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ORIGINAL ARTICLES

Association of Hyperlipidaemia with Vascular Dementia among Stroke Patients Attending a Tertiary Level Hospital in Bangladesh

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Abstract:

Background: *Stroke is a major cause of physical disability in the elderly and the second most common cause of dementia. The prevalence of Alhzeimer's dementia is increasing in western societies. But vascular dementia (VaD) is increasing in developing countries like Bangladesh and in Japan, because of the decline in mortality after stroke and aging of population. Conflicting data shows that hyperlipidaemia, a modifiable risk factor for ischemic stroke is associated with a higher risk of vascular dementia.* ***Objective:*** *The objective of this study was to evaluate association of hyperlipidaemia with vascular dementia. Method: It was a cross-sectional descriptive study conducted in the Department of Neurology, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka from August 2014 to November, 2015. All stroke patients above 18 years of age and both sexes, attending the department of Neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka presenting at least 3 months after stroke were the study population. Patients attending to the above mentioned hospital and after meeting the inclusion and exclusion criteria a purposive sampling technique were applied for selecting cases. Total 73 cases were evaluated. These patients were examined by MMSE for evidence of dementia. Severity and risk factors of vascular dementia were assessed. Serum fasting lipid profile was estimated in all cases and evaluated their association with VaD.* ***Results:*** *In this study it was observed that most of the stroke patients and VaD patients were in the age group of 5th and 6th decade. Among stroke patients it was 17(23.3%) and 31(42.5%) and among VaD patients it was 10(25.6%) and 18 (46.6%). Male outnumbered female (in stroke male-63%, Female-37%; in VaD male-59%, Female 41%). In this study out of 73 patients 40(54.8%) were smoker, 67(91.8%) had hyperlipidemia, 54(74%) had hypertension, 35(47.9%) had diabetes mellitus, 15 (20.5%) had IHD, 64(87.7%) had ischemic stroke, 9(12.3%) had hemorrhagic stroke, 25(34.25%) had recurrent stroke. Most of the patients were house-wife 16((21.9%) and read upto primary level 22 (30%). Out of 73 stroke patients 39(53.4%) had VaD. Of them 12(30.8%) had mild, 16(41%) had moderate and 11(28.2%) had severe dementia. Again out of 39 VaD patients 38(97.4%) had history of ischemic stroke and 1(2.6%) had history of hemorrhagic stroke who was moderately demented. Among VaD and non-vascular dementia patients the mean S. total cholesterol, S. triglyceride, S. LDL-C and S.HDL-C were 185.35±44.07, 149.82±57.05, 133.58±44.53, 31.07±11.16 (mg/dl) and 178.70±48.40, 151.35±76.12, 116.48±42.39, 33.61±11.82 (mg/dl) respectively.* ***Conclusion-:*** *In this study there is a non-significant positive association with high S. total cholesterol, high S. LDL-C, Low S. HDL-C but not with S. triglyceride. So, we can conclude that hyperlipidemia has weak association with VaD.*

Key words : *Stroke, Vascular dementia, hyperlipidemia.*

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Introduction :

Throughout the whole world, stroke is a major cause of physical disability in the elderly and the second most common cause of dementia behind Alzheimer's disease[1].Vascular dementia (VaD) is defined as permanent cognitive impairment produced by vascular damage to the brain[2]. In western countries among dementia cases over the age of 65, 25-33% are of vascular dementia. It is more in developing countries like ours and in Japan[3]. The diagnostic criteria for vascular dementia includes, documented intellectual loss, definite vascular damage to the brain, a relationship in time between the occurrence of strokes and the appearance of intellectual symptoms. In some community-based studies it is found that the prevalence of dementia in people with a history of stroke is about 30% (3.5-5.8 times higher than in those who have not had stroke)[4,5].In hospital based studies, the prevalence of Vascular dementia (VaD) ranges from 5.9 to 32%[6-10]. In a community-based study done over 25years, the cumulative incidence of VaD was 7% after 1 year, 10% after 3 years, 15% after 5 years, 23% after 10 years and 48% after 25 years[11].The risk of VaD and its severity are not influenced by the type of stroke (ischemic or hemorrhagic)[12-14]. Patient related variables associated with increased risk of VaD are increasing age[6-10], low education level, pre-stroke cognitive decline without dementia, high blood pressure [15], diabetes mellitus[13]; atrial fibrillation, myocardial infarction[16], epileptic seizures, sepsis, cardiac arrhythmias, congestive heart failure, silent cerebral infarcts, and white matter changes. Still there is no cure for VaD. So, the treatment for vascular dementia is prevention. Most vascular damages to the brain can be avoided through control of blood pressure, lipids, heart disease, obesity, diabetes mellitus, smoking cessation and regulation of heart rhythm. The medications presently available for Alzheimer's disease (AD) are not effective for patients with vascular dementia. Vascular dementia can be distinguished from other dementias through careful attention to clinical history and neurological examination. The clinical presentation of VaD may differ from AD because VaD patients may have stair-step progression, focal neurological deficits and vascular damage on brain imaging. The Lewy body dementia patients frequently present with early hallucinations while the VaD patient usually demonstrate intellectual decline. The Lewy body dementia patient has extrapyramidal symptoms while the VaD patients have focal neurological deficits. Alzheimer's and frontal lobe dementias rarely manifest with focal neurological signs or evidence of extensive stroke on brain imaging.

The prevalence of vascular dementia is increasing in western societies and also in developing countries like Bangladesh. Conflicting data show that hyperlipidemia, a modifiable risk factor for stroke is associated with a higher risk of vascular dementia. Reduced high density lipoprotein cholesterol (HDL-C)[17,18] and apolipoprotien A-1 levels [19], as well as increased levels of lipoprotein (a)[19], have been observed in vascular dementia in some but not in all studies [20,21]. Contradictory results have been found in studies relating to total cholesterol [22,23], HDL-C [19,24] and LDL-C [22,24] levels with VaD. The present study was done to evaluate the association of hyperlipidemia in a group of patients with VaD. Objective of the study was to evaluate association of hyperlipidemia with vascular dementia 3 months after stroke by Mini Mental State Examination (MMSE).

Methodology:

It was a cross-sectional descriptive study conducted in the department of Neurology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka, from August 2014 to November 2015. All stroke patients above 18 years of age and both sexes presenting at least 3 months after stroke were the study population. Patients attending to the above mentioned hospital and after meeting the inclusion and exclusion criteria a purposive sampling technique was applied for selecting the cases.

Selection criteria:

Inclusion criteria:

All patients clinically diagnosed first or recurrent stroke (Ischemic or hemorrhagic) confirmed by CT/MRI scan presented with at least 3 months after stroke and patients with stroke age 18 years and above of both sexes.

Exclusion criteria:
Patients of age less than 18 years, having pre-existing dementia, on lipid lowering medications, severe neuropsychiatric disorders (schizophrenia, major depressive disorder, alcohol or drug abuser etc), advanced medical conditions (acute myocardial infarction, left ventricular failure, end stage renal failure, malignancy etc), metabolic and toxic states resembling stroke, severe communication difficulties (severe aphasia, blindness, deafness etc) and patient unwilling to participate in the study

Data collection tools and procedure
The suspected cases of ischemic and hemorrhagic stroke were identified on the basis of history, clinical examination and findings of CT scan or MRI scan of brain. The following information's were collected from each patient: age, sex, occupation, educational status, detailed history of stroke, hypertension, diabetes mellitus, coronary artery disease, family history of stroke or dementia, current or previous history of smoking, alcohol consumption, tobacco chewing, dietary history and others. Examination findings including hemiparesis/monoparessis, dysphasia, plantar response, pulse, BP, carotid bruit, cardiac murmur were noted. Investigations like serum lipid profile (fasting), blood sugar, serum creatinine, Serum electrolytes, ECG, Chest X-ray, echocardiogram and related investigations were also done. Total 73 cases were included in the study. Patients with scores 24 or lower on MMSE considered as demented. Severity and risk factors of dementia (association with hyperlipidemia) were assessed with types of stroke, location of stroke (lesion), 1st or recurrent strokes etc.

Statistical analyses:
Data were collected in a pre-designed questionnaire. Data processing work consists of registration schedules, editing, computerization, preparation of tables and figures, analyzing and matching of data. Patients were divided into 2 groups according to the presence or absence of VaD and hyperlipidemia. Data analysis was done by using SPSS (Statistical Package for Social Science) software for windows version 18. Scatter plots were done to evaluate association between hyperlipidemia (total cholesterol, LDL-c, HDL-c and TG) and Vascular dementia. The horizontal axis (X-axis) represents lipids and vertical axis (Y-axis) represents vascular dementia.

Results & observations:

Table-I
Distribution of patients according to age (n=73)

Age	Frequency	Percentage
≤ 40	3	4.1
41- 50	7	9.6
51 - 60	17	23.3
61 -70	31	42.5
71 - 80	10	13.7
>80	5	6.9
Total	73	100.0

Table I. shows distribution of patients according to age. Most of the patients were above 50 years old. Maximum 31 (42.5%) patients were in age group of 61-70 years followed by 17 (23.3%), and 10 (13.7%), in age of group 51 – 60 years, and 71 – 80 years, respectively.

Table-II
Distribution of patients according to gender (n=73)

Gender	Frequency	Percentage
Male	46	63.0
Female	27	37.0
Total	73	100.0

Table II.shows distribution of patients according to gender. Male 46(63%) were predominant than female 27(37%). Male female ratio was 1.7:1.

Table-III
Distribution of patients according to educational status (n=73)

Education	Frequency	Percentage
Illiterate	9	12.3
Primary	22	30.1
Secondary	21	28.8
Higher secondary	14	19.2
Graduate and above	7	9.6
Total	73	100.0

Table III. shows distribution of patients according to educational status. Maximum 22 (30.1%) patients completed their primary education followed by 21 (28.8%) and 14 (19.2%) completed their secondary and higher secondary education respectively.

Table-IV

Distribution of patients according to occupation (n=73)

Occupation	Frequency	Percentage
Housewife	16	21.9
Service holder	13	17.8
Business	4	5.5
Others	40	54.8
Total	73	100.0

Table IV.shows distribution of patients according to their occupation. Sixteen (21.9%) patients were housewife, 13 (17.8%) were service holder, and 40 (54.8%) patients had miscellaneous occupation.

Table-V

Distribution of patients according to weakness of part of the body (hemiplegia) (n=73)

Weakness of part of the body (hemiplegia)	Frequency	Percentage
Yes	60	82.2
Right	12	16.40
Left	22	30.13
Bilateral	26	35.61
No	13	17.8
Total	73	100.0

Table V.shows distribution of patients according to weakness of part of the body (hemiplegia). Sixty (82.2%) patients had weakness of the body. Of them 26 (35.6%) patients had weakness in both side of the body, 22 (30.1%) had weakness in the left side of the body and 12 (16.4%) had weakness in the right side of the body.

Table-VI

Distribution of patients according to relevant past history (n=73)

Vascular risk factors	Frequency	Percentage
Stroke	73	100
Ischemic	64	87.7
Haemorrhagic	09	12.3
Hyperlipidaemia	67	91.8
HTN	54	74.0
DM	35	47.9
IHD	15	20.5
Recurrent Stroke	25	34.25

Table VI. shows relevant past history of the patients. Sixty four (87.7%) patients had ischemic stroke and 9 (12.3%) patients had hemorrhagic stroke. Hyperlipidemia was present in 67 (91.8%) patients; HTN, DM and IHD were present in 54 (74.0%), 35 (47.9%) and 15 (20.5%) patients respectively. History of recurrent stroke was present in 25(34.25%) cases.

Table VII

Distribution of patients according to smoking habit (n=73)

Smoking habit	Frequency	Percentage
Non-smoker	33	45.2
Ex-smoker	31	42.5
Smoker	9	12.3
Total	73	100.0

Table VII. shows distribution of patients according to smoking habit. Nine (12.3%) patients were smoker, 31 (42.5%) patients were ex-smoker and 33 (45.2%) patients were non-smoker.

Table-VIII

Distribution of patients according to family history of stroke and dementia (n=73)

Family history	Yes n (%)	No n (%)
Stroke	15(20.55%)	58 (79.45%)
Dementia	2 (2.74%)	71 (97.26%)

Table VIII. shows distribution of patients according to family history of stroke and dementia. Positive family history of stroke was present in only 15 (20.55%) cases and dementia in only 2(2.74%) cases.

Table IX

Distribution of patients according to hyperlipidemia in stroke patients with VaD (n-39) and without VaD (n=34)

	Hyperlipidaemia		Total
	Yes	No	
Stroke with VaD (n-39)	37(55.2%)	2(43.3%)	39 (53.4%)
Stroke without VaD (n-34)	30 (44.8%)	4 (66.7)	34 (46.6)
Total	67 (100.0)	6 (100.0)	73 (100.0)

Table IX: shows distribution of patients according to hyperlipidemia in stroke patients with VaD and without. Among 67 hyperlipidemia patients 37 (55.2%) patients had stroke with VaD and 30 (44.8%) patients had stroke without VaD.

Table-X

Distribution of vascular dementia patients according to gender (n-39)

Gender	Frequency	Percentage (%)
Male	23	59
Female	16	41

Table X. shows distribution of VaD patients according to gender, where 23(59%) cases were male, 16(41%) cases were female. Male: Female ratio was 1.4:1

Table XI

Distribution of fasting lipid profile of stroke patients (n=73) with VaD (n-39) and without VaD (n=34)

S. Lipid profile	Vascular dementia (VaD)		Total (n-73)Mean
	Yes (n-39)	No(n-34)	
S. Total cholesterol (mg/dL)	185.38 ± 44.07	178.70 ± 48.10	182.27 ± 45.79
S. Triglyceride (mg/dL)	149.82 ± 57.05	151.35 ± 76.12	150.53 ± 66.14
S.LDL-C (mg/dL)	133.58 ± 44.53	116.48 ± 42.39	125.75 ± 44.10
S.HDL-C (mg/dL)	31.07 ± 11.16	33.61 ± 11.82	32.26 ± 11.46

Table XII

Frequency and severity of vascular dementia (VaD) according to type of stroke.

Type of stroke	Vascular dementia (VaD)(n-39)			Total
	Mild (20-23)	Moderate (10-19)	Severe (<10)	
Ischaemic stroke	12 (100.0%)	15 (93.8%)	11 (100.0%)	38 (97.4%)
Haemorrhagic stroke	0 (0.0%)	1 (6.2%)	0 (0.0%)	1 (2.6%)
Total	12 (100.0)	16 (100.0)	11 (100.0)	39 (100.0)

Table XI. Shows fasting lipid profile of stroke patients (n-73) with VaD (n-39) and without VaD (34). Vascular dementia patients had higher s. total cholesterol, & s. LDL-C and lower s. triglyceride & s. HDL-C in comparison to that of non-vascular dementia patients.

Table XII. shows frequency and severity of vascular dementia (VaD) according to type of stroke. Among 39 VaD cases 38(97.4) had h/o ischemic stroke, of them 12 (100%) had mild, 15 (93.8) had moderate and 11(100%) had severe dementia. Among hemorrhage stroke patients only 1(2.6%) had moderate dementia.

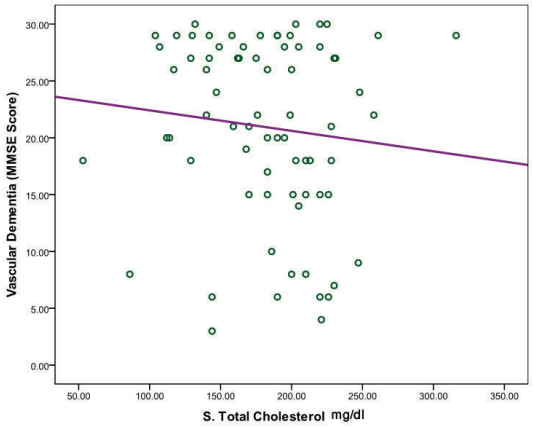

Fig.-1: *shows correlation of vascular dementia with S. Total cholesterol. (Pearson correlation, r=-0.104, p = 0.381). There was a non-significant negative correlation of MMSE score with S. total cholesterol.*

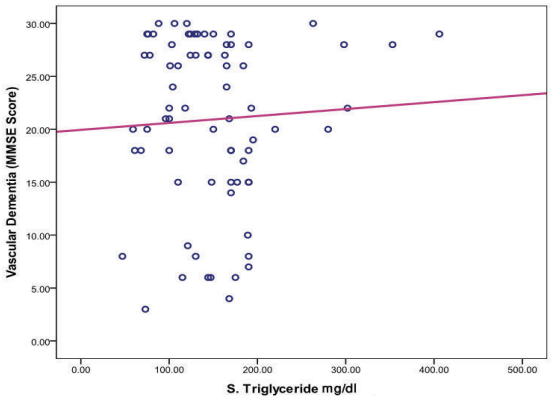

Fig.-2: *shows correlation of vascular dementia with S. Triglyceride. (Pearson correlation, r=0.055, p = 0.646). There was a non-significant positive correlation of MMSE score with S. Triglyceride.*

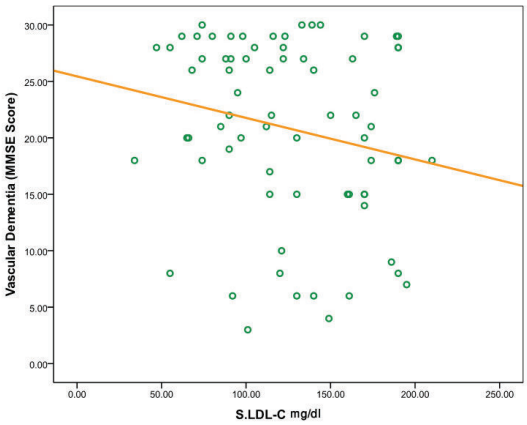

Fig.-3: *shows correlation of vascular dementia with S. LDL-C. (Pearson correlation r=-0.205, p = 0.084). There was a non-significant negative correlation of MMSE score with S. LDL-C.*

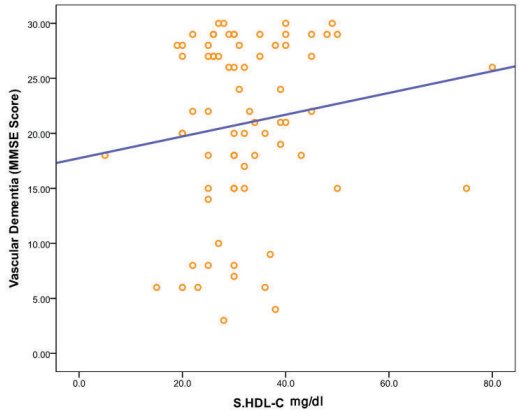

Fig.-4: *shows correlation of vascular dementia with S. HDL-C. (Pearson correlation, r=0.143, p = 0.227). There was a non-significant positive correlation of MMSE score with S. HDL-C.*

Discussion:

This cross-sectional descriptive study was carried out in the department of Neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka to find out whether there is any association of hyperlipidemia with VaD among stroke patients. In this study it was observed that (Table-I) the mean age of stroke patients was 67.5±42.5 years and most of the patients 63(86.3%) were above 50 years old. Maximum 31(42.5%) patients were in the age group of 61-70 years, followed by 17 (23.3%) in age group of 51–60 years which is consistent with some other

studies done in home and abroad[25,26]. Among these stroke patients (Table-II) males 46(63.0%) were predominant than females 27(37.0%). Male female ratio was 1.7:1. Stroke is a male predominant disease shown in different studies in Bangladesh[25,27,28]. They found M:F ratio 2.75:1, 2.53:1 and 3.44:1 respectively. Again VaD (n-39) was also found common 18(46.2%) among stroke patients in the age group of 61-70 years, followed by 10 (25.6%) among 51-60 years age group (Table-X) and also found common 18(46.6%) among male VaD (Table XI) patients than female 16(41%), ratio M:F= 1.4:1 in this study. A Swedish study also found that incidence of dementia was more in male and in older patients[29]. The subjects with VaD were significantly older than individuals without dementia or than controls seen by Reitz et al 2004 in his study[30]. Educational status (Table-III) and occupation (Table-IV) of the patients were recorded. Only 7 (9.6%) patients were graduate and 9 (12.3%) were illiterate. Maximum (30.1%) patients completed their primary education followed by 21 (28.8%) and 14 (19.2%) completed their secondary and higher secondary education respectively. The subjects with VaD were significantly less educated than individuals without dementia or than controls [1,30-33]. Nagndu et at 2007 also found most of the dementia patients were either illiterate or read up to primary school level[34]. Sixteen (21.9%) patients were housewife, 13 (17.8%) were service holder, and 40 (54.8%) patients had miscellaneous occupation. In this study out of 73 patients (Table-VII), 40 (54.8%) were either smoker or ex-smoker and 33 (45.2%) were non-smoker. In another study done in this country showed 39.5% and 44% stroke patients were smoker [35] respectively. Among 73 cases 15(20.55%) patients had family history of stroke and 2(2.74%) patients had family history of dementia (Table-VIII) which is consistent with the study of Sarker; 2015, where 20% cases had positive family history of stroke and 2.5% had family of dementia, reflecting that stroke runs more in families than dementia[25]. Relevant past history of the patients was recorded (Table-VI). Sixty four (87.7%) patients had ischemic stroke and 9 (12.3%) patients had hemorrhagic stroke. Ischemic stroke patients were more likely to develop dementia [35,36]. Hyperlipidemia was present in 67 (91.8%) patients, HTN in 54 (74.0%), DM in 35 (47.9%) and IHD in 15 (20.5%) patients respectively. Sarker; 2015. found dyslipidaemia in 53.75% of his stroke patients and HTN in 60%, DM in 27.5%, IHD in 11.3% and recurrent stroke in 20% cases respectively[25]. So, this study is consistent with the study of Sarker, 2015[25]. Reitz et al; 2004 showed 62% had a history of Hypertension, 23.3% had a history of heart disease, and 19.9% had a history of DM[30]. Dimopoulos et al; 2007 found hypertension and DM in 50.0% dementia patients respectively[33]. It is well established that blood pressure can increase the risk of stroke. Many studies including Framingham, the Kungsholmen and the Honolulu-Asia aging studies have implicated impaired cognitive function to hypertension in geriatric patients [37,38]. In this present study 54(74%) patients were hypertensive which correlated with previous studies. Again, the previous two studies showed in their series of patients having HTN in 58.6% and 65% cases respectively [27,39].

DM or hyperglycemia have been associated with worse cognitive performance after stroke, but most assessments of these markers are confounded by the fact that these might both occur in response to stroke in the acute phase, or might be present in the setting of a large stroke. Additionally data on hyperglycemia were conflicting[40]. This study shows 35 (47.9%) patients had diabetes mellitus which is consistent with similar studies done in our country which showed diabetes as a risk factor for stroke in 32.1% and 21% cases respectively [27,39]. The association between VaD and diabetes was also described by other researchers [40,41]. Among 67 hyperlipidemia patients (Table-V) 37(55.2%) patients had stroke with VaD and 30(44.8%) patients had stroke without VaD in this study. In this study serum fasting lipid profile among VaD patients showed that total cholesterol, LDL-C, HDL-C and triglycerides were 185.38±44.07, 133.58±44.53, 31.07±11.06 and 149.82±57.05mg/dl respectively. In another two studies done by sarker; 2015, and Das; 2013, where these were 202.3±25.11, 117.28±18.88, 37.06±6.45, 208.88±15.41 (mg/dl) and 204.36±39.57, 117.07±42.44, 39.75±6.5,

237.67±6.1(mg/dl) respectively. So, the result of this current study coincides with the study of sarker, 2015 and Das, 2013[25,42]. In this study vascular dementia patients had higher s. total cholesterol (185.38 ± 44.07 vs 178.70 ± 48.10mg/dl), & s. LDL-C (133.58 ± 44.53 vs 116.48 ± 42.39mg/dl) and lower s. triglycerides (149.82 ± 57.05 vs 151.35 ± 76.12mg/dl) & s. HDL-C (31.07 ± 11.16 vs 33.61 ± 11.82mg/dl) in comparison to than that of non-vascular dementia patients. Reitz et al; 2004. found mean level of total cholesterol was 198.8 mg/dL, HDL-C 47.4 mg/dL, triglycerides 155.9 mg/dL and LDL-C 120.1 mg/dL among his patients[30]. Result of this study regarding HDL-C is consistent with the Reitz et al; 2004. study[30]. S. HDL-C level was significantly lower in VaD patients in comparison to normal subjects found by Dimopoulos et al; 2007[33]. Zuliani et al; 2001. found lower levels of HDL-C in subjects with VaD compared with controls[43]. Kuriyama et al; 1994. reported lower HDL-C levels in patients with VaD compared with controls[17]. Van Exel et al; 2002. found a significant association between decreased HDL-C levels and cognitive impairment[44]. Reitz et al; 2004. found an association between higher LDL-C levels and a higher risk of VaD[30]. Frequency and severity of vascular dementia (*VaD*) according to type of stroke was recorded (Table-XII) where 38(97.4%) patients had past history of ischemic stroke out of 39 VaD patients. Of them among 12 mild VaD patients all (100%) had ischaemic stroke, among 16 moderate VaD patients 15 (93.8%) patients had ischaemic stroke and rest 1 (6.3%) patient had hemorrhagic stroke, among 11 severe VaD patients all (100%)of them had ischemic stroke. Almost similar result was also seen by Sarker; 2015, in his study where 80% VaD patients had past history of ischemic stroke[25]. Desmond et at; 2000. also got similar result in his study [45].

In this study (Fig 1-4) there was a non-significant negative correlation of MMSE score with S. total cholesterol (Pearson correlation r=-0.104, p = 0.381), a non-significant negative correlation of MMSE score with S. LDL-C (Pearson Correlation r=0.205, P=0.84), a non-significant positive correlation of MMSE score with S. Triglyceride (Pearson correlation r=0.055, p = 0.646), and a non-significant positive correlation of MMSE score with S. HDL-C(Pearson correlation r=0.143, p = 0.227). S. HDL-C concentrations presented a positive linear correlation with the score on the MMSE rating scale seen by Dimopoulos et al, 2007 which is consistent with this study[33]. Lower S. HDL-C levels were associated with a slightly higher risk of VaD also seen by Reitz et al; 2004 in both either cross-sectional & prospective analysis[30]. They also found an association between higher S. LDL-C levels and a higher risk of VaD which is consistent with this study. Trkanjee et al; 2009 done a pilot study on stroke patients and evaluated the levels of cholesterol (Total, HDL-C and LDL-C) in patients with vascular dementia on 23 patients where 11 patients had cholesterol values within normal range and 12 patients had elevated levels of Total cholesterol – 5.78±1.06, and LDL-C-3.72±0.85 (mmool/L) and lower level of HDL-C-1.44±0.57mmol/L, however the difference was not statistically significant[46]. Again Zuliani et al; 2001 estimated S. lipoprotein profile in 60 older patients (age>60 years) in a cross-sectional study where he found, low HDL-C level only among VaD patients, values of other S. Lipoprotein were within normal range[43]. Moroney et al; 1999 conducted a prospective longitudinal community-based study over a 7 year period (1991-1998) on 1111 non-demented participants (mean age- 75±5.9 years) and were followed up for an average of 2.1 years (range 1-7.8 years)[47]. Of them 61 (21.3%) developed dementia following stroke. Levels of S. LDL-C were significantly associated with an increased risk of dementia with stroke but not other components of lipid in his study. In another study done by Solomon et al, 2009 in Department of Neurology, University of Kuopio, Kuopio, Finland; where they investigated Mild-life serum cholesterol in relation to Alzheimer's disease and vascular Dementia three decades later[48]. They selected 9,844 multiethnic participants of both sexes during 1964-1973 at ages 40-45 years. The researcher evaluated them for AD and VaD in 1994 and 2007 and found midlife serum total cholesterol was associated with an increased risk of both AD and VaD. Even moderately elevated cholesterol increased dementia risk. Another study done by

Cankurtaran et al; 2004. in Hacettepe University Division of Geriatric Medicine, Ankara, Turkey. They examined the relationship between dyslipidaemia and dementia on 1251 admitted patients[49]. The fasting Lipoprotein levels were measured in all patients and analyzed the data by using X^2 and one-way analysis of variance methods. But no relation was found with VaD patients in their study. In another done by Meilke et al, 2005 on association between plasma total cholesterol and triglyceride level and dementia among elderly patients aged>70 years[50]. They found high cholesterol in late life was associated with decreased dementia risk, which is not consistent with some previous studies suggesting high cholesterol in midlife is a risk factor for later dementia.

So, considering the results of studies done in home and abroad where some studies showed hyperlipidemia is associated with VaD [25,30,33,43,46-48] but association is weak which is consistent with our study. But some other studies shows no association [49,50].

Conclusion

This cross-sectional descriptive study done in a tertiary level hospital over a small sample (only 73 patients) demonstrates that VaD is common (53.4%) among stroke patients, where ischemic stroke occupies almost the whole bulk (97.4%). Hyperlipidemia is a modifiable risk factor for ischemic stroke and in this study it was also found that there is a non-significant positive association of VaD with high total cholesterol, high LDL-C, and low HDL-C and not with S. triglyceride. We can conclude that hyperlipidemia has weaker association with vascular dementia.

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Association between Herpes Simplex Type 1 Virus Infection and Bell's Palsy

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Abstract:

Background: *Idiopathic facial paralysis is one of the commonest conditions in neurological practice. Objective: The purpose of this study is to see whether Bell's palsy is associated with serological marker of Herpes Simplex virus type 1, and to study the clinical signs and symptoms manifested by Bell's palsy. Methodology: This retrospective observational study was carried out in neurology OPD of ShSMCH, Dhaka from June, 2014 to May, 2016. All the patients who came to the OPD were selected as study population. All relevant data, those who fulfill the inclusion criteria were recorded in pre-designed data collection sheet.* ***Result:*** *A total number of 60 were recruited in this study. 30 were case group and 30 were control group. In our study, more than one quarter of cases (26.7%) was found between 26-30 years, while lowest age incidence was 16-20 years (6.7%). More than 37% of cases had their attack of Bell's palsy in monsoon season, only 3% in autumn. 52.3% had pain in or around the ear. Taste abnormalities were found in 23.3%. Conclusion: From this study, it can be concluded that, Herpes simplex type 1 may be an important causative agent for Bell's palsy. But a large scale study is needed for establishment of Herpes Simplex type 1 as an important infective agent for causation of Bell's palsy.*

Keywords: *Bell's palsy, Herpes simplex type 1.*

Introduction:

Idiopathic facial paralysis also called Bell's Palsy is one of the commonest conditions seen in neurologic practice, accounting for approximately 50 percent of cases of peripheral facial paralysis[1]. Bell's Palsy causes considerable functional, psychosocial and aesthetic disturbance to patients. Histological and clinical evidence suggests that the site of lesion within the confluence of the facial canal, particularly at its medial end[2]. However, most recent studies have shown that herpes simplex virus 1 may be the most likely candidate virus and polymerase chain reaction of endoneural fluid revealed Herpes simplex virus 1 genome in more than three quarter of bell's palsy cases, whereas Varicella Zoster virus or Epstein Barr virus have not been found therein[3,4,5,6]. Reactivation of herpes simplex virus 1 probably results in the initial facial weakness and virus will become undetectable with recovery[4]. Serum antibody titre to herpes simplex virus is a reliable diagnostic tool for Bell's Palsy[5]. Salivary polymerase chain reaction for herpes simplex virus type 1 is more likely to confirm virus during the replicating phase, but these tests remain research tools. Serological test for Bell's Palsy (IgG, IgM) are essential for diagnosis of Bell's Palsy, where PCR testing is not possible. In our study, we have done serum anti- HSV1 IgM for bell's Palsy cases and control groups. The laboratory diagnostic value ISR (Immune status ratio) e"1.10 were taken as positive; ISR 0.91-1.09 were considered negative results. Histological studies of facial nerve during acute stage of Bell's palsy, either at autopsy or during surgery, have shown signs of oedema, perivascular perineurial lymphocytic and macrophage infiltration of the nerve, an increase in axon: myelin surface ratio (thinning of myelin) and a decrease in the total fiber count[6]. Bell's palsy

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is equally frequent in men and women (ratio 48:52). This disease occurs on either side of the face and approximately 5% of the patients will have a recurrent palsy affecting the same or opposite side. Pregnancy, diabetes mellitus and arterial hypertension have all been associated with an increased incidence of Bell's palsy[7-9].

Materials and methods:

This is a retrospective observational study. This study was carried out in Neurology outpatient department (NOPD), Shaheed Suhrawardy Medical College Hospital (ShSMCH), Dhaka from June 2014 to May 2016.The study subjects were divided into cases and controls.

Selection Criteria:

Inclusion criteria for cases:

1. Flaccid paresis of all the muscles of face on the involved side
2. Affected side is smooth and brow droops, but palpebral fissure is widened.
3. Angle of mouth is depressed
4. Cheeks balloons on expiration
5. Dysarthria, drooling of saliva
6. Food collected between the gum and the cheeks
7. Lid remains open (lagophthalmos).
8. Lower lid is everted with excessive tearing (epiphora).
9. Bell's phenomenon –On attempted to closure of eye globe turns up and out.
10. Perversion of taste and hyperacusis
11. Various facial reflexes are lost.
12. Those cases of Bell's palsy who came within two weeks of onset of attack.

Exclusion criteria for cases:

1. History of trauma
2. Gradual evolution over several weeks
3. Persistence of severe symptoms for longer than 3 months
4. Vesicular eruption on external ear, pinna of ear, base of the tongue or soft palate
5. Slowly progressive facial paralysis
6. Pain, hearing loss in association with facial paralysis
7. Involvement of lower cranial nerves in association with CN VII lesion
8. Recurrent facial nerve lesion
9. Any form of treatment received for the disease before attending at neurology OPD, ShSMCH

Selection Criteria for controls:

All the patients were medically stable, mentally sound without any features of other systemic diseases like diabetes, leukemia, sarcoidosis, Lyme diseases and neoplasm. Other than facial nerve all the patients had no evidence of other neurological signs.

In a non-directed fashion, each of the patients was assessed by a standard questionnaire. All the patients were asked about any treatment they received before coming to us like any homeopathic or ayurvedic medication or any history of toxic exposure. After getting the negative answers, they were included in the study group.

Data collection

All relevant data were recorded in a predesigned data collection sheet which included history taking with particular aspects relevant to this study, general examination, and neurological examination. Viral antibody was detected by ELISA method.Three cc of blood was collected into plain test tube, avoiding haemolysis, mixed by inverting sample tube several times and left to clot for one hour at room temperature (18° – 28° C) and protected from direct light. Serum samples were stored at -17°C or lower if not assayed on the same day. Blood was collected between the 7-15 days of illness. The patient's ISR (Immune Status ratio) values are interpreted as follows: d"0.90 is negative: i.e. No significant level of detectable IgM antibody to HSV. 0.91-1.09 is equivocal: i.e. samples should be retested. e"1.10 is positive: i.e. significant level of detectable IgM antibody to HSV-1, that's Indicative of current or recent infection.

Data analysis

Data were analyzed using SPSS version 11.5 (Statistical Package for Social Sciences). The test

statistics used analyze the data were descriptive statistics, Chi-square, Fisher's Exact Probability Test and Student's t-test.

Results and observations:

Table-I

Demographic profile of study population

Age of the patient (years)	Group		P-values
	Case (n=30)	Control (n=30)	
≤15	6(20.0)*	1(3.3)	0.290
16-20	2(6.7)	4(13.3)	
21-25	7(23.3)	4(13.3)	
26-30	8(26.7)	6(20.0)	
>30	7(23.3)	15(50.0)	
Mean ± SEM	23.83 ± 1.37	25.90 ± 1.37	

*Figures in the parentheses indicate corresponding percentage %

**Student's t-test was done to analyze the data and the level of significance was 0.05.

Table-II

Clinical presentation of study subjects

Symptoms	Number of occurrence / Percentage (n=30)
Pain in and around the ear	16(53.3%)
Taste abnormalities	07(23.3%)
Facial tingling	63%
Neck pain	17(56.7%)
Hearing problem	13%
Blurred vision	12(40%)
Involved side	Left = 53% , Right = 47%

Table-III

Distribution of cases by season of occurrence (n=30)

Seasons	Percentage
Winter	10%
Spring	10%
Summer	33%
Monsoon	37%
Autumn	3%
Post-autumn	7%

Table-IV

Comparison of paraclinical parameters between case and control

Paraclinical Parameters#	Group		P-values*
	Group A (n=30)	Group B (n=30)	
RBS (mg/dl)	110.4 ±1.62	117.5± 2.21	0.012
WBC (per cu mm of blood)	8600 ±187	5800 ±425	<0.001
Lymphocytes (%)	41 ±1	30 ±1	<0.001
Neutrophil (%)	52 ±1	65 ±1	<0.001

#Data were analyzed using students' t-test and values were expressed as Mean ± SEM

*level of significance was 0.05 and p<0.05 was considered significant

Table-V

Association between serum anti-HSV1 IgM in Bell's palsy:

Serum anti-HSV1 IgM (ISR)#	Group		P-value*
	Case (n=30)	Control (n=30)	
+ve (≥1.10)	01(3.3)	00	<0.001
-ve (≤0.90)	29(96.7)	30(100)	
Equivocal (0.91 – 1.09)	00	00	
Mean anti-HSV1 IgM	0.46 ±0.02	0.12 ±0.02	

ISR means Immune Status Ratio: Data pertaining was analyzed using Student's t-test and values were expressed as Mean SEM

*level of significance was 0.05 and p<0.05 was considered significant

Discussion:

This was a retrospective observational study, which included 60 subjects. Among the study population 30 were in case group with Bell's palsy and another 30 were in control group without Bell's palsy. The study was carried out to see whether Anti-HSV type 1 IgM has any association with Bell's palsy or not. ELISA method was used to detect the presence of Anti-HSV type 1 Antibody (IgM) in blood samples of both groups. Bell's palsy can occur in any age group. In our study more than one-quarter of case (26.7%) was found between 26-30 years, while in lowest age incidence was found between 16-20 years of age (6.7%)[10-13]. In our study females are affected a bit higher (56.5%) in compared to male

group (43.3%). So our study showed that females were affected more than males. It does not coincide with the study group that showed no difference in incidence between the sexes[10,13,14]. In respect to seasonal occurrence more than 37% of cases at their attack of Bell's palsy in the monsoon season, only 3% in autumn[15]. Among the clinical features 53.3% had pain in or around the ear. Taste abnormalities were found in only 23.3% cases[16]. Finally in our study the association between serum Anti-HSV1 IgM level and Bell's palsy, in 1 (3.3%) case was found to be positive for serum Anti-HSV1 IgM of cases were more than 3 times higher (0.46±0.02) than that of controls (0.12±0.02) (P<0.01). Though this result is statistically significant but immunologically only one of the cases the titre level was found to be positive (ISR e"1.10) and rest 29 cases and 30 control patients had immunologically insignificant titre i.e. titre result is negative. This statistical significance is due to inclusion of negative results of cases that has no immunological significance. So this statistical significance is not so important in this study.

Summary:
Serum Anti-HSV 1 Antibody (IgM) was detected by ELISA method in both control and case groups. Immunologically significant titre was found in only one case (ISRe"1.10) but rest of the 29 cases had immunologically insignificant titre (results were negative). The mean Anti HSV-1 IgM of cases was about three times higher than that of controls (P<0.001). So this result is statistically significant as because negative values were also considered same as positive values, but actually negative values had not such importance as positive values.

Conclusion:
From this study it can be concluded that herpes simplex type 1 may be an important causative agent for Bell's palsy. But a large scale study is needed for establishment of herpes simplex type 1 as an important infective agent for causation of Bell's palsy.

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Clinical Profile of Stroke Patients Attended in a Tertiary Care Hospital- Study of 219 cases

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Abstract:

Background: Stroke is serious pathology with a immense impact on the functional and vital prognosis. It is the leading cause of death worldwide. The objective of the study was to observe clinical profile of stroke patients and important risk factors. Methods: It was a cross-sectional descriptive study conducted in the department of Neurology, Bangabandhu Sheikh Mujib Medical Universiy(BSMMU), Shahbag, Dhaka from August 2014 to November 2015. All patients above 18 years of age and both sexes attending the above mentioned department meeting all inclusion and exclusion criterias and confirmed CT/MRI scan of Brain were included in this study. Results: A total of 219 patients were studied. Maximum 93(42.5%) patients were in age group of 61-70 years followed by 51(23.3%) and 30(13.7%), in the age group of 51-60 years and 71-80 years respectively. Male 138(63%) were predominant than female 81(63%). 78(35.61%) patients had weakness in both sides of the body, 66(30.1%) had weakness in the left side and 36(16.4%) had weakness in the right side of the body. 190 (87.7) patients had ischemic stroke and 29(12.3%) had hemorrhagic stroke. Among risk factors dyslipidemia was in 185(84.5%) patients, hypertension, smoking habits, diabetes mellitus and ischemic heart disease were present in 165(75.3%), 120(54.8%), 105(47.9%) and 42 (19.2%) patients respectively. H/O recurrent stroke was present in 55(25%) cases. Conclusion: Stroke cases were male predominant where dyslipidaemia was the most common risk factor, most common type of stroke was ischemic, most common presentation was hemiplegia/monoplegia and commonest age of presentation was seventh decade.

Introduction:

Stroke is a devastating and disabling cerebrovascular disease with significant amount of residual neurological deficit leading to great economic loss. It has been defined as a rapidly developing signs of focal (or global) disturbance of cerebral function with symptoms lasting for e"24hours or leading to death with no apparent cause other than vascular origin[1]. It is a collection of clinical syndromes resulting from cerebral ischemia or hemorrhage. In the west, it is the 3rd most common cause of mortality and commonest cause of morbidity among the elderly persons[2]. Some of the recent studies have found that the stroke prevalence is of considerable extent in this subcontinent[3]. A recent study identified that 7% of medical and 45% of neurological admissions were due to stroke with a fatality rate of 9% at hospital discharge and 20% at 28 days[4]. Dyslipidemia, hypertension, smoking and diabetes mellitus are the common causes of stroke among the elderly,[5] and smoking, dyslipidemia, increased BMI, diabetes mellitus and hypertension are significantly associated with strokes among young people[6]. Ischemic strokes account for 50-80% of all strokes worldwide[7]. Heamorrhagic strokes are due to sub-arachonoid hemorrhage or intracerebral hemorrhage. They account for 1-7% and 7-27% respectively of all strokes worldwide[8]. Recently Bangladesh Baureu of statistics has estimated that

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the number of strokes has increased significantly and it occupies the number one position (16.4%) of mortality among elderly persons, ischemic heart disease being the 2nd (12.6%) and respiratory tract infection being the 3rd (11.4%).[8] The global burden of disease study also projects the similar findings worldwide by the year 2020. [10] Hence this study was undertaken in our setup to study various aspects of stroke which will help young physicians to deal with this deadly and disabling disease.

Meterials and methods:

It was a cross-sectional descriptive study conducted in stroke clinic, In-patients and out-patients department of Department of Neurology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka from August, 2014 to November, 2015. All patients above 18 years of age and both sexes attending the above mentioned department meeting all inclusion and exclusion criteria were included in this study. Total 219 consecutive patients were selected on the basis of history, clinical examination and findings of CT or MRI scan of Brain. The following information's were collected from each patient- age, sex, occupation, educational status, past history of stroke, hypertension, diabetes mellitus, coronary artery disease, family history of stroke, current or previous history of smoking , alcohol consumption, tobacco chewing, dietary history and others. Examination findings including hemiplegia/monoplegia, dysphasia/dysarthria, pulse, BP, carotid bruit, cardiac murmur etc were noted. Fasting serum lipid profile, blood sugar, S. Creatinine, S. electrolytes, ECG, eco-cardiogram, X-ray chest and relevant other investigations were done. Data analysis was done by using SPSS (statistical package for social science) soft ware version 18. Results were expressed in frequencies and percentages.

Selection Criteria:

Inclusion criteria: All patients clinically diagnosed as first or recurrent stroke (ischemic or hemorrhagic) confirmed by CT/MRI scan of Brain, age 18years or above and of both sexes.

Exclusion criteria: Patients less than 18years of age, advanced medical conditions (acute myocardial infarction, left ventricular failure, end stage renal disease, malignancy etc), metabolic and toxic states resembling stroke and patients unwilling to participate in the study.

Results and observations:

Table-I

Distribution of patients according to age (n-219).

Age	Frequency	Percentage
d"40	9	4.1
41-50	21	9.6
51-60	51	23.3
61-70	93	42.5
71-80	30	13.7
>80	15	6.3
Total	219	100.00

Table-: I. *Shows most of the Patients were above 50 years of age. Maximum 93(42.5%) patients were in the age group of 61-70 years, followed by 51(23.3%) and 30 (13.7%) in the age group of 51-60years and 71-80years respectively.*

Table-II

Distribution of Patients according to gender (n-219).

Gender	Frequency	Percentage
Male	138	63.0
Female	81	37.0
Total	219	100.0

Table-II: *Shows distribution of patients according to gender. Male 138(63%) were predominant than female 81(37%). Male female ration was 1.7:1*

Table-III

Distribution of patients according to educational status (n-219)

Education	Frequency	Percentage
Illiterate	27	12.3
Primary	66	30.1
Secondary	63	28.8
Higher Secondary	42	19.2
Graduate & above	21	9.6
Total	219	100.0

Table-III *Shows distribution of patients according to educational status. Maximum 66(30.1%) patients completed their primary education followed by 63(28.8%) and 42(19.2%) patients completed their secondary and higher secondary education respectively*.

Table-IV

Distribution of patients according to occupation (n-219)

Occupation	Frequency	Percentage
Housewife	48	21.9
Service holder	39	17.8
Business	12	5.5
Others	120	54.8
Total	219	100.0

Table-: IV. *Shows distribution of patients according to their occupation. Forty eight (21.9) patients were house-wife, 39(17.8%) were service holder and 120(54.8%) patients had miscellaneous occupation.*

Table-V

Distribution of patients according to weakness of part of the body (hemiplegia/ monoplagia)(n-219).

Hemiplegia/ monoplagia	*Frequency*	*Percentage*
Right	36	16.40
Left	66	30.13
Bilateral	78	35.61
No	39	17.8
Total	219	100.00

Table-V. *Shows distribution of patients according to hemiplegia/monoplegia. Among them 78(35.61) patients had bilateral hemiplegia, 66(30.13%) had left sided and 36(16.40%) patients had right sided hemiplegia.*

Table-VI

Distribution of patients according to type of stroke (n-219)

Stroke type	Frequency	Percentage
Ischemic	190	87.7
Hemorrhagic	29	12.3
Total	219	100.0

Table-: VI. *Shows distribution of patients according to type of stroke. 190(87.7%) patients had ischemic and 29(12.3%) patients had hemorrhagic stroke.*

Table-VII

Distribution of patients according to risk factors(n-219)

Risk factors	Frequency	Percentage
Dyslipidemia	185	84.5
Hypertension	165	75.3
Smoking habit	120	54.8
Diabetes mellitus	105	47.95
P/H/O stroke	55	25.1
Ischemic heart disease	42	19.2
Alcohol	12	5.5
Rheumatic Heart disease	03	1.4

Table-: VII. *Shows distribution patients according to risk factors. Here dyslipidemia (84.5%), hypertension (75.3%), smoking habit (54.8%) and diabetes mellitus (47.95%) were the common risk factors.*

Table-VIII

Distribution of patients according to clinical presentation(n-219)

Clinical Features	Frequency	Percentage
Altered sensorium	31	14.15
Instability of gait	15	6.85
Convulsions	18	8.22
Speech involvement	62	28.31
Headache	05	2.28
Vomiting	25	11.41
Hemiplegia/monoplegia	180	82.19

Table-VIII *Shows distribution of patients according to clinical presentation. Hemiplegia/monoplagia 180 (82.19%), speech involvement 62(28.31%) and altered sensorium 31(14.15%) were the common presentations.*

Table-IX

Gender wise distribution of different types of stroke (n-219)

Gender	Ischemic	Hemorrhagic	Total
Female	70(32%)	11(5%)	81(27.00)
Male	120(54.8%)	18(8.2%)	138(63.0)
Total	190 (86.77%)	29(13.3)	219(100)

Table-: IX. *Shows gender wise distribution of patients according to different types of stroke. Here among 190(86.77%) ischemic stroke patients 120(54.8%) were male and 70(32%) were female. And among 29(13.3%) hemorrhagic stroke 29(13.3%) patients 18(8.2%) were male and 11(5%) were female. So, in both types of stroke male is predominant than female.*

Discussion:

In this study it was observed that mean age of stroke patients was 67.5±42.5 years which correlates with study done by Chirayu et al(mean age 64years)[9], Maskay et al (mean age 63 years)[11] and Awad et al(mean age 63.66years)[12]. The common age group was in between 61-70years (42.5%) which correlated with the studies done by Upoha et al[13], and Maskey et al[11]. Young stroke (age<50years) comprised of 13.7% of all patients which closely correlated with study done by Sallam et al (13.6%)[14] and Gauri et al (19%)[15]. Among stroke patients males 138(63%) were predominent than females 81(37%). Male female ration was 1.7:1. Stroke is male predominant disease shown in different studies in Bangladesh[16-18]. They found M:F ratio 2.75:1, 2.53:1 and 3.44:1 respectively. This study also shows both ischemic & hemorrhagic strokes are male predominant [Ischemic-male 120(86.77%), female 70(32%); hemorrhagic-male 18(8.2%) and female 11(5%)], which also correlated with another study done abroad[9]. In this study out of 219 patients, 120(54.8%) were either current smoker or ex-smoker and 99(45.2%) were non-smoker. In another two studies done in this country showed 39.5% and 44% stroke patients were smoker respectively[16,19]. Regarding hemiplegia/ monoplegia 78(35.61%) patients had weakness in both sides of the body, 66(30.13%) patients had weakness on his left side and 36(16.4%) had weakness in right side of the body. This observation closely correlates with the study done in India by Chitrambalam et al (hemipegia <45years 93.3%, in >45years 89.2)[20].

In this study common risk factors correlated with the study done both in home and abroad. Dyslipidaemia was present in 185(84.5%) patients, HTN in 165(75.3%), smoking habit in 120(54.8%), DM in 105(47.95%) and IHD in 42(19.2%) patients respectively. H/O recurrent stroke was found in 52(25.1.25%) cases. This observation correlates with the study of Sarker, 2015(found dyslipidemia in 53.75%, HTN in 60%, DM in 27.5%, IHD in 11.3% and recurrent stroke in 20% cases)[18] and HTN in 58.6%, DM in 32.1%, in khan;2000[16] and HTN series in 65% and DM in 21% ullah et al 1993[19] series. This study shows 190(87.79%) patients had Ischemic stroke and 29(12.3%) had hemorrhagic stroke. This data correlated with studies done in home and abroad. In studies done by Aiyar et al[21] shows infraction in 70% and hemorrhage in 26% cases. Eapen et al[5] showed infraction in 68% and hemorrhage in 32% cases. Regarding clinical presentation 180(82.19%) patients had hemiplegia, 62(28.3%) patients had speech involvement and 31(14.15%) cases had altered sensorium which also correlates with the studies in home & abroad [9, 16, 19].

Conclusion:

In this study it was found that ischemic stroke (87.7%) was more common than hemorrhagic stroke (12.3%). Most of the patients (42.5%) were in between 61-70 years of age. Dyslipidemia was most frequent among risk factors (84.5%), followed by HTN(75.3%), smoking habit (54.8%), DM (47.9%). H/O recurrent stroke (25%), IHD (19.2%). Most common clinical presentation was hemiplegia/ monoplegia followed by speech involvement.

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Effect of Mannitol on Serum Electrolytes in Stroke Patients

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Abstract:

Mannitol, an osmotic agent and a free radical scavenger with neuroprotective properties, have been reported in many studies to decrease cerebral oedema , infarct size and neurological deficit in patients with stroke. The present study was carried out in the Department of Pharmacology and Therapeutics in collaboration with the Departments of Medicine and Neurology of Sylhet M.A.G Osmani Medical College and Hospital to evaluate the effect of mannitol on serum electrolytes in stroke patients. A total number of Forty five (45) acute stroke patients were randomly allocated in two groups- 23 patients received mannitol and 22 patients did not receive mannitol. On Day 1 after measuring serum electrolyte levels of both groups, mannitol receiving group was given infusion mannitol 1 gm/kg IV bolus followed by 0.5 gm/kg IV 6 hourly till 3rd day and then again on Day 3 serum electrolyte levels of both groups were measured. Predisposing risk factors, eg- smoking, hypertension, dyslipidaemia were also analyzed. RBS (Random Blood Sugar) and serum creatinine were estimated before treatment initiation with aim to assess hyperglycaemia and renal impairment respectively. Statistical analysis was done by SPSS program using unpaired 't' test between two groups and between Day 1 and Day 3 by paired 't' test. The result showed that serum sodium and potassium at Day 1 and Day 3 were almost similar between mannitol receiving group and mannitol non-receiving group (P>0.05 for each component). After infusion of mannitol till third day, no electrolyte imbalance was noted. The study depicts that mannitol can be safely given to stroke patients as there were no change in electrolyte balance till third day.

Key words: *Stroke, Mannitol therapy, Serum electrolyte.*

Introduction:

Stroke is a focal neurological deficit of acute onset whose symptoms may last for more than 24 hours[1] and which may lead either to recovery or physical disability or impairment of bodily functions or may culminate in death of the person[2]. It is most frequently caused by blockage of cerebral artery by embolus or atherosclerotic hemorrhagic plaque leading to insufficient oxygen supply to parts of the brain dependent on the patency of the artery[3] (figure 1) or when a blood vessel in the brain bursts spilling blood into spaces surrounding brain cells (figure 2). Stroke is the third leading cause of death and probably the most important cause of long term disability in most western nations[4], its incidence is progressing in Bangladesh as well[5]. Cerebral oedema is a major cause of early death and long term disability after stroke[6]. Cerebral injury have shown that there is a dense central core, surrounded by a less dense zone of penumbra. Neuronal death occurs in this central focus. On the other hand, cells in the zone of penumbra remain viable for upto several hours after stroke and may be salvaged by reperfusion or by neuroprotective agents to prevent further damage[7].

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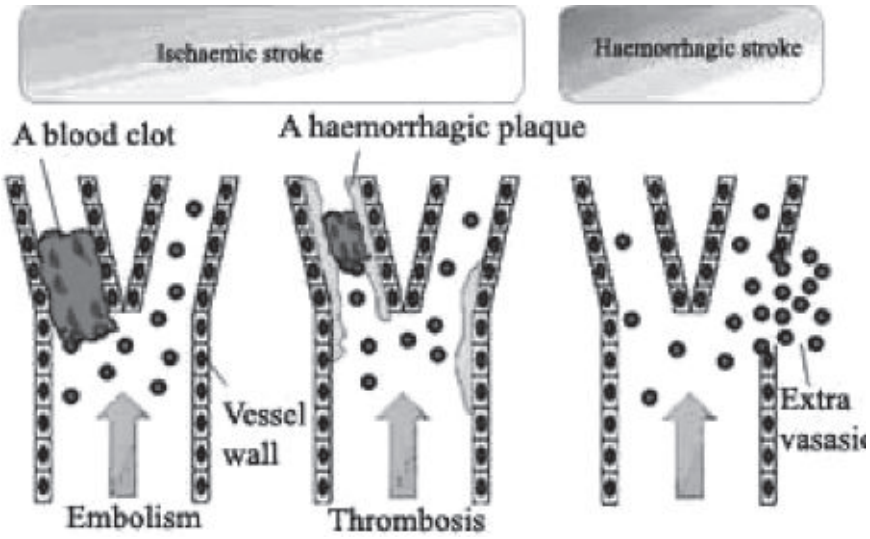

Fig.-1: *Mechanisms of ischaemic and haemorrhagic strokes*

Nerve cell injury most likely occurs from production of nitric oxide, changes in Na/K gradients, release of glutamate and subsequent formation of free radicals [7]. CT scan appearance of ischaemic stroke is hypodensity in brain (figure 2) and that of haemorrhagic stroke is hyperdensity in brain (figure 3).

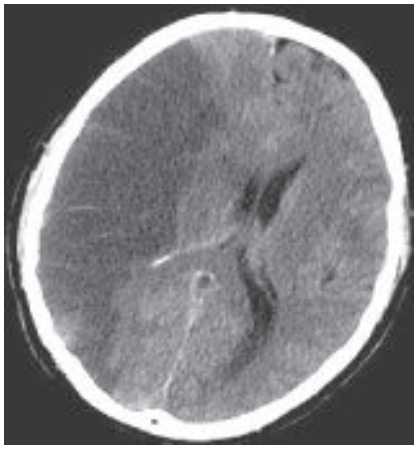

Fig.-2: *CT scan slice of the brain showing a right hemispheric stroke (left side of image)*

Classes of drugs under investigation for the treatment of acute stroke include those that promote early cerebral perfusion, neuroprotective agents and drugs to reduce cerebral oedema. Osmotic diuretics are among the agents that are widely used in the treatment of cerebral oedema[8]. Mannitol, an osmotic diuretic, decreases ICP (intracranial pressure), improves cerebral perfusion, acts as a

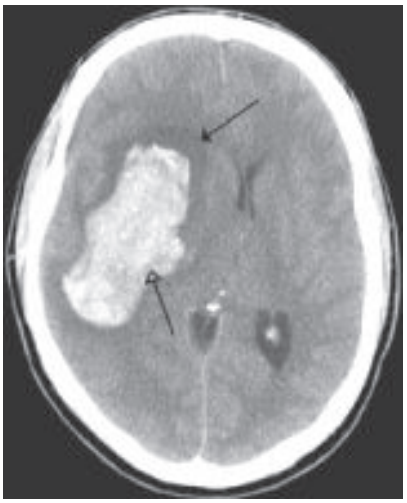

Fig.-3: *An intraparenchymal bleed (bottom arrow) with surrounding oedema (top arrow)*

free radical scavenger and also exerts neuroprotective effect. Mannitol decreases ICP by decreasing overall water content of the brain & CSF (Cerebrospinal fluid) volume and by reducing blood volume due to vasoconstriction[9]. Mannitol also improves cerebral perfusion by decreasing viscosity and by improving red blood cell rheology

(flow and shape of RBC), which results in increase brain oxygenation in large hemispheric stroke[10]. Most patients who survive the acute phase of a stroke regain some of the lost function[11]. The improvement of motor and sensory functions is accompanied by increased blood flow in impaired region surrounding the focal region[12]. Recovery after stroke is accelerated and facilitated by rehabilitation therapy, which might be supported by various drugs[13]. Therefore many trials were undertaken to enhance recovery of cognitive functions after stroke with the use of many pharmacological agents [14] and have focused mainly those agents which improve cerebral reperfusion or neuroprotection [15] . The neuroprotective effect of mannitol thus takes place by reducing infarct size and number of apoptotic cells[16]. The neuroprotective effect of mannitol may also be due to scavenging of free radicals, which protects against biochemical injury. Mannitol has been used in human ischaemic brain damage for over 30 years [17].

Materials and Methods

This interventional prospective comparative study was carried out during the period from 1st July, 2011 to 30th June, 2012 in the Department of Pharmacology and Therapeutics, in collaboration with the Departments of Medicine and Neurology of Sylhet M.A.G Osmani Medical College and Hospital. Newly diagnosed patients with stroke admitted into the Departments of Neurology and Medicine of this hospital within the study period were taken for the study. Patients with previous history of stroke, patients with serious co-morbid conditions, e.g.severe renal dysfunction, hepatic dysfunction, heart failure, malignancy, diabetes mellitus, diabetes insipidus, electrolyte imbalance, hyponatraemia, anaemia and hypovolaemic patients were excluded from the study. 73 patients were taken in the study. After fulfilling the inclusion and exclusion criteria, 45 acute stroke patients were selected for the study. History and clinical examination were recorded in a prescribed data collection form. Then patients were randomly allocated and categorized into two groups by all odd registration numbers in group-I and all even registration numbers in group-II. Patients who received mannitol belonged to group-É and who did not receive mannitol belonged to group-ÉÉ. Serum electrolyte levels of both groups were measured on Day 1 and Day 3. On Day 1 after measuring serum electrolyte level of both groups , group 1 was given infusion Mannitol 1gm/kg I.V. bolus over 10-15 minutes followed by 0.5-1gm/kg I.V. 6 hourly[18] till 3rd day and then again on Day 3 serum electrolyte level of both groups were measured. Other drugs, such as antiplatelet, anticoagulant, antihypertensive etc were given according to individual patient's need. Data from each patient were recorded in previously designed data collection sheet. Data were processed manually and analyzed with the help of SPSS (Statistical Package for Social Sciences) version 16.0. Then these parameters between two groups were compared. Comparison was done between mannitol receiving group and mannitol non-receiving group by unpaired "t" test and between day 1 and day 3 by paired "t" test. A probability value (p) of less than 0.05 was considered statistically significant.

Results:

For this study 73 (seventy three) stroke patients admitted in the Department of Medicine and Neurology of SOMCH were enlisted. Out of them, forty five (45) patients with acute stroke of first attack were selected during the study period from 1st July, 2011 to 30th June, 2012 after fulfilling the inclusion and exclusion criteria. 23 patients with acute stroke receiving mannitol at day 1 were enrolled as group-I and 22 patients with acute stroke without receiving mannitol were enrolled as group-II. Among the total stroke patients, the mean age was 62.6±11.6 years. The mean age of patients of mannitol receiving group was 61.3±12.3 years and mannitol non-receiving group was 64.0±11.0 years respectively, which did not differ significantly (t=-0.760; p=0.451) suggesting an age matched study.

Figure IV shows that among the total stroke patients, 35 (77.8%) patients were male and 10 (22.2%) patients were female. There were 17 (73.9%) male and 6 (26.1%) female patients in the mannitol receiving group; while 18 (81.8%) male and 4 (18.2%) female patients in mannitol non-receiving

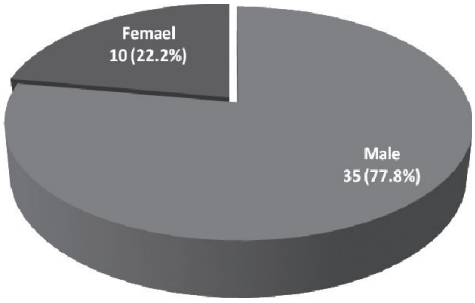

Fig.-4: Pie chart showing distribution of patients by sex (n=45)

group. The sex difference between the two groups was not statistically significant ($\div^2$=0.407; p=0.524) suggesting a sex matched study.

Table-I showed distribution of patients according to stroke type. It was observed that among the stroke patients, 34 (75.6%) patients had haemorrhagic stroke and 11 (24.4%) patients had ischaemic stroke. This table also showed that 18 (78.3%) patients had haemorrhagic stroke and 5 (21.7%) patients had ischaemic stroke in mannitol receiving group; while 16 (72.7%) patients had haemorrhagic stroke and 6 (27.3%) patients had ischaemic stroke in mannitol non-receiving group. The difference between the two groups was not statistically significant ($\div^2$=0.186; p=0.737).

Table-II showed the comparison of serum electrolytes between mannitol receiving group (Group-I) and mannitol non-receiving group (Group-II). It was observed that serum sodium in mannitol receiving group on Day 1 was 138.7±1.9 and in non-receiving group was 139.0±3.1, which was almost similar between two groups [t=-0.390; p=0.699]. On Day 3, serum sodium was recorded as 140.1±2.7 in mannitol receiving group and as 140.1 ± 2.6 in non-receiving group, which was almost similar between two groups [t=0.049; p=0.961]. In mannitol receiving group serum sodium level at day 3 was significantly higher than that of day 1 [t=3.591; p=0.002]. In mannitol non-receiving group serum sodium level at day 3 was also significantly higher than that of day 1 [t=2.483; p=0.022].

Serum potassium in mannitol receiving group on Day 1 was 4.1 ± 0.5 and in mannitol non-receiving group was 4.3 ± 0.5. It was almost similar between two groups [t= -0.994 ; p=0.326]. On Day 3 serum potassium was recorded as 4.3 ± 0.5 in mannitol receiving group and as 4.5 ± 0.5 in mannitol non-receiving group. It was almost similar between two groups [t= -0.910; p=0.368]. In mannitol receiving group serum potassium level at day 3 was significantly higher than that of day 1 [t=2.750; p=0.012]. In mannitol non-receiving group serum potassium level at day 3 was also significantly higher than that of day 1 [t=2.699; p=0.013].

On Day 1 serum chloride in mannitol receiving group was 102.9 ± 3.7 and in non-receiving group was 102.4 ± 3.2, which was almost similar between two groups [t=-0.249; p=0.804]. On Day 3 serum chloride was recorded as 103.7± 3.5 in mannitol receiving group and as 103.2 ± 2.8 in non-receiving group, which was almost similar between two groups [t=0.530; p=0.599]. In mannitol receiving group serum chloride level at day 3 was significantly higher than that of day 1 [t=3.280; p=0.003]. But in mannitol non-receiving group serum chloride level was almost similar at day 3 and day 1 [t=1.178; p=0.252].

Table-I

Distribution of patients according to stroke type.

Study subjects

Stroke type	Group-I (n=234	Group-II	Total (n=45)	P value
Haemorrhage	18(78.3%)	16(72.7%)	34(75.6%)	
Ischaemic	5(21.7%)	*6(27.3%)*	11(24.4%)	0.737
Total	23 (100.0%)	22 (100.0%)	45 (100.0%)	

Group-I: Mannitol receiving group of stroke patients.
Group-II: Mannitol non-receiving group of stroke patients.

Table-II

Serum sodium, potassium and chloride levels of Group-I and Group-II patients at Day1 and Day 3. Data from mannitol receiving (targetted group) and non-receiving (control group) stroke patients.

Time	Serum sodium (mmol/1) Mean ± SD			Serum potassium (mmol/1) Mean ± SD			Serum Chloride (mmol/1) Mean ± SD		
	Group-I (n=23)	Group-II (n=22)	p value	Group-I (n=23)	Group-II (n=22)	P value	Group-I (n=23)	Group-II (n=22)	p value
Day I	138.7 ± 1.9	139.0 ± 3.1	*0.699	4.1 ±0.5	4.3 ±0.5	*0.326	102.9 ± 3.7	102.4 ± 3.2	*0.804
Day 3	140.1 ± 2.7	140.1 ± 2.6	°0.961	4.3 ±0.5	4.5 ±0.5	°0.368	103.7 ± 3.5	103.2 ± 2.8	°0.599
Pvalue	*0.002	*0.022		•0.012	•0.013		▲0.003	△0.252	

Group-I: Mannitol receiving group of stroke patients.

Group-II: Mannitol non-receiving group of stroke patients.

* = No significant difference in sodium, potassium and chloride between mannitol receiving group of stroke patients and non-receiving group of stroke patients on Day 1 at p> 0.05 (Unpaired 't' test)

° = No significant difference in sodium, potassium and chloride between mannitol receiving group of stroke patients and non-receiving group of stroke patients on Day 3 at p> 0.05 (Unpaired 't' test)

† = Significant difference in sodium in mannitol receiving group of stroke patients and non-receiving group of stroke patients on day 1 and Day 3 at p=0.002 and p=0.022 respectively (Paired 't' test)

• = Significant difference in potassium in mannitol receiving group and non-receiving group on Day 1 and Day 3 at p=0.012 and p=0.013 respectively(Paired 't' test)

▲ = Significant difference in chloride in mannitol receiving group on Day 1 and Day 3 at p= 0.003 (Paired ' t ' test)

△ = No significant difference in chloride in mannitol non-receiving group on Day 1 and Day 3 at p= 0.252 (Paired ' t ' test)

Discussion:

Mannitol is reported to decrease cerebral oedema, infarct size and neurological deficit in several experimental models of stroke [16, 19], mostly when administered within six hours after stroke onset. A prospective, interventional, comparative study was done to see the effect of mannitol on serum electrolytes in stroke patients. It was observed that serum sodium (138.7±1.9 vs 139.0±3.1; p=0.699) and serum potassium (4.1 ± 0.5 vs 4.3 ± 0.5; p=0.326) at Day 1 were almost similar between mannitol receiving group and non-receiving group.

At Day 3, serum sodium (140.1±2.7 vs 140.1±2.6; p=0.961) and serum potassium (4.3±0.5 vs 4.5±0.5; p=0.368) were also almost similar between mannitol receiving and non-receiving groups.

In this observation, significant variation was seen in the level of sodium and potassium levels between 1st day before infusion of mannitol (Day 1) and on 3rd day after infusion of mannitol (Day 3). In mannitol receiving group serum sodium and potassium levels at Day 3 were significantly higher than that of Day 1 (140.1±2.7 vs 138.7±1.9; p=0.002 and 4.3±0.5 vs 4.1±0.5; p=0.012 respectively).

In mannitol non-receiving group serum sodium and potassium level on Day 3 was also significantly higher than that of Day 1 (140.1±2.6 vs 139.0±3.1; p=0.022 and 4.5±0.5 vs 4.3±0.5; p=0.013 respectively).

These findings were supported by Rautaray[18]. They have done an observational study in MGM Medical College, Indore, India and found that mean values of sodium and potassium before giving mannitol (Day 1) were 130.4 meq/l and 3.9 meq/l respectively. After 3rd day of giving mannitol (Day 3) the mean values were 138.1meq/l and 4.36 meq/l for sodium and potassium respectively. In their study, statistically significant values for serum sodium (P<0.001) and potassium (P<0.02) were obtained when comparison was done between Day 1 and Day 3.

Current study revealed that infusion of mannitol 1gm/kg stat and then 0.5 gm/kg 6 hourly till 3rd day was sufficient to improve the clinical condition in stroke patients. The findings were in close

conformity to the previously reported results that lower dosage of mannitol is quite effective with less chance of inducing hyperosmolar problems that have been noted with frequent high dose therapy[20].

Regarding age and sex there were no significant difference between two groups, suggesting an age and sex matched study. The mean ± SD age of total patients was 62.6±11.6 years. Peak age of occurrence of stroke was 61-70 years (42.2%) and the males were predominant which is consistent with the findings of Yao[20] . They have analyzed 1027 patients with acute stroke. The average age of the study population was found to be 67.5 years and peak age of occurance of stroke was 59.5 - 73.2 years and the majority of stroke patients were male (60.5%). In this study, number of ischaemic stroke and haemorrhagic stroke was almost similar between two groups. There was no significant difference in diagnosis between two groups (P=0.737). The overall result indicates that mannitol can be successfully used in stroke patients, but further larger studies are needed to confirm the routine use of mannitol in stroke patients.

Conclusion:

A prospective interventional comparative study was conducted to evaluate the effect of mannitol on serum electrolytes in stroke patients. Forty five (45) patients of stroke were randomly allocated in two groups: 23 patients received mannitol and 22 patients did not receive mannitol. On Day 1, after measuring serum electrolyte level of both groups, mannitol receiving group was given infusion mannitol 1 gm/kg IV bolus followed by 0.5 gm/kg IV 6 hourly till 3rd day and then again on Day 3 serum electrolyte levels of both groups were measured. It was observed that serum sodium, potassium and chloride on Day 1 and Day 3 were almost similar between mannitol receiving group and mannitol non receiving group (P> 0.05 for each component). The study revealed that serum electrolyte levels rise within normal range and there was no adverse effect of mannitol infusion on serum electrolytes in stroke patients. Mannitol therefore may be safely given to patients of stroke as there was no electrolyte imbalance till third day. This study had some limitations. Firstly, the follow-up period of this study was only few days which might impede the total outcome of stroke. Secondly, sample size was small. Also there was lack of medical education in mass people. Despite the limitations and draw back we tried to do our work sincerely. The study needs further extensive investigation in large scale and for long term period. Further prospective interventional randomized trials and larger follow-up are needed for better assessment of long term efficacy and safety profile.

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Association between Admission Hyperglycemia and Outcome in Actue Ischemic Stroke Cases: An Observational Study

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Abstract:

Background: *A high proportion of patients suffering from an acute stressful condition asuch as stroke or myocardial infarction may develop hyperglycemia even in the absence of a preexisting diagnosis of diabetes. The study evaluates the effect of hyperglycemia in the severity and outcome during the acute phase of stroke. Methods: This was a descriptive cross-sectional study. Baseline variables (eg: age, sex, smoking, hypertension, diabetes OHA/insulin) and outcome measures (mortaily, disability) were statistically analysed and compared with a control group of 50 patients of acute ischemic storke without admission hyperglycemia.* ***Result:*** *the base line characteristis of the two patient groups were comparable. The 1st week mortality was 16% in case group and 2% in the control group. the 30 days mortality in the case group and control group was 28% and 12% respectively, 58.33% were disabled & dependent in the hyperglycemia group, in comparison to 36.36% subjects in the control group.* ***Conclusion:*** *Admission hyperglycemia seems worsen the outcome and functional disability during the acute phase of Ischemic stroke. Admission glucose level is an important risk factor and should be immediately treated to reduce morbitidity & mortality in acute Ischemic stroke cases*

Key words: *Stroke, Hyperglycemia, Cerebral Ischemia, cerebro vascular Injury disability.*

Introduction:

Stroke is one of the leading causes of death and disability world wide and more so in underdeveloped countries like Bangladesh where health support system including rehabilitation is not expectedly available. At least 50% of the neurological disorder in a general hospital is stroke. World Health Organizasion (WHO) defined Stroke as rapidly developiong clinical signs of focal or global disturbance of cerebral function, with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than vascular origin[1]. Most of the stroke is due to cerebral infarction ((80%) the rest is due to haemorrhage. Modifiable risk factors for stroke include hypertension, diabetes, atrial fibrillation, dislipidemia, smoking and alcohol abuse. About one third of patients with acute stroke and no prior diagnosis of diabetes have hyperglycemia during acute phase of stroke. Wether this is an acute stress response or a reflection of underlying diabeties is controversial[2]. Hyperglycemia has been reported to worsen the lolerance of the brain to ischemia[3,4]. The early recognition of disorder of glucose metabolism in stroke patients is important because hyperglycemia during the acute phase worsens the outcome probably by reducing the salvage of penumbral tissue medicated by high lactate level of brain tissue [5]. Despite these observations, the relationship between glucose level and outcome after stroke in diabetic and nondiabetic patients has not been well characterised and those studies that have examined this relationship have reported conflicting results[6]. The present study is carried out to find out the relationship of admission hyperglycemia and its

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outcome in terms of mortality and morbidity after an acute ischemic stroke.

Methods:

This descriptive cross- sectional study was done among patients admitted in Shaheed Suhrawardy Medical College Hospital between July 2012 – June 2013. Tomographic (CT) diagnosis of ischemic stroke with admission hyperglycemia (RBS>8mmol/L) were included in the study. Patterns with intracerebral haemohage, subarachnoid haemorrhage transient Ischemic attack and with non-stroke cause of focal neurological deficit eg. brain tumour were excluded from the study. Those patients with associated co-morbidity like myocardial infraction, atrial fibrailation, cancer was not included in the study. 100 patients were selected by purposive type of nonprobability sampling technique. A random blood glucose was measured on admission (or within 24 hours of admission) to define admission hyperglycemia (RBS> 8mmol/L). Among them 50 patients who fulfilled the inclusion criteria were selected as case group and another 50 patients with RBS < 8mmol/L were selected as control group. Data were collected by taking medical history,clinical evaluation and laboratory investigations in a structured data sheet.

The samples under study were examined for assessment and follow up during admission, one week after admission and after one month of discharge from the hospital. Outcome was assessed in terms of fatality and functional recovery after 30 days adjusting age, stroke severity and comorbid conditions parameters used for assessment of stroke severity and outcome were the NIHSS (National Institute of Health stroke scale) and the modified Rankin Scale (MRS) [7]. Data were analyzed by statistical package for social science (SPSS) programme.

Result:

The mean age of the control was 60.10+11.35 years and that of cases was 60.80(+12.37) years. Majority of the patients belonged to the 6th & 7th decade of life. Analysis found no statistically significant difference between the mean age of the control and the cases (P>0.05). This is shown in Table I

Tabel-I

Age distribution of study subjects (n= 100, control 50, case 50)

Age group	Study Subjects		p value
	Case No. (%)	Control No. (%)	
21-30	1(2)	2(4)	
31-40	2(4)	0(0)	0.769
41-50	9(18)	6(12)	
51-60	11 (22)	21 (42)	
61-70	19 (38)	14 (28)	
71-80	7(14)	7(14)	
81-90	1 (2)	0 (0)	
Total	50 (100)	50(100)	
Range	21-90	21-90	
Mean +SD (years)	60.80+12.37	60.10+11.35	

Chi square test was done, which was not significant (P>0.05)

Out of 50 cases 31 (62%) were male and 19(38%) were female given a male to female ratio of 1.6:1. Among the 50 controls, 32 (64%) were male and 18(36%) were female giving a male to female ratio of 1.7:1. Analysis revealed that no statistically significant difference was found between the sex distribution of the subjects of two groups (P>0.05). This is shown in Table II

Tabel-II

Sex distribution of study subjects (n=100, Control 50, case 50)

Sex	Study Subjects		p value
	Case No. (%)	Control No. (%)	
Male	31 (62)	32 (64)	0.836
Female	19 (38)	18 (36)	
Total	50 (100)	50(100)	
M:F	1.6:1	1.7:1	

Chi square test was done, which was not significant (P>0.05)

Observation shows 30(60%) subjects of case group and 34(68%) subjects of control group have the history of hypertension before ischemic stroke. Analysis revealed no statistically significant difference between the case group and control group regarding previous history of hypertension (P>0.05). This is shown in Table III

Table-III

Comparison of hypertension between case and control group (n=100, Control 50, case 50)

Study Subjects	Hypertension			p value
	Present No. (%)	Absent No. (%)	No. (%)	
Case	32 (60)	20 (40)	50 (100)	0.405
Control	34 (64)	16 (32)	50 (100)	

Chi square test was done, which was not significant (P>0.05)

The mean blood glucose level in case group was 11+2.58 mmol/L (Mean +SD) and that of control group was 5.8+0.72 mmol/L (Mean +SD). Unpaired "t" test showed that there was significant difference of mean admission blood glucose level between the case and the control group (P<0.05). This is shown in Table IV.

In the case group 8(16%) subjects died in 1st week in the case group and 1(2%) subject died in 1st week in control group. Statistical analysis showed that there is significance in mortality during first week between the case and control group (P<0.05). This is shown in Table V

Table-IV

Comparison of blood glucose between case and control group (n=100, Control 50, case 50)

Admission RBS	Case group Range (8-20)		Control group Range (4.3 – 7.6)		P value
	Number	Mean +SD	Number	Mean +SD	
4-4.9		11+2.58	6	5.8+0.72	0.001
5-5.9			17		
6-6.9			25		
7-8			2		
8-8.9	11				
9-9.9	10				
10-10.9	7				
11-11.9	10				
12-12.9	4				
13-13.9	2				
14-14.9	3				
15-15.9	1				
16-16.9	0				
17-17.9	0				
18-18.9	0				
19-20	2				
Total	50		50		

Unpaired "t" test was done, which was significant (P<0.01)

In another observation 14 (28%) subjects of case group and 6(12%) subjects of control groups died after 30 days of ischemic stroke. Statistical analysis showed that there is significant difference in mortality after 30 dayss between the case and control group (P<0.05). This is shown in Table VI

Table VII shows 21(58.33) subjects of case group and 16(36.36%) subjects of control group has become dependent after 30 days of ischemic stroke. On the other hand 15 (41.67%) subjects in the case group and 28(63.64%) subjects in the control group become independent after 30 days of the event. Statistical analysis shows significant disability among case group after 30 days of the event (P<0.05).

Table VIII shows that 8 (40%) subjects who were treated for hyperglycemia became dependent whereas 13(81.25%) subject who were not treated for hyperglycemia became dependent. Statistical analysis shows significant difference between the treated and non treated group of admission hyperglycemia.

Table-V

Comparison of mortality in 1st week between case and control group (n=100)

Study	Death in 1st week			p value
Subjects	Yes No. (%)	No No. (%)	Total	
Case	8 (16)	42 (84)	50 (100)	0.036
Control	1 (2)	49 (98)	50 (100)	
Total	9	91	‘100	

Chi square test was done, which was significant (P<0.05)

Table-VI

Comparison of mortality in 30 days between case and control group (n=100)

Study	Death in 30 days			p value
Subjects	Yes (%)	No (%)	Total	
Case	14(28)	36 (72)	50	0.046
Control	6 (12)	44 (88)	50	
Total	20	80	100	

Chi square test was done, which was significant (P<0.05)

Table-VII

Comparison of disability among survivors after 1st week and after 30 days in case and control group (n=100)

Study	Death in 30 days					p value
Subjects	On admission No (%)	After 1st week No. (%)	After 30 days			
			Total Disability	Dependent No. (%)	Independent No (%)	
Case	50 (100)	42 (84%)	36(72%)	21 (58.36)	15 (41.67)	0.049
Control	50 (100)	44 (98%)	44(88%)	16 (36.66)	28 (63.64)	
Total	100	90	80	37	43	

Chi square test was done, which was significant (P<0.05)

Table-VIII

Comparison of disability among survivors after 30 days between treated and non treated group of hyperglycemia (n=36, treated 20, non treated 16)

Study Subjects	Disability after 30 days		Total	p value
	Dependent No. (%)	Independent No. (%)	No (%)	
Treated	8 (40)	12 (60)	20 (100)	0.031
Non treated	13 (81.25)	3 (18.75)	16 (100)	
Total	21	15	36	

Chi square test was done, which was significant (P<0.05)

Discussion:

The present study was carried out to show the effect of admission hyperglycemia in patients with ischemic stroke irrespective of the cause of hyperglycemia. The study was done to find out the association of socio-demographic factors like age, sex, socioe-conomic status, personal habit like smoking, family history of stroke and other disease like hypertension as risk factor in the development of ischemic stroke. One hundred subjects with ischemic stroke were included in this study of which 50 subjects with ischemic stroke were in the case group with admission hyperglycemia (RBS > 8mmol/L) during admission and 50 subjects in control group were without hyperglycemia (RBS<8 mmol/L) during admission. Regarding sex distribution, both the controls and cases were well matched with no significant statistical difference (P>0.05).The study also showed that 26% of control group and 28% of case group had the family history of stroke. Statistical analysis found no significant difference between the two group regarding family history of stroke (P>0.05). The study by Hayee MA et all[8] also found positive family history in 26.06%of patients. In the present study, 60% of subjects in the case group and 68% of subjects in the control group were hypertensive. No statistically singnificant difference was noted between the two groups (P>0.05).Previous study by Uddin J[9] also found 60%of patients with ischemic stroke were hypertensive. Hyperglycemia is frequently seen in the acute phase of ischemic stroke affecting up to 20% to 50% of patients at presentation. In the present study, the mean admission blood glucose level was 11+2.58 mmol/L (mean+SD) in the case group and 5.8+0.72 mmol/L (mean+SD) in the control group with a cumulative mean value of 8.4+1.65 mmol/L (mean +SD). Statistical analysis revealed significant difference between admission blood glucose level in the case and control group (P<0.05). In a previous study Nina T[10] showed mean blood glucose level at admission was 8.4±5.2 mmol/L (mean ± SD). This finding closely resembles the finding of the present study. Admission hyperglycemia was associated with higher mortality rate than was euglycemia. In this study, 16% patients of hyperglycemia group died in the first week in comparison with only 2% in the euglycemic group which is statistically significant (P<0.05). Death in 1st week was more in 61-70 years age group (6%) in the cases in comparison to (2%) in the controls of the same age group. The result implies that admission hyperglycemia is an independent predictor of mortality in patients with ischemic stroke. The higher rate of death in the present study may be due to lack of early reperfusion and thrombolytic therapy and inadequate supportive treatment facilities in our hospital set-up.

Regarding mortality after 30 days of ischemic stroke, the hyperglycemic group showed mortality rate 28% in comparison with 12% in the euglycemic group. This indicates a 2.3 fold increase in mortality among the patients with admission hyperglycemia which is also statistically significant (P<0.05). In this study, 58.33% survivors of the case group and

36.3% of the control group were severely disabled after 30 days of ischemic stroke. The remainder 41.67% of patients of the case group and 63.64% of the control group become functionally independent despite some residual disability ($P<0.05$). Study done by Jose Alverez S et al[11] showed 51% become severely disabled and 49% become functionally independent at 3 months. The present study shows higher incidence of significant disability ($P<0.05$) in the hyperglycemic group than the previous study.

Conclusion:

The study revealed that there is an association between on admission hyperglycemia and poor outcome after acute ischemic stroke. Admission hyperglycemia worsen the outcome and functional disability during the phase of ischemic stroke. The study also suggests that on admission glucose level is an important risk factor and should be immediately treated to reduce morbidity and mortality in acute ischemic stroke.

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Association of Hypertriglycerideamia with Ischaemic Stroke

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Abstract:

Stroke is one of the foremost causes of morbidity, mortality and is a socioeconomic challenge. This is particularly true for developing countries like Bangladesh, where health support system including the rehabilitation system is not within the reach of common people. Hypertriglyceradeмia has an effective influence in the pathogenesis of Ischaemic Stroke (IS). So, the focus of this study was to evaluate and assess the association of serum triglyceride level in patients of IS.

This case control study was carried out in the Department of Neurology in collaboration with Department of Biochemistry, BSMMU, Dhaka from July 2011 to June 2013. In this study, 60 diagnosed cases of ischaemic stroke patients and 60 age and sex matched healthy controls were enrolled. Risk factors of Ischemic Stroke (IS) patients were assessed (adjusted Odds Ratio) in comparison with healthy adults. In this study, being married [OR. 1.95, 95% CI (0.40-9.42), p=0.409] , smoker [OR.1.65, 95% CI (0.57 - 4.82),p= 0.357], DM [OR. 1.48, 95% CI (0.36-6.06), p=0.582], IHD [OR. 1.51, 95% CI (0.29 – 7.89), p=0.624] , HTN [OR. 3.66, 95% CI (1.11–12.12), p=0.033] , overweight [OR.2.31, 95% CI (0.77 – 6.91), 0.135] and obesity [OR. 16.19, 95% CI (1.31–200.6), p=0.030] , increased level of serum TC [OR.8.24, 95% CI (2.07 – 32.83), p=0.003], TG [OR. 9.40, 95% CI (1.17 -75.86), p=0.035], LDL [OR. 0.45, 95% CI (0.10–2.05), p=0.308],and decreased level of HDL [OR. 3.37, 95% CI (1.03 - 12.25), p=0.045] were found as risk factors in developing IS. Independent t-test was done to find out the statistically significant differences of continuous variables like serum lipid profile between case and control group. The mean (SD) value of TG which is focus of this study, was found 237.67 (61.74) in case group, and 169.97 (26.95) in control group which was highly statistically significant (p < 0.0001).

All of the significant variables were entered into stepwise logistic regression analysis model. From the logistic regression model, it can be finally concluded that hypertension, obesity, increased level of TC, increased level of TG and decreased level of HDL were statistically significant risk factors for development of IS.

***Abbreviation:** IS (ischemic stroke), TC (total cholesterol), TG (triglyceride), HDL (high density cipoprotein), LDL (low density lipoprotein).*

Introduction:

Stroke is one of the leading causes of death in the world [1] and low and middle income countries have the largest burden of stroke, accounting for more than 85% of stroke mortality worldwide [2]. Each year, about 4.4 million people die of stroke globally, of whom almost three millions are from developing countries [3]. According to WHO, stroke will remain second leading cause of death both in developed and developing countries in 2020[4]. A survey carried out by the Indian Council of Medical Research in Kolkata, showed the average annual incidence of stroke as 145 per 100,000 persons per year[5]. Estimated annual incidence in Pakistan is 250/ 100,000 translating to 350,000 new cases every year [6]. Incidence of stroke in Bangladesh is 2.55 per 1000 population per year in both sexes [7]. Another study showed prevalence of stroke is 46.2% in rural area, 27.4% in semi urban area and 26.4% in urban population[8].

Multiple risk factors are associated with Stroke. The Non-modifiable risk factors are age, sex, family history, race and ethnicity and the modifiable risk factors include hypertension, cardiac disease, diabetes mellitus, dyslipidaemia, cigarette smoking, alcohol abuse, physical inactivity, carotid stenosis, and transient ischaemic attack[9]. Hyper-

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choleterolaemia, high LDL and low HDL are established risk factor for ischaemic stroke[10,11] but some studies[12-15] showed significant correlation between hypertriglyceridemia and others[16-18] failed to prove this.Hypertriglyceridemia may lead to IS as Triglyceride-rich lipoproteins, including very-low-density lipoprotein and intermediate-density lipoprotein, in addition to LDL-C particles, become trapped in blood vessel walls and have been demonstrated in human atherosclerotic plaques. Hypertriglyceridemia may also endothelial dysfunction, oxidative stress due to lipid-derived free radicals, and impairment of endothelium-dependent vasodilatation[19]. In addition to a direct atherogenic effect of triglyceride rich lipoproteins, elevated triglycerides have been associated with several abnormalities of the clotting-fibrinolytic systems[20].

In Bangladesh, food grain, particularly rice plays a key role in the consumption of food as well as for supplying calories and nutrients for the people of Bangladesh [21].As the content of dietary carbohydrate is elevated (>55% of energy)and fat in the diet is reduced, triglycerides in the blood rises. This paradoxical phenomenon is known as carbohydrate-induced hypertriglyceridemia[22].As a result, Bangladeshi people may have high triglyceride level and this study is carried out to see the association between ishchemic stroke and serum triglyceride level.

Methodology:

This case control study was carried out on 60 ischaemic stroke patients admitted in the Neurology Department, BSMMU and 60 age and sex matched controls fromJuly 2011 to June 2013. All participants were above 18 years of age and ischaemia was confirmed by either CT scan or MRI of brain. Patients having venous thrombosis, cardioembolic events – AF, MI (within 6 weeks), prosthetic heart valve, endocarditis or taking anti lipid drugs are excluded from the study. After overnight fasting, serum lipid profile was done by automated analyzer in Biochemistry Department within 72 hours of stroke onset. Diabetes Mellitus was defined as per ADA diagnostic criteria. Hypertensive were those people having blood pressure more than 140/90 mmHg. Hypercholesterolaemia, having TC more than 200 mg/dl; hypertriglycerideamia, having TG more than 150mg/dl; high LDL having LDL more than 130mg/dl and low HDL, having HDL less than 40mg/dl was set to define abnormal lipid profile. Smoker were those people who had a smoking history for a certain period of time (e" 1 years) either regularly or irregularly. Overweight was defined as having BMI more than 25 but less than 30 and obese were those people having BMI 30 or more.SPSS 21.0 was used for analysis of the data. TheChi-square test was used to compare proportions and Student t test to compare continuous variables between groups. Logistic regression analysis was used to assess the independent contribution of risk factors to stroke. For all statistical tests, we considered p value <0.05 as statistically significant.

Results:

The mean age(SD) in the study was found 58.95 (12.23) years in case group and 52.90 (13.78) years that of control group(p=0.94). Most of the correspondents were belong to 60-69 years age group. Among the study sample, 56 were married in case group and 48 in control group. Statistically significant (p=0.018) difference was noted regarding the smoking status of case and control (36 Vs 22). 65% of the case and 68.3% of the control lived in urban area. (Table I) Around 51.67% of cases presented with hemiparesis, 20% monoparesis, 16.67% aphasia, 5% visual disturbance and 6.67% had cranial nerve involvement.The mean value of TG was found 237.67 (61.74) in case group, and 169.97 (26.95) in control group which was highly statistically significant (p < 0.0001). There was also statistically significant difference (p<0.05 in other parameters in case and control groups [TC: 204.36 (39.57) vs. 179.83 (22.08)mg/dl ; HDL: 39.75 (6.51) vs. 43.54 (5.04) mg/dl and LDL: 117.07 (42.44) vs 102.30 (22.59) mg/dl].(Figure 1)

Table-I

Characteristics of case and control group

		Case(n=60)	Control(n=60)	p value
1.	Age (SD) years	58.95 (12.23)	52.90 (13.78)	0.94
2.	Married (%)	56 (93.3%)	48 (80.0%)	0.60
3.	Urban dweller	39 (65.0%)	41 (68.3%)	0.846
4.	Smoker	36 (60.0%)	22 (36.7%)	0.018#
5.	Overweight	53.33%	36.67%	0.025#
6.	Obesity	10.0%	3.33%	0.025#
7.	Hypercholesterolaemia	51.7%	20.0%	0.001#
8.	Hypertriglyceridaemia	96.7%	75.0%	0.034#

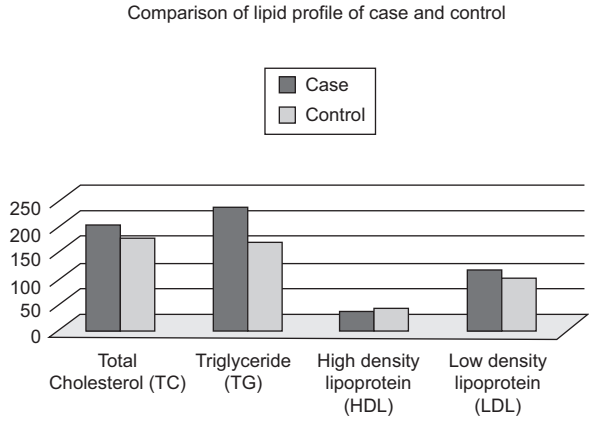

Fig.-1: *Bar diagram showing mean value of lipid profile in case group and control group.*

The following variables were entered into logistic regression model to find out adjusted OR for ischemic stroke: Marital status, smoking, urban living, Diabetes Mellitus, IHD, hypertension, overweight, obesity, hypercholesterolemia, Hypertriglyceridemia, high LDL and low HDL. This model revealed having hypertension [adjusted or(95% CI), 3.66 (1.11 - 12.12); p =0.033], obesity [adjusted or(95% CI), 16.19 (1.31 - 200.69); p=0.03], increased level TC [adjusted or(95% CI), 8.24 (2.07 - 32.83); p=0.003], increased level TG [adjusted or(95% CI), 9.40 (1.17 - 75.86); p= 0.035] and decreased level of HDL [adjusted or(95% CI), 3.37 (0.93 - 12.25); p = 0.05] as statistically significant risk for ischemic stroke. Other risk factors did not attain statistically significant value. (Table II)

Table-II

Risk factors for ischemic stroke

		Adjusted OR (95% CI)	p value
1.	Married	1.95 (0.40-9.42)	0.409
2.	Smoking	1.65 (0.57 - 4.82)	0.357
3.	Urban living	0.86(.40 - 1.84)	0.699
4.	Diabetes Mellitus	1.48 (0.36 -6.06)	0.582
5.	IHD	1.51 (0.29 - 7.89)	0.624
6.	Hypertension	3.66(1.11-12.12)	0.033#
7.	Overweight	2.31(0.77-6.91)	0.135
8.	Obesity	16.91(1.31-200.6)	0.030#
9.	Hypercholesterolemia	8.24(2.07-32.83)	0.003#
10.	Hypertriglyceridemia	9.40(1.17-75.86)	0.035#
11.	High LDL	0.45(0.10-2.05)	0.308
12.	Low HDL	3.37(0.93-12.25)	0.045#

Statistically significant
Logistic Regression Analysis was done to find correlation

Discussion:

The main findings in this study were high triglycerides which constitutes an independent risk factor for ischemic stroke along with high cholesterol, low HDL, hypertension and obesity. Multiple studies along with a meta-analysis showed association of TG with ischemic events. Triglycerides are present in all plasma lipoproteins and make triglyceride-rich lipoproteins highly heterogeneous. This heterogeneity leads to complex relationship between triglycerides and cardiovascular disease. Although concurrent hypertriglyceridemia, hypertension, diabetes mellitus, obesity, and other dyslipidemias are well known as “metabolic syndrome”, Hyper-triglyceridemia can cause stroke independently.

The metabolic pathways of triglycerides and HDL-C are related, and an increase in one will usually be accompanied by a decrease in the other[23] . Predicting ischemic risk in light of low HDL may most likely underestimate the role of triglyceride. The meta-analysis of prospective studies by the Asia-Pacific Cohort Studies Collaboration (APCSC) showed significant correlation between triglyceride and ischemic stroke[13] . In the Copenhagen City Heart Study, Lindenstrom et al founda strong linear association between nonfasting triglyceride levels and cerebral ischemic events[15]. For every 1 mmol/l increment in non-fasting triglycerides, the RR increment for ischemic events was 1.12 (95% CI 1.07–1.16). In the Blood Lipids and First-Ever Ischemic Stroke/Transient Ischemic Attack in the Bezafibrate Infarction Prevention (BIP) registry the odds ratio for IS of triglyceride levels >200 mg/dl was 1.47 (95% CI 1.19–1.8) [12].Wiely et al in their prospective study showed completely opposite result, where stroke was not associated with total cholesterol, triglyceride or HDL but increased risk of ischemic stroke of those having LDL>130 mg/dl (adjusted HR, 3.81; 95% CI, 1.53–9.51)[24].In Finnmark study, a significant association between nonfasting triglyceride levels and stroke was found for women only [RR 1.29 (95% CI 1.05–1.57)][14]. In Bangladesh Uddin et al, although found significant correlation between all components of lipid profile but not for TG[10]. Again, Bowman et al and Sridharan found no association of triglyceride level and ischemic stroke[11, 18] . To our best knowledge, this is the first study in Bangladesh to show correlation between TG and ischemic stroke. In the present analysis, we demonstrate the additive risk conferred by cholesterol fractions and high triglycerides.

Limitations:

Recall bias, inherent to all case- control study, and we are not different. This study is conducted in a single center involving small number of sample, which might not represent the actual condition of whole Bangladeshi people. In logistic regression model, we found wide confidence interval, which may be occurred due to small sample size.

Conclusion:

Blood lipids improve the prediction of ischemic stroke beyond traditional risk factors. Specifically, this study shows for the first time that high triglycerides is associated with increased risk of ischemic stroke. The renewed interest in the role of lipids for stroke, further research should focus on blood lipids, including serum triglycerides, as part of the global risk assessment and potentially modifiable risk factors for ischemic stroke.

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CASE REPORTS

Pulsatile Midline Solitary Plasmacytoma in the Frontal Head Region-A Case Report"

MD. ATIKUR RAHMAN[1], AKLAQUE HOSSAIN KHAN[2] , KANAK KANTI BARUA[3]

Abstract

Primary craniocerebral plasmacytomas are uncommon and represent only 0.7 % of all plasmacytomas. In this case solitary plasmacytoma in the midline frontal head region of the skull and discuss the clinical features and prognosis of this tumor. Plasmacytoma can present as multiple myeloma, solitary plasmacytoma of the bone or extramedullary plasmacytoma. Solitary plasmacytoma is a rare entity that composes of malignant plasma cells and involves the bone to form only one or two lesions without evidence of disease dissemination. It accounts for only 4% of malignant plasma cell tumors. 50 years old male was suffering from plasmacytoma in the frontal head region in our case which is pulsatile. On images showed multiple differential diagnosis but after operation histological examination revealed plasmacytoma.

Keywords: *Plasmacytoma, Pulsatile, Solitary*

Abbreviations: *CT (Computed Tomography), MRI (Magnetic Resonance Imaging), MRV (Magnetic Resonance Venography), CSF(Cererbrospinal Fluid).*

Introduction:

Solitary plasmacytoma is a circumscribed neoplastic lesion with no clinical or radiological signs of systemic involvement and accounts for some 7 % of myelomas[1,2,3,4]. Solitary bone plasmacytoma is described as a single lytic lesion without signs of myeloma cells on bone marrow examination, even when paraproteins are present in serum and/or urine. This neoplasm appears in about 5 % of patients with plasmacytoma and most frequently localizes in the vertebral column. Primary craniocerebral plasmacytomas are uncommon they represent 0.7 % of cases[3,5]. We report one case of solitary plasmacytoma of the skull and discuss the clinical features and treatment of this uncommon tumor in the light of the published cases.

Case report:

50 years old male had been suffering for five months from a oval swelling in the midline of frontal head region which was gradually increasing in size (Figure 1). On local examinations following features are found: Midline swelling is in frontal head region of coronal suture which is

- oval
- overlying skin shiny
- pulsatile
- measurement about 10X10 cm
- firm in consistency
- not fluctuating.
- fix with underlying structures
- Little bit fix with overlying skin
- Local temperature raised,
- Prominent superficial vein was seen

Skull radiographs showed a big osteolytic area localized in the midline frontal bones in front of coronal suture (Figure1). CT scan of brain showed a midline frontal mixed intensity osseous lesion with an electron density slightly greater than the brain and contrast enhancement. The bone is mild hypertrophied. MRI demonstrated a midline frontal homogeneous mass, isointense in Tl-weighted images with the cerebral parenchyma and slightly hyperintense in T2-weighted images (Figure 2). The lesion presented a contrast enhancement but

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intra or extradural could not identify clearly. MRV showed occlusion of anterior third part of the superior sagittal sinus (Figure 2). Then it was diagnosed as a case of parasagittal meningioma. Midline frontal craniotomy was done followed by macroscopical total removal of a nodular tumor which fully extradural and mild adherent with the dura mater. Involved dura and bone was removed followed by duruplasty and cranioplasty respectively (Figure 3). The histological diagnosis was plasmacytoma. Tumor tissue consisted of sheets of mature plasma cells. The plasma cells showed an increased nucleocytoplasmatic ratio and infrequent mitotic figures. Giemsa stain showed that the cells had moderately pleomorphic nuclei with clumped and marginated chromatin. CSF analysis showed nothing pathological, and the urine test for Bence Jones protein was negative. Bone marrow study was

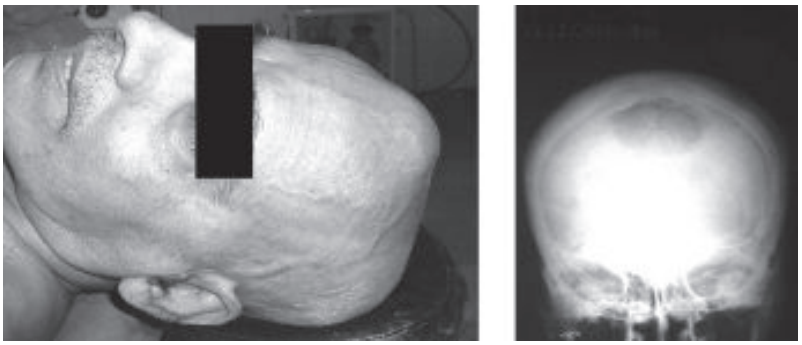

Fig.-1: *The patient with midline frontal swelling and x-ray skull shows big oesteolytic lesions.*

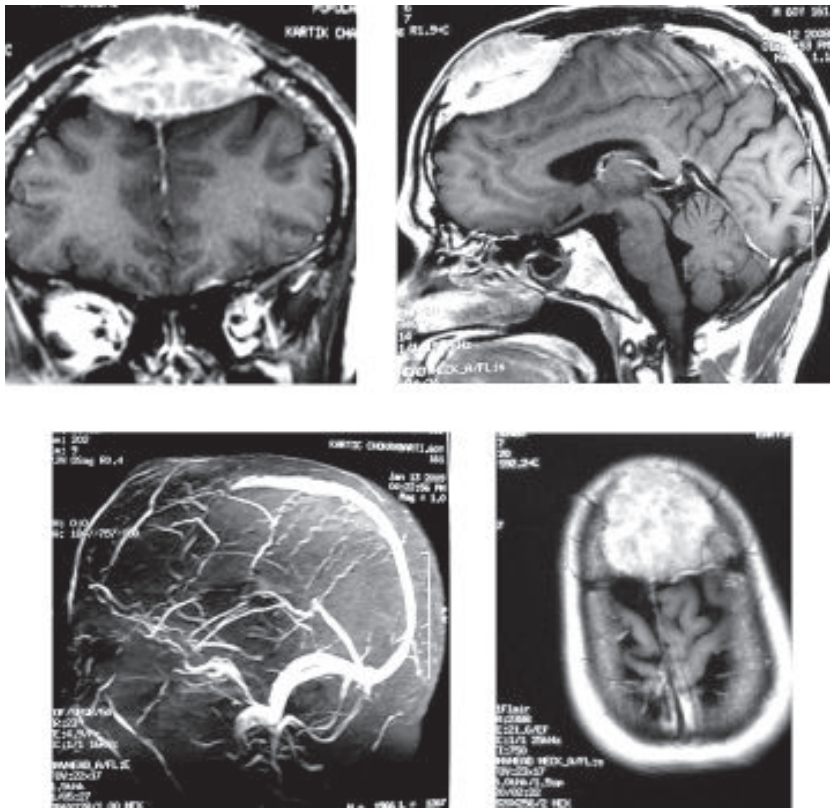

Fig.-2: *MRI of brain shows contrast enhanced lesions in different views and MRV shows obstructions of anterior part of superior sagittal sinus.*

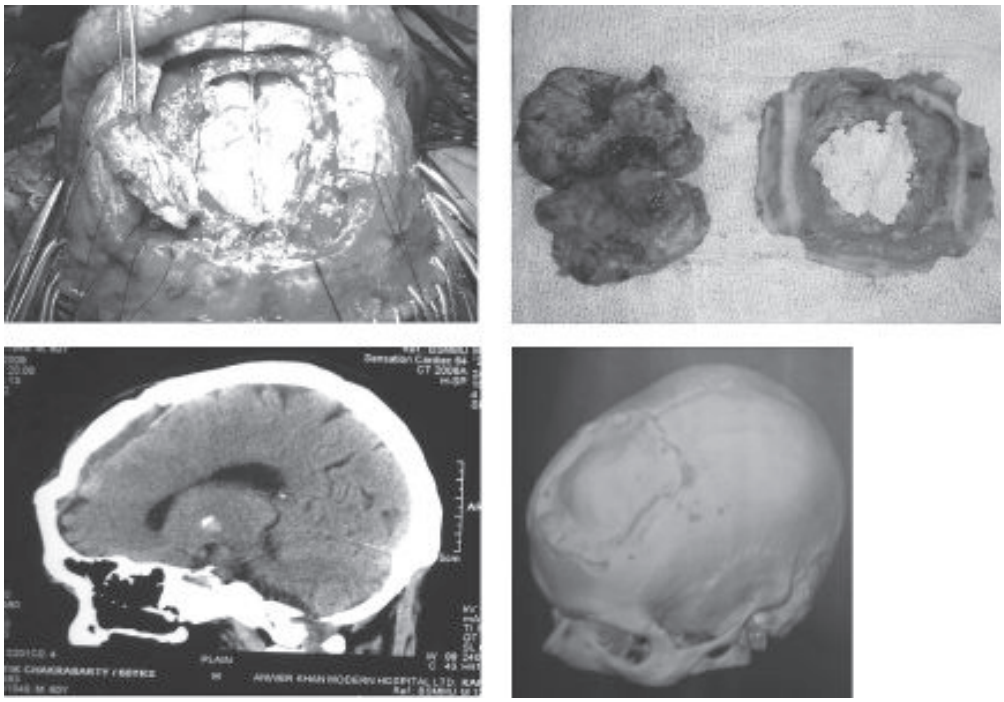

Fig.-3: *Per operative picture after removing the bone and involved portion of dura mater. Tumor and involved bone on the top right side. Bone shows oesteolytic area. Post operative CT scan shows total removal of the tumor and 3D picture shows cranioplasty areas in the frontal region.*

also normal. He never suffered from systemic neoplastic disease. Post operative CT showed total removal of tumor and cranioplasty was in proper place (Figure 3). Follow up after six months he was very well and no further deterioration.

Discussions:

Multiple myeloma (or simply myeloma) is a neoplasm of a single clone of plasma cells characterized by proliferation of plasma cells in bone marrow, infiltration of adjacent tissues with mature and immature plasma cells, and the production of an immunoglobulin, usually monoclonal IgG or IgA . Circulating pre-myeloma cells lodge in appropriate microenvironments (e.g. in bone marrow) where they differentiate and expand. Although multiple myeloma is often referred to in the context of “metastatic lesions” to bone, it is also sometimes considered a primary bone tumor. If only a single lesion is identified, then it is referred to as a plasmacytoma[6]. In this case patient was suffering from single lesion in skull bone. Cranial plasmacytomas are rare lesions that can arise from the calvarium, dura or skull base and could be the harbinger of a more widespread systemic myeloma. Very rarely, it has been described as the sole presenting feature of underlying multiple myeloma. On imaging, these lesions can be confused with meningioma, cranial secondaries or lymphoma. Zigouris *et al*. described a case of an elderly male with cranial plasmacytoma, who presented with progressive right hemiparesis[7]. This type differential diagnosis we had also thought regarding our case. But histopathology finally confirm the diagnosis, it was a case of plasmacytoma.

Conclusions:

Varieties of patient we have found in neurosurgical department. Sometimes actual diagnosis is very difficult even after lots of investigation. Clinical evaluation, imaging studies and histopathology report may be different in some patient. If we make proper plan for surgery before going to operate or in per operative, then we can significantly reduce the morbidity and mortality rate of the patient, even when diagnostic dilemma is present.

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Cerebellar Ataxia, An Unusual Neurological Manifestation of Coeliac Disease- A Case Study

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Abstract:

Coeliac disease was considered as a gluten sensitive enteropathy but now due to its wide clinical presentation is considered as multisystem autoimmune disorder. Ataxia with peripheral neuropathy is a rare manifestation of gluten sensitivity. The presence of gluten-related immune markers in normal population however complicates the reliable diagnosis of gluten related neurological disorders and clinical improvement on gluten free diet can serve as a diagnostic tool for this disease. We report a case of sporadic progressive cerebellar ataxia with peripheral neuropathy with positive anti tissue transglutaminase (anti-tTG) antibodies and subtotal villous atrophy in duodenal biopsy. This case highlights an important diagnostic and therapeutic principle in management of late onset idiopathic ataxia.

Keywords: *Coeliac disease, Ataxia, Anti TTG ab*

Case Presentation

A 65-year-old diabetic, normotensive female housewife (fig-1) presented to us with five years history of gradually progressive unsteadiness of gait. He denied any motor weakness but complaints of tingling and numbness sensation in gloves and stocking pattern and complained of tremulousness of the hands with clumsiness in doing fine work and a tendency to sway to either side while walking, with occasional falls. Within 3 years of the onset of the illness, she was unable to walk without support but she had no speech difficulty and sphincter disturbance. She also complained of forgetfulness and difficulty in calculating and handling money but there was no history of fits, headache, hallucinations, delusions or any change in behavior or personality. She also complained of chronic diarrhea with 6-7 semisolid, non-foul smelling loose stools without blood or mucus per day for last 15 years. Diarrhea was not associated with vomiting, abdominal pain, loss of appetite, weight loss or fever. Patient also diagnosed as DM for last 5 years. She was on oral hypoglycemic agents with good compliance and well controlled. No history of consanguinity among her parents and there was no family history of any similar illness in the parents or siblings. Besides the habit of betel nut chewing she had no other addiction.

On examination, patient was fully conscious and alert. She was moderately anaemic, nonicteric with vitiligo over extremities and around lips. There was diffuse non tender thyromegaly. Her vitals and other systemic examination were normal. Higher mental functions were essentially normal (MMSE-27/30). All the cranial nerves were intact with normal fundus examination and full ocular movements without nystagmus. There was no motor weakness but all the deep tendon reflexes were diminished and planters were bilaterally flexor. Pain & Temperature is lost in gloves and stocking pattern. Vibration is lost distally in both upper and lower limbs with positive Rhomberg's sign. She had bilateral cerebellar signs with in-coordination of finger nose test, impairment of heel shin test, and gait was broad based ataxic type.

On laboratory examination, complete blood count revealed Hb-8gm/dl, ESR-70 mm/1st hour with normal differentials, blood film shows microcytic hypochromic anaemia with elliptical, pencil and few

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target cells, Serum ferritin – 8.88µgm/l (↓), Iron-35 µgm/dl (↓) , TIBC-411 µgm/dl (↑) Serum Vitamin B12- 326 pgm/ml (Normal), HbA1c- 6.8%, Routine blood chemistry including blood sugar, LFT, RFT, Thyroid function test, and Serum electrolytes levels were within normal range. For evaluation of diarrhea stool r/e was done which was normal, anti TTG (tissue trans-glutaminase) antibody was positive (68.5 U/ml). Patient then undergone endoscopy of upper GIT and duodenal biopsy. It reveals chronic duodenitis with partial villous atrophy. MRI of brain showed cerebellar atrophy more marked over vermis (fig 2).

In view of a history of progressive cerebellar ataxia and peripheral neuropathy being accompanied by chronic diarrhea and a positive blood test for anti TTG (tissue trans-glutaminase) antibody and positive histopathology report of partial villous atrophy, a diagnosis of gluten sensitive disorder was confirmed. The patient was advised to follow a strict gluten free diet, following which her loose motions abated within a few days and was given some supportive management like iron and vitamin supplementation including vitamin E and she was discharged home with the advice to remain compliant with her diet plan and regular follow up.

Fig-1: *A 65 year female diabetic and normotensive patient*

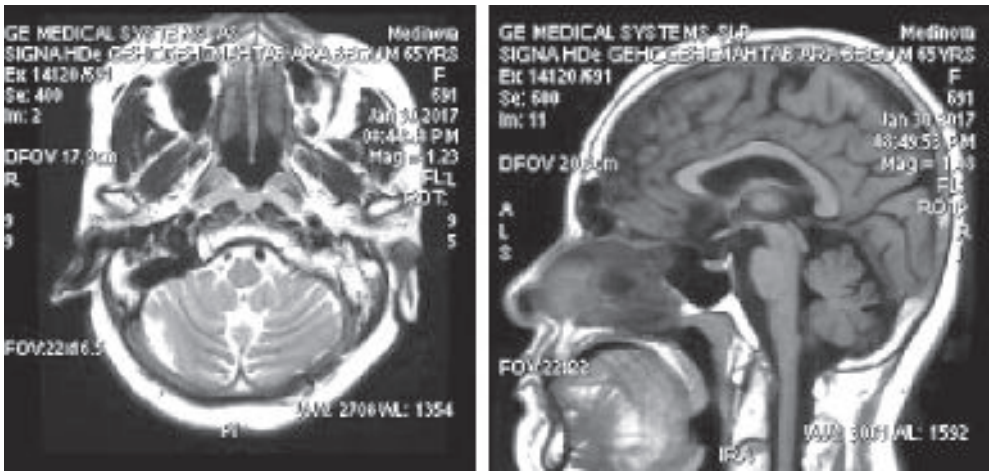

Fig-2: *MRI of Brain axial & saggital view showing bilateral cerebellar atrophy including vermis.*

Discussion:

Coeliac disease (CD) is a life-long gluten-sensitive autoimmune disease of the small intestine affecting genetically susceptible individuals worldwide and is seen more commonly in association with HLA DQ2 and DQ8 positivity[1]. CD individuals may present gastrointestinal symptoms, extraintestinal symptoms or no signs or symptoms. The classical symptoms include gastrointestinal-related symptoms such as diarrhea, steatorrhea and weight loss due to malabsorption. About 50% of CD patients present with extraintestinal or atypical symptoms, such as anemia, osteoporosis, dermatitis herpetiformis, neurological problems and dental enamel hypoplasia[2, 3]. The prevalence of CD has been estimated to approximate 0.5%-1% in different parts of the world[4]. A study from north India reported a prevalence of 1 in 310 individuals[5]. Overall prevalence of gluten sensitivity is probably much higher, since Coeliac disease is frequently referred to as 'iceberg disease.

Neurological complications occur in about 8%-10% of patients with the disease [6] including peripheral neuropathy [7,8], progressive multifocal leucoencephalopathy[9], cerebellar ataxia[6,10,11], progressive myoclonic ataxia [12,13], dementia[14] and myopathy[15].

Coeliac disease occurs in approximately 9% of patients with idiopathic cerebellar ataxia. Patients can present with ataxia of limb and/or dysarthria, oculomotor, sensory, or bladder dysfunction[16].The ataxia occasionally improves after a prolonged gluten-free diet[17]. Ataxic patients also have a higher incidence of gluten sensitivity, defined as the presence of antibodies to gliadin or transglutaminase in the absence of histological evidence of coeliac disease[16].

In patients with neurologic manifestations, gastrointestinal symptoms are detectable in 10% of the cases only, but biopsy evidence of coeliac disease can be found in upto one-third of the patients. In our case, the patient had a history of chronic diarrhea but the intestinal biopsy also shows partial villous atrophy.

Serological tests used to confirm the diagnosis of gluten sensitivity include: IgA anti gliadin antibody, IgA anti tissue trans-glutaminase (Anti-TTG) and anti endomysial antibodies. Anti TTG and endomysial antibodies are specific for enteropathy but these are often undetectable in patients with neurological manifestations but in our case this test also reveals positive at low titre. MR imaging shows cerebellar atrophy in around 60% of the cases, as similar lesion was found in the present case also (fig-2).

IVIg has had a beneficial effect in patients with sporadic cerebellar ataxia, in the context of GAD antibodies[18] and gluten sensitivity[19] but has not yet been shown to work for the combination of ataxia and coeliac disease. It would be interesting to test plasmapheresis or corticosteroids, as an alternative to costly IVIg, and to ascertain whether all ataxic patients with coeliac disease eventually respond to therapeutic long-term immunosuppression.

The mechanisms for neurological manifestations of coeliac disease remain uncertain. The first proposed mechanism is malabsorption of nutrients exerting neurotrophic and neuroprotective effects[20] but dietary gluten restriction and vitamin supplementation rarely improve the neurological deficits[8, 12]. Now an immunological mechanism is given priority in the literature: Anti gliadin Abs have been suggested to be directly or indirectly neurotoxic[15].

Conclusions:

Neurologic manifestations can also be encountered in cases with gluten sensitivity and which may occur with or without gastrointestinal symptoms and can often be missed if it occurs in isolation. As gluten ataxia is a potentially treatable and reversible disorder, all patients presenting with sporadic, unexplained chronic cerebellar ataxia should be tested for serological evidence of gluten sensitivity. Patients testing positive for antigliadin or anti TG antibodies, should be put on a strict gluten free diet to reduce disability and arrest further disease progression. To the best of our knowledge, we report the first case of elderly lady with cerebellar atxia due to coeliac disease.

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Miller Fisher Syndrome- a Case Report and Review of Literature

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Abstract:

Background and Objective:: Miller Fisher syndrome (MFS) is a variant of Guillan Barre syndrome characterized by ophthalmoplegia, ataxia and areflexia. Although self-limiting disease course is expected, disease modifying treatment options for MFS are no different than for GBS and include intravenous immune globulin (IVIG) and plasmapheresis. Here, we report a case of MFS presented with bilateral ptosis, ophthalmoplegia, ataxia with quadriparesis and normal NCS. Patient - Methods: A 14- year-old young boy was admitted to our hospital with the complaints of double vision, vertigo, difficulty in walking, imbalance. He had no diarrhea or upper respiratory tract infection prior to this illness. On neurological examination, he had limited ability to move his eyes up and out, had bilateral ptosis, ataxia. The muscle strength was mildly impaired. The plantar reflexes were flexor and the deep tendon reflexes were absent. Results: The blood laboratory, CT and brain MRI were normal. In the first sample of CSF, there was no change. Subsequent sample after 14 days revealed high protein with albuminocytological dissociation. The NCS and EMG were normal. Anti GQ 1b antibody was negative. He showed marked improvement with conservative management. Conclusion: MFS is a rare disease that must be diagnosed with the clinical findings and in the following days the diagnosis can be supported by the laboratory findings.

Key words: *Ataxia, Cerebrospinal fluid , Miller Fisher Syndrome, Ophthalmoplegia etc.*

Abbreviations: *CSF (Cerebrospinal Fluid), EMG (Electromyography), GBS (Guillain Barre Syndrome), IVIg (Intravenous Immunoglobulin), MFS (Miller Fisher Syndrome), NCS (Nerve Conduction Study).*

Introduction:

Miller Fisher Syndrome (MFS) is an acquired disease of nervous system which is considered as a rare variant of Guillain-Barré Syndrome (GBS). It is also called Fisher's syndrome, was first recognized by James Collier in 1932 as a separate clinical triad of ophthalmoplegia, ataxia, and areflexia. Later, MFS was named after Charles Miller Fisher who reported it in 1956 as a limited variant of Guillain- Barré syndrome (GBS) [1]. Miller Fisher Syndrome (MFS) is a geographically variable variant of GBS observed in about 1% - 5% of all GBS cases in Western countries, yet up to 19% and 25% in Taiwan and Japan, respectively [2]. There is an estab-lished male predominance at a ratio of 2:1 and a mean age of onset of 43.6 years, although cases of MFS have been reported in all age ranges [3]. Despite its rarity, MFS has played an important role in under-standing the pathogenesis of immune-mediated neuropathies, which is thought to involve molecular mimicry incited by an-tecedent infection [4, 5]. Chiba et al first reported the presence of anti-GQ1b antibodies in strong association with MFS in 1992 [6]. This serological marker, present in well over 90% of afflicted patients, has become an important diagnostic tool in MFS and has been implicated in other variants of GBS that involve ocular muscles [4, 5] . Although self-limiting disease course is expected, disease modifying treatment options for

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MFS are no different than for GBS and include intravenous immune globulin (IVIG) and plasmapheresis. Benefits of treatment are not as clear in MFS, but a rationale for treatment is to encourage faster resolution of symptoms and perhaps decreased likelihood of complications [7]. Here we are reporting a case of MFS having weakness of all four limbs, ptosis along with ataxia, areflexia, ophthalmoplegia conservatively managed. The patient gradually improved in symptoms including power, ataxia, ophthalmoplegia without intravenous immunoglobulin. After 2 weeks, the patient was discharged from hospital with marked recovery.

Case Report:1

A 14 year old young boy presented to the department Neurology, National Institute of Neurosciences and Hospital, Dhaka with sudden onset of both lower limb weakness followed by weakness of all four limbs, bilateral drooping of eyelids, more on the left and double vision for past 7 days. Drooping of eyelids is not of fatigable type and there was no diurnal variation. After two days of onset of symptoms, he developed unsteadiness of gait, while walking he had tendency to fall on either side and was able to walk only with support. His imbalance was not proportionate to weakness. There was no history of fever, headache, loose motions and upper respiratory tract infections in the past one month. There was no history of bladder and bowel incontinence. There was no recent history of trauma, drug abuse, alcohol addiction and vaccination.

General physical examination was normal with stable vitals. On neurological examination higher cerebral functions were normal. Cranial nerve examination revealed bilateral external opthalmoplegia with ptosis, more on the left (Figure 1). There was no nystagmus, optic fundus was normal. On motor system examination, muscle tone decreased in both lower limbs, power is 4/5 in both lower limbs and normal in upper limbs. There was no muscular wasting / atrophy, involuntary movements were not present. In all four limbs deep tendon reflexes were absent, plantars were flexors bilaterally. Sensations like thermal, pain and touch including lower limbs Joint position sense and vibration sense were normal. Romberg's test was positive in open eyes. He had ataxic gait with grossly impaired tandem walking and tendency to fall on either side. Finger nose test and other cerebellar signs were normal.

His routine investigations are normal. CT and MRI of brain, thyroid function tests, S. Vit B-12, VDRL were normal. CSF Analysis was done for 2 times at 14 days interval. First time it showed 0 cells with normal protein and sugar. Subsequent CSF study showed 3 cells, all are lymphocytes, protein 80 mg%, albuminocytological dissociation present. Gm stain, AFB stain, ADA and Gene Xpert were negative. Anti GQ 1b antibody was negative. Nerve conduction study showed normal sensory and motor nerve action potential.

As the patient shown triad symptoms of MFS - ataxia, areflexia, ophthalmoplegia and weakness of lower limbs, clinically he was diagnosed to have Miller Fisher variant of GBS.. The patient was managed conservatively and he had shown gradual improvement in symptoms including power, ataxia, ophthalmoplegia without intravenous immunoglobulin (IVIg). We discharged and followed up the patient. After 30 days the patient was recovered completely (Figure 2).

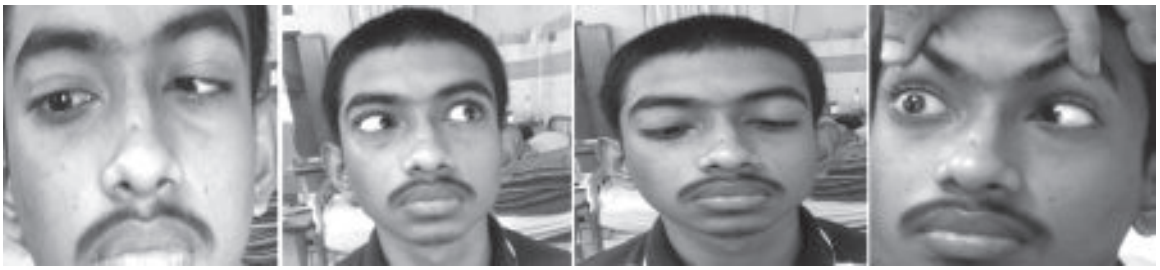

Fig.-1: *Bilateral ptosis with external ophthalmoplegia (lateral rectus, inferior oblique, superior rectus palsy).*

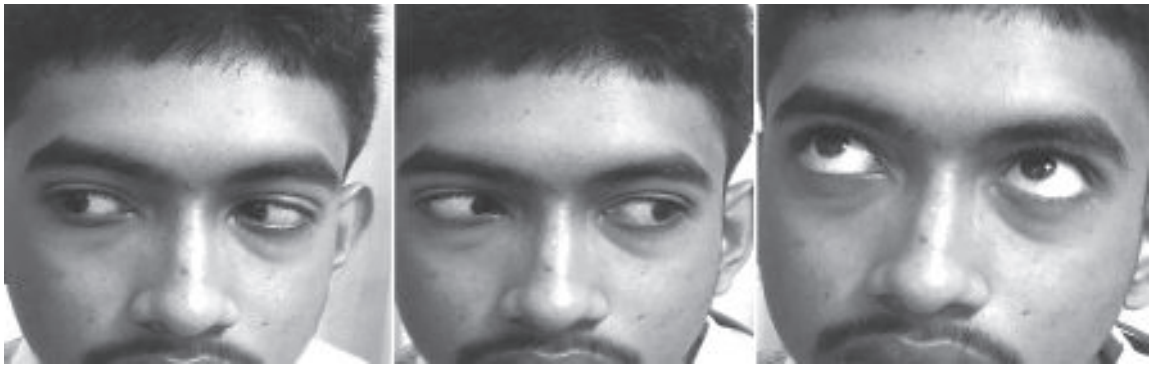

Fig.-2: *After recovery all EOM works with full range of motion (30 days after event).*

Discussion:

Miller-Fisher syndrome (MFS) is known for the characteristic triad of opthalmoplegia, ataxia, and areflexia without overt sensory deficits. It is considered a variant of GBS, which is also known as acute idiopathic neuritis. An increasing body of evidence sug-gests that a rather wide range of neurological features may be present and significant overlap exists in MFS and other forms of GBS. MFS accounts for one to five percent of all GBS cases in Western countries, but 19% and 25% in Taiwan and Japan, respectively [2]. MFS is twice as common in men as women 8. It affects people of all ages, with the median age of onset being in the fifth decade [8]. MFS presents commonly with diplopia (78%), ataxia (48%), and both (34%). The less frequent symptoms consist of limb dysesthesia; blepharoptosis; face, bulbar, and pupillary palsies; mild (grade 4) motor weakness; and micturition disturbance [2]. These clinical signs are preceded by signs of upper respiratory tract infection in 56–76% of the patients. The most common pathogens are Campylobacter jejuni and Haemophilus influenzae. However, Mycoplasma pneumoniae and cytomegalovirus are also found to be associated. MFS onset is typically acute, beginning with neurologic symptoms approximately 8–10 days (range of 1–30), following the antecedent illness [2,3]. The disease then progresses until a clinical nadir is reached approximately a week (range of 2–21) after the initial neurologic symptoms [2]. A diagnosis of MFS can be made with compatible clinical history taking, cardinal symptoms, normal findings on CT or MRI, and presence of albuminocytologic dissociation in the CSF of affected patients. Anti-GQ1b antibodies, which act against GQ1b (a ganglioside component of nerves), blocks acetylcholine release from the motor nerve terminals. It relates to the disease activity and can be used as a diagnostic marker in MFS [6]. It is not unique to MFS, but helps in serological confirmation to allow for more definite diagnostic certainty in the presence of confounding symptoms. Kusunoki et al found 5 patients with a variant form characterized by ataxia but no ophthalmoplegia in 149 patients who had the IgG anti-GQ1b antibody without profound weakness. These cases could fit with autoimmune ataxic neuropathy, having pathological lesions mainly in the dorsal root ganglion. GD1b antibody plays the key pathogenic role in autoimmune ataxic neuropathies. Because of the existence of cross-reactivity between GQ1b and GD1b, it is thought that the pathogenesis of this form is similar to that of MFS [9].

Numerous case reports and series of patients with MFS treated with immunotherapy [generally plasma exchange, intravenous immunoglobulin G (IVIG) or a combination including one of these] have been reported. Analysis of the largest MFS case series failed to show any beneficial effects in the group who had received plasmapheresis when compared with the group who received no immunotherapy [10]. Furthermore, in a recent randomized trial of patients with GBS, the addition of intravenous methylprednisolone with IVIG did not confer any additional effect on recovery from disability at 4 weeks, when compared with that of IVIG therapy alone [11]. MFS is generally regarded as a self-

limiting, benign condition. All of 28 untreated MFS patients in the largest published case series returned to normal activities 6 months after the neurological onset. The respective median (range) periods between neurological onset and the disappearance of ataxia and ophthalmoplegia were reported as 32 (8-271) and 88 (29-165) days. However, cases progressing to respiratory failure and requiring mechanical ventilation have also been described, particularly in children. Other serious complications reported include coma, ballism, cardiomyopathy from dysautonomia, lactic acidosis, and pain [3].

Differential Diagnosis of Opthalmoplegia, Ataxia, and Areflexia [12]

Opthalmople-gia caused by MFS is often rapid in onset compared to a more gradual course in chronic diseases such as myotonic dystrophy, thyroid eye disease, and myasthenia gravis. More than 50% of patients with MG present with ptosis and/or diplopia. The weakness of the ocular muscles may switch from one eye to another and improve or worsen over the course of a day, unlike MFS which progressively worsens until the nadir of symptoms has been reached before any recovery is seen. Ataxia can be seen in many conditions, often affecting the cerebellum, the spinocerebellar tracts, or the proprioception channels in peripheral nerves and dorsal columns. Cerebellar ischemia occurs due to compromise of the posterior circulation and often presents with non-specific symptoms of unsteady gait, dizziness, headache, eye movement dysfunction, as well as nausea and vomiting. Though both MFS and vascular compromise are acute events, ataxic patients with MFS typically lack lateralization of ataxia which helps to differentiate MFS from the majority of cerebel-lar lesions. Toxins and medications also have the capability of inducing acute onset ataxia. Sodium channel modulators such as phenytoin and chemotherapeutic agents such as fluorouracil can precipitate ataxic episodes. Arguably the most frequent cause of ataxia, alcohol consumption, mostly affects the lower extremities and is also associated with poor fine motor control of the hands, slurred speech, and impaired vision. The natural history of MFS is progression of weakness in a “head down” fashion, whereas the initial symptom would not be weakness and ataxia in the lower extremities. Often alcohol consumption can be determined through the patient’s history or urine toxicol-ogy screen. Areflexia is indicative of a lower motor neuron deficit, which would not be seen in many of the conditions affecting the central nervous system. Paradoxically, patients with spinal shock—seen in transection or compression of the spinal cord—are areflexic or hyporeflexic in the subacute stage of the disease, which then progresses to hypereflexia as the pathology evolves. Peripheral neuropathy, seen most often in diabetics and malnourished individuals, can lead to areflexia in severe cases. Anterior horn cell destruction, seen in polio and amyotrophic lateral sclerosis (ALS), will leave patients areflexic as well. Like MFS, spinal shock is an acute condition, while ALS typically has a gradual onset. Temporary paralysis and areflexia similar to that of MFS and Guillain-Barre can also be due to poliovirus infection, with functional recovery occurring 4-6 weeks after paralysis. Our case describes a patient who presented with quadriaresis, diplopia and ataxia. On examination he was dysdi-adochokinetic, dysmetric, and severely ataxic, with prominent opthalmoplegia. Our top differential for this clinical scenario included Brainstem encephalitis, Brainstem stroke, MG, and Miller Fisher variant of GBS. A clinical triad of ataxia, areflexia, ophthalmoplegia and high protein count in his CSF with albuminocytological dissociation were consistent with MFS variant of GBS, as was the favorable response with conservative management and his gradual recovery to improved function.

Conclusion:

Although uncommon, MFS is an important diagnosis to make since the presenting symptoms of ataxia and ophthalmoplegia may confuse the clinician and suggest an upper motor neuron sign or central cause. The presence of additional neurological symptoms may make clinical evaluation more challenging. Therefore, high clinical suspicion is needed to diagnose Miller Fisher Variant of Guillain-Barré Syndrome because all symptoms may not appear at the same time. It is necessary to rule out other clinical conditions with rapid onset of

ophthalmoplegia and ataxia, such as brainstem stroke, Wernicke's encephalopathy, Bickerstaff brainstem encephalitis and also other acute painful ophthalmoplegias such as bilateral cavernous sinus thrombosis, Tolosa-Hunt syndrome and superior orbital fissure syndrome before the clinical diagnosis of MFS in Primary health care setups.

Conflicts of interests: None

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