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CONTENTS

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- Original papers should have a structured abstract, must not exceed 3,000 words and should not include more than 4-6 illustrations and tables. Each separate part of a figure (a, b, etc.) counts as an illustration. Up to 40 references are permitted.
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ORIGINAL ARTICLES

Association Between Serum C- Reactive Protein With Migraine: A Case Control Study

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Abstract:

Objective: *The present case-control study was undertaken to find the association between serum level of CRP and attack of migraine.* ***Methods:*** *The study was carried out at the Headache Clinic and Outpatient Department of Neurology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka over a period of 2 years from January 2010 to December 2011. Migraine patients attending at the above mentioned places were enrolled as cases, while apparently healthy attendants of cases and other healthy persons, who did not have any history of migraine, were included as control. Based on predefined enrollment criteria, a total of 163 subjects were included in the study. Of them 87 were cases and 76 were controls. The serum levels of CRP of both cases and controls were measured and a serum level of > 6 mg/L was considered as raised/ elevated CRP. Levels of CRP were compared between groups (case and control) using appropriate statistical tests.* ***Result:*** *The findings of the study showed that the age and sex distribution of case and control groups were almost comparable. The behavioral factors like food or smoking habit and tobacco leaf chewing had no difference between the groups. Over 20% of migraine patients had abnormally high CRP as compared to 7.9% in the control group (p = 0.021). The migraine patients were 3(95% CI = 1.1 - 8.1) times more likely to be associated with raised CRP (> 6 mg/L) than their healthy counterparts. There were 7 migraine patients with aura and 80 without aura. The level of CRP was not found to be associated with type of migraine (with or without aura) (p = 0.960).****Conclusion:*** *Every one in five patients exhibits abnormally high CRP. The level of CRP does not vary whether the migraine is being associated with or without aura. The migraineurs carry higher risk of developing elevated CRP than their normal counterparts.*

Key words: *Migraine, C-reactive protein, acute attack etc.*

Introduction:

Migraine is a disorder characterized by recurrent attacks of headache, widely variable in intensity, frequency and duration. Attacks are commonly unilateral and are usually accompanied by anorexia, nausea and vomiting. According to International Headache Society (IHS), migraine constitutes 16% of the primary headaches and it affects 10-20% of general population. About 15-20% women and 10-15% men suffer from migraine[1]. Over two-thirds of migraine sufferers either have never consulted a

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doctor or stopped doing so, which greatly affects quality of life (causing disability). Of the Bangladeshi patients suffering from headache 16.05% had migraine and 12.27% had co-existing migraine and THA[2].

Diagnosis of migraine is made by International Headache Society (IHS) criteria. Headache diary, migraine triggers, medical history, investigations like EEG, CT scan, 3D CT angiogram and MRA of brain (only to exclude secondary causes) are needed to diagnose the disease[3]. Migraine is a risk factor for ischemic stroke, in particular in young woman suffering from migraine with aura[4]. Migraine is also associated with silent brain infarcts and deep white matter lesions detected by magnetic resonance imaging[5]. Both types of brain lesion have been shown to increase stroke risk in the general population[6]. Although the mechanisms underlying the association between migraine and ischemic cerebrovascular disease are unknown, it is believed that inflammation within certain brain tissues resulting from neuronal activation and the subsequent release of proinflammatory neuropeptides from perivascular nerve endings occur during a migraine attack[7,8]. However,

C-reactive protein (CRP), an acute-phase reactant, synthesized by the liver in response to factors released by fat cells (adipocytes) and macrophages[9], has been identified as a sensitive indicator of active systemic inflammation and an independent risk marker for cardiovascular morbidity, including ischemic stroke[10]. A small, uncontrolled retrospective review found abnormal CRP levels in migraineurs[11]. CRP levels rise dramatically during inflammatory processes occurring in the body. It rises above normal limits within 6 hours and peaks at 48 hours depending of the severity of the disease and precipitating cause.

Therefore, CRP values can prove useful in determining disease progress or the effectiveness of treatment. Normal concentration in healthy human serum is usually lower than 6 mg/L, slightly increasing with ageing. Higher levels are found in late pregnant women, mild inflammation and viral infections (10-40 mg/L), active inflammation, bacterial infections (40-200 mg/L) and burns (> 200 mg/L)[12]. As normal concentration of CRP in healthy human serum is usually lower than 6 mg/L, any cut-off value > 6 is considered pathognomic and as a marker of inflammation. In migraine, different inflammatory markers have been observed in the systemic circulation, including increased levels of C-reactive proteins (CRP)[11,13].

Repeated attacks of migraine have been suggested to carry the risk of inflammatory arteriopathy disrupt the vascular endothelial function and structure, ultimately leading to increased risk of atherosclerosis and ischemic stroke in migraine[14,15]. Stroke is the most disabling of all the neurological diseases and poses a huge burden both socially and economically. The treatment is often frustrating and rehabilitation is not readily available. As CRP has been identified as a sensitive indicator of active inflammation and is frequently associated with migraine, abnormally high

CRP in migraineurs could be detected early to prevent ischemic heart disease and stroke.

Materials & Methods:

This case-control study was conducted over a period of period of 2 years from January 2010 to December 2011 at the Headache Clinic and Out-patient Department of Neurology of Bangabandhu Sheikh Mujib Medical University, Dhaka. The study commenced after having ethical clearance from Institutional Review Board of the university. Migraine patients attending at the above mentioned places were enrolled as cases. Healthy attendants of case and other healthy adult persons visiting the OPD of BSMMU, who did not have a history of migraine, were included as control. A total of 87 cases and 76 controls were included in the study. Adult (18 – 50 years) migraine patients (diagnosis was based on International Headache Society criteria) of either sex who were not on prophylactic medications like pizotifen, propanolol, amitryptyline, pizotifen, topiramate, sodium valproate etc. were included in the study. Data were processed and analysed using software SPSS (Statistical Package for Social Sciences) version 11.5. Data presented on categorical scale were compared between groups using Chi-square (χ^2), Fisher's Exact Test, while data presented on continuous scale were compared between groups using Unpaired t-Test. The risk of having elevated CRP in migraineurs was computed with the help of Odds Ratio and its 95% confidence interval. Level of significance was set at 0.05 and $p < 0.05$ were considered significant.

Results:

The age and sex of the case and control groups were almost comparable between groups. Married population was significantly higher in the case group than that in the control group (0.039). Lower middle class people were much higher in the case group (25.3%) than that in the control group (6.6%) (p = 0.001). There was no significant difference between the groups with respect to BMI

(p = 0.089) (Table I). Very few subjects in the case and control groups had smoking and betel-nut chewing habit with no significant intergroup difference (p = 0.609 and p = 0.632). All the subjects in either group were accustomed to Bengali food (Table II).

Majority (97 .7%) of the migraine patients experienced throbbing nature of pain and only 2.3% had dull-aching pain. Nearly three-quarter (74.7%) of patients felt pain of moderate severity, 23% of mild severity and only 2.3% had severe pain. In more than three-quarters (78.1 %) of the cases the pain lasted for 4 - 72 hours and in 21.8% cases it persisted for up to 4 hours. Pain was mainly unilateral (74.7%) followed by bilateral (24.1%) and generalized (1.1%) ((Table III). Of the associated symptoms, over 95% complained of nausea, 77% vomiting, and 28.7% photophobia. Phonophobia, vertigo, insomnia, one-sided weakness and unconsciousness were rarely reported. Some 7(8%) cases have had aura during an attack with visual aura being predominant (85.7%) (Table IV). Comparison of blood pressure between case and control groups did not reveal any significant difference with mean systolic and diastolic blood pressures within normal physiological ranges (p = 0.767 and p = 0.756 respectively) (table V).

The mean C-reactive protein was significantly higher in the case group than that in the control group (p = 0.041). The mean ESR was also significantly higher in the case group than that in the control group (p < 0.001). The case and controls were almost alike with respect to total count of WBC and neutrophil (p = 0.776 and p = 0.190 respectively), but esinophils and lymphocytes were much lower in the case group (p = 0.003 and p = 0.072 respectively) (Table VI). Serum CRP was observed to bear a significantly linear correlation with ESR (r = 0.379, p < 0.001), but it was not found to be correlated with total count of WBC (r = 0.129, p = 0.101) (Fig. 1 & 2).

Table-I

Distribution of demographic characteristics between groups

Demographic characteristics	Groups		p-value
	Case(n = 87)	Control(n = 76)	
Age#	25.6 ± 6.7	25.1 ± 6.8	0.671
Sex*			
Male	25(28.7)	22(28.9)	0.976
Female	62(71.3)	54(71.1)	
Marital status*			
Married	53(60.9)	34(47.7)	0.039s
Unmarried	34(39.1)	42(55.3)	
Residence*			
Urban	50(57.7)	69(90.8)	<0.001s
Rural	37(42.5)	7(9.2)	
Social status*			
Upper-middle class	8(9.2)	17(22.4)	0.001s
Middle class	57(65.5)	54(71.1)	
Lower-middle class	22(25.3)	5(6.6)	
BMI*			
<25	55(63.2)	38(50.0)	0.089
≥25	32(36.8)	38(50.0)	

Figures in the parentheses indicate corresponding %;
*Chi-squared Test (c^2) was done to analyzed the data.

Data were analyzed using Unpaired t-Test and were presented as mean ± SD.

Table-II

Association between behavioral factors and migraine

Behavioral factors	Groups		P value
	Case(n = 87)	Control(n = 76)	
Smoking*	5(5.7)	3(4.0)	0.609
Betel-nut chewing with tobacco leaf**	2(2.3)	2(2.7)	0.632
Food habit (average Bengali food)*	87(100.0)	75(100.0)	——

Figures in the parentheses indicate corresponding %;
*Chi-squared Test (÷2) was done to analyze the data; **Fisher's Exact Test was done to analyze the data.

Table-III

Distribution of patients by detailed history of migraine (n = 87)

Symptoms	Frequency	Percentage
Throbbing	85	97.7
Dull-aching	02	2.3
Severity of pain		
Mild	20	23.0
Moderate	65	74.7
Severe	02	2.3
Duration of each episode		
Up to 4 hours	19	21.8
4-72 hours	68	78.1
Location		
Unilateral	65	74.7
Bilateral	21	24.1
Generalized	01	1.1
Family history of migraine	16	18.4
Antimigraine medications used		
Analgesics/Paracetamol	87	100

Table-IV

Distribution of patients by associated symptoms (n = 87)

Associated symptoms	Frequency	Percentage
Nausea	83	95.4
Vomiting	67	77.0
Photophobia	25	28.7
Phonophobia	3	3.4
Vertigo	2	2.3
Insomnia	01	1.1
Weakness (one-sided)	01	1.1
Unconsciousness	01	1.1
Aura	07	8.0
Type of aura (n = 7)		
Visual	06	85.7
Sensory	01	14.3

Table-V

Comparison of blood pressure between case and control groups

Blood pressure (mm Hg)#	Groups		P value
	Case(n = 87)	Control(n = 76)	
Systolic BP	120.1 ± 10.2	121 ± 10.9	0.767
Diastolic BP	75.0 ± 8.1	74.5 ± 8.5	0.756

Data were analyzed using Unpaired t-Test and were presented as mean ± SD.

Table-VI

Association of inflammatory markers and haematological variables with migraine

Inflammatory markers & haematological variables#	Groups		p-value
	Case(n = 87)	Control(n = 76)	
Serum CRP (mg/L)	5.7 ± 6.1	4.2 ± 6.0	0.041
ESR (mm in 1st hour)	20.3 ± 16.1	11.3 ± 7.5	<0.001
Total count of WBC (/cu-mm)	8700 ± 240	8410 ± 790	0.776
Neutrophil(%)	57 ± 15	64 ± 6	0.190
Lymphocyte(%)	34 ± 8	32 ± 15	0.164
Esinophil (%)	3.6 ± 1.5	2.1 ± 1.0	0.003
Monocyte(%)	3.6 ± 1.5	1.9 ± 1.2	0.072
Basophil(%)	0.8 ± 0.4	0.0 ± 0.0	0.186
Hb (g/dl)	13.0 ± 2.0	14.1 ± 1.0	< 0.001

Data were analyzed using Unpaired t-Test and were presented as mean ± SD.

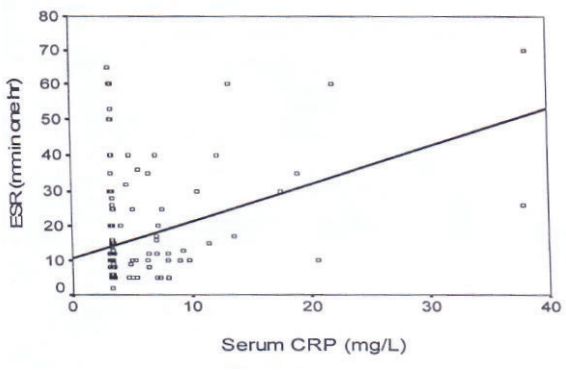

Fig. 1: *Correlation between serum CRP and ESR*

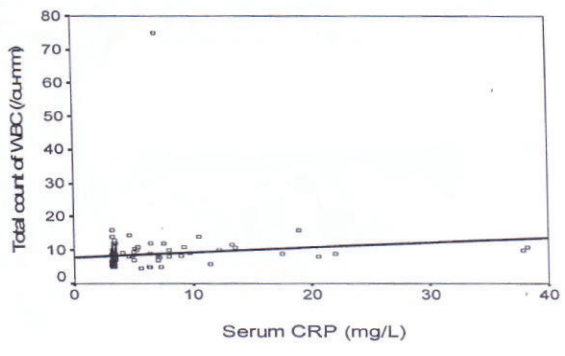

Fig.-2: *Correlation between serum CRP and total count of WBC*

Table VII

Association of CRP with migraine

Serum CRP (mg/L)	Groups		p-value	Odds Ratio
	Case(n = 87)	Control(n = 76)		(95% CI of OR)
> 6 (Raised)	18(20.7)	6(7.9)	0.021	3.1(1.1- 8.1)
≤6 (Normal or low)	69(79.3)	70(92.1)		

Figures in the parentheses indicate corresponding %;
Data were analyzed using Unpaired t-Test and were presented as mean ± SD.

Table-VIII

Association between CRP and migraine with or without aura

Serum CRP (mg/L)**	Migraine		p-value
	With aura(n = 7)	Without aura(n = 80)	
Raised	2(28.6)	16(20.0)	0.960
Normal or low	5(71.4)	64(80.0)	

Figures in the parentheses indicate corresponding %;
**Fisher's Exact Test was done to analyze the data.

Over 20% of the case group had abnormally high CRP (> 6 mg/L) as compared to 7.9% of the control group. The likelihood of having raised CRP in patients with migraine was more than three-fold (95% of CI = 1.1- 8.1) higher than that of their healthy control (p = 0.021) (Table VII). There were 7 migraine patients with aura and 80 without aura. Level of CRP did not differ between migraine with and without aura (p = 0.960) (table VIII).

Discussion:

In the present study, the major demographic characteristics (age and sex) and behavioral factors (food habits, smoking and tobacco leaf chewing) were almost comparable between migraineurs and healthy controls. The mean age of the patients was 25 years with a female preponderance (71%). Smoking habit was very less (5.7%) and betel-nut chewing with tobacco leaf was even less (2.3%). The body mass index (BMI) also did not differ between the groups with mean BMI in case and control groups were 23.8 and 24.8 kg/m^2 respectively. The mean age of the migraineurs were 24.6 years and mean BMI 21.6 kg/m^2 with a female predominance (78 %) and was consistent with other findings[13] but smoking habit was, however, somewhat higher (14%).

In our study, CRP level parallelly increased with ESR as it happens in most of the inflammatory process and as migraine attacks are associated with sterile inflammation[16] and as WBC count did not show any linear increase along with CRP, we can say that this increased level of CRP is not due to infection. But we did not find any similar study which shows the association between ESR and serum CRP level. The age and sex distribution were almost comparable between migraineurs and control subjects and no behavioral factors like food habit or smoking habit, tobacco leaf chewing were any different between the case and control groups, it can be conceived that the raised CRP in the case group is associated with migraine, unless otherwise proved.

It was found that over 20% of migraine patients (cases) exhibited abnormally high CRP (> 6 mg/L) which was almost 3 times more than that found in control group (7.9%) and this raise was not associated with presence or absence of aura (p = 0.934)[11] and found raised CRP in 43% of migraine patients, which compares well with our findings but they found raised CRP level more in without aura group (55.1%) than that of aura group (32.2%), which is not similar with these study. After adjustment for

confounding variables, the relationship between serum CRP and migraine remained significant.

As migraine attacks are accompanied by repeated vascular inflammation of the cranial blood vessels and CRP is a marker of inflammation, repeated attacks of migraine have been suggested to carry the risk of inflammatory arteriopathy of the cranial vessels[16] and consequent thrombosis. Inflammatory processes within the vasculature are well-recognized to play a central part in the pathogenesis of ischemic stroke[17,18]. Repeated episodes of perivascular inflammation during migraine attacks might, therefore, contribute to the increased risk of stroke in migraine[19,20]. The exact mechanisms underlying the association between migraine and ischemic cerebrovascular disease are still elusive. However, it is believed that inflammation within certain brain tissues resulting from neuronal activation and the subsequent release of proinflammatory neuropeptides from perivascular nerve endings occur during a migraine attack[8]. A retrospective review on a small sample found abnormal CRP levels in migraine patients with complex clinical features referred to secondary or tertiary clinics indicating that this protein might play a significant role in the pathogenesis of migraine[11].

The inflammatory process in migraine carries the potential disruption of the vascular endothelial function and structure. This increases the risk of atherosclerosis and vascular diseases. Repeated episodes of perivascular inflammation during migraine attacks might therefore contribute to the increase risk of ischemic stroke in migraine[15]. Stroke is one of the most disabling of all the neurological diseases and in the context of our country it poses a huge social burden. The treatment cost-benefit is frustrating and rehabilitation is not expectedly available. So we should concentrate more on prevention of stroke. As CRP is a marker of inflammation and a risk factor for ischemic stroke[16] , migraine patients should be treated appropriately as early as possible otherwise it will go a long way in controlling migraine and reducing the incidence of ischemic stroke.

Conclusion:

The study concluded that, C-reactive protein is a marker of migraine and migraine is an inflammatory process. More than one-fifth of the patients of migraine possess abnormally high CRP and the level of CRP does not vary whether the migraineurs being associated with or without aura. The migraineurs carry significantly higher risk of developing elevated CRP than their normal counterparts.

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Association of Serum Uric Acid and Parkinson's Disease: A Case Control Study

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Abstract:

Aim*: Recent studies have provided evidence that uric acid (UA) is supposed to play a neuro-protective role in Parkinson's disease (PD). Uric acid is a natural antioxidant that may reduce oxidative stress, a mechanism thought to play a role in the pathogenesis of PD. This study aimed to evaluate whether the serum UA level was associated with PD in a relatively small population of Bangladeshi patients.* ***Materials and methods:*** *An observational prospective case control Study was conducted in Neurology department of Sir Salimullah Medical College & Mitford Hospital including both the male and female wards during July 2012 to December 2013. Serum uric acid were determined from 40 PD patients and compared with 70 age and sex matched control; following the uric acid colorimetric method, the serum creatinine (Scr) levels were also measured to reduce the bias caused by possible differences in renal excretion function. Data were analyzed with software SPSS 16 and statistical descriptive methods (mean percentage, SD) and* t*-test.* ***Result:*** *In this study, 22 men (55%) and 18 women (45%) with PD were evaluated. The mean serum uric acid in patients was 3.7±0.97 and in the control group was 5.32 ±0.44. This difference was statistically significant.(p=0.001) Also, the mean serum uric acid in both men (3.48±0.98) and women (4.1±1.17) patients group was statistically lower than both men (5.39±0.46) and women (5.17±0.35) in control group.(p=0.001).* ***Conclusion:*** *This present study showed a positive association between low serum UA and PD .*

Key Word: *Serum Uric Acid, Parkinson's disease*

Abbreviation: *Uric Acid(UA), Parkinson's disease(PD)*

Introduction:

PD is the second commonest neurodegenerative disease, clinically characterized by rest tremor, rigidity, bradykinesia, and gait impairment and pathologically, there are degeneration of dopaminergic neurons in the substantia nigra pars compacta, reduced striatal dopamine, and intracytoplasmic proteinaceous inclusions known as Lewy bodies [1].

UA is the final oxidation product of purine metabolism and is excreted in urine. It is a marker of oxidative stress, and may have a potential therapeutic role as an antioxidant [2,3].

It is reported that uric acid could suppress oxidative stress and prevent dopaminergic cell death in animal models of Parkinson's disease. Reduced UA levels have been found not only in the substantia nigra but

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also in the cerebrospinal fluid and serum of PD patients[4,5,6]

The association between UA and risk of PD has been investigated in several previous prospective studies and higher serum uric acid levels might have been correlated to a significantly reduced risk of PD [7,8]. There is also evidence that higher uric acid levels could slow the clinical progression of PD [9,10].

Some recent studies show that UA can decrease the onset of the disease or its intensity, because of having the antioxidant effects and this effect must be considered in the therapeutic process of the disease [11]. Some other studies indicate that high uric acid levels lead to the decrease of the free radicals and subsequently the onset of the disease [3].

Another 14 years period research in America revealed that the risk of onset of PD in people with higher dietary intake of uric acid index was much lower than others; instead, the onset of Gout and renal stones was higher than other people [7,12]. Some studies also show that the risk of PD is much lower in patients suffering from Gout [13,14].

Despite the above researches, results of the recent researches are not yet adequate for a general conclusion. Yet there are many studies indicating the need for more investigations, [5,15,16,17].

Here, with considering the above studies, we would like to embark on measuring the serum UA levels in PD patients in Bangladesh to find out their association, so that the study result might open new era of future research regarding alternative management of PD.

Materials and Methods:

This is a observational prospective case control study, carried out on Parkinson patients in the Department of Neurology of Sir Salimullah Medical College & Mitford Hospital, Dhaka Bangladesh from July 2012 to December 2013. Being manifested with the disease was confirmed through clinical examinations by a neurologist and the Para clinical measures according to Brain Bank clinical criteria for diagnosis of Parkinson's disease. All of the patients suffering from Gout, blood diseases and vasculitis, those who had a history of using the drugs effective on the uric acid levels (Corticosteroids, Colchicine, Alluporinol), and also the patients taking medications other than the anti – Parkinson drugs were excluded from the study. Then, 40 patients were included in the research. Meanwhile, 70 people of age and sex matched healthy individual from patient's attendants and yet had taken no specific medications were selected as the control group. The ethical committee of the Sir Salimullah Medical College, Dhaka, Bangladesh had approved the research. The serum uric acid levels were measured by milligram per deciliter, and the results were evaluated with 95% confidential interval. The values were registered with the demographic information of the questionnaire and were statistically analyzed by the use of the SPSS-16 software, the descriptive statistics methods (the number of percentage and average) and the analytic statistics (comparing the mean and the T- test and ANOVA).

Results:

In this study, the age distribution of study population in case group 15(37.5%) patients belonged to age 71-80 years and their mean age was found 69.15±10.08 years. In control group, 27(38.6%) patients belonged to 51-60 years and their mean age was 67.14±10.25 years. The mean age difference was not statistically significant ($p>0.05$) between two groups.(Table:I)

The observation of sex distribution of the study was, male 22(55.0%) and female 18(45.0%) in case group. The male were 40(57.1%) and female were 30(42.9%) in control group. Male female ratio was found 1.22:1 & 1.33:1 in case and control group respectively. The difference was not statistically significant ($p>0.05$) between two groups.(Table:II)

In Table III shows serum uric acid of the study population. It was observed that mean serum uric acid was found 3.7±0.97 mg/dl in case group and 5.32±0.44 mg/dl in control group. The mean difference was statistically significant ($p<0.05$) between two groups.

Table-I

Distribution of the study population by age (n=110)

Age (in years)	Case (n=40)		Control (n=70)		P value
	No	%	No	%	
d”50	2	5.0	1	1.4	
51-60	8	20.0	27	38.6	
61-70	13	32.5	24	34.3	
71-80	15	37.5	9	12.9	
>80	2	5.0	9	12.9	
Mean±SD	69.15±10.08		67.14±10.25		0.321ns
Range (min, max)	48,100		50,90		

ns= not significant
P value reached from unpaired t-test

Table-II

Distribution of the study population by sex (n=110)

Sex	Case (n=40)		Control (n=70)		P value
	No	%	No	%	
Male	22	55.0	40	57.1	0.827ns
Female	18	45.0	30	42.9	

ns= not significant
P value reached from chi square test

Table-III

Distribution of the study population by serum uric acid (n=110)

	Case (n=40)		Control (n=70)		P value
	Mean	±SD	Mean	±SD	
Serum uric acid (mg/dl)	3.7	±0.97	5.32	±0.44	0.001s
Range (min,max)	1.8	,5.8	4.5	,6.2	

s= significant
P value reached from unpaired t-test

Discussion:

This observational prospective case control study was carried out with an aim to determine the relation of serum UA level with prevalence of PD and also to find out the correlation of UA with severity of PD.

In this study it was observed that in case group 37.5% patients were in 8th decade and their mean age was 69.15±10.08 years, varied 48 – 100 years. In control, 38.6% patients were in 6th decade and their mean age was 67.14±10.25 years, varied 50 – 90 years. The mean age was almost alike between the two groups. In a recent research showed that the mean age of male patients of the control group was 64.7±6.4 years and the mean age of the female patients of the control group was 63.2±5.6 years[18]. There were no statistical differences between the mean ages of the estimated groups. 20 % of patients were under 60, 18% between 61–65, 28% were between 66–70 and 34% were more than 70 years old, which is consistent with the current study[18]. Another researcher mentioned in his study that one in seven patients with PD is under the age of 50 years, and there is an increase in prevalence with increasing age[19]. In this study only 5% of patients were 50 years or below which is much lower than that of previous study. The prevalence of PD in

industrialized countries is thought to be approximately 0.3%[20]. This rises to 1.0% in people over the age of 60 and 3% in people over 80 years[21]. In the UK, PD is estimated to affect 100–180 per 100,000 of the population and has an annual incidence of 4–20 per 100,000[22]. Finding of present study regarding age also consistent with these previous studies.

In this study it was observed that male was 55.0% and 57.1% in case and control group respectively, which indicates that Parkinson's disease is more common in male subjects. Male to female ratio was 1.2:1 in case group and 1.3:1 in control group. The difference was not statistically significant ($p>0.05$) between two groups. In a recent research showed, 52.0% of the people in both groups of case and control were males and 48.0% were females[18]. A similar previous study showed 53.8% were males and 46.2% were females[23]. Our present study supports previous studies.

In this present study it was observed that mean ± SD serum uric acid was 3.7±0.97 mg/dl varied from 1.8 to 5.8 mg/dl in case group and 5.32±0.44 mg/dl varied from 4.5 to 6.2 mg/dl in control group. The mean serum uric acid level was significantly lower in case group ($p<0.05$). Similarly, it was observed that the mean uric acid levels were 4.79±1.21 mg/dl in the patients group, and it was 5.85±1.14 mg/dl in the control group[18]. The serum uric acid levels in the case group was significantly lower than the control group ($p<0.001$), which also consistent with the current study[18]. When compared male and female individually it was observed that serum uric acid was significantly lower in Parkinson's disease patients of both male and female separately. [3.48±0.98 mg/dl Vs 5.39±0.46 mg/dl ($p<0.05$) in male and 4.1±1.17 mg/dl Vs 5.17±0.35 mg/dl ($p<0.05$) in female]. A recent study observed that the mean uric acid levels were significantly lower when compared male and female separately (4.87 ±1.2 mg/dl and 4.70 ± 1.23 mg/dl in male and female cases respectively Vs 5.42 ±1.25 mg/dl and 5.91 ± 1.62 mg/dl in male and female controls respectively) which is supported by this study[18].

Evaluation of serum uric acid level with disease severity observed that though it is not statistically significant; mean serum uric acid level was steadily lower with disease severity in stage II to IV but in stage V there was a slight raise of serum uric acid level than that of stage IV. Schwarzschild et al. did a large prospective study among subjects in the early stages of PD enrolled in a randomized clinical trial and found that the rate of progression declined with increasing level of serum urate level [10]. Another study had observed among subjects with early PD participating in a large randomized trial, that both serum and CSF urate concentrations measured at baseline were inversely related to clinical progression of PD[6]. But a discriminating report was found in the study by Hau and Eugene, who observed that there was no significant correlation serum uric acid level and staging of PD except a trend of lower uric acid level in stage 5 patients[24].

There was no relationship between the uric acid and the duration of illness (Table II), and this was in line with other studies. More researches still deem necessary in this area [25-27]. The main limitation of the research was the lack of comparison between the serum uric acid levels and the severity of illness which has to be considered in future studies [28-30].

Conclusion:

This present study showed that the uric acid levels in the Parkinson's patients were lower than healthy people. This means that the decrease of the uric acid levels lead to more outbreak of Parkinson both in men and women. This finding confirms the previous studies, emphasizes on the role of uric acid levels on the PD, and also indicates the necessity of more studies specially the cohort studies to achieve a final result and to clarify a part of the treatment process.

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Authors' Contributions:

All authors had equal role in design, work, statistical analysis and manuscript writing.

Conflict of Interest:

The authors declare no conflict of interest.

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A Study of Surgical Outcome of Supratentorial Meningioma

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Abstract:

This was descriptive study. This study was carried out at the Department of Neurosurgery Bangabandhu Sheikh Mujib Medical University from April 2010 to April 2014. We have studied 35 cases. After collecting patients admission data, a brief history and clinical examination was done. Supratentorial meningioma was diagnosed primarily by contrast CT scan and MRI of brain which was confirmed by surgery & histopathological examination. After surgery close follow up were done. Most of the sufferer were female 19(54%). The commonest age group was 40-59 years (37.14%). The commonest site of tumors were frontal convexity8(22.9%) and the commonest histological types were meningotheliomatous 12 (34.3%). All of the patients were undergone surgery. Majority of patients were improved after treatment 31(88.6%).

Key words: *Meningioma, craniotomy, intracranial pressure, Computerized Tomography scan, Magnetic Resonance Imaging*

Introduction:

The term meningioma is the noncommittal all encompassing name coined by Harvey Cushing, for this tumor of the meninges which is usually benign[1]. Meningiomas account for 15% of intracranial tumors. They commonly occur in the fourth to sixth decades. Females have meningiomas more than males and this varies according to site from a ratio of 3:2 in the supratentorial area. Ninety per cent of meningiomas are intracranial and of these about 90% are supratentorial.

As with virtually all other brain tumors the etiology of menigiomas is unknown. Cases exist however in which the tumor has arisen under a fracture from an area of scarred dura or around a retained foreign body,[2] conceivably these factors contributed to the formation of the mennigiomas but there is no definitive in meningioma formation especially during child hood[3].

Neuro fibromatosis I and 2 (NF-I and NF-2) genetic diseases inherited in autosomal dominant fashion may be associated with meningiomas.

The arachnoidal cap cells are most prevalent near collection as of arachonoid villi at the dural – venous sinuses and their large tributaries meningiomas may arise anywhere the cap cells are located[4].

Meningiomas are well demarcated round or oval and frequently multilobulated. They are firm and pink and vary in consistency from soft and easily aspirable to rock hard[5].

According to the site, the distribution meningioma are followers: convexity, parasaggittal, falx, olfactory groove, tuberculum Sella, sphenoid ridge, posterior fosa, intraventricular, intraorbital[6].

Methodology:

This was a descriptive cross sectional study, which was carried out at the Department of neurosurgery BSMMU from April 2010 to April 2014. A total of 35 cases were selected before entry to the study and an informed written consent was taken from each patient. A structured questionnaire was made and data were collected. Diagnosis was confirmed by CT scan and MRI of brain and histopathological examination. The study was analysed by SPSS program.

Results:

A total of 35 patients were included in the Study (table I). Out of the female (54.60%) outnumbered the male (table II). The age group of 40-59 years gripped the major proportion (34.14%) of patients. Headache was the commonest (71.4%) presenting symptoms followed by vomiting (34.38%). Hemiparesis (51.14%) was the presenting symptoms and followed by vomiting (34.38%).

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Hemiparesis (51.14%) was the findings major proportion of patients (table III & IV).

The commonest site of lesion (table V) was frontal convexity (22.9%). Meningotheliomatous (34.31%) was the major varieties of lesion (table VI). All of the patient were treated by surgery (table VII). Only eight patient develop different complication (table-VIII). After surgery about 88.6% improved, 8.6% deteriorated and one died (table IX).

Table-I

Distribution of the patients by age (n=35)

Age	Number	Percentages (%)
>20	05	14.3
20-39	12	34.38
40-59	13	37.14
<60	05	14.3
Total	35	100

Table-II

Distribution of the patient by sex (n=35)

Sex	Number	Percentages (%)
Male	16	45.4
Female	19	54.6
Total	35	100

Table-III

Distribution of the patient by presenting symptoms

Presenting Symptoms	Numbers	Percentages
Headache	25	71.4
Vomiting	12	34.38
Convulsion	12	34.35
Altered Consciousness	5	14.3
Visual blurring	5	14.3

Table-IV

Distribution of patients by clinical findings

Clinical Features	Numbers	Percentages
Impaired higherPsychic functions	12	34.38
Cranial nerve palsy	7	20
Hemi paresis	18	51.14
Mono paresis	12	34.38

Table-V

Distribution of patients by the site of lesions (n =35)

Site	Numbers	Percentages
Frontal convexity	8	22.9
Sphenoid wing	8	22.9
Fronto-Parietal convexity	6	17.1
Parietal convexity	5	14.3
Temporal	3	8.6
Olfactory groove	1	2.9
Falcine	2	5.7
Sellar	1	2.9
Optic nerve sheath meningioma	1	2.9
Total	35	100%

Table-VI

Distribution of patients by histologicals types of the tumor (n=35)

Histological Types of the tumor	Who Grade	Number	Percentage
Meningotheliomatous	I	12	34.3
Fibrous	I	8	22.9
Transitional	I	6	17.1
Psammomatous meningioma	I	4	11.4
Angiomatous Atypical meningioma	I	2	5.7
Atypical meningioma	II	2	5.7
Anaplastic Meningioma	III	1	2.9

Table-VII

Distribution of patients by treatments options (n=35)

Treatment Option	Number	Percentages
Surgery	34	97.1
Surgery+Gammaknife surgery	1	2.9

Table-VIII

Distribution of patients by post operative complication (n=35)

Complication	Number	Percentages
Post operative haematoma	3	8.6
Seizure	2	5.7
Limb weakness	1	2.9
Cranial nerve palsy	1	2.9
Brain edema	1	2.9

Table-IX

Distribution of patients by outcome after treatment (n=35)

Outcome	Number	Percentages
Improved	31	88.6
Deteriorate	3	8.6
Death	1	2.8

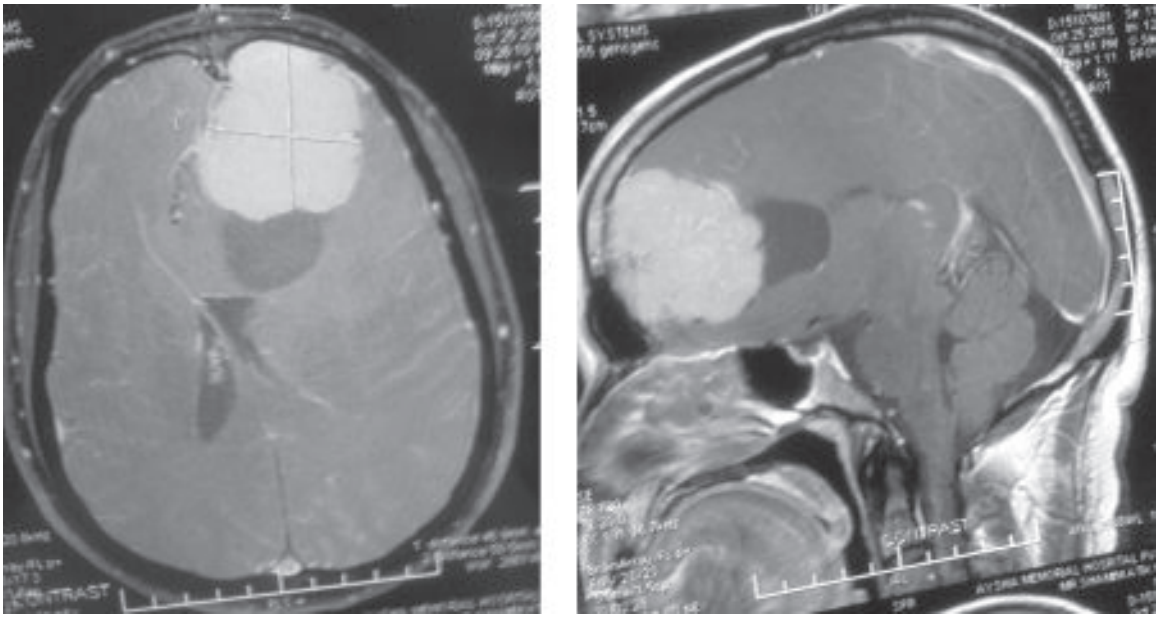

Fig. -1: *Frontal falcine meningioma axial & saggital section*

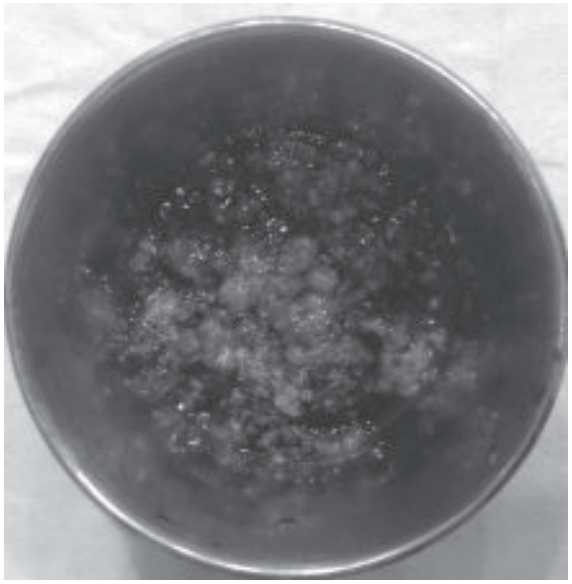

Fig. -2: *Excise tumor*

Fig. -3: *Postoperative patient after three months*

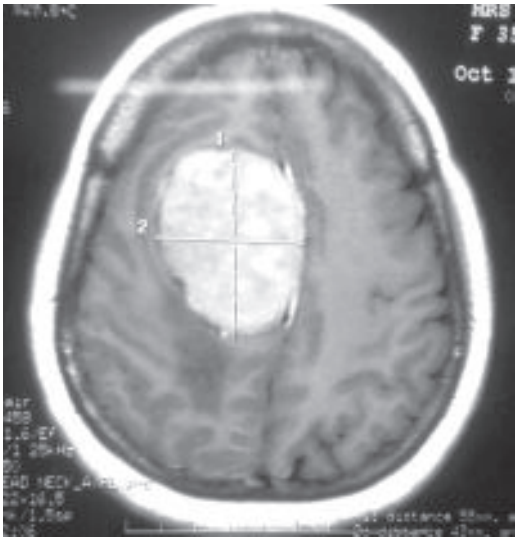

Fig. -4: *Frontoparital convexcity & paragittal meningioma*

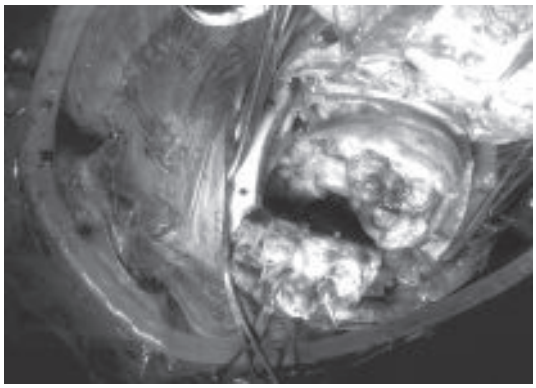

Fig. -5: *Peroperative photograph*

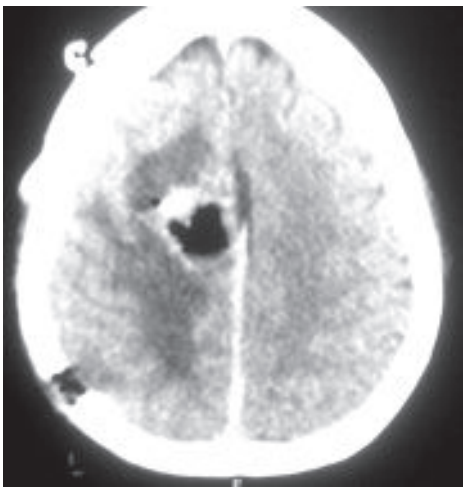

Fig. -6: *Postoperative photograph*

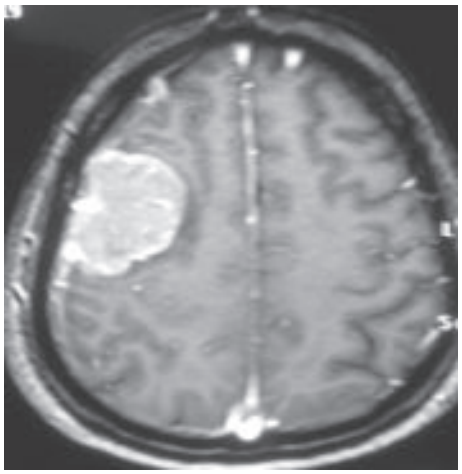

Fig. -7: *Right frontoparietal meningioma*

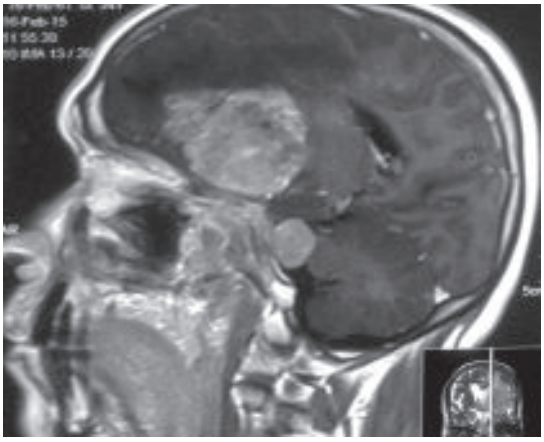

Fig.-8: *Frontotemporal meningioma*

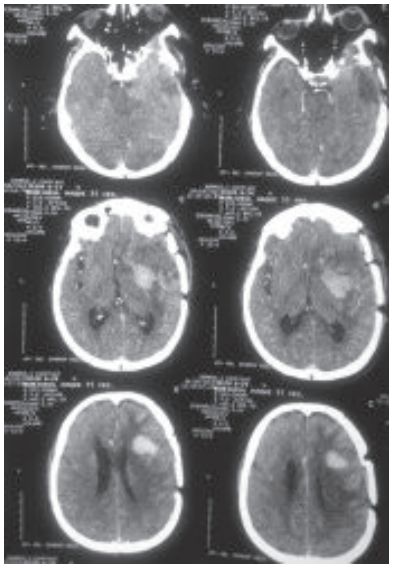

Fig.-9: *Postoperative film with hematoma*

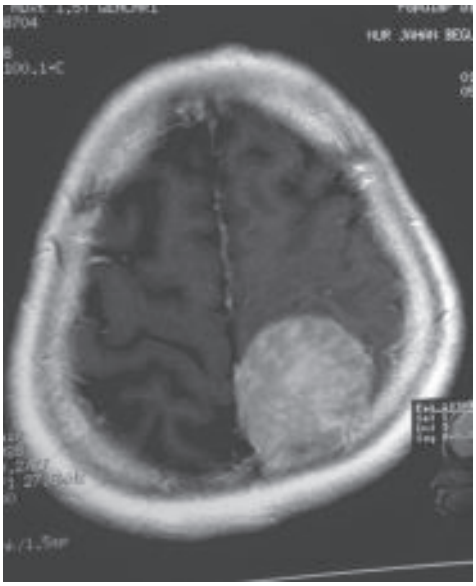

Fig.-10*: Left parietal meningioma*

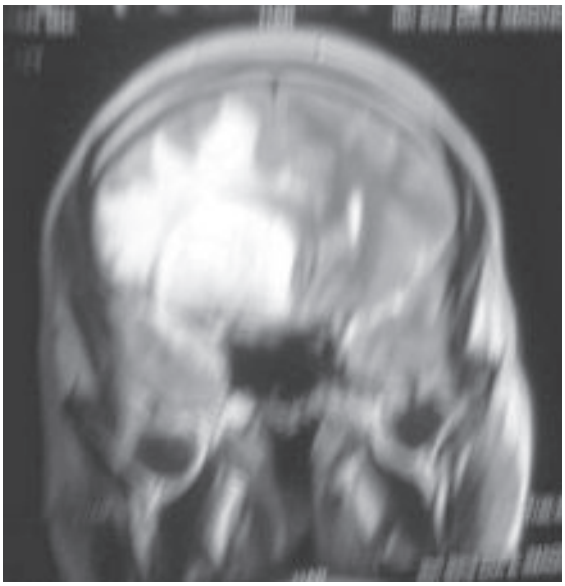

Fig.-11*: Right sphenoid wing meningioma*

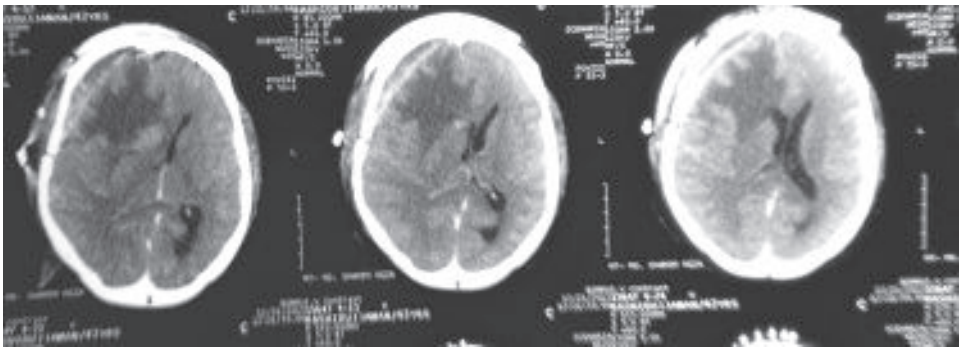

Fig.-12*: Postoperative scan*

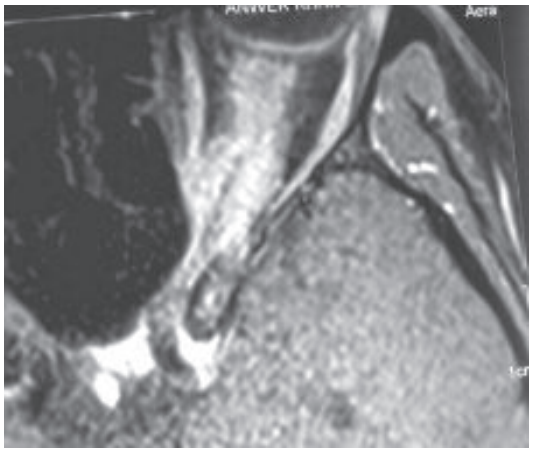

Fig.-13*: Left optic nerve sheath meningioma*

Discussion:

This was descriptive study which was carried out at the Department of Neurosurgery, BSMMU. The female & male ratio of patients were 19:1 which was more or less concomitant with the study of Perry A[7]. The result of that study reveled female & male ratio were 18:1

It was documented in a study the prevalence was more at 4th to 6th decade[8].

In this study where the age group of 40-59 years were the major proportion of patients (37.14%). The second highest proportion of age group were 20-39 years (31.38%).

In this series the commonest sites of tumors were frontal convexity meningioma i.e. frontal & anterior to the central sulcus.

In a study the majority of histological types were meningotheliomatous 08(32%). In previous study meningotheliomatous was the commonest type in this study 21(84%) patients improved after surgery, 8.4% patients remain same as before, 8.4% patients were detoriorated after surgery, previous study shows surgery was the treatment of choice in meningioma[9].

In this study (2.9%) only one patient was treated by radiotherapy+ surgery in previous study 32% of patient was treated by partial resection with radiotherapy[10].

Conclusion:

The present study was concluded that surgery is, the choice of treatment of meningiomia and further study is recommended.

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A Study of Pituitary Adenoma Surgery: Transphenoidal Microscopic Versus Endoscopic Endonasal Approach

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Abstract:

Background: *Transphenoidal endoscopic approach is minimal invasive surgery in case of pituitary adenoma.* ***Objective :*** *To see the outcome of transphenoidal endoscopic and microscopic approach in case of pituitary tumor.* ***Results :*** *This study showed among the 37 patients, 25 (67.6%) were done by transphenoidal microscopic approach and 12 (32.4%) patients were done by endonasal endoscopic approach. Among the 12 patients 8(66.7%) were male and 4(33.3%) were female. Among the 25, patients 15(60%) were male and 10(40%) were female. It was documented that in 12 patients, 10(83.3%) were macroadenoma and 2(16.7%) were microadenoma. It was evident that among the 25 patient 18(72%) were macroadenoma and 7(28%) were microadenoma. Among 12 patients, 11 (91.7%) had preoperative visual disturbance and 1(8.3%) had normal vision. It was observed that among 25 patients, 23(92%) patients had preoperative visual disturbance and 2 (8%) patients had normal vision. Tumor was totally removed in 9(75%) patients in endoscopic approach and 14(56%) in microscopic approach. Clinically 10(83.3%) patients were improved in endoscopically and 16(64%) patients were improved in microscopic group.* ***Conclusion:*** *It was concluded that endoscopic endonasal approach is better than transphenoidal microscopic approach.*

Key word: *Pituitary adenoma, transphenoidal approach, endoscopic endonasal approach, microscopic approach, acromegally, cushing's syndrome.*

Introduction:

Pituitary adenomas are the third most common intracranial neoplasm, accounting for 10%–25% of intracranial neoplasms with a prevalence of 16.9% in autopsy studies[1].

In March 1907, Schloffer reported the first successful removal of a pituitary tumor via a superior nasal transsphenoidal approach, which was based on Giordano's experimental work[2]. The sublabial transsphenoidal route to the sella turcica, originally pioneered by Harvey Cushing[3].

In 1967, Hardy introduced the use of the operating microscope for this procedure and developed and designed his own microsurgical instrumentation, which transformed transsphenoidal surgery.The excellent visualization and surgical results provided by the endoscope in sinus surgery have prompted neurosurgeons to explore its potential application to transsphenoidal surgery[4].

The endonasal microscopic transsphenoidal approach has several variations, including the transseptal submucosal technique, the septal pushover and the direct sphenoidotomy[5].

Authors reported the first use of the endoscope in pituitary surgery in 1978 but its application to the sella turcica did not grow in popularity, however, until the mid-1990s, when endoscopic sinus surgery had virtually replaced conventional open techniques in use by otolaryngologists for the treatment of inflammatory sinonasal disorders. Many modifications of the transsphenoidal approach have been developed; they range from sublabial transnasal, transnasal, and pure endonasal endoscopic approaches and are used with an

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increasing popularity in endoscopic over microscopic procedures[6].

Technological advances in the areas of endoscope-assisted microneurosurgery, frameless stereotaxy and three-dimensional computer-assisted neuronavigation, color Doppler ultrasonography and real-time intraoperative magnetic resonance imaging have been applied to the classic transsphenoidal operation.

Methods:

It was a prospective cross sectional study. Sampling technique was purposive consecutive. Total 25 cases of pituitary adenoma by transphenoidal microscopic approach and 12 cases were done by endonasal endoscopic approach from January 2010 to December 2014 at the Department of Neurosurgery, Bangababdhu Sheikh Mujib Medical University, Dhaka. Patients with pituitary adenoma who had visual impairment and hormonal imbalance requiring surgery for it and who had post-operative histological confirmation of pituitary adenoma were included in this study. Exclusion criteria are patients who had concomitant intra-ocular disease making visual assessment difficult, systemic disorders other than pituitary adenoma that affected visual function, presence of any other intracranial pathology. Data were collected pre-designed data collection sheet. Data were analysis using computer based programme statistical package for social science (SPSS) for windows version 20.

Operation procedure:

Under general anaesthesia with supine position head is raised slightly from body. Nose was parallel to the floor, head was 20^0 flexed and rotated to left shoulder, surgeon will stand towards the right shoulder. Disinfectant was used providone iodine soaked gauze. Killian type nasal speculum and Hardy nasal speculum were used. The middle turbinate was identified and passage was make between the narrow space of middle turbinate and nasal septum. Ostium of sphenoidal air sinus and choana were identified.

Bilaterally nasal mucosa was dissected. Hadat flap were made those who were operated by endoscopic approach. Keel of the vomer was identified and was removed. Anterior wall of sphenoidal air sinus, sinus cavity, sinus mucosa and posterior wall of sphenoidal air sinus was removed. Dura was opened after coagulation and tumour was excised by suction ring currete and micro ronger. Seller floor was reconstructed and nasal pack was given with ribbon gauze and merocele.

Results:

Table-I

Sex distribution of patients by sex

Sex	Endoscopic group (n=12)		Microscopic group (n=25)		P value
	No	%	No	%	
Male	8	66.7	16	64.0	0.873
Female	4	33.3	9	36.0	

Table-I shows male predominated than female.

Table-II

Distribution of the patients by age

Age	Endoscopic group (n=12)		Microscopic group (n=25)		P value
	No	%	No	%	
<20	1	8.3	1	4.0	0.547
21-39	4	33.3	4	16.0	
40-59	5	41.6	16	64.0	
≥60	2	16.6	4	16.0	

It was evident that 40-59 years age group belongs to the highest group.

Table-III

Distribution of patients by the size

Size	Endoscopic group (n=12)		Microscopic group (n=25)		P value
	No	%	No	%	
Microadenoma	2	16.6	7	28.0	0.329
Macroadenoma	10	83.3	18	72.0	

It was documented that macroadenema occupied 83.37 in endoscopic group & 72% in microscopic group.

Table-IV

Distribution patients by visual disturbance

Sex	Endoscopic group (n=12)		Microscopic group (n=25)		P value
	No	%	No	%	
Normal vision	1	8.3	2	8.0	0.876
Blind of only one eye with temporal hemianopia other eye	4	33.3	5	20.0	
Bilateral papiloedema	1	8.3	1	4.0	
Complete blindness	3	24.9	5	20.0	
Bitemporal haemianopia	2	16.6	7	28.0	
Bilateral hand movement only	1	8.3	5	20.	

Table-V

Distribution of patients with pituitary apoplexy

	Endoscopic group (n=12)		Microscopic group (n=25)		P value
	No	%	No	%	
Present	1	8.3	3	12.0	0.7366
Absent	11	91.3	22	88.0	

Pituitary apoplexy was present 8.3% in endoscopic group & 12.8 in microscopic group.

Table-VI

Distribution of patients by functional types of tumour

	Endoscopic group (n=12)		Microscopic group (n=25)		P value
	No	%	No	%	
Non functional tumour	3	24.9	7	28.0	0.944
Acromegally	3	24.9	7	28.0	
Giantism	0	00	1	4.0	
Prolactinoma	5	41.7	8	32.0	
Cortisol secreting tumour		1	8.3	2	8.0

Majority of tumor were prolactinoma in (endoscopic had group 41.71 and microscopic group had 32.6%).

Table-VII

Distribution of the patients by excision of tumour

	Endoscopic group (n=12)		Microscopic group (n=25)		P value
	No	%	No	%	
Total resection	9	75.0	14	56.0	0.474
Subtotal resection	2	16.6	9	36.0	
Partial resection	1	8.3	2	8.0	

Table VII showed 75% tumors were excised totally (endoscopically & 56% tumors were excised microscopically).

Table-VIII

Distribution of the patients by postoperative complication

	Endoscopic group (n=12)		Microscopic group (n=25)		P value
	No	%	No	%	
Diabetes insipidus	5	41.6	14	52.0	0.808
Cerebral salt wasting	2	16.6	4	12.0	
CSF leakage	1	8.3	3	12.0	
Pnemocephalus	0	00	1	4.0	
Intracerebral haemorrhage	0	00	1	4.0	
SIADH	0	00	1	4.0	
Meningitis	0	00	1	4.0	
Septal perforation	0	00	1	4.0	

Table VIII showed different complications after surgery (i.e. endoscopic and microscopic groups).

Table-IX

Distribution of patients by postoperative outcome of tumour

	Endoscopic group (n=12)		Microscopic group (n=25)		P value
	No	%	No	%	
Visual status					
Improved	10	83.3	16	64.0	0.159
Same as before	1	8.3	7	28.0	
Deterioration	1	8.3	2	8.0	
Hormonal status					
Improved	6	50	12	48	0.835
Same as before	5	41.8	12	48	
Deterioration	1	8.3	1	4	

The table IX showed that 83.3% patient's visual status had imrpved endoscopic surgery & 64% had improved microscopic surgery.

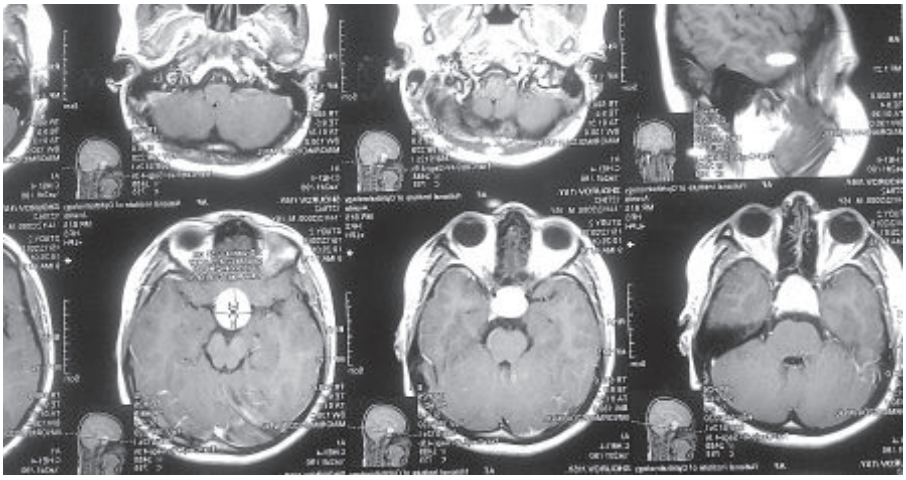


Fig. 1: *Preoperative MRI show macroadenoma (Axial)*

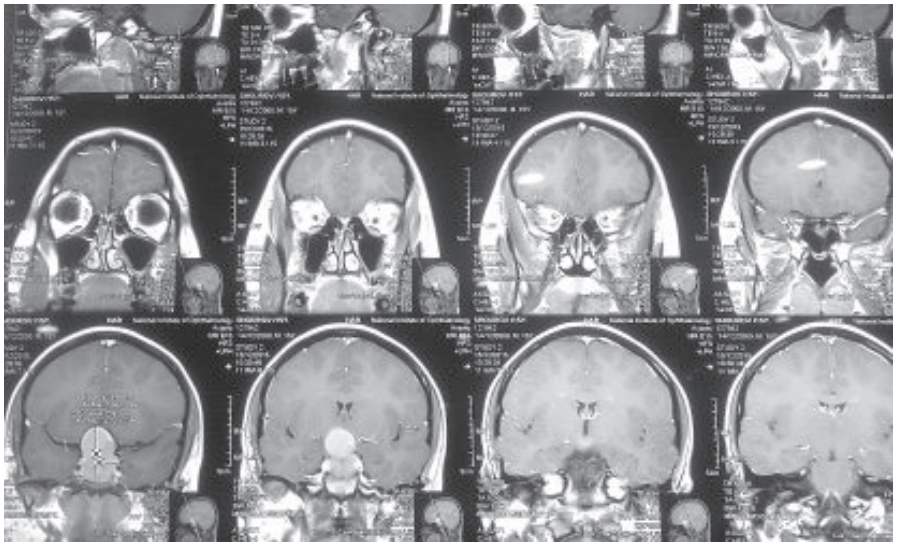


Fig. 2: *Preoperative MRI show macroadenoma (Coronal)*

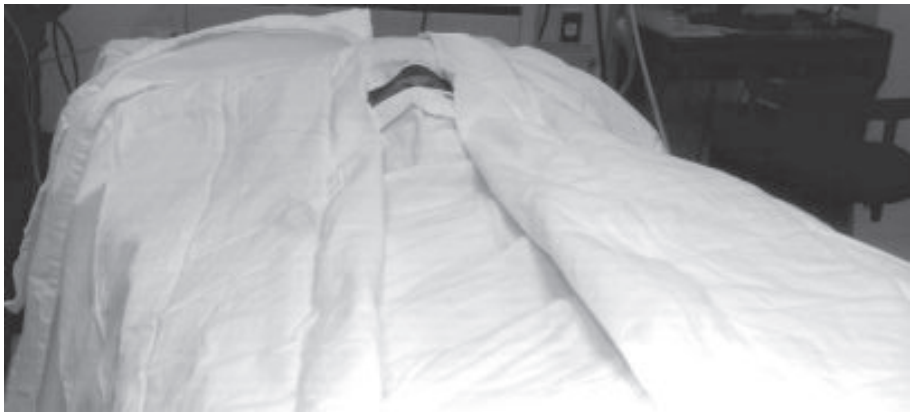


Fig. 3: *Peroperative photograph after drapping of the patient*

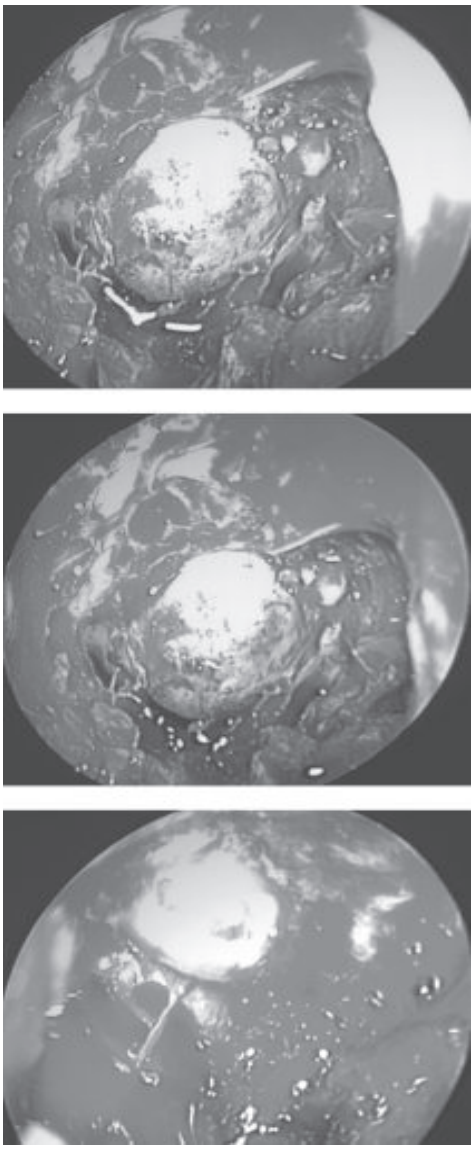


Fig. 4: *Endoscopic preoperative photograph of the tumour in different view*

Fig. 5: *Postoperative photograph*

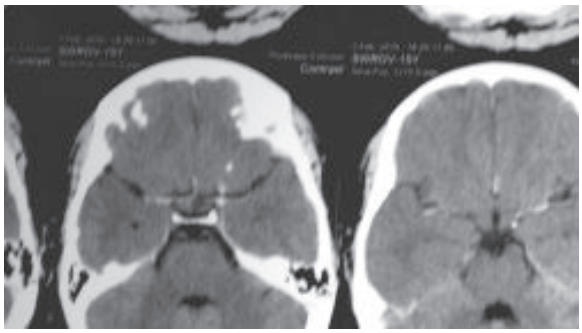
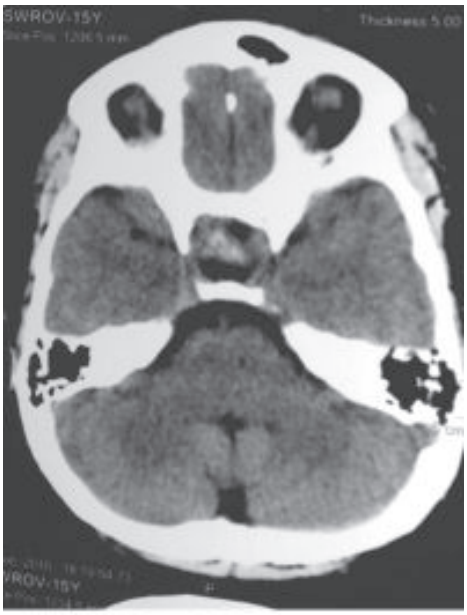


Fig. 6: *Postoperative CT-scan with contrast*



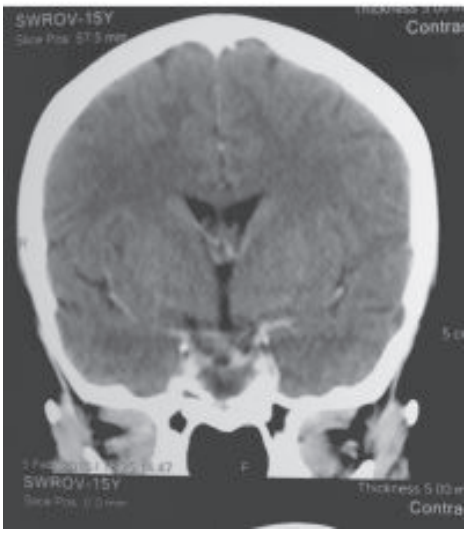


Fig. 7: *Peroperative view*

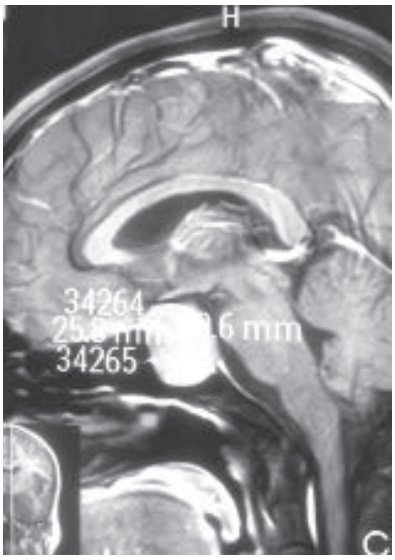


Fig. 8: *Postoperative CT-scan with contrast in different view*

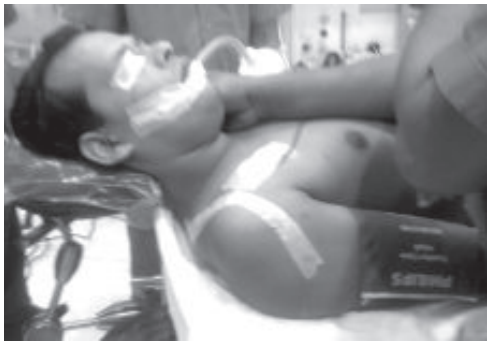


Fig.-9: *Preoperative view*

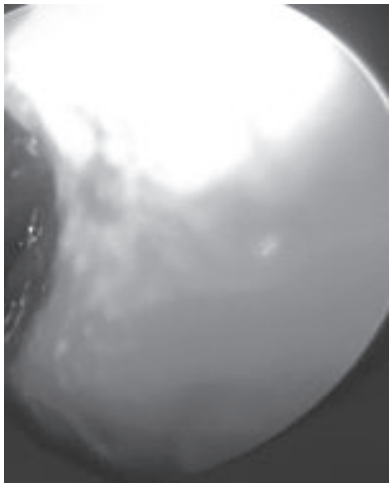
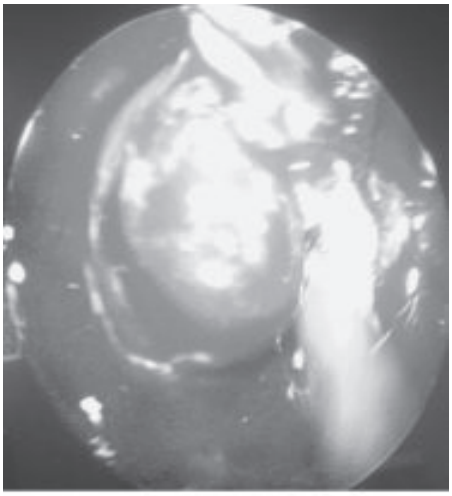


Fig.-11: *Endoscopic different view of tumour*



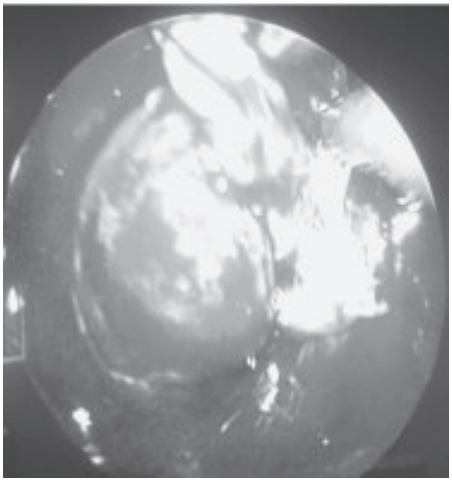


Fig.-10: *Endoscopic different view of tumour*

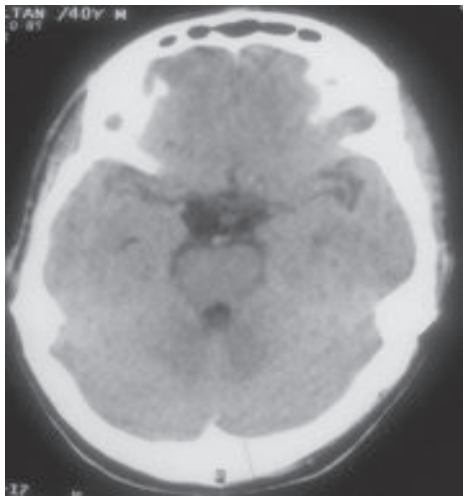


Fig.-12: *Postoperative CT scan of brain*

Discussion:

Over the last century, pituitary adenoma surgery has evolved from a craniotomy approach toward less invasive approaches. In the past twenty years, there is growing evidence to support the use of endoscopic techniques as an alternative approach in the treatment of pituitary adenomas[6-11].

Several authors have discussed the potential outcomes of the endoscopic technique. DeKlotz *et al*.[8] used a meta-analysis to reveal the superior rate of gross total resection (GTR) (79% versus 65%, *P*<0.0001) as well as the lower rates of CSF leak (5% versus 7%, *P*<0.01), septal perforation (0% versus 5%) for the endoscopic approach compared with the sublabial approach. Rotenberg *et al*.[9] concluded that the two approaches had similar outcomes (GTR, hormonal abnormality resolution) but that the endoscopic approach was associated with fewer complications as well as a shorter hospital stay and length of operation. Goudakos *et al*.[10] demonstrated that the rates of GTR/CSF leakage were similar between the two techniques. However, other study also revealed a lower incidence of post-operative DI and a shorter hospital stay in the studied endoscopic groups[12]. Other systematic reviews also support the safety and short-term efficacy of endoscopic pituitary surgery[6,10]. Interestingly, Ammirati *et al*.[13] recently reported a meta-analysis concluding that endoscopic removal of pituitary adenoma, in the short term, does not seem to confer any advantages over the microscopic technique and the incidence of vascular complications was higher with endoscopic than with microscopic removal of pituitary adenomas. In our study showed CSF leakage 1(8.3%) in endoscpic approach and 3(12%) in microscopic approach. Diabetes insipidus was 5(41.6%) in (table-VIII) edoscopic approach and 14(56%) was in microscopic approach. In endoscopic approach penumocphalus and intracerebral haemorrhage were none but in microscopic approach these complication were only in 1(4%).

The primary explanation is that most of the previous reports pertain to single-armed studies in the absence of a reliable comparison. Second, the inclusion and exclusion criteria are key factors in each study, which may lead to different conclusions. In addition, the complication rate in microscope-based surgery is already low and the rates of GTR are high. Demonstrating a statistically significant difference between endoscopic and microscopic techniques will require a larger number of cases. In our study total removal of tumour by endoscopic approach were 9(75%) and microscopically total removal were done 14(56%) (Fig. 1-10).

The results of previous study were clearly favor the endoscopic approach for pituitary surgery over the microscopic approach. The endoscopic approach yielded a significantly improved rate of gross total removal (GTR) with lower rate of post-operative septal perforation. It is important to recognize that the above analysis represents only the results of early outcomes and complications. There are few publication long-term studies following these patients beyond the initial post-operative period. This study shows complication more in microscopic approach than endoscopic approach.

Conclusions:

In conclusion, the results of our study support the safety and effectiveness of endoscopic transsphenoidal pituitary adenoma surgery is more than tranphenoidal microscopic approach. Future studies with a long-term follow-up are required to determine the outcomes and complications of endoscopic pituitary surgery.

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"Short Segment pedicle screw fixation for the treatment of unstable thoracolumbar fracture"- a study of 50 cases.

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Abstract:

Introduction: *Short segment pedicle screw fixation is a popular procedure for treating unstable thoracolumbar burst fracture. But due to lack of adequate neurological improvement, progressive kyphosis and hardware failure- the efficacy of different methods remain debatable.* ***Method :*** *50 patients with isolated thoracolumbar burst fractures were treated by short segment pedicle screw fixation and transforaminal thoracolumbar inter body fusion (TLIF) between January 2010 to December 2013. All patients were followed up for a minimum 2 years. Demographic data, Neurological improvement (Frankel) grade and Hardware failure related complication were evaluated.* ***Results:*** *All patients recovered with solid bony fusion by inter vertebral bone graft and pedicle screw without complications like misplacement of screw, nerve or vessel lesion or hardware failure. The post-operative radiographic demonstration reveals- good fracture reduction and it was well maintained until the bone graft fusion. Neurological recovery of the one to three Frankel grade was seen in 42 patients with partial neurological deficit. Among the 30 patients 3 grade improvements was seen in 4 patients, 2 grade of improvement was observed in 20 patients and 1 grade of improvement was found in 18 patients. 3 patients with Franke-D on admission showed no improvement. 5 patients with no paraplegia/hemiplegia on admission remained neurological intact.* ***Conclusion:*** *Posterior short segment pedicle fixation in conjunction with TLIF seems to be a feasible option in the management of selected thoracolumbar burst fracture with good neurological improvement.*

Key words: *Short segment fixation, unstable burst failure, pedicle screw, TLIF*

Introduction:

Management of thoracolumbar burst fracture still remains controversial[1]. Surgical treatment is generally recommended for patients with neurological deficit or those with instability. Currently posterior short segment pedicle screw fixation is one of the most common operative approaches to treat unstable thoracolumbar burst fracture. The clinical results of this surgery are usually satisfactory but progressive kyphosis persistence of neurological deficit and hardware failure remain a concern[2]. Kyphosis and hardware failure problems can be solved by bone grafting, balloon- assisted vertrbroplasty and corpectomy & cage placement . We retrospectively studied a consecutive series of 50 thoracolumbar burst fractures with posterior short segment pedicle screw fixation (one level cephalad to and one level caudal to a fracture) in conjunction with TLIF to evaluate the feasibility and efficacy of the technique.

Methods:

This retrospective study includes a consecutive series of 50 patients (35 males & 15 females)

with anti-traumatic thoracolumbar fractures who were operated between January 2010 to December 2013

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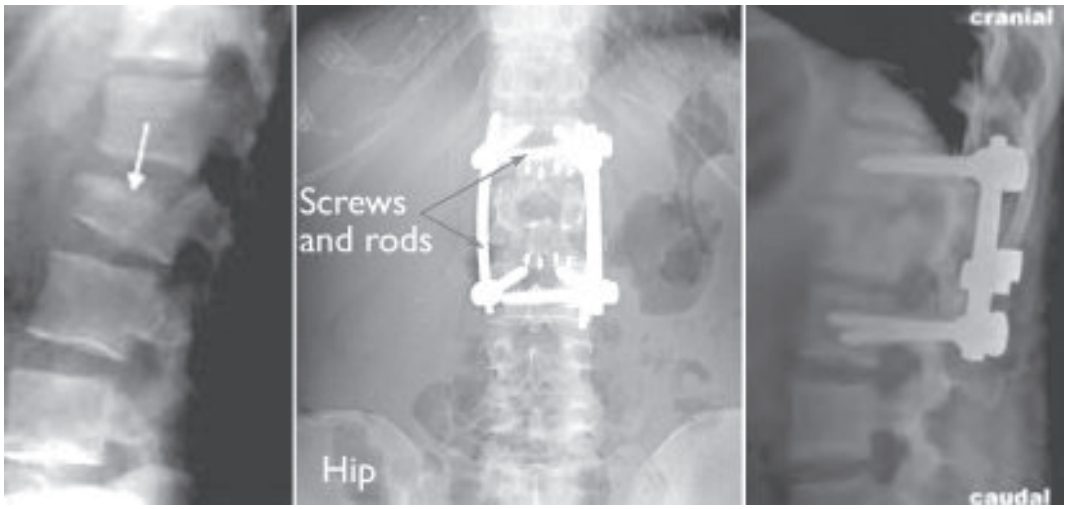
in department of Neurosurgery, Dhaka Medical Collage Hospital. The patients aged from 20 to 60 years mean 39.2 years and indication for surgery were the presence of anyone or more of the following: 1) Presence of neurological involvement caused by fracture or CT scanning of the affected level showed more than 50% spinal canal compromise; 2) More than 50% loss of anterior vertebral height or local kyphosis angle exceeds 25 degrees[3]. Plan X ray and CT scan of affected level was done to show fracture morphology before surgery. MRI was done to assess canal encroachment and for signal abnormalities in the spinal cord and other soft tissue changes. All patients underwent plain radiography in the early post-operative period within 7 days and then after 3, 6 ,9 & 12 months as per demand. CT scan and MRI of respective level done only for selected patients. For clinical assessment, neurologic deficit was assumed using Frankel motor score system[4].

Surgical Technique:

The patient was placed in prone position. X-ray monitoring C-arm localization of fracture was done. A posterior mid line straight incision centered on the affected level was made to expose the Laminae 1 level above and below affected level. Subperiosteal dissection was carried out with an electric cautery until the facet joints on the both sides were visualized. Pedicle screws were introduced one level below and above the affected level[5]. Spinous process was removed to decompress the posterior aspect of the thecal sac. The thecal sac & nerve root were gently retracted to expose the intervertebral disc which was completely removed subsequently. The retro pulsed fragments of the fractured vertebral body were removed thereby decompressing the anterior aspect of the thecal sac. Then granulated bone graft made from removed bone tissue was packed into the intervertebral space and vertebral body through fractured end plate. When the decompression procedure was finished the final verification of the screws & rod position was done. Drain was placed; muscle fascia and skin were closed in proper fashion.

Results:

Among 50 patients, 35 were male and 15 were female. The patients aged from 20-60 years, mean age 39.2 years. The affected levels were: T_{12} level in 12 patients, L_1 in 7, L_2 in 20, L_3 in 8 and L_4 in 3. Neurologic deficit was graded according to Frankel motor score system. 7 Patients were classified as Frankel B, 15 as Frankel C, 13 as Frankel D, 15 as Frankel E. There was no patient classified as Frankel-A in the series. The cause of injury included 30 cases due to fall from height, 16 cases due to road traffic injury, 4 cases due to fall with heavy weights over head. The average injury surgery interval was 20 days, ranging from 2 to 30 days. All



Pre-operative Post-operative AP view Post-operative Lateral view

patients were treated with posterior short segment pedicle screw fixation in conjunction with TLIF. Average hospital stay was 45 days ranging from 20 to 60 days. In neurologically intact patients average hospital stay decreased to 20 days, ranging from 15 to 30 days. Neurological recovery of one to three Frankel grades was seen in 30 patients, three grades of improvement was seen in 4 patients(from grade B to E), two grades of improvement was observed in 20 patients and one grade of improvement was found in 18 patients. In 3 patients with partial neurological deficit (frankel grade D) on admission, no improvement was observed. All the neurologically intact patients (5 cases) remained so during the follow up period. 45 patients recovered with solid fusion of the intervertebral bone graft without any complications, remaining 5 cases with some complications, like hardware failure in 3 cases (one case-screw broken, one case screw dislodged, one case rod extruded subcutaneously) and remaining two patients experienced cerebrospinal fluid leakage because of initial dural injury while introducing pedicle screw.

Discussion:

Burst fractures of thoracolumbar spine can cause neurological complications and kyphotic deformity[6] which may have a great impact on the patient's quality of life. The treatment option of burst unstable thoracolumbar fracture (where height of vertebral body loss >50% and kyphotic angulation deformity >25 degree) is posterior short segment transpedicular screw fixation with TLIF. It is a common surgical option and it's acceptability is established. There are other surgical techniques but each technique has its own advantages and disadvantages. Although the combination of both anterior and posterior approach can provide the most stable biomechanical repair but the operation time, complications and morbidity is higher than that of single approach. Considering everything, the standard is posterior approach which relatively is an easy procedure where reduction of fractured vertebral body and augmentation of the anterior column without any complications is possible[7]. The posterior approach instrumentation can be 1) short segment fixation - involving one level above and one level below the fractured level and 2) long segment fixation involving more than two upper and lower level below the fractured segment. Now a days short segment pedicle screw instrumentation is a well described and popular technique to reduce and stabilize thoracolumbar spine fractur[8]. Short segment fixation offers the advantage of saving motion segments when compared with longer instrumentations. But disadvantages are - earlier impact failure and correction loss of kyphotic angle[9,10].

Conclusion:

Posterior short segment pedicle screw fixation and TLIF might be an optimal surgical treatment option for selected thoracolumbar unstable burst fractures. Most neurosurgeons are familiar with posterior decompression by laminectomy with TLIF with canal clearance by removing the protruding fracture fragments releasing spinalcord and nerve root. So posterior short segment pedicle screw fixation and TLIF is the best choice for the treatment of unstable thoracolumbar fracture. Lack of comparison group , proper record keeping and follow up facilities are the limitations of this study. Further investigations should be carried out to evaluate the effect of this technique in unstable thoracolumbar fracture groups.

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REVIEW ARTICLE

Cerebrospinal Fluid Biomarkers for Diagnosis of Alzheimer's Disease

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Abstract:

Alzheimer's disease is the most common cause of dementia among elderly people. The major pathological hallmarks of AD are the loss of neurons, occurrence of extracellular senile plaques as well as intracellular neurofibrillary tangles (NFT). Biochemical changes in the brain are reflected in the cerebrospinal fluid (CSF), and intense research efforts have been made to develop biomarkers for the central pathogenic processes in AD that can be used as diagnostic tools. Biomarkers are essential part of disease management as they are essential for diagnosis, monitoring the disease progression, detecting early onset of the disease, monitoring the effect of therapeutic intervention, and also avoiding false diagnosis of the disease. Unfortunately, none of the biomarkers presently available are able to accomplish the disease diagnosis single-handedly. Three CSF biomarkers, Aâ42, Total-tau (t-tau), and phosphorylated-tau (p-tau), have been found to have the highest diagnostic potential.

Keywords: *Dementia, Alzheimer's disease, CSF Biomarker, Tau protein, Amyloid beta.*

Introduction:

Alzheimer's disease (AD) is a progressive neurodegenerative disorder that causes dementia in approximately 10% of individuals older than 65 years [1]. It is estimated to afflict more than 27 million people worldwide[2]. AD accounts for at least 60% of all dementia diagnosed clinically. Alzheimer's disease is the most common cause of dementia among elderly people and will become a public health crisis within two to three decades if left untreated. Diagnosing AD and distinguishing it from other dementias depends primarily on clinical evaluation, and, ultimately, on investigator judgment[3]. There is also no definite clinical method to determine which patients with mild cognitive impairment (MCI) will develop AD. The major pathological hallmarks of AD are the loss of neurons, occurrence of extracellular senile plaques as well as intracellular neurofibrillary tangles (NFT) . Senile plaques are primarily composed of amyloid *â*-protein (A*â*), which is produced from the amyloid precursor protein (APP) by sequential proteolytic cleavages made by two proteolytic enzymes, *â*-secretase (*â*-site APP-cleaving enzyme; BACE) and *ã*-secretase (Figure 1)[2]. A definitive diagnosis of AD can only be made after death, when autopsy can reveal these senile plaques and neurofibrillary tangles in brain tissue. It is well known that the pathological processes in the brains of AD patients start more than a decade before the first symptoms are noticed. The temporal dynamics of biomarker levels in relation to changes in cognition have been described in a hypothetical model on the continuum of AD[4]. In line with this, the revised diagnostic guidelines identify three different stages of AD: preclinical AD, mild cognitive impairment (MCI) due to AD and AD with dementia. The main focus of this review is to provide insights on the various potential biomarkers with particular emphasis on CSF biomarkers characteristics of these three stages for AD diagnosis.

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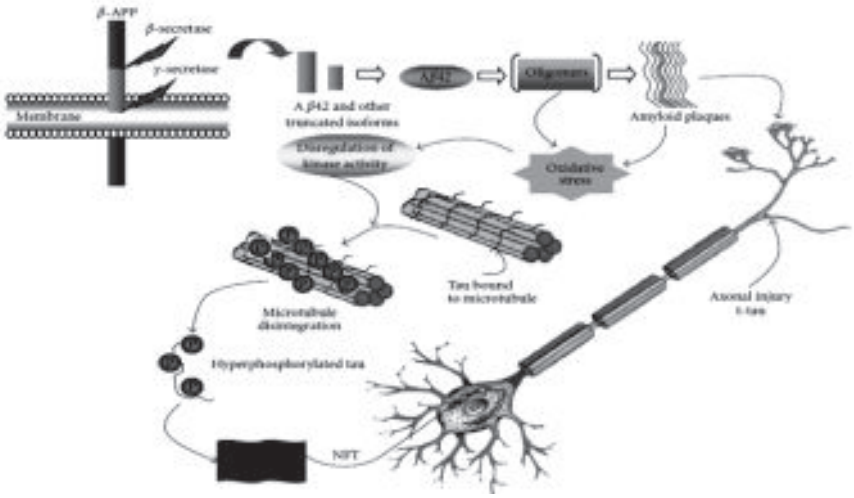

Fig.-1: *Pathological cascades and potential biomarkers of AD.*

Importance of diagnostic markers for AD and MCI:

The introduction of acetylcholine esterase (AChE) inhibitors as symptomatic treatment has highlighted the in the population of the availability of drug treatment has also made patients seek medical advice at an earlier stage of the disease, making the percentage of MCI cases at dementia clinics increase. This has increased the diagnostic challenge for physicians, because the characteristic clinical picture of AD with slowly progressive memory disturbances combined with parietal lobe symptoms has not yet developed in MCI cases. Accordingly, there is no clinical method to determine which MCI cases will progress to AD with dementia except for a very long clinical follow-up period. Thus, new diagnostic tools to aid the diagnosis of early AD and to identify incipient AD in MCI cases would be of great importance[5].

Biomarkers:

The biomarkers are the entities whose concentration, presence, and activity are associated with disease. Biomarkers are essential part of disease treatments as they are essential for diagnosis, monitoring the disease progression, detecting early onset of the disease, monitoring the effect of therapeutic intervention, and also avoiding false diagnosis of the disease[6]. An ideal biomarker (1) should be highly specific, (2) should predict the course of illness accurately, and (3) should reflect the degree of response to treatment[7]. The biomarker research for AD has significantly advanced in recent years (Table-1). The neuroimaging techniques like CT, PET, PIB-PET, MRI assess the regional structure and function of the brain, as well as assist in identifying the biochemical profile of brain dysfunction[8-10].

The body fluids such as cerebrospinal fluid (CSF), plasma, and urine are considered as important sources for the AD biomarker development. Plasma biomarkers like α_{2-} Macroglobulin, Complement factor H, βâ 42 are noninvasive but less sensitive and specific tests for AD diagnosis[11-13]. But CSF is considered a better source for biomarker development as it is in direct contact with the extracellular space of the brain and can reflect biochemical changes that occur inside the brain. Thus far, three CSF biomarkers, Aβ42, total-tau (t-tau), and phosphorylated-tau (p-tau), have been found to have the highest diagnostic potential[10, 14]. Biomarkers of inflammation and oxidative stress and urine-based biomarkers are among the other sources that provide vital information on development and progression of AD. Unfortunately, none of the biomarkers presently available are able to accomplish the disease diagnosis single-handedly. Monitoring more than one biomarker at the same time is suggested to be suitable for detecting the disease progression.

Table-I

Some promising biomarkers in diagnosis of AD.

Category	Markers	Advantages	Limitations
Imaging	CT, PET, PIB-PET, MRI	(1)Noninvasive (2) Provides structural and functional details of brain immediately (3) Can reveal disease progression	(1) Expensive (2) Requires experienced personal (3) Sensitivity and specificity not satisfactory
Plasma	α_{2}- Macroglobulin, Cmplement factor H, Aβ 42	(1) Noninvasive (2) Samples are easily accessible	(1) Less correlation to AD (2) Less sensitive and specific for AD diagnosis
CSF	Aβ 42, t-tau,p-tau, p-tau/ Aβ 42, t-tau/ Aβ 42	(1) Can correlate AD directly (2) Highly sensitive and specific (3) Can detect AD progression	(1) Invasive , sample to be collected by LP (2) Irreproducible diagnosis due to sample storage and transportation

CSF Biomarker:

Biochemical changes in the brain are reflected in the cerebrospinal fluid (CSF), and intense research efforts have been made to develop biomarkers for the central pathogenic processes in AD that can be used as diagnostic tools. Early studies indicated that CSF biomarkers could be useful for defining a subgroup of patients with MCI at especially high risk of developing AD[15]. The best studied fluid proteins in AD have been CSF levels of Aβ42, the primary constituent of amyloid plaques, and tau protein, the primary component of neurofibrillary tangles. Levels of CSF Aβ42 are typically reduced in AD[16] reflecting its aggregation and deposition as amyloid in the brain , whereas levels of CSF tau and phosphorylated tau (p-tau) species are increased in AD[17]and are hypothesized to reflect the presence of neurofibrillary tangles, neurodegeneration, or both although not all studies support this conclusion[18]. Indeed, there is no proof that plaque formation is reason for Aβ42 concentration decrease, only correlation. A tau protein/ Aβ42 index, usually increased in AD patients, has high sensitivity, high specificity and also high negative predictive value in AD diagnosis.

CSF Amyloid-β

Amyloid-β (Aβ) is a secreted peptide of unknown physiological function that is cleaved from the amyloid precursor protein (APP) by the sequential activities of β-secretase and β-secretase enzymes. The majority of Aβ is produced in the brain and secreted into the brain extracellular space. Some fraction of CNS-produced Aâ diffuses into the CSF, appearing in modest concentrations (~10–15 ng/ml). Aβ occurs in multiple forms, including those ranging from 37 to 43 amino acids in length (Fig.2). Among these, Aâ40 is the most abundant species, but Aβ42 seems to be essential for initiating amyloid-â aggregation and is considered central to the amyloid cascade hypothesis of AD[19]. Of these two species, Aâ42 has emerged as a useful biomarker for AD.

CSF Tau

Tau is a cytosolic protein predominantly expressed in neurons, wherein its primary function seems to be regulation of microtubule stability within the axon. The tau proteins are the product of alternative splicing from a single gene that in humans is designated *MAPT* (microtubule-associated protein tau) and is located on chromosome 17[20]. They were discovered in 1975 in Marc Kirschner's laboratory at Princeton University[21]. This function is regulated by several different post-translational modifications, principally phosphorylation of numerous serine and threonine residues. In AD, hyperphosphorylated tau often fills the dystrophic neurites of neuritic plaques, and is the principal component of the paired helical

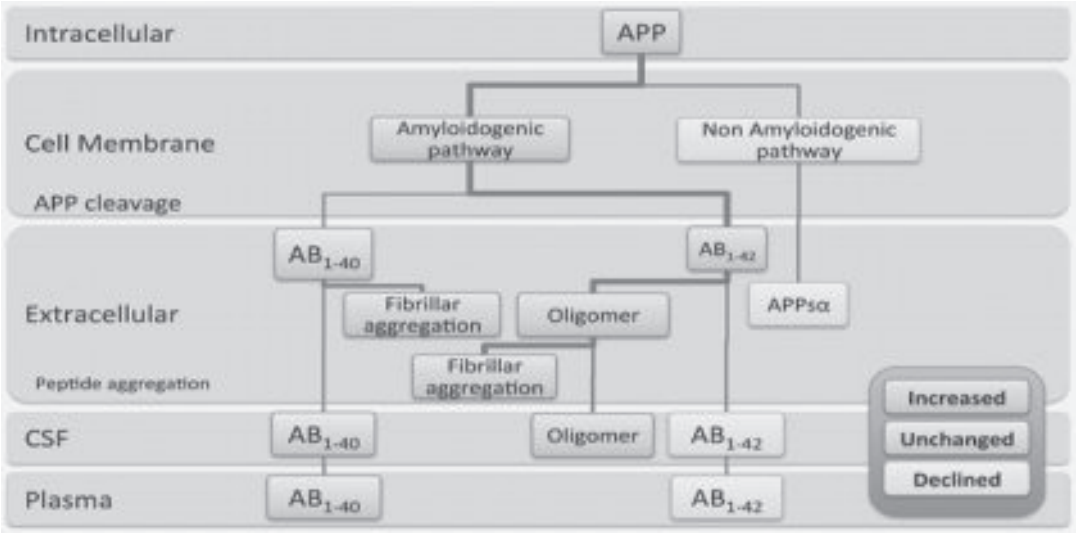

Fig.-2: *Amyloid precursor protein metabolism and biomarker of amyloid pathology.*

filaments that constitute NFTs that are present in neuronal cell bodies. The precise forms of tau that appear in the CSF, and the mechanism or mechanisms by which they get there, are not entirely understood, but recent studies demonstrate that virtually all domains of the protein are represented, and it is widely assumed (but not proven) that the major sources of increases in tau and phosphorylated tau (Fig. 3) in the CSF in AD are either due to synaptic/neuronal injury, cell death, or possibly neurofibrillary tangles.

Total (T)-Tau

Tau is the major protein component of intra-neuronal NFT and is elevated in the CSF in most patients with AD. In addition to the presence of tau in neurofibrillary tangles, it has been shown that tau levels in CSF can increase rapidly as a result of neuronal injury, and therefore, may indicate the severity of the underlying neurodegeneration. Over 50 studies have demonstrated an increase in the concentration of total tau (t-tau) by approximately 2–3 fold in AD compared with non-demented elderly subjects .Elevation of CSF tau differentiates AD from non-demented, age-matched elderly with a sensitivity and specificity of ~90%[22]. As mentioned previously, tau elevation seems to occur at the early symptomatic stages of disease (MCI/ very mild dementia) and in some cognitively normal individuals, where its levels correlate with the amount of amyloid

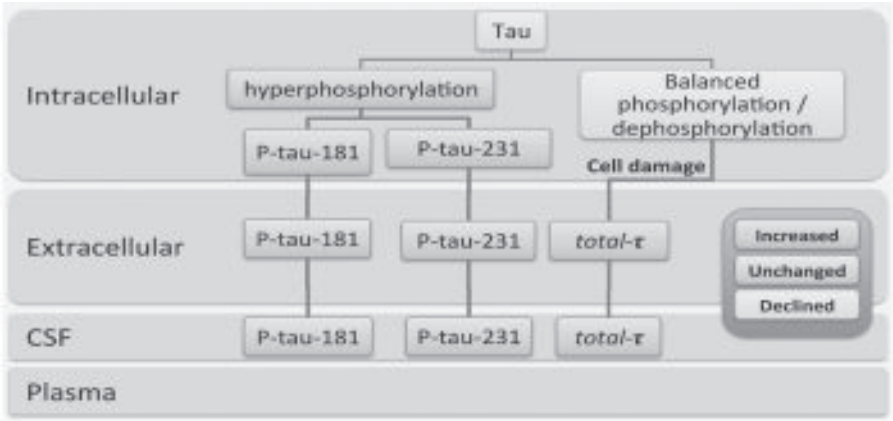

Fig.-3: *Biomarkers of tau pathology*

deposition and together with Aβ42 predict cognitive decline (see below). Cognitively normal individuals with evidence of amyloid deposition and increased tau are likely to have preclinical AD (see below). However, it is important to consider that tau elevation can be seen in other neurodegenerative diseases, potentially limiting the utility of tau alone in the differential diagnosis of AD .Tau, as a marker of neuronal injury, can be transiently increased after any acute brain injury (such as stroke or trauma)[23]. Moreover, tau levels seem to remain relatively stable throughout the clinically symptomatic period of AD and do not correlate well with dementia severity. Age might affect the CSF levels of tau; however, studies have been conflicting regarding the direction and significance of such an effect.

Phosphorylated (P)-tau

Abnormal tau phosphorylation is present in neurofibrillary tangles and has been investigated as a marker of AD pathology. As many as 30 different phosphorylation sites of p-tau have been identified[24], and ELISAs (enzyme-linked immunoassays) have been developed for at least 5 of them. Studies examining the utility of different forms of p-tau in the early diagnosis of AD, and in the differentiation from other causes of dementia, have consistently shown that p-tau 181[25], p-tau 231-235, or p-tau 396-404 offer at least equivalent diagnostic utility for AD as compared to total tau. Studies comparing the diagnostic performance of different phosphorylation sites (p-181, p-199, and p-231) suggest that all three assays are equally effective in differentiating AD from non-demented controls. P-tau 231 may provide diagnostic specificity for AD and may improve the differentiation between AD and FTD, while there is some evidence that p-tau 181 improves the differentiation between AD and DLB. P-tau 396-404, and the ratio of p-tau 396-404/t-tau, but not tau alone, has been shown in one study to differentiate AD from vascular dementia. In contrast to t-tau, p-tau does not appear to be increased secondary to acute brain injury, further adding to its diagnostic specificity.

Combination of Aâ42 and tau

Based on current data, the use of CSF Aβ42 alone but especially together with t-tau or ptau181 is very useful in both diagnosis and prognosis of individuals with MCI/very mild dementia and also in predicting progression from cognitive normalcy to MCI/very mild dementia. This is likely due to the fact that the levels of the markers together can identify two aspects of AD pathology, plaques (Aβ42) and tauopathy / neurodegeneration (tau).

Use of AD Biomarkers in CSF in Clinical Practice

The diagnostic performance of AD biomarkers has been evaluated in clinical practice in two studies[26, 27]. In these studies, the CSF markers have been evaluated on prospective patient samples from clinical practice, and ELISA assays have been run each week in clinical neurochemical routine. The diagnostic performance of CSF T-tau[26] and the combination of CSF T-tau and Aβ42[27] has been similar to that found in other studies, with a high ability to differentiate AD from normal aging, depression, and PD, but lower specificity against other dementias like VAD and LBD. A summary of the diagnostic performance of T-tau, P-tau, and Aβ42 is given in Table 2. Details on the performance of these CSF markers in the separation between AD and nondemented aged individuals have been published previously.

The diagnostic performance of the CSF markers seems to be highest in the differentiation between AD and several important differential diagnoses, including normal aging, depression, alcohol dementia, and PD (Table 2). Another useful clinical application is the identification of CJD in cases with rapidly progressive dementia, in which the combination of very marked increased CSF T-tau and normal or mildly increased P-tau has high diagnostic value. Lastly, these CSF markers may be useful in identifying mixed AD/VAD dementia.

Candidate biomarkers

The search for new AD biomarkers may be facilitated by the core CSF AD biomarkers. By including patients with signs of an AD pathological process and ensuring that control subjects lack this profile, future biomarker studies may be more successful.

BACE1

For Aβ to be produced, the amyloid precursor protein (APP) is cut by two different enzymes, â-secretase

Table-II

Summary of the Specificity of CSF Markers for Alzheimer's Disease

Disorder	Total Tau	Phospho-Tau	Aβ42
Alzheimer's disease	Moderate to marked increase	Moderate to marked increase	Moderate to marked decrease
Normal aging	Normal	Normal	Normal
Depression	Normal	Normal	Normal
Alcohol dementia	Normal	Normal	Normal
Parkinson's disease	Normal	Normal	Normal
Creutzfeldt-Jakob disease	Very marked increase	Normal, but some cases with mild increase	Normal to marked decrease
Frontotemporal dementia	Normal to mild increase	Normal	Mild to moderate decrease
Lewy body dementia	Normal to mild increase	Normal to mild increase	Moderate decrease
Vascular dementia	Inconsistent data, some studies with normal and some with increased levels	Normal	Mild to moderate decrease
Acute stroke	Mild to very marked increase, depending on the infarct size	Normal	Normal
Non-acute CVD without dementia	Normal	N.E.	Normal

CVD = cerebrovascular disease; N.E. = not examined.

and â-secretase. The major â-secretase in the brain is called β-site APP cleaving enzyme-1 (BACE1). Several studies have investigated the levels of CSF BACE1 activity in patients with MCI and AD, but the results are not univocal.

Ubiquitin

Ubiquitin is a small (8.7 kDa) protein involved in the ATP-dependent degradation of proteins, in which it is covalently conjugated to lysine residues of target proteins, for which it serves as a signal for degradation of the protein by proteases.

NF proteins

NF proteins are structural components in the neuronal axons that are important for axonal structure and transport. Neurofilaments are composed of three subunits based on the molecular weight, termed high (NF-H), medium (NF-M), and light (NF-L).

GAP43 (neuromodulin)

GAP43, or neuromodulin, is a protein localized in the presynaptic terminals and axons of cortical neurons. In AD brain, GAP43 is found in the dystrophic neuritis in plaques. GAP43 protein levels are decreased in the frontal cortex and the hippocampus in AD.

NTP and AD7c protein

NTP was identified a brain protein cross-reacting with antibodies against pancreatic thread protein (PTP). Both brain NTP immunoreactivity and mRNA levels are increased in AD.

Limitations:

Although CSF biomarkers have proved to be highly informative, sensitive, and specific for detection of clinical AD and early stage of AD, their regular use in clinic is still limited. One of the major reasons against the vast applicability of CSF in AD diagnosis is lumbar puncture, an invasive method to collect the CSF sample. However, the technique of lumbar puncture has considerably improved and, as a consequence, the incidence of headache after lumbar puncture in elderly patients is 2% or less. Other issues including inconsistency of data analysis of CSF sample due to sample collection, transportation, storage, and high expense of the test might limit the use of CSF for routine diagnosis. The major and inherent limitation of fluid biomarkers is the lack of anatomical precision in the measurements. Another limitation is the lack of assay standardization. Different assays for, e.g., Aâ42 correlate but give different absolute concentrations of the protein. This prevents from the use of global reference limits and diagnostic cut-points.

Conclusion:

The potential uses for AD biomarkers are many. Besides from diagnostics, CSF biomarkers may be utilized for prognosis, assessing disease

progression, developing treatments, monitoring treatment effects and studying disease mechanisms. Intense research has led to the development of CSF biomarkers reflecting different aspects of AD pathogenesis. Currently, validated and reliable biomarkers exist for amyloid pathology and axonal degeneration. Measuring CSF Aβ42, t-tau and p-tau alone or in combination may be especially useful for the selection of pre-symptomatic individuals with known MCI/ pre-clinical AD pathology and for enrollment in prevention trials of disease modifying therapies. Apart from the core biomarkers, there are several candidate CSF and blood biomarkers in the pipeline, but they need verification in further studies.

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CASE REPORT

GBS with Bilateral plantar extensor – A case report

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Abstract:

GBS is an immune mediated polyradiculoneuropathy classically characterized by acute symmetrical ascending lower motor type weakness and areflexia. But sometimes, in axonal variants of GBS, reflexes are preserved or exaggerated. We report a case of GBS with bilateral extensor plantar response during the course of the disease. A 36-year-old male presented with acute quadriplegia with asymmetrical muscle weakness and extensor plantar response. Sensory, bowel and bladder function was intact. He was treated with intravenous methylprednisolone daily for 5 days without improvement. NCS revealed AIDP and AMAN variants of GBS. So, in any patient presenting with acute quadriplegia with extensor plantar response, GBS should be considered as differential diagnosis.

Abbreviation: *NCS (nerve conduction study), AIDP(acute inflammatory demyelinating polyradiculoneuropathy), AMAN ((acute motor and axonal polyradiculoneuropathy), GBS (Guillain-Barré syndrome), CSF(cerebrospinal fluid), AMSAN(acute motor sensory axonal neuropathy).*

Introduction:

Guillain-Barré syndrome is an acute, immune mediated, frequently severe and fulminant polyradiculoneuropathy[1]. It is clinically characterized by acute, progressive, symmetrical ascending muscle weakness and areflexia with or without sensory, autonomic or brainstem involvements. Cranial nerve involvement occurs in 45% to 75% of cases in different series. Facial paresis, usually bilateral, is present in 50% of affected individuals[2]. Although, the diagnosis of GBS is based on clinical criteria, the presence of suggestive findings in the nerve conduction studies (NCS) or albuminocytological dissociation in the cerebrospinal fluid (CSF) analysis help to confirm the diagnosis[3]. We reported a case of GBS with asymmetrical weakness and extensor plantar response during the course of the disease.

Case presentation:

A 36-year-old male was admitted with weakness of all 4 limbs for 5 days. It was sudden onset and gradually progressive. Weakness started in left upper limb, then right upper limb and subsequently involved both lower limbs 1 day later. Initially, he performed his daily activities with assistance, later 2 days prior his admission, he become bedridden. There was no history of fever, respiratory tract infection, diarrhea, vaccination prior to his illness within 1 month. On examination, bulk and tone of muscles were normal. The weakness of all 4 limbs were asymmetrical and muscle power were of 2/5 in both upper limbs and 3/5 in both lower limbs with more marked on proximal than distal part. All deep tendon reflexes were present with bilateral plantar extensors. All modalities of sensation were intact except C_5 and C_6 was absent. There were no involvement of cranial nerves, respiratory system and autonomic systems. He was treated with intravenous methylprednisolone daily for 5 days without improvement. The investigations showed normal findings of total and differential leukocyte counts and serum electrolytes. Vasculitis screening was negative. MRI of brain (Fig. 1), MRI of cervical spine with screening of whole spine was normal. CSF examination showed

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albuminocytological dissociation. CSF protein was 100 mg/dl and cell count only 2 (100% lymphocyte). All causes of infectious radiculopathies were ruled out by analysis of serological test for infectious agent. Nerve conduction study(Table I) showed demyelinating and axonal polyradiculopathy. Later on the patient was treated with 5 courses of plasmapharesis every alternate day. The patient was gradually improved after plasmapheresis and subsequently he was discharged from hospital.

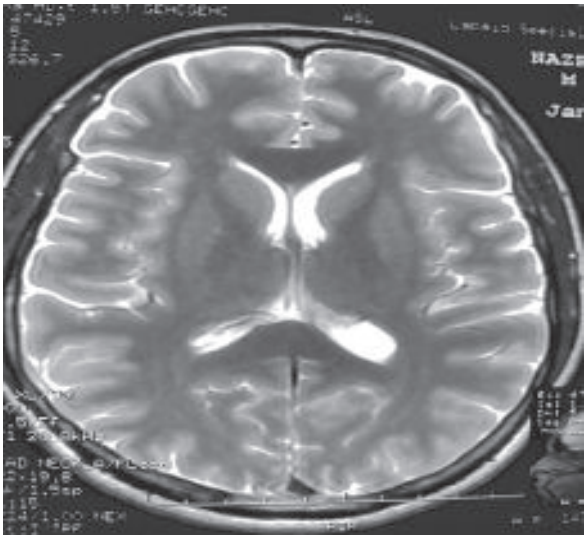


Fig.-1: *MRI of Brain revealed Normal.*

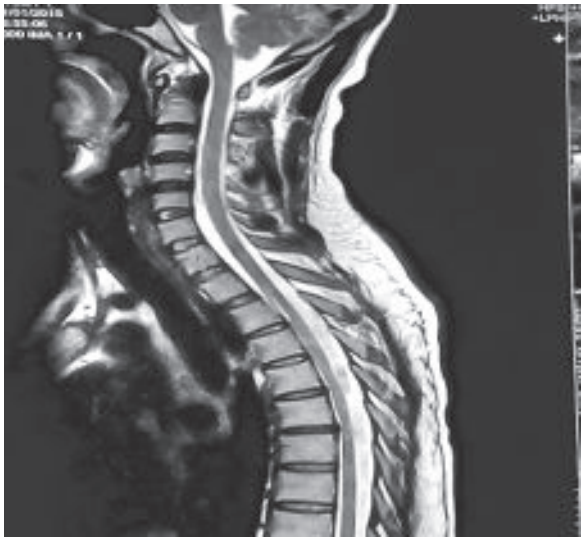
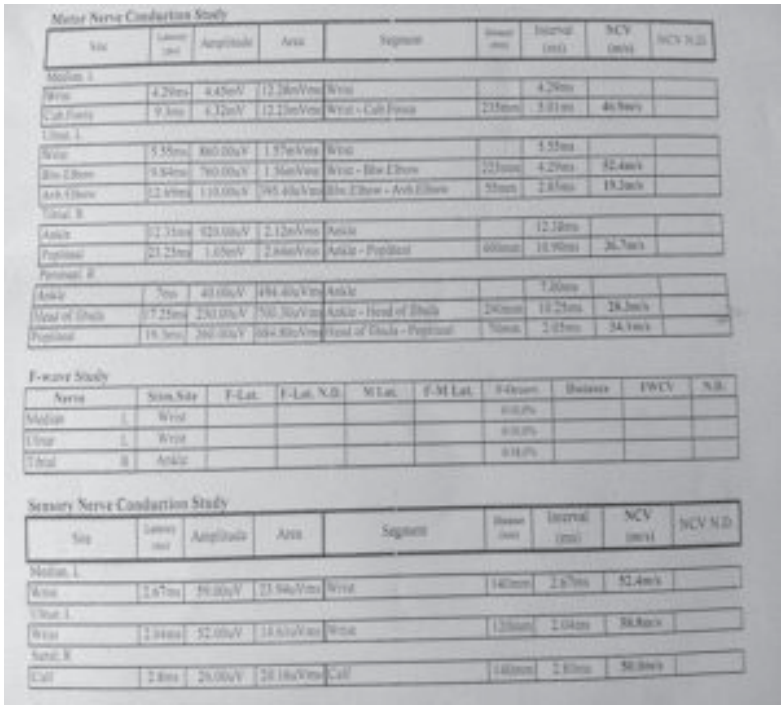


Fig.-2: *MRI of cervical spine and dorsal spine with screening of other spine revealed normal.*

Table-I

Nerve conduction study (NCS) revealed demyelinating and axonal polyradiculoneuropathy



Motor Nerve Conduction Study

Site	Latency (ms)	Amplitude	Area	Segment	Distance (mm)	Interval (ms)	NCV (m/s)	NCV N.D
Median, L								
Wrist	4.29ms	4.45mV	12.28mVms	Wrist		4.29ms		
Cub Fossa	9.3ms	4.32mV	12.23mVms	Wrist - Cub Fossa	235mm	5.01ms	46.9m/s	
Ulnar, L								
Wrist	5.55ms	860.00uV	1.97mVms	Wrist		5.55ms		
Bw Elbow	9.84ms	760.00uV	1.56mVms	Wrist - Bw Elbow	223mm	4.29ms	52.4m/s	
Arb Elbow	12.69ms	110.00uV	295.40uVms	Bw Elbow - Arb Elbow	55mm	2.85ms	19.2m/s	
Tibial, R								
Ankle	12.33ms	920.00uV	2.12mVms	Ankle		12.38ms		
Popliteal	23.25ms	1.05mV	2.64mVms	Ankle - Popliteal	400mm	10.90ms	36.7m/s	
Peroneal, R								
Ankle	7ms	40.00uV	484.40uVms	Ankle		7.00ms		
Head of Fibula	17.25ms	230.00uV	760.30uVms	Ankle - Head of Fibula	240mm	10.25ms	28.3m/s	
Popliteal	19.5ms	360.00uV	884.80uVms	Head of Fibula - Popliteal	55mm	2.05ms	34.1m/s	

F-wave Study

Nerve	Stim.Site	F-Lat.	F-Lat. N.D	M-Lat.	F-M Lat.	F-Amp	Distance	FWCV	N.D.
Median L	Wrist					0.0uV			
Ulnar L	Wrist					0.0uV			
Tibial R	Ankle					0.0uV			

Sensory Nerve Conduction Study

Site	Latency (ms)	Amplitude	Area	Segment	Distance (mm)	Interval (ms)	NCV (m/s)	NCV N.D
Median, L								
Wrist	2.67ms	59.00uV	23.94uVms	Wrist	140mm	2.67ms	52.4m/s	
Ulnar, L								
Wrist	2.04ms	52.00uV	18.61uVms	Wrist	120mm	2.04ms	58.8m/s	
Sural, R								
Calf	2.8ms	26.00uV	20.18uVms	Calf	140mm	2.83ms	50.0m/s	

Discussion:

This is a case of GBS with atypical clinical presentation, characterized by acute quadriplegia with asymmetrical weakness and bilateral extensor plantar responses. Our patient had no history of antecedent infection. We diagnosed him as GBS on the basis of acute progressive quadriplegia, albuminocytological dissociation on CSF and NCS revealed demyelinating and axonal polyradiculo-neuropathy. Despite an atypical pattern of clinical signs and symptoms, the plasmapharesis was started which leaded to the functional recovery of our patient.

GBS is an immune mediated acute progressive inflammatory polyradiculoneuropathy that characterized by symmetrical muscle weakness and areflexia. Several types of GBS are recognized, acute inflammatory demyelinating poly-radiculoneuropathy (AIDP) is common variant. Additionally, there are two axonal variants, are well recognized that are acute motor axonal neuropathy (AMAN) and acute motor sensory axonal neuropathy (AMSAN)[2]. Axonal variants are commonly associated with preserved or brisk reflexes. Hyperreflexia seen in GBS has a common association with antecedent C jejuni infection and positive anti-GM_1 ganglioside antibody. Although, all patients have IgG anti-GM1 ganglioside antibody and anti-c jejuni antibodies are frequently negative[4]. Antibody testing is not widely available in our country which makes the diagnosis.

Conclusion:

GBS patient may present with signs and symptoms associated with CNS involvement. So, Neurologist as well as internist should have a high degree of suspicion towards the diagnosis of GBS, if a patient present with acute motor paraparesis or quadriparesis with extensor plantar response. In that case, NCS and CSF analysis can confirm the clinical findings. Early diagnosis and treatment of GBS may prevent mortality and morbidity.

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Dorsal Spine Giant Cell Tumor with paraplegia: A Case Report

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Abstract:

Patients of Giant cell tumors (GCT) of the spine is rarely seen . We reported a case of GCT of the eleventh dorsal vertebra presented by severe backache with paraplegia in a 30 year old woman. Imaging showed an osteolytic lesion invading the vertebral body, the posterior arch and compression of the spinal cord. Neurological decompression was performed but pain recurred after 2 months. The MRI of spine revealed recurrence of tumor and again surgical decompressions was done along with long segment transpedicular fixation and patient was significantly improved. A surgical biopsy was obtained at the same time to confirm the diagnosis. Giant cell tumor is not so common in thoracic region. We believe that the gross removal of tumor provide good outcome for the patient.

Key word: *Giant cell tumors, dorsal spine, tumor recurrence*

Abbreviation: *GCT (Giant cell tumors)*

Introduction:

Osteolytic lesions are seen in the giant cell tumors of the bone, which are usually located in the epiphysis. This is a benign tumors and frequently recurs. Surgery is the treatment of choice[1]. Except for the sacrum, spinal forms of GCT are rare[2]. The more severe forms of this entity result in recurrence, malignant degeneration and neurotoxicity[3]. The percentage of local recurrence in the literature is approximately 30% [1]. We present a case of GCT of the eleventh dorsal vertebra initially treated by laminectomy and was taken biopsy may be tutor removal was incomplete. The aim of this study is to present the clinical and radiographic characteristics of these tumors and tumor recurrence with immediate outcome after surgery.

Case report:

The patient was a 30-year-old woman, a housewife. She had developed severe pain in the mid dorsal region that radiated to her low back and also to both lower limbs (right> left). Pain was dull, progressively increasing and more marked after 8-10 pm daily and disturbed her sleep despite in any posture. She was evaluated to have spine tumor at D11 vertebral body and underwent a surgery to remove which was a Giant cell tumor (laminectomy Dorsal11).

She received 45Gy post operative radiotherapy and was pain free with no weakness for the next 2 months. 2 months after the surgery pain was reappeared and became more unforgiving and was aggravated by the slightest of movement in the mid dorsal spine. Pain was only minimally relieved with injectable analgesics and started developing weakness of both lower limbs which was rapidly progressive, requiring support for basic needs and became bedridden, the cause of which she states to be pain more than weakness. Clinical examination showed partial loss of dorsal lordosis and pain during palpation of the D11 vertebrae with paravertebral dorsal contraction. Neurological examination revealed gross motor deficit in both lower limbs (muscle power grade 2 in right and 1 in left) with sensory level at D12 level. Genito-sphincter area also involved. The rest of the clinical tests and the biological results were normal except high ESR. Xray dorsal spine showed osteolytic lesion with decrease of hightof body of D11 (Fig. 1). MRI of dorsal spine revealed expansion of the residual tumor at D11 which affected the whole body and the pedicles(right>left) partially, forming an anterior

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epidural compression on the spinal cord (Fig. 2, 3). Then posterior decompression was done with gross total removal of tumor including vertebral body and cavity filled up with bone chips at D11 and transpedicular fixation D9,10 with D12 and L1 vertebra (figure 4) . Just after surgery dorsal pain was significantly improved and muscle power became normal within very short period. 10 Days after surgery she was normal and able to walk independently (Fig. 5).We referred her to radiotherapy department for further treatment.

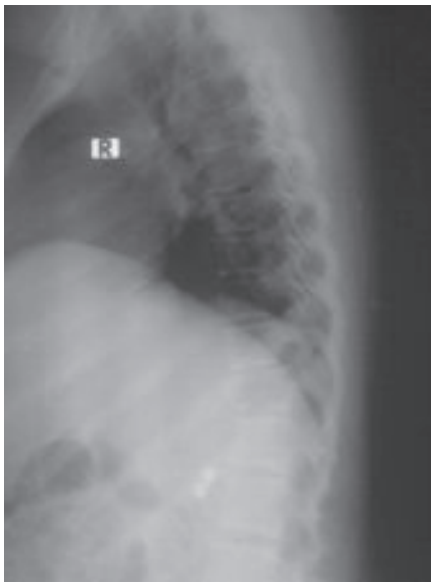

Fig.-1: *X-ray dorsal spine lateral view shiws oesteolytic lesion in the body of D11 vertebra including posterior arch.*

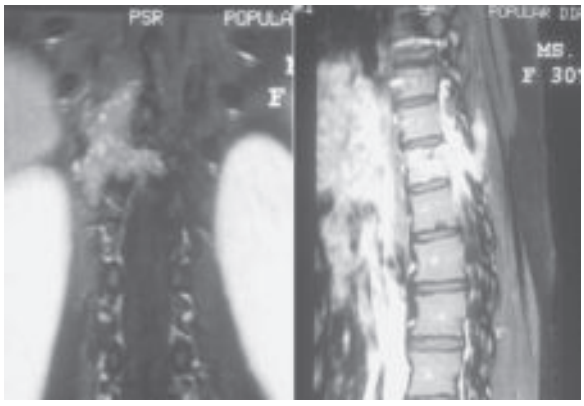

Fig.-2: *MRI Dorsal spine with contrast coronal and lateral view (Before first operation) revealed contrast enhanching lesions at D11 which affected the body of vertebra and arch (right>left) partially, forming an anterior epidural mild compression on the spinal cord.*

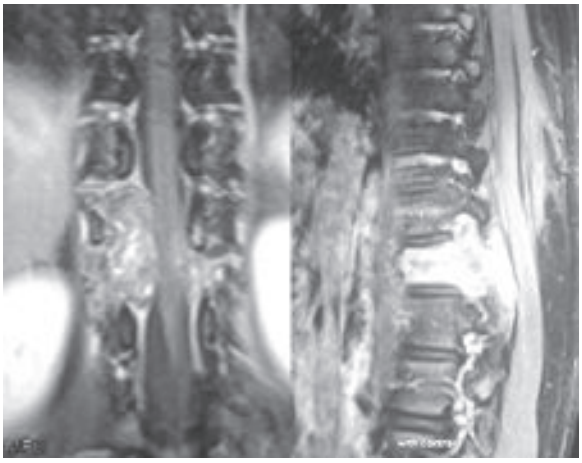

Fig.-3 : *MRI Dorsal spine with contrast coronal and lateral view (After first operation) revealed expansion of the residual tumor at D11 which affected the whole body and the pedicles(right>left) forming an anterior epidural compression on the spinal cord.*

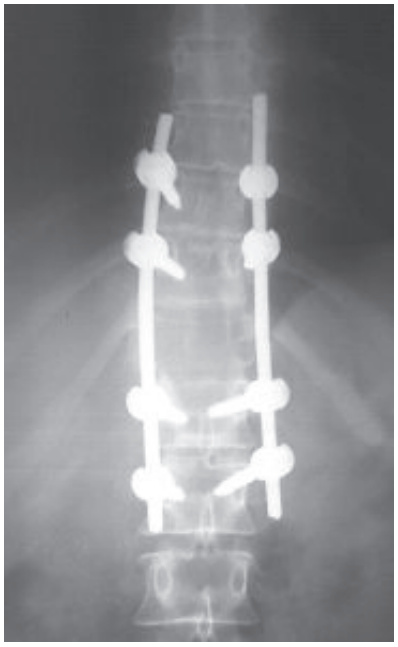

Fig.-4: *X-ray dorsal spine anterior and lateral view shows transpedicular screws and rods fix with above and below two vertebral body from affected D11.*

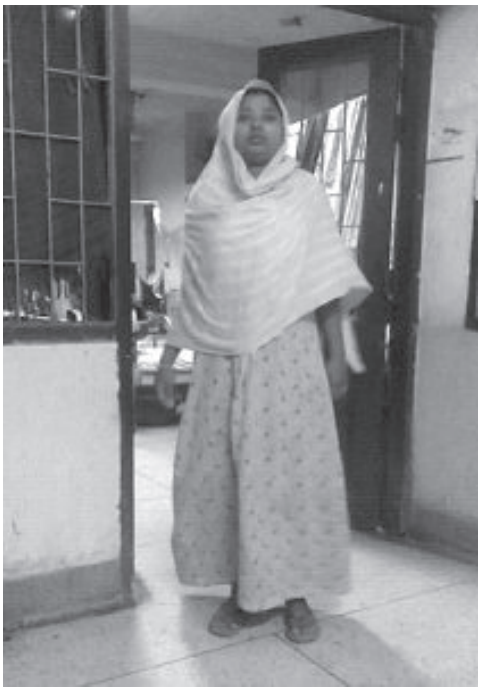

Fig.-5: *Patient could walk independently on 10 days after operation.*

Discussion:

According to the Mayo clinic, Spinal GCTs are rare; they represent 6.5% of bone GCTs[3] and 1—9% of bone GCTs according Bedwell et al.[4]. In 1993, Sanjay et al.[3] reported 24 cases of spinal giant cell tumors from cases in the Mayo Clinic between 1955 and 1989. Although this lesion often only involves one vertebra, Kos et al.[5] published a case of multifocal thoracic and sacral spine GCT and Erdogan et al.[6] published a case of GCT in the sixth cervical vertebra. The different reported cases often occurred in patients between 20 and 30 years old and especially in women [7].

Spinal pain with or without radiculalgia is the most frequent cause for consulting[3]. However, the diagnosis of GCT is often made after a neurological deficit has developed with medullary compression can also be obtained[8]. At present, MRI is the gold standard for evaluating locoregional invasion in spinal GCT, to determine the size of the tumor and look for intracanal extension. The signal is usually mixed, with a low intensity signal on T1 and a high intensity signal on T2-weighted images[9].

Histological confirmation of the diagnosis requires a surgical biopsy[2] or a CT scan guided puncture biopsy, whose reliability is 65% [10]. In this report we performed a surgical biopsy at the same time as decompressive laminectomy with transpedicular fixation. A CT scan guided puncture biopsy is safe[11], and was performed to confirm tumor recurrence. In most cases, the histological examination confirms the diagnosis of GCT and excludes the main differential diagnoses, in particular aneurysmal cyst[1]. Sanerkin is the reference classification for the histological grading of a bone GCT[1]. Grade I is the benign form of the disease, while grade III is osteosarcoma, and grade II is a borderline form. Treatment of these tumors must take into account three problems: mechanical because of the extensive osteolysis of the vertebral body, neurological and tumoral with the risk of recurrence [3]. Treatment of spinal GCT is usually surgical[1,2,7]. The possibilities of extratumoral surgery are extremely limited[12]. An isolated lesion of the vertebral body can be treated by total spondylectomy by the anterolateral approach[13]. Unfortunately, extension into one of the two pedicles makes extratumoral resection impossible[12]. Partial spondylectomy, corporectomy or resection of the posterior arch is a viable option in well-circumscribed lesions [14]. Lafarge et al.[2] filled bone defects with autologous grafts alternating with slices of allograft strengthened with transversal screws and screw plate osteosynthesis. Li et al.[3] used fibular grafts to strengthen vertebrae above and below with compression screws. Smartis et al.[13] performed posterior resection and short-term osteosynthesis, then anterior corporectomy with a cage implant for filling, then a posterior approach for pedicular reconstruction. The use of adjuvant radiotherapy is considered to be a factor favoring the development of sarcoma in an estimated 10% of cases[3]. It can be indicated in inoperable GCT[7], incomplete GCT resections, recurrent GCT[3] or as adjuvant therapy to surgery[15]. The role of biphosphonates in the prevention of recurrent bone GCT was confirmed in a study by Tse et al.[16]. Its efficacy in spinal forms was reported by Fujimoto et al.[17] but in association with radiotherapy. Bleeding during surgery of spinal GCT is a severe complication, which can make it

impossible to complete the surgical procedure[18]. Preoperative embolisation can prevent this complication and reduce the size of the tumor, facilitating resection [19].

Recurrent GCT after surgery is a serious complication, and treatment is a problem. Most authors believe that it is due to marginal surgical resection[3]. Sanjay et al.[6] reported 10 cases of recurrence in 24 spinal GCT. According to Campanacci et al.[20], 90% of recurrence developed in the first three years after surgery. He noted that recurrence had not occurred in total spondylectomy 13 years after surgery. The complication in our report is mainly explained by insufficient resection, which was limited to simple anterior curettage. Recently, Junming et al.[15] published a series of 22 cervical spine GCTs. The rate of recurrence with subtotal spondylectomy was 71% while for total spondylectomy it was only 7.7%.

Conclusion:

Dorsal spine GCTs are rare and their clinical and radiographic characteristics are not specific. MRI is indispensible to evaluate local extension and especially to identify nerve compression. If the vertebral body and the posterior arch are affected, curettage of the lesion is insufficient to prevent tumor recurrence. This occurred in the present report, where a total spondylectomy should have been performed with autologas graft of bone chips and transpedicular stabilisation to minimise this risk.

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Myasthenia gravis as a presenting feature in a patient with SCLC: A case report

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Abstract:

Small cell lung cancer (SCLC) is the most frequent cancer histology associated with paraneoplastic syndromes. These syndromes are typically caused by ectopic hormone production or immune-mediated tissue destruction caused by neural antigen expression from cancer cells. Lambert-Eaton myasthenic syndrome is well known to be a classical paraneoplastic syndrome of small cell lung carcinoma (SCLC).Only a few cases of myasthenia gravis (MG) and SCLC were previously reported. The causal association between lung cancer and non-thymomatous myasthenia gravis has not been clarified yet. To date, there has been no evidence supporting the speculation that association of myasthenia gravis with lung cancer might be one of the phenotypes of paraneoplastic syndrome. We present a case of a 47-year-old male ex-smoker with SCLC associated with myasthenia gravis evidenced by the clinical findings of ptosis, dysphagia, proximal weakness, and positive repetitive nerve stimulation (RNS) test.

Abbreviation: *MG(myasthenia gravis) ,SCLC(Small cell lung cancer), RNS (repetitive nerve stimulation), NMJ (neuromuscular junction), LEMS(Lambert-Eaton myasthenic syndrome). (LEMS),*

Introduction:

Myasthenia gravis is an autoimmune neuromuscular disease caused by autoantibodies to postsynaptic acetylcholine receptors, blocking their attachment at the postsynaptic junction. This results in a lack of the excitatory effects of acetylcholine at the postsynaptic nicotinic receptors. MG is considered as a paraneoplastic syndrome associated with thymoma in 15% of MG patients. Extrathymic malignancies have been also reported to happen simultaneously with MG.[1–5] . Here we reported this case of lung cancer presenting with postsynaptic NMJ disorder (MG).

Case Report:

A 47 years old diabetic, hypertensive, ex-smoker gentleman got admitted under Neurology Unit II with the complains of progressive weakness of both upper and lower limbs for one month and difficulty in swallowing of liquid food for ten days. He also gave history of weight loss in past six months but had no change in bowel and bladder functions, muscle twitching and gave no preceding history of anorexia , fever, cough or hemoptysis .

On examination, the patient was ill looking with below average body built . His vitals signs were normal. A hard, non tender, immobile swelling was noted over thye sternum. On neurological examination, he had dysarthia , nasal intonation, ptosis on right side ,left facial weakness, absent gag reflex and palatal palsy. Muscle power was 4/5,reflexes were normal and planters were bilaterally flexor. He had diminished ability and difficulty to sustain upward gaze for greater than 20 seconds. The patient was unable to maintain a sustained hold against gravity of the upper extremities while holding the arm in an outstretched position (Fig-1).

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Fig-1: *Pictorial profile of patient*

Respiratory system examination revealed diminished breath sound and dull percussion note over left lower lung field. All other systemic examination were normal.

His Hb% was 12.9 gm/dl,Total and differential white cell count was normal, Platelet count 2,34000/ cumm , ESR- 40 mm in 1st hr. His fasting Blood Sugar was 6.1 mmol/l and after breakfast was 9.7 mmol/l, HbA1C- 6.1% .Routine biochemical tests including renal function, liver function,electrolytes were normal.ECG was normal .Chest XR revealed opacities occupying left lung field with collapse of left lower lobe as evidenced by elevation of left hemi diaphragm(Fig-2).

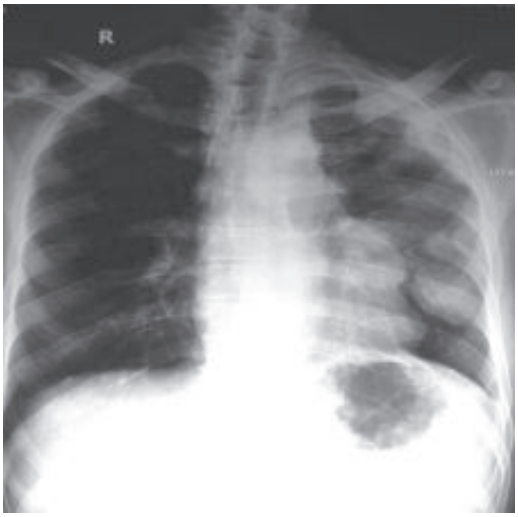

Fig-2: *CXR PA showing opacities occupying left lung field with collapse of left lower lobe*

No abnormality was detected in MRI of brain as well as MRI of cervical spine.

We performed standard repetitive nerve stimulation (RNS) test, which is one of the most sensitive diagnostic tests in patients with NMJ disorders, to evaluate patient's muscle weakness. We first performed nerve conduction study (NCS) in upper and lower limbs that were normal in distal latency, velocity and amplitude. Repetitive nerve stimulation (RNS) study of facial and ulnar nerve showed significant decremental response from 6th onward; thus suggesting neuromuscular junction disorder(Fig-3). After these procedures, needle electromyography was done in upper and lower limb muscles; that was normal in every parameter.

AChR-ab or Voltage gated calcium channel antibody was not tested . To evaluate the findings in the chest x-ray and to search for the presence of thymoma, chest CT scan with contrast was done. No evidence of thymoma was noticed.

CT scan of chest revealed a broad non- enhancing based soft tissue mass suggestive of consolidation(?Primary) with pleural base in left para vertebral , left anterior chest wall, anterior mediastinum, extending up to chest wall in left para sternal region and right para tracheal lymphadenopathy(Fig-4).

FNAC from subcutaneous nodule over sternum was done by orthopedic surgeons. Smear shows

anaplastic cells with scanty cytoplasm round to oval hyperchromatic nuclei with coarse cromatin and inconspicuous nucleoli.These cella are arranged in clusters,rossetes and singly; compatible with metastatic small cell carcinoma of lung and hstopathology report was positive for malignant cells; compatible with metastatic small cell carcinoma of lung(Fig-5).

Specialist consultation was taken from oncologist , and a CT guided FNAC from lung lesion was done , which was positive for malignancy suggestive of SCLC.

So, the patient was finally diagnosed as a case of Metastatic small cell carcinoma of lung with concurrent Myasthenia Gravis and DM ,HTN,CAD (S/P PCI to LCX)

For his treatment he received Pyridostigmine 30mg 8 hourly, dietary adjustment to control diabetes, Aspirin (75 mg) OD, Bisoprolol (5mg) OD , Losartan potassuim (25 mg)OD. Chemotherapy combined with thoracic radiation therapy (TRT) was his next treatment plan. Unfortunately the patient died 10 days later before therapy could be started.

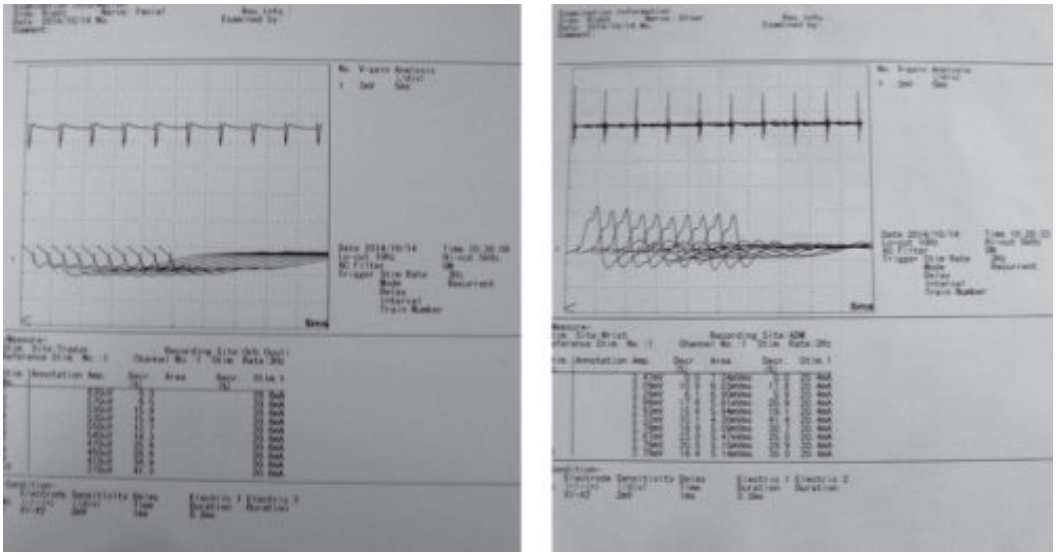

Fig-3: *Repetitive nerve stimulation (RNS) study data of facial and ulnar in reported patient.*

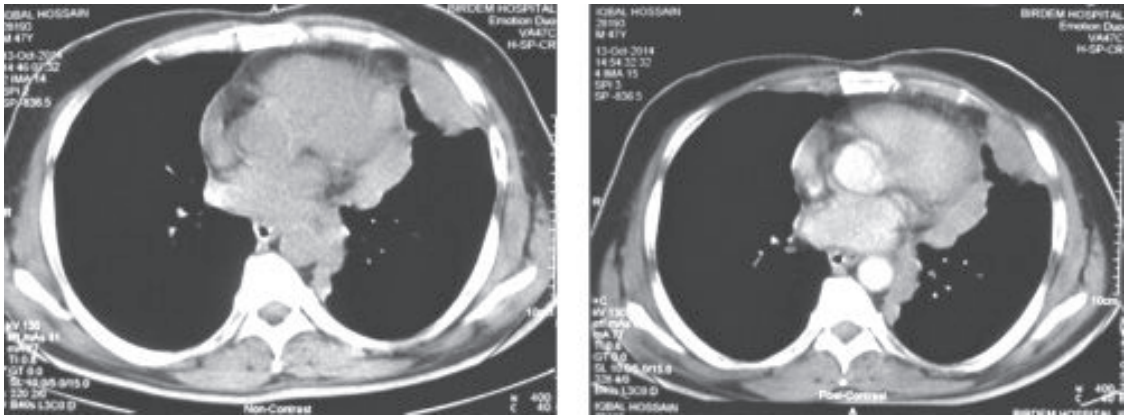

Fig-4: *CT scan of chest revealed a broad non- enhancing based soft tissue mass and right para tracheal lymphadenopathy*

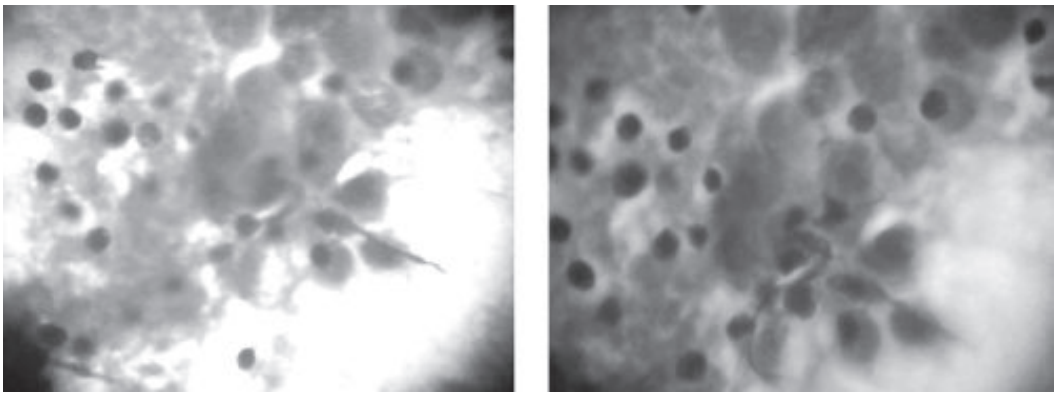

Fig.-5: *Smear showed anaplastic cells compatible with metastatic small cell carcinoma of lung*

Discussion:

Paraneoplastic syndromes are common findings in lung cancer. They often are incidental

findings serving as a harbinger to the underlying disease. They comprise syndromes involving the neuromuscular junction, vascular, hematologic, and metabolic syndromes as well as connective tissue and skeletal tissue disorders[6]. Paraneoplastic disorders are diagnosed in up to 15% of patients with the highest incidence occurring in NSCLC. Neurological paraneoplastic syndromes have an incidence of 0.01% of cancer patients, often imposing a burden on the patient's ability to carry out their activities of daily living[7]. These neurological syndromes comprise syndromes such as Lambert-Eaton myasthenic syndrome (LEMS), limbic encephalopathy, polyneuropathy, cerebellar degeneration, opsoclonus-myoclonus, and autonomic neuropathy[6,7].

Traditionally myasthenia gravis has been associated with several autoimmune diseases including lupus erythematosus, rheumatoid arthritis, diabetes mellitus type 1, Hashimoto's thyroiditis, grave's disease, and part of the paraneoplastic spectrum in thymic diseases such as thymoma[8].

The correlation between myasthenia gravis and primary lung carcinomas has not been established, as has clearly been defined for Lambert-Eaton syndrome and small cell carcinoma of the lung. There are few reports on primary lung carcinomas which complicate MG, in the medical literature[9-14] .

According to literature review, there are two types of association between lung cancer and MG.The more common is the occurrence of lung cancer in MG patients after many years of treatment that can be a coincidental finding[9-17]. Another type is presentation of cancer simultaneously with MG, which is a rarer report[17-19].

Only a few cases showing combined MG and SCLC features have been reported[20,21]. They were male and aged 49 to 56. Three cases were seronegative. In two cases, SCLC was found at the time when the diagnosis of MG was made. In Myoshi's case, SCLC was found 18 months after the diagnosis of MG. Three cases had classical oculo-proximal muscle weakness of MG.[21] One case had bulbar weakness. One case presented with MG crisis[22].

Anti-acetylcholine receptor antibodies (Anti-AChR abs) are the causative agents in myasthenia gravis[23]. These antibodies affect neuromuscular transmission by functional impairment of the AChR and accelerated degradation and complement activation at the AChR, ultimately leading to the loss of neurotransmission. 20% of these individuals, however, are referred to as seronegative patients. These individuals do not possess the classic anti-AChR abs rather they possess Anti-MuSK abs, an antibody towards argin/MuSK signaling pathway responsible for the functional maintenance of the postsynaptic neuromuscular junction [24].

The standard diagnosis of myasthenia gravis relies on the reliable demonstration of anti-AChR abs or anti-MuSK abs; however, these may not always be

available. Electrophysiologic testing through repetitive nerve stimulation may be used alternatively to detect a neuromuscular transmission defect (sensitivity 95–99%).In 1992, Chini et al. demonstrated the potential for small cell lung carcinoma, non-small lung carcinoma, and neuroblastomas to express the á3 subunit nAChR[25]. They further established the cross reactivity of autoantibodies against á3-nAChR against the a1 nAChR [25-27].In our case ,considering the diagnosis of SCLC and cost of testing for anti – ACR abs or anti-MuSK abs ,these tests were not done.

In conclusion, this case was a typical MG but his symptoms were the only clinical presentation of his underlying lung cancer; it means that MG can be a paraneoplastic syndrome, such as Lambert-Eaton myasthenic syndrome.

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