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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.

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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: Yu WM, Hawley TS, Hawley RG, Qu CK. Immortalization of yolk sac-derived precursor cells. Blood. 2002 Nov 15; 100(10):3828-31. Epub 2002 Jul 5.

2. Books and Other Monograph Personal author(s):

Murray PR, Rosenthal KS, Kobayashi GS, Pfaller MA. Medical microbiology. 4th ed. St. Louis: Mosby; 2002.

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Original Article

Efficacy of Different Doses of Dexmedetomidine in Blood Pressure to Laryngoscopy in Controlled Hypertensive Patient: A Randomized Control Trial

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Abstract

Control of blood pressure during anesthesia is very crucial. Laryngoscopic manipulation and endotracheal intubation are always a matter of concern which capable of producing tachycardia, arrhythmias and hypertension which is generally well tolerated in healthy patient. In hypertensive patient cardiovascular response to laryngoscopy and intubation is exaggerated. This study was conducted to assess the efficacy of different doses of dexmedetomidine in reduction of blood pressure during laryngoscopy and intubation in controlled hypertensive patient. This prospective Randomized controlled trial was carried out among 60 patients belonging to American Society of Anesthesiologists (ASA) Physical Status II posted for elective general anesthesia. Patients were randomly divided into three groups where each groups contain twenty with fixed card sampling. Group A consisted of twenty (20) patients who were received IV dexmedetomidine 0.5 µg/kg diluted to 50 ml with normal saline. Group B consisted of twenty (20) patients who were received IV dexmedetomidine 0.75 µg/kg diluted to 50 ml with normal saline. Group C consisted of twenty (20) patients who were received IV dexmedetomidine 1 µg/kg diluted to 50 ml with normal saline. Each infusions were started 10 minutes prior induction of general anesthesia and were given over 10 minutes. Baseline systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial blood pressure (MAP) were measured by one volunteer anesthesiologists by non-invasive blood pressure monitor. Following laryngoscopy and endotracheal intubation, the parameters recorded were SBP, DBP and MAP at 1, 3 and 5 min after intubation by non-invasive blood pressure monitor. The primary outcome measures were blood pressure responses after intubation and secondary outcome measures were to note down any adverse effects associated with drugs.

In this study baseline readings of SBP, DBP and MAP were almost similar in all three groups and statistically not significant. Maximum intubation response was seen at 1 min post intubation in all the three groups. The mean SBP of group A varied from 144.8±8.4 mmHg to 118.5±4.4 mmHg that of group B varied from 134.8±4.1 to 122.0±4.2 mmHg and then group C varied from 126.5±15.5 mmHg to 103.8±8.4 mmHg during different evaluation period ($p<0.05$). The mean DBP of group A varied from 91.8±7.6 mmHg to 72.4±5.8 mmHg that of group B varied from 81.3±5.2 to 70.3±2.5 mmHg and then group C varied from 80.9±6.7 mmHg to 63.4±2.4 mmHg during different evaluation period ($p<0.05$). The mean MAP of group A varied from 109.0±5.6 mmHg to 87.5±4.4 mmHg that of group B varied from 98.7±2.5 to 86.3±3.4 mmHg and then group C varied from 95.5±9.2 mmHg to 76.5±3.4 mmHg during different evaluation period ($p<0.05$). The mean SBP at 1st hour was found 127.9±6.5 in group A, 131.6±6.4 group B and 131.5±7.1 group C. The DBP at 1st hour was found 126.8±6.4 in Group A, 131.4±6.8 in Group B and 131.8±6.1 in Group C. The mean MAP at 1st hours was found 93.2±3.7 in group A, 95.4±3.4 in Group B and 96.2±4.9 in Group C($p>0.05$). Dexmedetomidine in doses of 0.75 µg/kg was more effective compared to 0.05 µg/kg and 1µg/kg in attenuating blood pressure response to laryngoscopy and endotracheal intubation without producing adverse effects in control hypertensive patients.

Keywords: *Efficacy; different doses; dexmedetomidine; blood pressure; laryngoscopy; controlled hypertensive patient; randomized control trial*

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INTRODUCTION

Dexmedetomidine is effective during intubation at the time of anaesthesia.[1] In addition, it maintained intraoperative cardiovascular stability. These drugs decrease tachycardia, hypertension, and sympathetic activity, which are beneficial for the cases with a presence of myocardial ischemia.[2]

Various researchers of different countries have suggested that dexmedetomidine is significantly reduced the haemodynamic responses during laryngoscopy and endotracheal intubation among the hypertensive patients.[3] Choudhury et al[4] and Sulaiman et al[3] have both performed two separate studies by using dexmedetomidine with a dose of 0.05 μg/kg for reduction of blood pressure responses during laryngoscopy and endotracheal intubation. The pretreatment with dexmedetomidine 0.05 μg/kg attenuate the stress responses, but did not totally abolish the cardiovascular and catecholamine surge responses to tracheal intubation. Smitha et al[5] have used dexmedetomidine with the dose of 0.5 and 1μg/kg and have found that the dose of 1μg/kg is more effective for the reduction of stress response to laryngoscopy and endotracheal intubation. However, this is a promising results; furthermore the dose of 1 μg/kg is associated with some incidence of cardiovascular system. Sebastian et al[6] have used dexmedetomidine (0.75 μg/kg) for reduction of stress response to laryngoscopy and endotracheal intubation. In 0.75 μg/kg group, intubation responses is completely obtunded when compared to 0.5 μg/kg without any adverse effects.

Appropriate premedication can prevent the associated risks of heamodynamic pressure response to laryngoscopy and intubation in controlled hypertension patients; which is essential to prevent negative outcomes such as tachycardia, hypertension, myocardial ischemia, ventricular arrhythmias. Dexmedetomidine is highly specific and selective potent alpha-2 agonist which produces dose dependent sedation anxiolytics and analgesia. It can potentially offer a superior effect in attenuating stress-induced sympathoadrenal responses during laryngoscopy. In addition, many perioperative beneficial characteristics stated earlier, made it an attractive drug to study. It reduces the requirement of both intravenous and inhalational anaesthetics[7], thus reducing their side effects, achieve hemodynamic stability during the intra-operative period and maintains intraoperative cardiovascular stability.

Therefore, the search of effective dose of dexmedetomidine premedication for controlled hypertensive patients uncovering the possibilities for better management of those patient with less side effects in perioperative period and reduce mortality and morbidity. So the aim of the present study was to assess the effectiveness of dexedetomidine in attenuation of blood pressure due to laryngoscopy and endotracheal intubation with different doses of intravenous dexmedetomidine in controlled hypertensive patients.

MATERIALS AND METHODS

Study Population and Settings: This single blind, parallel randomized controlled trial was conducted in Department of Anaesthesia, Analgesia, Palliative and intensive Care Medicine, Dhaka Medical College Hospital, Dhaka from August 2016 to July 2018 for a period of two (02) years. Data was gathered after approval of protocol by ethical review committee. Patients who were categorized as American society of Anesthesiology (ASA) class II, patients who had a history of essential hypertension for which they were being treated and controlled as well as posted for elective surgeries under general anesthesia were selected as study population. Any anticipated difficult intubation or patients who had a history of bronchial asthma, drug or alcohol abuse, patients who had a history of cerebrovascular, neurologic, respiratory or ischemic heart disease and renal or hepatic dysfunction, patients who were physically dependent on narcotics, known drug allergy to dexmedetomidine, patients on antidepressants, anxiolytics, anticonvulsant or antipsychotics, pregnant or nursing woman, participation in another drug study during the preceding 1 month period were excluded from this study.

Randomization and Blinding: A total number of sixty (60) patients belonging to ASA Physical Status II posted for elective general anaesthesia was finally selected. All the information were recorded in a prefixed data sheet. Patients were randomly divided into three groups and each group had twenty patients. Randomization allocated by fixed card sampling. One assigned anesthesiologist performed the grouping. Data were collected by the volunteer anaesthesiologist who was expert enough take data and was fully unaware of the study.

INTERVENTION

Group A consisted of twenty (20) patients who were received IV dexmedetomidine 0.5 μg/kg diluted to 50 ml with normal saline as infusion over 10 min. Group B consisted of twenty (20) patients who were received IV

dexmedetomidine 0.75 µg/kg diluted to 50 ml with normal saline as infusion over 10 min. Group C consisted of twenty (20) patients who were received IV dexmedetomidine 1 µg/kg diluted to 50 ml with normal saline as infusion over 10 min. All infusions were started 10 minutes prior induction of general anesthesia. All patients were evaluated a day before surgery. The patients were kept fasting overnight after 10:00 pm and was received tablet Ranitidine 150 mg orally and tablet midazolam 7.5 mg orally as premedication at night before surgery. The same anaesthesiologist prepared the intravenous (IV) infusions of dexmedetomidine. All patients monitored with non-invasive blood pressure monitor (philips sure signs VS3). An IV line was secured, and the patients were administered 500ml of IV fluid Ringer's lactate. Baseline systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MAP) were measured by one volunteer anaesthesiologists by non-invasive blood pressure monitor. Then study drug infusion was given over 10 min by principal investigator. All the patients were pre-oxygenated for 3 minutes. Then, patients was induced with IV Thiopental Sodium 5 mg/kg body weight, IV fentanyl 1 µg/kg, endotracheal intubation was facilitated by IV succinylcholine 1.5 mg/kg body weight. Laryngoscopy and intubation was done by principal investigator.

Follow up and Outcome Measures: Following laryngoscopy and endotracheal intubation, the parameters recorded was SBP, DBP and MAP at 1, 3 and 5 min after intubation by non-invasive blood pressure monitor. After adequate recovery, patients were shifted to post-anaesthesia care unit and monitored for 2 hours. The principle investigator was assessing the patients directly postoperatively in the recovery room and was also personally follow-up the patients in the ward for monitoring purposes. If any unforeseen complication occurs in the ward, the principle investigator was available to come and examine the patient, address and manage any problems.

Statistical analysis: All the parameters were expressed as mean and standard deviation (mean ± SD) and percentage. ANOVA for repeated measures followed by post hoc analysis with Least Significance Difference (LSD) was performed for comparing continuous variables within the groups at different time points. For intragroup comparison at the same time point, between the groups, Students't' test was applied. *p* value <0.05 was accepted as level of significance. Statistical analyses were performed by using a computer based statistical program SPSS (Statistical Package for Social Sciences) Version 22 with the help of a biostatistician.

RESULT

Table I shows this present study was carried out with an aim to find out the specific dose of Dexmedetomidine in attenuation of blood pressure response to laryngoscopy and tracheal intubation in controlled hypertensive patients without adverse effects. The groups were well matched for their demographic data. Male to female ratio was 1:1 in all three group. The basal readings of blood pressure were similar in all the three groups. Maximum intubation response was seen at 1 min post-intubation in all the three groups. Regarding the side effects it was observed that Hypotension was found in 6(30.0%) cases in group C and hypertension was found in 4(20.0%) cases of group A. The difference was statistically significant (p<0.05) among three groups. The mean age were 45.2±3.1 years in group A, 50.3±7.4 years in group B and 47.5±7.9 years in group C. Male was found 10(50.0%) in group A, 10(50.0%) in group B and 10(50.0%) in group C. The difference was statistically not significant (p>0.05) among three groups (Table 1).

Table 1: Age and Gender Distribution of the Study Participant (n=60)

Variables	Group A (n=20)	Group B (n=20)	Group C (n=20)	P value
Mean Age (Years)	45.2±3.1	50.3±7.4	47.5±7.9	[a]0.053[ns]
Range(min-max)	33 to 43	40 to 60	35 to 60	
Gender				[b]1.000[ns]
• Male	10(50.0%)	10(50.0%)	10(50.0%)	
• Female	10(50.0%)	10(50.0%)	10(50.0%)	

ns= not significant; [a]p value reached from ANOVA test; [b]p value reached from Chi- square test; Data are expressed as Mean±SD

Table II shows the baseline mean Systolic blood pressure was found 130.2±6.5 (mmHg) in group A, 135.6±4.3 (mmHg) in group B and 134.9±11.9 (mmHg) in group C. The Baseline difference was statistically not significant (p>0.05) among three groups. The mean SBP of group A varied from 144.8±8.4 mmHg to 118.5±4.4 mmHg that of group B varied from 134.8±4.1 to 122.0±4.2 mmHg and then group C varied from 126.5±15.5 mmHg to 103.8±8.4 mmHg during different evaluation period. The difference was statistically significant (p<0.05) among three groups.

Table II: Distribution of the Study Participant by Systolic Blood Pressure (n=60)

Systolic blood pressure (mmHg)	Group A (n=20)	Group B (n=20)	Group C (n=20)	P value
Baseline	130.2±6.5	135.6±4.3	134.9±11.9	0.086ns
Range(min-max)	120 to 140	130 to 142	127 to 158	
After drug administration	118.5±4.4	129.0±5.5	124.5±10.9	0.001s
Range(min-max)	110 to 122	120 to 137	110 to 143	
1 min	144.8±8.4	134.8±4.1	126.5±15.5	0.001s
Range(min-max)	130 to 155	130 to 140	105 to 145	
3 min	128.6±5.8	126.3±5.7	112.2±8.9	0.001s
Range(min-max)	118 to 135	120 to 135	100 to 124	
5 min	119.1±8.0	122.0±4.2	103.8±8.4	0.001s
Range(min-max)	105 to 128	118 to 130	90 to 120	

s=significant; ns=not significant; p value reached from ANOVA test; Data are expressed as Mean±SD

Table III shows the baseline mean diastolic blood pressure baseline (DBP) was found 79.8±2.2 (mmHg) in group A, 80.6±3.7 (mmHg) in group B and 82.2±4.5 (mmHg) C. The Baseline difference was statistically not significant (p>0.05) among three groups. The mean DBP of group A varied from 91.8±7.6 mmHg to 72.4±5.8 mmHg that of group B varied from 81.3±5.2 to 70.3±2.5 mmHg and then group C varied from 80.9±6.7 mmHg to 63.4±2.4 mmHg during different evaluation period. The difference was statistically significant (p<0.05) among three groups.

Table III: Distribution of the study participant by diastolic blood pressure (n=60)

Diastolic BP (mmHg)	Group A (n=20)	Group B (n=20)	Group C (n=20)	P value
Baseline	79.8±2.2	80.6±3.7	82.2±4.5	0.108ns
Range(min-max)	75-82	75-87	80-92	
After drug administration	72.4±5.8	73.7±4.2	78.1±5.7	0.003s
Range(min-max)	60-80	70-82	70-86	
1 min	91.8±7.6	81.3±5.2	80.9±6.7	0.001s
Range(min-max)	79-100	78-85	71-90	
3 min	86.3±6.5	75.7±2.9	73.1±6.7	0.001s
Range(min-max)	75-95	70-80	68-90	
5 min	77.8±3.9	70.3±2.5	63.4±2.4	0.001s
Range(min-max)	70-82	65-75	60-68	

s=significant; p value reached from ANOVA test; Data are expressed as Mean±SD

Table IV shows the baseline mean MAP was found 96.8±4.1 (mmHg) in group A, 98.3±3.8 (mmHg) in group B and 100.3±7.1 (mmHg) in Group C. The Baseline difference was statistically not significant (p>0.05) among three groups. The mean MAP of group A varied from 109.0±5.6 mmHg to 87.5±4.4 mmHg that of group B varied from 98.7±2.5 to 86.3±3.4 mmHg and then group C varied from 95.5±9.2 mmHg to 76.5±3.4 mmHg during different evaluation period. The difference was statistically significant (p<0.05) among three groups.

Table IV : Distribution of the study participant by MAP (n=60)

MAP (mmHg)	Group A (n=20)	Group B (n=20)	Group C (n=20)	P value
Baseline	96.8±4.1	98.3±3.8	100.3±7.1	0.113ns
Range(min-max)	91 to 106	93 to 105	95 to 114	
After drug administration	87.5±4.4	91.9±3.7	92.6±7.7	0.007s
Range(min-max)	80 to 94	88 to 99	83 to 104	
1 min	109.0±5.6	98.7±2.5	95.5±9.2	0.001s
Range(min-max)	101 to 117	96 to 103	84 to 108	
3 min	99.9±4.3	91.8±4.2	85.9±5.4	0.001s
Range(min-max)	94 to 106	85 to 97	80 to 96	
5 min	91.4±3.4	86.3±3.4	76.5±3.4	0.001s
Range(min-max)	84 to 96	80 to 93	70 to 82	

s=significant; p value reached from ANOVA test; Data are expressed as Mean±SD.

Table V shows the mean SBP at 1st hour was found 127.9±6.5 in Group A, 131.6±6.4 Group B and 131.5±7.1 Group C. The DBP at 1st hour was found 126.8±6.4 in Group A, 131.4±6.8 in Group B and 131.8±6.1 in Group C. The mean MAP at 1st hours was found 93.2±3.7 in group A, 95.4±3.4 in Group B and 96.2±4.9 in Group C. The difference hour was statistically not significant (p>0.05) among three groups.

Table V : Distribution of the Study Participant by Blood Pressure in Post-Operative period (n=60)

BP in Post-Operative Period	Group A (n=20)	Group B (n=20)	Group C (n=20)	P value
SBP (mmHg)				
• 1st hour	127.9±6.5	131.6±6.4	131.5±7.1	0.145ns
• Range(min-max)	115 to 138	120 to 140	115 to 140	
• 2nd hour	127.2±6.4	131.4±6.8	131.8±6.1	0.0510ns
• Range(min-max)	120 to 137	123 to 142	120 to 142	
DBP (mmHg)				
• 1st hour	76.3±3.4	77.7±2.83	79.0±4.3	0.065ns
• Range(min-max)	70 to 80	75 to 82	70 to 84	
• 2nd hour	76.0±3.8	76.8±3.7	78.4±2.4	0.081ns
• Range(min-max)	72 to 82	72 to 82	72 to 80	
MAP (mmHg)				
• 1st hour	93.2±3.7	95.4±3.4	96.2±4.9	0.061ns
• Range(min-max)	85 to 99	91 to 100	85 to 101	
• 2nd hour	93.2±4.1	95.3±4.3	96.1±3.1	0.058ns
• Range(min-max)	88 to 99	89 to 100	89 to 100	

s=significant; ns=not significant; p value reached from ANOVA test; Data are expressed as Mean±SD.

DISCUSSION

In this present study, the mean age was 45.2±3.1 years in group A, 50.3±7.4 years in group B and 47.5±7.9 years in group C. The difference was statistically not significant (p>0.05) among three groups. Samala et al[8], Pramanick et al[9] and Smitha et al[5] found almost similar mean age and age ranged in their respective studies. On the other hand Sebastian et al[6] found the mean age was 32.50±9.12 years in Group A, 36.96±10.33 years in Group B, 31.20±9.30 years in Group C, which is smaller with the present study. The lower mean age and age range maybe due to geographical variations, racial, ethnic differences, and genetic causes.

In this study, dexmedetomidine is effective significantly in blunting the increase in mean SBP and DBP due to laryngoscopy and intubation. However, the baseline difference of mean SBP and DBP is not statistically significant (p>0.05) among the group A, B and C. Though mean SBP and DBP have been increased at 1 minute after intubation in all three groups. The haemodynamic variables fell below the base line in group B and C all the time. The findings indicates that there is a disparity of SBP and DBP in group A and group C but in group B it was almost unswerving from baseline to 5 minutes follow-up. Inter group comparison revealed statically significant among three groups (p<0.05). Smitha et al[5] compared the effect of 0.5 and 1 μg/kg of dexmedetomidine with normal saline in attenuating stress response. They found out that dexmedetomidine 1 μg/kg was more effective than dexmedetomidine 0.5 μg/kg in controlling haemodynamic responses to tracheal intubation. The intergroup comparison revealed a statistically significant (p<0.05). Similar observations regarding the SBP and DBP were also Samala et al[8], Pramanick et al[9] and Sebastian et al[6].

At baseline, the MAP (P=0.113) is almost same among the group A, B and C. However, it has been also found that group B and group C have a significantly lower MAP (p=0.001) to 5 min follow up. Dexmedetomidine attenuates sypathatoadrenal response by activation of presynaptic α2 receptors in sympathetic nerve endings resulting in decreased release of noradrenaline. Moreover, stimulation of postsynaptic α2 receptors of locus coeruleus causes inhibition of norepinephrine release[10]. Patel et al[11] have administered dexmedetomidine intravenously as loading dose of 1 μg/kg over 10 min prior to induction in group B and observed, dexmedetomidine significantly attenuated stress response to intubation with lesser increase in systolic (6% vs. 23%) and diastolic (7% vs. 20%) blood pressure as compared to the control group (P <0.05).

In this current study, the baseline mean MAP is 96.8±4.1 (mmHg) in group A; however, in group B and group C the MAP are slightly higher that group A which are 98.3±3.8 (mmHg) and 100.3±7.1 (mmHg) respectively. The baseline difference of mean arterial pressure among these three groups is not statistically significant (p>0.05). Maximum intubation response is found at 1 min post-intubation among the three groups. In group B, they approached near the baseline by 3 minutes. Interestingly, the variables fell below the baseline by 3 min in group C. In group A statistically higher values of SBP, MAP at all-time intervals are found in post-intubation when compared to group B and group C. Therefore, it can be inferred that the haemodynamic response is better observed in group B and group C, when it is compared with group A. However, the parameters fell below the baseline value at 1 min after intubation in group C. This clearly indicates that the dexmedetomidine in a dose of 0.75 μg/kg and 1 μg/kg is superior to dexmedetomidine in a dose of 0.5 μg/kg.

Similarly Sebastian et al[6] showed the mean of Mean Arterial Blood Pressure (MAP) in first minute 114.57±5.14 mmHg in Group A, 98.87±5.86 mmHg in Group B and 96.33±5.40 mmHg in Group C (p<0.001). In third minute 108.47±4.97 mmHg in Group A, 94.83±5.13 mmHg in Group B and 90.27±5.49 mmHg in Group C (p<0.001). In fifth minute 103.37±4.51 mmHg in Group A, 91.80±5.48 mmHg in Group B and 85.47±5.08 mmHg in Group C(p<0.001). Similar observations regarding the MAP pressure was also reported by Smitha et al[5].

In this present study, hypotension is found in 6(30.0%) in group C. In group A hypertension has found in 4(20.0%) cases. The differences among the three groups is statistically significant (p<0.05). Smitha et al[5] have reported that different doses of dexmedetomidine has shown irregular breathing with varied episodes of apnoea. Furthermore, dexmedetomidine (1 μg/kg) has been associated with the increased incidence of adverse effects like bradycardia and hypotension observed by Kartik et al[12] and Menda et al[13]. It has been established that the activation of post-synaptic α-2 receptors in CNS brings the decreased sympathetic activity which can lead to bradycardia as well as hypotension[14]. Furthermore dexmedetomidine (1 μg/kg) is associated with increased incidence of adverse effects[13].

Yallapragada et al[15] have been reported that the dexmedetomidine (1 μg/Kg) is effective on the blood

pressure responses during laryngoscopy and intubation showed that BP increased by 4.0% initially but later declined by 11.0% following a 5 minute infusion of dexmedetomidine. After intubation the SBP rose only slightly above baseline. In four patients in dexmedetomidine Group hypotension (SBP <90 mmHg) was observed following induction of anaesthesia. In this study also six patients had developed hypotension in group C.

Patients have been shifted to the post anaesthesia care unit after complete clinical recovery and they have been observed for 2 hours for nausea, vomiting, bradycardia, hypotension and sedation. In present study results suggested that to control blood pressure during laryngoscopy and tracheal intubation, Dexmedetomidine is a better drug and 0.75 μg/kg dose is more effective than Dexmedetomidine with the dose of 0.5 μg/kg and 1 μg/kg which causes no significant side effects in controlled hypertensive patients. In this study no significant respiratory depression, apnea, muscle rigidity or decrease in SpO_2 was seen in any patient in post-operative period.

CONCLUSIONS

It can be concluded that Dexmedetomidine dose of 0.75 μg/kg is safe and effective in obtunding the blood pressure response to laryngoscopy and endotracheal intubation without producing side effects compared to doses of 0.5 μg/kg and 1 μg/kg .

REFERENCES

1. Agarwal, S., Gupta, K., Singh, V.P., Sharma, D. and Pandey, M.N., 2016. Comparative evaluation of dexmedetomidine with clonidine as premedication for attenuation of hemodynamic responses during laryngoscopy and endotracheal intubation under general anesthesia. International Journal of Research in Medical Sciences, 4(9), pp.4026-32.
2. Krishna K.N.G., 2011. Effect of Dexmedetomidine on perioperative haemodynamics, anaesthtic requirements and recovery characteristics in patients undergoing transnasal trans sphenoidal resection of pituitary tumor. Thesis.
3. Sulaiman, S., Karthekeyan, R.B., Vakamudi, M., Sundar, A.S., Ravullapalli, H. and Gandham, R., 2012. The effects of dexmedetomidine on attenuation of stress response to endotracheal intubation in patients undergoing elective off-pump coronary artery bypass grafting. Annals of Cardiac Anaesthesia, 15(1), pp.39-43.
4. Choudhary, K.R., Kaushik, A., Sharma, S. And Puri, S.K.S., 2017. A Randomized Controlled Study on Effect of Dexmeditomidine for Stress Response Attenuation due to Laryngoscopy and Intubation. International Journal of Medical Research Prof, 3(3), pp. 219-22.
5. Smitha, K.S., Shukla, D., Sathesha, M., Rao, N.S. and Sudheesh, K., 2014. Comparison of two different doses of dexmedetomidine in attenuating hemodynamic changes during laryngoscopy. Journal of Evolution of Medical and Dental Science, 3, pp.13501-8.
6. Sebastian, B., Talikoti, A.T. and Krishnamurthy, D., 2017. Attenuation of haemodynamic responses to laryngoscopy and endotracheal intubation with intravenous dexmedetomidine: A comparison between two doses. Indian Journal of Anaesthesia, 61(1), pp.48-54.
7. Aantaa, R., Kanto, J., Scheinin, M., Kallio, A. and Scheinin, H., 1990. Dexmedetomidine, an alpha2-adrenoceptor agonist, reduces anesthetic requirements for patients undergoing minor gynecologic surgery. Anesthesiology, 73(2), pp.230-235.
8. Samala, S. and Indurkar, P.S., 2017. Effect of intravenous dexmedetomidine (1μg/kg) in obtunding the pressor response to laryngoscopy and tracheal intubation compared to intravenous preservative free 2% lignocaine (1.5 mg/kg). International Journal of Research in Medical Sciences, 4(7), pp.2750-55.
9. Pramanick, S., Sadaqat S.H. and Banerjee, P.B.D., 2016 Attenuation of haemodynamic response to different doses of dexmedetomidine during extubation in patients undergoing peripheral vascular surgery. Indian Journal of Basic and Applied Medical Research, 5(4), pp.740-751.
10. Prasad, S.R., Matam, U.M. and Ojili, G.P., 2015. Comparison of intravenous lignocaine and intravenous dexmedetomidine for attenuation of hemodynamic stress response to laryngoscopy and endotracheal intubation. Journal of Dr. NTR University of Health Sciences, 4(2), pp.86-90.
11. Patel, N.D., Patel, J.J. and Patel, D.D., 2015. A study on comparison of intravenous dexmedetomidine with intravenous fentanyl for suppression of hemodynamic responses to laryngoscopy and endotracheal

intubation during general anaesthesia. *National Journal Medical research* 5(2), pp.127-131.

12. Kartik, S., Bunty S., Gian C. And Avinash G., 2018. Dexmedetomidine Versus Esmolol for Attenuation of Haemodynamic Response to Laryngoscopy and Tracheal Intubation in Hypertensive Patients. International Journal of Anatomy, Radiology and Surgery 7(1), PP.1-5.
13. Menda, F., Koner, O., Sayin, M., Ture, H., Imer, P. and Aykac, B., 2010. Dexmedetomidine as an adjunct to anesthetic induction to attenuate hemodynamic response to endotracheal intubation in patients undergoing fast-track CABG. Annals of Cardiac Anaesthesia, 13(1), pp. 16-20.
14. Paranjpe, J.S., 2013. Dexmedetomidine: Expanding role in anesthesia. Medical Journal of Dr. DY Patil Vidyapeeth, 6(1), pp.5-13
15. Yallapragada, S.V., Vidadala, K.S., Vemuri, N.N. and Shaik, M.S., 2014. Comparison of the efficacy of dexmedetomidine with that of esmolol in attenuating laryngoscopic and intubation response after rapid sequence induction. Anesthesia, Essays and Researches, 8(3), pp.383-387.

Original Article

Comparison between Flexor Carpi Radialis and Flexor Carpi Ulnaris Tendon Transfer for Fingers' Extension in High Radial Nerve Palsy

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Abstract

The hand grip is severely impaired following high radial nerve palsy due to loss of extension of the wrist, metacarpo-phalangeal joint of fingers and thumb. If radial nerve does not show neural recovery following conservative or surgical repair during the optimum time, tendon transfer is considered the standard treatment. To evaluate and compare the clinical outcome between flexor carpi radialis and flexor carpiulnaris tendon transfer for fingers' extension in high radial nerve palsy. This randomized controlled trial study was carried out in the Department of Orthopedic Surgery, Bangabandhu Sheikh Mujib Medical University, Dhaka over a period of two years from January 2013 to December 2014. A total of 30 patients with high radial nerve palsy were recruited, 15 patients were gone through Flexor Carpi Radialis tendon transfer procedure (FCR group) and the rest 15 patients were gone through Flexor Carpi Ulnaris tendon transfer procedure(FCU group). The patients were followed up for 12 weeks after surgical intervention. Out of all patients, 86.7% male were encountered in each group. The mean age was found 31.07±9.14 years in FCR group and 33.60±10.79 years in FCU group. Humerus fracture was remained a major cause of radial nerve palsy in both FCR and FCU groups (26.7% vs. 33.3%). In final follow-up at 12th week, no extension deficit was observed at MCP joint (93.3% vs. 80.0%, p>0.05). The end result of surgical intervention was found satisfactory equally in both the groups (86.7%). In case of high radial nerve palsy, both FCR and FCU tendon transfer procedures are effective forfingers' extension at MCP joint.

Keywords: *Flexor carpi radialis, flexor carpi ulnaris, fingers' extension and radial nerve palsy.*

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INTRODUCTION

Hand is a highly specialized organ as it has grasping, pinching and hooking function carried out by musculotendinous units. It can give information about the position, size and shape of an object by its highly developed sensory mechanism and described as third eye.[1]

Injury to radial nerve may occur at different level. A very high level radial nerve injury occurs at the level of axilla. Loss of extension at the elbow, wrist, fingers and thumb occur in very high level lesions. A high level radial nerve palsy happens due to injury above elbow to below axilla where elbow function is intact but wrist drop is obvious and associated with loss of fingers and thumb extension. A low level lesion occurs due to injury just below the elbow where elbow and wrist spared but fingers and thumb extension are lost.[2]

Most surgeons have used the pronator teres (PT) to extensor carpi radialis brevis (ECRB) transfer to restore wrist extension.[3] Restoration of finger extension may be done using the flexor carpi radialis (FCR), flexor carpi ulnaris (FCU) or flexor digitorum superficialis (FDS).[4-6] Currently many surgeons prefer to use FCR because it is simpler than using the FDS and it spares the strong wrist stabilizer.[7]

The best technique of thumb extensor/radial abduction remains controversial. The most commonly used technique is the transfer of Palmaris longus(PL) to the rerouted extensor pollicis longus (EPL). The EPL must be transposed from the third compartment toward the PL. This transposition eliminates the thumb adduction vector of the EPL and the new 'EPL' then acts as both an extensor and radial abductor of the thumb.[3,8] Surgeons who do not

re-route the EPL have addressed radial abduction of the thumb by transferring the PL or FCR to the abductor policis longus (APL).[4,5,7] Radial abduction of the thumb may also be restored by a tenodesis of the APL to the brachioradialis(BR).[7]

The rationale for choosing the FCR is preservation of the FCU as a strong wrist stabilizer; preservation of wrist flexion with ulnar deviation (hammering activity for manual workers).[9] Clinical findings may have the significant implication on the choice of the tendon transfer. In general tendon transfer is indicated when there is little or no likelihood that a damage radial nerve will regenerate sufficiently to innervate lost motor function. If the nerve, the extensor muscles supplied by the nerve or both has been damaged beyond repair, tendon transfer should be considered as soon as sufficient wound healing and maturation have occurred to produce tissue equilibrium.[10]

Previous studies recommended for further studies to be carried out to makea comparison between FCR versus FCU tendon transfer for EDC function (fingers' extension) in the cases of high radial nerve palsy. Limited data are available regarding this topic in our country. Available information from above studies had provided a rationale to conduct the current study.

MATERIAL AND METHOD

This randomized controlled trial was carried out at the Department of Orthopedic Surgery, Bangabandhu Sheikh Mujib Medical University, Dhaka over a period of two years from January 2013 to December 2014. A total of 30 patients with high radial nerve palsy were recruited, 15 patients were gone through Flexor Carpi Radialis tendon transfer procedure (FCR group) and the rest 15 patients were gone through Flexor Carpi Ulnaris tendon transfer procedure (FCU group). Patients had duration of radial nerve injury less than 6 months, stiff joints, epilepsy or paralyzed hand and patients with absence of palmaris longus muscle were excluded from this study. They were diagnosed on the basis of presenting complaints, clinical examinations & investigations. The patients were followed up for 12 weeks after surgical intervention. In this study, baseline data and four follows up were recorded from each patient and measured the clinical response, complications and Bincaz scalewas used for the overall assessment of tendon transfers for high radial nerve palsy.

RESULTS

Tabble I shows the range (min-max) (18-46) (11-53). In both groups 13.3% were female and 86.7% were male. The mean age was found 31.07±9.14 years with the range of 18 to 46 years in FCR group and mean age was 33.60± 10.79 years with the range of 11 to 53 years in FCU group.

Table I: Demographic profile of the study population (n=30)

	Group		p value
	FCR n (%)	FCU n (%)	
Gender			1.000
Female	2 (13.3)	2 (13.3)	
Male	13 (86.7)	13 (86.7)	
Age (years)			
Mean±SD)	31.07±9.14)	33.60±10.79)	0.493

Table II shows the soaked dressing in first POD (26.7% vs. 20.0%), second POD (20.0% vs. 14.3%) in FCR and FCU group respectively. Hand swelling in first POD was 64.3 % and 53.3% in second POD; 26.7% and 20% in FCR and FCU groups respectively.

Table II: Distribution of the patients according to Post-operative follow-up (n=30)

	1st POD		2nd POD	
	FCR n (%)	FCU n (%)	FCR n (%)	FCU n (%)
Dressing (Soaked)	4(26.7)	3(20.0)	3 (20.0)	2(14.3)
Hand Swelling	9 (64.3)	8 (53.3)	4(26.7)	3(20.0)

Table III shows the wound condition in both FCR and FCU group (100.0% vs. 100.0%).

Table III: Distribution of the patients according to wound condition (n=30)

Wound condition-(Healthy)	Group		p value
	FCR n (%)	FCU n (%)	
At 12th week	15 (100)	15(100)	

Table IV shows the extension deficit >10° was found nil in both groups at 12th week after surgical intervention. Extension deficit <10° was found 20.0% in FCR group and 26.7% in FCU group at 12th week after surgical intervention. No extension deficit was accounted 80.0% in FCR group and 73.3% in FCU group at 12th week after surgical intervention.

Table IV: Distribution of the patients according to Finger's active extension (n=30)

Finger's active extension (at 12th weeks)	Groups		P value
	FCR n (%)	FCU n (%)	
Extension deficit >10°	-	-	
Extension deficit <10°	3 (20.0)	4 (26.7)	0.666 ns
No extension deficit	12 (80.0)	11 (73.3)	

Table V shows the fairly satisfaction was found 6.7% cases in FCR group and 26.7% cases in FCU group at 12th week after surgical intervention. Satisfied was found 66.7% in FCR group and 60.0% in FCU group at 12th week after surgical intervention. Patients with very satisfied were accounted in FCR group was 26.7% and in FCU groups 13.3% at 12th week after surgical intervention. No statistically significant difference was found in two groups in cosmetically satisfaction of patients.

Table V: Distribution of the patients according to cosmetically satisfaction of patients (n=30.)

Cosmetically satisfaction of patients (at 12th weeks)	Groups		P value
	FCR n (%)	FCU n (%)	
Fairly satisfied	1 (6.7)	4 (26.7)	
Satisfied	10 (66.7)	9 (60.0)	0.657
Very satisfied	4 (26.7)	2(13.3)	

Table VI shows the follows up at 12th week, 6.7% patients had extension deficit <10^0 of metacarpo-phalangeal joint in FCR group but in FCU group, was 20%. No-significant difference in level of metacarpo-phalangeal joint extension was observed.

Table VI: Distribution of the patients according to Metacarpo-phalangeal joint extension at final follow-up at 12th week (n=30).

Metacarpophalangeal joint extension (at 12th weeks)	Groups		p value
	FCR n (%)	FCU n (%)	
Extension deficit >100	-	-	
Extension deficit <100	1(6.7)	3(20.0)	0.591ns
No extension deficit	14 (93.3)	12 (80.0)	

Table VII shows that no significant difference was found regarding overall satisfaction between both groups (93.3% vs. 80.0%). In FCR group 93.3% of the patientsand in FCU group, 86.7% of the patients able to return their previous job.

Table VII: Distribution of the patients according to overall satisfaction of patients with the operation (n=30).

	Groups		P value
	FCR n (%)	FCU n (%)	
Overall Satisfaction	14 (93.3)	12 (80.0)	0.591ns
Able to return previous job	14(93.3)	13 (86.7)	0.543ns

Table VIII shows the end result of surgical intervention excellent in FCR group and FCU group 26.7% vs. 6.7%, (p> 0.5). 60.0% and 80.0% patients declared as good surgical intervention in FCR and FCU group respectively. Fair surgical intervention was found same in both groups which was 13.3%. There was no significant differencein surgical intervention between two groups.

Table VIII: Distribution of the patients according to end result of surgical intervention (n=30)

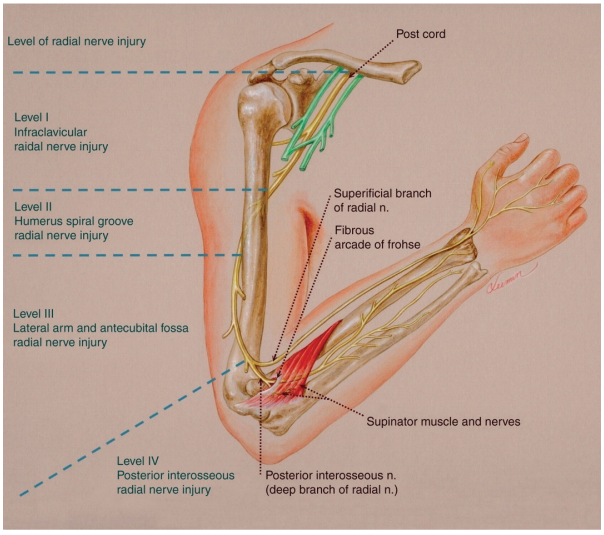
Result	Groups		P value
	FCR n (%)	FCU n (%)	
Excellent	4 (26.7)	1 (6.7)	
Good	9 (60.0)	12 (80.0)	0.308 ns
Fair	2 (13.3)	2 (13.3)	

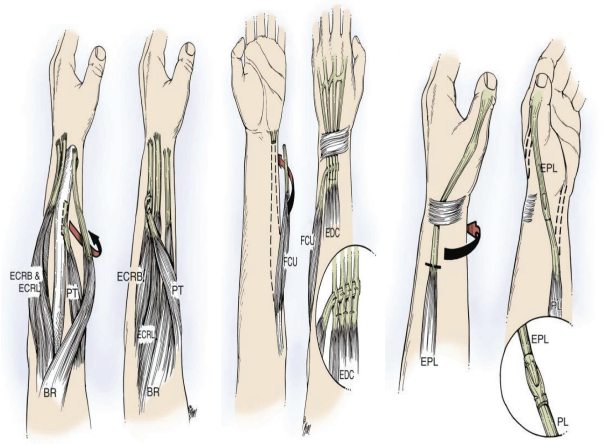
Table IX shows the among the 30 case, complications developed in 8 (26.66%) of cases, but 3(20%) of case in FCR group and 5(33.33%) of cases in FCU group. Those patient developed infection subsequently developed adhesion formation and extension or flexion lag. There was no statistical difference between two groups.

Table IX: Distribution of the study population by complications (n=30)

Complication	Groups		p value
	FCR n (%)	FCU n (%)	
Infection	2 (13.3)	2 (13.3)	0.881ns
Adhesion formation	2 (13.3)	3 (20.0)	
Ugly scar	2 (13.3)	2 (13.3)	
Muscle bulging	1 (6.7)	3 (20.0)	
Extension lag	1 (6.7)	1 (6.7)	
Flexion lag	1 (6.7)	1 (6.7)	

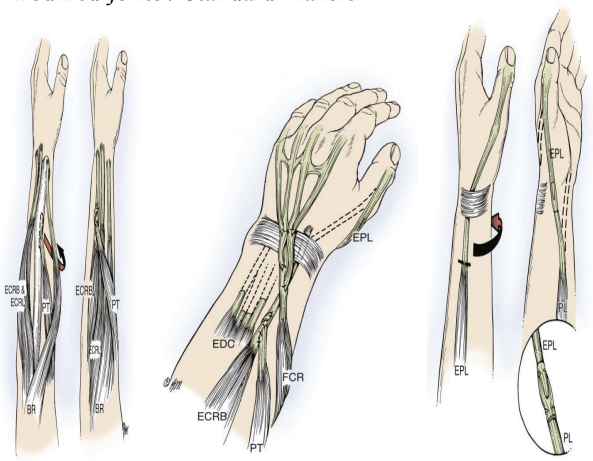
Complications were almost same in both groups.





FCU Set of Transfer

Modified Jones / Standard Transfer



FCR Set of Transfer

Brand Transfer

FCU set of Tendon Transfer for High Radial Nerve Palsy

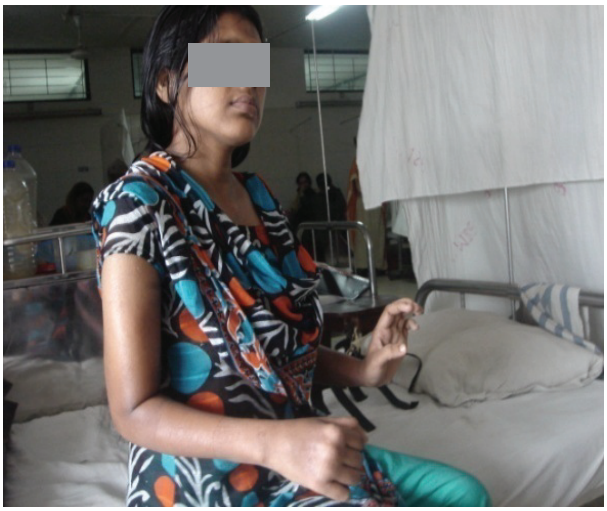


Fig: Pre-Operative Photograph of high Radial Nerve palsy

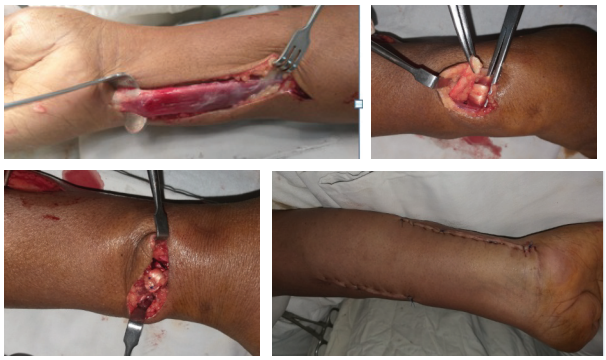


Fig: Per-Operative Photo of FCU to EDC transfer.

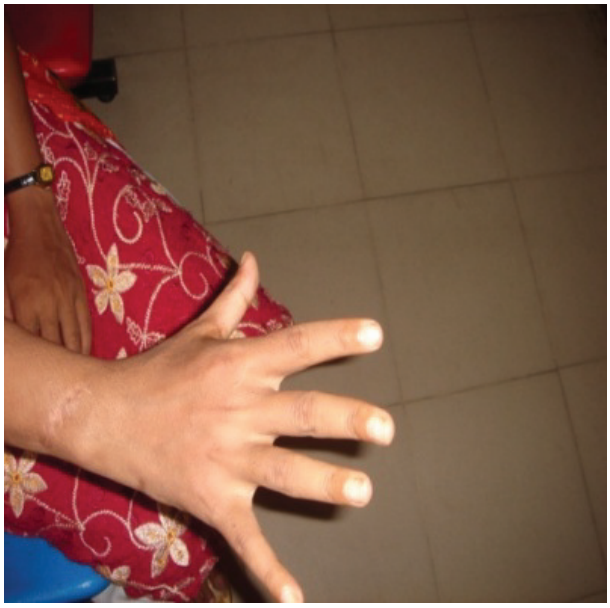


Fig: Post Operative MCP Extension

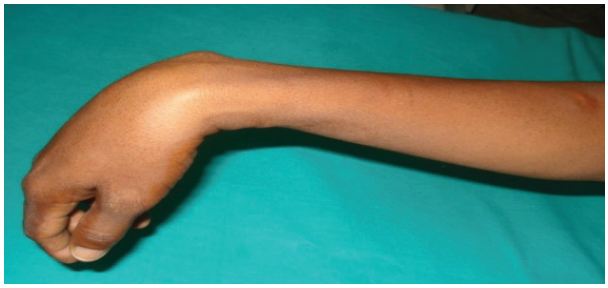


Fig: Pre-Operative Photograph of high Radial Nerve palsy

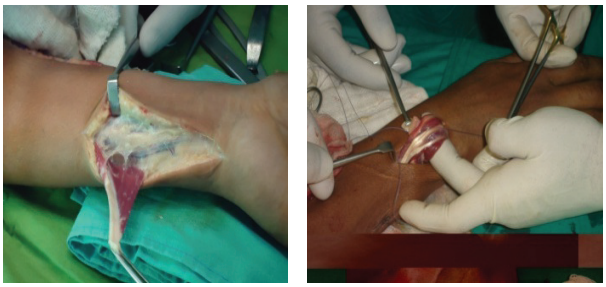


Fig: Per-Operative Photo of FCR to EDC transfer.

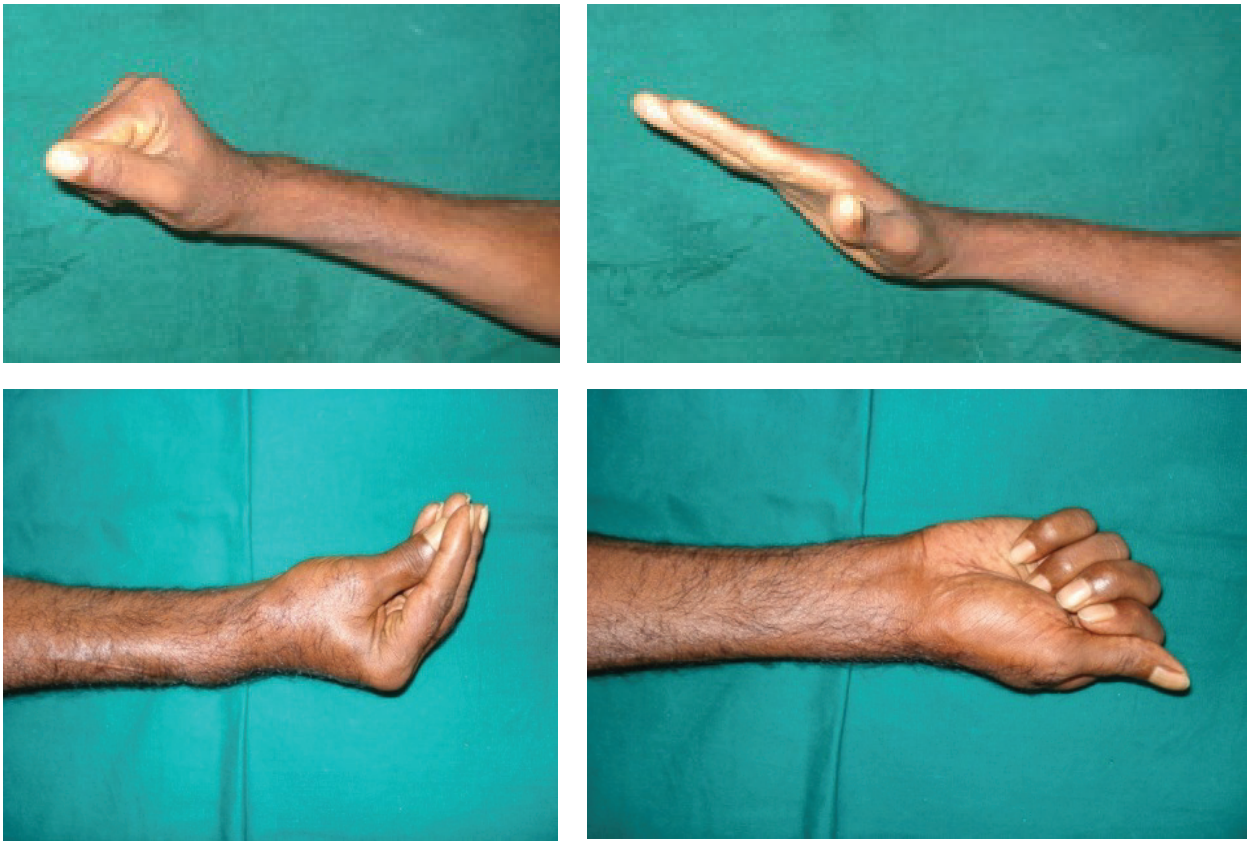


Fig: Post Operative Photograph of MCP Extension and finger with thumb flexion and extension.

DISCUSSION

Male was found predominant in this study. Out of all patients, 86.7% male were encountered both in FCR and FCU group. Zareezadeh et al.[11] also found that about 98.0% of the study population was male.

Mean age was found 31.07±9.14 years with the range of 18 to 46 years in FCR group and 33.60±10.79) years with the range of 11 to 53 years in FCU group.Zareezadeh et al. and Moussavi et al.[12] found no statistical significant difference in age between two groups.

After surgical intervention, soaked dressing was found more in first POD (26.7% vs. 20.0%) than second POD (20.0% vs 14.3%) in FCR and FCU group respectively. Moreover, hand swelling in first POD was 64.3 % and 53.3% whether it was declined in second POD 26.7% and 20.0% in two groups but it remained non-significant in two groups. In a study in Iran by Zareezadeh et al.[11], they also found non-significant association regarding hand swelling including forearm and wrist between FCR and FCU groups.

Fairly satisfaction was found 6.7% cases in FCR group and 26.7% cases in FCU group at 12th week after surgical intervention. Satisfied was found 66.7% in FCR group and60.0% in FCU group at 12th week after surgical intervention. Patients with very satisfied were accounted in FCR group was 26.7% and in FCU groups was 13.3% at 12th week after surgical intervention. No statistically significant difference was found between two groups incosmetically satisfaction of patients. But Zareezadeh et al.[11] found significant difference in consideration of cosmetic results of FCR and FCU groups.

At 12th week, only 6.7% patients had extension deficit<10^0 of metacarpo-phalangeal joint in FCR group but in FCU group, that was noted 20.0%. It was also found that at 12th week, no-significant difference in level of metacarpo-phalangeal joint extension was observed.On the opposite of our study result, Zareezadeh et al.[11] found significant difference between finger's active extension of FCR and FCU group ($p < 0.05$).

After surgery, complications such as infection, scarring, formation of abnormal deformation was also observed. There was no significant difference between groups regarding complications. This result is agreeable with the study by Zareezadeh et al.[11]

According to overall satisfaction of patients with the operation, Overall satisfaction in FCR group was 93.3% and in FCU group was 80.0%.93.3% of the patients in FCR group and 86.7% patients in FCU group were able to return their previous job. Gousheh and Arasteh[13] conducted a study on only FCU for tendon transfer, also reported that 86.0% of the patients were able to do their daily work after 45 days. Another study by Moussavi et al.[12] who worked on tendon transfer for radial nerve paralysis and compared three methods FCU, FCR & FDS found the ability to return to previous job without difficulty was 73.2% of the patients. As well, they also reported non-statistical significant difference in between three method counting the ability, time of return to job, satisfaction with the operation ($P>0.05$). This findings support our study findings totally.

Surgical intervention was found excellent more in FCR group than FCU group (26.7% vs. 6.7%, $p> 0.05$)according to Bincaz scale. However, 60.0% and 80.0% patients declared as good surgical intervention in FCR and FCU group respectively. Fair surgical intervention was found same in both groups which was 13.3%. There was no significant difference in surgical intervention between two groups. Qattan[14] observed the study results according to Bincaz scale and found that 80.0% patients showed excellent result in finger extension. Moussavi et al.[12], done a DASH (disabilities of the arm, shoulder and hand) score for comparing three method of tendon transfer in radial nerve paralysis namely FCR, FCU and FDS also found non-significant association among three groups. This result is completely agreeable with our study finding.

CONCLUSIONS

In case of high radial nerve palsy,both FCR and FCU tendon transfer methods are equally effective in the improvement of fingers' extension at MCP joint.

REFERENCES

1. Davies D. Plastic and reconstructive surgery. The hand--I. British medical journal (Clinical research ed.). 1985;290(6482):1650.
2. Solomon L, Warwick D.J &Nayagam S. Apley's system of orthopaedics and fractures, 9th ed. Hodder Arnold Co. Ltd. 2010; 224-301.
3. Ratner JA, Peljovich A, Kozin SH. Update on tendon transfers for peripheral nerve injuries. Journal of Hand Surgery. 2010;35(8):1371-81.
4. Altintas AA, Altintas MA, Gazyakan E, Gohla T, Germann G, Sauerbier M. Long-term results and the disabilities of the arm, shoulder, and hand score analysis after modified Brooks and D'Aubigne tendon transfer for radial nerve palsy. Journal of Hand Surgery. 2009;34(3):474-8.
5. Krishnan KG, Schackert G. An analysis of results after selective tendon transfers through the interosseous membrane to provide selective finger and thumb extension in chronic irreparable radial nerve lesions. Journal of Hand Surgery. 2008;33(2):223-31.
6. Lowe JB, Sen SK, Mackinnon SE. Current approach to radial nerve paralysis. Plastic and reconstructive surgery. 2002;110(4):1099-113.
7. Ropars M, Dreano T, Siret P, Belot N, Langlais F. Long-term results of tendon transfers in radial and posterior interosseous nerve paralysis. Journal of Hand Surgery. 2006;31(5):502-6.
8. Raskin KB, Wiglis ES. Flexor carpi ulnaris transfer for radial nerve palsy: functional testing of long-term results. Journal of Hand Surgery. 1995;20(5):737-42.

9. Brand PW, Hollister A. Operations to restore muscle balance to the hand. In: Brand PW, Hollister A, eds. Clinical mechanics of the hand, 2nd ed.St. Louis: Mosby–Year Book. 1993; 180–189

10. Tsuge K. Tendon transfer for radial nerve palsy. Aust Hz J Surg, 1980;50(3):267-272.

11. Zareezadeh A, Dehghai M, Zarezadeh A, Nasri E. Results of Flexor Carpi Radialis and Flexor Carpi Ulnaris Tendon Transfers in Chronic Radial Nerve Palsy. Journal of Isfahan Medical School. 2011; 28(121): 1-10.

12. Moussavi AA, Saied A, Karbalaeikhani A. Outcome of tendon transfer for radial nerve paralysis: Comparison of three methods. Indian journal of orthopaedics. 2011;45(6):558-562.

13. Gousheh J, Arasteh E. Transfer of a single flexor carpi ulnaris tendon for treatment of radial nerve palsy. Journal of Hand Surgery. 2006;31(5):542-6.

14. Al-Qattan MM. Tendon transfer for radial nerve palsy: a single tendon to restore finger extension as well as thumb extension/radial abduction. Journal of Hand Surgery (European Volume). 2012;37(9): 855-62.

Original Article

Status of Serum Magnesium Level in Bangladeshi Children and Adolescents with Type 1 Diabetes Mellitus and its Relationship with Glycemic Control

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Abstract

Type 1 diabetes mellitus is one of the most common endocrine and metabolic disorder in children and adolescents. Alteration of serum magnesium level may be associated with metabolic control and diabetic complications. The aim of the study was to evaluate serum magnesium level and find out its relationship with glycemic control in type 1 diabetic children and adolescents. For this study 80 type 1 diabetic children & adolescents with age range 1 to 18 years and 80 aged matched healthy controls were enrolled from the outpatient department of Changing Diabetes in Children, Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine & Metabolic disorders, General Hospital, Dhaka. Using a cross sectional design, we measured anthropometric parameters and serum magnesium level of all study subjects. We also estimate the fasting plasma glucose and HbA1c levels of the diabetic children and adolescents and controls. The mean ± SD of serum magnesium level was significantly lower in patient with type 1 DM compared to control (0.7 ± 0.1 vs 0.8 ± 0.1 mmol/L respectively; p= < 0.001). Lower level of magnesium was found in subjects with poor glycemic control compared to good glycemic control (0.6 ± 0.1 vs 0.8 ± 0.1 mmol/L respectively; p= < 0.001). This study showed that serum magnesium level was lowered in type 1 diabetic children and adolescents and it was strongly associated with poor glycemic control which potentially contributing to the early development of diabetic complications.

Keywords: *Type 1 diabetes mellitus, serum magnesium level, glycemic control*

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INTRODUCTION:

Diabetes Mellitus is a major non communicable disease and a leading cause of death & disability worldwide. Type 1 diabetes mellitus (T1DM) is a disorder that arises following the autoimmune destruction of insulin- producing pancreatic beta cells.[1,2] Type 1 diabetes mellitus is a chronic disease that usually develops during childhood and adolescence. Globally, the number of children (0-14 years) with type 1 diabetes is 542,000 & the number of newly diagnosed cases each year is 86,000.[3] The incidence of type 1 DM in Bangladesh as 4.2 new cases /100,000 children (0-14 years) per year.[4]

Diabetes mellitus has been suggested to be the most common metabolic disorder associated with magnesium deficiency, having a prevalence of 25% to 39%.[5] Magnesium (Mg) is an essential cofactor of more than 300 enzymes including those important in glycolysis, transcellular ion transport, neuromuscular transmission and synthesis of carbohydrates, proteins, lipid and nucleic acids. Numerous causes for low magnesium levels in diabetes are diets low in magnesium, osmotic diuresis that leads to high renal excretion of magnesium, insensitivity to insulin that affects intracellular magnesium transport and causes increased loss of extracellular magnesium, usage of loop and thiazide diuretics that promote magnesium wasting, diabetic autonomic neuropathies and reduced tubular reabsorption due to insulin resistance.[6] Hypomagnesaemia has been implicated in various long- term complications of DM, such as increased carotid wall thickness, coronary artery disease, dyslipidemia, diabetic retinopathy, neuropathy, nephropathy, ischemic stroke and foot ulcerations.[7,8] Some researchers found in their studies that hypomagnesaemia occurred in 28.2% & 37.3% type 1 diabetic patient respectively with poor glycemic control.[6,9] Oral or intravenous supplementation of magnesium in T1DM patients results in increased levels of magnesium and optimization of glycemic control.[10,11]

In the present study, we measured serum magnesium level in children and adolescents with T1DM and evaluated its relationship with glycemic control.

MATERIALS AND METHODS

This was a cross sectional study conducted in the department of Biochemistry and Molecular Biology of BIRDEM-2 General Hospital from July 2016 to June 2017. The research protocol was approved by Ethical Institutional Review Board (IRB) of BIRDEM Academy, Dhaka. Total 80 type 1 diabetic patients & 80 healthy controls aged 1-18 were selected from the outpatient department of Changing diabetes in Children (CDiC), BIRDEM-2 General Hospital. All diabetic subjects were being treated with insulin.

After selection of the subjects, the aims and objectives of the study along with procedure, risks and benefits of this study were explained to the guardian of the study subjects. When their parents were agreed for participation then an informed written consent was obtained from them and a structured questionnaire was filled up for each patient. Participants below 1 year and above 18 years, with any chronic illness and any medication that may influence serum magnesium level were excluded from the study. Detail personal, medical and family histories of the participants were recorded.

Data collection technique

Weight and height were measured (in kilogram and meter respectively) and body mass index (BMI) was calculated as weight divided by height squared. Systolic and diastolic blood pressure were also recorded. Then under all aseptic precaution 5 ml blood sample was collected from study subjects after an overnight fasting of 8-10 hours, 4 ml of which was delivered in a plain test tube for estimation of fasting plasma glucose, serum magnesium and remaining 1ml blood was delivered into EDTA tube for estimation of HbA_{1c}.

Serum magnesium was assessed by Beckman Coulter AU-480 auto-analyzer .Plasma glucose level was estimated by Enzymatic Glucose-Oxidase (GOD-PAP) method using Biosystem BTS 350 analyzer. Glycemic control was estimated for each patient through HbA_{1c} which is asessed by Clover A_{1c} analyzer using HPLC method.

To define "glycemic control", we used standard international criteria. Based on HbA_{1c} level, subjects were divided into two groups: (i) Those with good glycemic control (normoglycemic group), defined as HbA_{1c} levels < 9 %; and (ii) Those with poor glycemic control, defined as HbA_{1c} levels ≥ 9%. Normal magnesium level considered as 0.7-1.0 mmol/L. So, the value < 0.7 mmol/L was labeled as hypomagnesaemia.

All data were collected, tabulated and statistically analyzed using software SPSS version 20. Quantitative data was expressed as mean ± SD and unpaired Student's't' test was done to see the level of significance. Qualitative data were expressed as frequency & percentage and chi-square test was done to obtain the level of significance. The p-value of < 0.05 was considered statistically significant.

RESULTS

Table-I shows that 50% of the cases were male and 50% were female, 48.8% of controls were male and rests were female. There were no statistically significant differences in age, weight, height, BMI, systolic and diastolic blood pressure between case and controls. However, FPG and HbA_{1c} levels were found statistically significant between them.

Table I: General and biochemical parameters of the study population (n=160)

Variables	Case (n=80) Mean ± SD	Control (n=80) Mean ± SD	p- value
Gender			
• Male	40 (50%)	39 (48.8%)	
• Female	40 (50%)	41 (51.2%)	
Age of the respondent	14.9 ± 2.9	14.8 ± 2.9	> 0.05^{ns}
Age of onset during diagnosis (in year)	10.5 ± 3.6	-	-
Duration of diabetes (in year)	4.5 ± 2.7	-	-
Weight of the respondent (in Kg)	50.5 ± 16.7	48.7 ± 13.5	
Height of the respondent (in cm)	150.8 ± 13.7	151.7 ± 12.2	
BMI of the respondent (kg/sqm)	21.5 ± 4.7	20.9 ± 3.9	> 0.05^{ns}
SBP of the respondent (mm of Hg)	101.0 ± 11.6	102.1 ± 10.9	
DBP of the respondent (mm of Hg)	68.2 ± 8.1	67.1 ± 7.9	
FPG (mmol/L)	9.2 ± 4.2	5.6 ± 0.1	< 0.001
HbA_{1c} (%)	9.2 ± 2.2	5.6 ± 0.1	

Data was expressed as mean ± SD and comparison between groups was done by Student's unpaired 't'test. n= number of subjects, p-value < 0.05 is significant, ns= not significant

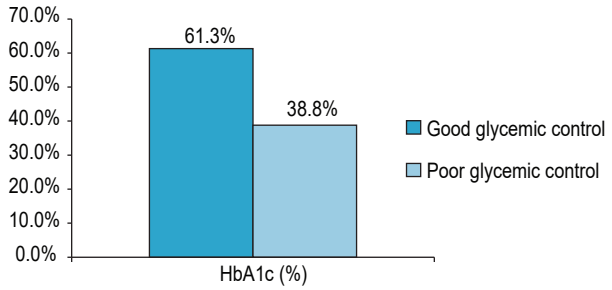

Fig.-1: *Glycemic status of the diabetic children and adolescents*

Figure-1 among the total diabetic children and adolescents 61.3% had good glycemic control and 38.8% had poor glycemic control.

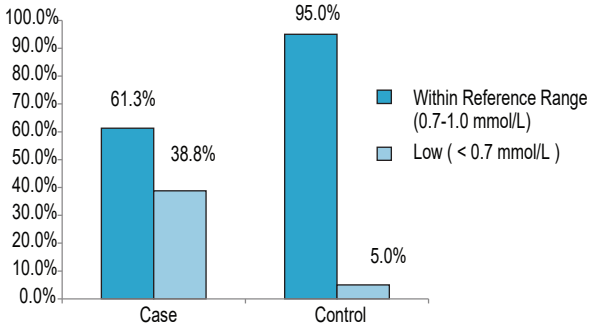

Fig.-2: *Serum magnesium status of the study population*

Almost 38.8% of the total participants in cases and 5.0% of controls had hypomagnesaemia as shown in Figure 2.

Table II shows significantly lower level of serum magnesium (0.7 ± 0.1) in cases with T1DM compared to controls. The serum magnesium level was significantly lower (0.6 ± 0.1) in patient with poor glycemic control compared to good glycemic control which was also shown in table-II.

Table-II: Comparison of serum magnesium level in study population (n=160) and relationship of serum magnesium level with glycemic status in cases (n=80)

Variable			**p- value**
Serum magnesium (mmol/L)	Case	0.7 ± 0.1	< 0.001
	Control	0.8 ± 0.1	
	In good glycemic control (HbA_{1c} < 9)	0.8 ± 0.1	
	In poor glycemic control (HbA_{1c} ≥ 9%)	0.6 ± 0.1	

Data was expressed as mean ± SD and comparison between groups was done by Student's unpaired't' test. n= number of subjects, p-value < 0.05 is significant, ns= not significant

Table III shows the serum magnesium level in cases; it was significantly lower in patients who have duration of diabetes mellitus more than 5 years compared to those who have duration of diabetes mellitus less than that.

Table –III: Relationship of duration of DM with serum magnesium level in cases (n=80)

Variables		**Relationship with duration of DM**		**p-value**
		< 5 years	≥ 5 years	
Serum magnesium	Low (< 0.7 mmol/L)	12 (38.7%)	19(61.3%)	< 0.001
	Within reference range	39(79.6%)	10(20.4%)	
	(0.7-1.0 mmol/L)			

Statistical analysis was done by Chi-square test to compare among the groups. n= number of the subjects, p-value < 0.05 is significant, ns= not significant

DISCUSSION

In the present study we measured serum magnesium level, as well as other clinical and biochemical parameters, in children and adolescents with T1DM. Inadequate metabolic control can affect the concentrations of magnesium, developing hypomagnesaemia, which may be directly related with some micro and macrovascular complications observed in diabetes, as cardiovascular disease, retinopathy and neuropathy.[12]

In this study, we estimated serum magnesium level in children and adolescents with T1DM. Taking cut off level of serum magnesium < 0.7 mmol/L, we detected 38.8% of diabetic patient had hypomagnesaemia which is significantly lower compared to control. A recent study in Egypt showed that there were 37.3% of the diabetic subjects had hypomagnesaemia.[9] Seyoum et al.[13] found a higher percentage of hypomagnesaemia (65%) in their study. Contrary to our result, Zargar et al.[14], did not found any significant alteration in plasma magnesium level in type 1 diabetes mellitus.

We also found that serum magnesium was significantly lower (< 0.001) in patient with poor glycemic control compared to good glycemic control. In poor glycemic control uncontrolled hyperglycemia and glycosuria may increase magnesium excretion through osmostic diuresis. This result is similar with the study of many researchers.[6,9,15,16] Inconsistent with our result, some researchers did not observe any relationship between serum magnesium and glycemic status[17-19]. This difference could be attributed to the difference in study populations, degree of diabetic control among them and to the different methods of evaluating serum magnesium and HbA_{1c}.

In our study we found serum magnesium was low with patient having duration of DM ≥ 5 years. This result is consistent with Shahbah et al.[6] who found that duration of diabetes were more in participants with hypomagnesaemia.

CONCLUSIONS

Present study demonstrated a significantly lower serum magnesium level in T1DM cases and a low serum magnesium level was associated with poor glycemic control. So, it is advocated that proper glycemic control, close monitoring, supplementation of magnesium might be beneficial for preventing complications in type 1 diabetic children and adolescents.

Conflict of interest: The authors declare no conflict of interest.

REFERENCES

1. Atkinson MA, Eisenbarth GS. Type 1 diabetes: new perspectives on disease pathogenesis and treatment. Lancet. 2001; 358:221–9.
2. Bluestone JA, Herold K, Eisenbarth G. Genetics, pathogenesis and clinical interventions in type 1 diabetes. Nature. 2010; 464:1293–300.
3. The global picture.IDF Diabetes Atlas. 2015; 7th ed.47-63.
4. The global burden and regional overviews. IDF Diabetes Atlas. 2013; 6th ed. 29-68.
5. Rude RK. Magnesium deficiency and diabetes mellitus. Causes and effects. Postgrad Med. 1992; 92:217–24.
6. Shahbah D, El Naga AA, Hassan T, Zakaria M, Beshir M, Al Morshedy S, et al. Status of serum magnesium in Egyptian children with type 1 diabetes and its correlation to glycemic control and lipid profile. Medicine. 2016; 95(47):1-7
7. Pham PC, Pham PM, Pham SV, Miller JM, Pham PT. Hypomagnesemia in patients with type 2 diabetes. CJASN. 2007; 2(2):366-73.
8. Sakaguchi Y, Shoji T, Hayashi T, Suzuki A, Shimizu M, Mitsumoto K, et al. Hypomagnesemia in type 2 diabetic nephropathy: a novel predictor of end-stage renal disease. Diabetes care. 2012; 35 (7), 1591-7.
9. Asmaa MN, Samira SZ, Aliaa MM, Bassem HG. The Relationship between Hypomagnesaemia and Glycemic Control in Children with Type 1 Diabetes Mellitus. J Diabetes Metab. 2016; 7(8): 1-5.
10. Yeh GY, Eisenberg DM, Kaptchuk TJ, Phillips RS. Systematic review of herbs and dietary supplements for glycemic control in diabetes. Diabetes care. 2003; 26(4):1277-94.
11. Shahbah D, Hassan T, Morsy S, El Saadany H, Fathy M, Al-Ghobashy A, et al. Oral magnesium supplementation improves glycemic control and lipid profile in children with type 1 diabetes and hypomagnesaemia. Medicine. 2017; 96(11): 1-6.
12. Sales CH, Pedrosa LD. Magnesium and diabetes mellitus: their relation. Clinical Nutrition. 2006; 25(4):554-62.

13. Seyoum B, Siraj ES, Saenz C, Abdulkadir J. Hypomagnesemia in Ethiopians with diabetes mellitus. Ethnicity and disease. 2008; 18(2):147-51.

14. Zargar AH, Bashir MI, Masoodi SR, Laway BA, Wani AI, Khan AR, et al. Copper, zinc and magnesium levels in type-1 diabetes mellitus. Saudi Med J. 2002; 23(5):539-42.

15. Galli-Tsinopoulou A, Maggana I, Kyrgios I, Mouzaki K, Grammatikopoulou MG, Stylianou C, et al. Association between magnesium concentration and HbA1c in children and adolescents with type 1 diabetes mellitus . J. Diabetes. 2014; 6(4):369-77.

16. Shaikh M, Devrajani B, Soomro A, Ali Shah S, Devrajani T, Das T. Hypomagnesemia in Patients with Diabetes mellitus. World Appl. Sci. J. 2011; 12(10) :1803-6.

17. Lin CC, Tsweng GJ, Lee CF, Chen BH, Huang YL. Magnesium, zinc, and chromium levels in children, adolescents, and young adults with type 1 diabetes. Clin. Nutr. 2016; 35(4):880-4.

18. Salmonowicz B, Krzystek-Korpacka M, Noczynska A. Trace elements, magnesium, and the efficacy of antioxidant systems in children with type 1 diabetes mellitus and in their siblings. Adv Clin Exp Med. 2014; 23(2):259-68.

19. Matthiesen G, Olofsson K, Rudnicki M. Ionized magnesium in Danish children with type 1 diabetes. Diabetes care. 2004; 27(5):1216-7.

Original Article

Risk Factors and Clinical Profile of Respiratory Distress in Newborn: A Hospital Based Study in Bangladesh Army

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Abstract

Neonatal respiratory distress (NRD) is a main cause of neonatal morbidity and mortality in developing countries. Early detection of its risk factors and early treatment of its causes are major challenges. There are many causes of respiratory distress, among them, transient tachypnea of newborn (TTN), respiratory distress syndrome (RDS) and perinatal asphyxia are commonest causes. Timely and appropriate therapy is essential to prevent ongoing injury and improve outcome. The aim of this study was to determine the risk factors and to identify the causes of respiratory distress in neonatal intensive care unit (NICU) in Combined Military hospital (CMH) Sylhet and to observe the hospital outcome of these babies. Descriptive type of cross- sectional study was conducted in CMH Sylhet over a period of one year from April 2018 to March 2019. During the study period a total of 287 live newborns were found and included as study subjects to observe for development of respiratory distress. The overall prevalence of respiratory distress was 19.2%. There was male predominance (63.6%) and more than two third (71.1%) were born by cesarean section. Prematurity (38.2%), low birth weight (52.7%), male gender (63.6%), APGAR at 1 min <7 (10.9%), caesarean delivery (76.4%), less antenatal care visit (52.7%), more than 4 pervaginal examinations 49.1%, acute fetal distress 43.6% and gestational diabetes mellitus 34.5% were the most common risk factors for development of NRD. The main causes were transient tachypnea of newborn 47.3%, respiratory distress syndrome 29.1% and perinatal asphyxia 10.9%. All babies required high flow oxygen initially, subsequently Bubble Continuous Positive Airway Pressure (CPAP) and mechanical ventilation was required in 14.5% and 1(1.8%) cases respectively. Mortality was 1.8% in neonates with respiratory distress syndrome with pneumothorax with septicaemia requiring mechanical ventilation. NRD is a frequent emergency and causes high morbidity and mortality. Risk factors like prematurity, low birth weight, male gender, APGAR at 1 min <7, caesarean delivery, less antenatal care visit, more than 4 pervaginal examinations, acute fetal distress and gestational diabetes mellitus were associated with respiratory distress in newborns. Majority of cases are due to TTN followed by respiratory distress syndrome and perinatal asphyxia. Mortality was in RDS mainly related to pneumothorax with septicaemia. Better obstetrical care and timely intervention may improve the outcome of newborn respiratory distress.

Keywords: *Meconium aspiration syndrome (MAS), respiratory distress (RD), respiratory distress syndrome (RDS), transient tachypnea of the newborn (TTN)*

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INTRODUCTION

Respiratory disorders are the most frequent cause of admission for neonatal intensive care in both term and preterm infants.[1] Fifteen percent of term infants and 29% of late preterm infants admitted to the neonatal intensive care unit develop significant respiratory morbidity; this is even higher for infants born before 34 weeks gestation.[2] It occurs in 0.96 to 12% of live births and is responsible for about 20% of neonatal mortality.[3] The severity of respiratory distress can be assessed by Downe's scoring system which includes parameters such as respiratory rate, cyanosis, retractions, grunting and air entry in both the lungs.[4]

The risk factors include prematurity, male gender, asphyxia, caesarean delivery, maternal diabetes mellitus, and hypertensive disorders of pregnancy, antepartum

hemorrhage, multiple pregnancies, and rapid labor.[5,6] The causes of respiratory distress in neonates include transient tachypnea of newborn (TTN), respiratory distress syndrome (RDS), meconium aspiration syndrome (MAS), congenital pneumonia, congenital heart disease (CHD), perinatal asphyxia (PNA), and congenital anomalies as tracheo-oesophageal fistula, and congenital diaphragmatic hernia.[7]

Early detection of its risk factors and anticipation of the management of its etiologies are imperative.[8] There has been a tremendous advance in the management of respiratory distress such as ventilator therapy with different modes such as Continuous Positive Airway Pressure (CPAP), conventional mechanical ventilation; ultra high frequency jet ventilation, liquid ventilation, surfactant replacement therapy, sophisticated monitoring and extracorporeal membrane oxygenation all have improved the outcome among the babies with respiratory distress.[9]

In spite of the varying recent advance in clinching diagnosis and management there have been very less clinical studies on the neonatal respiratory distress in our country. So, the aim of the study was to find out the risk factors and causes of respiratory distress among the admitted newborns in neonatal intensive care unit (NICU) in CMH Sylhet and to observe the hospital outcome of these babies.

MATERIAL AND METHODS

This descriptive type of cross-sectional study was carried out at NICU, CMH Sylhet during April 2018 to March 2019. Any newborn showing one or more of the following signs (for >2 hours) was considered to have respiratory distress which includes parameters such as tachypnea or respiratory rate of more than 60/minute, retraction or increased chest in-drawing on respirations (subcostal, intercostal, sternal, and suprasternal) and noisy respiration in the form of grunt, stridor or wheeze were included in this study and babies with multiple congenital malformations were excluded. The ethical approval of the study was obtained from ethical review committee of the area headquarter, Sylhet cantonment, Sylhet. Diagnosis was done within 24 hours of admission according to their clinical presentation and relevant investigations. Inform consent was taken from each patient before enrollment. Data were collected by checkup sheet and appropriate questionnaire who were admitted in NICU.

After the initial assessment and cardio respiratory management, a history was obtained. Maternal and obstetrical histories were taken which provided invaluable information. Intra-partum details with special reference to the fetal well-being, maternal age, antenatal care visits, pervaginal examinations, duration of rupture of membranes, quantity and quality of liquor, gestational diabetes mellitus ,drugs especially analgesics and sedatives given to the mother were recorded. Apgar score, resuscitation details, sex, and gestational age was assessed by modified Ballard score and clinical examination, birth weight and findings suggestive of respiratory distress were also noted. Data regarding use of mechanical ventilation, Bubble CPAP or required only oxygen were recorded. Statistical analysis was performed using the commercial statistical software Epi info version 3.5.

RESULTS

The total number of live births during the study period was 287. Total number of caesarean section deliveries were 204 (71.1%) and spontaneous vaginal deliveries were 83 (28.9%). Out of all these cases 55 (19.2%) newborns developed respiratory distress. Among respiratory distress male was 35 (63.6%) and female was 20 (36.4%). Full term newborns were 31 (56.4%), premature newborns were 21 (38.2%), and post term was 3 (5.4%). The overall prevalence of respiratory distress was 19.2%. Mean gestational age was 35.6 ± 3.1wks (range - 31 to 41 weeks). Mean weight was 2447 ± 826gm (range - 1400 to 4100 gm). Fifty two (52%) babies had normal birth weight, 28 (50.9%) were low birth weight, 1(1.8%) were very low birth weight and 1(1.8%) were macrosomic (weight >4000gm) babies. The risk factors associated with neonatal respiratory distress are shown in (Table 1).

Table 1 shows neonatal risk factors include prematurity (38.2%), male gender (63.6%), Low birth weight <2500 gm) (52.7%), meconium stained liquor (21.8%), APGAR at 1 min < 7 (10.9%) and maternal risk factors include caesarean delivery (76.4%), attending less than three antenatal visits (52.7%), more than four pervaginal examinations (49.1%), fetal distress (43.6%), gestational diabetes mellitus (34.5%) and advanced maternal age >35 years (25.5%) were the most common risk factors for development of NRD.

Table I: Risk factors associated with neonatal respiratory distress (n=55)

Risk factors	Number of factors	Percentage (%)
Neonatal factors		
Prematurity	21	38.2%
Male baby	35	63.6%
Low birth weight <2500 gm)	29	52.7%
Meconium stained liquor	12	21.8%
APGAR at 1 min < 7	06	10.9%
Knotting of the cord	06	10.9%
Post maturity	03	5.4%
Obstetrical factors		
Cesarean section	42	76.4%
Number of antenatal care visits <3	29	52.7%
>4 pervaginal examinations	27	49.1%
Fetal distress	24	43.6%
Gestational diabetes mellitus	19	34.5%
Advanced maternal age >35 years	14	25.5%
Oligohydramnios	12	21.8%
Pregnancy induced hypertension	11	20.0%
Prolonged rupture of membrane >12 hours	10	18.2%
Maternal fever at the time of delivery > 38°c	09	16.4%
Bad obstetrical history (abortion, still birth)	08	14.5%
Prolonged labor	07	12.7%
Twin pregnancy	04	7.3%

Table 2 shows TTN was found to be the commonest cause of respiratory distress (47.3%) and it was found to be the commonest cause of respiratory distress among both term and preterm babies. RDS was the second commonest cause of respiratory distress (29.1%) and it was found in preterm babies. PNA was the third commonest cause of respiratory distress (10.9%) and it was found in term and post term newborns. Congenital pneumonia, CHD, septicaemia, and MAS were found in 3.6%, 3.6%, 3.6%, and 1.8% of cases respectively.

Table-II : Causes of respiratory distress of studied newborn (n=55)

Disease	Number	Percentage
Transient tachypnea of newborn (TTN)	26	47.3%
Respiratory distress syndrome (RDS)	16	29.1%
Perinatal asphyxia (PNA)	6	10.9%
Congenital pneumonia	2	3.6%
Congenital heart disease (CHD)	2	3.6%
Septicaemia	2	3.6%
Meconium aspiration syndrome (MAS)	1	1.8%

Table III shows causes of respiratory distress with obstetrics and gestational history are shown in

Table III : Causes of respiratory distress with obstetrics and gestational history

Criteria	TTN	RDS	PNA	Congenital pneumonia	CHD	Septicaemia	MAS
M:F	1.4:1	1.3:1	2:1	1:1	1:1	1:1	1:1
Term (%)	88.5%	6.3%	66.7%	50%	50%	0%	100%
Preterm (%)	11.5%	93.7%	33.3%	50%	50%	100%	0%
Mean GA (weeks) ± SD	37.1 (±1.1)	32.5 (±0.8)	37.3 (±1.2)	37.1 (±1.0)	36.2 (±1.1)	34.5 (±1.1)	41 (±1.2)
Mean weight (grams) ± SD	2900 (±880)	1500 (±770)	2700 (±565)	2740 (±630)	2500 (±820)	1850 (±785)	3100 (±740)
C/S	69.2%	87.5%	83.3%	100%	100%	50%	100%
NVD	30.8%	12.5%	16.7%	0%	0%	50%	0%

Table IV shows all babies required high flow oxygen initially by head box 55 (100%), subsequently Bubble CPAP and mechanical ventilation was required in 8 (14.5%) and 1(1.8%) cases respectively.

Table IV: Treatment of patients of respiratory distress

High flow oxygen through head box	55 (100%)
Bubble CPAP	8 (14.5%)
Mechanical ventilation	1(1.8%)

Mortality was 1.8% in neonates with respiratory distress syndrome with pneumothorax with septicemia requiring mechanical ventilation.

DISCUSSION

Respiratory distress, the most common cause for which baby needed intensive care support and death rate was 2-4 times more in this group of patients than those required admission without respiratory distress.[10] The overall prevalence of respiratory distress in this study was 19.2%. Results from our study are comparable with results from developed countries with reported prevalence rates of 4.24% in Pakistan.[11] 18.5% in France[12], 23% in Ivory Coast[13] and 14.5% Burkina Faso.[14]

In the present study, neonatal risk factors include prematurity (38.2%), male gender (63.6%), Low birth weight <2500 gm) (52.7%), meconium stained liquor (21.8%), APGAR at 1 min < 7 (10.9%) and maternal risk factors include caesarean delivery (76.4%), attending less than three antenatal visits (52.7%), more than four pervaginal examinations (49.1%), fetal distress (43.6%), gestational diabetes mellitus (34.5%) and advanced maternal age >35 years (25.5%) were the most common risk factors for development of NRD (Table 1).

Low gestational age at the time of delivery was a risk factor for respiratory distress also observed by Dani C et al, and Lureti M et al.[15, 16] Lureti M et al, and Miller HC shows the frequency of neonatal respiratory distress was higher in males than compared with females.[16, 17] The studies conducted by Dani C et al, Lureti M et al, Miller HC et al and Lee K et al, also mentioned that low birth weight is a risk factor for respiratory distress among newborn baby[15-18].The studies conducted by Rygal M,[19] where meconium stained liquor had more chances of developing respiratory distress. Lureti M et al, Fidanovski D et al and Gouyon J et al observed that low APGAR score were associated with increased RD and prolonged NICU stay.[16, 20, 21]

The studies conducted by Dani C, Gouyon J, Geller EJ where it was noticed that caesarian delivered babies have more chances of neonatal respiratory distress when compared to normal vaginal delivery.[15, 21, 22] Dani C et al has shown that the number of PV examination above 4 was significantly associated with respiratory distress.[15] Advanced maternal age responsible for newborn respiratory distress also reported by Dani C et al and Smith A et al respectively. [15, 23]

In the present study, the most common causes of respiratory distress found were TTN (47.3%), RDS (29.1%), PNA (10.9%), septicemia (3.6%), congenital pneumonia (3.6%) and congenital heart disease (3.6%) (Table II). Santosh S[24] et al also reported near similar finding.

TTN was the commonest (47.3%) cause of respiratory distress in this study. In many study, TTN was found to be the commonest cause which was consistent with this study.[25, 26] Among the neonates with TTN 88.5% were term and their mean Gestational age was 37.1 weeks, and their mean weight was 2900 gm. Two third (69.2%) were delivered by C/S. Different studies showed cesarean section, term babies and male predominance to be associated with TTN.[27,28] In this study similar result was found but more than half of the TTN cases were term baby but their birth weight was normal. Assisted ventilation in the form of bubble CPAP (bCPAP) was required in 14.5% cases without any mortality. Zaazou MH et al. found 37.9% neonates had respiratory distress due to TTN among them 11.5% cases required nasal CPAP with no mortality.[27] Many other studies also reported cases with TTN requiring assisted ventilation without any mortality.[26, 29]

RDS is an important cause of respiratory distress in our set up and also was the second common cause in our study. It constituted 29.1% of cases. Majority (93.7%) were preterm with mean gestational age 32.5 weeks and mean weight of 1500 gram. One study showed that RDS was the second commonest cause of respiratory distress which constituted 31%, like our finding[27]. In many other studies showed low percentage (2-7%) of RDS.[26, 30, 31] Assisted ventilation was required for the management of RDS, in the form of bCPAP and mechanical ventilation in 14.5% and 1.8% cases respectively. Mortality was 1.8% among the ventilated baby who required mechanical ventilation associated with pneumothorax with septicemia while no death observed who required bCPAP. One study showed

that 83.2% cases of RDS required ventilator support and mortality rate was 76.0% who put on IMV mode.[26]

Perinatal asphyxia still remains one of the major cause of neonatal respiratory distress.[32, 33] Perinatal asphyxia was the third common (10.6%) cause of respiratory distress in this study. Their mean gestational age 37.3 weeks and mean weight 2600 grams. Nessa L et al found 52% newborn had respiratory distress who had perinatal asphyxia[30] which is much higher than our study but on the contrary, many other study showed low incidence of perinatal asphyxia.[26, 27]

In this study, among all cases with respiratory distress, mechanical ventilation was required in 1.8% cases and bCPAP required in 14.5% cases. There was no death who required bCPAP but mortality rate was 1.8% among the babies who required mechanical ventilation. One study reported that mortality was high (80%) in perinatal asphyxia who required mechanical ventilation.[27] Lawn et al. reported that mortality rate in cases of perinatal asphyxia is as high as 25-50%.[34]

Neonatal sepsis is an important and common cause of neonatal morbidity and mortality.[35-37] We found septicemia as the fourth (3.6%) cause of respiratory distress in this study. Majority (100%) of them were preterm, mean gestational age was 34.5weeks and mean weight was 1850 grams. Mechanical ventilation and bCPAP were required in 1.8% and 14.5% cases respectively among these babies. Among these babies, 1 (1.8%) died who required mechanical ventilation but no death was observed who required bCPAP. One study reported that case fatality rate is 33.3% in the cases with neonatal sepsis.[30]

Congenital pneumonia was found in 3.6% cases. 50% were preterm mean gestational age was 37.1 weeks. Dutta A et al found pneumonia as the second common cause of respiratory distress in his study,[26] where in most cases it was part of septicemia and 34.28% was primary pneumonia. In another study, pneumonia was found to be a cause of respiratory distress in 8% cases,[30] which is near to our finding. Mechanical ventilation and bCPAP were required in 1.8% and 14.5% cases respectively among these babies. No death was observed in cases required bCPAP or mechanical ventilation.

CONCLUSIONS

Neonatal respiratory distress is a major cause of neonatal admissions and has a high mortality rate. Risk factors like prematurity, low birth weight, male sex, meconium stained liquor, APGAR at 1 min < 7, attending less than three antenatal visits, more than 4 per vaginal examinations, fetal distress and cesarean delivered newborns were associated with severe respiratory distress in newborns. Most common causes of respiratory distress are TTN, RDS, perinatal asphyxia and septicemia. Better obstetrical care and awareness of the risk factors of birth asphyxia among mothers and fetus, along with adequate follow-up of pregnancy and labor for early detection of risk factors and timely intervention may improve the outcome of neonatal respiratory distress.

REFERENCES

1. Carlo WA, Ambalavanan N. Respiratory Distress Syndrom. In: Kliegman RM, Stanton BMD, St. Geme J, Schor NF, editors. Nelson Textbook of Pediatrics. 20th edition. Elsevier: 2016; 20(1): 579-80.
2. Hibbard JU, Wilkins I, Sun L, Gregory K, Haberman S. Respiratory morbidity in late preterm births. JAMA. 2010; 304(4): 419-25.
3. Kommawar A, Borkar R,Vagha J, Lakhkar B, Meshram R, Taksandae A. Study of respiratory distress in newborn. Int J Contemp Pediatr. 2017; 4(2): 490-94.
4. Singh M. Care of the newborn. Revised 8th ed. CBS Publishers and Distributors Pvt Ltd; September 2016: 350-54.
5. Lorotte-Namoumi C, Clamadieu, Jarreau PH. Détresses respiratoires du nouveau-né en dehors des malformations et des maladies génétiques ou constitutionnelles. Encycl Med Chir (Elsevier Paris) Pédiatrie. 2004; 4:10-1.
6. Chalacon M, Debillon T, Plantaz D, Ego A. Facteurs de risque détresse respiratoire chez les prématurés modérés (32 a 34 semaines d'aménorrhées). Thèse. Université Joseph Fourrier. 2012. Google Scholar
7. Am Fam. Physician American Academy of Family Physicians. 2007; 76: 987-94.
8. Fedakar A, Aydogdu C. Clinical features of neonates treated in the intensive care unit for respiratory distress. Turk J Pediatr. 2011; 53(2):173-79.
9. Rao GC, Rao MSP. Etiological profile of respiratory distress in first day of life of a newborn baby. Int J Contemp pediatr. 2017; 4(1): 210-14.

10. Misra PK. Respiratory distress in newborn. Indian Pediatrics. 1987; 24: 77-80.

11. Saeed Z, Lutufullah G, Hassan R. Prevalence and Etiology of Respiratory Distress in newborns. PAFMJ. 2013; 63(1): 22-25.

12. Chalacon M, Debillon T, Plantaz D, Ego A. Facteurs de risque détresse respiratoire chez les prématurés modérés (32 a 34 semaines d'aménorrhées). Thèse. Université Joseph Fourrier. 2012.

13. Lasme E, Amon TD, Akaffou E, Ehua-Amangoua E, Koffi O, Kangah D. Les facteurs de risque des détresses respiratoires néonatales en milieu hospitalier a Abidjan. Ann Pediatr (Paris). 1997; 44(9): 635-39.

14. Kam KI, Ye D, Sawadogo A, Sanou I, Traore A, Koueta F et al. Les Détresses Respiratoires du nouveau-né dans L'unité de Néonatologie du centre hospitalier National de Ouagadougou, Burkina Faso. Burkina Médical. 1998; 2: 447.

15. Dani C, Reali MF, Bertini G. Risk factors for the development of respiratory distress syndrome and transient tachypnoea in newborn infants. European Respiratory J. 1999; 14:155-59.

16. Lureti M. Risk factors for respiratory distress syndrome in newborn infants: A multi centre Italian survey. Acta Obstetr Gynecol Scandinavica. 1993; 72: 359-64.

17. Miller HC. Respiratory Distress Syndrome of Newborn Infants: Statistical Evaluation of Factors Possibly Affecting Survival of Premature Infants. Pediatr.1998; 31 (4): 573-79.

18. Kwang-sun Lee, Arthur I Eidelman, Po-I Tseng, Stephen R. Kandail, Lawrence M: Respiratory Distress Syndrome of the Newborn and Complications of Pregnancy. Pediatrics. 1976; 58: 675-80.

19. Rygal M. Neonatal respiratory distress syndrome: anautopsy study of 190 cases. Indian J Pediatr. 1985; 52: 43-46.

20. Fidanovski D, Milev V, Sajkovski A. Mortality risk factors in premature infants with respiratory distress syndrome treated with mechanical ventilation. Srp Arh Celok Lek. 2005; 133: 29-35.

21. Gouyon J, Ribakovsky C, Ferdyns C. Severe respiratory distress in term neonates. Pediatr Perinatal Epidemiol. 2001; 22: 22-30.

22. Geller EJ, Wu JM, Jannelli ML, Nguyen TV. Neonatal outcomes associated with planned vaginal versus planned primary cesarean delivery. Journal of Perinatology. 2010; 30: 258-64.

23. Smith A, Malhotra A. Respiratory distress in newborn treated with ventilation. Indian J Pediatr. 1995; 3: 207-11.

24. Santosh S, Kumar K, Adarsha E. A clinical study of respiratory distress in newborn and its outcome. Indian J Neonatal Med Res. 2013; 1: 2-4.

25. Kumar A, Bhat V.B. Epidemiology of respiratory distress of newborns. Indian Journal Pediatrics. 1996; 63(1): 93-98.

26. Dutta A, Sinhamahapatra KT. Spectrum of respiratory distress in newborn: A study from a tertiary care hospital in Kolkata. The Child and newborn. 2011; 15(2): 45- 48.

27. Zaazou MH, Kamal MM, Ali R M, Hussieny NE, Sayed ME. Descriptive study of cases of respiratory distress in NICU in Ahmed Maher Teaching hospital. Medical Journal Cairo University. 2011; 79(1): 441-48.

28. Rawlings JS and Smith FR. Transient tachypnea of the newborn: An analysis of neonatal and obstetric risk factors. American Journal of Diseases of Children. 1984; 138 (9): 869-71.

29. Helve O, Andresson S, Kirjavainen T, Pitkanen OM. Improvement of lung compliance during post natal adaptation correlates with airway sodium transport. American Journal of Respiratory and Critical Care Medicine. 2006; 173: 448-52.

30. Nessa L, Khatun S, Banu NA, Rouf A, Khan MSR, Haque N et al. Etiology and outcome of respiratory distress in newborn. Chest & Heart Journal. 2011; 35 (1): 1-4.

31. Banu K, Rahman MS. Disease in the neonatal period: A study in the special care baby unit of Dhaka Shishu Hospital. Bang J Child Health. 1982; 6(3): 133- 39.

32. Mishra PK, Srivastava N, Malik GK, Kapoor RK, Srivastava KL, Tastogi S. Outcome in relation to APGAR score in term neonates. Indian J Pediatrics. 1994; 3:1215-18.

33. Suresh GM, Sarker S. Delivery room management of infants born through thin Meconium stained liquor. Indian J Pediatrics. 1994; 31: 1177- 81.

34. Lawn J, Shibuya K and Stein C. No cry at birth: Global estimates of intrapartum stillbirths and antrapartum related neonatal deaths. Bull. World Health Organ June. 2005; 83 (6): 409-17.

35. Jamal M, Khan N. Neonatal Morbidity and Mortality in high risk pregnancies. JCPSP. 2002; 12(11): 657- 61.

36. Aurangzeb B, Hameed A. Neonatal sepsis in hospital borne-babies; bacterial isolates and antibiotic susceptibility patterns. JCPSP. 2003; 13(11): 629- 32.

37. Report of the National Neonatal Perinatal Database (National Neonatology Forum), India 2002-03.

Original Article

Role of Urinary Calcium and Creatinine Ratio in Assessing Bone Resorption in Lepromatous Leprosy.

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Abstract

Bony changes in lepromatous leprosy are one of the causes of deformity and disability. Fasting calcium and creatinine ratio in urine is used as a bone resorption marker in a number of diseases such as hyperthyroidism, osteoporosis, multiple myeloma, paget's disease and sarcodosis. In lepromatous leprosy assessment of bone resorption might be done with that marker. To assess the role of fasting urinary calcium and creatinine ratio as a marker of bone resorption in patients with lepromatous leprosy. A case control study was conducted on 28 patients diagnosed as lepromatous leprosy and 28 age-matched healthy control. The participants who fulfilled all inclusion and exclusion criteria were studied by measuring fasting urinary calcium and creatinine level as well as observing X-rays of both hands and feet of affected individuals. The mean age of cases 38.1±14.2 years and 38.9±12.9 years was in control group. Male - female ratio was 3.6: 1. It was observed that 10.7% leprosy patients showed urinary Ca/Cr ratio >0.20 (0.13±0.12) and 10.7% healthy control showed urinary Ca/Cr ratio ratio>0.20 (mean ±SD 0.11±0.7). the difference was not statistically significant (p>0.05). X-ray finding was positive in 14.3% leprosy patients and none of the control group. That difference was not significant statistically (p>0.05). there was no relation between raised urinary Ca/Cr ratio and positive findings of bone resorption on x-rays among the leprosy cases.

Keywords: *Leprosy, urinary calcium creatinine ratio, bone resorption, lapromatous leprosy*

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INTRODUCTION

Leprosy is caused by Mycobacterium leprae, discovered in 1873 by Hansen at Bergen in Norway. It is believed to be transmitted via droplets from the nose and mouth, through close contact with a person affected by the disease who has not received treatment. The bacillus multiplies slowly and it can take up to 20 years before symptoms appear. Leprosy primarily affects the skin, peripheral nerves, the nasal tissues, the bones and can damage the eyes and testes. Delayed treatment can result in physical and sensory disability; including damage to fingers and toes, contractures, inability to close the eyelids and blindness which often lead to social isolation.[1]

Bony changes usually occur in Leprosy patients of long duration. About 80% of joint lesions are in the metatarso-phalangeal joints of the foot or in theinterphalangeal joints of the hands and feet. Bone changes are divided into specific and secondary changes. Specific bone changes are caused by direct invasion of the bones by M. leprae causing granulomatous lesions seen as focal areas of rarefaction on X-rays. Nasal bone changes have described asspecific for lepromatous leprosy infection.[2] Incidence of bony changes in Leprosy found 15%, 29% and 95% in different studies.[3,4,5] In the small bones of lower limbs these changes include honeycombing, pseudocysts, enlarged nutrient foramina, and areas of bone destruction leading to concentric cortical erosion and thinning to collapse of bone.

Secondary bone changes are caused by destruction of nerve supply as well as vascular changes, trauma and secondary infection contribute to non-specific changes. The changes may be of four types: distal absorption of the digits,

osteoarthritis, osteomyelitis,osteoporosis.[6]Histologically, these lytic bone lesions present foamy macrophages with numerous bacilli, few lymphocytes, epitheloid cells and Langerhans giant cells.Osteoporosis is the second most common sign in patients with leprosy. It is thought to be due to high bacillary load and or reaction to an active lesion in the secondary area or due to immobilization and disuse atrophy. Testicular atrophy and subsequent low levels of testosterone contribute to generalized osteoporosis in males usually in patients with lepromatous leprosy.[7] Motor denervation is sometimes associated with absorption of the cancellous bone and the development of a concentric type of bone atrophy. It affects both the length and width of bone. Osteoporosis mainly causes vertebral fractures, intertrochanteric fractures and colles fractures.[8] Leprotic deformities are more common in males, usually after 40 years of age. Secondary changes are more common in Lepromatous leprosy patients.Bone resorption is well documented in Leprosy patients by radiological studies. Various radiological studies have shown bone resorption in leprosy patients usually involve limbs, alveolar bones and face. Archeological studies have found bone resorption in skeleton of leprosy patients.[9,10]

Very few biochemical studies have been done to evaluateboneresorption in leprosy patients with conflicting results. Calcium metabolism was studied in 47 patients with borderline or lepromatous leprosy.[11] This was measured by serum total and ionized calcium, phosphorus, creatinine, total alkaline phosphatase, parathyroid hormone, 25-hydroxy vitamin D, and 1, 25 –dihidroxy vitamin D; calcium and total hydroxyproline , two important bone resorption markers were determined in urine. Although all values were within the normal ranges, lepromatous leprosy patients had lower total calcium, higher alkaline phosphatase, and higher urinary hydroxyproline than borderline leprosy patients.

Progression of bone disease may still occur even several years after having completed specific treatment for leprosy, meaning such treatment is necessary, but that is not sufficient to cure the bone lesions.[12]A study was done to evaluate the therapeutic effect on oral administration of risedronate in male osteoporotic patients with leprosy.It had shown that oral administration of risedronate apparently prevented vertebral fractures by increasing lumber BMD and caused a significant reduction in urinary cross linked N-telopeptides of type 1 collagen (NTX), a marker of bone resorption. So treatment modality can certainly be changed to some extent by adding calcium supplement and anti- resorptive therapy with Bisphosphonates to prevent deformity resulting from bone resorption. Therefore, our honest effort has been made to evaluate bone resorption by measuring urinary calcium and creatinine level in lepromatous leprosy patients who are gravely suffered by mainly secondary bony changes and compared to controls.

MATERIAL AND METHOD

Clinically suspected LL patients were taken to panel of expert for confirmation and then detailed history taking and clinical examination were done and recorded. Then slit skin smear was done in all patients to confirmed the multibacillary leprosy. Then informed written consent was taken and all bacteriologically positive patients were included in the study procedure. Skin biopsies for histopathology were done in case of highly suspected B.I negative patients.

28 age and sex matched apparently healthy persons without any history of leprosy was included in this study procedure ascontrol group. Objective and purpose of this study was explained to the participants and then informed consent was obtained from them before initiation of the study. A detailed family history and medical examination were performed at screening stage for all participants. Controls were chosen from attendants of patients, staffs of BSMMU. After thorough physical examination, urinary calcium/creatinine was done as investigative procedure. As x-ray is hazardous to health this procedure was done in selected controls whose urinary Ca/Cr was>0.20. Questionnaire was filled up like LL patients. 5 ml of random urine sample was collected after 14 hours of fasting from the diseased and control individuals in a clean, sterile glass bottle.Urinary calcium concentration was measured by an automated chemistry analyzer using the O-cresolphthaleincomplexone method with the calcium-C test. Urinary creatinine was analyzed by the same chemical analyzer using the standard Jaffe kinetic reaction with picric acid.Urinary calcium/creatinine (mg/mg) was calculated as fasting urinary calcium (mg/dl) excretion divided by fasting urinary creatinine excretion (mg/dl). A normal reference interval for the urinary calcium (mg/dl): urinary creatinine (mg/dl) ratio is <0.20. Values exceeding 0.20 was found in patients with hypercalciuria indicating resorption process in bone.

RESULTS

A total of 28 cases and 28 controls were enrolled in that study. Cases of LL were considered as group I and apparently healthy controls were considered as group II.

Table I shows majority of 10(35.7%) patients belonged to age ≤30 years, in group I and 8(28.6%) healthy control in group II. The mean age was found 38.1±14.2 years in group I and 38.9±12.9 years in group II. There are no difference in age of two groups.

Table I: Distribution of cases and control according to age.

Age (years)	Case N=28		Control N=28		P value
	n	%	n	%	
30	10	35.7	8	28.6	
31-40	6	21.4	7	25	
41-50	8	28.6	6	21.4	
51-60	2	7.1	5	17.9	
>60	2	7.1	2	7.1	
Mean ± SD	38.1± 14.2		38.9 ± 12.9		0.826^{ns}
Range (years)	56		50		

^{ns}= P value non significant

Table II shows the male out-numbered female. About 79% cases were male as well as in control group.

Table II: Distribution of cases and control according to sex.

Sex	Case N=28		Control N=28		P value
	n	%	n	%	
Male	22	78.6	22	78.6	1.000^{NS}
Female	6	21.4	6	21.4	
Male to female ratio	3.67 : 1		3.67 : 1		

ns= P value non significant

Table III shows the urinary calcium and creatinine ratio. There was no significant difference in urinary calcium and creatinine ratio of case and control group (p-value >0.05).

Table III: Distribution of cases and control by urinary calcium creatinine ratio

Calcium/Creatinine ratio	Case N=28		Control N=28		P value
	n	%	n	%	
≤0.20	25	89.3	25	89.3	
>0.20	3	10.7	3	10.7	
Mean ± SD	0.13 ± 0.12		0.11 ± 0.07		0.449ns
Min-max	0.01-0.54		0.01-0.27		
Range	0.53		0.26		value non

significant

Table IV shows the mean fasting urinary calcium level was 13 in cases and it was 9.3 in controls but the difference was not significant statistically (p-value >0.05).

Table IV: Distribution of cases and control fasting urinary calcium.

Fasting urinary calcium	Case N=28	Control N=28	P value
Mean ± SD	13.0 13.5	9.3 11.45	0.273^{ns}
Min-max	0.04-45	1.1-60.7	
Range	44.96	59.6	

^{ns}= P value non significant

Table V shows the distribution of cases and control on x-ray findings. Positive x-ray finding was found in 14.3% cases and 3.6% in control.

Table V: Distribution of cases and control on x-ray finding.

x-ray findings	Case (n=28)		Control (n=28)		P value
	n	%	n	%	
Positive	4	14.3	1	3.6	0.35^{ns}
negative	24	85.7	27	96.4	

^{ns}= P value non significant

DISCUSSION

This case control study was done for early detection of bone resorption by measuring fasting urinary calcium/creatinine ratio in Lepromatous leprosy patients. A total of 28 cases of LL patients (newly diagnosed, old and or treated) along with 28 age and sex matched healthy controls were included in this study who attended the outpatient department of Dermatology & Venereology of Bangabandhu Sheikh Mujib Medical University (BSMMU) and Leprosy and Tuberculosis Control Institute of Mahakhali. The study period was from August 2014 to August 2016. Patients of LL were confirmed by history, clinical examination followed by conclusive investigations of slit skin smear and skin biopsy for histopathology.

The present study showed that the mean age was 38.1±14.2 in group 1 and 38.9±12.9 years in group 2 (in healthy controls).The difference was not statistically significant (P= 0.826) between two groups. The youngest patient in this study was 10 years old boy and the oldest was 65 years old. The maximum number of patients who showed bone changes in this study belonged to 20 to 65 years of age. In a Study the youngest patient of Lepromatous Leprosy was 12 years old and the oldest was 75 years old. The maximum number of patients 13 (18.57%) who showed bone changes in that study belonged to the 40-49 years of age group, whereas the least number of patients 2(2.87%) belonged to the 10-19 years age group.[13]

In this study it was observed that 78.6% patients were male and 21.4% were female. Male female ratio was 3.6:1, which indicates lepromatous leprosy is predominant in male subject. In a similar study 56 (80%) patients were male and 14(20%) were female with a male: female ratio was 4:1. Ishida et al (1997) showed 238 (46%) patients were male with LL and 139 (27%) patients were female, which clearly indicates male predominance among the LL cases.[14] These studies closely resemble the present study. Eighty percent of people in Bangladesh live in rural areas. Patients of LL came to Dermatology and Venereology department of BSMMU and TB and Leprosy control institute of Mahakhali from different rural areas. In contrast, patients of LL were few who came from urban as well as from affluent society. The study showed 21 patients (75%) were from rural areas and 7 (25%) from urban areas. 13 (46.4%) healthy controls who participated in this study from rural areas and 15 (53.5%) were from urban areas. The difference was statistically significant (P= 0.028).In this study 14 (50%) patients had duration of illness ≤1year and 14(50%) patients had >1 year. None of the patients had disease duration more than 3 years. As a result, only 3 LL (10.71%) patients showed urinary Ca/Cr ratio >0.20.

Another 4 (14.28%) LL patients showed flexion deformity of interphalangeal joints of right hand and erosion of distal phalanges of right foot, lucent lesion in medullary cavity at proximal phalanx of right hand, Osteoarthosis and lytic area in medial aspect of proximal phalanx of left hand. A study among 70 leprosy patients where most of the patients had the disease for more than 10 years and were in the cured category, but all the patients had permanent residual deformities. Bone resorption is an early event in leprosy and is frequently already present at diagnosis.[15] In this study 2 LL patient (7.14%) presented with urinary Ca/Cr ratio >0.20 and one LL patient (3.57%) presented with lucent lesion in medullary cavity at proximal phalanx of right hand on X-ray when they were first diagnosed as cases of Lepromtous Leprosy. Urinary calcium excretion corrected for creatinine was used as a marker of bone resorption in LL patients in this study. From the present study, it was observed that only 3 LL patients (10.7%) showed urinary Ca/Cr ratio >0.20 (Mean±SD 0.13±0.12) and 3 healthy controls (10.7%) showed urinary Ca/Cr ratio >0.20 (Mean±SD 0.11±0.7. The difference was not statistically significant (P>0.05) between two groups. There was a study where urinary Ca/Cr ratio was also used as a bone resorption marker. In that study, it was observed that there was a statistically significant increase in mean value of urinary calcium/ creatinine (0.13 Vs 0.09) in cases as compared to controls.[16] Another study showed urinary hydroxyproline, which was used as a bone resorption marker markedly elevated in LL patients.[17] On the contrary, another study among 24 lepromatous leprosy patients where urinary calcium, urinary creatinine and urinary excretion of hydroxyproline were within normal range. This study closely resembles the present study.[18]

Some investigatorsmentioned that bone resorption has been well established by radiographic studies. In this present study x-ray findings were positive in 4 patients (14.3%) out of 28 cases and none of the control groups showed positive findings on x-ray. The difference was not statistically significant (p>0.05) between two groups. This study showed flexion deformity of interphalangeal joints of right hand in 1 patient (25%),Lucent lesion in medullary cavity at proximal phalanx in 1patient (25%), Osteoarthosis in 1 patient (25%) and lytic area in medial aspect of proximal phalanx of left hand in 1 patient (25%). In the present study, all the 4 patients (14.3%) showed non-specific bone changes. On the contrary, another group of researchers showed specific bone changes were more prevalent among the LL and BB types of leprosy (100%).[19] But other researchersshowed 75% specific bone changes, 100% non-specific and 75% osteoporosis among the LL cases. In another study there was non-specific bone changes among 26.7% of LL cases. In a similar study it was observed that 46% of multibacillary patients were belonged to bone changes. In other studiesthat figure was 11% and there were more patients belonged to the multibacillary group.[20] Multidrug therapy has limited impact on bone loss.[21] In this study, itwas observed, 2 LL patients (14.3%) who received treatment <1 year among the 14 patients, had urinary Ca/Cr ratio>0.20 and 1LL patient (14.3%) who received no treatment among 7 patients, had urinary Ca/Cr ratio>0.20. The mean was found 0.12±0.10 in first group, 0.18±0.17 in second group and 0.95±0.06 in third group who received treatment more than one year and urinary Ca/Cr ratio was <0.20. The P value was .001 which was statistically significant between the groups. This present study also showed flexion deformity of IP joints of right hand and erosion of distal phalanges of right foot in 1 LL patient(50%),osteoarthrosis in another patient among 2 patients who got treatment for <1 year. Lytic area in medial aspect of proximal phalanx of left hand was found in 1 patient (100%) who got treatment for more than 1 year, and 1 patient (100%) had lucent lesion in medullary cavity at proximal phalanx of left hand, who was newly diagnosed. Ina cohort study of 105 newly-diagnosed adult multibacillary leprosy patients admitted for treatment between 1990-1992.[22] The patients were surveyed until 1999. Progression of bone resorption (BR) in cured leprosy patients was observed up to 8 years after release from MDT. Twenty three percent of the patients were found to have acralresorption. BR was found to be associated with male sex, grade of disability at diagnosis with other deformities and with the occurrence of four or more lepra reactions.A positive correlation was tried to find out between raised urinary Ca/ Cr ratio and positive x-ray findings (both hands and feet) indicative of bone resorption among the LL patients. But such finding was not observed in this study. The 3 LL patients who showed raised urinary Ca/Cr ratio>0.20 did not show any bone changes on x-ray. Similarly, all the 4 LL patients who showed bony changes on x-rays had normal urinary Ca/Cr ratio. A study was conducted among 47 borderlines and LL patients where calcium and hydroxyproline were measured in urine and total subperiosteal diameter and medullary cavity were measured on an x-ray of the hand of all patients.[23]

CONCLUSIONS

This study was carried out for the first time in Bangladesh to detect early bone resorption in LL patients by measuring urinary calcium/creatinine ratio. This bone resorption marker was not used in LL patients widely over the world. Sufficient data and information were unavailable. The test

was also done among healthy controls. But no statistically significant difference was found between cases and controls from this study. Furthermore, this test was not well correlated with resorption findings on x-ray. May be it is due to bone resorption closely related with long duration and severity of the disease.

REFERENCES

1. Srinivasan H. The problem and challenge of disability and rehabilitation in leprosy. Asia Pacific Disability Rehabilitation Journal. 1998;9(2):48-54.
2. Andersen JG, Manchester K, Ali RS. Diaphysealremodelling in leprosy: a radiological and palaeopathological study. International Journal of Osteoarchaeology. 1992 Sep;2(3):211-9.
3. Kanaji A, Higashi M, Namisato M, Nishio M, Ando K, Yamada H. Effects of risedronate on lumbar bone mineral density, bone resorption, and incidence of vertebral fracture in elderly male patients with leprosy. Leprosy review. 2006 Jun 1;77(2):147-53.
4. Illarramendi X, Carregal E, Nery JA, Sarno EN. Progression of acral bone resorption in multibacillary leprosy. Actaleprologica. 2000;12(1):29-37.
5. MacMoran JW, Brand PW. Bone loss in limbs with decreased or absent sensation: ten year follow-up of the hands in leprosy. Skeletal radiology. 1987 Aug 1;16(6):452-9.
6. Faget GH, Mayoral A. Bone changes in leprosy: a clinical and roentgenologic study of 505 cases. Radiology. 1944 Jan;42(1):1-3.
7. Ishikawa A, Ishikawa S, Hirakawa M. Osteoporosis, bone turnover and hypogonadism in elderly men with treated leprosy. Leprosy review. 2001 Sep;72(3): 322-9.
8. Andersen JG, Manchester K, Roberts C. Septic bone changes in leprosy: a clinical, radiological and palaeopathological review. International Journal of Osteoarchaeology. 1994 Mar;4(1):21-30.
9. Choudhuri H, Thappa DM, Kumar RH, Elangovan S. Bone changes in leprosy patients with disabilities/ deformities (a clinico-radiological correlation). Indian journal of leprosy. 1999;71(2): 203-15.
10. Chhabriya BD, Sharma NC, Bansal NK, Agrawal GR. Bone changes in leprosy. A study of 50 cases. Indian journal of leprosy. 1985;57(3):632-9.
11. Moonot P, Ashwood N, Lockwood D. Orthopaedic complications of leprosy. The Journal of bone and joint surgery. British volume. 2005 Oct;87(10): 1328-32.
12. de Lagrán ZM, Arrieta-Egurrola A, González-Pérez R, Soloeta-Arechavala R. Bone complications in a patient with lepromatous leprosy. Actas Dermo-sifiliogr. 2009 Jan 1;100(07):615-7.
13. Balachandra AS, Hombal A, Sudhakar R, Varna NM. Radiological changes in the hands and feet of leprosy patients with deformities. Journal of Clinical and Diagnostic Research. 2011 Aug 1;5(4):703-7.
14. Kumar WJ, Kothari SY, Swamy MK. Deformities and bone changes in leprosy. IJPMR. 2014;25:13-7.
15. Ribeiro FB, de Assis Pereira F, Muller É, Foss NT, de Paula FJ. Evaluation of bone and mineral metabolism in patients recently diagnosed with leprosy. The American journal of the medical sciences. 2007 Nov 1;334(5):322-6.
16. Swathi M, Rao R, CR WD. Evaluation of bone resorption markers in leprosy. International Journal of Clinical and Diagnostic Research 2004; vol. 2, no.2.
17. Mautalen CA, Vega EM, Einhorn TA. Are the etiologies of cervical and trochanteric hip fractures different?. Bone. 1996 Mar 1;18(3):S133-7.
18. Vidal MC, Bottasso OA, Lehrer A, Puche RC. Altered calcium-binding ability of plasma proteins as the cause of hypocalcemia in lepromatous leprosy. International journal of leprosy and other mycobacterial diseases. 1993 Dec 1;61:586-.
19. Paira SO, Roverano S. The rheumatic manifestations of leprosy. Clinical rheumatology. 1991 Sep 1;10(3): 274-6.
20. Olmos JM, Hernández JL, Martínez J, Castillo J, Valero C, Pajares IP, Nan D, González-Macías J. Bone turnover markers and bone mineral density in hypertensive postmenopausal women on treatment. Maturitas. 2010 Apr 1;65(4):396-402.
21. Kanaji A, Higashi M, Namisato M, Nishio M, Ando K, Yamada H. Effects of risedronate on lumbar bone mineral density, bone resorption, and incidence of vertebral fracture in elderly male patients with leprosy. Leprosy review. 2006 Jun 1;77(2):147-53.
22. Bührer-Sékula S, Illarramendi X, Teles RB, Penna ML, Nery JA, Sales AM, Oskam L, Sampaio EP, Sarno EN. The additional benefit of the ML Flow test to classify leprosy patients. Actatropica. 2009 Aug 1;111(2):172-6.
23. Barbieri RR, Sales AM, Illarramendi X, Moraes MO, Nery JA, Moreira SJ, Sarno EN, Machado AD, Bozza FA. Diagnostic challenges of single plaque-like lesion paucibacillary leprosy. Memorias do Instituto Oswaldo Cruz. 2014 Nov;109(7):944-7.

Original Article

Intraoperative Consultation (Frozen Section) in the Diagnosis of Ovarian Tumour

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Abstract

Ovarian cancer is a devastating disease preoperative evaluation of the patients with an ovarian tumour is difficult. So frozen section biopsy of ovarian tumour is important to determine the extent of surgery. This retrospective cross-sectional study was carried out in the Department of Gynaecological Oncology, Bangabandhu Sheikh Mujib Medical University from August 2016 to July 2017 to determine the validity of frozen section biopsy in the diagnosis of ovarian tumour. Fifty cases of ovarian tumour underwent frozen section biopsy were included by purposive sampling. Histopathological finding was taken as the gold standard. Data was analyzed by SPSS version 16. The sensitivity of frozen section in the diagnosis of benign, borderline and malignant were 100%, 100% and 97.67% respectively as well as the specificities were 100%, 97.96% and 100% respectively. Similarly the accuracy, PPV, NPV for the benign, borderline and malignant ovarian tumour were also high except the borderline tumour which had low PPV.

Keywords: *Ovarian tumour, intraoperative consultation, frozen section.*

INTRODUCTION

Ovarian cancer is the 7th most common cancer among female globally[1]. It is a devastating disease as it is often diagnosed late, hence related to poor diagnosis and survival.[2] Among the cancers of the female genital tract, ovarian cancer is the second leading cause of death world wide.[3] Patients with ovarian masses are presenting a persistent agonizing problem due to their inconsistent clinical presentation, difficulties in early diagnosis and wide variations in histological architecture. Preoperative evaluation of the patients with an ovarian tumour is usually made by imaging and estimation of the serum tumour marker. Since these methods have limited value for the recognition of ovarian cancer. The diagnosis of ovarian cancer and the extent of surgery are usually determined by frozen section examination during the surgical procedure[4]. So, the accuracy of frozen section biopsy of ovarian tumour is important as it will influence the line of management, such as conservative versus radical surgery. Conservation of the uterus and the other ovary can be vital to the young patients to whom fertility is an important concern.[5] In the literature, the reported frozen section utilization ratios for ovarian lesions range from 7.4% to 47%.[6]

Frozen section diagnosis should not be seen merely as a microscopic examination of the tissue. Rather, it is an intraoperative consultation method in which other diagnostic tests such as gross examination, touch imprints are used in combination. Hence, some have preferred that the term "frozen section examination" be eliminated in favor of the term "intraoperative consultation"[7] Careful gross examination of the specimen is of utmost importance for both correct sampling and arriving at the correct diagnosis.

This retrospective study was performed to determine the validity of frozen section biopsy in the diagnosis of ovarian tumour in the Department of Gynaecological Oncology at Bangabandhu Sheikh Mujib Medical University.

MATERIALS AND METHODS

This retrospective cross-sectional study was carried out in the Department of Gynaecological Oncology, Bangabandhu Sheikh Mujib Medical University from August 2016 to July 2017. Fifty cases of ovarian tumour were evaluated according to frozen and paraffin section diagnosis in the Department of Pathology, BSMMU during this period. So, these 50 cases were included in this study by purposive sampling by reviewing the hospital record form. Regarding the ethical implications, as this was a retrospective study using the hospital record form, so

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permission was taken from the Unit head of the then Gynaecological Oncology division of BSMMU. The demographic features of the study population, standard biochemical tests and the reports were recorded in a pre-designed data collection sheet.

Preparation of frozen section:

The frozen and paraffin section diagnosis were reported by two pathologists of the Department of Pathology, BSMMU experienced in gynaecological pathology. Following gross inspection, representative samples of suspicious areas with emphasis on solid, papillary or thickend regions was collected for frozen section evaluation. During this procedure portions of resected specimens were taken in the cryostat machine. After quick freezing (at -20 to -25°C), these blocks was sectioned at thickness of 5 micrometer in the cryostat. Frozen sections were then quickly immersed in Koplin's jar containing 95% alcohol for 20 seconds. The slides were then stained with rapid Haematoxyline and eosin staining method. After staining cover slips were mounted over the sections with Di-N-butyle Phthalate in Xylene (DPX). Frozen slides were and results were documented as negative for malignancy or positive for malignancy or suspicious.

Histopathological finding was taken as the gold standard. The frozen section diagnosis was compared with the final paraffin section diagnosis in terms of whether it was a non neoplastic lesion or a benign, borderline, and malignant tumour. Data was analyzed by SPSS version 16. Quantitative observations were indicated by frequencies and percentages.. For the validity of study outcome, sensitivity, specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV) of frozen section biopsy in the evaluation of ovarian masses was calculated. The results were presented in tables

RESULTS

This retrospective cross sectional study was carried out with an aim to find out the sensitivity, specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV) for diagnosis of ovarian tumour evaluated by frozen section biopsy.

A total of 50 cases with ovarian tumour who underwent laparotomy in the Gynaecological Oncology Division of Bangabandhu Sheikh Mujib Medical University, from August 2016 to July 2017 were included in this study. The mean age of the patients was 47.54 ± 12.49 years. Clinically 78% patients were suspected having malignant ovarian tumor. Frozen section biopsy revealed that 12% cases were benign, 4% were borderline and 84% cases were malignant. Histopathological examination revealed that 12% cases were benign, 2% cases were borderline and 86% cases were malignant. The sensitivity of frozen section in the diagnosis of benign, borderline and malignant were 100%, 100% and 97.67% respectively as well as the specificities were 100%, 97.96% and 100% respectively. Similarly the accuracy, positive predictive value (PPV), negative predictive value (NPV) for the benign, borderline and malignant ovarian tumour were also high except the borderline tumour which had low PPV.

Table - I shows the age distribution of the study subjects, it was observed that 42% of patients belonged to less than 50 years age group. The mean age of the patients was 47.54 ± 12.49 years with the age range 18-72 years.

Table I: Age distribution of the study patient (n=50)

Age (in years)	Number of Patients	Percent
<20	2	4.0
20-30	4	8.0
31-40	10	20.0
41-50	13	26.0
>50	21	42.0
Total	50	100.0

Table - II shows the clinical features of the study subjects, it was observed that majority 39(78.0%) of the study subjects were diagnosed as malignant ovarian tumour, 6(12%) as tubo ovarian cyst/mass and 5 (10.0%) were as benign ovarian tumour.

Table II: Distribution of the patients according to clinical feature (n=50):

Clinical feature	N. of patients	Percent
Tubo-Ovarian mass	6	12.0
Benign Ovarian Tumour	5	10.0
Malignant Ovarian Tumour	39	78.0
Total	50	100.0

Table-III shows the serum CA-125 level among the study subjects, it was observed that majority (86.0%) had raised CA-125 (>35 IU/ml) & it was normal in 7(14.0%) cases.

Table III: Distribution of the patients according to CA – 125 (n=50).

Level of CA - 125	Number of patients	Percent
≤ 35	7	14.0
> 35	43	86.0
Total	50	100.0

Table-IV shows the Frozen section of the ovarian tumour revealed malignant in 42(84.0%) cases, benign in 6(12.0%) cases and borderline in 2 (4%) cases.

Table IV: Distribution of the patients according to diagnosis of ovarian mass by frozen section

Ovarian mass by frozen section	No. of patients	Percent
Benign	6	12.0
Borderline	2	4.0
Malignant	42	84.0
Total	50	100.0

Table V shows the Final histopathological diagnosis of the ovarian tumour revealed, 43(86%) cases were malignant, 6(12%) as benign and 1(2%) as borderline ovarian tumour.

Table V: Distribution of the patients according to histopathological diagnosis

Histopathological diagnosis	No. of patient	Percent
Benign	6	12.0
Borderline	1	2.0
Malignant	43	86.0
Total	50	100.0

Table VI : A total of 6 cases were evaluated as benign and all of them revealed as benign by histopathology as well, 2 cases were borderline on frozen biopsy but histopathology confirmed 1 case as borderline, and 42 cases revealed as benign in frozen but final histopathology confirmed as malignant in 43 cases. One case of borderline tumour was over diagnosed and one case of malignant was missed by frozen section biopsy.

Table VI: Comparison between histopathological diagnosis and frozen section biopsy report of ovarian masses

Variable	Histopathological diagnosis(n=50)			Total (n=50)
Frozen Section (n=50)	Benign	Borderline	Malignant	
Benign (n=6)	6	0	0	6
Borderline(n=2)	0	1	1	2
Malignant(n=42)	0	0	42	42
Total	6	1	43	50

Table VII : The sensitivity of frozen section diagnosis for benign, borderline and malignant ovarian tumour were 100%, 100% and 96.67% respectively as well as the specificities were 100%, 97.96% and 100% respectively. The accuracy was 100% for benign tumours and , 98% for both borderline & malignant tumours of ovary. PPV and, NPV for the benign tumours was 100%; PPV & NPV for the borderline ovarian tumour were 50% & 100% respectively and for the malignant ovarian tumours were 100% & 87.5% respectively.

Table VII: Sensitivity, specificity, accuracy, positive and negative predictive values of frozen section in the diagnosis of ovarian tumour.

	Sensitivity (95% CI)	Specificity (95% CI)	Accuracy (95% CI)	PPV	NPV
Benign	100% (54.07 - 100%)	100% (91.96 -100%)	100% (92.89% - 100%)	100	100
Borderline	100% (2.50% - 100.00%)	97.96% (89.15% - 99.95%)	98% (89.35% - 99.95%)	50	100
Malignant	97.67% (87.71% - 99.94%)	100% (59.04% - 100.00%)	98% (89.35% - 99.95%)	100	87.5

DISCUSSION

Frozen section diagnosis is an important and reliable tool in the clinical management of patients with ovarian tumours. However, little information has been published concerning the utilization ratio of frozen section in ovarian tumour. In the literature, the reported frozen section utilization ratios for ovarian lesions range from 7.4% to 47%.[6,8,9] Since most of the patients with ovarian tumour undergo surgery without a definite tissue diagnosis, the diagnosis and the course of the surgery are usually determined by performing frozen section. Benign lesions are managed conservatively, borderline and malignant ovarian tumours are managed by definitive surgery, omental biopsy or omentectomy and comprehensive surgical staging or debulking surgery depending on the stage of the disease.[10,11] So, accurate intraoperative diagnosis is imperative.

Many studies have assessed the accuracy of frozen section in ovarian tumours. In the present study, 6 benign ovarian tumours were diagnosed intraoperatively as benign by frozen section and no false positive cases evaluated by histopathology. This result showed that there is agreement with frozen section and histopathology in the diagnosis of benign ovarian tumour. But 1 out of 2 cases of borderline ovarian tumours there was disagreement in the diagnosis and 1 out of 43 cases of malignant ovarian tumours was misdiagnosed as borderline. In that casee, the frozen section diagnosis of 1 borderline tumour (mucinous borderline tumour) turned out to be malignant on final histology and that was mucinous cystadenocarcinoma. Borderline ovarian epithelial tumours have always been a major cause of pitfall in frozen section diagnosis with less reliable results compared to benign and malignant tumours.[5,610,12,13,14]

Houck et al reviewed 140 borderline ovarian tumours which showed that in 60% of cases, frozen section diagnosis agreed with permanent diagnosis[13]. Over diagnosis was reported in 10.7% and 29.3% of cases were under diagnosed[13].Other studies also report a less than 90% overall sensitivity for borderline tumours.[10,11,12,14] In the literature, frozen section examination has a high accuracy rate in ovarian tumours, reported at greater than 90%[9,15-22].

In this present study, the accuracy was 100%, 98% and 98% for benign, borderline and malignant ovarian tumours respectively. The sensitivity rates for benign, borderline and malignant tumours were found as 100 %, 100% and 97.67% respectively which correlate with the other series.[9,17,19-21]

In this study the positive predictive value of frozen section evaluation in the diagnosis of ovarian malignancies was 100 %. This finding is consistent with the other studies which reported positive predictive values of 99.1% to 100%, making overtreatment an unlikely event [9,1518,23]

Several literatures have shown that the causes of discordance between frozen section and histology are due to sampling error, misinterpretation, lack of communication with the surgeons, and technical problems.[17]

At BSMMU during the intraoperative consultation, the pathologists are able to communicate with a responsible surgeon from the surgical team and also receive the clinical information and intraoperative findings which is also an important component during frozen section.

CONCLUSION

This study confirms that frozen section diagnosis is a reliable method in the intraoperative evaluation of ovarian tumour in our instituition. However, diagnostic problem can occur in borderline ovarian tumour during frozen section biopsy and the pathologists as well as the surgeons must be aware of the limitations of this procedure, and a good communication between pathologists and surgeons is required to obtain more accurate results.

Limitations of the study

The study population was selected from one selected hospital in Dhaka city with limited sample size, so that the results of the study may not be reflect the exact picture of the whole country.

REFERENCES

1. Bhatla N, Denny L. FIGO's updated Cancer Report 2018. Int J Gynecol Obstet 2018; 143(suppl.2):2-3.
2. American Cancer Society. Cancer facts and figures 2020.https://www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/cancer-facts-figures-2020.html.
3. Modugno F. Ovarian cancer and polymorphism in the Androgen and Progesterone receptor genes: A HUGE Review. Am J Epidemiol 2004; 159: 319- 335.
4. Lim FK, Yeoh CL, Chong SM, Arulkumaran S. Pre and intraoperative diagnosis of ovarian tumours: how accurate are we? Aust NZ J Obstet Gynaecol 1997; 37:223-7.

5. Gol M, Baloglu A, Yigit S, Dogan M, Aydin C, Yensel U. Accuracy of frozen section diagnosis in ovarian tumors: Is there a change in the course of time?. Int J Gynecol Cancer 2003; 13: 593-597.

6. Twaalfhoven FC, Peters AA, Trimbos JB, Hermans J, Fleuren GJ. The accuracy of frozen section diagnosis of ovarian tumors. Gynecol Oncol 1991; 41: 189-92.

7. Fechner RE. Frozen section (intraoperative consultation). Hum Pathol 1988; 19: 999-1000.

8. Maiman M, Selzer V, Boyee J. Laparoscopic excision of ovarian neoplasm subsequently found to be malignant. Obstet Gynecol 1991; 77: 563-5.

9. Puls L, Heidtman E, Hunter JE, Crane M, Stafford J. The accuracy of frozen section by tumor weight for ovarian epithelial neoplasms. Gynecol Oncol 1997; 67: 16-9.

10. Ilvan S, Ramazanoglu R, Akyildiz EU, Calay Z, Bese T, Oruc N. The accuracy of frozen section (intraoperative consultation) in the diagnosis of ovarian masses. Gynecologic Oncology 2005; 97: 395-399.

11. Pinto PB, Andrade LA, Derchain SF. Accuracy of intraoperative frozen section diagnosis of ovarian tumors. Gynecol Oncol 2001; 81: 230-2.

12. Maheshwari A, Gupta S, Kane S, Kulkarni Y, Goyal BK, Tongaonkar HB. Accuracy of intraoperative frozen section in the diagnosis of ovarian neoplasm: experience at a tertiary oncology center. World J Surg Oncol 2006;4:12.

13. Houck K, Nikrui N, Duska L, Chang Y, Fuller AF, Bell D. et al. Borderline tumours of the ovary: correlation of frozen and permanent histopathological diagnosis. Obset Gynecol 2000;95(69):839-43.

14. Kim JH, Kim TJ, Park YG, Lee SH, Lee CW, Song MJ,et al. Clinical analysis of intra-operative frozen section proven borderline tumours of the ovary. J Gynecol Oncol 2009;20(3):176-80.

15. Obiakor I, Maiman M, Mittal K, Awobuluyi M, DiMaio T, Demopooulos R. The accuracy of frozen section in the diagnosis of ovarian neoplasms. Gynecol Oncol 1991; 43(1):61-3.

16. Tangjitgamol S, Jesadapatrakul S, Manusirivithaya S, Sheanakul C. Accuracy of frozen section in diagnosis of ovarian mass. Int J Gynecol Cancer 2004;14(2): 212-9.

17. Wang KG, Chen TC, Wang TY, Yang YC, Su TH. Accuracy of frozen section diagnosis in gynecology. Gynecol Oncol 1998; 70: 105-10.

18. Crum CP. 'The female genital tract' in Robbins and Cotran Pathologic Basis of Disease, 7th edition, Kumar V, Abbas AK, Fausto N (eds), Elsevier Saunders, Philadelphia 2004; pp. 1092-1117.

19. Mills SE, Carter D, Greenson JK, Oberman HA, Reuter V, Stoler MH. Sternberg's Diagnostic Surgical Pathology. 4th ed. Philadelphia: Williams & Wilkins;2004.

20. Benedet JL, Bender H, Jones H, 3rd, Ngan HY, Pecorelli S. FIGO staging classifications and clinical practice guidelines in the management of gynecologic cancers. FIGO Committee on Gynecologic Oncology. Int J Gynaecol Obstet 2000;70(2):209-62.

21. Robinson WR, Curtin JP and Morrow CP. Operative staging and conservative surgery in the management of low malignant potential ovarian tumors. Int. J. Gynecol. Cancer 1992; 2: 113–118.

22. Kim K, Chung HF, Kim JW, Park NH, Song YS, Kang SB. Clinical impact of under-diagnosis by frozen section examination is minimal in borderline ovarian tumors. Eur J Surg Oncol 2009;35(9):969-73.

23. Brun JL, Cortez A, Rouzier R, Callard P, Bazot M, Uzan S, et al. Factors influencing the use and accuracy of frozen section diagnosis of epithelial ovarian tumors. Am J Obstet Gynecol 2008;199(3):244-7.

Original Article

Habitual Physical Exercise and Osteoarthritis of the Knee in Female

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Abstract

The study aimed to evaluate the association of recreational (habitual) physical activities with the osteoarthritis (OA) of the knee in the female. The case-control study was carried out at the Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka in the year 2016 and 2017. The total participants were 174 female selected purposively with the age range of 40 – 70 years, among them 87 were the cases with OA of the knee, and the same number of the same age group were included as the control without OA of the knee. A structured interviewer-administered questionnaire was used to collect data. High level of physical activities (20 or more miles per week) was associated with OA of the knee, whereas moderate level of physical activities (10-20 miles/per week) and low level of physical activities (<10miles/per week) had no significant association with the OA of the knee. This study reveled the relationship of the physical activity and OA of the knee. Continue physical activity according to the public health guideline, may eliminate this such physical problem for the general health promotion and particularly to prevent the OA of the knee.

Keywords: *Osteoarthritis, physical activity, exercise, risk factor*

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INTRODUCTION

The biomechanical influence of anthropometric changes and habitual physical activity levels are important linked contributory factors which may play a role in the prevalence and symptomatology of osteoarthritis in aging women.[1]

The beneficial health effects of physical activity are well known, include increased longevity and decreased incidence of cardiovascular disease, diabetes, obesity, and hypertension.[2-3] One of the potentially hazardous effects of physical activity is osteoarthritis.[4] Female gender, age, obesity, previous joint injury, occupational activities are known risk factors for both hip and knee osteoarthritis.[5]

There is an increased risk of developing hip and knee OA with specific strenuous exercise and long term physical activity were detected among general population, here wear and tear theory of joint degeneration related to repetitive joint loading.[6-8]

Other studies report that moderate and strenuous physical activities including recreational running do not significantly increase the risk of OA.[9-10]

While many kinds of physical activity require repetitive joint use that may cause cartilage attrition, physical activity can help in preventing OA in different ways like strengthening the muscular support around joints and thereby reduces the risk of joint injury, improve and maintains joint mobility by preventing the joints from 'freezing up' and physical activity helps to avoid obesity, a risk factor for some forms of OA. Finally, mature cartilage cells receive nourishment only from the diffusion of substances through the cartilage matrix from the joint fluid as because cartilage has no blood vessels or nerves, and physical activity enhances this process.[11]

A widely promoted way to improve and maintain health is leisure-time physical activity. The potential effect of physical activity on OAis important to understand.

Previous studies on the impact of physical activity on the knee joint have reported conflicting findings. Moreover, few studies have been carried out on this fact in Bangladesh.

Therefore, this study was aimed to explore theinteraction between physical activities with the osteoarthritisof the knee inthe female.

MATERIALSAND METHODS

Thecase-control study was done on 174female participants who were selected purposively with the age range of 40-70 years at BSMMU in the year 2016 and 2017. They were divided into the two groups where 87 patients withosteoarthritis of the knee as the caseand 87 without osteoarthritis of the knee werein the control group. A structured interviewer-administered questionnaire, enquiring about demographic data and details of the exercise pattern was used to collect the data. The Institutional Review Board of the BSMMU reviewed and approved all the procedures of this study. The physical, psycho-social and legal risk were minimum. The participants were well informed to give written consent before enrollment and they had the right to participate or refuse or even withdraw from the study at any point in time.The privacyof the data information was maintained strictly.

The chosen physical activitieswere walking, running, jogging here because they were the most common activity for this population and they were assessed by self-reported regular exercise patterns. Among those who reported any regular exercise, three levels of activity were defined. The high level- physical activity more than 20 miles per week; moderate level - physical activity between 10 and 20 miles per week andlowlevel - physical activity up to 10 miles per week.

TheStatistical Package for Social Sciences version 23.0 for Windows was used to analyze all relevant information. The quantitative observations were in frequencies and percentages. Thecategorical variables were analyzed by the Chi-Squared test, showed with cross tabulation. The considered statistically significantp-value was <0.05.

RESULTS

The mean age was 57 years.

Table-I: shows regular physical activity of the respondents. Among the 87 patients, 55 were doing a high level of physical activities, the value was 41 in the control group and the P value was significant (<0.05). The low level of physical activities and a moderate level of physical activities were not statistically significant (p >0.05) between the two groups.

Table I: Regular physical activity of the respondents

Regular physical activity (miles /per week)	Case (n=87)	Control (n=87)	OR (95% CI)	P value
Low (<10)	7	14	2.19 (0.77-6.40)	0.103^{ns}
Moderate (10-20)	25	32	0.69 (0.35-1.37)	0.258^{ns}
High (>20)	55	41	1.93 (1.01-3.70)	0.032^{s}

s= significant, ns= not significant

DISCUSSION

This study gives an idea about the relation of physical activity to the OA of the knee in female aged 40 to 70 and above in this region.

This study revealed a positive association between the high level of physical activity and the OA of the knee where the mean age was 57 years. However, the OA of the knee was not significantly associated with the physical activities in low level and physical activities in a moderate level.

It proves the Marti et al study where they have explained that the exercise of high-intensity over a long period of time may be responsible for the premature OA.[12]

Another study favors this studywhere it is observed that the weight-bearing sports like running, jogging, etc. can increase the risk of radiographic OA of the knees in women.[13]

Some studies reported conflicting findingsinvestigating the impact of physical activity on the knee joint. Few of them declaredthe physical activity as a risk factor for the OA of the knee.[6, 13-14]

Among the walkers and runners the female gender is contributing along with the other risk factors for the OA of the Knee.[15]

The high level of physical activity was showed significant for the OA of the knee in a study and so did ours.This is may be happening due to cartilage degeneration by transmitting repetitive impact and torsional loads to the large weight-bearing joints such as the hip and knee.[16]

In this study, the moderate level of physical activity and low level of physical activity were not associated with the osteoarthritis of the knee and that was seen in other studies. They all explored, the physical activity in moderate level did not increase the risk of OA without significant joint injury.[1, 7, 17-23]

It wasdescribed in a study thatthe recreational exercises did not increase the risk of the radiographic OA of the knee in middle-aged and elderly persons.[24]

Other studies observed that the degenerative changes of the knee joint might not be caused by the physical activity moreovercould even be protected by it.[8, 24-26]

The similarity of this study with others is the high level of physical activities have an association with the OA of the knee while it differs in the moderate level and low level of physical activities which are not associated.

The suggestion is to follow the public health guideline and continue regular physical exercise.[27-28]This message will be helpful for the health promotion in general and particularly theOAof the knee can be prevented.

CONCLUSIONS

This study findings support the conclusion that a high level of physical activities has a significant association with osteoarthritis of the knee in the female. Whereas, moderate level and low level of physical activities have no effect on osteoarthritis of the knee.

RECOMMENDATION

To avoid the OA of the knee, low level (<10miles/per week) and a moderate level (10-20 miles/per week) of habitual/regular physical exercise like walking, jogging or running is recommended.

Acknowledgment

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REFERENCES

1. White JA, Wright V, Hudson AM. Relationships between Habitual Physical Activity and Osteoarthrosis in Ageing Women. Public Health 1993; 107: 459-470.
2. Pate R, Pratt M, Blair S, Haskell W, Macera C, Bouchard C, et al. Physical activity and public health: a recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine. JAMA 1995; 273(5):402–7.
3. Blair S, Kohl H, Barlow C, Paffenbarger R, Gibbons L, Macera C. Changes in physical fitness and all-cause mortality: a prospective study of healthy and unhealthy men. JAMA 1995; 273(14):1093–8.
4. Pate R, Macera C. Risks of exercising: Musculoskeletal injuries. In: Bouchard C, Shepard R, Stephens T, editors. Physical activity, fitness and health: international proceedings and consensus statement. Champaign, IL: Human Kinetics Publishers, 1994: 1008–18.
5. Felson D, Zhang Y. An update on the epidemiology of knee and hip osteoarthritis with a view to prevention. Arthritis Rheum 1998; 41(8): 1343–55.
6. Cheng Y, Macera C, Davis D, Ainsworth B, Troped P, Blair S. Physical activity and self-reported, physician-diagnosed osteoarthritis: Is physical activity a risk factor?. J Clin Epidemiol 2000;53:315–22.
7. Cooper C, Snow S, McAlindon T, Kellingray S, Stuart B, Coggon D, et al. Risk factors for the incidence and progression of radiographic knee osteoarthritis. Arthritis Rheum 2000;43(5):995–1000.
8. Hart D, Doyle D, Spector T. Incidence and risk factors for radiographic knee osteoarthritis in middle-aged women: the Chingford Study. Arthritis Rheum 1999;42(1):17–24.
9. Hannan M, Felson D, Anderson J, Naimark A. Habitual physical activity is not associated with knee osteoarthritis: the Framingham Study. J Rheumatol 1993;20(4):704–9.
10. Lane N, Oehlert J, Bloch D, Fries J. The relationship of running to osteoarthritis of the knee and hip and bone mineral density of the lumbar spine: a 9-year longitudinal study. J Rheumatol 1998;25(2):334–41.
11. Hall AC, Urban JPG, Gehl KA. The effects of hydrostatic pressure on matrix synthesis in articular cartilage. J Orthop Res 1991;9:1–10.
12. Marti B, Tschopp KA, Jucker A, Howald H. Is excessive running predictive of degenerative joint disease?. Controlled study of former elite athletes.

British Medical Journal, 1989;299: 91-93.

13. Spector TD, Harris PA, Hart DJ, Cicuttini FM, Nandra D, Etherington J, Wolman R, Doyle DV. Risk of osteoarthritis associated with long-term weight-bearing sports: a radiologic survey of the hips and knees in female ex-athletes and population controls. Arthritis Rheum 1996;39:988–95.
14. Szoeke C, Dennerstein L, Guthrie J, Clark M, Cicuttini F. The relationship between prospectively assessed body weight and physical activity and prevalence of radiological knee osteoarthritis in postmenopausal women. J Rheumatol 2006;33:1835-1840.
15. Gabriel SE. Update on the epidemiology of the rheumatic diseases. Curr Opin Rheumatol 1996; 8:96-100.
16. Buckwalter J, Lane N. Athletics and osteoarthritis. Am J Sports Med 1997;25(6):873–81.
17. Hootman JM, Macera CA, Helmick CG, Blair SN. Influence of physical activity-related joint stress on the risk of self-reported hip/knee osteoarthritis: a new method to quantify physical activity. Prev Med 2003;36:636-644.
18. Sandmark H, Vingard E. Sports and risk for severe osteoarthritis of the knee. Scand J Med Sci Sports 1999;9(5):279–84.
19. Panush RS, Schmidt C, Caldwell JR, Edwards NL, Longley S, Yonker R, et al. Is running associated with degenerative joint disease?. JAMA 1986; 255: 1152–4.
20. Cooper C, McAlindon T, Snow S, Vines K, Young P, Kirwan J, et al. Mechanical and constitutional risk factors for symptomatic knee osteoarthritis: differences between medial tibiofemoral and patellofemoral disease. J Rheumatol 1994;21:301–13.
21. Bagge E, Bjelle A, Eden S, Svanborg A. Factors associated with radiographic osteoarthritis: results from the population study 70-year old people in Goteborg. J Rheumatol 1991;18(8):1218–22.
22. Lau E, Cooper C, Lam D, Chan V, Tsang K, Sham A. Factors associated with osteoarthritis of the hip and knee in Hong Kong Chinese: obesity, joint injury and occupational activities. Am J Epidemiol 2000;152(9): 855–62.
23. Manninen P, Riihimaki H, Heliovaara M, Suomalainen O. Physical exercise and risk of severe knee osteoarthritis requiring arthroplasty. J Rheumatol 2001;40:432–7.
24. Felson D, Niu J, Clancy M, Sack B, Aliabadi P, Zhang Y: Effect of recreational physical activities on the development of knee osteoarthritis in older adults of different weights: The Framingham Study. Arthritis Rheum 2007; 57:6-12.
25. Rogers LQ, Macera CA, Hootman JM, Ainsworth BE, Blair SN. The association between joint stress from physical activity and self-reported osteoarthritis: an analysis of the Cooper Clinic data. Osteoarthritis and Cartilage 2002; 10: 617–622.
26. Urquhart DM, Soufan C, Teichtahl AJ, Wluka AE, Hanna F, Cicuttini FM. Factors that may mediate the relationship between physical activity and the risk for developing knee osteoarthritis. Arthritis Research and Therapy. 2008;10:203.
27. U.S. Department of Health and Human Services. Healthy People 2010. Washington, DC: U.S. Department of Health and Human Services 2000.
28. U.S. Department of Health and Human Services. Physical Activity and Health: A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion 1996.

Case Report

Temporomandibular Joint Monoarthritis in Rheumatoid Arthritis - A Rare Case Report

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Abstract

Rheumatoid arthritis (RA) is a chronic, systemic, autoimmune inflammatory disorder that is characterized by joint inflammation, erosive properties and symmetric multiple joint involvement. Temporomandibular joint (TMJ) is very rare to be affected in the early phase of the disease, thus posing diagnostic challenges for the rheumatologist. TMJ complaints are present in about more than 50% of patients of RA. TMJ is usually among the last joint to be involved and is associated with many clinical signs and symptoms of which pain is a major problem leading to inflammation, limited movements, swelling, joint stiffness, and muscle spasm. Here reported case is 64 years old male, ex-smoker, diagnosed case of diabetes mellitus for 7 years, hypertension for 2 years, came to hospital with the complains of pain in left jaw for 1 year. He had no history of other joint pain, morning stiffness or any deformities. The patient was diagnosed as a case of rheumatoid arthritis on the basis of inflammatory monoarthritis with high titer positive RA factor and anti CCP. The patient gradually improved after treatment with methotrexate. Inflammatory markers like ESR dropped down with the clinical improvement. TMJ is seldom joint to be affected first in the disease course.

Keywords: *Rheumatoid arthritis, temporomandibular joint arthritis*

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INTRODUCTION

Rheumatoid arthritis (RA) is a systemic autoimmune condition with variable manifestations, characterized by symmetric polyarticular inflammation, predominantly in small joints of upper limbs which can lead to progressive joint damage. It is associated with substantial functional disability, morbidity, and accelerated mortality. The prevalence of RA is estimated at 1% in most developed countries, with a frequency ranging from less than or equal to 0.1% to 1.9% in surveys from different parts of the world. More than 50% of patients with rheumatoid arthritis have involvement of the TMJ. The approximate female-male ratio is 3:1. This TMJ is very rare to be affected in the early phase of the disease and isolated TMJ involvement is rarer. Here we are presenting a patient who had isolated TMJ involvement and finally diagnosed as RA.

CASE SUMMARY

A 64 years old male, ex-smoker, diagnosed case of diabetes mellitus for 7 years, hypertension for 2 years, came to our hospital with the complaints of pain in left jaw for 1 year. Initially pain was mild; it was progressively increasing, more marked in the morning making him difficulty in opening mouth. For last 2 months pain was throbbing in nature, severe and radiating to upper and lower jaw. He was unable to chew solid food and he even used to feel pain during speaking. The patient also complained burning and tingling sensation over same area which was aggravated on exposure to cold water for last 5 months. There was no history of low back pain or pain in other joints. No history of headache, blurring of vision and dental pain. His blood sugar was well controlled with tablet metformin 500 mg daily and tablet Linagliptin 5mg daily. There was no history of hypoglycemic attack. He was a known case of hypertension for 2 years for which he was taking Bisoprolol 2.5 mg daily and his blood pressure was within normal limit. He developed myocardial infarction in March 2019 and primary PCI was done. There was no family history of skin lesion suggestive of psoriasis. No drug history like steroid and bisphosphonate.

On examination patient was ill looking and anxious. Pulse was 72 beats per minute; blood pressure was 130/70 mm of Hg, no postural hypotension, and respiratory rate was 17 breaths per minute, temperature was 98. There was no palpable lymph node. Thyroid gland was normal. There was grade tenderness over the left TM joint. Examination of all other system reveals no abnormalities.

Investigation reports reveal: Hb was 11.3 gm/dl, total leucocyte count was 6.8 $X10^9$/µL, platelet was 200X 10^3/µL and RBC count was 3.49X10^6 / µL. His ESR was 25 mm in 1st hour, CRP was 2.81 mg/dl, random blood sugar-7.2 mmol/L, HbA1c-6.1%, SGPT was 16 U/L, S. creatinine was 0.9 mg/dl. Lipid profile was- total cholesterol- 232 mg/dl (<240 mg/dl), HDL- 37 mg/dl (>40 mg/dl) mg/dl, LDL- 119.4 mg/dl (<130 mg/dl) and TG was 325 mg/dl <200 mg/dl). Urine RME showed normal, spot urinary micro albumin 31.71mg/dl (<30mg/dl), ECG was normal, CXR P/A view was normal, RA test 54.9 IU/ml (<15 IU/ml), AntI-CCP 365.2U/ml (25 U/ml), Anti SSA 0.58 U/ml (<0.95 U/ml), Anti-SSB 0.62 U/ml (<0.95U/ml), X-ray left TM joint shows joint space narrowing and sclerosis. (Figure no. 1a, 1b), X-ray of hand showed normal findings (Figure no. 2).

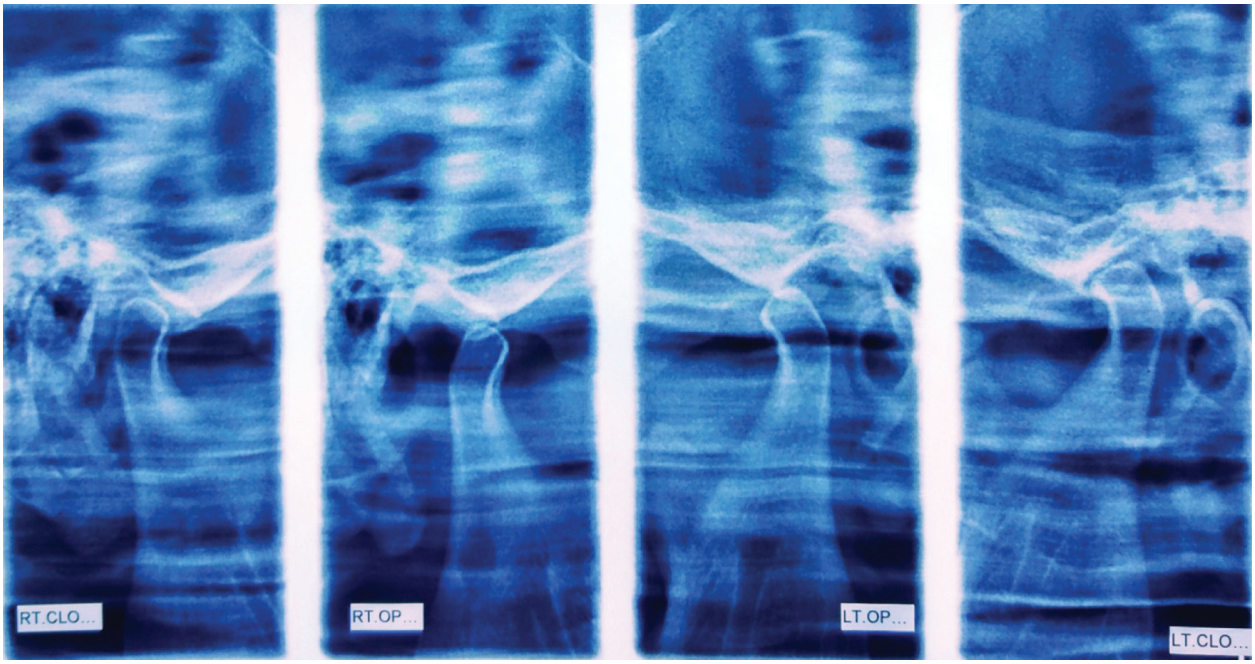

Figure-1a: *Joint space narrowing and sclerosis in left TM joint*

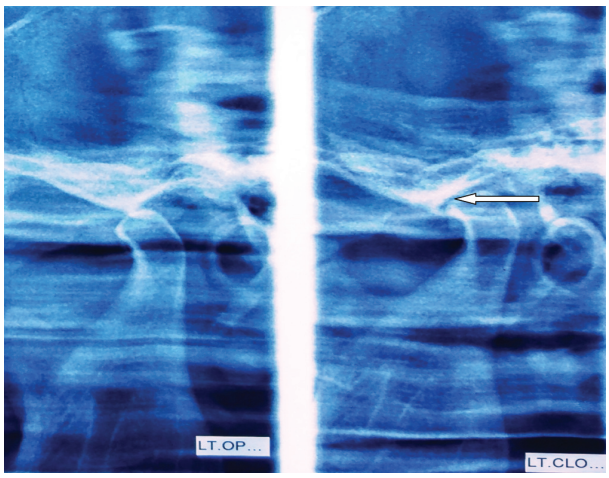

Figure-1b: *Joint space narrowing and sclerosis in left TM joint*

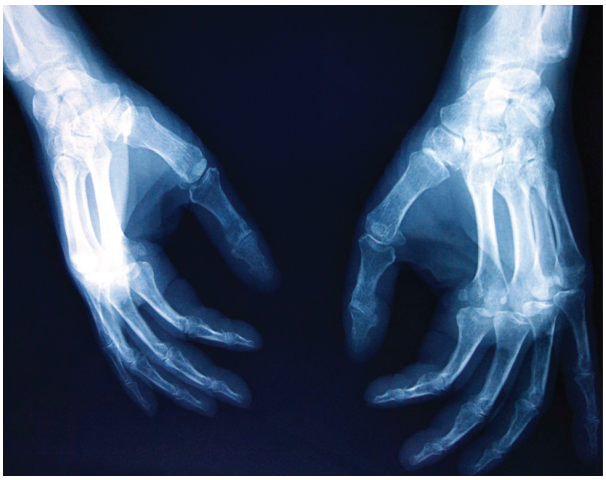

Figure-2: *X-ray of both hands showing normal findings*

DISCUSSION

Rheumatoid arthritis is a systemic autoimmune condition with fluctuating manifestations. It is characterized by symmetric polyarticular inflammation, which can lead to progressive joint damage and is associated with substantial functional disability, morbidity, and accelerated mortality. The prevalence of RA is estimated at 1% in most developed countries, with a frequency ranging from less than or equal to 0.1% to 1.9% in surveys from different parts of the world[6]. The characteristic patient with RA often reports pain and swelling of the small joints of the hands, wrists, and feet, with prolonged morning stiffness, often lasting more than an hour. Early in the natural course, patients with RA may experience difficulty using their hands with routine activity, and pain in the forefeet with weight bearing or walking. Articular symptoms most often begin with stiffness, pain, and swelling involving the small joints of the hands and feet in a symmetric distribution, including the metacarpophalangeal (MCP), proximal interphalangeal (PIP), and metatarsophalangeal (MTP) joints. Patients commonly report a "gelling" phenomenon following periods of rest, which improves with activity. The joint examination often reveals swelling, tenderness, increased warmth, and limited range of motion. Other findings may include palmar erythema and subcutaneous nodules on extensor surfaces. Extra-articular features are more commonly seen in later disease. The condition characteristically spares the distal interphalangeal (DIP) joints impacting <10% of cases[7] and also spares the thoracic and lumbosacral spine. With more advanced and longer duration of disease, RA may also involve atypical joints, including the temporomandibular joint.

The patient presented here was male and his age was 60 years and had only temporomandibular joint pain and stiffness without involvement of other joints and extra articular involvement of RA.

For diagnosis of RA, serological tests such as ESR, CRP, Rheumatoid Factor (RF), Anti CCP antibody was done. Our patient had raised ESR and CRP, high titer positive RF and Anti CCP antibody. X-ray left TMJ showed marginal sclerosis with joint space narrowing, right TMJ was normal. X-ray of both hands were normal.

Methotrexate remains the mainstay of treatment. Most of the patient responds well with this DMARD monotherapy. If does not respond or do not achieve treat to target to maximum tolerable dose of methotrexate then combination of other drugs like Sulfasalazine and/or Hydroxychloroquin of bDMARDs may be tried.

Our patient was treated with Methotrexate 10mg/week initially and later on dose was gradually increased to 20 mg/week with significant improvement on the basis of DAS28.

Isolated TMJ involvement as an initial presentation in RA is extremely rare, physician should be aware of this unusual presentation and RA should be considered as a differential diagnosis of TMJ arthritis even in the absence of other typical features of RA.

CONCLUSIONS

Isolated TMJ involvement as an initial presentation in RA is extremely rare. Physician should be aware of this unusual presentation and RA should be considered as a differential diagnosis of TMJ arthritis even in the absence of other typical features of RA.

REFERENCES

1. B. Bruce and G. Martin, "Temporomandibular disorders," in Burket's Textbook of Oral Medicine: Diagnosis and Treatment, pp. 271–306, Elsevier, Canada, 11th edition, 2008.
2. C. S. Crowson, E. L. Matteson, E. Myasoedova et al., "The lifetime risk of adult-onset rheumatoid arthritis and other inflammatory autoimmune rheumatic diseases," Arthritis & Rheumatism, vol. 63, no. 3, pp. 633–639, 2011.
3. K. Moen, L. T. Bertelsen, S. Hellem, R. Jonsson, and J. G. Brun, "Salivary gland and temporomandibular joint involvement in rheumatoid arthritis: relation to disease activity," Oral Diseases, vol. 11, no. 1, pp. 27–34, 2005.
4. Delantoni A, Spyropoulou E, Chatzigiannis J, Papademitriou P. Sole radiographic expression of rheumatoid arthritis in the temporomandibular joints: A case report. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006; 102:e37–40.
5. Seymour RL, Crouse VL, Irby WB. Tempo-romandibular ankylosis secondary to rheumatoid arthritis. Report of a case. Oral Surg Oral Med Oral Pathol. 1975; 40:584–9.
6. Silman AJ: Rheumatoid arthritis, ed 4, St. Louis, 2001, Mosby Elsevier
7. Ichikawa N, Taniguchi A, Kobayashi S, et al: Performance of hands and feet radiographs in differentiation of psoriatic arthritis from rheumatoid arthritis. Int J Rheum Dis 15(5):462–467, 2012.

Case Report

Cardiac Cephalgia: Angina in the Head

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Abstract

Cardiac cephalgia is a migraine like headache that occurs during episodes of myocardial ischaemia. Although most of the patients presenting with ischaemic heart disease have chest pain, there are other rare presenting symptoms like cardiac cephalgia. Headache can be the only presentation of coronary artery disease. We report a case of a 57 years-old man, Presenting with only headache during brisk walking, Exercise Tolerance Test (ETT) was positive for Electrocardiograph (ECG) evidence of provocable myocardial ischemia, who latter was diagnosed as double vessel coronary artery diseaseon Coronary Angiogram (CAG). As the patient preferred remaining without revascularization, he was put onto optimum medical management for ischaemic heart disease. A follow up visit after one month revealed, marked improvement of the headache with anti anginal medications. Early evaluation and diagnosis of the headache symptom should be done because treatment with anti-migraine drugs may deteriorate headache and undermine the diagnosis of coronary artery disease.

Keywords: *Cardiac cephelgia, coronary artery disease, headache.*

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INTRODUCTION

Headache is found in 6% of all cardiac ischaemic cases.[1] According to the International Classification of Headache Disorders (ICHD) 3rd edition cardiac cephalgia is a 'migraine like' headache, usually but not always aggravated by exercise, occurring duringepisode of myocardial ischaemia and it is relieved by nitroglycerine.[2] Cardiac cephalgia is a typical secondary headache disorder, usually initiated by exertion that is related to myocardial ischaemia. Primary exertional headachesuch as sex cough or exercise induced headache are typically benign. Cardiac cephalgia, on the other hand, can have life threatening complications thereare a total of 36 cases that have been reported in literature so far.[3] We report a case of a 57 year old male, presenting to a neurologist with headache as sole symptom, who later was diagnosed having severe coronary artery disease.

CASE REPORT

A 57 year old Muslim male, hypertensive, diabetic, nonsmoker without any positive family history of ischaemic heart disease, presented to us with a history of post exertional headache for last 2 years. It spread to the occipital region and back of neck after exertion. Initially it occurred in moderate to severe exertion, later worsened and presently it occurs with minimal exertion relieves on taking rest. The headache was not associated with watering of eyes, nausea or vomiting. With this complaint he presented to a neurologist and underwent neurological examinations and investigations including magnetic resonance imaging (MRI) of brain and cervical spine, Magnetic resonance venogram (MRV) and carotid duplex study which failed to reveal any abnormality.

Initially diagnosed as a case of migraine and treated accordingly without any improvement, the patient underwent an exercise tolerance test (ETT). During the test, he developed headache without chest pain. It was associated with ST-T change in stage-1 which persisted up to recovery stage. Accordingly sublingual nitrate was given which relieved headache.

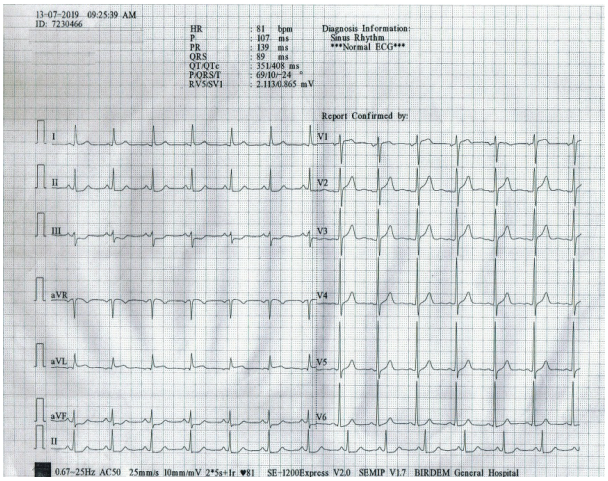

Fig.-1: A) Resting ECG showing mild ST depression at inferior leads

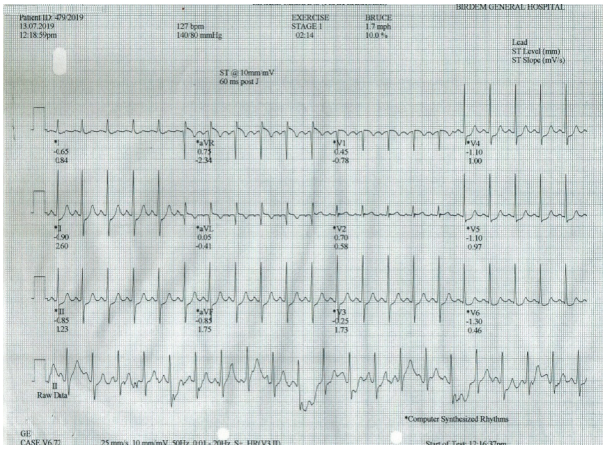

Fig.-1: B) ST change at inferior and lateral leads in stage 1 of ETT

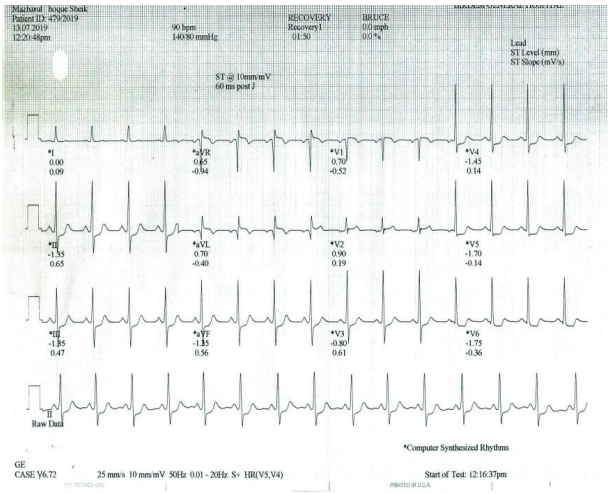

Fig.-1: C) ST change at inferior and lateral leads in recovery stage of ETT

Few days later, coronary angiogram was done which revealed 99% stenosis in proximal Left circumflex coronary artery (LCX), total occlusion of proximal Right coronary artery (RCA) and minor plaques in left anterior descending (LAD) artery at proximal part. Carotid and vertebral arteries were free of disease.

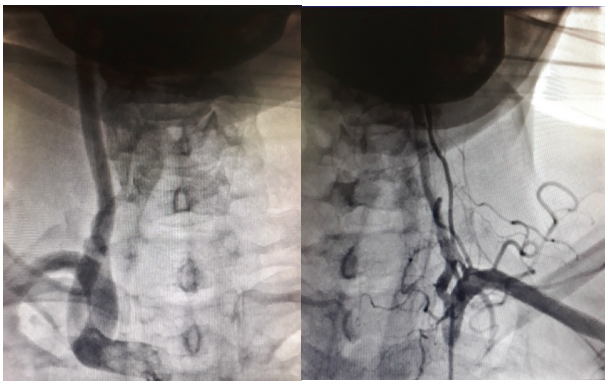

Fig.-2: Angiographic view of Right and left carotid and vertebral artery showing no stenosis.

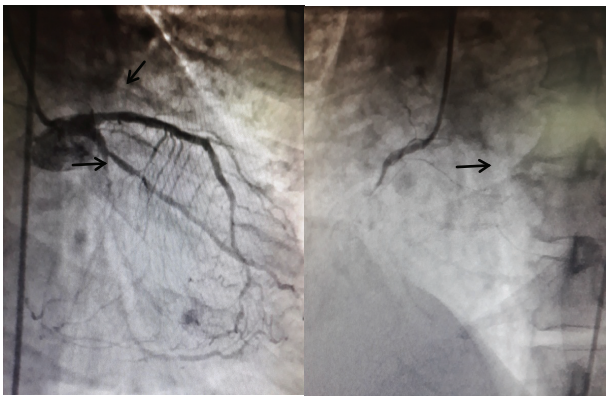

Fig.-3: Coronary angiogram showing diseased coronary vessels.

Patient was advised revascularization with angioplasty. But due to some constraints patient refused to do this and we discharged him with optimum medical management. On follow up visit after one month symptomatic improvement was found with anti anginal drugs.

DIFFERENTIAL DIAGNOSIS

It is important to distinguish cardiac cephalgia from migraine with or without autonomic symptoms and other forms of exertional headache.

DISCUSSION

The term Cardiac Cephalgia was coined by Lipton et al.[4] In 1997 as a form of exertional headache. The diagnosis of

Cardiac cephalgia depends on the presence of severe headache worsened by physical exercise or stress and relieved with rest and or administration of nitrates. The International Headache Society has included Cardiac cephalgia as a specific entity in its international classification of Headache Disorders and proposed diagnostic criteria.[7]

A. Headache, which may be severe, aggravated by exertion and accompanied by nausea and fulfilling criteria "C" and "D".
B. Acute Myocardial ischaemia.
C. Headache develops concomitantly with acute myocardial ischaemia.
D. Headache resolves and does not recur after effective medical therapy for acute myocardial ischaemia or coronary revascularization.

Our case meets each of the mentioned criteria. Cardiac Cephalgia is also called by several synonyms such as angina capitis, angina cranialis or simply as 'headache angina.[5, 6]

Bini et al[5] reviewed 30 cases with cardiac cephalgia and showed a mean age of 62.4 years (range 35-85 years). Pain is usually not localized, and may be unilateral or bilateral. Pain is almost always severe and has been described as having different characteristics. There may or may not be other accompanying symptoms and if there are, 30% may have autonomic in nature. In 27% of the cases headache is the only manifestation of a cardiovascular ischaemia. The headache starts immediately after physical exertion. In 33% cases headache appeared at rest. The frequency of this headache is highly variable and is 57% of patients show ECG abnormalities at rest[7] as well as elevated cardiac enzymes[8] and in the remaining ECG changes appear only during stress.[9]

Four theories have been proposed as a pathophysiologic mechanism. The first suggests that Cardiac cephalgia is a referred pain, as there is a connection between central nervous system (vagus nerve) and the cranial pain afferents (trigeminal nerve) is the upper part of the spinal cord. [4, 10] The second theory proposed that cardiac cephalgia is secondary to elevated intracranial pressure due to venous stasis caused by transient decrease in cardiac output due to ischemic ventricular dysfunction.[4] According to the third theory, it is secondary to the local release in the heart muscle of the chemical mediators capable of inducing remote pain, in this case headache.[4] Among others, serotonin, bradykinin, histamine and substance P have been proposed as potential pain producing substances. The increase in intra-cardiac pressure during anginaattacks could also result in release of natriuretic peptides with consequent vasodilatation of cerebral vasculature resulting in headache.

Finally Cardiac cephalgia could be due to concomitant presence of vasospasm in both coronary and cerebral vasculature.[11]

When the headache occurs as the only manifestation of as acute coronary event, the diagnosis could be difficult if occurred in our case. Useful clues are older age at onset, no previous history of headaches, and presence of risk factors for cardiovascular disease and the onset of headache under stress. Misdiagnosis as migraine and prescribing anti-migraine drug may cause suffering of the patient. Even delayed diagnosis can be fatal. So awareness should be build up among the concerned physicians and further study is needed to see the prevalence of headache in IHD patients.

CONCLUSIONS

Headache is a common symptom associated with various clinical conditions. It is rarely considered in cardiac diseases. Cardiac cephalgia though a very rare condition should not be underestimated. As if not properly addressed it may culminate into serious conditions like acute coronary syndrome and may even be life threatening.When the headache occurs as the only manifestation of an acute coronary event, the clues for suspicion are a) older age at onset, b) no past medical history of headache, c) presence of risk factors for vascular disorders and d) onset of headache under stress[5].

REFERENCES

1. Wei J.H. Wang H.F. Cardiac cephalgia case report and review. Cephalgia International Journal of Headache 2008; 288:892-6
2. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorder, 3rd edition (beta version) Cephalgia 2013; 33:629-808
3. Wasse I. N. Ali A. T. Kalsanevaki A. Z.Cardiac Cephalgia.Cardiol Res 2014; 5(6):195-197
4. Lipton RB, Lowenkopf T, Bajwa ZH, Leckie RS, Ribeiro S, Newman LC, Greenberg MA. Cardiac

cephalgia: a treatable form of exertional headache. Neurology. 1997;49(3):813–816. doi: 10.1212/WNL. 49.3.813.

5. Bini A, Evangelista A, Castellini P, Lambru G, Ferrante T, Manzoni GC, Torelli P. Cardiac cephalgia. The Journal of Headache and Pain. 2009;10:39. doi: 10.1007/s10194-008-0087-x.
6. Sathirapanya P (2004) Anginal cephalgia: a serious form of exertional headache. Cephalalgia 24(3):231–234
7. Seow VK, Chong CF, Wang TL, Ong JR. Severe explosive headache: a sole presentation of acute myocardial infarction in a young man. Am J Emerg Med. 2007;25(2):250–251. doi: 10.1016/j.ajem. 2006.11.014.
8. Korantzopoulos P, Karanikis P, Pappa E, Dimitroula V, Kountouris E, Siogas K (2005) Acute non-St-elevation myocardial infarction presented as occipital headache with impaired level of consciousness. Angiology 56:627–630
9. Lanza GA, Sciahbasi A, Sestito A, Maseri A. Angina pectoris: a headache. Lancet. 2000;356(9234):998. doi: 10.1016/S0140-6736(00)02718-5.
10. Meller ST, Gebhart GF. A critical review of the afferent pathways and the potential chemical mediators involved in cardiac pain. Neuroscience. 1992;48(3):501–524. doi: 10.1016/0306-4522 (92)90398-L.
11. Ramadan NM. Headache caused by raised intracranial pressure and intracranial hypotension. CurrOpin Neurol. 1996;9(3):214–218. doi: 10.1097/00019052 -199606000-00011.

Obituary News September-2019

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

Sl.No.	Name & Address	Age	Date of Death
1	Dr. Md Ahsanul Habib Consultant, Dept. of Cardiac Anesthesiology, Square Hospital		07/5/2019
2	Dr. Parvez Iftekhar Ahmed Palash Associate professor of Nephrology, Dhaka Medical College, Dhaka		15/07/2019
3	Dr. Md. Shahadat Hossain Hazra Civil Surgeon, Hobiganj		21/07/2019
4	Freedom Fighter Dr. Willian Srong Physician & Ex-Student of Mymensingh Medical College (40 Bach)		26/07/2019
5	Dr. Tania Sultana Ex-Student of (FCPS part-2), Dhaka Medical College, Dhaka		26/07/2019
6	Dr. Nigar Nahid Dipu Junior Consultant, Dept. of Radiology & Imaging Kuwait Bangladesh Friendship Hospital	80	03/07/2019
7	Dr. Polas Dey Student of Bagura Medical College (21 Bach)	82	08/08/2019
8	Freedom Fighter Dr. Mujibur Rahman Ex- Joint Secretary, Bangladesh Medical Association (BMA)		14/08/2019
9	Professor Dr. Sayada Nurzahan Bhuiyan Ex- Vice President, Central Executive Committee, BMA	71	29/08/2019

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.

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