, TC:1000-3500/cu mm, L:80-90%,N:5-10%, plenty of RBC, No AFB, Xpert Gene for MTB was not detected, PCR of MTB was negative, malignant cell was not found. MT (07/01/2017): Negative (02 mm).

Synovial biopsy on August, 2015 showed dense infiltration of acute & chronic inflammatory cells. The synoviocytes were hypertrophic. No granuloma or malignancy is seen. Chronic non-specific arthritis was commented. In Dec' 2016 biopsy report finding was fibro-cartilagenous fatty tissue infiltrated by chronic inflammatory cells including a few haemosiderin laden macrophages and comment was features were consistent with chronic inflammatory tissue.

He was also negative for HLAB27 alleles. After exclusion of all possibilities and two episodes of synovial biopsy was done without conclusive remarks. Then he was labeled as spondyloarthritis and treated with NSAIDs, salfasalazine, intra-articular steroid for two years without significant improvement. He was referred to a tertiary hospital in Bangladesh. Here patient was reevaluated and further drive was given to reach diagnosis. Radiographs of the right knee shows no bony abnormality. Ultrasonography shows synovial hypertrophy and moderate fluid collection but no Doppler activity.

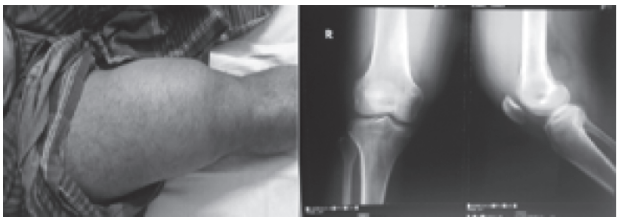

Fig:1 Picture of right Knee joint and X-Ray of right knee

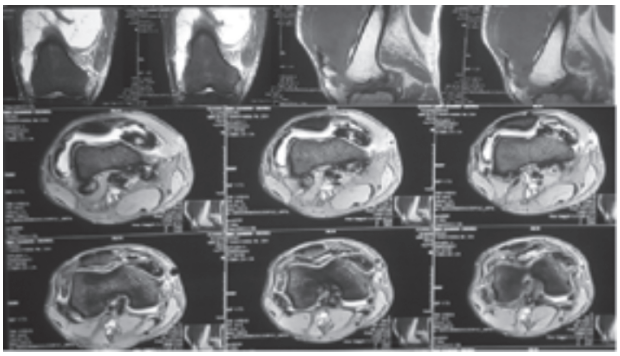

Fig:2 MRI of knee joint- Coronal, Sagittal and Axial view

MRI (Fig: 2) reveals- a large loculated joint effusion seen in pre-patellar region, low to Intermediate signal intensity on T1WI & T2WI on the Hoffa's fat pad, posterior to distal femur, medial and posterior aspect of knee joint with some high signal intensity. A multilobulated lesion is seen in continuity with the synovium in the anteromedial, anterolateral, and patello-femoral joint space with few internal septations. Bone erosion involving distal femur was present.

Again synovial biopsy was done and which revealed- The synoviocytes are hypertrophic, infiltration of chronic inflammatory cells and presence of haemosiderin laden macrophages with no granuloma. Multilobulated lesion in antero-medial and antero-lateral aspect of knee joint with loculated effusion- suggestive of Pigmented villonodular synovitis.

DISCUSSION

Clinical feature may not be typical and varies a great extent and it depends whether the lesion is intra or extra-articular. Extra-articular PVNS generally presents as a mass of soft-tissue (83%-99%) may have pain (22%-71%). Here pain was mild and discomfort was complained. Joint dysfunction and swelling reported rarely (0%-4%).16 Intra-articular type of PVNS usually have pain and swelling with limitation of movement11, joint dysfunction is less (26%-28% cases) and soft tissue mass found in 6%-19% of cases.16

The duration of symptoms varies widely from 1 to 120 months with an average of 2-3 years before presentation. Here it took four year to reach diagnosis. Laboratory findings including blood count and sedimentation rate are normal like this case.11

In synovial biopsy from PVNS there is synovial cell proliferation, hemosiderin laden macrophages, xanthomatous cell accumulation .The mechanism of bone erosion in PVNS is somewhat unclear. It was believed that erosion results from raised intra-articular pressure while some believe that the synovium releases substances causes erosion and progress to destruction.17

The appearances of PVNS on MR imaging are often characteristic, with low to intermediate signal intensity in all pulse sequences due to hemosiderin deposition. Other features of may include synovial proliferation, joint effusion and bone erosion. The combination of hemosiderin deposits, villonodular soft tissue masses and/or multiple bone erosion is highly diagnostic for PVNS.The deposit of hemosiderin, appearing as a low signal area best seen on FFE sequence, is diagnostic for PVNS.18

For both localized and diffuse PVNS surgical excision is the treatment of choice. Outcome depends on complete resection with clear margins. For diffuse PVNS, open surgical excision is the primary method. Another method is arthroscopic synovectomy but has reported recurrence rate is as high as 46%.19 Totalsynovectomy is difficult to perform and the neurovascular structures adjacent to the affected synovium may be injured. One report suggests that total synovectomy seems to be effective in preventing recurrence but osteoarthritis risk is increased, so subtotal synovectomy is preferred than total synovectomy.20 PVNS has been reported to have a high recurrence rate (14-56%). It rarely in becomes malignant.19 To prevent recurrence, radiation therapy to a dose of 35 to 50 Gy has been effective. Radiotherapy is particularly useful in patients with mitotic

figures or incomplete excision.20 Kotwal et al reported no recurrence after post-operative radiotherapy in comparison to 6% recurrence.

CONCLUSIONS:

PVNS is a rare and benign but recurrence is the problem. Diagnosis can be delayed. Hemarthrosis may be the first clue and histopathololgist and clinician may exchange views to give attention for rare conditions like PVNS. So that sufferings may be minimized.

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Case Report

Thrombocyteapheresis for The Treatment of Essential Thrombocythemia Presented As A Digital Ischaemia- A Case Report

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Abstract

Thrombotic manifestations of essential thrombocytosis (ET) may be a life threatening condition. The conventional cytoreductive therapy or radioisotopes may take long time to reduce the platelet counts whereas thrombocyteapheresis can reduce the count more rapidly. Here the reported case is an essential thrombocytosis presented with digital ischaemia and was managed with intermittent flow centrifugal thrombocyteapheresis combined with hydroxyurea to reduce the platelet count. Thrombocytopharesis is an effective method and safe to reduce platelet count acutely. Thrombocyteapheresis has been done for the first time for the treatment of essential thrombocythemia (ET) in BSMMU probably also in Bangladesh.

INTRODUCTION

Essential thrombocythaemia is a rare myeloproliferative disease and the incidence is 0.4–2.5 per 100,000 per year .18 It has female preponderance and usually occurs at the fifth or sixth decade of life.29 The JAK2 V617F mutation is positive in 50–60% of cases.3 ET presents with haemorrhagic complications, due to platelet dysfunction, or thrombotic disorders like stroke, myocardial infarction, venous thrombosis, and digital ischaemia.3 Platelet count is usually reduced with cytoreductive agents and thrombocyteapheresis. Because the usually used cytoreductive agents takes 7 to 10 days or more to reduce the platelet count in life-threatening increases of platelets or thrombotic condition , can only be lowered by removal of platelets.3 Here we report a case of ET with digital ischaemia resistant to hydrooxyurea. Dramatic reduction of the platelet count by intermittent flow thrombocyteapheresis was achieved safely and swiftly in this patient .

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CASE RECORD

A 45- year- old woman was admitted in the department of Internal Medicine, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh with pain and change of color of left hand and both feet for two months and blackening of left fourth toe for 14 days (figure-1) which is not aggravated on exposure to cold. She was also suffering from intermittent headache and vertigo. She had a spontaneous miscarriage at first trimester and was on oral contraceptive pill for 5 years. Physical general examination revealed , she was mildly anemic, pulse was 100 beat per min and all peripheral pulses are present, blood pressure was 120/80 mm of Hg, respiratory rate was 14 breaths per min and on examination of the limbs , there was bluish discoloration of fingers of left hand & all toes , reddish coloration of left palm of hands and sole of feet, raised temperature, tender and dry gangrene in left 4th toe and levedo reticularis over sole of the feet (Figure-1). Systemic examination revealed normal. Investigations revealed FBC: Hb-11.7 gm/dl, ESR-35 mm 1st hour, RBC-4.15x10^12/L, Platelet-3500x10^9/L (35 lacs/cumm) , WBC count revealed total count-17.36x10^9/L, neutrophil-71%, lymphocyte- 24%, monocyte-4%, eosinophil-1%, basophil-0%, PCV-0.36 l/l,MCV-86.3 fl,MCH-28.2 pg,MCHC-32.7 g/dl, RDW(CV)-15.3% and peripheral blood film demonstrated ; RBC- anisocytosis and anisochromia, WBC-mature with above distribution, Platelet- markedly increase in number and plenty of platelet clumps and the comment was features suggestive of essential thrombocythaemia. (Figure-3) Bone marrow trephine biopsy revealed hypercellular marrow with increased M:E ratio with active erythropoesis and granulopoesis and grossly hyperactive with giant megakaryocytes with hyperlobulated nuclei ,features consistent with essential thrombocythaemia. (Figure-4) The liver function, renal function, urine R/M/E and electrolyte was normal. CRP was 3 mg/dl, PT was 13

seconds, APTT was 33 seconds. The ANA, anti-phospholipid antibody, C-ANCA & P-ANCA, anti-CCP, HBs-Ag, anti-HCV all were negative. USG of abdomen and duplex scan of the both lower limbs were normal. JAK-2 V617F was negative. Her condition had initially improved after treatment with aspirin, hydroxyurea and antibiotic to treat super added infection in the hand. But it later, was refractory to medical treatment and platelet counts remained around thirty lacs and digital infarction progressed despite adequate dose titration of the drugs for two weeks. So, she underwent one episode of thrombocyteapheresis (figure-2) and her platelet count (Table-1) and digitral ischaemia was improved. After that she was on hydroxyurea and aspirin and followed up.

DISCUSSION

Essential thrombocythaemia presents with hemorrhagic complications, due to platelet dysfunction, or thrombotic disorders like stroke, myocardial infarction, venous thrombosis, and digital ischaemia. Thrombotic event are frequent when JAK2 V617F mutation is present.3 Most of the time , the platelet count is elevated above 1000 × 109/L but the studies agrees a median level of around 800 × 109/L .4

Our patient presented with the persistent redness and pain of the feet and hands which suggest erythromelagia. We reached the diagnosis by excluding the all causes of reactive thrombocytosis by appropriate investigations. We used the revised diagnostic criteria for ET that were proposed in 2005.5 We treated our patient with aspirin and hydroxyurea at first but she required one episodes of thrombocyteapharesis because she had inadequate response to medical therapy and consulted general surgery department for management of the gangrene.

Previous studies have shown that thombocyteapheresis can reduce the platelet count in a patient with thrombocytosis using intermittent flow centrifugation devices.6,7 It is believed that patients with thrombotic or haemorrhagic manifestations associated with ET should be treated with thrombocyteapheresis in combination with cytoreductive therapy .

Our target was to remove 30% of the platelet count from the baseline according to ASFA guideline.8 We used intermittent flow centrifugation (Haemonetic MCS+) by doing venous access using 16 G needle in the left anticubital vein. About 1.5 times of total blood volume was processed. The total procedure took 3 to 4 hours. Intermittent flow centrifugal technique was performed with only one vene puncture and blood is drawn and reinfused through same needle. 9

During the procedure we observed pulse, blood pressure temperature and partial pressure of oxygen .After one episode of thrombocyteapharesis she had significant improvement of symptoms and platelet count was reduced (table-1) and after one episode of thrombocyteapharesis patient was maintained on hyhroxyurea. She was on follow up and remained well.

CONCLUSIONS

In summary, thrombocyteapheresis is effective measure of reducing platelet count and relieving acute symptoms quickly attributed to elevated platelet count in ET .We believe that procedure may reduce the morbidity associated with thrombotic manifestations of ET during the interval between administration and maximum effectiveness of the hydroxyurea.

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Lists of figures and table

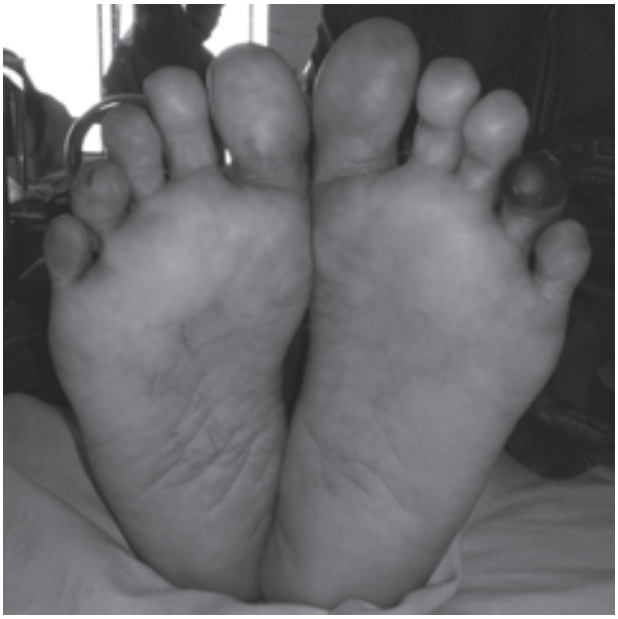

Figure: 1 Picture of feet showing redness, bluish discoloration and gangrene of the 4th toe

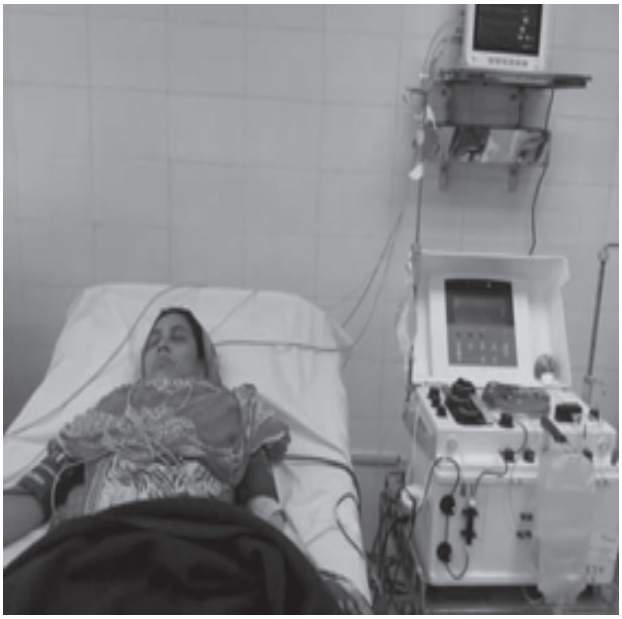

Figure : 2 procedure of thrombocytopharesis

Table-1: Serial platelet count before and after treatment

Table I: General Risk Factors of Burst Abdomen (n=100)

Date	Platelet count(10^9/ L)	Treatment
20.03.17	4660	
21.03.17	5000	Hydroxyurea – 1 gm
25.03.17	2500	
28.03.17	2000	
01.04.17	2600	Hydroxyurea – 1.5 gm
03.04.17	1200	
04.04.17	2500	
06.04.17	3080	Thrombocyteapharesis
08.04.17	850	

Case Report

Managing Progressive Subcutaneous Emphysema in Patient on Invasive Positive Pressure Ventilation

Jafra A[1], Kapoor D[2]

Abstract

Subcutaneous emphysema (SE) results from air leak from lung parenchyma into the least resistance subcutaneous tissues. Mostly a self limiting condition but extensive subcutaneous emphysema (ESE) may lead to anxiety, disfigurement, discomfort, respiratory embarrassment, upper airway obstruction and systemic air embolism and requires active management. We report successful management of progressive SE in a patient on invasive positive pressure mechanical ventilation using a newer approach and also discuss the role of surgical tracheostomy as a rescue measure.

Key Words: Subcutaneous emphysema; Positive pressure ventilation; Cannula.

To the editor,

Subcutaneous emphysema (SE) may spread to face, arms, thorax, abdomen and lower limbs. SE may develop spontaneously or following trauma, pneumothorax, infections, malignancies, positive pressure ventilation (PPV) and thoracic surgical procedures.1 Mostly a self limiting condition but Extensive Subcutaneous Emphysema (ESE) may lead to anxiety, disfigurement, discomfort, respiratory embarrassment, upper airway obstruction, pacemaker dysfunction and systemic air embolism and requires active management.1 We discuss the troubleshooting technique and role of surgical tracheostomy for progressive SE in a patient on invasive PPV for management of Acute Respiratory Distress Syndrome (ARDS).

A 15 year old boy was kept on invasive PPV in our intensive care unit (ICU) for management of ARDS. He was managed on low tidal volume with high positive end expiratory pressures (PEEP) of 18 cm of H2O (keeping plateau pressures≤ 30 cmH2O). Two days later, patient developed ESE on neck, chest and abdomen, causing rise in peak and plateau airway pressures (≥ 44cmH2O and≥ 40 cmH2O respectively). After ruling out the possibility of pneumothorax, we decided to drain SE with improvised fenestrated cannula.

The fenestrated cannula was constructed by creating circumferential, equidistant, punched-out holes in a 16G intravenous cannula by surgical blade under strict asepsis.(Figure 1A). These cannulas were inserted in subcutaneous plane at fourth intercostal space in the mid-clavicular plane bilaterally and connected to underwater seal. Thereafter, active compressive massage was done with direction of force pointing towards the catheter tip to vent-out the entrapped air. (Figure1B). However, due to the continuous positive pressure ventilation with high PEEP, we were not able to vent the entrapped air effectively. Meanwhile, we decided for surgical tracheostomy in view of the anticipated prolonged ventilation and ICU stay. Surprisingly, following surgical tracheostomy we observe rapid resolution of subcutaneous emphysema. There was dramatic fall in peak and plateau airway pressures with improvement in lung compliance. No further incidence of ESE observed during the stay of patient in ICU.

During PPV, there is one-way valve mechanism leading to progressive accumulation of air in tissues with each successive breath which leads to rapid and progressive SE. The incidence of barotrauma and development of SE in patients on PPV is 4-15%, whereas in patients with ARDS, it may further increase to a nearly 50%.2 Specific measures includes high flow oxygen therapy and surgical procedures such as subcutaneous chest drains, infraclavicular “blow holes”, pigtail drains, cervical mediastinotomy, trochar-type drains with suction and Jackson pratt drain.3,4 Micro-drainage techniques such as fenestrated angiocatheters are minimally invasive and may reduce morbidity (5). We observe that for effective management of progressive ESE during PPV, requires a more definitive method for vent of entrapped air. Surgical tracheostomy may act as an effective rescue procedure in this subset of patients as there maybe continuous vent of entrapped air from the stoma site. In addition, the aforesaid procedure may further minimise spread of Subcutaneous Emphysema (SE) to deeper tissue and therefore preventing the resultant thoracic inlet compression and chest wall restriction, which may lead to ventilation failure.

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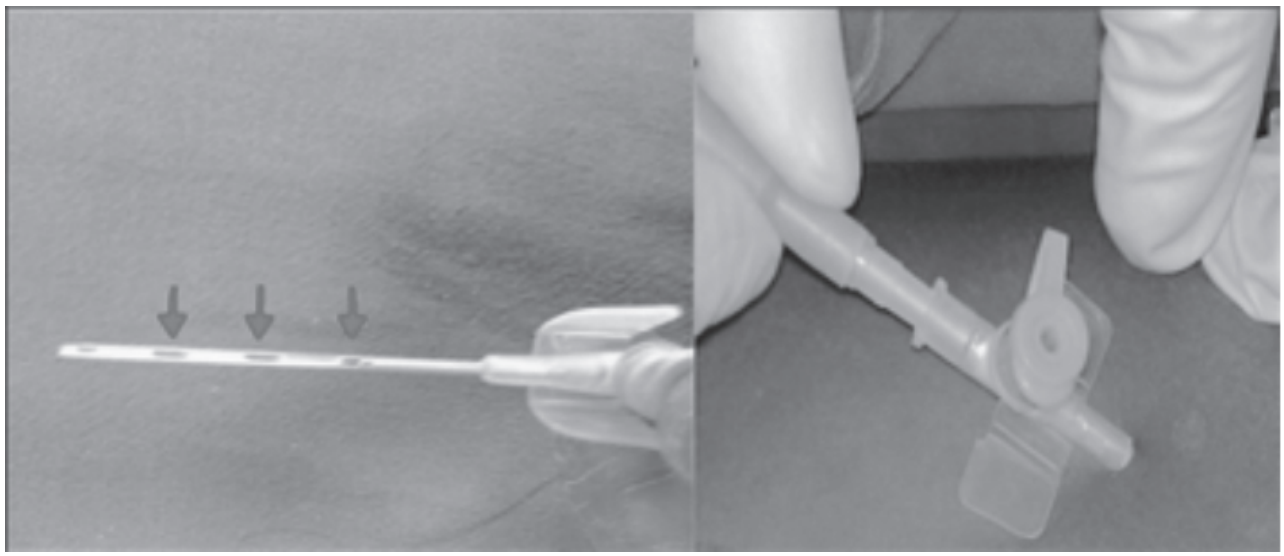

Figure 1A. Improvised Fenestrated Cannula. (Black arrows indicating punched-out holes)

Figure 1B. Subcutaneous Insertion of Cannula.

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