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CONTENTS

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Bangladesh Journal of Neuroscience

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- Review articles are subject to the peer review process. They should contain a maximum of 4000 words and 75 references.
- 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 of Dyslipidaemia in Young Patients with Recent Ischaemic Stroke

MOSTAFA HOSEN [1], MD. RAFIQUL ISLAM[2] , ABU NASIR RIZVI[2], MONIRUZAMMAN BHUYIAN[2]

Abstract:

Background*: The relation between serum lipids and ischemic stroke remains controversial in young patients. The aim was to determine the serum lipid profile and the vascular risk factors for ischaemic stroke in a series of patients under 45 with an ischemic stroke and to compare them with a series of controls of the same age.* ***Material and method:*** *This case-control study was conducted in the Department of Neurology and Department of Biochemistry of BSMMU, Dhaka, between the period of July 2007 and June 2009 for duration of two years. A total number of 50 patients presented with recent ischemic stroke and 50 control person were enrolled in this study. All patients of both sexes, aged between 15 to 45 years presented with ischemic stroke, from 0 day to 1 month that was confirmed by CT scan of head/MRI of brain. Vascular risk factors were recorded and blood sample was collected from the cases and the controls and analyzed at the Dept. of Biochemistry, BSMMU for estimation of serum fasting lipid profile.* ***Result:*** *Multivariate analyses showed that other than serum lipids- family history of dyslipidaemia, family history of stroke or TIA, history of HTN and smoking habit are found significant risks for stroke in young adult.* ***Conclusion:*** *The present study does not confirm the role of serum lipids as risk factors for ischemic stroke in young adult. Other than serum lipids- family history of dyslipidaemia, family history of stroke or TIA, history of HTN and smoking habit are found significant risks for stroke in young adult.*

Keywords: *Ischemic stroke; young people; lipoproteins.*

Introduction:

Stroke is a major global health problem. It is a major cause of mortality, morbidity and disability in developed and increasingly in less developed countries. ischemic stroke in young adults has been considered a relatively rare event, with fewer than 5% of all cerebral infarctions occurring below the age of 45 years, (Nedeltchev et al. 2005)[1].Studies of lipid related risk factors in cerebrovascular disease have varied greatly in their findings and also in their definition of the cerebrovascular end points[2-3]. Several clinical trials showed an association between high concentrations of serum cholesterol and ischemic stroke[4-6]. On the other hand, case-control studies of stroke which examined cholesterol as a risk factor have generally produced negative findings[7-8] and prospective studies have generally failed to show a direct and strong association[9]. Present study is designed to evaluate the serum lipid profile as a risk factor for young ischemic stroke patients less than 45 years in Bangladesh.

Materials and Methods:

This case control study was conducted in the Department of Neurology, BSMMU, Dhaka from July 2007 to June 2009 for duration of two years. Total 100 subjects were included in this study and of them 50 were young ischemic stroke patients, who were enrolled as cases and 50 were clinically healthy individual, enrolled as controls.

Subjects were selected following the inclusion and exclusion criteria-

1. Assistant professor. Department of Neurology. Sylhet M A G Osmani Medical College.
2. Professor. Department of Neurology. Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka

Inclusion criteria for cases:

1. Patients with clinical features of ischemic stroke proved by computed tomography scan and/MRI of head within 4 weeks of attack.
2. Young patients in between the age of 16 to 45 years.
3. Patients, who gave consent and complied with the study procedure, were included.

Exclusion criteria for cases:

1. Patients who refused to be included in the study
2. Patient with intracranial space occupying lesion (ICSOL) presenting with stroke like features.
3. Systemic disease like vasculitis, e.g. systemic lupus erythematosus (SLE), polyarteritis nodosa (PAN).
4. Head injury
5. Infective disease of brain and meninges
6. Abnormal cardiac condition giving rise to stroke e.g. valvular heart disease, atrial fibrillation.
7. Those patients who were on lipid lowering drugs.

Inclusion criteria for control:

1. Age group and sex matched with the cases
2. Clinically healthy individual voluntarily agreed to undergo the study protocol.
3. Agreed to collection of blood sample for biochemical test

Exclusion criteria for control:

Those who did not voluntarily agree to the study protocol after full explanation.

Data were collected in a structured questionnaire at stroke clinic and neurology ward in BSMMU. Collection of blood sample & estimation of serum lipid profile from the cases and the controls were done at the department of Biochemistry, BSMMU.

Statistical analysis:

The relationships between different variables of both case and control group was analyzed with the Chi-squared test; Student's t test where applicable. Risk factor was analyzed by multiple logistic regression model. The findings of the study are presented here.

Results:

Table 1, showed the distribution of the respondents by age. Mean ± SD of age of the cases was 39.88 ±7.26 years. Among the cases most common age group was 36-45 years (82.0%) followed by 26-35 and 16-25. Mean ± SD of age of the control was 39.68 ± 5.90 years. There is statistically no significant difference in age between the case and control (p>0.05).

Table II showed the sex distribution of the respondents of both case and control group. Male and female ratio was approximately 2:1 in each group. There is statistically no significant difference in sex between the case and control (p>0.05).

Table III revealed that out of all respondent of case and control group 40.0% and 10.0% had family history of diabetes mellitus, 34.0% and 16.0% had hypertension, 12% and 8.0% had familial history of

Table-I

Distribution of the respondents by age (n=100)

Age (in year)	Group		Total
	Case (n=50)	Control (n=50)	
16-25	3 (6.0)#	3 (6.0)	6 (6.0)
26-35	6 (12.0)	6 (12.0)	12 (12.0)
36-45	41 (82.0)	41 (82.0)	82 (82.0)
Total	50 (100.0)	50 (100.0)	100 (100.0)
Mean ± SD	39.88 ±7.26	39.68 ± 5.90	

#Figure within parenthesis indicates in column percentage.

Table-II

Distribution of the respondents by sex (n=100)

Sex	Group		Total
	Case (n=50)	Control (n=50)	
Male	32 (64.0)#	32 (64.0)	64 (64.0)
Female	18 (36.0)	18 (36.0)	36 (36.0)
Total	50 (100.0)	50 (100.0)	100 (100.0)

#Figure within parenthesis indicates in column percentage.

Table-III

Distribution of the respondents by family history of different diseases by group (n=100)

Family history	Group		p value*	Odd ratio
	Case	Control		
Diabetes	20 (40.0%)#	5 (10.0%)	0.001	6.00 (2.03-17.73)
HTN	17 (34.0%)	8 (16.0%)	0.038	2.71 (1.04-7.04)
IHD	6 (12.0%)	4 (8.0%)	0.505	1.568 (0.41-5.93)
Dyslipidaemia	18 (36.0%)	3 (6.0%)	0.001	8.81 (2.39-32.41)
Stroke/TIA	24 (48.0%)	9 (18.0%)	0.001	4.205 (1.69-10.45)

*Chi-square test was done to measure the level of significance.
#Figure within parenthesis indicates in column percentage. Multiple responses

IHD, 36.0% and 6.0% had dyslipidaemia and 48.0% and 18.0% had family history of stroke/TIA respectively. There is statistically significant difference in family history of diabetes, hypertension, IHD, dyslipidaemia and stroke/TIA between the case and control ($p<0.05$).

From Table IV, in case group 34.0% and in control group 10.0% had diabetes and patients with diabetes mellitus showed a risk of having stroke 4.64 times more than that of non diabetics. Out of all patients of case group 62.0% and in control group 10.0% had hypertension. Respondents having hypertension are 14.48 times more prone to develop stroke. There is statistically significant difference in respondents history of diabetes, hypertension in the case and control ($p<0.05$).

In table V, 24.0% of the case group and 13.0% in control group had smoking habit, in case group 14.0% and in control group 03.0% had history of alcohol intake, in case group 25.0% and in control group 09.0% were tobacco chewer .

Table VI showed mean (±SD) total serum cholesterol, triglyceride, HDL and LDL level for case group were 201.32 (±43.47), 145.48(±40.11), 34.26(±8.59), 137.96(±41.38) mg/dl respectively and in control group were 178.18(±38.62), 136.38(±57.11), 40.16(±8.05), and 110.74(±35.03) mg/dl respectively.

The table VII showed that in case group 54.0% had normal and 46.0% had abnormal level of total cholesterol. In control group 80.0% had normal and 20.0% had abnormal level of cholesterol. Statistically significant difference was observed between groups in term of total serum cholesterol level ($p<0.05$).

Table VIII showed In case group 60.0% had normal and 40.0% had abnormal level of triglyceride. In control group 68.0% had normal and 32.0% had abnormal level of triglyceride. No statistically significant difference was observed between groups in term of triglyceride level ($p>0.05$

Tabled IX showed In case group 24.0% had normal and 76.0% had abnormal level of HDL cholesterol. In control group 44.0% had normal and 56.0% had abnormal level of HDL cholesterol. Statistically significant difference was observed between groups in term of HDL cholesterol level ($p<0.05$).

Table-IV

Distribution of the respondents history of diseases by group (n=100)

Diseases	Group		p value	Odds ratio (CI)
	Case (n=50)	Control (n=50)		
Diabetes	17 (34.0)#	5 (10.0)	0.004*	4.64(1.55-13.84)
HTN	31 (62.0)	5 (10.0)	0.001*	14.48(4.96-43.51)
IHD	5 (10.0)	0 (.0)	0.056**	
Dyslipidaemia	4 (8.0)	1(2.0)	0.360**	
Stroke	2 (4.0)	0 (.0)	0.153**	

*Chi-square test was done to measure the level of significance.
**Fisher's exact test was done to measure the level of significance.
#Figure within parenthesis indicates in column percentage. Multiple responses

Table-V

Distribution of the respondents by personal habit by group (n=100)

Personal habit	Group		p value*	Odds ratio (CI)
	Case	Control		
Smoking habit	24 (48.0)	13 (26.0)	0.023	2.63(1.13-6.09)
Alcohol intake	7 (14.0)	3 (6.0)	0.182	2.55(0.62-10.49)
Tobacco leaf chewer	25 (50.0)	9 (18.0)	0.001	4.56(1.83-11.32)

*Chi-square test was done to measure the level of significance.
#Figure within parenthesis indicates in column percentage .Multiple responses

Table-VI

Distribution of the respondents fasting lipid profile level by group

Fasting lipid profile	Normal value	Mean ± SD	
		Case	Control
Total serum cholesterol	<200mg/dl	201.32 ± 43.47	178.18 ± 38.62
Triglyceride	<150mg/dl	145.48 ± 40.11	136.38 ± 57.11
HDL cholesterol	>40mg/dl	34.26 ± 8.59	40.16 ± 8.05
LDL cholesterol	<130mg/dl	137.96 ± 41.38	110.74 ± 35.03

Table-VII

Distribution of the respondents by total serum cholesterol by group (n=100)

Total serum	Group		p value*	Odd ratio
cholesterol	Case(n=50)	Control (n=50)		
Normal	27 (54.0)	40 (80.0)		
Abnormal	23 (46.0)	10 (20.0)	0.006	3.41 (1.40-8.28)
Total	50 (100.0)	50 (100.0)		

*Chi square test was done to measure the level of significance.

Table-VIII

Distribution of the respondents by triglyceride level by group

Triglyceride	Group		p value*	Odd ratio
	Case (n=50)	Control (n=50)		
Normal	30 (60.0)	34 (68.0)		1.42 (0.62-3.22)
Abnormal	20 (40.0)	16 (32.0)	0.405	
Total	50 (100.0)	50 (100.0)		

*Chi square test was done to measure the level of significance.

Table-IX

Distribution of the respondents by HDL cholesterol by group

HDL cholesterol	Group		p value*	Odd ratio
	Case	Control		
Normal	12 (24.0)	22 (44.0)		2.49 (1.06-5.86)
Abnormal	38 (76.0)	28 (56.0)	0.035	
Total	50 (100.0)	50 (100.0)		

*Chi square test was done to measure the level of significance.

Table X showed In case group 44.0% had normal and 56.0% had abnormal level of LDL cholesterol. In control group 76.0% had normal and 24.0% had abnormal level of LDL cholesterol. Statistically significant difference was observed between groups in term of LDL cholesterol level ($p<0.05$).

Table XI showed, logistic regression analysis of Odds ratios for characteristics of the patients likely to develop stroke. The variables revealed to be significantly associated with stroke by bivaraite analyses were all entered into the model directly. Variables entered into the model were family history of DM, HTN, dyslipidaemia, stroke/TIA, personal history of DM, HTN, smoking habit, tobacco leaf chewer, total serum cholesterol, HDL cholesterol LDL cholesterol were found to be the independent predictors of stroke with Odd ratios being 4.60, 1.66, 21.27, 4.48, 1.23, 11.70, 4.71, 2.44, 3.72, 3.25 and 2.52 respectively. Of them family history of dyslipidaemia, family history of stroke/TIA, personal history of HTN and smoking habit were found significant predictors.

Table-X

Distribution of the respondents by LDL cholesterol level by group

LDL cholesterol	Group		p value*	Odd ratio
	Case (n=50)	Control (n=50)		
Normal	22 (44.0)	38 (76.0)		4.03 (1.71-9.49)
Abnormal	28 (56.0)	12 (24.0)	0.001	
Total	50 (100.0)	50 (100.0)		

*Chi square test was done to measure the level of significance.

Table-XI

Logistic regression analysis for predictors of stroke in young

	B	S.E.	Wald	Sig.	Exp(B)	95.0% C.I.for EXP(B)	
						Lower	Upper
Family H/O DM	1.527	0.952	2.571	0.109	4.604	0.712	29.768
Family H/O HTN	0.504	0.743	0.461	0.497	1.656	0.386	7.103
Family H/O dyslipidaemia	3.057	1.180	6.717	0.010*	21.267	2.107	214.663
Family H/O stroke/TIA	1.500	0.726	4.272	0.039*	4.481	1.081	18.584
H/O DM	0.204	0.866	0.055	0.814	1.226	0.225	6.697
H/O HTN	2.460	0.764	10.379	0.001*	11.702	2.620	52.262
Smoking habit	1.550	0.769	4.061	0.044*	4.711	1.043	21.268
Tobacco leaf chewer	0.890	0.696	1.638	0.201	2.436	0.623	9.525
Total serum cholesterol	1.314	1.093	1.444	0.229	3.720	0.437	31.703
HDL cholesterol	1.180	0.762	2.394	0.122	3.253	0.730	14.495
LDL cholesterol	0.926	0.907	1.041	0.307	2.524	0.426	14.936
Constant	-4.455	1.018	19.165	0.001	.012		

* Significant predictor

Discussion::

All respondents were enrolled in this study from the age group of 16 to 45 years with a male and female ratio of 2:1. Majority of the cases presented at 36 to 45 years of life [Mean (± SD) age of case group was 39.88 (± 7.26) and control group was 39. 68 (± 5.90)] with male and female ratio of 2:1.There is no statistically significant difference in sex between the case and control (p>0.05) (Table 2).

In present study out of all respondent of case and control group 40.0% and 10.0% had family history of diabetes mellitus, 34.0% and 16.0% had hypertension, 12% and 8.0% had family history of IHD, 36.0% and 6.0% had dyslipidaemia and 48.0% and 18.0% had family history of stroke/TIA respectively.

Respondents having family history of diabetes, hypertension, IHD, dyslipidaemia and stroke/TIA are 6.0, 2.71, 1.57, 8.81 and 4.20 times more chance to develop stroke than respondents not having this type of family history respectively. These risk factors were measured by bivariate analysis.

Respondents having family history of stroke/TIA had 4.20 times more chance to develop stroke (p<0.05) than respondents not having this type of family history. Few studies have examined FHS as a risk factor for specific stroke types or in early-onset stroke cases. A matched case-control study conducted in India showed a significant 2.5-fold increased risk of stroke associated with FHS after adjusting for stroke risk factors (Zodpey et al. 2000) [10]. In a population-based case-control study of Japanese men and women aged 20 to 70 years, the risk of ischemic stroke was significantly increased in those with a FHS in any first- or second-degree relative (Kubota 1997) [11]. In a large prospective study conducted in Finland, an adjusted RR of 1.8 (*p* =0.03) for ischemic stroke and 2.8 (*p* =0.11) for SAH was found in those with an early parental history of stroke compared to those with no parental history in women aged 25 to 64 years (Jousilahti et al. 1997)[12]. These risk estimates were very similar in magnitude to those found in the current study of young patients aged 35 to 45 years (unadjusted OR [95% CI] =4.205 [.69-10.45]) and adjusted OR [95% CI] = 4.48 [1.08-18.58] for ischemic strokes.

In a study conducted by Jalal Uddin (2006), 20% of the patients with ischemic stroke had family history

of stroke while in control only 2% had positive family history[13]. All these findings are consistent with the findings of present study.

In case group of present series 34.0% and in control group 10.0% had history of diabetes and participants with positive personal history of diabetes mellitus showed a risk of having stroke 4.64 times that of negative personal history of diabetes mellitus. In Jalal Uddin (2006) [13] series diabetic persons had 3.917 times higher risk of ischemic stroke than non diabetic persons which is consistent with our findings. In Albucher et al (2000) [14]series Odds ratio for development of stroke in diabetes mellitus patients was 1.058.

Hypertension was one of the most important risk factor of cerebral infarction in this study, found in 62% of patient. This figure is almost similar to that reported by Safeer et al (2008)[15], Ali-L et al (1997) [16]and Al-Rajeh et al (1993)[17] and lower than reported by Burgin et al (65%)[18] and Feigin et al (85%)[19].

In the present study respondents not having hypertension were 14.48 times more prone to develop stroke than respondents not having hypertension. In multivariate analysis this risk reached 11.70 times. In Albucher et al (2000)[14] series Odds ratio for development of stroke for hypertensive patients were 18.67.About 60% patients of stroke group and 20% respondents of control group were hypertensive in Jalal Uddin series (2006) (P<0.05). Hypertensive persons showed a risk of having ischemic stroke 6 times higher than those of non-hypertensive persons in their series. Similar observation was also made in the present series.

In the present series among all respondents of case and control group 48.0% and 26.0% were smoker respectively. Smoker had 2.63 in bivariate analysis and 4.71 in multivariate analysis, times more chance to develop stroke than non smoker.

In Jalal Uddin series, 54% of case and 52% of the control group were smokers (p>0.05). Smokers showed a risk of having ischemic stroke 1.084 times higher than those of non-smokers in his series[13]. Similar result was found by Khan (2000)[20]. In his series 55% of ischemic stroke patients were smoker but in control group, only 33% were smoker.

Smoking is associated with increased risk of cerebral infarction (Pancioli 1998)[21]. In Safeer et al (2008) [15]study smoking was found in 31% of patients. The figure is slightly higher than other reported studies in Pakistan (Javed 1998)[22] and much lower than studies reported in Greenland (81%) (Kjaergaard and Gelvan 2004)[23].

The serum cholesterol–stroke association remains an enigma. If low serum cholesterol concentration is associated with an increased risk of hemorrhagic stroke (Iso et al., 1989; Yano et al., 1989)[24,25], increased cholesterol is associated with an increased risk of ischemic stroke (Iso et al., 1989; Knuiman and Vu, 1996)[24,26]. Studies in men subsequently showed increases in ischemic stroke rates at higher levels of total cholesterol, particularly for levels above 240 to 270 mg/dl (Iso et al., 1989 ;). The Asia Pacific Cohort Studies Collaboration found a 25% increase in ischemic stroke rates for every 1 mmol/L increase in total cholesterol (Zhang et al; 2003)[27]. Dyslipidaemia was present in 32% of Khan et al (2009) series which is higher than 11-23% reported in other studies (Ali et al., 1997;)[16].

In Jalal uddin (2006) series the total cholesterol level was 210±7.89 (mean±SE) mg/dl and 187±4.53 (mean±SE) mg/dl in case and control groups respectively (p<0.05). Previous case-control study conducted by Khan (2000) found the value of serum total cholesterol 201±5.52 (mean±SE) mg/dl in ischaemic stroke patients and 169.13±3.49 (mean±SE) mg/dl in corresponding control (p<0.05). Thus the result of the present study is consistent with the previous studies mentioned above although the age strictly was not mached.

LDL cholesterol level of patients with ischemic stroke in Jalal Uddin (2006) study was 156.99±7.53 (mean±SE) mg/dl in stroke group and was 126.44±4.47 mg/dl in control group (p<0.01). The values of HDL-c in case and control groups of the Jalal Uddin series were 30.34±0.91 vs. 41.04±0.87 (mean±SE) mg/dl (p<0.01). Low level of serum HDL-c was significantly associated with ischemic stroke in a previous case-control study conducted by Khan (2000) [20].

In this study high level of total serum cholesterol and LDL-c level and low level of HDL-c have odds of 3.41, 2.49 and 4.03 to develop stroke than that of normal level of these lipid profiles.

After adjustment with other predictors increased level of total serum cholesterol, lower level of HDL and higher value of LDL cholesterol had ODDs ratio (95% CI) of 3.72 (0.44-31.70), 3.25 (0.73-14.50) and 2.52 (0.43-14.94) respectively to develop stroke in young people.

In the present study after doing multiple logistic regression model- family history of DM, HTN, dyslipidaemia, stroke/TIA ; personal history of DM, HTN, smoking habit, tobacco leaf chewer ; total serum cholesterol, HDL cholesterol LDL cholesterol were found to be the independent predictors of stroke with Odd ratios being 4.60, 1.66, 21.27, 4.48, 1.23, 11.70, 4.71, 2.44, 3.72, 3.25 and 2.52 respectively. Of them family history of dyslipidaemia, family history of stroke/TIA, personal history of HTN and smoking habit were found significant predictors ($p<0.05$).

In this study bivariate analysis showed lower level of HDL- cholesterol and higher value of total cholesterol and LDL-c as risk factors for stroke but after adjusted these variables by other known risk factors no significant result has come out. So, this study does not conclude having any relation between ischemic stroke in young patients and serum lipid profile.

Conclusion :

The present study does not confirm the role for lipids as risk factors for ischemic stroke in young adult. Rather than lipids, family history of dyslipidaemia, family history of stroke or TIA, personal history of HTN and smoking habit were found significant risks for stroke. As the present study conducted in a single center in Dhaka city with small sample size, to find out such potential risk factors, more study is needed to see association of serum lipids as a risk factor for young ischemic stroke in our ethnic population.

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Serum Lead Level and Polyneuropathy among Bangladeshi Patients

SWAPON KUMAR GHOSE[1], KAZI GIAS UDDIN AHMED[1], AHMED HOSSIAN CHOWDHURY[2], A T M HASIBUL HASAN[3], KANOL SAHA[2], HASHMI SINA[2], MD. ARIFUZZAMAN[2], IFTIKHER ALAM[4], AMIT WAZIB[4], ASM REZAUL KARIM[5], MD. RAFIQUL ISLAM[6], MANSUR HABIB[7], QUAZI DEEN MOHAMMAD[8]

Abstract:

Background: *Heavy metals may produce various symptoms among the exposed, of which polyneuropathy is a matter of real concern. Our aim was to determine the pattern and association between polyneuropathy and blood lead level.* ***Methods:*** *This case control study was done in the department of Neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka in collaboration with Bangladesh Atomic Energy Centre from July 2001 to June 2002. The lead concentration in the blood was detected by X-ray fluorescence (XRF) technique. Nerve conduction study and CSF examination were done among the cases.* ***Result:*** *Data were collected from 92 respondents, of whom cases and controls were equal in number with a male to female ratio of 8.17:1. Mean age of the cases and controls were 30.87 +14.53 years and 30.91+ 12.03 years respectively. Among the cases, 55% had sub acute type of polyneuropathy, followed by acute and chronic type of polyneuropathy among 30% and 15% respondants respectively. The mean CSF protein level was 112.00 + 65.04 gm/L. The mean CSF protein was higher in acute polyneuropathy than in subacute and chronic cases (p<.001). The mean blood lead level among cases was 45.5587 with a standard deviation (SD) of +35.2625 and among control were 33.2065 with a SD of +5.6793. The difference was statistically significant (p= 0.021).*

Conclusion: *Increase blood level of lead is associated with polyneuropathy.*

Key words*: Polyneuropathy, lead concentration in blood.*

Introduction:

With industrialization and a tendency to keep a higher growth rate Bangladesh is driving towards becoming a middle income country. As a consequence of industrial revolution the chances of environmental and occupational exposure to these toxins are increasing. Toxicity from environmental exposure to lead has long term consequences. The non-biodegradable nature of lead poses a persistent threat for public health. Exposure to lead leads to breakdown of cellular homeostasis with a major effect on central and peripheral nervous system[1]. The usual form of lead neuropathy consists of motor weakness that primarily involves the wrist and finger extensors, especially among the painters but later spreads to other muscles with only minimal sensory involvement. Infrequently, there is a more typical toxic neuropathy with predominant distal sensory and motor involvement. The motor neuropathy is more likely to develop following relatively short-term exposure to high lead concentrations and evolves in a sub acute fashion[2-4].

1. Associate Professor of Neurology, Dhaka Medical College Hospital
2. Assistant Professor of Neurology, Dhaka Medical College Hospital
3. Registrar (Neurology),Dhaka Medical College Hospital
4. Junior Consultant, Dept of Neurology, Dhaka Medical College Hospital
5. Senior Consultant (Medicine), Nilphamari Sadar Hospital, Nilphamari
6. Professor of Neurology, Bangabandhu Sheikh Mujib Medical University
7. Professor of Neurology, Dhaka Medical College Hospital
8. Professor and Director, National Institute of Neurosciences and Hospital, Dhaka

Nerve conduction studies (NCS) have been carried out by several investigators in chronically exposed industrial workers with raised blood lead concentrations to see the electrophysiological evidence of neuropathy[5-9]. Interestingly enough, electrophysiology was found to be normal in many of these patients, who had minimally slowed motor conduction with slightly reduced compound muscle action potentials. These minimal abnormalities tended to improve once lead exposure ceased. Abnormalities of sensory nerve action potentials were noted only in a few of these subjects[9]. There is a generally weak relationship between the development of lead neuropathy and blood lead levels, at least for the subacute motor neuropathy, leading to speculation that the metabolic basis for the neuropathy is interference with porphyrin metabolism[10]. So we wanted to investigate the relationship between polyneuropathy and serum lead level among Bangladeshi patients.

Methods:

This hospital-based case- control study was carried out in the department of Neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka in collaboration with Bangladesh Atomic Energy Centre, Dhaka from July 2001 to June 2002. A total number of 120 polyneuropathy patients were selected during the study period. Out of them 46 patients fulfilling the inclusion criteria were finally selected as cases. The controls (46) were selected randomly who were non-polyneuropathy patient. The diagnosis was confirmed by a senior neurologist and nerve conduction study was done. Written informed consent was taken from all patients. Each of them was screened for possible common etiologies. Past medical history, family history, drug history, occupational history of exposure of lead and detailed clinical examination including examination of nervous system and cardiovascular system was done. The following investigations were done – routine blood examination, urine R/E, X-ray chest, random and fasting blood sugar, ECG, blood urea, serum creatinine, serum electrolytes. The lead concentration in the blood were detected by X-ray fluorescence (XRF) technique on both case and control groups. Nerve conduction study and CSF examination were done among the cases. All relevant information from history, clinical findings and investigation results were documented in predesigned interview schedule and check list. Recorded data were compiled and possible statistical analysis was done. The study protocol was approved by the institutional ethical committee.

Inclusion criteria:

- Typical history of polyneuropathy and fulfilling the lead induced neuropathy diagnostic criteria
- Age between 6-60 years
- Patient with positive nerve conduction study consistent with polyneuropathy
- CSF findings consistent with polyneuropathy

Exclusion criteria:

- Debilitated patient
- Patient with intercurrent illness
- Patient with diabetes mellitus, thyroid dysfunction, kidney dialysis and alcoholic polyneuropathies
- Occupational H/O exposure of lead.

Consent to participate:

Informed written consent was obtained from each of the respondent after appropriate explanation of the study procedure.

Consent to publish data:

The manuscript does not contain any individual image, video or any detail of individual patient, the publication of which might be subjected to prior consent to publish the data

Ethical approval:

Ethical permission was granted by the ethical review committee of Dhaka Medical College (DMC) after proper submission of the study protocol.

Result:

Total 92 respondents were studied, among them 46 were cases and 46 were controls. Mean age of the cases and controls were 30.87 +14.53 years and 30.91+ 12.03 years respectively. Of the total respondents, 89.1% were male and 10.9% were female (Table-1). Among the cases, more than half of the respondents (55%) were in sub acute type of polyneuropathy, followed by acute (30%) and chronic

(15%) type of polyneuropathy (Fig.1). The mean CSF sugar level among the cases was 4.8191+ 2.7442 mmol/L and mean CSF protein level was 112.00 + 65.04 gm/L. The mean CSF protein was higher in acute polyneuropathy than in subacute and chronic cases, which was also statistically significant (p<.001)(Table-2). The mean blood lead level among cases was 45.5587 with a standard deviation of +35.2625 and among control were 33.2065 with a standard deviation of +5.6793. The difference was statistically significant (p= 0.021) with a higher blood lead level among the cases (Table-3).

Table-I

Demographic characteristics of the respondents

Characteristics	Group	Case	Control
Age in year	30.83+ 14.83	30.91+12.03	
(Mean +SD)			
Sex	Male	41(89.1%)	5(10.9%)
	Female	41(89.1%)	5(10.9%)

Figure 1 showing the majority (55%) of the cases had sub acute polyneuropathy, followed by acute (30%) and chronic (15%) polyneuropathy.

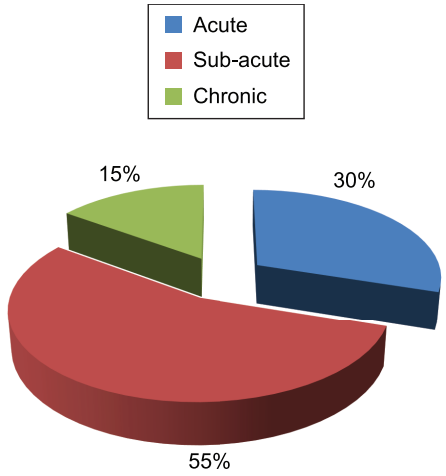

Fig.-1: *Distribution of the cases by types of polyneuropathy*

Table-II

Distribution of the cases by biochemical analysis of CSF

CSF sugar(mmol/l)	No.	Mean(mmol/l)	SD(mmol/l)	F	Sig.
Acute	14	6.1886	3.97	2.916	.065
Sub-acute	25	4.0656	1.76		
Chronic	07	4.7714	1.74		
CSF protein(gm/l)					
Acute	14	170.8571	30.59	15.997	.000
Sub-acute	25	96.28	63.56		
Chronic	07	50.4286	1.61		

Table-III

Lead level in blood among cases and controls

Characteristic	Respondents	No.	Mean	SD	t	df	p
Blood level of lead	Case	46	45.5587	35.2625	2.346	90	.021
(µgm/dl)	control	46	33.2065	5.6793			

Discussion:

Lead, being an ubiquitous and versatile metal, has become widely distributed and mobilized in the environment and with a consequent increase in human exposure. Exposure of human populations to environmental lead has increased with industrialization and large-scale mining[11]. Global lead contamination, of lead in soil, water and air is attributable to increased of human activities[12]. The pre-industrial blood lead level in humans was estimated to be about 0.016 mg/dl, which is 50–200 times lower than the lowest reported levels in human today. [13]. The matter of huge concern is that this level is about 625 times lower than the current level of concern for children (i.e. 10 mg/dl) proposed by the Centers for Disease Control and Prevention in the USA[14].

In this study, majority of our cases had sub acute form of polyneurpathy along with higher CSF protein level in comparison to the age and sex match control. The mean serum lead level was also higher among the cases.

Age of the respondents was found to have no relation among the groups but younger the age, more would be the susceptibility to develop polyneuropathy. Brody DJ et al also showed similar findings[15]. But Reinhard K et al[16] showed that lead concentration was found to be increasing with age. One possible reason for this discrepancy might be that they had been residing close to high lead exposure, like highway or busy traffic. But our study had age matched in between cases and control. So the effect of increasing age, if any, is minimal. Most of the previous electrophysiological studies have concentrated on groups of workers exposed to lead with or without neuropathic symptoms, or on those occasional patients with subacute motor weakness associated with lead toxicity. Minor changes in distal motor nerve conduction or CMAP amplitudes have been noted when the level of safe chronic occupational exposure was exceeded[3,5-7]. But the uniqueness in our study is that we excluded the definite occupational exposure of lead among respondents.

The nervous system is the most sensitive and chief target for lead related toxicity. Both the central and the peripheral nervous system may be affected[17]. The effect also depends on age of exposure of the patient and the duration. The effects on the peripheral nervous system are more pronounced in adults while the central nervous system is the target in children[18]. The earliest lead-induced changes are observed in the endothelium of the microvasculature, which is an essential component of the blood– brain barrier[19]. Electrophysiological studies showed that neurosensory processing may be affected by lead and provided a direct link between lead exposure and neurologic deficits[20].

In this study, the mean blood lead level was significantly higher in neuropathic respondents. This finding was supported by O Rubens et al, and Ruth Lilis et al[21, 22]. Though these studies had some difference in methodology than this one, the result was comparable. This is probably attributed to recent industrial development in Bangladesh. Our finding about blood level also supports the conclusion World Health Organization (WHO) have made in a theme paper about environmental lead exposure and public health concern, mentioning that rapid industrialization and the persistence of lead in the environment, exposure is likely to remain a significant public health problem in most developing countries for many years[23].

Limitations:

Non-uniform nerve conduction velocity study was carried out in all respondents to detect particular nerve conduction velocity in the case group only. Again different nerves were tested in different respondents. Although X-Ray Fluorescence spectrometry is a powerful tool for elemental analysis, it cannot trace out the actual normal limit of lead level in blood.

Conclusion:

This study finding showed that increase blood level of lead was associated with polyneuropathy. Additional in depth research is needed to determine the causal factors of polyneuropathy.

Conflict of interest: None

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Efficacy of low-dose Topiramate in Migraine Prophylaxis

MUHAMMAD ABDUL MOMEN KHAN[1], MOHAMMAD BAHADUR ALI MIAH[2], MD.SHAHIDULLAH[2], MD. RAFIQUL ISLAM[3], SUBASH KANTI DAY[2], JANNATUL FERDOUS[4], MD. AMIR HOSSAIN[5]

Abstract:

Background: *Anticonvulsants are now commonly used for migraine prophylaxis, among them topiramate, one of the newer anticonvulsants, recently has been demonstrated to be effective as mono-therapy for migraine prophylaxis.* ***Objectives:*** *To observe the efficacy and safety of low dose topiramate in migraine prophylaxis.* ***Methods:*** *This prospective trial was carried out in the Out Patient Department (OPD) & Headache Clinic, Department of Neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka. Total 60 patients around the age range of 18 to 50 years diagnosed as migraine (with aura or without aura) according to ICHD-3 criteria, were recruited as the study population. Total 60 patients were administered by Tab.Topiramate 50 mg/ day. Out of them, total 47 patients had completed the study due to drop out of 13 patients. During trial, three follow up visits were taken, 1st follow up after 4 weeks of baseline information (Before starting prophylactic medication), 2nd follow up after 4 weeks of treatment, 3rd follow up after 8 weeks of treatment. Efficacy of treatment was measured by headache frequency, duration and severity as measured by the VAS. Effectiveness was assessed by comparing baseline & on-treatment migraine status.* ***Results:*** *The mean (SD) age of patients were found 29.72 (9.58) years. Female sex was predominant. The mean (SD) value of frequency of migraine at baseline level with 1st and 2nd follow up were statistically significant [Baseline 9.28 (2.39) vs. 1st FU 7.55 (3.07), p=0.001; Baseline 9.28 (2.39) vs. 2nd FU 4.72 (2.80), p<0.001]. Duration of each episode of migraine ,comparing the mean (SD) value of duration of migraine of baseline level with 1st and 2nd follow up were statistically significant [Baseline 10.85 (5.26) vs. 1st FU 8.06 (4.11) hr, p<0.001; Baseline 10.85 (5.26) vs. 2nd FU 5.53 (2.98) hr, p<0.001]. According to severity of migraine based on VAS in base line period all patients had experienced moderate & severe headache but in 1st follow up, few patients had experienced mild headache from moderate headache, few patients had experienced moderate headache from severe headache & in 2nd follow up, patients had better condition and had experienced mild and moderate headache, no patient had experienced severe headache. In this study, 23.4% patients developed adverse effects. Among the adverse effects, 8.5% develop dizziness, 6.3% drowsiness, 4.2% anorexia & blurring of vision.* ***Conclusion:*** *The present study suggest that low dose topiramate are effective for migraine prophylaxis in reduction of frequency, severity and duration of migraine headache .*

Key words: *Efficacy, low-dose Topiramate, Migraine*

Abbreviations: *VAS- Visual Analogue Scale, ICHD- International Classification of Headache Disorder, SD- Standard Deviation*

Introduction:

Migraine is an episodic central nervous system disorder characterized by vascular headache associated with vasodilatation of extra-cranial vessels but may be due to disturbed neuronal activity in the hypothalamus [1]. Migraine headache ranges from moderate to very severe in intensity and lasts from 4 to 72 hours [2], often accompanied by photophobia, phonophobia and vomiting [3].

According to World Health Organization (WHO) migraine is the global burden of health related issue. That study was conducted in 2000 and was reported

1. Assistant Professor, Department of Neurology,Manikgonj Medical college
2. Associate Professor, Department of Neurology, BSMMU
3. Professor, Department of Neurology, BSMMU
4. Resident, Department of Paediatrics, SSMC & Mitford Hospital
5. Assistant Professor, Department of Neurology,SBMC,Barisal

in the World Health Report 2001. Migraine included for the first time in years lived with disability (YLD) & contributing 1.4% of YLD, is the 19th cause of disability in both sexes of all ages & 12th in case of women, accounting for 2.0% of YLD, in case of women[4]. Successful management of migraine requires intensive patient's educations and through physician knowledge about available treatment options and strategies. Use of a prophylactic medication reduces headache duration, frequency, severity and risk for rebound headache [5].

Migraine is a common condition, annually affecting 12% of the United States population, including 18% of women, 6% of men and 4% of children. Migraine is generally more common in people who are in lower socioeconomic groups [6].

In Bangladesh there is no data regarding the prevalence of migraine. In a study conducted in BSMMU headache clinic total 3440 of headache patients were studied and 16.05% of them had a diagnosis of migraine [7].

Different elements need to be considered in migraine management. They include: avoidance of triggering factors, lifestyle modifications, non-pharmacological therapies and lastly medications. Pharmacological treatment is traditionally divided into acute treatment, and preventive treatment. Many migraine patients can be treated using only acute treatment that are used only during headache attacks to abort an ongoing attack or to stop its progression to severe pain and associated symptoms. Patients with severe and/or frequent migraine require long-term preventive therapy [8].

Prophylaxis is recommended to reduce the frequency and/or intensity of migraine headaches when patients experience more than three to five attacks per month. A variety of drugs from diverse pharmacological classes are in use for migraine prevention. Adrenergic receptor blockers (e.g. propranolol), tricyclic antidepressants (e.g. amitriptyline), anticonvulsants (e.g. topiramate and valproate), and serotonergic drugs (e.g. methysergide) are most commonly administered for this purpose, as summarized in US Headache Consortium Guidelines .More recently, topiramate was tested prospectively. Topiramate showed statistically significant efficacy in migraine prevention .Topiramate appeared to be safe and had an acceptable safety profile. Among several treatment-emergent adverse events dose dependent weight loss is common. For these reason, slow titration of target dose of topiramate is advisable [9].

The impact of migraine on the sufferer and his or her productivity in national level is innumerable. For the last decade, anticonvulsants are in use as prophylactic medication for migraine, among which sodium divalproex & sodium valproate are the most studied. For the last few years, high dose (100- 200 mg/day) of topiramate was used in migraine prophylaxis, but with such high doses, usually significant side effect could have occurred.

In this context, the present study was designed to observe the effect of low dose topiramate (50 mg/ day) in migraine prophylaxis

Materials and Methods:

A clinical trial was conducted in Out Patient Department (OPD) & Headache Clinic, Department of Neurology, BSMMU, Dhaka. Informed written consent was taken from all patients. Migraine was diagnosed according to the criteria of the Headache Classification Committee of the International Headache Society, 2013(ICHD-3). Considering 10% drop out in every follow up, sample size was 60. A total 60 patients were selected according to selection criteria.

Inclusion criteria

1. Patient of migraine (with typical aura or without aura) according to ICHD-3 criteria.
2. Age at entry: 18-50 years.
3. Patients not on any prophylactic medication.
4. Patients willing to take part in the study.
5. Patient being able to fill a headache diary successfully & reliably.

Exclusion criteria

1. Age <18 years or >50 years.
2. Patients having headache other than migraine.
3. Patients on prophylactic medication.
4. Any co-morbidity such as hepatic or renal impairment, malignancy, intracranial vascular aneurysm, pregnancy & breastfeeding etc.

5. Patients not willing to take part in the study.
6. Patient having known hypersensitivity to topiramate

Detailed history, general examination, neurological examination, routine laboratory investigations and other relevant investigations were carried out accordingly. They were taught to maintain their headache character on a headache diary supplied to them & advised them to report at the headache clinic after 4 weeks. Intensity of headache was measured by Visual Analogue Scale (VAS). VAS is graded as mild, moderate and severe in intensity.

The analysis was done by comparing the number of days (duration) with headache, frequency and intensity of headache according to visual analogue pain scale before starting of prophylaxis and that of 4 weeks and 8 weeks after treatment. Outcome measured were reduction of visual analogue pain scale score, duration and frequency of acute attacks of headache compared to the baseline with subsequent follow up, adverse effects were individually registered .The trial evolved into 2 stages:

Stage-1(4 weeks): The base line period or medication(Topiramate) free period. During this period the subjects were taught to fill their headache diary to record the baseline headache characters, they act as control group in this study. Those who filled the headache diary reliably entered into the stage-2. Stage- 2(8 weeks): Tab.Topiramate was given & headache character was recorded by the patients themselves on headache diary. Patient was treated by Tab Topiramate 25 mg at night for 1 week, followed by 25 mg twice daily for another 7 weeks. Continuous data were expressed as mean and standard deviation and qualitative data were expressed as frequency distribution and percentage. Statistical analysis was performed by using SPSS-21. Data were analyzed by Wilcoxon signed ranks test as data shows asymmetric distribution. For all statistical tests, we considered p value <0.05 as statistically significant. Approval from the IRB of BSMMU was obtained prior to the commencement of this study.

Results:

Total 60 patients in the age range of 18 to 50 years diagnosed as migraine (with aura or without aura) according to ICHD-3 criteria, were enrolled as study population. Of them total 47 patients completed the study due to drop out of 13 patients in different steps of follow up. Table-I showed that there were 72.3% female & 27.7% male. A total 20 (42.3%) patients were in age group of 28-25 years and 12 (25%) were in the age group of 26-35 years(Table-II).Table-III showed that there were 14.9% patients experienced aura & 85.1% patients were free from aura.

Table-I

Study population by gender

Gender	Number of patients	Percentage
Female	34	72.3
Male	13	27.7
Total	47	100

Table-II

Study population by age

Age (year)	Number of Patients	Percentage
18-25	20	42.6
26-35	12	25.5
36-45	8	17.00
46-50	7	14.9
Total	47	100

Mean (SD) [yrs] 29.72 (9.58)
Range (min-max) [yrs] (18-48)

Table-III

Aura of migraine among study population

Type of Migraine	Number of Patients	Percentage
With Aura	7	14.9
Without Aura	40	85.1
Total	47	100

Table-IV showed distribution of the patients according to baseline, 1st & 2nd follow up in frequency of migraine attack , comparing the mean (SD) value of frequency of migraine attack at baseline level with 1st and 2nd follow up were statistically significant [Baseline 9.28 (2.39) vs. 1st FU 7.55 (3.07), p=0.001;

Baseline 9.28 (2.39) vs. 2nd FU 4.72 (2.80), p<0.001]. Table-V shows distribution of the patients according to duration of each episode of migraine (hours) ,comparing the mean (SD) value of duration of migraine of baseline level with 1st and 2nd follow up were statistically significant [Baseline 10.85 (5.26) vs. 1st FU 8.06 (4.11) hr, p=<0.001; Baseline 10.85 (5.26) vs. 2nd FU 5.53 (2.98) hr, p<0.001]. Table-VI shows distribution of the patients according to severity of migraine based on categories of Visual Analogue Scale (VAS). During clinical trial of 1st follow up, patients were distributed in all mild, moderate and severe groups . In 2nd follow up, patients had better condition and distributed in mild and moderate groups. Table-VII shows distribution of patients according to adverse effects. In this study, 23.4% patients developed adverse effects. Among the adverse effects, 8.5% develop dizziness that was followed by 6.3% drowsiness.

Table-IV

Frequency of migraine attacks

Type of patients	Frequency of migraine attack Mean (SD)	p-value*
Baseline level	9.28 (2.39)	
1st Follow up (after 4weeks)	7.55 (3.07)	0.001s
2nd Follow up (after 8weeks)	4.72 (2.80)	<0.001s

s=significant

*Wilcoxon signed ranks test was done to measure the level of significance.

Table-V

Duration of each episode of migraine (hours)

Type of patients	Duration of each episode of migraine (hour) Mean (SD)	p-value*
Baseline level	10.85 (5.26)	
1st Follow up (after 4 weeks)	8.06 (4.11)	<0.001s
2nd Follow up (after 8 weeks)	5.53 (2.98)	<0.001s

s=significant

*Wilcoxon signed ranks test was done to measure the level of significance.

Table-VI

Severity of migraine based on Visual Analogue Scale (VAS)

Severity of migraine	Number of patients	Percentage
Baseline level		
Moderate	25	53.2
Severe	22	46.8
1st followup		
Mild	24	51.1
Moderate	15	31.9
Severe	8	17.00
2nd followup		
Mild	29	61.7
Moderate	18	38.3
Total	47	100

Table-VII

Adverse effects among study population

Adverse effects	Number of Patients	Percentage
Yes	11	23.4
Dizziness	4	8.5
Drowsiness	3	6.3
Blurring of vision	2	4.2
Anorexia	2	4.2
No	36	76.6
Total	47	100

Discussion:

Various drugs have been used for migraine prophylaxis. Recently, antiepileptic drugs including topiramate (TPM) are more commonly used in adults and adolescents for migraine prophylaxis. In several randomized, double-blind, placebo-controlled, dose-ranging trials involving adult patients with episodic migraine, topiramate treatment resulted in significant benefit compared with placebo, with efficacy observed within the first month of treatment [8].

Analysis of age distribution showed that, the mean age was found 29.72 (9.58) years and range were (18-48). A good number of the study patients were 18- 25 years age group. A study done by Dahlöf et

al. (2007)[10] found mean (SD) age, 39.8 years who studied on topiramate placebo-controlled clinical trials. Silberstein et al. (2012)[8] and Brandes et al. (2004)[9] also obtained mean age 40.4 ± 11.5 and 38.3 ± 12.0 years respectively. In this study, patients were younger than the patients of above mentioned studies.

Out of all patients, 72.3% was female and 27.7% male. Dahlöf et al (2007)[10] also found as female groups more prone to develop migraine. Diener et al. (2004)[11] and Brandes et al. (2004)[9] also found more female patients of migraine 76% and 82%, respectively. These results are similar to this study.

Out of all patients, 7 (14.9%) patients had migraine with aura & 40 (85.1%) were free from aura. Among them major portion of patients had visual aura (12.76%), followed by sensory aura (2.14%).

The efficacy of topiramate, based on frequency of migraine attack was observed where mean (SD) value of frequency of migraine attack of baseline level with 1st and 2nd follow up were statistically significant [Baseline 9.28 (2.39) vs. 1st FU 7.55 (3.07), p=0.001; Baseline 9.28 (2.39) vs. 2nd FU 4.72 (2.80), p<0.001]. Ashtari et al. (2008)[12] found that the topiramate group showed more reduction in migraine frequency, so present study results is similar with that study.

The efficacy of topiramate based on duration of each episode of migraine (hour) was observed, where mean (SD) value of duration of migraine of baseline level with 1st and 2nd follow up were statistically significant [Baseline 10.85 (5.26) vs. 1st FU 8.06 (4.11) hr, p<0.001; Baseline 10.85 (5.26) vs. 2nd FU 5.53 (2.98) hr, p<0.001]. Ashtari et al. (2008)[12] found, headache duration decreased more in topiramate group, so present study results is similar with that study .

At baseline level, patients were distributed into moderate and severe groups. During clinical trial of 1st follow up, patients was distributed in all mild, moderate and severe groups. At the end of the trial 2nd follow up, patients had better condition and distributed in mild and moderate group. Ashtari et al. (2008)[12] measured headache intensity, lessened more in topiramate group.

Regarding adverse effects, 23.4% patients developed adverse effects. Among the adverse effects 8.5% develop dizziness that was followed by drowsiness 6.3%. Adverse effects of topiramate are 16% in the study of Silberstein et al. (2012)[8] which was relatively similar with the present study.

In present study, efficacy and adverse effect of topiramate were observed and results showed that topiramate was effective in recducing frequency and severity of headache.

Conclusion:

Considering statistical analyses, a conclusion can be made that low dose topiramate are safe and effective for migraine prophylaxis in reducing of frequency, severity and duration of migraine headache.

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Association of Serum Ferritin with Amyotrophic Lateral Sclerosis: A Case Control Study

MD. KABIRUZZAMAN[1], AKM ANWAR ULLAH[2], MA HANNAN[2], MD, REZAUL KARIM KHAN[2], MD RAFIQUL ISLAM[2], ABU NASER REZVI[2], BAHADUR ALI MIAH[3], MOHAMMAD SHAH ZAHIRUL HOQUE CHOWDHURY[4], NURUDDIN MOAHMMAD EUSUF[5], ABU JAFOR MD. SALAUDDIN[6], ABDUL ALIM[7], MD. KHAIRUL KABIR PATWARI[7], LT. CON. HUMAYUN[8], MOHAMMAD SAYEED HASAN[7], RASHED IMAM ZAHID[9], AKM GOLAM KABIR[10], MD. MASUD RANA[11].

Abstract:

Background: *Despite conflicting results from prospective studies, substantial evidence is accumulating suggesting that high Serum Ferritin was associated with Amyotrophic Lateral Sclerosis.* ***Objective:*** *Our aim was to find out the association of serum ferritin with Amyotrophic Lateral Sclerosis.* ***Methods:*** *This was a retrospective, case-control study done in the Neurology, Department of Bangabandhu Sheikh Mujib Medical University on 76 subjects with equal number of cases and controls with their age ranging from 15 to 70 years. Results: The analysis revealed that serum ferritin were significantly high in ALS patients 158.9 ± 16.6 and p= 0.004 as compared to control 104.8 ± 7.9. The proportion of patients below 40 years of age was a bit higher. Predominance in male 73.7% and female 26.3%, predominantly workers or housewife 65% followd by day labourers 26%. A large proportion of patients in both groups were non-smoker (73.7% in case and 78.9 in control group).* ***Conclusions:*** *High Serum ferritin is an important risk factor for ALS. A strong positive correlation was also observed between high serum iron and ALS in our study.*

Key words: *Serum ferritin serum iron and ALS.*

Introduction:

Amyotrophic lateral sclerosis, or ALS, were reported as early as 1824 by Charles Bell and others[1,2]. However, Charcot was the first to describe the condition in detail, based on careful clinico-pathological correlation and he coined the term amyotrophic lateral sclerosis[3]. Motor neuron disease, or MND, as used by Brain in the first edition of this textbook[4], is the name used for the disease most commonly in the United Kingdom and represents an umbrella term encompassing amyotrophic lateral sclerosis and three other disorders that are considered its clinical variants: primary lateral sclerosis, progressive muscular atrophy, and progressive bulbar palsy. In the USA, amyotrophic lateral sclerosis is sometimes known as Lou Gehrig's disease after the famous Yankee baseball player who developed the disease at the peak of his sports career and died in 1941. Amyotrophic lateral sclerosis is sometimes referred to as LAS/MND.

The incidence of ALS reported from recent epidemiological studies ranges from 1 and 3 per 100 000, with point prevalence rates of 6-8 per 100

1. Assistant Professor, National Institute of Neurosciences and Hospital, Dhaka.
2. Professor, Dept. of Neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka.
3. Associate Professor, Dept. of Neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka.
4. Associate Professor cum RP, National Institute of Neurosciences and Hospital, Dhaka.
5. Assistant Professor, Adin Medical College Hospital, Dhaka.
6. Assistant Professor, Satkhira Medical College, Dhaka.
7. Assistant Professor, National Institute of Neurosciences and Hospital, Dhaka.
8. Neurologist, CMH, Dhaka.
9. Medical Officer, National Institute of Neurosciences and Hospital, Dhaka.
10. Assistant Professor, Dept. of Radiology, National Institute of Neurosciences and Hospital, Dhaka.
11. Medical Officer, Dept. of Neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka.

000[5,6]. Most of the studies have been conducted in developed countries and relatively little is known of the incidence and prevalence in developing countries, or in specific racial or ethnic groups. Pockets of high incidence are described amongst the Chamorro indigenous population of the Western Pacific Island of Guam, on the Kii peninsula of Japan and amongst the Auyu and Jakia people of Irian Jaya[7,8]. The explanation for the strikingly increased incidence and prevalence of motor neurone disease in these geographical foci remains uncertain. Although the prevalence remains high in Guam compared to typical populations in western countries, there has been a substantial decrease over the last half century.

The disease usually begins with weakness and wasting of hand muscles, associated with cramping and fasciculations in the arm muscles and then shoulder girdles. Less often, the symptoms begin in one leg as a foot drop, soon followed by weakness of plantar flexor and other leg muscles. Before long, the triad of atrophic weakness of the hands and forearms, slight spasticity of the legs, and generalized hyperreflexia with Babinski and Hoffman signs- all in the absence of sensory changes- leaves little doubt as to the diagnosis. Early or late in the illness, dysarthria, dysphagia, and dysphonia set in, and the tongue may wither and fasciculate; or a spastic bulbar paralysis (pseudobulbar palsy) may become prominent.

Diagnosis of ALS is clinical and based on diagnostic criteria. The EL Escorial diagnostics criteria is established since 1994. These criteria were subsequently revised and the key feature of the revised criteria are summarized[9]. Electrophysiological study demonstrating neurogenic changes that cannot be explained by a single nerve, root, or plexus lesion[10]. Assessment of the thoracic paraspinal muscles can be particularly valuable in differentiating amyotrophic lateral sclerosis from multilevel spondylotic radiculomyelopathy[11]. In ALS pathology has been considered traditionally a pure motor disorder now regarded as multi system disease in which motor neurons tend to be affected earliest and most severely[12].

In ALS patients will typically have lost 50 per cent of the lower motor neurons in the limb enlargement areas of the spinal cord at autopsy[13]. Many of the remaining lower motor neurons show atrophic and basophilic changes that are likely to represent part of the spectrum of an apoptosis, programmed cell death pathway[14]. The depletion of lower motor neurons is accompanied by diffuse astrocytic gliosis in the spinal grey matter. There is relative preservation of motor neurone in the nucleus of Onufrowitz, Onuf's nucleus, in the sacral spinal cord[15], which innervates skeletal muscles of the pelvic floor, and in the cranial motor nuclei of the oculomotor, trochlear, and abducens nerve which control eye movements.

The primary pathogenetic processes underlying amyotrophic lateral sclerosis are multifactorial and the precise mechanisms underlying selective cell death in the disease are at present incompletely understood. There may be complex interplay between multiple mechanisms including genetic factors, oxidative stress, excitotoxicity, and protein aggregation as well as damage to critical cellular processes, including axonal transport and organelles such as mitochondria[16,17,18]. Recently there has been growing interest in the role played in motor neuron injury by neighboring non- neuronal glial cells and in dysfunction of particular molecular signaling pathways. The relative importance of these different pathways may well vary in different subgroups of patients.

The cause of ALS is unknown. Many hypothesis have put forward, including that of viral infection, activation of the immune system, exogenous toxins, and hormonal disturbances. However, there has been insufficient evidence to implicate any of these as the major cause of motor neuron degeneration in ALS patients.

The only proven risk factors with the development of ALS disease are gender, a positive family history, and increasing age. Search for linked with environmental, occupational, or physical factors have been done but not yet established. Recently several studies show high serum Ferritin associated with neurodegenerative disease. Several studies also revealed that there was a association of high serum

Ferritin with ALS patient. Elevated levels of Ferritin also have been reported in the spinal cord of ALS patients compared to controls and in Guamanian ALS patient brain samples. High Ferritin promotes oxidative agent in ALS patient. As we know abundant neurofilaments are present in the cytoskeleton of motor neuron, where they are vital for bidirectional axonal transport, oxidative stress causes slow axonal transport, ultimately neurofilament injury. Higher serum Ferritin also causes uncontrolled release of iron, which donate electron for the generation of the super oxide radical and can participate in the generation of hydroxyl radicals via the Fenton reaction (Fe (II) + H2O2'!Fe (III) + OH- + OH) and generation of such reactive species directly damage DNA, lipids and proteins leading to profound cellular toxicity specially motor neuron cell[19].

Materials and Methods: Study populations: This was an observational, retrospective, case control study done in the Department of Neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka, from January 2010 to December 2011. Study population was patient of 15 to 70 years of age. Age and sex was matched apparently healthy person and cases.

Statistical Analysis: All data were recorded systematically in preformed data collection form. Unpaired 't' tests were used to compare group means and Chi square test, Odds ratio with 95% confidence interval were done to evaluate differences between groups for other variable. Risk factors analysis was performed by computer based software Statistical Package for Social Science (SPSS for windows version 16.0). Probability value <0.05 was considered as minimum level of significance.

Results and Observation:

A total 76 subjects were studied and out of them 38 were ALS patients and 38 were normal healthy individuals. In this study the age range was 15 to 70 years with mean (±SD) 37.1 ± 12.9 in case and 39.9 ± 13.5. in control group.

Table I demonstrates that the proportion of patients below 40 years was more than 60% in case group compared to 52.6% in control group. However, the mean ages of case and control groups were almost identical (p = 0.480).

Table-I

Comparison of age between two groups

Age# (years)	Group		p value
	Case (n = 38)	Control (n = 38)	
**<40	23(60.5)	20(52.6)	
40 – 60	12(31.6)	13(34.2)	
e" 60	3(7.9)	5(13.2)	
Mean ± SD	37.1 ± 12.9	39.2 ± 13.5	0.480^{NS}

NS- Not significant

Figures in the parenthesis denote corresponding %;

Data were analysed using Student's t-Test and were presented as mean ± SD.

**Most of the people of our country are illiterate and they have no clear idea about there age.

Males demonstrated their predominance in male 28(73.7%) and female 10(26.3%) in cases group. In male 29(76.3%) and female 9(23.7%) in control groups. The groups were almost identical in terms of sex distribution (p= 0.791).

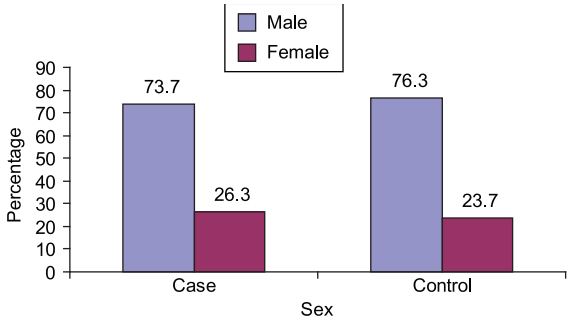

Fig.-1: *Comparison of sex between groups*

The study subjects in both case and control groups were predominantly workers/ housewife (65%) followed by day laborers (26%). Very few were students and service holders. There was no significant difference between groups in terms of occupation (p = 0.392).

Table-II

Comparison of occupation between two groups

Occupation	Group		p value
	Case (n = 38)	Control (n = 38)	
Student	3(7.9)	1(2.6)	
Service	00	2(5.3)	0.392^{NS}
Workers/House wife	25(65.8)	25(65.8)	
Day labourers	10(26.3)	10(26.3)	

NS- Not significant

Figures in the parenthesis denote corresponding %; c^2 Test was employed to analyse the data.

Figure 2 shows that a large proportion of patients in the both groups were non-smoker (73.7% of cases and 78.9% of controls). Approximately 11% of patients in case group and 5.3% patients in control group were ex-smoker. Current smoker was equal in the both case and control groups (each of 15.8%) (p = 0.692).

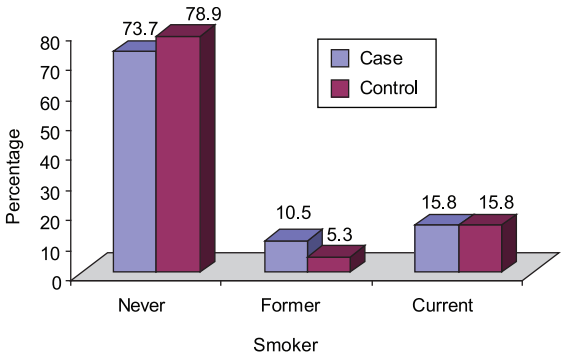

Fig.-2: *Comparison of smoker between groups*

Half (50%) of the patients in case group was habituated of chewing betel nut compared to 44.7% of patients in control group (p = 0.646). All of the patients in the both groups had usual food habit. Majority of the patients in case and control used to drink tube-well water (94.7% vs. 97.4%, p = 0.500).

Table-III

Comparison of behavioral factors between two groups

Behavioral factors	Group		p value
	Case (n = 38)	Control (n = 38)	
Betel nut-chewing*	19(50.0)	17(44.7)	0.646^{NS}
Food habit (usual)	38(100.0)	38(100.0)	-
Source of drinking water			
Tube-well	36(94.7)	37(97.4)	0.500^{NS}
Ponds	2(5.3)	1(2.6)	

NS- Not significant
*Chi-square (c^2) Test was employed to analyse the data.
Data were analysed using Fisher's Exact Test.

Biochemical investigations of the patients demonstrated that the mean serum Ferritin and serum total iron were significantly higher in patients of case group than those in patients of control group (158.9 ± 16.6 vs. 104.8 ± 7.9 µgm/L, p = 0.004 and 111.1 ± 9.2 vs. 81.3 ± 9.3 µgm/dL, p = 0.029 respectively).

Table-IV

Comparison of biochemical investigations between two groups

Biochemical investigations	Group		p value
	Case (n = 38)	Control (n = 38)	
Serum Ferritin (µgm/L)	158.9±16.6	104.8±7.9	0.004
Serum total iron (µgm/dL)	111.1 ± 9.2	81.3 ± 9.3	0.029

Data were analysed using Student's t Test and were presented as mean ± SD.

A staggeringly higher proportion of cases 14(36.8%) had elevated serum Ferritin as opposed to only 2(5.3%) of the control group (p = 0.001). Serum iron was also significantly higher in the former group 11(28.9%) than that in the latter group 2(5.3%) (p = 0.006). The likelihoods of having raised serum Ferritin and serum iron in patients with Amyotrophic lateral sclerosis were observed to be 10.5(95% of CI = 2.2 – 50.4) and 7.3(1.5 – 35.8) times higher respectively compared to their control counterpart (Table V).

Table-V

Risk of increased serum Ferritin and iron in Amyotrophic lateral sclerosis

Iron parameters	Group		p value	Odds Ratio (95% CI of OR)
	Case (n = 38)	Control (n = 38)		
Serum Ferritin (µgm/L)				
Raised	14(36.8)	2(5.3)	0.001	10.5(2.2 – 50.4)
Normal	24(63.2)	36(94.7)		
Serum iron (µg/dL)				
Raised	11(28.9)	2(5.3)	0.006	7.3(1.5 – 35.8)
Normal	27(71.1)	36(94.7)		

Figures in the parentheses indicate corresponding percentage;
Data were analysed using Chi-square (Ç2) Test.

Discussion:

The study was carried out in the Department of Neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka from January, 2010, December 2011 for the duration of two years. A total of 76 participants were allocated into two groups– case group 38 (28 male and 10 female) with ALS and control group 38 (29 male and 9 female) to evaluate the association of serum Ferritin with ALS. Patients

of ALS and age & sex matched normal participants in the above mentioned place were included the study population. The demographic variables were age, sex and occupation. The behavioral factors were smoking, alcoholism, betel nut chewing, food habit and source of drinking water. The biochemical investigations were serum Ferritin, serum total iron, Hb%, TC, DC, ESR and CRP. The test statistics used to analyze the data were Chi-square (c2) tests, Fisher's Exact Test and Student's t-Test. For all analytical tests, the level of significance was set at 0.05 and p <0.05 was considered significant. The proportion of patients below 40 years of age was a bit higher. In our study demonstrated their predominance in male 28(73.7%) in cases group. And 29(76.3%) in control groups. The study subjects in both case and control groups were predominantly workers/ housewife (65%) followed by day laborers (26%), few students and service holders. A large proportion of patients in both groups were non-smoker (73.7% of cases and 78.9% of controls). Approximately 11% of patients in case group and 5.3% patients in control group were ex-smoker. Current smoker was equal in the both case and control groups (each of 15.8%). Half (50%) of the patients in case group was habituated chewing betel nut compared to 44.7% of patients in control group. All of the patients in both groups had usual food habit. Majority of the patients in case and control group drink tube-well water. The mean serum Ferritin and serum total iron were significantly higher in patients of case group than those in patients of control group (158.9 ± 16.6 vs. 104.8 ± 7.9 µgm/L, and 111.1 ± 9.2 vs. 81.3 ± 9.3 µgm/dL respectively).In our study we have excluded inflammation, infection, iron overloading condition and found that out of 38 ALS patients 36.8%(14) had higher serum Ferritin level and 28.9%(11) had higher serum iron level. Out of 14 ALS patients with high serum Ferritin 10 were male and 4 were female (in 10 male ALS patients serum Ferritin level was >300¼gm/L and in 4 female ALS patients serum Ferritin level was >120¼gm/L). Out of 11 ALS patients with higher iron level 8 were male and 3 were female (in all cases total serum iron level was >150¼gm/dL). Our study also found that the proportion of patients below 40 years of age was a bit higher and this maybe due to most our patients were illiterate and they have no idea about their age.

But in a previous study in Qureshi et al 2008[20] series, in Neuromuscular Clinic at the Massachusetts General Hospital (MGH) about 321 patients of ALS over ten years period between January 1994 and December 2003 and found serum Ferritin levels elevated in ALS patients and the majority of participants were male (59%) and the mean age was 56.3 years (mean ± SD =13.0). The mean serum Ferritin level in the ALS population was significantly higher (ANOVA: males p=0.037, females p=0.032). The mean serum Ferritin level in the 17 males with ALS was 269.9 ng/ml (±126.4 SD) compared to 164.1 ng/ml (±142.2 SD) in 14 healthy controls. The mean serum Ferritin value in 13 female with ALS was 183.5 ng/ml (±186.9SD) compared to 71.3 ng/ml (±60.4 SD) in 16 female control subjects. The other series Goodall, 2008[21] associates demonstrated that serum Ferritin level was increased in ALS patients. In their series 60 patients of ALS (41 male and 19 female) and 44 age-matched controls (14 male, 30 female) were studied. Serum Ferritin levels were significantly elevated in ALS patients compared to controls (p<0.001).

In another study Molfino and colleagues findings of 84 patients (40 male, 44 females) mean age of 62.38± 10.19 (range of 32-79 years) those presented with dysphasia. In their nutrition Unit for nutritional evaluation and treatment found that 34(40.4%) patients had increased levels of serum Ferritin and in 36 (43%) serum Ferritin was above the upper level of normality and rest (16.6%) are normal.

Comparison of the results of our study with those from previous studies, our study revealed similar to their study report[22] and 40.4% of ALS patients had high levels of serum Ferritin vs our study that found 36.8% had higher serum Ferritin level although selection criteria, methodology and examination were also same in our and pervious study. In previous study they were unable to do genetic study and environmental factors but they concluded that increased serum Ferritin levels in their cases could reflect the ongoing muscle degradation. or greater storage of iron of patients

In our study we found that Ferritin level were increase in ALS patients and this could signify a greater storage of iron of ALS patients or reflect the ongoing muscle degeneration characteristics of the disease, like previous study, as we also unable to do genetic study and environmental factor study. So, high serum ferritin in our study indicating that high serum ferritin was associated with amyotrophic lateral sclerosis.

Conclusion:

In the present study serum Ferritin was found to be elevated in patients with ALS indicating that high serum Ferritin was associated with amyotrophic lateral sclerosis (ALS) which was consequence of disease process itself. This increase may be due to iron overloading conditions like environmental or genetic factors which were not ruled out by concomitant investigations and limitations of study.

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Epilepsy Patients in Bangladesh - The Experience of a Referral Hospital

ABDUS SALAM[1], MD. RAFIQUL ISLAM[2], HASAN ZAHIDUR RAHMAN[3]
ANIS AHMED[4], MD. RUHUL QUDDUS[5]

Abstract:

***Purpose**: To analyze the socio-demographic and electro-clinical data of Epilepsy patients presenting in the 'Epilepsy Clinic' of a referral hospital. **Method**: Epilepsy patients came to this weekly clinic after referral from this hospital OPD, other hospitals and from private practitioners. All the patients were enrolled from November, 2012 to December, 2015. Then clinical diagnosis was established by the chief investigator. Routine EEG was done. MRI was advised in appropriate cases. Finally the clinical findings and investigation reports were correlated. **Results**: Among 331 patients, 63% were male and 37% were female. 86% patients were in the younger age group (0-29years). 75% patients were suffering from various forms of LRE, 19% from Generalized Epilepsy Syndrome, 2.7% were unclassified and 2.7% had pseudo-seizure. Total 224 EEG could be done. Among them 118 (52.7%) had different types of abnormalities. Among total 158 MRI, 120 (76%) were abnormal. 6.3% patients could not go to school, 3.3% left study and 12.7% patients remain unemployed due to the disease burden. **Conclusion**: This is a hospital based study. In this study LRE comprises 75% of total patients which is relatively higher than other reports. Males were predominating and younger people were affected more with epilepsy. Due to this disease various social problems were occurring regarding study and employment. This result demands community based larger study in our country.*

Introduction:

Epilepsy is the commonest neurological condition affecting people of all ages, race and social class. There are an estimated 50 million people with epilepsy in the world, of whom up to 75% live in resource-poor countries with little to or no access to medical services or treatment[1,2].

Epilepsy is clinically similar in developing and developed countries, but the extent to which patients with epilepsy are recognized, investigated, and managed is different. Epidemiology, etiology, socio-cultural, and economic factors all contribute to these differences[3].

Diagnostic accuracy is a particular problem in epilepsy as seizures are a symptom of diverse underlying cerebral etiologies and usually do not have any physical manifestations. Consequently a definitive diagnosis of epilepsy is often only made after an extended period of follow up, as evidenced in the Rochester study and the National General Practice Study of Epilepsy (NGPSE), a community-based study of epilepsy in the United Kingdom. Moreover it has been found that 20-30% of those attending tertiary referral centers with refractory epilepsy do not in fact have epilepsy, with the most common differential diagnoses being dissociative seizures and syncope. As expected, neurologists are better at the diagnosis of epilepsy than non-specialists (mistake rate 5.6% vs. 18.9%), but a misdiagnosis rate of 5% should be considered as the absolute minimum[4].

1. Assistant Professor, Neurology, Shaheed Sheikh Abu Naser Specialized Hospital, Khulna.
2. Professor, Neurology Department, Bangabandhu Sheikh Mujib Medical University, Dhaka.
3. Professor, Neurology Department, Bangabandhu Sheikh Mujib Medical University, Dhaka.
4. Assistant Professor, Neurology Department, Bangabandhu Sheikh Mujib Medical University, Dhaka.
5. Assistant Professor, Neurology, Shaheed Sheikh Abu Naser Specialized Hospital, Khulna.

Many people with epilepsy may not come to medical attention, either due to ignorance or lack of awareness of the symptoms. This is particularly true of absence and minor complex partial seizures, which may only be recognized in retrospect following presentation with a generalized seizure. Indeed in one study of general practices only 20% of patients with seizures suspected the diagnosis prior to medical consultation[4].

In Bangladesh epidemiological surveys confirm that seizure disorders are common. A study showing prevalence rate of 68 out of every 1000 for 'any seizure history' and 9 out of every 1000 for 'any unprovoked seizure', in children aged 2 to 9 years. However, there is very little information on the types of epilepsy or on their clinical presentations, EEG records, or clinical outcomes. These are important for planning management and for developing wider services within the country[5].

Bangladesh is one of the densely populated countries in the world where infectious diseases, malnutrition and many chronic neurological disorders are quite common. Although there is no national statistics yet in the country but there are some hospital based studies that reflect to some extent the situation of epilepsy in Bangladesh. Studies in developed countries shows prevalence rate of about 5 per 1,000 populations whereas in developing countries it is higher. Men are more often affected than female and rural populations are affected more than the urban populations[6]. Based on the prevalence rate of 10 per 1,000 populations it is estimated that out of 160 million, there are at least 1.6-2.0 million people with epilepsy in Bangladesh[7]. The common ages of epileptic patients in Bangladesh are between 16 to 31 years. The etiology varies with age. Birth trauma, birth asphyxia, central nervous system infections are common in neonate and infancy whereas head trauma, brain tumor, stroke, infections are common causes in middle aged and elderly. Vast majority of the people in Bangladesh does have superstitious belief about Epilepsy. This belief usually is a strong barrier for total care of patients with epilepsy. Misunderstanding and negative attitude of the parents, family members and society towards epilepsy are still prevalent. Thus, many patients with epilepsy are still neglected in diagnosis, treatment, education, rehabilitation and other social needs. The epilepsy patients are often reluctant to seek advice from physicians. Rather they believe epilepsy has no cure and they seek advice from indigenous medicine practitioner *'Kabiraj',* snake charmer *'Ojha'* and spiritual healers. A report of 130 patients from the epilepsy clinic of BSMMU (a government post-graduate medical center) showed that close to 70% of patients visited indigenous medicine practitioners, exorcists, spiritualists prior to consulting the clinic, only 29% perceived epilepsy as a disease, 50% dropped out from school (58% of whom due to epilepsy), and 52% of patients had to change job because of epilepsy. Appropriate antiepileptic drugs are sometime unavailable in Bangladesh. The BSMMU study showed 23% of patients found it difficult to continue treatment due to financial problem. Financial factor is likely to partly accounts for the drug non-compliance[7].

The aim of our study was to obtain a baseline profile of epilepsies, to determine the types of epilepsies and epileptic syndromes in patients attending the outdoor epilepsy clinic in a tertiary care hospital and to compare the data with other centers of this country and rest of the world.

Materials and Methods:

This is an observational study carried out from records in weekly Epilepsy outdoor clinic of Department of Neurology, Shaheed Sheikh Abu Naser Specialized Hospital, Khulna (a government specialized hospital) from November 2012 to December, 2015. This is the only center in this division (comprising 10 districts and 15,563,000 inhabitants)[8] which is providing such type of facilities. So patients are referred from all over the division. They are consulted free of cost. During this period a total of 331 patients with history of seizure disorder attended the clinic. All patients who had been seen consecutively in the epilepsy clinic were retrospectively enrolled into this study. There is a case record proforma for every patient attending the clinic which contains all relevant information and findings. A preformed questionnaire was used containing information on age, sex, habitat, clinical history from patients and observers, examination findings, previous and current medications, result

of EEG and imaging studies for data collection from hospital records. A review of baseline clinical information, EEG reports, other investigations, and follow-up records was performed. If the information was insufficient, a further follow-up review was undertaken by recalling the patients and the care-givers by telephone calls[9].

EEG: An EEG is advised routinely to all patients. EEG was performed at either first presentation or at any stage during the follow-up period. The EEG was obtained with a 32–channel digital machine with the electrodes placed in accordance with the International 10–20 system. In most cases recordings were obtained in both the awake and sleep states for 30-40 minutes. Photic stimulation and hyperventilation were routinely done. The EEGs were interpreted and reported by the chief investigator.

The findings were grouped into two main categories: 'normal' and 'abnormal'. The abnormal EEG was defined as the presence of interictal or ictal epileptiform discharges and/or the presence of background abnormal activity with focal or generalized, excessive slow waves or excessive fast waves, abnormal for the age and state of the patients noted during the recording. The abnormal was further classified as FED (Focal Epileptiform Discharge), GED (Generalized Epileptiform Discharge) and Others (Focal or generalized slowing, multi-focal epileptiform discharge with burst attenuation pattern). EEG abnormalities were considered focal if there was a localized spike or sharp wave discharge or focal slowing present.

Other investigations like 'MRI of Brain' was advised for all patients clinically diagnosed as suffering from LRE, symptomatic generalized epilepsy, most patients with late onset epilepsy and also for patients with clustered seizures, frequent seizures, isolated seizures, intractable epilepsy, and patients who had unexplained break-through seizures in otherwise well-controlled epilepsies. Routinely CT scan was not advised. But patients presenting with a CT done previously were documented. The available films were interpreted jointly by the radiologist and the investigator (as there is no epilepsy expert radiologist in this institute). All clearly abnormal focal lesions (e.g., tumour, infarct, gliosis, atrophy) revealed on CT and magnetic resonance imaging (MRI) scans of the brain were documented.

Diagnosis and classification of epilepsy: Epilepsy was diagnosed when there was a history of two or more unprovoked seizures. These were classified with a simplified International League Against Epilepsy classification (ILAE 1989, 1993)[10,11] as: (a) generalized epilepsy, which included myoclonic seizures, infantile spasms, absence seizures, atonic seizures, generalized tonic–clonic seizures, generalized clonic seizures, or tonic seizures; (b) partial epilepsy, which included simple or complex partial seizures, or secondarily generalized seizures; and (c) unclassifiable seizures, which were atypical or those in which the children were not sure whether their seizure were focal or generalized in presentation[10-13] .

By using standard clinical and investigation criterions (ILAE 1989, 1993) epilepsy was further classified as 'symptomatic' if there was a clear antecedent history (e.g., significant head trauma, CNS infection) and when a structural lesion was documented on neuroimaging and 'idiopathic' if there was no such evidence of a cerebral lesion. Patients with recurrent seizures, and with clinical or EEG evidence of focal onset but no evidence of causation were included under 'cryptogenic' localization related epilepsy. Epileptic disorders with mental retardation and frequent seizures which lacked the characteristic features of the defined syndromes were included under "other symptomatic generalized epilepsies not defined" [10, 11] .

Partial seizures were further sub-classified chiefly on the basis of whether or not consciousness was impaired during the attack and whether or not progression to generalized convulsions occurred.

A. Simple partial seizures (when consciousness not impaired).
B. Complex partial seizures (when consciousness was impaired).
C. Partial seizures (simple or complex) evolving to secondarily generalized (tonic–clonic or tonic or clonic) seizures.

Complex partial seizures were further sub-classified chiefly on the basis of involvement of temporal lobe or not:

1) Complex partial seizures-Temporal (CPS-T)
2) Complex partial seizures-Extra-Temporal (CPS-ET)

Temporal lobe epilepsy was diagnosed if the history, seizure semiology, EEG and/or imaging showed evidence in favor of seizure originating over the temporal lobes. Rest of the CPS cases which did not fit to temporal lobe origin or showed evidence of origin over other parts of brain, were considered to be CPS Extra-Temporal (CPS-ET).

As in the International League Against Epilepsy classification (ILAE 1989, 1993) there is no special entity for 'Status Epilepticus' or 'Epilepsia Partialis Continua'(EPS), the cases of EPC have been included in the partial seizure group. As all the patients were referred to this 'Epilepsy Clinic' by various physicians, the patients whose history were not convincing enough to fit for seizure, were considered to be suffering from 'Pseudo-Seizure' and the data was included in the study so that the real picture of our patients come to light.

Result:

These were 331 patients were included in this study and out of them 123(37.166) were female and 208(62.84%) were male. The majority of patients attending outdoor clinic were <30 years age group (86%) (Table-I). There was a male (62.8%) predominance (Table-II). A large number of patients were student (35%), followed by preschool child (14.8%) (Table-III).

Table-I

Age distribution of patients (n=331)

Age Group	Number of Patient	Percentage
0-9 yrs	99	29.9
10-19 yrs	123	37.2
20-29 yrs	62	18.7
30-39 yrs	22	6.7
40-49 yrs	17	5.1
>50 yrs	08	2.4
Total	331	100.0

Table-II

Sex distribution of patients (n=331)

Male	208	62.84
Female	123	37.16
Total	331	100.0

Table-III

Sex distribution of patients (n=331)

Occupation of the patients	Number of Patient	Percentage
Non-school	21	6.3
Pre-school	49	14.8
Left school	11	3.3
Student	116	35.0
House wife	31	9.4
Business	15	4.5
Service	19	5.8
Unemployed	42	12.7
Others	27	8.2
Total	331	100.0

Table-IV

Types of Seizure & their distribution (n=331)

Seizure Type	Frequency	Percentage
LRE	249	75.3
Gen. Epilepsy	64	19.3
Unclassified	08	2.4
Pseudo-Sz	09	2.7
Total	331	100.0
Findings	Frequency	Percentage
Normal	106	47.3
FED	79	35.3
GED	22	9.8
Others	17	7.6
Total	224	100.0

Table-V

Distribution of occupation of patients (n=331)

Seizure Type	Frequency	Percentage
Focal Motor Seizure	5	1.5
CPS-T	112	33.8
CPS-ET	27	8.2
Partial Seizure with secondary generalization	102	30.8
EPC	2	0.6
BRE	1	0.3
Symptomatic Generalized Epilepsy	39	11.8
Sturge Weber Syndrome	1	0.3
Tuberous Sclerosis Complex	2	0.6
IGE	13	3.9
CAE	4	1.2
JME	3	0.9
JAE	1	0.3
Gelastic Seizure	1	0.3
SSPE	1	0.3
Unclassified	8	2.4
Pseudo-Seizure	9	2.7
Total	331	99.9
(Reflex seizure)	5	

Table-VI

EEG findings of the patients

Findings	Frequency	Percentage
Normal	38	24
Abnormal	120	76
Total	158	100

Table-VII

CT scan findings of the patients

Findings	Frequency	Percentage
Normal	106	47.3
FED	79	35.3
GED	22	9.8
Others	17	7.6
Total	224	100.0

Table-VIII

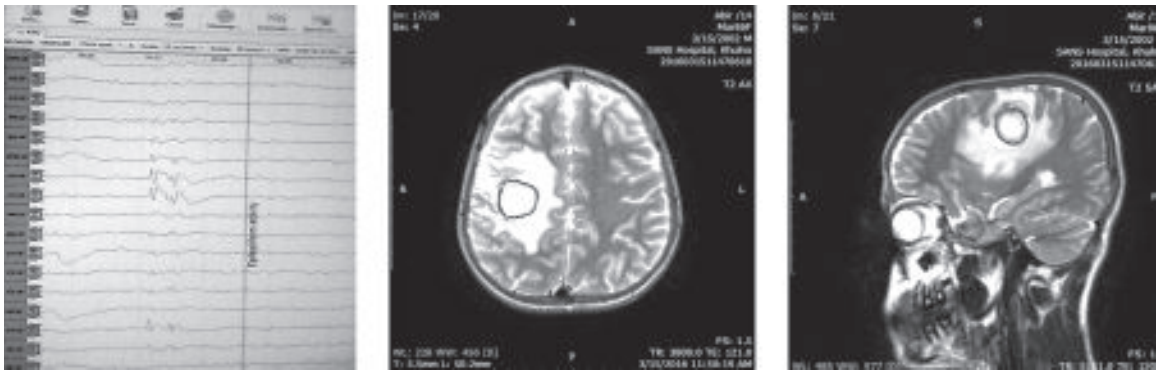
MRI findings of the patients

Findings	Frequency	Percentage
Normal	6	27.3
Abnormal	16	72.7
Total	22	100.0

Among the 331 patients, 75% had been suffering from various forms of localization related epilepsy (LRE), 19% from generalized epilepsy, 2.4% were unclassified and 2.7% from pseudo-seizure (Table-V). 11.8% patients had been suffering from symptomatic generalized epilepsy (most of them were child and had history of perinatal asphyxia and head injury), 2 patients were found to have Tuberous sclerosis complex, 1 patient was found to have Sturge Weber syndrome and 1 patient was diagnosed as SSPE and 3.9% patients had IGE (Table-VI). Five patients were identified to have reflex seizures. The seizures were precipitated by eating, sound and light. But these patients have primary features suggestive to be included in other classifications of epilepsy like CPS-T, CPS-ET and IGE (Table-VI). So they are not showed in the main sub-groups of epilepsy. EEG could be done in 224 patients. Of them 35.3% showed FED, 9.8% showed GED, 7.6% showed focal or generalized slowing or multi-focal epileptiform discharge with burst attenuation pattern and 47.3% were normal (Table-6). Among total 158 MRI, 76% showed various types of abnormal findings and among total 22 CT Scan 72.7% were abnormal (Table-VII, VIII).

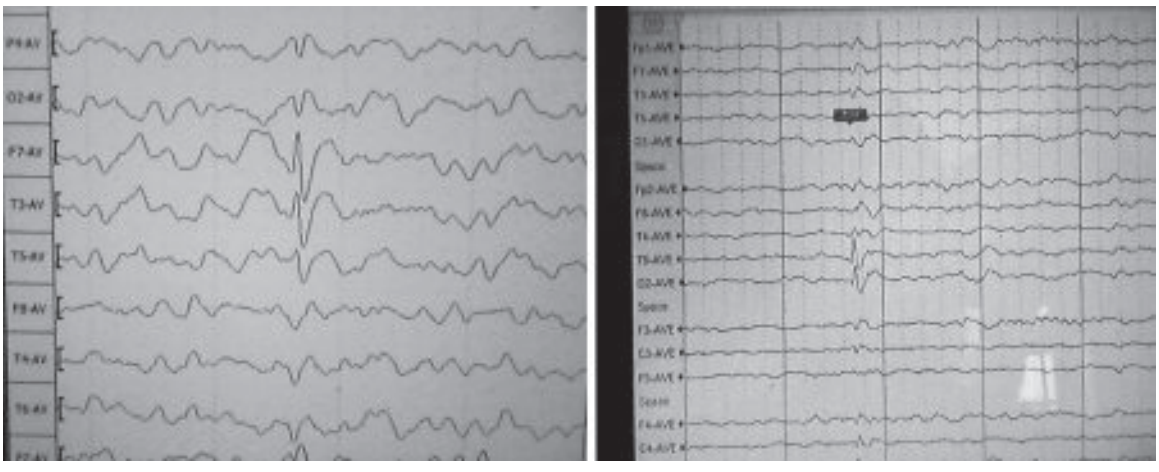
In figure 1, a young patient of 14 years presented with the history of 'Partial Seizure with secondary generalization'. He had been suffering from 'Ventricular Septal defect with Reverse Shunt'. His EEG shows Focal Epileptiform Discharge (FED) over right fronto-centro-temporal region. His MRI shows abscess over the same area of brain. Figure 2 shows 2 cases of Temporal Lobe Epilepsy, 'a' shows FED over left anterior temporal (CPS-T-Lt.) and 'b' shows FED over right posterior temporal area (CPS-T-Rt.). In figure 3, the patient presented with Simple Partial Seizure–Left sided. His EEG was normal, MRI showing

tuberculoma over right parietal area. Figure 4 patient presented with the features of Cerebral Palsy and Complex Partial Seizure – Extra-Temporal. His EEG shows FED over left posterior head region. MRI also shows gliosis over the same area with left sided cerebral atrophy. The patient in figure 5 presented with CPS. He had mental retardation and adenoma sebaceum. He was diagnosed as Tuberous Sclerosis with CPS. His CT scan of brain shows tubers. The patient in figure 6 presented with repeated drop attacks, poor mental condition. His EEG shows runs of spike and slow wave discharge at 1-1.5 Hz (Status of Atypical Absence Seizure). His MRI showing bilateral gliosis (Rt.>Lt.) with right sided cerebral atrophy. These features are consistent with Symptomatic- LGS. In figure 7 the EEG of 13 month child showing multi-focal Epileptiform discharge with burst attenuation pattern which is suggestive of Epileptic Encephalopathy. In figure 8 a child of 8 years showing Spike and wave discharge at 3 Hz during which she was unresponsive which is a classical feature of Absence Seizure.



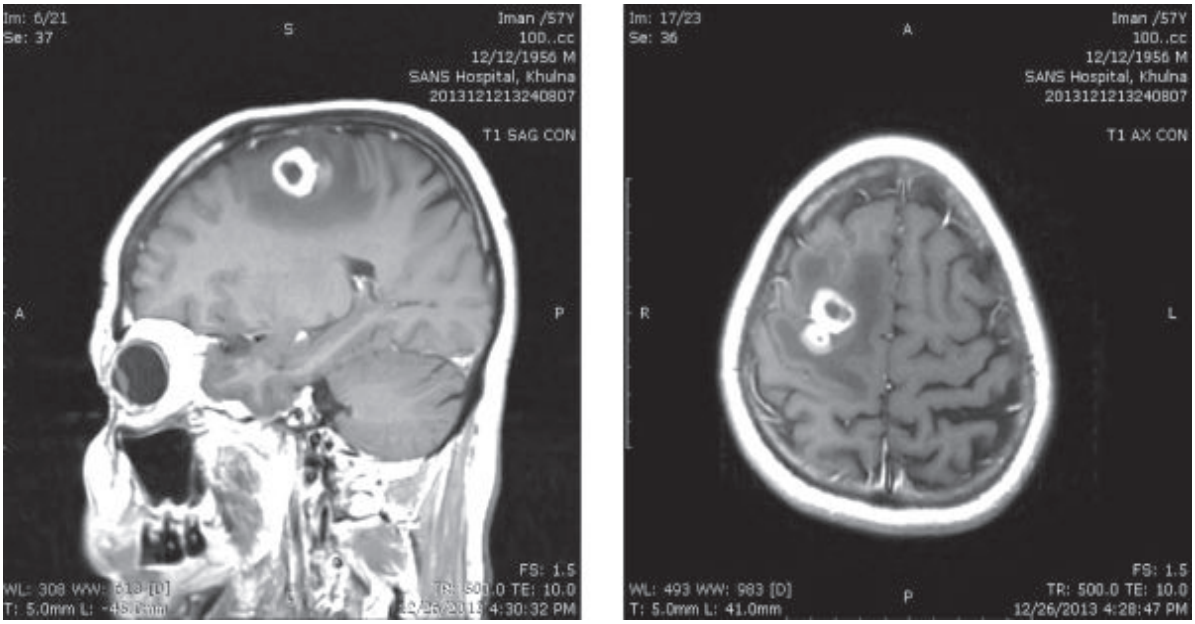
A B C

Fig.-1: *Abir, 14y: A-EEG - FED-Rt-Fronto-Centro-Temporal, B- MRI (b-Axial, c-sagital view) = Brain Abscess over right frontal lobe*
DIAGNOSIS = Partial Sz. with secondary generalization due to Brain Abscess + VSD with reverse shunt.



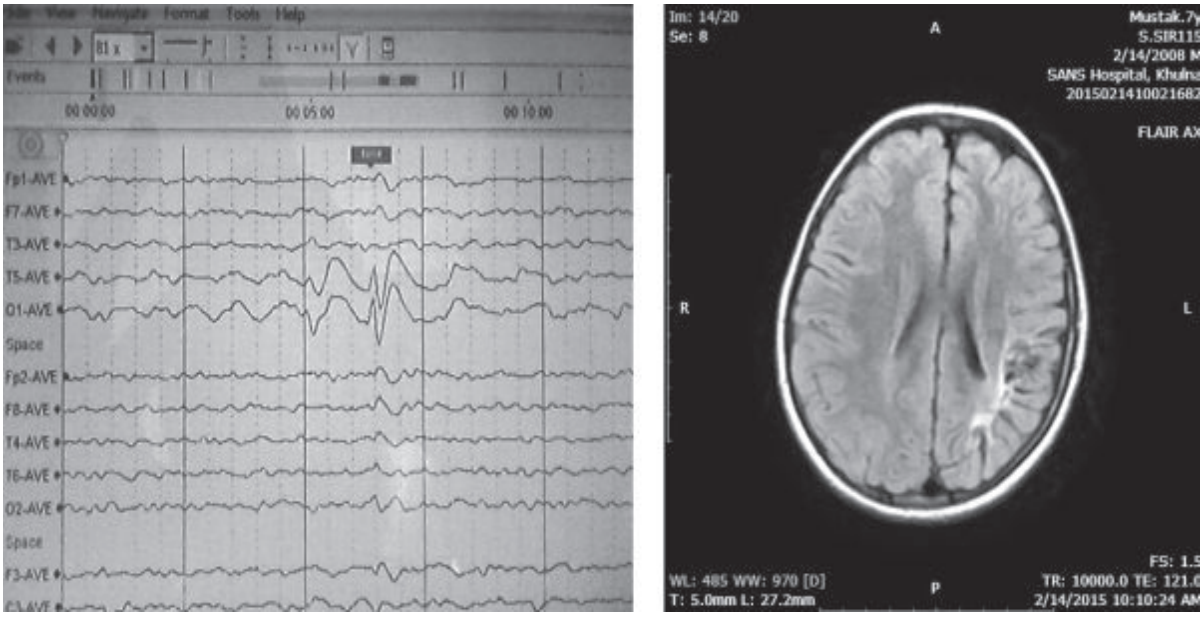
A B

Fig.-2: *EEG of Temporal Lobe Epilepsy. a = Left Anterior Temporal Spike, b = Right Posterior Temporal Spike*



A B

Fig.-3: *Iman, 57Y - MRI of Brain (a-Sagital, b-Axial view) = Tuberculoma Diagnosis = Simple Partial Seizure due to CNS-TB*



A B

Fig.-4: Mustak, 7y a*) EEG = Focal Epileptiform Discharge over left posterior head region with delta slowing b) MRI of Brain = Gliosis & Atrophy (Left Parieto-Occipital) Diagnosis = Cerebral Palsy + Complex Partial Seizure –Posterior Head Region*

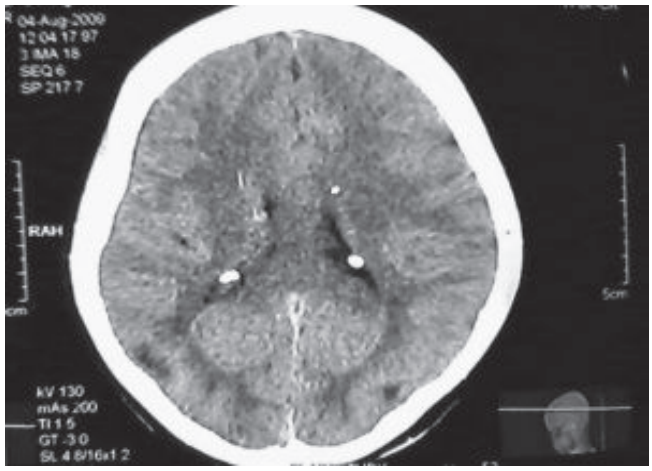


Fig.-5: *CT Scan of Head (Tubers): Mominul, 18Y Diagnosis = Complex Partial Seizure due to Tuberous Sclerosis Complex*

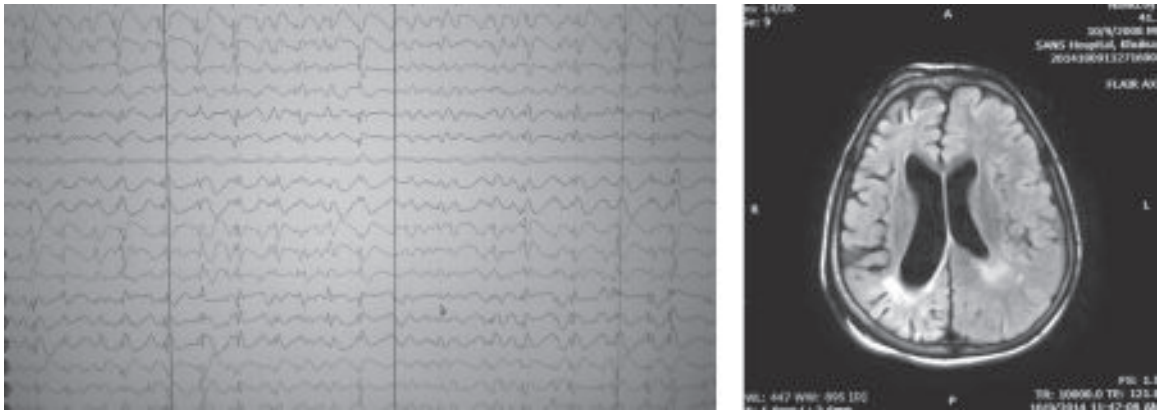


Fig.-6: *Nahid, 6y: a) EEG= Atypical Absence Seizure (Status). b) MRI of Brain= Bilateral gliosis (Rt.>Lt.) & Right Cerebral Atrophy; sequele of Encephalitis at age 4y. Diagnosis = Lennox-Gastaut Syndrome*

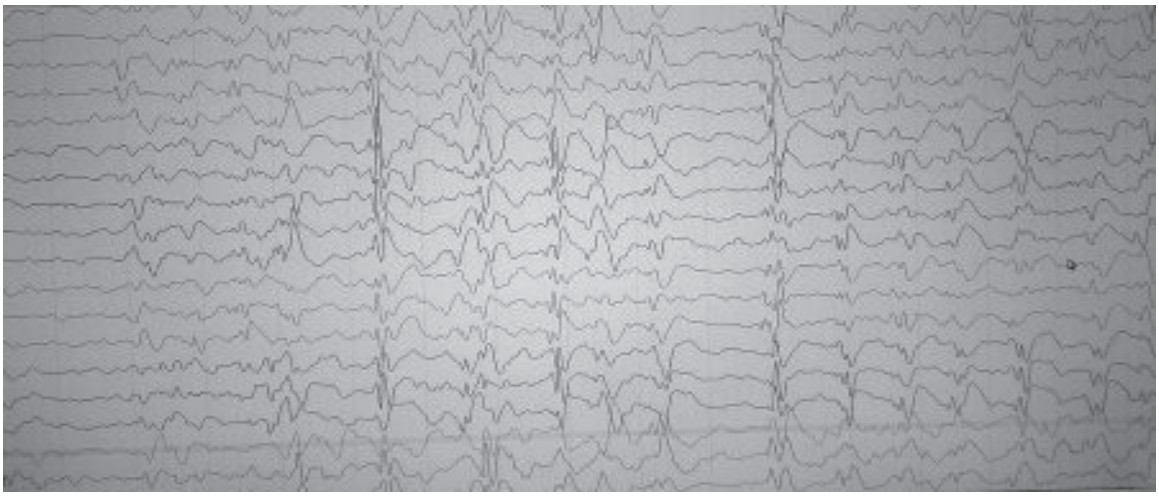


Fig.-7: *Siam,13m - Multi-focal epileptiform discharge with Burst Attanuation pattern Diagnosis = Symptomatic Generalized Epilepsy with Epileptic Encephalopathy*

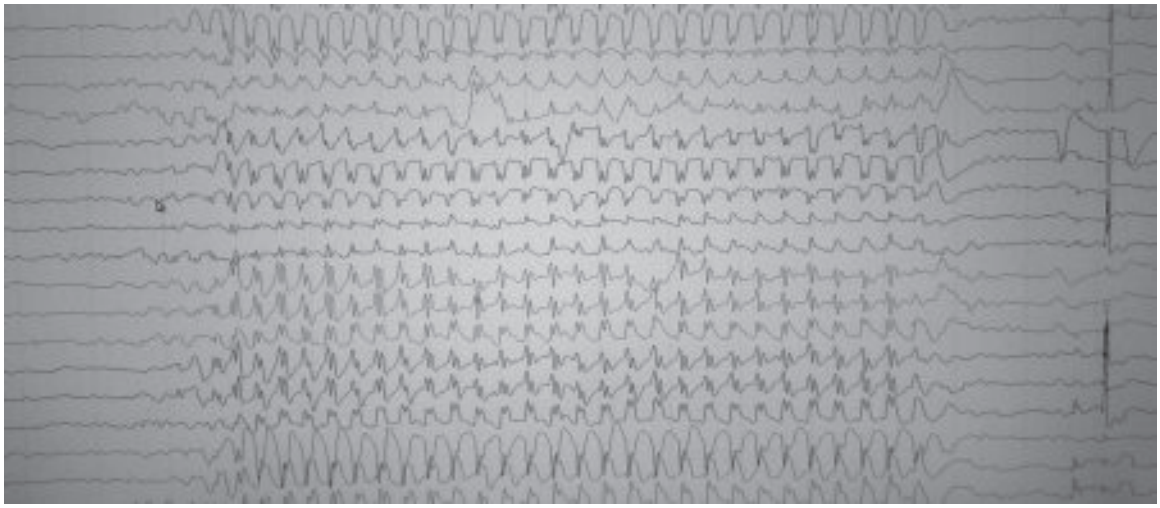


Fig.-8: *Khadiza, 8y: EEG= Generalized Spike and dome discharge at 3 Hz (Absence Sz.)*

Discussion:

Based on the findings of this study several issues demand attraction. The most common age of presentation of epilepsy was <30 years (86%). In a study done by Sridharan and Murthy[14], similar findings was seen; 'age-specific prevalence rates were higher in the younger age group, with the onset of epilepsy reported mostly in the first three decades of the sample population's lives'. Except for Shanghai in China, most of the Asian countries have younger epileptic patients. The probable reason for the missing peak in the older age group in many Asian countries is due to the fact that the population in general is younger[15].

Here a male predominant (62.84%) picture is seen. Epilepsy is slightly more common in men than in women but the sex-specific prevalence is not, in general, significantly different.[15] Reports are similar in other Asian countries[16]. Although our country has almost same socio-economic condition like the surrounding countries (India and Pakistan) here women are more home bound and neglected. Regarding epilepsy various social stigma remains. So people try to hide the illness of their daughters and sisters. As males are more exposed to outer world, their diseases come to the attention easily and people bring them to doctors. Also, as they are the earning members, their illness gets more importance for the uninterrupted continuation of earning source.

The students (35%) came to epilepsy clinic as they are the knowledgeable group of society who has an easy access to a tertiary health care system. They draw attention through their teachers and fellows and also the parents are more concerned with the illness of their kids.

Regarding distribution of seizures 75.3% patients are suffering from various forms of LRE. Studies from India also recorded a high frequency of partial epilepsies: 62.9%,[17] and 57%[18]. Data in other developing[19-22] and developed countries shows same finding[23]. Earlier study of Bangladesh also showed a high frequency of partial epilepsies: 54%[24].

In this study Partial seizure with Secondary generalization comprises 41% which appears to be relatively more than other's findings. These patients usually present with convulsion and draw attention of the attendants and physicians early. Many patients showed lesions (gliosis, atrophy in MRI) in occipital and posterior head region which indicates birth injury, asphyxia and trauma which may be the reason for increased number of these patients in this area.

Although few patients were ultimately diagnosed as having pseudo-seizure, this issue should be taken into account as all of them were getting anti-epileptic drugs along with all the restrictions and burden of epilepsy.

EEG findings were positive in almost 52.7% cases. This also matches with the findings of other authors[25].

There are some limitations in the study. We could not apply the recent ILAE proposal for classification of epilepsy syndrome. The study from hospital records may not completely represent the scenario in the community. Finally, also due to the retrospective nature, some aspects like the attitude of patients and attendants to epilepsy, the real burden of the disease on the family and society could not be evaluated.

Conclusion:

This study highlights some facts. Localization Related Epilepsy are more common in our country. Facilities should be improved to identify the etiology and provide extra care to reduce the burden. This is a hospital based study. Males are predominating and younger people are affected more with epilepsy. Due to the disease various social problems are occurring regarding study and employment. This result demands community based larger study in our country.

Declarations:

Funding: This research project was not funded by any group or any institution.

Ethics: The study protocol was approved by institutional ethical committee of Shaheed Sheikh Abu Naser Specialized Hospital, Khulna, Bangladesh

Data Sharing: There is no other unpublished data to share.

Conflict of interest: There is no conflict of interest relevan1t to this paper to disclose.

Abbreviation :

BRE = Benign Rolandic Epilepsy

BSMMU = Bangabandhu Sheikh Mujib Medical University

CAE = Childhood Absence Epilepsy

CPS = Complex Partial Seizure

EPC = Epilepsia Partialis Continua

FED = Focal Epileptiform Discharge

GED = Generalized Epileptiform Discharge

IGE = Idiopathic Generalized Epilepsy

JAE = Juvenile Absence Epilepsy

JME = Juvenile Myoclonic Epilepsy

LGS= Lennox Gastaut Syndrome

LRE = Localization Related Epilepsy

OPD = Out Patient Department

PHR= Posterior Head Region

SSPE= Sub-acute Sclerosing Pan Encephalitis

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Intraventricular Tumor: An Analysis of 18 Cases

SHAMSUL ALAM[1], A.N. WAKIL UDDIN[2], MASHIUR RAHMAN MAJUMDER[3], MD MOTASIMUL HASAN. ANIS AHMED[5]

Abstract:

Objective: *To describe the transcallosal and transcortical approach to deal with intraventricular tumors.* ***Methods:*** *Details of the transcallosal and transcortical approach to intraventricular tumors of the lateral and third ventricles were presented.* ***Results:*** *Intraventricular tumors are ideal indications for microscopic neurosurgery. They often cause cerebrospinal fluid (CSF) pathway obstruction, resulting in ventricular dilatation. The general principle of removal of intraventricular tumors was interruption of the blood supply to the tumor and subsequent tumor debulking. In general, a piecemeal resection was performed; however, in some tumors such as meningioma, it was possible to detach the lesion from the surrounding brain tissue and remove it in toto. When the tumor found in the anterior part of the third ventricle, the craniotomy was done at the coronal suture. When the tumor was located in the posterior part, the entry craniotomy was selected more anteriorly in order to pass the foramen of Monro in a straight line.* ***Conclusion:*** *Intraventricular tumors and related CSF pathway obstructions can be safely and effectively treated with micro neurosurgical techniques, either by transcallosal or transcortical approach. The aim should be the total extraction of the tumor with minimum damage and the chosen operative corridor should optimize tumor access and the protection of vulnerable neurovascular structures. Lateral ventricle tumors can be removed via transcortical approach when having hydrocephalus which provides a wider and more direct approach to the tumor than the transcallosal one. It allows the surgeon to achieve good functional outcome and maximum excision of the tumor. Transcallosal is an excellent midline exposure with preserving the callosomerginal and pericallosal arteriesto the midline tumor of lateral and 3rd ventricles.*

Key Word: *Intraventricular Tumor, Meningioma,Central Neurocytoma.*

Introduction:

Intraventricular neoplasms are uncommon, representing just 1–10% of all CNS tumors. Lateral ventricular neoplasms are rare and account for half of all intraventricular tumors in adults and one quarter of those in children. While these neoplasms are easily detected with computed tomography (CT) and magnetic resonance imaging (MRI) [1,2].

The ventricles are surrounded by a layer of ependymal cells and a subependymal plate formed by glial cells. Such layers give origin to ependymomas, subependymomas and subependymal giant cell astrocytomas. Such a lining and the septum pellucidum that is located between the corpus callosum and the fornix, separating the lateral ventricles, also give origin to central neurocytoma, a unique glial neuronal tumor of the ventricular systems[2,3].

Tumors are more frequently found in the posterior portion of the lateral ventricles, but their location may vary according to the type of tumor. Choroid plexus papillomas occur mainly in children, with predilection for the lateral ventricles in this age range, while in adults it usually is more frequently

1. Assistant Professor, Department of Neurosurgery, Bangabandhu Sheikh Mujib Medical University, Dhaka.
2. Research Assistant, Department of Neurosurgery, Bangabandhu Sheikh Mujib Medical University, Dhaka.
3. Registrar, Department of Neurosurgery, Comilla Medical College, Comilla.
4. Resident. Department of Neurosurgery, Bangabandhu Sheikh Mujib Medical University, Dhaka.
5. Medical Officer, Department of Neurology, , Bangabandhu Sheikh Mujib Medical University, Dhaka.

found in the fourth ventricle. Ependymomas are most frequent in the posterior fossa in children, and in adults they are generally supratentorial[3,4].

Tumors of the lateral ventricle can be removed via two major approaches, either through the transcallosal or transcortical route. The purpose of this study is to discuss the techniques and outcomes in transcallosal and transcortical surgery of tumors located in the lateral ventricle and 3rd ventricle[4,5].

The transcallosal route is preferred by some neurosurgeons for a variety of reasons. The transcallosal approach may decrease the risk of postoperative seizures and functional deficits.It is recognized that the transcallosal route to the ventricles can be safely performed to excise lesions in the ventricular body, anterior horn, atrium and 3rd ventricles[5,6].

The transcortical approach to the lateral ventricles is a simple and attractive alternative to the transcallosal approach for many deep-seated tumors. It has the advantage of simplicity. Tumors located in certain regions of the lateral ventricle, specifically the temporal horn or atrium, are often more safely and easily approached through a cortical incision. Transcortical approach provides superior working space and more flexibility in traversing the lateral ventricle[5,6].

We used either transcallosal or the transcortical routes for the excision of lateral ventricular masses. This article is based, in part, on our recent 5-year experience with excising mass lesions in the lateral ventricle and 3rd ventricle via the transcortical and transcallosal route.

Relevant Surgical Anatomy:

An appreciation of the relevant anatomy is extremely helpful when performing transcortical and transcallosal approaches to the lateral ventricles.

The lateral ventricles are paired C-shaped structures that wrap around the ipsilateral thalamus. Each ventricle is divided into five sections: anterior horn, body, temporal horn, atrium, and occipital horn. Each of these five sections has a roof, a floor, and a medial and lateral wall.[7,8](Fig-1).

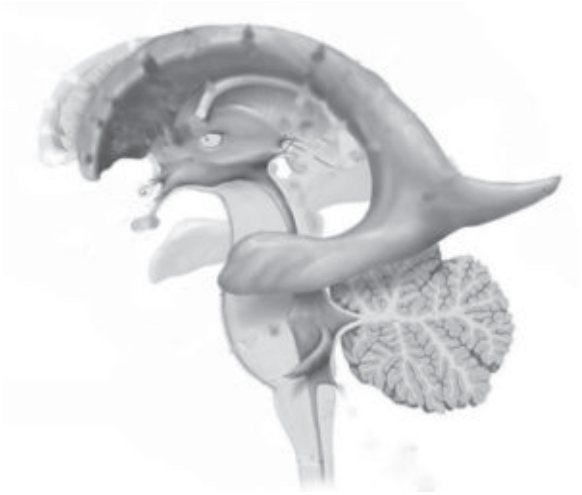

Fig.-1: *Shows the normal anatomy of ventricular system.*

The walls of the lateral ventricles are formed by the thalamus, septum pellucidum, corpus callosum and its radiations, caudate nucleus, and the fornix. The caudate nucleus is also an almond-shaped structure that forms the lateral wall of the body, anterior lateral wall of the atrium, and roof of the temporal horn. The fornix starts as the fimbria of the hippocampi in the medial temporal horn and runs along the thalamus in the anterior wall of the atrium. After giving off commissural fibers, it continues in the inferior medial wall of the body. Finally, it forms the superior and anterior borders of the foramen of Monro[8].

Although it provides limited access to tumors in the posterior trigone, temporal horn or superior frontal horn, the transcallosal approach to the lateral and third ventricles can provide maximal exposure to tumors arising body of lateral ventricle and foramen Monro. Patients harboring tumors arising in those locations are best managed by transcortical approaches. Each of these surgical options has its own set of potential complications[8,9].

The primary arteries to the choroid plexus are the anterior and posterior choroidal arteries, the branches of which provide the vascular supply to tumors in this region. Understanding the course of the arteries helps the surgeon choose an approach for each lesion and thus permits early control, when possible, of the feeding vessels[9].

The anterior choroidal artery arises from the internal carotid artery, distal to the posterior communicating artery. It leaves the anterior incisural space and enters the lateral ventricle through the choroidal fissure, coursing posteriorly to lie near the lateral posterior choroidal artery. The anterior choroidal artery generally supplies the choroid plexus in the temporal horn and atrium. Because the choroidal arteries pass through the choroidal fissure, opening this fissure early will facilitate proximal control of the feeding vessels[9].

The posterior choroidal arteries are grouped into lateral and medial divisions. The lateral posterior choroidal artery is comprised of one to six branches, which arise in the ambient and quadrigeminal cisterns from the PCA. These branches then pierce the ventricle and pass around the pulvinar and through the choroidal fissure at the level of the crus of the fornix to supply the choroid plexus in the posterior temporal horn, atrium, and body of the ventricles.The medial posterior choroidal arteries arise as one to three branches from the PCA in the interpeduncular and crural cisterns. These arteries circumnavigate the mid-brain and move to the pineal gland to enter the roof of the third ventricle. This vessel then passes in the velum interpositum, between the thalmi, adjacent to the internal cerebral veins. The medial posterior choroidal arteries travels through the velum interpositum (tela choroidea), sending inconstant branches to the lateral ventricle through the choroidal fissure and foramen of Monro. The medial posterior choroidal artery supplies the choroid plexus in the roof of the third ventricle and sometimes the choroid plexus of the lateral ventricle[9].

The veins are useful as landmarks to direct the surgeon to the foramen of Monro, especially in cases in which hydrocephalus is present. There are many important veins composing the lateral and medial groups, but perhaps the best known for surgical and angiographic orientation is the thalamostriate vein. The thalamostriate vein courses from the lateral wall of the body of the ventricle through the sulcus between the caudate and thalamus toward the foramen of Monro, where it forms the venous angle with an acute posterior turn to empty into the internal cerebral veins. The veins, which drain the frontal horn and usually anterior lateral ventricle, drain into the internal cerebral vein as it travels in the roof of the third ventricle within the velum interpositum. The veins in the temporal horn drain into the basal vein of Rosenthal (basal vein) as it passes through the ambient cistern. Veins from the atrium and occipital horn drain into the basal internal cerebral veins as well as the vein of Galen[9,10].

There are several options for accessing the third ventricle via the transcallosal approach. The foramen of Monro provides access to the anterior third ventricle; however, lesions in the middle and posterior third ventricle require an alternative exposure. An expanded foramen does not routinely need to be enlarged by sacrifice of a fornix. If a lesion located within the third ventricle can be decompressed and delivered into the foramen, then this is the most appropriate use of this approach[10].

A common approach to the middle and posterior third ventricle is through the choroidal fissure into the velum interpositum. This space is defined laterally by the insertion of the choroid plexus, superiorly by the fornix, and inferiorly by the dorsomedial thalamus. The choroid plexus can be removed along its insertion in the choroidal fissure[10].

The fornix is then gently elevated along with the internal cerebral vein, which opens the velum interpositum. The tumor is decompressed into the area of exposure and mobilized away from the ependymal surface of the ventricle[10].

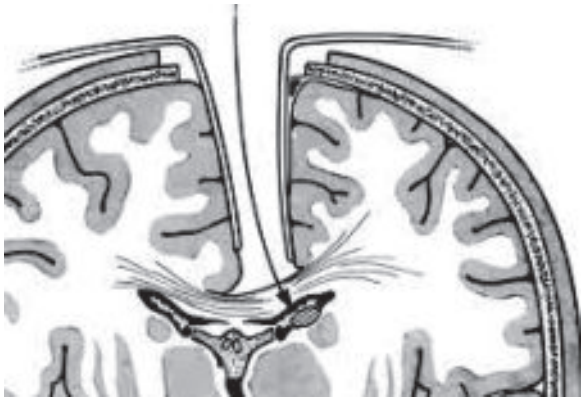

Fig.-2: *Picture of transcallosal approach.*

Methods and Materials:

An experience with 18 consecutive lateral and 3rdventricular tumors resected via the transcortical and transcallosal route, over a 5-year period, was presented. The risks, complications, and outcomes of this surgical series, as well as those reported in the literature, we discussed.

Following tumor resection by piecemeal fashion, it is important to ensure complete hemostasis. To prevent delayed ventricular obstruction, care is taken to irrigate blood that may have pooled in the lateral and third ventricles. The ventricles are filled with warm saline at the end of the surgery,

to remove air that may have become trapped. A ventricular catheter is left in the lateral ventricle for approximately 96 hours postoperatively to monitor intracranial pressure and to demonstrate that the ventricular system is patent. It is routine to obtain a CT scan on the 1st postoperative day to evaluate the extent of the tumor resection and to check for obstruction. The catheter can be removed at the bedside prior to mobilization of the patient to ward or before discharge.

Symptomatology:

The most common symptoms and signs of intraventricular tumor were intracranial hypertension, hydrocephalus and hemiparesis. Hydrocephalus are common in those tumor which were located at the foramen of Monro. Parinaud syndrome and diabetes insipidus are common in patients harboring a third ventricle tumor.

Results:

We did surgery in 18 cases of intraventricular tumor. Among them 10 were male and 8 were female (Table-I).

Table-I

Shows the Sex of patients(N-18)

Sex	No. of Patient	Percentage
Male	10	55.55%
Female	8	45.45%
Total	18	100%

Ages varies from 10-65 years. Mean age was 33 years (Table II).

Table-II

Shows the age of patients(N-18)

Ages	No. of Patient	Percentage
>10	1	5.56%
10-20	2	11.11%
21-30	4	22.22%
31-40	7	38.88%
41-50	1	5.56%
51-60	2	11.11%
<60	1	5.56%
Total	18	100%
Mean Age	33 Years	

Most of the tumor well located in the body of lateral ventricle. Only 3 cases were anterior 3rd ventricular tumor (Table III)

Table III

Location of Tumor(N-18)

Location	No. of cases	Percentage
Body of Lateral ventricular	9	50.00 %
Trigone of Lateral Ventricle	3	16.66 %
Foramen monro	3	16.66 %
3rd Ventricle	3	16.66 %
Total	18	100 %

The transcallosal (44.44%) or transcortical (55.56%) approach was used depending upon the ventricular dilatation, tumor location and proximity of the tumor in relation to approach (Table-IV)

Table-IV

Table of Approach(N-18)

Name of approach	No of cases	Percentage
Transcortical	10	55.56 %
Transcallosal	8	44.44 %
Total	18	100 %

Gross total removal was done in 13 (72.23%) cases, subtotal in 3 (16.67%) cases, near total in one case (5.55%) and partial removal was done in one case (5.55%). (Table-V)

Table-V

Shows the Extent of Tumor Removal(N-18)

Extent of Tumor Removal	No. of Patient	Percentage
Gross Total	13	72.23%
Sub Total	3	16.67%
Near Total	1	5.55%
Partial	1	5.55%
Total	18	100%

At surgery, three neurocytomas appeared as originating from the septum pellucidum and another appeared as arosed from the head of the caudate nucleus. Three cases of meningioma are arosed from choroid plexus. All three ependymomas appeared as originating from the septum pellucidum and one SEGA from the head of the caudate nucleus. Two cases of pilocytic astrocytoma arised from thalamus. (Table VI)

Table-VI

Shows the Histopathology(N-18)

Histopathology	No. of Patient	Percentage
Neurocytoma	4	22.23%
Meningioma	3	16.68%
Lateral Ventricular Ependimoma	3	16.68%
Pilocytic astrocytoma	1	5.55 %
Epidermoid	1	5.55%
Subependymal Giant Cell astrocytoma	1	5.55%
Thirdventricular tumor Ependimoma	1	5.55%
Thalamic glioma	2	11.11%
Choroid plexus papilloma	1	5.55%
Adenomas carcinoma Cyst	1	5.55%
Total	18	100%

Radiation therapy was given to a patients who had adenoid carcinoma cyst, of lateral ventricle which was recurred one year after surgery.

Seizure following surgery occurred in 2 cases(28.57%). Meningitis was developed in 3 cases (42.85 %) which was improved by injection Meropenum.

VP Shunt was done by 2 cases(28.57 %) (Table VII).

Table-VII

Table of Complication(N-18)

Name of complication	No of cases	Percentage
Meningitis	3	42.85 %
VP Shunt	2	28.57 %
Seizure	2	28.57 %
Total	7	100 %

One year after surgery, 77.78% of patients had good functional outcome. (Table VIII)

Table-VIII

Table of Glasgow outcome following surgery(N-18)

Functional outcome	No of cases	Percentage
Good Recovery	14	77.78 %
Moderate Disability	2	11.12 %
Severe disability	1	5.55 %
Vegetative	1	5.55 %
Death	0	0
Total	18	100 %

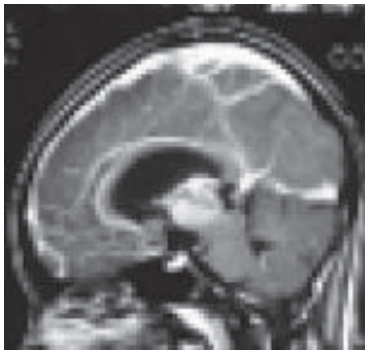

Fig.-3: Preoperative picture of 3rd ventricular ependyomoma.

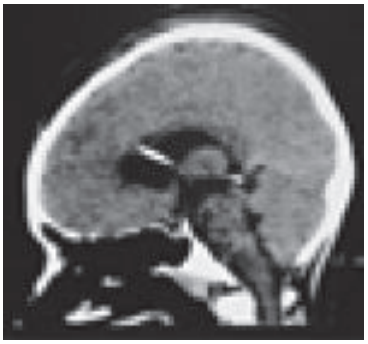

Fig.-4: Postoperative picture of 3rd ventricular ependyomoma done by transcallosal approach.

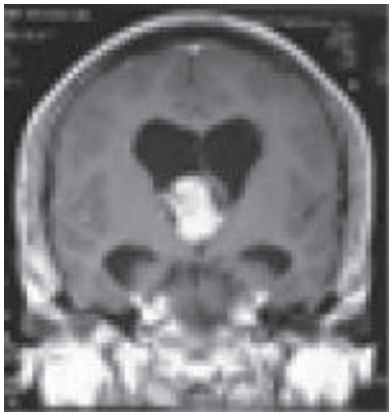

Fig.-5: *Preoperative picture of Pilocytic astrocytoma.*

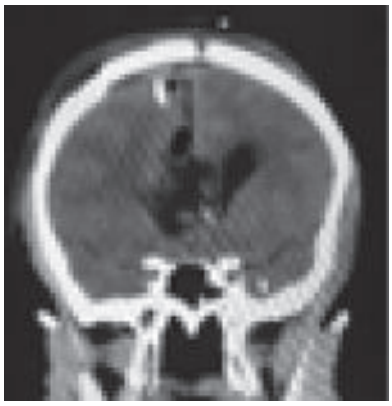

Fig.-6: *Postoperative picture of Pilocytic astrocytoma done by transcallosal Approach.*

Discussion:

The incidence of cortical incision-related postoperative epilepsy is hard to determine because there are many factors that can contribute to a seizure disorder, including the tumor histological type, presence of preoperative seizures, presence of residual tumor, subdural hygroma, and electrolyte imbalance. Any patient who undergoes a craniotomy or has his/her cortex broached is at risk for postoperative seizures. Rates of postoperative seizures have been noted to be as low as 19% in a recent study and as high as 75% in a study reported in the pre-microsurgical age.It is difficult to isolate surgical technique accurately in the various studies and arrive at an incidence of transcortical incision-induced postoperative epilepsy[7]. In our recent series at 1-year follow up, we found an incidence of 22.22% of persistent postoperative epilepsy that required medication.

Postoperative neurological deficits include hemiparesis and language deficit. A mild to moderate hemiparesis is not uncommon when a large trigone or ventricle body tumor is excised via a middle fossa transcortical approach. Most weakness is presumably the result of retraction pressure and will resolve; however, the incidence of permanent motor loss has been reported to be as high as 30% in some series[12]. However we have found 11.11% hemiparesis in all 18 cases.

Cognitive deficits and personality disorders are much more difficult to quantitate, especially if preoperative neuropsychological studies are not conducted. It is wise to leave tumor, especially if it is attached to critical structures such as the basal ganglia or fornices, and particularly if the lesions is benign[11].

Subdural hygroma formation is a well-recognized problem, especially in patients in whom an enormous tumor is associated with ventriculomegally. This is especially true in pediatric series in which large choroid plexus neoplasms and hydrocephalus are treated. The cortical surface may fall or pull away from the dura and create a hematoma or hygroma, which may eventually require the placement of a shunt. In their 1989 series of transcortical approaches to intra- and periventricular tumors in 38 patients, Tanaka, et al found that persistent subdural fluid accumulations developed in 24% of the patients; 11% required surgical treatment. Patients with preoperative hydrocephalus and those who underwent a transfrontal approach were at greatest risk. Filling the ventricles with sterile saline or lactated Ringer solution before the completion of the surgery and leaving both subdural and intraventricular catheters in place may reduce the incidence of hygroma and hydrocephalus[11].

Postoperative ventriculomegally is common complication.The number of patients requiring a shunt will vary based on different factors. Approximately 10 to 50% of patients will ultimately require CSF diversion. We did 2 VP shunt(28.57 %) out of 18 cases in our series.

All patients may suffer some form of meningeal irritation caused by the presence of blood products

in the CSF. This type of chemical meningitis can be treated by administering analgesic agents and a tapered course of steroid medication[12]. In our series we report rates of infection is 3 cases. We have 3 cases(42.85 %) of pyogenic meningitis which was controlled by injection Meropenem.

Prior to the advent of microsurgery techniques, the mortality and morbidity rates were higher than those of the present day. In early studies the some authors reported mortality rates as high as 75%, mostly because result of intraoperative hemorrhage or cerebral edema.In the more modern series the authors have recorded mortality rates far lower than 10%. The deaths in the microsurgical era are usually secondary to catastrophic postoperative hemorrhage or pulmonary emboli. In our current study we had only one mortality due to intraventricular massive hemorrhage[13].

As a general principle, the number of veins sacrificed during a transcortical approach should be kept to a minimum. Sacrifice of both deep and superficial veins can cause inconstant deficits, which have been reported as severe by some surgeons. This is a controversial neurosurgical issue. The variation in outcome may be the result of differences in individual anatomy. Dandy claimed that one internal cerebral vein can be sacrificed without effect, and, occasionally, even the great vein of Galen has been ligated without causing death. Other surgeons have found this observation to be incorrect. We made every effort to avoid sacrificing any vein unless it clearly compromises access to the ventricular mass but yet one cortical cerebral vein was injured which leads to hemorrhagic transformation of venous infracts.

All patients was monitored in post-operative setting for at least 24 hours and should undergo non-contrast CT scanning within 72 hours to assess ventricular size and tumor residual (Figure 4,6). Repeating the neuroimaging study in a week is useful for assessing the presence of extra cerebral fluid collections. It is useful to remove the external catheters/drains as soon as possible and to mobilize the patient. Patients with persistent ventriculomegaly or subdural hygroma are monitored longer and receive antibiotic therapy for as long as a drain is in place. Adequate levels of anticonvulsant agents are monitored at regular intervals and electrolyte imbalance is aggressively treated[13,14].

The transcortical technique makes it possible to resect lesions in each of the five regions of the lateral ventricle. It provides superior microsurgical working space and flexibility for maneuvering within the lateral ventricle. The key to a successful transcortical approach is an understanding of the functional anatomy of eloquent cortex to be broached, the location of the lesion, and its vascular supply. A clear understanding of the advantages and limitations of the transcortical approach makes performing this procedure for resection of large lesions in the ventricle both safe and effective. The majority of the patients in this series (77.78 %) had a good outcome, returning to baseline functional status and suffering minimal morbidity. In the microsurgical era, transcortical surgery-related postoperative morbidity and outcome are dependent more on tumor histological type and site of origin than on approach[14].

The transcallosal approach to the lateral and third ventricle lesions offers an important surgical option (Figure 3,5). There are several advantages to this approach over the transcortical route. With appropriate brain relaxation and minimal retraction, the surgeon can reduce the risk of brain injury. Care to preserve medial draining veins prevents venous infarction. Partial sectioning of the callosum leads to minimal long-term consequences unless additional brain injury is induced. Because this approach is not commonly used in the average neurosurgical practice, it is important to review the anatomy and to pay careful attention to the techniques that optimize a favorable outcome[14].

Transcallosal surgery carries a reduced risk of postoperative seizures, porencephalic cyst formation, and subdural hygroma formation compared with transcortical surgery.Limited exposure of the posterior lateral ventricle and the apex of the frontal horn, however, reduces the utility of the transcallosal approach for lesions arising in these regions[14].

Conclusion:

Intraventricular tumors and related CSF pathway obstructions can be safely and effectively treated with micro neurosurgical techniques, either by transcallosal or transcortical approach. The aim should be the total extraction of the tumor with minimum damage and the chosen operative corridor should optimize tumor access and the protection of vulnerable neurovascular structures. Lateral ventricle tumors can be removed via transcortical approach when having hydrocephalus which provides a wider and more direct approach to the tumor than the transcallosal one. It allows the surgeon to achieve good functional outcome and maximum excision of the tumor. Transcallosal is an excellent midline exposure with preserving the callosomerginal and pericallosal arteries to the midline tumor of lateral and 3rd ventricles.

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Effects of Selective Rehabilitation on Neck Pain due to Cervical Spondylosis - A Clinical Trial

MD. ABDUS SHAKOOR[1], SHAMSUNNAHAR[2], NAYEEM ANWAR[3], MD. MUHIBBUR RAHMAN[4], FATEMA ZOHRA[5], MD. MOYEENUZZAMAN[1]

Abstract:

Background:*Pain in the neck is a common complaint of the patients attending the hospital. In clinical practice, neck pain is seen frequently as a presenting symptom and sometimes it becomes disabling and compromises the working capacity. One of the most common causes of pain in the neck is cervical spondylosis. Rehabilitation treatment may play an important role to improve the condition of the patients. For this purpose, the study was done to find out the effects of rehabilitation treatment on chronic neck pain to improve the present situation regarding treatment.* ***Methodology:*** *A randomized clinical trial was conducted in the department of Physical Medicine and Rehabilitation, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh. A total of 150 patients were included and they were divided into two groups: group-A and group-B. Group-A was treated with selective rehabilitation and Group –B was treated with NSAID only. History, clinical examination and relevant investigations were done. The findings were recorded at first attendance and follow up was done weekly for six weeks. The results were expressed as mean ± SD and the level of significance was expressed by* p-*value unless otherwise stated. Student's 't' tests was done to test the hypothesis.* ***Results:*** *Among the study subjects 48(32 %)were male and 102 (68 %) were female. The male female ratio was 1: 2.12. There was significant improvement in both the group after treatment (P= 0.001). But in comparison between two groups, all the baseline criteria were identical. There was no significant improvement between two groups up to 5th weak(P>05) but significant improvement was seen in Group-B than Group-A after six weeks treatment (P= 0.03). This results indicates that the improvement of the patient with cervical spondylosis was seen in selective rehabilitation group and in NSAIDs group. And improvementwas same in both the group up to 5th week and after six weeks more improvement was found in NSAIDs group.* ***Conclusions:*** *By this study, it may be concluded that to reduce symptom and disability, rehabilitation treatment can be used effectively for the treatment of chronic neck pain without analgesics and by this way nephropathy due to NSAIDs can be avoided.*

Key words:*Selective rehabilitation, neck pain, cervical spondylosis.*

Introduction:

Pain in the neck is a common complaint of the patients attending the hospital. In clinical practice, neck pain is seen frequently as a presenting symptom and sometimes it becomes disabling and compromises the working capacity. Many of the patients come to the department of Physical Medicine for proper treatment and rehabilitation. Most of them are suffering from cervical spondylosis.Osteoarthritis is the most common

1. Professor, Physical Medicine and Rehabilitation, Bangabandhu Sheikh Mujib Medical University, Shahbagh, Dhaka-1000, Bangladesh.
2. Professor and Chairman, Physical Medicine and Rehabilitation, Bangabandhu Sheikh Mujib Medical University, Shahbagh, Dhaka-1000, Bangladesh.
3. HMO, Department of Neurology, Bangabandhu Sheikh Mujib Medical University, Shahbagh, Dhaka-1000, Bangladesh.
4. Resident, Physical Medicine and Rehabilitation, Bangabandhu Sheikh Mujib Medical University, Shahbagh, Dhaka-1000, Bangladesh.
5. HMO, Physical Medicine and Rehabilitation, Bangabandhu Sheikh Mujib Medical University, Shahbagh, Dhaka-1000, Bangladesh.

rheumatological disease that affects more than 80% of the population aged 55 years and older [1]. Cervical spondylosis is one kind of osteoarthritis, disc degeneration of the intervertebral disc with associated osteophyte formation[2]. Degenerative changes in the cervical spine (cervical spondylosis) may be associated with neck pain but usually only when the degenerative changes are severe. Mild or moderate degenerative changes are often seen in asymptomatic individuals. In general, the pain of mechanical disorders is intermittent and related to use. Neurological examination will often reveal the level of entrapment [3]. Neck stiffness existed as a common disorder in the age group of 25 to 29 years in our working population and 25 to 30 percent had one or more attack of stiff neck. For working population over 45 years of age, this figure rises to 50 percent. Brachial neuralgia occurs later in life than stiff neck does with a frequency of 5 to 10 percent in the 25 to 29 years' age group, rising to 25 to 40 percent after the age of 45 years and overall 45% of working men experience at least one attack of stiff neck, 23% report at least one attack of brachial neuralgia and 51% suffer from both symptoms [4]. Pain and stiffness in the neck can originate from many tissue sites and can result from a number of mechanisms. One of the most common causes of pain and disability in the neck and arm is cervical degenerative arthritis (cervical spondylosis) [5]. Cervical spondylosis is a clinical syndrome in which cervical spine degenerates to such an extent that symptom arises [6]. It is characterized by osteophytosis, narrowing of intervertebral joint spaces and foramina and compression of the nerve roots and spinal cord.

It runs a prolonged course with intermittent periods of relief. It commonly affects people above the age of 40 and is responsible for varying grades of disability [7]. It may produce clinical symptoms and / or signs and these are very variable, ranging from neckache, with or without headache, to brachialgia, myelopathy and vertebro-basillar insufficiency and indeed there may be various combinations and permutations of one or more of these in the individual patients. A study was carried out by Alam et al. in 1995 in the Rheumatology clinic in the department of Physical Medicine, IPGMR and they showed that cervical spondylosis was the commonest lesion (23.5%) amongst the various rheumatic disorders [8]. However, there are few studies were found to see the effects of rehabilitation program. The use of physical therapies e.g. Transcutaneous Electrical Nerve Stimulation, other electromagnetic applications, exercises and aids & appliances are widely used by pain specialist [9,10]. Several types of physical therapy has potential effects on musculoskeletal pain [11, 12, 13]. Cervical traction is widely used in treating various types of neck disorders, opinions are divergent on methods of application and clinical results [14]. But rehabilitation treatment may play an important role to improve the condition of the patients. This large number of patients should be managed properly for improvement of their working capacity and thus they may be able to contribute themselves for the prosperity of the country. For this purpose, the study was done to find out the effects of rehabilitation treatment on neck pain due to cervical spondylosis to reduce disability & recurrence of symptoms.

Objectives:

The objectives of this research were to observe the effects of selective rehabilitation on cervical spondylosis

and comparing the effects of rehabilitation with that of drug therapy.

Materials and Method:

The patients having chronic cervical spondylosis were selected from the department of Physical Medicine, Bangabandhu Sheikh Mujib Medical University(BSMMU). A total 170 patients aged from 30 to 60 years were selected for the study as per the selection criteria. Selection was done randomly by the way of lottery. On arrival at the department, detailed history was taken and clinical examination was carried out properly. The patient was selected based on the criteria used in the trial of 1966 with some modification, sponsored by the British Association of Physical Medicine. Chronic pain in the neck and arm, the symptoms having a root distribution and being associated with limited and painful movement of the neck, chronic pain in the neck and arm of full root distribution with paresthesia

but without clinical evidence of abnormality in the neck and chronic pain and stiffness of the neck with or without any rootdistribution (mild) were included.Patients with acute / severe pain and stiffness of the neck or local lesion like rotator cuff tears, tennis elbow and carpal tunnel syndrome, abnormal neurological signs indicating cord compression, definite disorders of the cervical spine, such as rheumatoid arthritis, tuberculosis or any infection, or has a bony injury to the cervical spine were excluded. Before admission into the trial, informed consent of the patients was taken. History, clinical examination and relevant investigations were done. The findings were recorded at first attendance and followed up was done weekly for six weeks. They were divided into two groups by the way of lottery. In group-A, 72 patients were treated with selective rehabilitation program that is - exercise (isometric neck muscle exercisefor 10 repetitions twice daily), cervical collar, neck support, manual cervical traction at home, warm moist compression and instruction in posture while in Group-B, 78 patients were treated with NSAIDs with omeprazole coverage only. Cervical traction was given by a manual home cervical traction set in sitting position. The angle of pull was 15$^{>}$ flexion of the cervical spine. The traction was given continuously for 20 minutes every day. The weight of traction in the trial was 15 % (Approx.) of the subject's body weight. Posture correction regarding sitting, lying, reading, writing, shaving, chooking bending etc. was clearly explained to the patients. A cervical collar was prescribed for all the subjects for posture correction and it was used during activity but not during the time of sleeping. All the patients participated in the clinical trial were provided with vitamine-B_1(Thiamin) three times daily and NSAID were provided in the Group-B. NSAIDs were given in the form of Naproxen (250 mg) twice daily after meals and Omeprazole (20mg) was given twice daily to prevent drug induced peptic ulcer. The following tools were used for comparing the treatment:Physician's assessment of the severity of the conditions-pain score, tenderness index &pain frequency score and patient's assessment of pains by visual analogue scale.The numerical data was analyzed statistically. The results were expressed as mean ± SD and the level of significance was expressed by *p*-value unless otherwise stated. Statistical analysis was done by using SPSS package for Windows. Student's 't' tests will be done to test the hypothesis.

Results:

A total of 175 patients were selected but 150 patients with cervical spondylosis duly participated in the study. Twenty-five patients were dropped out from the study because they did not take treatments allocated to them and/or could not attend regularly and did not follow advice of the investigators. Among the subjects there were 48(32 %) male and 102 (68 %) female (Fig. No-1).

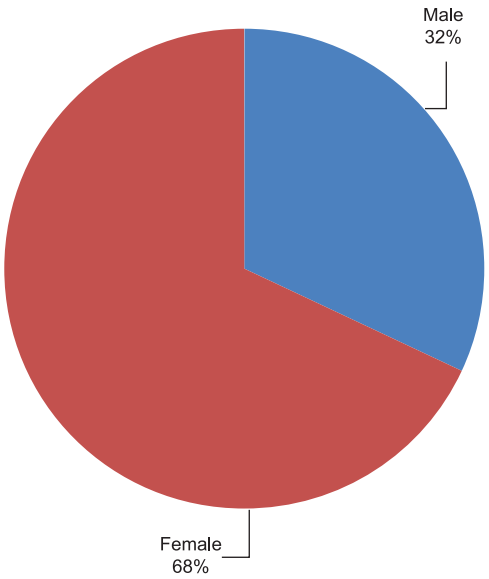

Fig. -1: *Sex distribution of the patients (N=150)*

The male female ratio was 1: 2.12. Most of the subjects were married (96.7%). Maximum patients were in the middle class (64%). The mean age of the subjects was 42.67 ± 8.85 years. The highest number of patients was in the 40- 49 years' age group (Fig No-II). And maximum female persons were affected in their earlier age than male (Fig No-III). Regarding occupation of the patients, maximum patients of cervical spondylosis were house wife 79 (52.70 %) and the private was in the second position (14%).

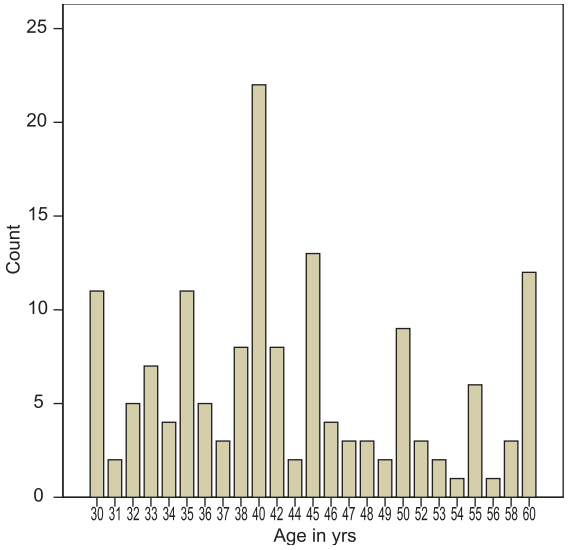

Fig.-2: *Age distribution of the patients (N=150).*

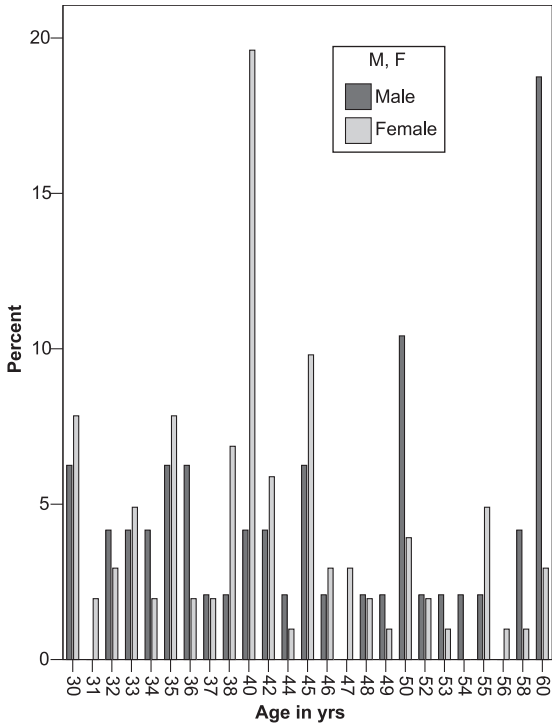

Fig.-3: *Age and sex distribution of the patients (N=150).*

Results of the clinical trial:

Base lines characteristics of the patients in both the Group were identical. This result showed that there was no significant deference between two groups regarding baseline clinical characteristics (Table No-I).

In group –A, there were 85 patients initially, but 13patients were dropped out from the study because of their irregularities to take treatments. There were 72 patients participated in the clinical trial and they took treatments and all suggestions properly. There was marked improvement of the condition of the patients in response to treatment for 6 weeks. The numerical data of pretreatment and after treatment assessment scores were compared statistically (paired student's 't`test) and found highly significant (*P* = 0.001). So selective rehabilitation was found significantly effective to reduce the sign & symptoms of cervical spondylosis.In group – B, there were 88 patients initially, but 10 patients were dropped out from the study because of their irregularities to take treatments. There were 78 patients participated in

Table-I

Distribution of baseline clinical characteristics of the patients included in the clinical trial.

Groups	Age in years	Pulse / m	Systolic BP (m m of Hg)	Diastolic BP (m m of Hg)	Height in Cm	Weigut in Kg
Group –A(n = 72)	43.08 ± 8.39	76.90 ± 4.27	127.71± 10.47	81.25 ± 6.32	157.93± 7.01	63.04±6.49
Group –B(n = 78)	42.29 ± 9.30	76.49 ± 4.84	126.03± 12.41	79.81 ± 7.70	157.46±7.57	61.84±6.46
p - value	0.58	0.47	0.38	0.24	0.69	0.26
95 % CI	- 2.06 to 3.64	- 1.05 to 1.88	-2.01to 5.38	- 0.82 to 3.71	- 1.88 to 2.82	- 0.89 to 3.28

n = Number of patients,
Results are expressed in mean ± standard deviation
p = 0.05 is considered the level of significance.
CI = Confidence interval

the clinical trial. There was improvement of the condition of the patients in response to treatment for 6 weeks. The numerical data of pre-treatment and after- treatment assessment scores were compared statistically (paired student's 't` test) and found highly significant (*p* = 0.001). So NSAIDs were found also effective to reduce the sign & symptoms of cervical spondylosis.At the time of first visit, there was no significant improvement between two groups up to 5th weak (P>05) but on the other hand there was significant improvement in Group-B than Group-A after six weeks treatment (P= 0.03,Table No-2). This result indicates that the improvement of the patient with chronic cervical spondylosis was seen in selective rehabilitation group and also in NSAIDs group. And improvement is more or less same in both the group upto 5th week and after six weeks more improvement was found in NSAIDs group (P= 0.03).

Table-II

Distribution of comparative improvementbetween two groups.

	pre-treatment scores	post-treatment scores
Group-A (n=72)	12.89 ± 3.38	6.69 ± 3.12
Group-B (n=78)	13.76± 3.83	5.65 ± 2.70
p-value	0.14	0.03
95% CI	-2.03 to 0.29	0.09 to 1.98

n = Number of patients, results are expressed in mean ± standard deviation;

p = 0.05 is considered the level of significance.CI = Confidence interval

Discussion:

Cervical spondylosis may affect people of wide range of groups. In our study maximum number of patients was in the 40-49 years age group (35.67%). The mean age of the patients in our study was found 42.67±8.85 years. Bhattecharjee B N et al. found, in their study on cervical spondylosis that maximum number of patients in the 40-49 years, which favoursthe same result found in our study. However, their sample size was small and they selected patients from different hospitals of Dhaka city. On the other hand, study of British Association of Physical Medicine showed most patients fell in the 40 to 60 years age group, which is also favourable to our study [15].Among the subjects there were 48(32 %) male and 102 (68 %) female. The male female ratio was 1: 2.12. But The British Association of Physical Medicinefound 203 male and 290 female patients during their study, where the male female ratio was 1:1.4 [15]. This is nearer to our study. The more female in our study may be due to awareness and increasing female education. Irvine et al. studied almost equal number (223 females and 230 males) of matched male and female patients and found slight preponderance of male over females [16]. The figure of this series does not reflect male-female ratio of general population because female patients attend hospitals less often because of shyness and social custom. If the general population could be studied, the number of female patients would be gone up.Regarding occupation of the patients, maximum patients of cervical spondylosis were house wife 79 (52.70 %) and the private was in the second position 14%. Highest number of patients seen in our study was housewife but Bhattecharjee B N et al. found that highest number of patients was table worker and housewife was second [17]. This may be due to more female participants in our study. The number of patients in this series can be attributed to the fact that prolonged neck flexion-extension movement during their household works. Most of our middle aged and elderly female patients have no occupation other than housewife. This may be important for the highest incidence of neck pain among housewives.

Treatment response: In our study, significant improvement was observed in response to selective rehabilitation, there was significant difference between pre-treatment and after treatment. The result is in the line with the results presented by the British Association of Physical Medicine [15]. They found that during traction relief of their symptoms was obtained in 105 of the 114 patients (92%). Bhattacharjee B.N et al. found in their study that cervical traction has no significant improvement but their sample size was only 18 in cervical traction group but our sample size was 100 in number and he used only cervical traction without exercise but we use isometric neck muscle exercise along with cervical traction. But Swezey R.L et al found significant improvement in response to home cervical traction [18]. They used simple, in-expensive over-

the-door home cervical traction method of treatment requiring 5 minutes of cervical traction twice daily for both cervical pain and radiculopathy syndromes. They found over-the-door home cervical traction modality provided symptomatic relief of 81 % of the patients with mild to moderately severe cervical spondylosis syndromes, which supports the findings of our study because we used home cervical traction daily for 15 minutes. On the other hand Wareham T et al found that very good results in their study, where 100 patients treated with cervical traction with radiculopathy, 90 obtained complete relief within about half a minute of the application of the traction [19]. Cervical traction is also effective to reduce deformity of the cervical spine. Graziano G.P et al. found that excellent correction of deformity and radiographic union were achieved in all patients with severe cervical deformity in rheumatoid arthritis [19]. Honet C.J et al found good to excellent results in 92% of patients treated with cervical traction [21]. This supports the results of our study also. Caldwell et al. treated 577 patients of cervical syndrome and found 82% good results with constant traction on an average of 13 session treatments, 92% exhibit good and 8% moderate improvement and there was no failure [22]. Shakoor et al. also found better improvement of cervical spondylosis with cervical traction in the hospital setting [23,24]. This is also in favour of our study we also used constant traction. The only effects which traction can be expected to achieve are some distraction between vertebrae at the intervertebral disc and apophyseal joints, tensing the longitudinal ligaments of the spinal column, and some slight widening of the intervertebral foramina[23]. The two general objectives in

applying cervical traction are (1) to stretch the posterior cervical region and (2) to enlarge the interspaces at the intervertebral foramina [14]. Probably due to this distraction there was good results we obtained in our study. In a study in the department of Physical Medicine & Rehabilitation, IPGM&R, Dhaka, it was found that there was significant improvement in response to cervical traction group, where cervical traction was given along with exercise and NSAIDs [23]. But in our study we used traction without NSAIDs.

In the study of Caldwell J.W et al. neck muscle exercises were applied and found good results[21]. In our study, we used isometric neck muscle strengthening exercises and we found significant improvement. This indicates that exercise also played an important role to improve the condition. In some studies, it was found that strength training was effective moderately to reduce pain and improving function and stiffness in osteoarthritis [25] More specific exercises were used to strengthen muscle to increase range of motion of a joint to re-educate patients in appropriate use of joints and reduce pain. Exercises to stretch the involved muscles are the key to sustained relief of myofascial pain [26]. Restoration of normal muscular length, posture and muscle overwork. improved conditioning (exercise tolerance or stamina) and increased strength through exercises, reduces the likelihood of their developing trigger points. A carefully graded exercise programme is needed to increase endurance. Strengthening exercises are recommended, which should be done smoothly and slowly, with a certain number of repetitions to achieve conditioning [27]. In our study we used certain number of repetitions (10 times) twice daily and found statistically significant improvement. However, we used cervical traction along with exercise, ADL advice and cervical collar as selective rehabilitation. Education interventions can be split into two main areas: providing information on the disease and how to alleviate the symptoms through behavioral changes (physical coping) or reducing symptoms through physiological strategies (physiological coping) [25]. In a study, Tanaka S et al. found significant relationship of activities of daily living on muscle atrophy in patients with joint disorders [27]. Chard J et al. found that there are moderate improvement of pain and function due to posture correction without side effects [25]. We applied

posture correction procedures in both the groups and found insignificant improvement regarding pain and range of motion. We also used cervical collar (one kind of brace) for maintaining good neck posture during working period, which also supported by Chard J et al. The results are in the line of Tanaka S et al. and Chard J et al.Education of the patient about the pain and the perpetuating and aggravating

factors is of major importance. It helps in the programme and allows satisfactory long-term results.

We found significant improvement in response to treatment with NSAIDs. We used tablet naproxen (250 mg) twice daily, as all the subjects were chronic in nature. Chard J et al. found in a review that NSAIDs were highly effective for pain and function but with potential side effects [25]. This is in favour of our study. NSAIDs therapy is the most prevalent category of adverse drug reaction. Thus NSAIDs may be used to reduce pain and improve function but it should be used very cautiously.

Comparative study: We compare between selective rehabilitation and non-steroidal anti-inflammatory drugs and found significant improvement in NSAIDs group than rehabilitation group after six weeks ($p = 0.03$) but there was no significant improvement throughout the study upto 5th week. But in the present study no NSAIDs was given to the selective rehabilitation group. In spite of that there was significant improvement after treatment in that group. In this study, NSAIDs were given in both the groups but cervical traction plus NSAIDs showed good results. In both the studies it was found that cervical traction is superior to other form of treatment, which also supports the results obtained in the present study because without giving NSAIDs same improvement was found in rehabilitation group upto 5thweek.. On the other hand there were potential side effects of NSAIDs rather than physical therapies [25]. Gastrointestinal (G I) complications related to NSAIDs therapy are the most prevalent category of adverse reaction [28,29]. These side effects includes –dyspepsia, gastric ulcer, perforation, gastric outlet obstruction, major or minor acute or chronic GI bleeding even death [29,30]. But rehabilitation has negligible side effects. In a study, Dabbs V et al. found that cervical manipulation for neck pain is much safer than the use of NSAIDs , by as much as a factor of several hundred times and there is no evidence that indicates

NSAIDs use is any more effective than cervical manipulation for neck pain. So NSAIDs should be used very cautiously. And if it is possible to avoid NSAIDs we should avoid it and go for non-pharmacological therapy like rehabilitation treatment.

Our study has it's obvious limitations. It was confined to a highly selected group of patients in a specialized hospital (BSMMU). Follow up period was also short. Only two types of conservative measures were observed in the study. However, it is necessary to investigate a large sample and a multicenter trial of rehabilitation for a longer period of follow up.

Conclusions:

From the present study in may be concluded that to reduce pain and disability, the patients with neck pain due to cervical spondylosis may be treated effectively with rehabilitation treatment. And by this way, use of NSAIDs can be reduced and ultimately kidney disease may be decreased.

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REVIEW ARTICLE

Sarcopenia, A Booming Concern of Ageing World: A Review

MD SHAHIDUR RAHMAN

Abstract:

Sarcopenia is a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength with a risk of adverse outcomes such as physical disability, poor quality of life and death. With the onset of advancing age, muscle tissue is gradually lost, resulting in diminished mass and strength, a condition referred to as sarcopenia. The sequelae of sarcopenia often contribute to frailty, decreased independence, and subsequently increased health care costs. This review article will introduce potential mechanisms that may contribute to sarcopenia, although no one mechanism has yet, and may not completely, define this process. Despite sarcopenia is an inevitable process of life, prevention and treatments are absolutely needed in order to improve the quality of life and quality adjusted life years. Adequate nutrition and structured exercises are essential components of treatment and prevention. However, even those individuals who maintain their fitness through exercise do not appear to be immune to sarcopenia.

Introduction:

The term *sarcopenia* (from the Greek *sarx* for flesh and *penia* for loss) was first coined by Rosenberg[1] in identifying the age-associated loss of muscle mass and function. Sarcopenia is determined by two factors: the initial amount of muscle mass and the rate at which it declines with age. The rate of muscle loss with age appears to be fairly consistent, approximately 1%–2% per year past the age of 50 years [2, 3]. With advancing age there are significant changes in body composition such that body fat increases while modest losses are observed in muscle mass [4, 5, 6]. This shift in body composition with advancing age is often masked by relative stability in overall body weight [3, 7]. Balagopal et al in a cross-sectional data demonstrates that young healthy men have a body composition of approximately 20% body fat at age 25, whereas in men aged 55 years, body fat was 30%, and greater than 35% in 75-year-old men[8]. Muscle mass was fairly stable between the 25- and 55-year-old men, but declined approximately 25% between 50 and 75 years of age[8]. Although physical activity and exercise status are important factors in the onset of obesity with age, the decline in muscle mass and gain in body fat are evident even in active older adults [3, 9, 10. 11]. In the New Mexico Elder Health Study[12], sarcopenia was defined as a muscle mass index [muscle mass (kg)/height (m) ^{2}] less than two standard deviations below the mean of a young reference population. Using this definition 10%–25% of persons under the age of 70 years were sarcopenic, whereas beyond the age of 80 greater than 30% of women and 50% of men were sarcopenic[12, 13].

Consequences of Sarcopenia

The consequences of sarcopenia include decreased strength[14, 15.], metabolic rate [16, 17, 18]and maximal oxygen consumption[19]. These physiologic decrements in maximal strength and fitness probably contribute to weakness and a loss of independence [20]. The loss of aerobic capacity with age is predominantly due to a loss of muscle mass [21]. This loss of fitness is also observable in highly active older adults, who continue to exercise regularly, yet display rates of decline are similar to their sedentary peers[22]. However, fitness remains greater at any age in those who exercise regularly as compared with those who do not.

Biology of Sarcopenia:Much like the underlying causes of aging, the biology of sarcopenia remains

Professor. Department of Physical Medicine and Rehabilitation
Bangabandhu Sheikh Mujib Medical University

elusive. Two key observations associated with sarcopenia include a loss of skeletal muscle fiber number [23]and a change in the cross-sectional area (CSA) of the remaining fibers[24]. Various mechanisms have been put forth to explain the change in total muscle mass observed including:

(a) A lack of regular physical activity ("use it or lose it"),

(b) A change in protein metabolism (a deficit between protein synthesis versus degradation),

(c) Alterations in the endocrine milieu (decrease in growth hormone (GH) and testosterone and an increase in cortisol and cytokines),

(d) A loss of neuromuscular function (denervation versus reinnervation),

(e) Altered gene expression, and

(f) Apoptosis; other factors may also contribute in part to sarcopenia.

Skeletal muscle is a dynamic tissue constantly turning over its proteins to amino acids. For muscle to maintain its mass, the rate of protein synthesis must be in balance with the rates of degradation to amino acids in combination with dietary absorption maintaining the difference in amino acid utilization. For sarcopenia to occur, only small imbalances between synthesis and degradation over many years are necessary to eventually result in a significant loss of muscle mass[25]. In young adults, muscle mass accounts for approximately 30% of whole body protein turnover, whereas in elderly persons, muscle mass only represents approximately 20% or less of whole body protein turnover [26]. With advancing age, illness, trauma, or inadequate dietary intake of amino acids can all decrease the rates of protein synthesis and ultimately exacerbate the onset of sarcopenia. Alternatively, the oxidized proteins, which increase with advancing age, may not be as efficiently removed by the proteolysis system (ubiquitination and lysosomal degradation) resulting in the accumulation of lipofuscin and cross-linked proteins[27]. An age-related accumulation of nonfunctioning proteins that are not efficiently removed from the muscle could increase the amount of non-contractile material in muscle, which might explain why muscle strength declines to a greater degree than total muscle mass in sarcopenia.

Hormonal effects onSarcopenia:With advancing age, there is a well-documented increase in insulin resistance that contributes to diabetes. Insulin has long been considered anabolic, primarily by reducing protein degradation[28. 29]. A recent review of the topic has suggested that insulin can also stimulate protein synthesis[30]. One mechanism by which insulin signaling may facilitate amino acid transport into the cell is via stimulating nitric oxide synthase[31]. Therefore, insulin resistance with age may contribute to sarcopenia via an inhibition of the nitric oxide cascade resulting in less absorption of available amino acids for protein synthesis. As well, GH, liver-derived insulin-like growth factor (IGF)-I[32]and testosterone [33, 34]all decrease with age. Although GH-induced IGF-I production in the liver is the major source of circulating IGF-I, and mediates many GH metabolic effects, local IGF-I production within target tissues, under the influence of both GH and testosterone[35], accounts for greater than 50% of total IGF-I production and appears to be important for stimulating muscle growth and repair[36].Cortisol, a potent stimulus to protein catabolism[37], increases slightly with age and may contribute to the age-related increase in adiposity [38]. Circulating levels of these various hormones are altered by the aging process, all potentially contributing to sarcopenia[32. 39]. One molecular pathway of interest involves the suppression of myostatin, a recently discovered member of the transforming growth factor (TGF) superfamily. Myostatin is an autocrine factor that inhibits muscle development.[40]. However, we recently demonstrated that circulating hormone levels were not related to the expression of myostatin in skeletal muscle [41]. Therefore, how myostatin ultimately interacts in sarcopenia remains unclear.

Pathogenesis: Age-related reductions in muscle mass and strength are also accompanied by a reduction in motor unit (MU) number [42] and histological changes (angulated fibers, fiber-type clumping), which are suggestive of neuronal remodeling[43] in elderly people. The muscle appears to compensate for this reduction in MUs by hypertrophy of existing smaller and slower MUs that attempt to re-innervate faster fibers and transform them into slower myosin fiber types[43, 44] thus

partially explaining why slower muscle is preserved in aging. Urbanchek[45]recently assessed the issue of whether denervated fibers significantly contributed to the age-related loss of muscle strength and observed that only 11% of specific force decrements were due to denervated fibers.

The decline in $VO_{2\,max}$with age has been primarily attributed to sarcopenia and a reduced cardiac output[21]. However, available evidence suggests that mitochondrial metabolism is also adversely affected by age [46]and may contribute to a reduction in $VO_{2\,max}$. Aiken and colleagues, and others [47]have demonstrated that mitochondrial DNA mutations and deletions are increased in the single fibers of aged skeletal muscle, and the abundance of these abnormal mitochondrial regions increase with age in both rats and nonhuman primates[48]. The frequency of mutations is greater in muscles more prone to sarcopenia[47]. Human studies have also demonstrated increased numbers of mitochondrial point mutations in older versus younger participants[49].

Benefits of nutrition and exercise for the prevention of sarcopenia: Nutrition and especially amino acid intake are important to maintain protein turnover. Exercise is beneficial and will decrease body fat, improve reserve capacity, and increase muscle strength (and maybe muscle mass). It could be that sarcopenia has both physiologic factors, as has been discussed, in combination with social issues resulting in older persons not taking up exercise. Sarcopenia is a process whereby a loss of reserve capacity will result in an increased sense of effort for a given exercise intensity. If one avoids exercise, then future performance will continue to decrease, as cardiovascular function and $VO_{2\,max}$ will diminish, again feeding back to the increased perception of exercise effort, thus exacerbating sarcopenia.

As regular physical activity decreases with age, there is a down-regulation of physiological systems adapting to reduced exercise/stress levels. As cardiovascular and skeletal muscle reserve functions decline, this contributes to an increased relative perception of effort for a similar absolute task as compared to when an individual was younger. If tasks are perceived to be more difficult, this will increase the likelihood for avoidance of physical work. As more physical work is avoided, exercise performance will continue to decline, therefore contributing to additional physiological decrements in an individual's functional reserve capacity, thus leading to more sarcopenia.

Conclusion:

The physiological and psychological factors that contribute to the process of sarcopenia are multifactorial, occurring over a prolonged time period, possibly with no identifiable single cause or mechanism, potentially explaining this age-related loss of mass and strength in and of itself. Our goal as researchers should be to gain an improved understanding of the complex biological factors leading to age-related muscle loss beyond those attributable to a simple decrease in physical activity. Populations are rapidly ageing worldwide with major implications for health systems. This situation is more prevalent in low-income and middle-income countries. High-income countries show some evidence that a compression of morbidity (a reduction over time in the total lifetime days of disability) is taking place, as noted from trends of functioning and disability status. However, uncertainty remains about the health of future older generations in view of the different risk factor exposures in different cohorts and increases in the prevalence of chronic diseases. Low-income and middle-income countries currently have no reliable evidence of compression, and morbidity might even be expanding, driven by lifestyle risk factors and increasing prevalence of chronic diseases.

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CASE REPORT

A Giant Hydatid Cyst at Right Frontoparietal Region: A Rare Case Report

HARADHAN DEB NATH[1], KANAK KANTI BARUA[2], MOHAMMAD SHAHNAWAZ BARI[3], AHMEDUL MURSALIN[4], MD MASUM ALI[4]

Abstract:

Background: *Hydatid cyst is a parasitic disease which can affect the central nervous system.* ***Objective:*** *The purpose of the study is to reveal the clinical findings and the effect of giant the intracranial hydatid cyst at frontoparietal region, which is a rare finding.* ***Results:*** *A patients with right frontoparietal hydatid cyst was admitted in our hospital with history of headache, seizure and left upper limb weakness. We operated the patient and postoperatively developed hydrocephalous and pseudocyst at the site of operation. Cystoperitoneal shunt was done. The patient was medically treated by albendazole. The patient cured postoperatively.* ***Conclusion:*** *Patients with intracranial hydatid cyst can be treated surgically and with albendazole.*

Key words: *Hydatid cyst, echinococcus granulosus, intracranial, craniotomy, magnetic resonance imaging.*

Introduction:

Parasitic zoonoses, transmittable from animals to humans, remain a serious and significant public health problem in developing countries[1,2]. Twenty five percent of the world's population could be suffering parasitic infestation. Among these parasitoses, neurocysticercosis, infection of the central nervous system by Taenia solium metacestodes, is the commonest encountered cerebral parasitic infection in the world. It is the first cause of epileptic seizures in developing countries. The other zoonosis with a world-wide distribution is the hydatid disease which will be the topic of this chapter[1,2].

Indeed, in Antiquity, according to Galen, Hippocrates (4th century AD) has evoke the disease as taught his students: when liver is distended with water, it breaks in the epiploon, so the abdomen is full of water and the sick dies". Arateus, Galen (first and 2nd century AD, respectively), Al Rhazes (860-932 AD) and Avicenna (980-1037) reported also on human involvement by hydatidosis. John Hunter in 1773 described the morphological picture and Goeze in 1782 the microscopic picture of the cyst. The first description of vertebral echinococcosis was by Chaussier in 1807[3]. Reydellet is believed to have performed the first surgical intervention for spinal hydatidosis in 1819. Virchow, for the first time in 1855, established the helminthic nature of alveolar cysts. The life cycle of the parasite was first described in 1862. In 1890, Graham and Clubb were the first neurosurgeons to perform removal of a brain hydatid cyst. Since the last century, it is usual to associate the following names with improvement of the surgical procedures of brain hydatid cyst: Dowling[4]. More recently Arana-Iniguez[5] perfected the procedure giving birth to an unbroken cyst by irrigating saline isotonic solution between cyst wall and brain.

The echinococcus granulosus cycle requires two hosts: one intermediate, usually sheep, camel or swine, and the other final hosts represented by dog

1. Associate Professor, Neurosurgery Bangabandhu Sheikh Mujib Medical University, Dhaka.
2. Professor Neurosurgery, Bangabandhu Sheikh Mujib Medical University, Dhaka
3. Medical Officer, Bangabandhu Sheikh Mujib Medical University, Dhaka.
4. Resident, Neurosurgery, Bangabandhu Sheikh Mujib Medical University, Dhaka.

or fox. Dogs are infected by ingesting faeces or butured infected animals containing cysts which develop into cestode, an adult tapeworm in their small intestine. Eggs included in some parts of the bowels pass out through faeces and contaminate pasture. When ingested by the sheep, the scolex or eggs be-immediately infective by releasing larvae which cross the intestine wall. Then they are carried through the portal system to liver, where they develop into hydatid cysts. Occasionally humans can take the place of sheep as accidental intermediate hosts through contact with infected dogs or by oral in-gestion of garden vegetables infected by the eggs of the parasite.

If the daughter cyst crosses the hepatic filter; then it is spread through the bloodstream to other organs, i.e. lungs, and less frequently to brain. Usually, the infestation goes up the systemic circulation to the parietal lobe via the middle cerebral artery as in all embolic diseases. Brain hydatid cysts (BHC) are spherical, or balloon-shaped, and are characterized by slow growth. At diagnosis, their size varies from few centimetres to huge volume of 15cm or more. Ventricles, brainstem and orbit are other exceptional localizations. The solitary aspect of the BHC is the most observed (85%), remaining cases are multilocular or multiple. Growth rate is slow and controversial, ranging between 1 and 10 cm per year. Rarely, BHC can be calcified, expression of their degeneration and death.

Case report:

A 14 years old boy was admitted at the Department of Neurosurgery, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka with the complaints of occasional headache for last two years. Headache was global in nature. Headache became worse at very early in the morning. There was history of occasional seizure for one year with temporary loss of consciousness. Seizure started at left upper limb and became generalized. There was history of tongue bite and history of micturation and defecation during seizure. On examination higher psychic function was normal. All cranial nerves were intact and weakness of left upper limb. Muscle power was grade four at left upper limb. There was no history of taking any burn meat. Magnetic Resonance Imaging (MRI) of brain with contrast and computerized tomography (CT scan) of brain with contrast showed a giant hydatid cyst at right frontoparietal region. The patient underwent surgery by wide craniotomy at right frontoparietal region under general anaesthesia. Dura was opened widely. Total excision of cyst was done with cotton dissection, saline irrigation and through the arachnoid plane. Irrigation was done with 3% sodium

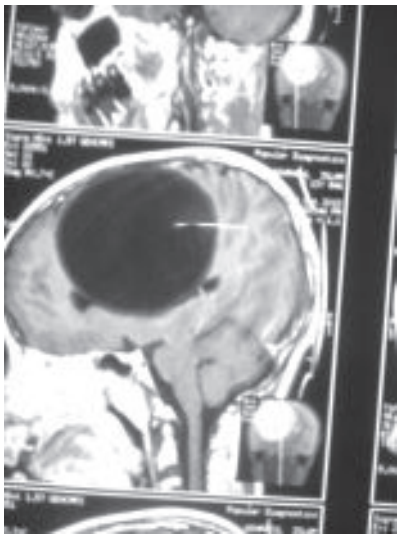

Fig.-1: *MRI of brain with saggital section frontoparietal giant hydatid cyst*

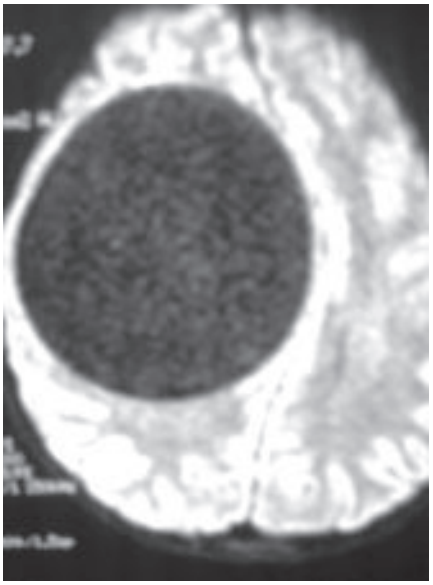

Fig.-2: *Diffusion axial film showed giant right frontoparietal hydatid cyst*

chloride, hydrogen peroxide and normal saline. Cyst size was 13x12 cm in diameter. Postoperatively patient developed right frontoparietal subdural hygroma which was treated conservatively. Diagnosis was confirmed by histopathological and microbiological examination. Post operatively patient developed hydrocephalus, subdural hygroma with pseudocyst. Cysto peritoneal shunt was done. Postoperative period was uneventful. Albendazole 400 mg was given 12 hourly for 4 weeks. Patient was totally improved clinically.

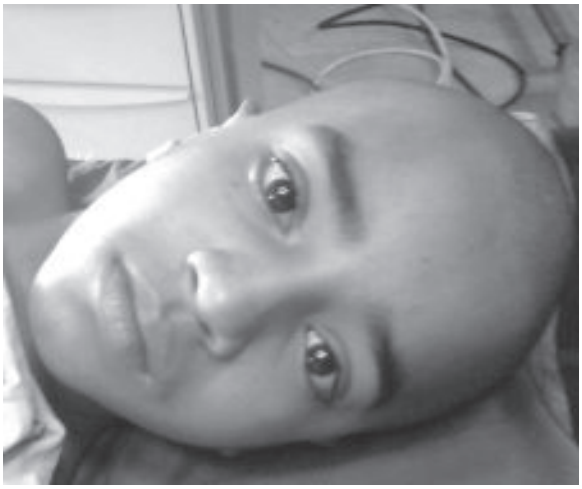

Fig.-3: *Preoperative photograph of the patients*

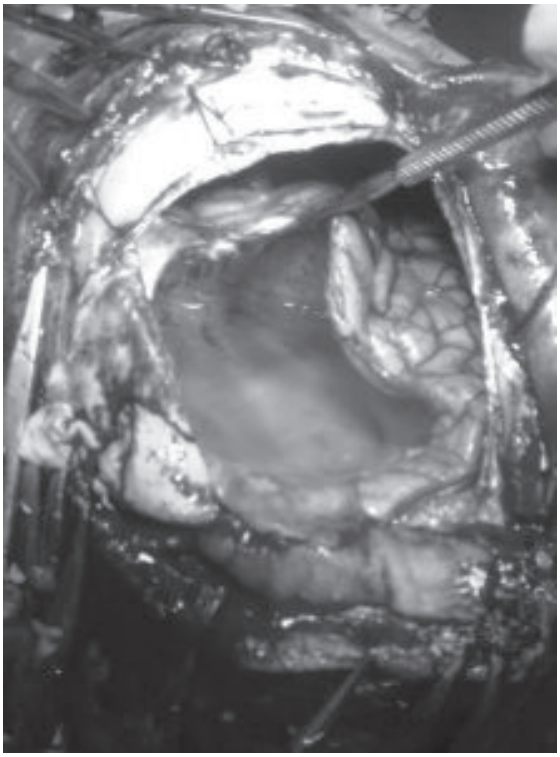

Fig.-4: *Peroperative photograph showed space after excision of the hydatid cyst*

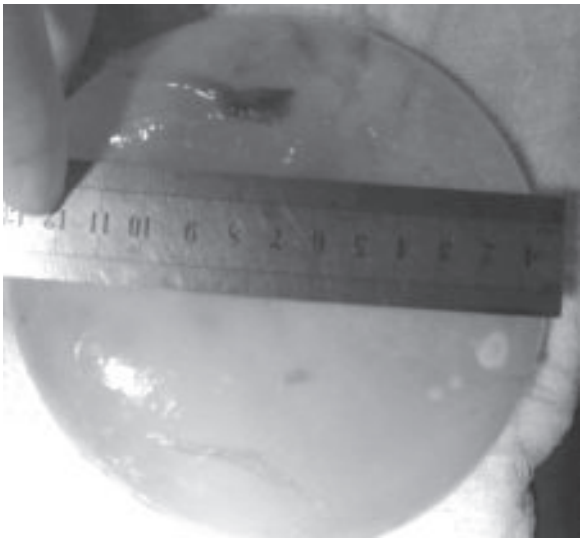

Fig.-5: *Postoperative photograph after excision of the hydatid cyst*

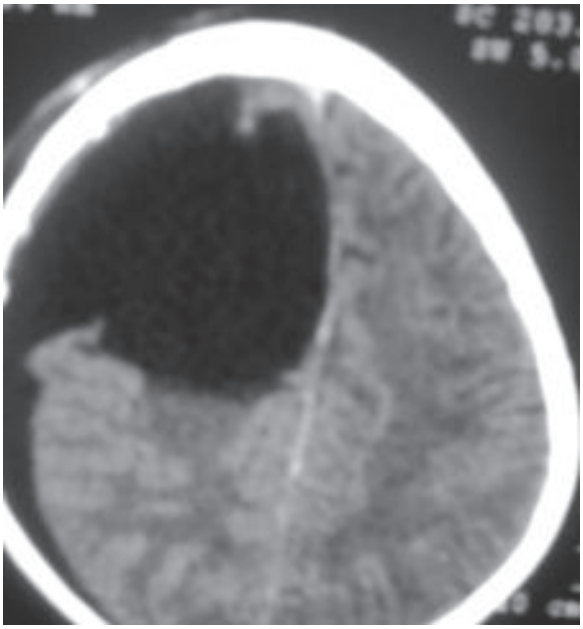

Fig.-6: *Postoperative CT scan of brain after excision of the hydatid cyst with subdural hygroma*

Fig.-7: *Postoperative photography of the patients without neurological deficit*

Discussion:

Hydatid is a word derived from the Greek "ydatos" which means water. Hydatid disease is a parasitic infestation caused by a dog tapeworm larvae of Echinococcus granulosus, a helminth belonging to the cestode group.

It is common in sheep farming in underdeveloped countries such as those in Asia, Africa, South and Central America or in the Mediterranean area. "It follows the sheep as his shadow". On the opposite, it is unusual in developed countries. Nevertheless, this notion should be attenuated by the movements of humans, especially migratory flows. Liver and lung as big filter of the portal system, are the most infested organs, whereas involvement of brain, 2-3% of all body localizations, and spine, less than 1%, are rare. However, these spinal hydatid cysts (SHC) represent around 50% of the bone localizations.

BHC occurs more frequently in children than in adults. This data was confirmed in our 99 patients operated on between 2000 and 2007 in 4 departments of neurosurgery: 2 in Algiers (Ait Idir and Salim Zemirli), one in Annaba and one in Constantine. Among them, 59 (59.5%) were less than 15 years old. The probable reason may be ductus arteriosus, or their close contact with infected dogs. There is no appreciable difference between males and females affected: sex-ratio 46/53. In children, loss of balance and rapid growth of head circumference are suspicious for the parents. Headaches, blurred or decreased vision and vomiting are usual reasons for consultation. Signs of increased intracranial pressure are of paramount importance in the diagnosis of this space occupying lesion. Focal neurological deficit depends on the involved area and the size of the hydatid cyst. Nevertheless, some infants present with ataxia and or dysmetria when imaging features show huge parieto occipital hydatid cyst. This can be explained by the hypothesis of a pressure cone on cerebellum through the tentorium. Untreated, patient become lethargic, stuporous, eventually comatose. In their series, location of hydatid cyst in the supratentorial compartment was present in 92 cases, 4 cases were in the brainstem one case was in the cerebellar hemisphere and two cases were in the orbit.

Children treated for head injury may sometimes show split sutures indicative of increased intracranial pressure, leading to the incidental discovery of intracranial mass lesion. Skull X-rays can be useful, showing signs of raised intracranial pressure as suture diastasis, unilateral enlargement or erosion of the inner table of the skull, or decalcification of the posterior clinoid process in older patients. CT scan demonstrates non contrast enhancing circular hypodense lesion[6,7] ipsilateral ventricles can be compressed, effaced with midline shift to the controlateral hemisphere. Sometimes one large cystic lesion with internal septations evocative of daughter cysts can be seen. Absence of surrounding oedema is usual. In previous series, a diameter of 5-10cm was the most frequent and was encountered in 56% of cases. In 51 cases (5 1%), BHC was single and multiple in 49 patients. Due to increased

intracranial pressure and worsening of the patient's condition, MRI was not performed on many patients and the decision was to operate as soon as possible. MRI, axial, sagittal and coronal views, reveal spherical or egg-shaped lesions with CSF-like signal intensity both in T1 and T2 sequences: hypointense in T1 and hyperintense in T2. On T1 weighted images, the thin capsule is iso- or slightly more hypointense than the fluid content; enhancing ring lesion is observed in case of infected cyst. T2W images show a low intensity rim which correlates to the external layer composed of fibrosis of surrounding brain tissue. On the whole, image of BHC is a well recognized entity on CT scan, which is superior to, MRI in depicting rare calcifications. On the other hand, MR imaging is more accurate in demonstrating the pen-cyst layer, which appears as a ring[5].

In our case the patient had been admitted with history of headache, upper limb weakness and seizure which was treated with excision of the tumor and medical treatment by albendazole for 4 weeks.

Conclusion:

Patients with hydatid cyst can be treated by surgical excision and with antimicrobial agent, like albendazole. The disease can be prevented by discouraging people by taking of burn meat and food hygiene by hand wash and uncooked vegetable washing properly.

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