VOL. 30 NO. 1 ISSN 1023-4853 January 2014

# BANGLADESH JOURNAL OF NEUROSCIENCE

## CONTENTS



OFFICIAL ORGAN OF BANGLADESH SOCIETY OF NEUROSCIENCES

# Bangladesh Journal of Neuroscience

# INSTRUCTIONS FOR AUTHORS

- Review articles are subject to the peer review process. They should contain a maximum of 4000 words and 75 references.
- Original papers should have a structured abstract, must not exceed 3,000 words and should not include more than 4-6 illustrations and tables. Each separate part of a figure (a, b, etc.) counts as an illustration. Up to 40 references are permitted.
- Brief communications should include brief original studies or reports on one or a small number of cases. They should not exceed 1,000 words; 1-2 illustrations and up to 10 references are permitted.
- Technical notes include description of an original surgical technique and its application on one or a small number of cases. Follow-up and outcome need to be clearly stated.
- Letters to the editors are published in the Correspondence section. They must not exceed 9000 types, 5 references and 5 authors. They should not have an abstract. They should be addressed to the Editor-in-Chief. Submitted letters will be subject to shortening and editorial revision.

**Manuscript Submission**

- Submission of a manuscript implies: that the work described has not been published before; that it is not under consideration for publication anywhere else; that its publication has been approved by all co-authors, if any, as well as by the responsible authorities – tacitly or explicitly – at the institute where the work has been carried out. The publisher will not be held legally responsible should there be any claims for compensation.

**Permissions**

- Authors wishing to include figures, tables, or text passages that have already been published elsewhere are required to obtain permission from the copyright owner(s) for both the print and online format and to include evidence that such permission has been granted when submitting their papers. Any material received without such evidence will be assumed to originate from the author

**Title Page**

The title page should include:

- *The name(s) of the author(s)*
- *A concise and informative title*
- *The affiliation(s) and address(es) of the author(s)*
- *The e-mail address, telephone and fax numbers of the corresponding author*

**Abstract**

Please provide an abstract of 150 to 250 words. The abstract should not contain any undefined abbreviations or unspecified references.

**Keywords**

Please provide 4 to 6 keywords which can be used for indexing purposes.

**Acknowledgments**

Acknowledgments of people, grants, funds, etc. should be placed in a separate section on the title page. The names of funding organizations should be written in full.

**Manuscript Submission**

Submission of a manuscript implies: that the work described has not been published before; that it is not under consideration for publication anywhere else; that its publication has been approved by all co-authors, if any, as well as by the responsible authorities – tacitly or explicitly – at the institute where the work has been carried out. The publisher will not be held legally responsible should there be any claims for compensation.

**Permissions**

Authors wishing to include figures, tables, or text passages that have already been published elsewhere are required to obtain permission from the copyright owner(s) for both the print and online format and to include evidence that such permission has been granted when submitting their papers. Any

material received without such evidence will be assumed to originate from the authors.

Reference list

The list of references should only include works that are cited in the text and that have been published or accepted for publication. Personal communications and unpublished works should only be mentioned in the text. Do not use footnotes or endnotes as a substitute for a reference list.

The entries in the list should be numbered consecutively.

- *Journal article – Gamelin FX, Baquet G, Berthoin S, Thevenet D, Nourry C, Nottin S, Bosquet L (2009) Effect of high intensity intermittent training on heart rate variability in prepubescent children. Eur J Appl Physiol 105:731-738. doi: 10.1007/s00421-008-0955-8*
- Ideally, the names of all authors should be provided, but the usage of "et al" in long author lists will also be accepted: Smith J, Jones M Jr, Houghton L et al (1999) Future of health insurance. N Engl J Med 965:325–329
- *Article by DOI - Slifka MK, Whitton JL (2000) Clinical implications of dysregulated cytokine production. J Mol Med. doi:10.1007/s001090000086*
- *Book- South J, Blass B (2001) The future of modern genomics. Blackwell, London.*
- *Book chapter-Brown B, Aaron M (2001) The politics of nature. In: Smith J (ed) The rise of modern genomics, 3rd edn. Wiley, New York, pp 230-257.*

**Ethical approval:**

"All procedures performed in studies involving human participants were in accordance with

the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards."

- For retrospective studies, please add the following sentence:
- "For this type of study formal consent is not required."

**Informed consent:**

"Informed consent was obtained from all individual participants included in the study."

- If identifying information about participants is available in the article, the following statement should be included:
- "Additional informed consent was obtained from all individual participants for whom identifying information is included in this article."

Bangladesh Journal of Neuroscience 2014; Vol. 30 (1) : 1-10

## *ORIGINAL ARTICLES*

# Association Between Carotid atherosclerosis And High Factor VIII Activity In Ischemic stroke

SUKUMAR MAJUMDER[1], ANIS AHMED[2], MD SHAHIDULLAH[3], MD RAFIQUL ISLAM[4], MD REZAUL KARIM KHAN[4], MASUD RANA[5]

**Abstract:**

***Background:*** *A sample of 60 subjects from population based study participated in a study on carotid color duplex ultrasonography that aimed to assess the relations of coagulation factors to stroke and carotid atherosclerosis. The association between severity of carotid atherosclerosis and high factor viii activity in ischemic stroke is still not clear.* ***Objective:*** *The present study was conducted to find out the association between carotid atherosclerosis and high factor viii activity in ischemic stroke.* ***Methodology:*** *This was a cross sectional analytical study carried out in the department of neurology,BSMMU during the period of july'2009 to june'2011.A total 60 subjects with ischemic stroke were included in this study and data were collected purposively. Chi square test was done and probability value <0.05 were considered as level of significance and 95% confidence limit were taken.* ***Result:*** *In patients with e"50% carotid stenosis, 7(23.33%) had high factor VIII activity and 23(76.67%) had normal factor VIII activity. In patients with <50% carotid stenosis, 2(6.67%) had high factor VIII activity and 28(93.33%) had normal factor VIII activity. No significant difference (P>0.05%) was found between the high factor VIII activity and normal factor VIII activity related to severity of carotid stenosis.* ***Conclusion:*** *The roles of hypertension, hypercholesterolemia, and hypertriglyceridemia have been implicated in the pathogenesis of the carotid atherosclerosis but in the present study did not find any association between the severity of the carotid atherosclerosis with high factor viii activity in ischemic stroke.*

***Key words:*** *Factor viii activity, Carotid atherosclerosis , Ischemic stroke.*

**Introduction:**

Stroke is a clinical syndrome characterized by rapid onset of focal or global neurological signs or disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than that of vascular origin, non-epileptic and non-traumatic in nature[1]. This definition includes stroke from both infarction and hemorrhage. Transient ischemic attack (TIA) is identical to that of stroke, except that the symptoms last less than 24 hours. About 85% of stroke is caused by primary cerebral ischemia resulting in infarction (ischemic stroke) and 15% are caused by cerebral hemorrhage (hemorrhagic stroke)[2,3].

Stroke is a major global health problem. It is a major cause of mortality, morbidity and disability in developed countries and increasingly in less developed countries. Worldwide, it is the leading cause of healthy years lost in late adulthood, and evidence indicates that the burden of stroke, particularly in terms of morbidity and disability, will almost certainly increase in the foreseeable future[4].

1. Registrar, Department of Neurology , Rangpur Medical College, Rangpur
2. Resident, Department of Neurology, BSMMU, Dhaka
3. Assistant Professor, Department of Neurology, BSMMU, Dhaka
4. Professor, Department of Neurology, BSMMU, Dhaka
5. Medical Officer, Department of Neurology, BSMMU, Dhaka

Stroke is the third most common cause of death in the developed world and is the most common cause of adult physical disability[5]. It is a common medical emergency with an annual incidence of approximately 160 per 100,000 population per year[6]. The incidence rises steeply with age; the incidence is rising in many developing countries due to adoption of less healthy lifestyle.

There are several risk factors associated with stroke. Some of which are non modifiable and some are modifiable. Non-modifiable factors are age, gender, race, heredity, previous vascular events (MI, stroke), high fibrinogen. Modifiable factors are high blood pressure, ischemic heart disease, diabetes mellitus, hyperlipidemia, smoking, excess alcohol consumption, polycythemia, elevated homocystiene, elevated anticardiolipin antibodies, obesity and oral contraceptives[7] .For ischemic stroke there are some potential new risk factors, which include some genotypes, inflammatory markers, infectious agents, biomarkers hemostasis, high factor VIII activity , Von-Willbrand factor and platelet related factors[8] .

The prevalence rate of stroke of India is 250-350/ 100,000 in last decade. Incidence of stroke in Bangladesh is 2.55/1000 population/year in both sexes (Bangladesh bureau of statistics, 2009). About 40-50% of beds are occupied by stroke patients in neurology ward which is reported in a developing country like ours[9].

It is interesting to note that coronary artery disease mortality was reduced in haemophilic patients with very low level of factor VIII observed both the 5-years and 16.1 years studies of the Northwick Park Heart Study. They also found modest association between high factor VIII activity and coronary artery disease[10]. These findings encourage the previous researchers to elucidate the association between carotid atherosclerosis and high factor VIII activity in ischemic stroke patients.

Factor VIII, an essential blood coagulation factor, is a large glycoprotein having a molecular weight of approximately 360,000 [11]. Factor III is a cofactor involved in activation of factor X by activated factor IX in the presence of membrane surfaces and calcium. Normal levels of factor VIII do not saturate this enzymatic reaction. When factor VIII level increase above the normal level, a given quantity of factor IX can generate larger quantities of activated factor X, which in turn generate large quantities of thrombin and thus fibrin[12]. Factor VIII and Von Willebrand factor as potential markers of endothelial cell injury[13]. Plasma factor VIII might interact with platelet glycoprotein-I, endothelium and subendothelium thus deposition of platelet on damage endothelium.

Deposited platelets may release growth promoting peptides which stimulate proliferation of intima and smooth muscle of blood vessels leading to atherosclerosis[14].This biochemical observation and previous reports of thromboembolic disease in patients with high factor VIII elevation, a causal relationship between high factor VIII and thromboembolic stroke appears likely.

Arteriography has been long regarded as the gold standard diagnostic tool for carotid stenosis. It is a costly and invasive technique with potentially serious complications. The results of arteriography have not been standardized which makes comparison of results from different laboratories difficult. Duplex ultrasound is a non-invasive, inexpensive and can provide functional and anatomical information about vessel stenosis and plaque morphology. Color duplex flow ultrasonography has thus became a routine noninvasive method of assessing extracranial cerebrovascular occlusive disease because it avoids the expense and risk of arteriography. The sensitivity and specificity of carotid duplex ultrasound range from 90% to 95% for measurement of carotid diameter reduction, and duplex ultrasound may be more sensitive for detection of minimum atherosclerotic plaque. The goals of carotid imaging can be described as early detection, clinical staging, surgical road mapping and postoperative therapeutic surveillance[15].

The purpose of the study was to evaluate the association between carotid atherosclerosis and factor VIII activity in ischemic stroke.

**Subjects and Methods:**

**Study population:**

It was a cross sectional analytical study done in the department of neurology ,Bangabandhu Sheikh Mujib Medical University, Dhaka from July 2009 to

June 2011.A total of 60 patients with ischemic stroke were included in this study. In this study normal range of plasma factor viii activity was defined by 50-150% and elevated range by >150%.The severity of carotid stenosis was defined by mild as <50%,moderate as 50-69% and severe as >70%.

acute thrombotic event Study population was WHO defined stroke patients, ischemic in type, confirmed by CT scan of head/MRI of brain, presented after 7 days after the event. The sampling technique was purposive and included both sexes. Patients were excluded from the study who refuse to participate, with cardioembolic conditions on clinical and electrocardiographic grounds, like atrial fibrillation, aortic or mitral valve disease, recent myocardial infarction (<6 weeks), prosthetic cardiac valve, heart failure, patients with, acute inflammatory conditions, malignancy, liver & renal disease, pregnancy, history of recent surgery.

**Statistical analysis:**

All data were recorded systematically in preformed data collection form and data were expressed as mean and standard deviation and qualitative data as frequency distribution and percentage. Risk factors were analyzed by Chi square test. Statistical analysis was performed by using SPSS for windows version 16.0. 95% confidence limit was taken. Probability value <0.05 was considered as level of significance.

**Observations and Results:**

This cross sectional study was conducted in the Department of Neurology, BSMMU, Dhaka from July'2009 to June' 2011 for duration of two years. Total 60 ischemic stroke patients were enrolled in this study. The findings of the study are presented here.

**Table-I**

*Age distribution of the study population (n=60)*

| Age | Number of Patients | Percentage |
|---|---|---|
| £40 | 4 | 6.7 |
| 41 – 50 | 12 | 20.0 |
| 51 – 60 | 19 | 31.7 |
| 61 – 70 | 17 | 28.3 |
| 71 – 80 | 7 | 11.7 |
| >80 | 1 | 1.7 |
| Mean ±SD | 58.0±10.7 | |
| Range | 35-85 | |
| Total | 60 | 100 |

The study included 60 patients and the mean age was 58.0±10.7 years with range from 35 to 85 years. Nearly one third 19(31.7%) of the patients was found in the age group of 51-60 years. The results are shown in the table I.

**Table-II**

*Sex distribution of the study population(n=60)*

| Sex | Number of Patients | Percentage |
|---|---|---|
| Male | 37 | 61.7 |
| Female | 23 | 38.3 |
| Total | 60 | 100 |

Table II shows the sex distribution of the patients and it was found that 37(61.7%) male and 23(38.3%) female. Male female ratio was almost 1.6:1 in this study patient.

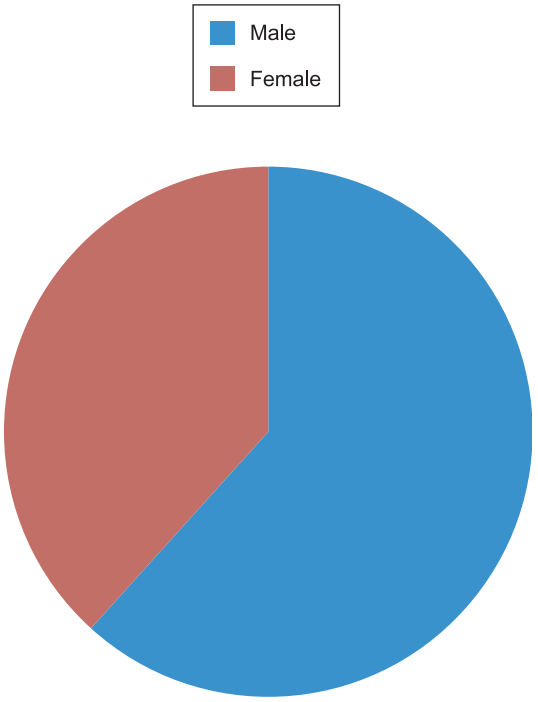


**Fig.-1:** *Pie chart shows sex distribution*

**Table-III**

*Distribution of 60 study population according to socioeconomic condition*

| Characteristics | Carotid stenosis >50% (n=30) | | Carotid stenosis <50% (n=30) | | P Value |
|---|---|---|---|---|---|
| Income (TK.) | N | % | n | % | |
| <10.000 | 8 | 26.67 | 13 | 43.33 | $0.175^{ns}$ |
| >10.000 | 22 | 73.33 | 17 | 56.67 | |
| Total | 30 | 100 | 30 | 100 | |

NS=Not significant
P value reached from chi square test.

In patient with >50% carotid stenosis, 8(26.67%) had monthly family income of d" 10,000 taka and 22(73.33%) had monthly family income of > 10,000 taka. In patient with <50% carotid stenosis, 13(43.33%) had monthly family income of <10,000 taka and 17(56.67%) had monthly family income of > 10,000 taka. No Significant (P>0.05) difference regarding socioeconomic status was found between < 50% and >50% Carotid Stenosis. The results are shown in the table III.

**Table-IV**

*The distribution and Status of Carotid Stenosis (n=60)*

| Carotid Stenosis | Number of patients | Percentage |
|---|---|---|
| Mild | 30 | 50.0 |
| Moderale | 16 | 26.7 |
| Severe | 14 | 23.3 |
| Total | 60 | 100 |

Among the 60 patients of the study showed mild Carotid Stenosis in 30 patients (50%), moderate carotid stenosis in 16 patients (26.7%) and severe carotid stenosis in 14 patients (23.3%) The results were shown in table IV.

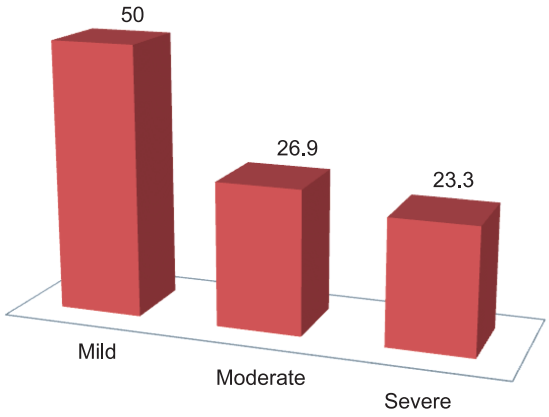


**Fig.-2:** *Bar diagram shows status of carotid stenosis*

**Table-V**

*Distribution of the study of subjects whose age was a risk factor for carotid stenosis (n=60)*

| Age group | Carotid stenosis >50% (n=30) | | Carotid stenosis <50%(n=30) | | OR | (95%CI) | P Value |
|---|---|---|---|---|---|---|---|
| | n | % | N | % | | | |
| >50 years | 28 | 93.33 | 12 | 40 | 21.33 | 3.71-85.7 | $0.001^{s}$ |
| <50 years | 2 | 6.67 | 18 | 60 | | | |
| Total | 30 | 100 | 30 | 100 | | | |

S=Significant
P value reached from chi square test.

In patient with >50% carotid stenosis, 28(93.33%) had age >50 years and 2(6.67%) had age d"50years. In patient with <50% carotid stenosis, 12(40%) had age>50 years and 18(60%) had age d"50years. Significant difference (p<0.05) was found regarding severity of carotid stenosis in age group betweend"50 years and >50 years. The results were shown in table V.

**Table-VI**

*Distribution of sex as a risk factor for carotid stenosis (n=60)*

| Sex | Carotid stenosis >50% (n=30) | | Carotid stenosis <50%(n=30) | | OR | (95%CI) | P Value |
|---|---|---|---|---|---|---|---|
| | n | % | N | % | | | |
| Male | 17 | 56.67 | 20 | 66.64 | 0.65 | 0.20-2.11 | 0.425$^{ns}$ |
| Female | 13 | 43.33 | 10 | 33.36 | | | |
| Total | 30 | 100 | 30 | 100 | | | |

NS=Not significant

P value reached from chi square test.

**Table-VII**

*Distribution of smoking as a risk factor for carotid stenosis (n=60)*

| Smoking | Carotid stenosis >50% (n=30) | | Carotid stenosis <50%(n=30) | | OR | (95%CI) | P Value |
|---|---|---|---|---|---|---|---|
| | n | % | N | % | | | |
| Yes | 22 | 73.33 | 21 | 70 | 1.18 | 0.33-4.19 | 0.774$^{ns}$ |
| No | 8 | 26.67 | 9 | 30 | | | |
| Total | 30 | 100 | 30 | 100 | | | |

NS=Not significant

P value reached from chi square test.

**Table-VIII**

*Distribution of hypertension as a risk factor for Carotid Stenosis (n=60)*

| Hypertension | Carotid stenosis >50% (n=30) | | Carotid stenosis <50%(n=30) | | OR | (95%CI) | P Value |
|---|---|---|---|---|---|---|---|
| | n | % | N | % | | | |
| Yes | 26 | 86.67 | 15 | 50 | 6.50 | 1.59-28.69 | 0.002$^{s}$ |
| No | 4 | 13.33 | 15 | 50 | | | |
| Total | 30 | 100 | 30 | 100 | | | |

S= Significant

P value reached from chi square test.

**Table-IX**

*Distribution of diabetes mellitus as a risk factor for carotid stenosis (n=60).*

| Diabetes | Carotid stenosis >50% (n=30) | | Carotid stenosis <50%(n=30) | | OR | (95%CI) | P Value |
|---|---|---|---|---|---|---|---|
| | n | % | N | % | | | |
| Yes | 16 | 53.33 | 7 | 23.33 | 3.76 | 1.09-13.34 | 0.016[s] |
| No | 14 | 46.67 | 23 | 76.67 | | | |
| Total 30 | | 100 | 30 | 100 | | | |

S= Significant

P value reached from chi square test.

**Table-X**

*Distribution of dyslipidaemia as a risk factor for carotid stenosis (n=60)*

| Dyslipidaemia | Carotid stenosis >50% (n=30) | | Carotid stenosis <50%(n=30) | | OR | (95%CI) | P Value |
|---|---|---|---|---|---|---|---|
| | n | % | N | % | | | |
| Yes | 17 | 56.67 | 20 | 66.67 | 0.65 | 0.20-2.11 | 0.425[ns] |
| No | 13 | 43.33 | 10 | 33.33 | | | |
| Total | 30 | 100 | 30 | 100 | | | |

NS=Not significant

P value reached from chi square test.

**Table-XI**

*Distribution of study of Factor VIII as a risk factor for carotid stenosis (n=60)*

| Factor activity | Carotid stenosis >50% (n=30) | | Carotid stenosis <50%(n=30) | | OR | (95%CI) | P Value |
|---|---|---|---|---|---|---|---|
| | n | % | N | % | | | |
| High | 7 | 23.33 | 2 | 6.67 | 4.26 | 0.70-33.16 | 0.072[ns] |
| Normal | 23 | 76.67 | 28 | 93.33 | | | |
| Total | 30 | 100 | 30 | 100 | | | |

NS=Not significant

Among the patient with e”50% carotid stenosis, 17(56.67%) had male gender and 13(43.33%) had female gender. In patient with <50% carotid stenosis, 20(66.67%) had male gender and 10(33.33%) had female gender. Severity of carotid stenosis was not significant (p>0.05) among male and female gender. The results were shown in table VI.

In patient with e”50% carotid stenosis, 22(73.33%) were smoker and 8(26.67%) were non smoker. In patient with <50% carotid stenosis, 21(70%) were smoker and 9(30%) were non smoker. No significant difference (p>0.05) was found between smokers and non-smokers group related to severity of carotid stenosis. The results were shown in table VII.

In patient with e”50% carotid stenosis, 26(86.67%) were hypertensive and 4(13.33%) were normotensive. In patient with <50% carotid stenosis, 15(50%) were hypertensive and 15(50%) were normotensive. Severity of carotid stenosis among hypertensive and normotensive group was statistically significant (p<0.05).The results were shown in table VIII.

In patient with e”50% carotid stenosis, 16(53.33%) diabetic and 14(46.67%) were non diabetic. In patient with <50% carotid stenosis, 7(23.33%) diabetic and 23(76.67%) were non diabetic. Significant difference (p<0.05) was found between diabetic and non-diabetic group related to severity of carotid stenosis. The results were shown in table IX.

In patient with e”50% carotid stenosis, 17(56.67%) were dyslipidaemic and 13(43.33%) were normal lipid profile. In patient with <50% carotid stenosis, 20(66.67%) had dyslipidaemic and 10(33.33%) had normal lipid profile . Severity of carotid stenosis was not significant (p>0.05) between dyslipidaemic and non-dyslipidaemic group. The results were shown in table X.

In patient with e”50% carotid stenosis, 7(23.33%) had high factor VIII activity and 23(76.67%) had normal factor VIII activity. In patient with <50% carotid stenosis, 2(6.67%) had high factor VIII activity and 28(93.33%) had normal factor VIII activity. No significant difference (P>0.05%)between high factor VIII activity and normal factor VIII activity related to severity of carotid stenosis. The result are shown in table XI.

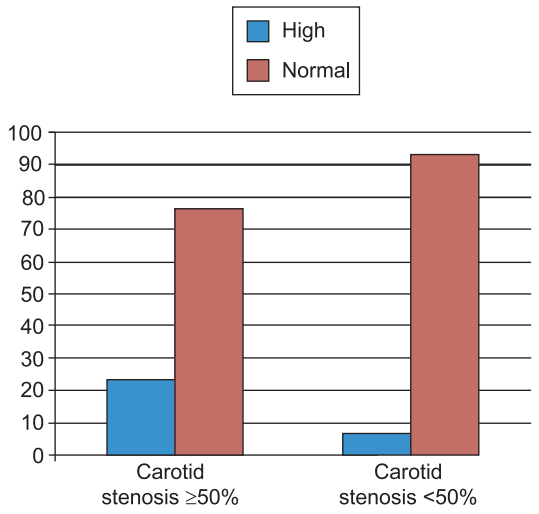


**Fig.-3:** *Bar diagram shows relation between severity of carotid stenosis and factor VIII activity*

**Discussion:**

This cross sectional study was carried out with an aim to explore the association between carotid atherosclerosis and high factor VIII activity in patients with ischemic stroke. For this purpose, a total 67 patients of ischemic stroke age ranging from 35 to 85 years were purposively selected who attended in the Department of Neurology of Bangabandhu Sheikh Mujib Medical University, Dhaka during July, 2009 to June, 2011. Among them, seven patients were excluded from the study because of four had chronic kidney disease, two had valvular heart disease and one had chronic liver disease. Finally 60 patients were enrolled in this study .

Previous population based study done by Beamer et al[16] shown the mean age of the patients having ischemic stroke was 66±8 years, whereas the mean age of patients in our study was 58.0±10.7 years.

In this study it was observed that 61.7% were male and rest 38.3% were female patients and male female ratio was 1.6:1 In a similar study done previously by Khan[17] the ratio was found 2.75:1. Another study found M:F 2.53:1 in stroke patients irrespective of types[18] . The present hospital based study may not reflect the actual ratio in the community because in our society female stroke patients usually do not get admitted to hospital because of religious ground and lack of attention by their family.

Regarding monthly family income, no significant (P>0.05) difference was found between <50% and >50% carotid stenosis in this study.

In the present cross sectional study of 60 ischemic stroke patients we found mild carotid stenosis in 30 patients (50%), moderate stenosis in 16 patients (26.7%) and severe stenosis in 14 patients (23.3%).This observation is supported by Hadi et al[19] and Razzaq et al[20].

Change et al [21] in their cross sectional study found the strongest correlation of age with >50% carotid stenosis. They had also explored, after age 20, every 10 year increase in age would double the risk of having <50% carotid stenosis to becoming >50% carotid stenosis. The present study also showed that age more than 50 year is a significant predictor of >50% carotid stenosis (OR: 21.33, 95%. CI: 3.71-

85.7, P=0.001). Similar observations were obtained from different investigators[22,23]. Our study did not find any association between gender and carotid stenosis (OR: 0.65, 95% CI: 0.20-2.11, P=0.425). Similar result was obtained in an other study(OR:0.055,95%CI:0.30-0.99,P value0.06)[23].However O'Leary et al[24] and Caplan et al[25] observed male sex was a significant predictor of moderate to severe carotid stenosis than female.

SU et al[26] in their community based observational study with 3602 ischemic stroke patients in Taiwan shows smoking is a significant predictor of >50% carotid stenosis (OR: 1.52, 95% CI: 1.30-1.89, P value <0.05) where as our study failed to display any association between smoking and carotid stenosis(OR:1.18,95%CI:0.33-4.19,P value=0.774). The difference is probably due to difference in selection criteria and small sample size in this study. Further large population based longitudinal studies are needed to identify the relation between smoking and severity of carotid stenosis.

The present study shows that hypertension is significant predictor of >50% carotid stenosis (OR: 6.50, 95% CI: 1.59-28.69, P=0.002).Similar observations were found by SU et al. [26] and Fisher et al.[27].

The present study reveals significant association between diabetes and severity of carotid stenosis (OR: 3.76, 95% CI: 1.09-13.34, P=0.016). Hillen et al [30] in their observational cross sectional study found a significant correlation between carotid stenosis and diabetes (OR: 2.92, 95% CI: 0.98-11.23, P<0.05).Several studies have shown diabetes is an independent risk factor of carotid atherosclerosis and atherothrombotic cerebral infarction[28,29],whereas Change et al. failed to confirm the result (OR: 1.28, 95% CI: 0.77-2.11, P= 0.34)[21].

Our study did not found any association between dyslipidaemia and severity of carotid stenosis (OR: 0.65, 95% CI: 0.20-2.11, P value 0.425).Several hospital based case control studies have suggested an association between high cholesterol and extracranial carotid stenosis[31,32] whereas other population based study showed a conflicting result both for high cholesterol and triglyceride in the prediction of carotid intima-media thickness[33].

The potential source of bias may be related to the study design since lipid lowering therapy were not taken into account. Further, multiple measurement and time integrated effect of longitudinal study are needed to identify the relation between dyslipidaemia and the severity of carotid stenosis.

In this study, patient with e"50% carotid stenosis, 7(23.33%) had high factor VIII activity and 23(76.67%) had normal factor VIII activity. In patient with <50% carotid stenosis, 2(6.67%) had high factor VIII activity and 28(93.33%) had normal factor VIII activity. No significant difference was found (P>0.05%) between high factor VIII activity and normal factor VIII activity related to severity of carotid stenosis. Our present study did not found any association between high factor VIII activity and severity of carotid carotid stenosis(OR:4.26,95% CI:0.70-33.16,P=0.072). Pan et al[34] in their case control study found high factor VIII activity was associated with moderate and severe carotid stenosis (OR: 3.35, 95% CI: 0.55-3.33, P value <0.05). Our study is not consistent with this study. The difference of result probably due to a potential source of bias, demographic variations between Chinese and Bangladeshi population and difference of study design. On the other hand as Von Willebrand antigen is the carrier protein for factor VIII, both factor VIII and Von Willebrand antigen should be measured to access the association between high factor VIII activity and carotid atherosclerosis.

The application of multiple measurements and time integrated effect of longitudinal study may further evaluate the association between degree of carotid stenosis and high factor VIII activity.

In regard to the relation between carotid stenosis and risk factors, evidence from the various literatures are quite discordant. Of all the risk factors investigated age, hypertension and diabetes has independent association with severity of carotid stenosis. Although sex, smoking, dyslipidaemia and high factor VIII activity were considered important risk factors for atherosclerosis, the present study did not find any association.

**Conclusion:**

The aim of the study was to explore the association between carotid atherosclerosis and high factor VIII activity in ischemic stroke. The present study did not find any association between severity of carotid atherosclerosis and high factor VIII activity in ischemic stroke.

**Limitation of the study**

This is a study based on data collected from Neurology department of BSSMU, Dhaka. The patients with ischemic stroke, who do not attend this department, were not included in this study population. Therefore, the sample lacks representation of the population. Furthermore, many confounding variables like age, sex, smoking, hypertension, diabetes, dislipidaemia & dietary habit may influence the result of the study. On the other hand, as Von Willebrand factor is the carrier protein for factor VIII further studies are needed to elucidate the role of both protein in relation to carotid atherosclerosis.

In order to include all of the patients suffering from ischemic stroke it will require such a study that would be conducted over a large population of vast area. But such an extensive study was not feasible for several constraints like time, resources and financial etc.

**Recommendations**

Besides traditional risk factors such as hypertension, diabetes and dyslipidaemia additional treatable risk factors that can be easily measured and highly prevalent in the general population. Although this study did not find any association between carotid atherosclerosis and high factor VIII activity, further application of multiple measurements and time-integrated effect of longitudinal study may evaluate the association between severity of carotid atherosclerosis and high factor VIII activity in ischemic stroke.

**References:**


1. Aho K, Harmsen P, Hatano S. Cerebrovascular disease in the community : results of a WHO collaborative study. *Bull WHO*1980; 58: 133-230.
2. Panicker JN, Thomas M, Pavithram k, Nair D, Sarma PS. 'Morbidity predictors in ischemic stroke' *Neurology India* 2003 51:49-51.
3. Markus HS.Stroke:Causes and clinical feature.*Medicine and International.*2005;32:36-40.
4. Kalache, A, Aboderin . Stroke the global burden health policy and planning 1995; 10:.l-21.
5. Neyer JR,Greenlund KJ, Denny CH, Keenan NL,Casper.Heart disease and stroke prevention :*National center for chronic disease and health protection* 2007;56 :469-74.
6. Singh N, Pearce WH.Atherosclerosis disease of the carotid artery. *Medscap* 2010;43:231-34.
7. Ropper AH, Brown RH. 'Cerebrovascular Diseases', Adams and victor's Principles of Neurology, 8th edn, *McGraw-Hill .*2005;1:661-740.
8. Hankey GJ. 'Potential new risk factors for ischemic stroke: What is their potential?,*'Stroke* 2000;37:2181-88.
9. Ullah AKMA, Miah GA, Islam KM, 'Pattern of admission in the department of neurology IPGMR- A one year study,*' Bangladeh Journal of Neuroscience* 1992.;8:17-23.
10. Rosendaal FR,Varkamp I,Smit C,Brocker-Vriends AHJT,van Dijck H,Vandenbroucke JP et al.Mortality and causes of death in Dutch haemophiliacs 1973-1986 *Thromb Br.J Haematol.*1989;71:71-76.
11. Firkin F, Chesterman C, Penington D, Rush B, 2005. Coagulation disorders. De Gruchys Clinical haematology in medical practice. Fifth revised edition. Blackwell science Ltd.London2005;76: 407-8
12. Blann A.Von willebrand factor and the endotheliumin vascular disease. Br J Biomed Sci.1993;50:125-134.
13. Tracy RP,Arnold AM, Ettinger W, Fried L, Meilahn E,Savage P.The relation ship of fibrinogen and factor VII and VIII toincident cardiovascular disease death in ealderly.*Arteriosclr Throm Vasc Biol*.1999;19:776-83.

14. Folsom AR,Wu KK,Shahar E,David CE.Atherosclerosis Risk in Communities(ARIC) Study Investigators. Association of hemostatic variables with prevalent cardiovascular disease and asymptomatic carotid artery atherosclerosis. *Arterioscler Thromb* 1993; 13:1829-36.

15. Jahromi AS, Cina CS, Liu Y, Clase CM. Sensitivity and Specificity of colour duplex ultrasound measurement in the estimation of internal carotid artery stenosis:A systemic review and meta-analysis.2005;41:962-72.

16. Beamer NB, Coull BM, Clark WM, Wynn M. 'Microalbuminuria in ischemic stroke,' *Arch Neurol*1999; 56:699-702.

17. Khan MRK . 'Relationship between blood lipids, lipoproteins and ischemic stroke,' [Thesis].2000 Dhaka, Bangabandhu Sheikh Mujib Medical University.

18. Hannan MA.'Study of seasonal variation of stroke'[Thesis]..1999.Dhaka: Bangabandhu Sheikh Mujib Medical University

19. Hadi NU, Rushhana, Awan KH, Iqbal N.Frequency of carotid artery stenosis in ischemic stroke by usuing carotid doppler ultrasonography in a teaching hospital.*Gomal journal of medical science.*2009;7:86-95.

20. Razzak A, Khan B, Jadoon C Baig S. Carotid doppler ultrasonography in young stroke patients.*Pak Med Associ*.1999;49:97-99.

21. Change CH, Chang YJ, Lee TH, Hsu KC, Ryu SJ.Risk factors of carotid stenosis in first-ever ischemic stroke.*Acta Neurol Taiwan* 2006;15:237-43.

22. Stevens J,Cai J,Pamuk ER.The effect of age on the association between body mass index and mortality.*N Engl J Med* 1998;55:1-7.

23. Howard G, Sharrett AR, Heiss G. Carotid artery intimal- medial thickness distribution in general populations as evaluated by B-mode ultrasound. ARIC Investigators. *Stroke.* 1993;24 :1297-304.

24. OLeary DH, Polak JF, Kronmal RA. Distribution and correlates of sonographically detected carotid artery disease in the cardiovascular health study. The CHS Collaborative Research Group. *Stroke*. 1992;23:1752-60.

25. Caplan LR, Gorelick PB, Hier DB .Race,sex and occlucive cerebrovascular disease. *Stroke*.1986;17:648-55.

26. Su TC, Jeng JS, Chien KL. Hypertension status is the major determinant of carotid atherosclerosis: a communitybased study in Taiwan*. Stroke* 2001;32:2265-71.

27. Fisher CM. Lacunar strokes and infarcts: a review. *Neurology* .1982;32:871-76

28. Abbott RD, Donahue RP, MacMahon SW. Diabetes and the risk of stroke. The Honolulu Heart Program. *JAMA*1987; 257:949-52.

29. Barrett-Connor, E, Khaw, K. Diabetes mellitus: an independentrisk factor for stroke? *Am J Epidemiol* 1988;128:116-23.

30. Hillen T, Nieczaj R, Munzberg H. Carotid atherosclerosis, vascular risk profile and mortality in a population based sample of functionally healthy elderly subjects: the Berlin ageing study. *J Intern Med*2000;247:679-88.

31. Ford CS, Course JR, Howard G.Therole of carotid bifurcation atherosclerosis. Ann Neurol.1985;17:301-03.

32. Anderson, K.M, Castelli, W.P, Levy, D. Cholesterol and mortality: 30 years of follow-up from the Framingham Study. *JAMA* 1987;l257:1276-80.

33. Cooper GR, Smith SJ, Myers GL. Estimating and minimizing effects of biologic sources of variation by relative range when measuring the mean of serum lipids and lipoproteins. *Clin Chem* 1994;l40:227-32.

34. Pan WH, Bai CH, Chen JR, Chiu HC. Association between carotid atherosclerosis and high factor viii activity, dyslipidaemia and hypertension. Stroke 1997;28(1):88-94.

Bangladesh Journal of Neuroscience 2014; Vol. 30 (1) : 11-15

# Identification of Central Nervous System Complications Related To Eclampsia

MURSHED BAQUI [1], MOHAMMAD SHAH JAHIRUL HOQUE CHOWDHURY[2], MD. TAUHIDUL ISLAM CHOWDHURY[3], PARITOSH KUMAR SARKAR[4], MD. NAHIDUL ISLAM[5], QUAZI DEEN MOHAMMAD[6]

**Abstract:**

***Background:*** *Eclampsia is a complex hypertensive disorder of pregnancy affecting multiple systems. Central nervous system is commonly affected and is a cause of significant morbidity and mortality in women. Various neurological complications are found in eclamptic patients.* ***Aims and Objectives:*** *The aim of this study was to explore the various CNS complications related to eclampsia.* ***Materials and Methods:*** *This retrospective observational study was carried out in the 'Eclampsia ward' of Department of Gynaecology and Obstetrics of Dhaka Medical College Hospital (DMCH), during the period of November, 2010 to October, 2011 in patients admitted with a history of eclampsia. Fifty(50) patients were included in this study. Data was collected by a semi-structured questionnaire. The patients were interviewed and a complete clinical examination was performed by the investigator. It was reviewed by a consultant neurologist.* ***Results & conclusion:*** *The results revealed that patients had headache, comatose state, stroke, focal neurological deficit, post partum psychosis, aphasia and cortical blindness. Death occurred in 6.0% of patients. As eclampsia is the third major cause of pregnancy related maternal death in Bangladesh (16%), and no study has yet not been reported in this field, this study might help in formulating management plan; predict prognosis and functional recovery in the individual cases.*

## Introduction:

Eclampsia is one of the dreaded complications of pregnancy as it carries high morbidity and mortality to the mother and baby. The incidence of eclampsia depends on a variety of factors and varies widely from region to region.

Both the International Society for the Study of Hypertension in Pregnancy (ISSHP) and the Working group on High Blood Pressure in Pregnancy (WGHBPP 1990) have recommended the following definitions. Accordingly pre-eclampsia is defined as occurrence of hypertension along with proteinuria or edema or both after 20 weeks of gestation and when convulsions or unexplained coma occur in the setting of gestational hypertension, the condition is referred to as eclampsia. In this context, hypertension is defined as blood pressure above 140/90 mmHg (measured on two occasions, 4 h apart) and proteinuria as urinary protein excretion over 300 mg per 24 h (~30 mg/dl on random sample or e" 1+ on dipstick). It is more common in developing countries because illiteracy, lack of health awareness and education, poverty, and superstitious believes prevent women from seeking medical advice during pregnancy[1,2].

The incidence of eclampsia is high in Bangladesh-7.9% (not including pre-eclampsia), according to the results of a house-to-house survey[3].

A neurological complication is defined as any manifestation secondary to neuronal dysfunction in patients with eclampsia. Common symptoms include

1. Medical Officer, National Institute of Neurosciences and Hospital, Sher-E- Bangla Nagar, Dhaka.
2. Assistant Professor cum Resident Physician, National Institute of Neurosciences and Hospital, Sher-E- Bangla Nagar, Dhaka.
3. Assistant Professor, National Institute of Neurosciences and Hospital, Sher-E- Bangla Nagar, Dhaka.
4. National Institute of Neurosciences and Hospital, Sher-E- Bangla Nagar, Dhaka.
5. Registrar, National Institute of Neurosciences and Hospital, Sher-E- Bangla Nagar, Dhaka.
6. Professor, National Institute of Neurosciences and Hospital, Sher-E- Bangla Nagar, Dhaka

headache, blurring of vision, aphasia, facial nerve palsy, cerebrovascular accident, transient ischaemic attack, cerebral edema, comatose state, postpartum psychosis, cortical blindness, transient blindness, retinal edema etc[4].

The World Health Organization (WHO) estimates that only 40% of births in developing countries take place in health facilities[5].When delivery care is sought, it is done late, after a lot of delays and this contributes to maternal mortality. The aim of this study to identify the central nervous system complications and its pattern related to eclampsia.

Methods and Materials: This retrospective hospital based observational study was carried out in the Eclampsia ward of Department of Gynaecology and Obstetrics, Dhaka Medical College Hospital. The study period was 1st November 2010 to 31st October 2011. Fifty(50) eclamptic patients were sampled by purposive (non-random) sampling. Patients with features of eclampsia confirmed by consultant gynaecologist and having central nervous system complications diagnosed clinically and evaluated by neurologist were included. Patients having any pre-existing neurological deficit were excluded. Data was collected by a semi-structured questionnaire. The patients of eclampsia were identified by a consultant gynaecologist on the basis of diagnostic criteria[1,2]. All patients of eclampsia during the study period were interviewed and examined. Patients with central nervous system complications were isolated. A complete clinical examination was performed by the investigator after 24 hours of proper management of eclampsia and was repeated 24 hourly for three occasions for newer central nervous system features. It was reviewed by a consultant neurologist before reaching final diagnosis. Information was obtained from the patient as well as from the witness usually a family member or hospital staff. Clinical features and examination findings were noted. Those patients found having central nervous system complications in clinical examination were sent for CT scan of head in Department of Radiology and Imaging, Dhaka Medical College Hospital. CT scans of head were performed by standard CT scan machine (Somatom emotion Duo, Duel slice, Siemens). The images were reported by the same radiologist in all cases. Relevant data and findings were recorded in a preformed data sheet for each patient. The different variables of the data were analyzed with the help of SPSS (Statistical Program for Social Science) software version 16. Statistical analysis was done by appropriate procedure. The results were presented as tables and analyzed accordingly. Prior to the commencement of this study, the research protocol was approved by the thesis committee (Local Ethical Committee).

**Results:**

In this retrospective hospital based observational study a total number of 50 eclamptic patients having central nervous system complications were enrolled and the results of the study were presented here.

**Table-I**

*Age distribution of the eclamptic patients associated with CNS complications (n=50)*

| Age of the patient (Years) | Number of patients | Percentage |
|---|---|---|
| 15-20 | 23 | 46.0 |
| 21-25 | 14 | 28.0 |
| 26-30 | 5 | 10.0 |
| 31-35 | 6 | 12.0 |
| 36-39 | 2 | 4.0 |
| Total | 50 | 100.0 |

Range : 15-39 years; Mean±SD : 22.9 ± 6.1

Table-I showed that the mean age of patients having features of eclampsia was found 22.9 ± 6.1 years ranging from 15-39 years and maximum number (46.0%) was found in the age group of 15-20 years. 28.0% of patients were found in the age group of 21-25 years and only 4.0% of patient were above 35 years of age.

**Table-II**

*Other socio-demographic characteristics of the subjects (n=50)*

| Variables | | Patients | |
|---|---|---|---|
| | | Number | Percentage |
| Habitat | Urban | 18 | 36.0 |
| | Rural | 32 | 64.0 |
| Education | Illiterate | 12 | 24.0 |
| | Primary | 29 | 58.0 |
| | Secondary | 6 | 12.0 |
| | SSC | 3 | 6.0 |
| Family Monthly income (Tk.) | <10000 | 39 | 78.0 |
| | 10001-20000 | 9 | 18.0 |
| | 20001-30000 | 2 | 4.0 |

Table-II showed sample descriptions of socio-demographic variables that 36.0% of patients were residing in urban area and 64.0% in rural area. 58.0% of patients were educated up to primary level, and 24.0% were illiterate. 78.0% of patients had a monthly family income of less than 10,000 Tk.

**Table-III**

*Distribution of antenatal care in eclamptic patients with CNS complications (n=50)*

| Antenatal care | Number of patients | Percentage |
|---|---|---|
| Never | 39 | 78.0 |
| 1-3 times | 11 | 22.0 |
| Total | 50 | 100.0 |

Table-III showed that 78.0% of the patients never went to any antenatal care center for present pregnancy and only 22.0% of the patients received antenatal care for 1 to 3 times.

**Table-IV**

*Distribution of time of development of eclampsia with central nervous system complications (n=50)*

| Time | Number of Patient | Percentage |
|---|---|---|
| Prepartum | 38 | 76.0 |
| Postpartum | 12 | 24.0 |
| Total | 50 | 100.0 |

Table-IV showed 76.0% of patients had prepartum eclampsia whereas 24.0% had post partum eclampsia that developed central nervous system complications.

**Table-V**

*Distribution of gestational age of pregnancy of prepartum eclamptic patient at admission (n=38)*

| Gestational age (Weeks) | Number of Patients | Percentage |
|---|---|---|
| 26-28 | 2 | 5.26 |
| 29-32 | 5 | 13.16 |
| 33-36 | 16 | 42.11 |
| 37-40 | 15 | 39.47 |
| Total | 38 | 100.00 |

Range : 26-40 weeks; Mean±SD : 35.1±3.4 weeks

Table-V showed that 42.11% of patients developed eclampsia during the gestational age of 33-36 weeks and 39.47% of patients at their late pregnancy. Only 18.42% of patients had eclampsia before gestational age of 32 weeks. Mean gestational age was 35.1 weeks with a standard deviation of 3.4 weeks.

**Table-VI**

*Distribution of parity of eclamptic patients with CNS complications (n=50)*

| Parity | Number of Patients | Percentage |
|---|---|---|
| Primigravida | 29 | 58.0 |
| 2-3 | 13 | 26.0 |
| >4 | 8 | 16.0 |
| Total | 50 | 100 |

Table-VI showed 58.0% of patients who developed eclampsia with central nervous system complications were primigravida while 26.0% of patients had 2-3 parity and only 16.0% of patients had e”4 parity.

**Table-VII**

*Pattern of CNS complications in eclamptic patients (n=50)*

| Complications | Number of Patients* | Percentage |
|---|---|---|
| Aphasia | 6 | 12.0 |
| Headache | 23 | 46.0 |
| Focal neurological deficits | 9 | 18.0 |
| Stroke | 11 | 22.0 |
| Cortical blindness | 4 | 8.0 |
| Post partum psychosis | 8 | 16.0 |
| Comatose state | 17 | 34.0 |
| Death | 3 | 6.0 |

*Multiple responses

Table-VII. showed that 46.0% of patients had headache, then 34.0% had comatose state, 22.0% stroke, 18.0% focal neurological deficits, 16.0% post partum psychosis, 8.0% cortical blindness. Death occurred in 6.0% of cases.

**Discussion:**

The present study was carried out with an aim to find out central nervous system complications related to eclampsia in the perspective of

Bangladesh. The socio-demographic profile (age, body weight, socio-economic status and parity) of the patients, antenatal care, gestational age, and its relation to develop central nervous system complications in eclampsia and maternal outcome were evaluated.

A Clinical Study of 100 Cases of Eclampsia In Rajshahi Medical College Hospital (RMCH) found the socioeconomic status, level of education, the quality of patients' nutrition and antenatal care of the patients were very low[6]. Another study found that eclampsia was more common below 20 years (6.97%) of age group, primi-mother (7.43%), lower socio-economic status (5.67%) and in unbooked (6.41%) cases[7]. The current study also featured almost same findings in the patients of eclampsia who developed central nervous system complications such as age below 20 years, primigravida, late gestational age, lower socioeconomic status, illiterate or primary level of education, no or a few antenatal care. These results were comparable with other results.

In a study at Eclampsia ward in Dhaka Medical College Hospital in the year of 1998 to 2000 with 2956 eclamptic patients found the incidence of eclampsia with different complications was 21.0%, which included central nervous system complications with coma (2.9%)[8]. Eclampsia study in RMCH found only 4.0% of patient as eclampsia with central nervous system complications[6]. Another study in Mayo Hospital Lahore found 7.0% central nervous system complications in a study[9]. Sibai and Ustav (1995) found that about 6.5% of the patients with eclampsia develop neurological complications[10]. In this current study the incidence of central nervous system complications found were 4.77%. These findings were consisted with the current study. While Okanloma and Moodley (2000) in a study in Darban, South Africa found neurological complication rate only 0.9% which truly reflects its better health services of their community[7].

In the same study it was revealed that out of 140 eclamptic women with neurological complications it was found that 37.5% of patients had hemiparesis, 12.5% hemiplegia, 6.25% monoparesis, 18.75% facial nerve palsy, 12.5% transient blindness (<6 hours), 6.25% cortical blindness (>48 hours), 18.75% post partum psychosis, 6.25% transient ischaemic attack and 6.25% comatose state[7]. Sibai and Ustav (1995) found followings as common neurological complications in eclampsia that include cortical blindness, aphasia, limb weakness, psychosis, coma or cerebrovascular accident[10]. Douglas et al. (1994) [11] ,Katz et al. (2000) [12] and Chames et al. (2002) [13] in separate studies found that persistent occipital or frontal headaches, blurred vision, photophobia, and altered mental status. Patients might experience at least one of these symptoms in 59–75% of the cases. Headaches were reported by 50– 75% of the patients, whereas visual changes were reported in 19–32% of the patients[11-13].In the current study shown that 46.0% of patients had headache, then 34.0% had comatose state, 22.0% stroke, 18.0% focal neurological deficits, 16.0% post partum psychosis, 8.0% cortical blindness. Death occurred in 6.0% of cases. These findings support the present study.

There were different range of maternal mortality in different region and different areas of same region. Eclampsia is an important cause of maternal death in many parts of Africa, Asia, the Caribbean, and Latin America. Nigeria has one of the highest rates of maternal mortality in the world. There are several studies in Nigeria. All of those study showed that eclampsia has been noted to be among the most common causes of maternal mortality in Nigeria. Tukur et al. (2007) [14] in Birnin Kudu found eclampsia contributed 43.1%, while Igbafe et al. (2004) [15] in Yenagoa 40.0% and Aboyeji et al. (2004) [16] in Ilorin 27.5% of all maternal deaths. Rathore et al. (2010) found maternal mortality due to eclampsia was around 24.0% in a hospital based study in Lahore, Pakistan[9]. In Rajshahi Medical College Hospital, Khanum et al. (2004) found maternal mortality due to eclampsia was 16.0%[6].[6]Pal (2011) found that the overall maternal mortality rate was 6.05% in Burdwan Medical College Hospital, Kolkata[7].In this current study maternal mortality due to central nervous study complications was 6.0%.

**Conclusion:**

Central nervous system complications remained as important cause of morbidity and mortality of eclampsia of pregnancy. Younger age groups, low

socioeconomic status, lack of education, primigravida, avoidance of antenatal care were commonly observed in patients who developed eclampsia with central nervous system complications.

**Referrances:**


1. Davey DA, MacGillivray I. The classification and definition of the hypertensive disorders of pregnancy. Am. J. Obstet. Gynecol. 1988; 158:892-898.
2. WGHBPP (Working Group on High Blood Pressure in Pregnancy), 1990. Consensus report. Am. J. Obstet. Gynecol. 1990; 163: 1689-712.
3. BIRPERT. Bangladesh Institute of Research for Promotion of Essential and Reproductive Health and Technologies. Proceeding of Dissemination Workshop on Maternal Morbidity Study. Hotel Sheraton, Dhaka 1994.
4. Okanloma KA, Moodley J. Neurological complications associated with the pre-eclampsia/ eclampsia syndrome. International Journal of Gynecology & Obstetrics 2000; 71: 223-25.
5. WHO. Coverage of maternity care. A list of available information. Geneva, Switzerland: Maternal and newborn health/Safe Motherhood. 1997.
6. Khanum M, Ashraf F, Sahrin H: A Clinical Study of 100 Cases of Eclampsia In Rajshahi Medical College Hospital. TAJ Dec 2004; 17( 2):80-3.
7. Pal A, Bhattacharyya R, Adhikari S, Roy A, Chakrabarty D, Ghosh P, Banerjee C. in Eclampsia-scenario in a hospital- a ten years study. Bangladesh Med Res Counc Bull 2011; 37: 66-70
8. Begum MR, Begum A, Quadir E. et al: Eclampsia: Still a Problem in Bangladesh. Med Gen Med 2004; 6(4): 52.
9. Rathore R, Butt NF, Iqbal A, Khan MZU. Complications and outcome of patients of pre-eclampsia and eclampsia presenting to medical wards of Mayo Hospital Lahore. Ann King Edward Med Uni 2010;16(1):17-9.
10. Sibai BM, Ustav IM. Emergent management of puerperal eclampsia. Obstet. Gynecol. Clin. North Am. 1995; 22: 315-335.
11. Douglas KA, Redman CW. Eclampsia in the United Kingdom. *BMJ*. Nov 26 1994;309(6966):1395-400.
12. Katz VL, Farmer R, Kuller J. Preeclampsia into eclampsia: toward a new paradigm. Am J Obstet Gynecol 2000;182: 1389–96.
13. Chames MC, Livingston JC, Invester TS, Barton JR, Sibai BM. Late postpartum eclampsia: a preventable disease? Am J Obstet Gynecol 2002;186:1174 –7.
14. Tukur J, Umar BA, Rabi'u A. Pattern of eclampsia in a tertiary health facility situated at a semi rural town in Northern Nigeria. Ann Afr Med 2007;6:164-7.
15. Igbafe AA, Bariweni AC, Bennibor J, Gharoro EP. The Contribution of eclampsia to maternal mortality at the Federal Medical Center, Yenagoa. Trop J Obstet Gynaecol 2004;21:S9-10.
16. Aboyeji AP, Ijaiya MA, Fawole AA. Maternal mortality in a Nigerian teaching hospital: A continuing tragedy. Trop J Obstet Gynaecol 2004;21:S8.

Bangladesh Journal of Neuroscience 2014; Vol. 30 (1) : 16-22

# Asymptomatic Neuropathy in Recently Diagnosed Diabetic Patients: Electrophysiological Evaluation

ABU SALEH MD BADRUL HASAN[1], BIPLOB KUMAR ROY[2], KAZI GIASUDDIN AHMED[3], MD RAFIQUL ISLAM[4], AKM ANWAULLAH[4], HASAN ZAHIDUR RAHMAN [4], QUAZI DEEN MOHAMMAD[5], SK MAHBUB ALAM[6]

**Abstract:**

***Aim & background:*** *As significant electrophysiological changes are found in asymptomatic neuropathy in diabetes mellitus and electrophysiological studies of nerve conduction velocity are our most sensitive tools to quantify early abnormalities, therefore, we tried to find out status of asymptomatic peripheral nerve dysfunction in recently diagnosed diabetic patients in Bangladesh perspective. Method :This study was carried out at BSMMU and BIRDEM during November 2005 and April 2006. The study included 60 subjects, 30 recently diagnosed diabetic subjects (14 male, 16 female).*

*None had neuropathic symptoms or signs. All cases were selected randomly diagnosed by ADA criteria accepted by WHO. Thirty healthy controls with mean age comparable to that of diabetic subject were selected from the friends of the subjects and patients attending neurology outdoor of BSMMU. Result:Findings (mean±SD) were (case and control, respectively): Tibial nerve, DML 4.05±0.81 and 3.84±0.70 msec (P>0.10), CMAP 16.90±5.14 and 19.49±4.73 mV (P<0.05), MCV 45.43±4.55 and 48.24±4.72 m/s (P<0.05), and F latency 45.09±12.43 and 42.50±8.93 msec (P>0.10); peroneal nerve, DML 4.12±1.10 and 4.03±0.67 msec (P>0.50), CMAP 5.80±2.89 and 6.97±1.79 mV (P>0.05), MCV 43.10±8.89 and 48.27±3.56 m/s (P<0.01), and F latency 50.27±10.81 and 41.32±3.05 msec (P<0.001); median nerve, DML 3.57±0.46 and 3.55±0.52 msec (P>0.50), CMAP 16.33±4.24 and 17.84±3.73 mV (P>0.10) and MCV 55.16±5.33 and 57.70±4.33 m/s (P<0.05), and F latency 25.08±5.28 and 24.39±4.83 msec (P>0.50); and ulnar nerve DML 2.57±0.33 an 3.17±0.61 msec (P<0.001), CMAP 14.65±3.32 and 17.29±6.83 mV (P>0.05), MCV 55.74±5.00 and 58.50±5.13 m/s (P<0.05), F latency 25.09±5.35 and 25.82±3.33 msec (P>0.50); sural nerve, DSL 2.46±0.68 and 3.12±0.45 msec (P<0.001), SNAP 19.44±10.25 and 25.32±7.88 iV (P<0.05), SCV 49.95±10.22 and 52.46±3.96 m/s (P>0.10); median nerve, DSL 2.52±0.39 and 2.77±0.49 msec (P<0.05), SNAP 30.23±12.79 and 31.69±11.02 iV (P>0.50), and SCV 56.90±6.77 and 57.41±5.85 m/s (P>0.50); and ulnar nerve, DSL 2.03±0.39 and 2.48±0.49 msec (P<0.001), SNAP 29.30±14.36 and 30.72±10.76 iV (P>0.50), and SCV 60.96±8.38 and 57.93±7.15 m/s (P>0.10). Mean (±SD) $HbA_1c$ was significantly high (P<0.001) in case group (7.10±0.80%) compared to control (5.51±0.65%). Mean (±SD) SGPT showed no significant difference between case (36.10±13.02 u/L) and control (36.20±7.94 u/L). Similarly, mean (±SD) total cholesterol also showed no significant difference between case (201.57±37.56 mg/dl) and control (191.00±17.17 mg/dl).*

***Conclusion:*** *Motor nerve conduction parameters are affected more than sensory nerves and F-wave latencies are more frequently and early involved in these subjects. Abnormalities on nerve conduction was started in the feet rather than the hands.Clinical*

1. Assistant Professor and head of Department of Neurology, Dinajpur Medical College and Hospital, Dinajpur
2. Associate Professor of neurology, Sylhet MAG Osmani Medical College & Hospital, sylhet
3. Asst Professor of Neurology,National Institute of Neurosciences and Hospital, Dhaka
4. Professor. Department of Neurology, Bangabandhu Sheikh Mujib Medical University. BSMMU, Dhaka
5. Professor of Neurology & Director, National Institute of Neurosciences and Hospital, Dhaka
6. Assistant Professor. Department of Neurology Bangabandhu Sheikh Mujib Medical University. BSMMU, Dhaka.

*spectrum of diabetic neuropathy is variable and may be asymptomatic, but once established as polyneuropathy, it is irreversible and may finally be disabling. Early detection of diabetic neuropathy is one of the major goals in the management of diabetes since timely intervention may substantially reduce mortality and morbidity.*

***Key words:*** *Neuropathy, Diabetes, Electrophysiology*

***Abbreviation:*** *MCV (motor nerve conduction velocity), DML (distal motor latency), CMAP (compound muscle action potential), SCV( sensory conduction velocity),SNC, DSL( distal sensory latency),SNAP(sensory nerve action potential),*

**Introduction:**

Diabetic neuropathy is defined as peripheral somatic or autonomic nerve damage attributable solely to diabetes mellitus[1].It is not a single entity but a diverse group of disorders exhibiting a wide range of natural histories and clinical manifestations.[1] Its manifestation ranges from subclinical alteration of nerve conduction, affecting practically all patients, who have diabetes for more than a few years, to extremely severe neuropathy with life threatening autonomic dysfunction[2].

This disorder is characterized by striking atrophy and loss of myelinated and unmyelinated fibres accompanied by Wallerian degeneration, segmental and paranodal demyelination and blunted nerve fibre regeneration. There is a significant relationship between clinical measures of neuropathic severity and myelinated nerve fibre loss. This progressive nerve fibre damage and loss parallels the degree and/or duration of hyperglycaemia[3].

Microvascular abnormalities, particularly basement membrane thickening and endothelial cell hyperplasia are early features of diabetic microangiopathy and relate to neuropathic severity[4]. It has been suggested that microvascular disease plays a more important role in the development of neuropathy in type 2 than in type 1 diabetes[4]. On the other hand, in type 1 diabetes, aetiology is metabolic rather than vascular[3].

Patients with recently diagnosed or poorly controlled diabetes frequently show reduced nerve conduction velocity that improves rapidly with establishment of euglycaemia[5]. There is progressive deterioration of nerve function with time and duration of diabetes.[6] Abnormal nerve function can be due to metabolic component, which can rapidly be reversed and is greatest in the early stages of neuropathy and a structural (more permanent) component occurring later in the disease process[6].

As significant electrophysiological changes are found in asymptomatic neuropathy in diabetes mellitus and electrophysiological studies of nerve conduction velocity are our most sensitive tools to quantify early abnormalities, therefore, this study was designed to find out the real asymptomatic peripheral nerve dysfunction in recently diagnosed diabetic patients in Bangladesh perspective.

**Methods:**

This observational study was carried out in the Department of Neurology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, and Endocrinology Outpatient Department, Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM), Dhaka, during November 2005 and April 2006.

A total number of 60 patients were randomly selected for this study. Out of 60 subjects, 30 were recently diagnosed diabetics and 30 were control (non diabetics). Healthy controls with mean age comparable to that of diabetic subjects were selected from the friends of the subjects and patients attending neurology outdoor at BSMMU. All were age and sex matched. All the volunteers were apparently healthy as assessed by detailed medical history and clinical examination. None of them had history of diabetes up to second degree relations. None of the female control was pregnant. Thirty recently diagnosed diabetic subjects attending Endocrinology Outpatient Department, BIRDEM, were included consecutively. All recently diagnosed diabetic subjects had no neuropathic symptoms or signs. All cases were selected randomly by ADA criteria accepted by WHO.

*Inclusion criteria:* Recently diagnosed diabetic subjects of either sex having no history of taking antidiabetic agent in the recent or remote past were included in this study. ADA criteria accepted by WHO were followed for the diagnosis of diabetes; age between 12 and 60 years.

*Exclusion criteria:* Presence of symptoms or signs of neuropathy; presence of other causes of neuropathy, such as CRF, alcohol, drugs and toxins, malignancy, etc.; presence of other comorbid conditions, such as stroke, PD, COPD, pregnancy, etc.; and presence of family history of neuropathy

*Neurophysiological examinations:* Were done by NCS of one upper and one lower limb to see motor and sural sensory nerve conduction parameters between case and control groups. For this purpose, median, ulnar, tibial, peroneal and sural nerves were investigated for underlying asymptomatic neuropathy.

*Measurement of nerve conduction parameters:* Nerve conduction velocity was measured by a standard EMG machine in a room with a temperature of 37°C. Nerve conduction parameters were included according to the protocol recommended by San Antonio Conference on Diabetic Neuropathy. For upper limb, unilateral studies of motor and sensory conduction of ulnar nerve and median nerve, including F wave latencies were measured. For lower limbs, unilateral study of tibial and peroneal nerves for motor conduction including F wave latency were measured. Unilateral study of sural nerve for sensory conduction was done in lower limbs.

All measurements were performed with surface electrodes and measurements were recorded in a form used in the Department of Neurology, BSMMU. Nerves were stimulated using 1 ms electrical pulse at a repetition rate of 1 per second with intensity sufficient to elicit maximum amplitude of compound muscle action potential (CMAP) and sensory nerve action potential (SNAP).

Collected data were recorded on predesigned data collections sheet. Comparison between the groups was done by unpaired Student's 't' test using computer based software, Statistical Package for Social Science (SPSS).

**Results:**

Table I shows characteristics of the study subjects. In case and control group, respectively, there were 13 (43.3%) and 14 (46.7%) male and 17 (56.7%) and 16 (53.3%) female. Mean (±SD) age was 40.37±12.48 years (case) and 40.37±12.48 years (control). No significant variation was observed between sex and age. Mean (±SD) $HbA_1c$ was significantly high ($P<0.001$) in case group (7.10±0.80%) compared to control (5.51±0.65%). Mean (±SD) SGPT showed no significant difference between case (36.10±13.02 u/L) and control (36.20±7.94 u/L). Similarly, mean (±SD) total cholesterol also showed no significant difference between case (201.57±37.56 mg/dl) and control (191.00 ±17.17 mg/dl).

Table II shows comparison of motor nerve conduction parameters between case and control groups.

**Table-I**

*Characteristics of the study subjects*

| Parameters | Case (n=30) | | Control (n=30) | | P value |
|---|---|---|---|---|---|
| Sex | No. | (%) | No. | (%) | $>0.50^{ns}$ |
| Male | 13 | (43.3) | 14 | (46.7) | |
| Female | 17 | (56.7) | 16 | (53.3) | |
| Mean±SD | Mean±SD | | | | |
| Age (years) | 40.37±12.48 | | 40.37±12.48 | | $>0.50^{ns}$ |
| $HbA_1c$ (%) | 7.01±0.80 | | 5.51±0.65 | | $<0.001^{***}$ |
| SGPT (u/L) | 36.10±13.02 | | 36.20±7.94 | | $>0.50^{ns}$ |
| Total cholesterol (mg/dl) | 201.57±37.56 | | 191.00±17.17 | | $>0.10^{ns}$ |

Chi square test/Unpaired Student's 't' test
ns = Not significant, *** = Significant

Tibial nerve: Mean (±SD) DML (4.05±0.81 and 3.84±0.70 msec) and F latency (45.09±12.43 and 42.50±8.93 msec) showed no significant difference between case and control. Mean (±SD) CMAP (16.90±5.14 and19.49±4.73 msec) and MCV (45.43±4.55 and 48.24±4.72 m/s) were significantly (P<0.05) low in case group.

Peroneal nerve: Mean (±SD) DML (4.12±1.10 and 4.03±0.67 msec) and CMAP (5.80±2.89 and 6.97±1.79 mV) showed no significant difference between groups. Mean (±SD) MCV was significantly low (P<0.01) in case group (43.10±8.89 m/s) compared to control (48.27±3.56 m/s). However, mean (±SD) F latency was significantly high (P<0.001) in case (50.27±10.81 msec) compared to control (41.32±3.05 msec).

Median nerve: Mean (±SD) DML (3.57±0.46 and 3.55±0.52 msec), CMAP (16.33±4.24 and 17.84±3.73 mV) and F latency (25.08±5.28 and 24.39±4.83 msec) showed no significant difference between case and control groups. However, mean (±SD) MCV was significantly low (P<0.05) in case group (55.16±5.33 m/s) compared to control group (57.70±4.33 m/s).

Ulnar nerve: Mean (±SD) CMAP (14.65±3.32 and 17.29±6.83 mV) and F latency (25.09±5.35 and 25.82±3.33 msec) showed no significant difference between case and control groups. Mean (±SD) DML was significantly low (P<0.001) in case group (2.57±0.33 msec) compared to control group (3.17±0.61 msec). Similarly, Mean (±SD) MCV was also significantly low (P<0.05) in case group (55.74±5.00 m/s) compared to control group (58.50±5.13 m/s).

Table III shows comparison of sensory nerve conduction parameters between case and control groups.

**Table-II**

*Comparison of motor nerve conduction parameters*

| Parameters | Case (n=30) (Mean±SD) | Control (n=30) (Mean±SD) | P value |
|---|---|---|---|
| Tibial nerve | | | |
| DML (msec) | 4.05±0.81 | 3.84±0.70 | >0.10$^{ns}$ |
| CMAP (mV) | 16.90±5.14 | 19.49±4.73 | <0.05$^{*}$ |
| MCV (m/s) | 45.43±4.55 | 48.24±4.72 | <0.05$^{*}$ |
| F latency (msec) | 45.09±12.43 | 42.50±8.93 | >0.10$^{ns}$ |
| Peroneal nerve | | | |
| DML (msec) | 4.12±1.10 | 4.03±0.67 | >0.50$^{ns}$ |
| CMAP (mV) | 5.80±2.89 | 6.97±1.79 | >0.05$^{ns}$ |
| MCV (m/s) | 43.10±8.89 | 48.27±3.56 | <0.01$^{**}$ |
| F latency (msec) | 50.27±10.81 | 41.32±3.05 | <0.001$^{***}$ |
| Median nerve | | | |
| DML (msec) | 3.57±0.46 | 3.55±0.52 | >0.50$^{ns}$ |
| CMAP (mV) | 16.33±4.24 | 17.84±3.73 | >0.10$^{ns}$ |
| MCV (m/s) | 55.16±5.33 | 57.70±4.33 | <0.05$^{*}$ |
| F latency (msec) | 25.08±5.28 | 24.39±4.83 | >0.50$^{ns}$ |
| Ulnar nerve | | | |
| DML (msec) | 2.57±0.33 | 3.17±0.61 | <0.001$^{***}$ |
| CMAP (mV) | 14.65±3.32 | 17.29±6.83 | >0.05$^{ns}$ |
| MCV (m/s) | 55.74±5.00 | 58.50±5.13 | <0.05$^{*}$ |
| F latency (msec) | 25.09±5.35 | 25.82±3.33 | >0.50$^{ns}$ |

Unpaired Student's 't' test

ns = Not significant, */**/*** = Significant

**Table-III**

*Comparison of sensory nerve conduction parameters*

| Parameters | Case (n=30) (Mean±SD) | Control (n=30) (Mean±SD) | P value |
|---|---|---|---|
| Sural nerve | | | |
| DSL (msec) | 2.46±0.68 | 3.12±0.45 | <0.001*** |
| SNAP (iV) | 19.44±10.25 | 25.32±7.88 | <0.05* |
| SCV (m/s) | 49.95±10.22 | 52.46±3.96 | >0.10ns |
| Median nerve | | | |
| DSL (msec) | 2.52±0.39 | 2.77±0.49 | <0.05* |
| SNAP (iV) | 30.23±12.79 | 31.69±11.02 | >0.50ns |
| SCV (m/s) | 56.90±6.77 | 57.41±5.85 | >0.50ns |
| Ulnar nerve | | | |
| DSL (msec) | 2.03±0.39 | 2.48±0.49 | <0.001*** |
| SNAP (iV) | 29.30±14.36 | 30.72±10.76 | >0.50ns |
| SCV (m/s) | 60.96±8.38 | 57.93±7.15 | >0.10ns |

Unpaired Student's 't' test
ns = Not significant, */*** = Significant

Sural nerve: Mean (±SD) SCV showed no significant difference between case (49.95±10.22 m/s) and control (52.46±3.96 m/s) groups. Mean (±SD) DSL (2.46±0.68 and 3.12±0.45 msec) was significantly low (P<0.001) in case group compared to control. Also mean (±SD) SNAP (19.44±10.25 and 25.32±7.88 ìV) was significantly low (P<0.05) in case group.

Median nerve: Mean (±SD) SNAP (30.23±12.79 and 31.69±11.02 ìV) and SCV (56.90±6.77 and 57.41±5.85 m/s) showed no significant difference between case and control groups. However, mean (±SD) DSL (2.52±0.39 and 2.77±0.49 msec) was significantly low (P<0.05) in case group.

Ulnar nerve: Mean (±SD) SNAP (29.30±14.36 and 30.72±10.76 ìV) and SCV (60.96±8.38 and 57.93±7.15 m/s) showed no significant difference between groups. However, mean (±SD) DSL (2.03±0.39 and 2.48±0.49 msec) was significantly low (P<0.001) in case group compared to control.

**Discussion:**

The present study was undertaken to evaluate the asymptomatic neuropathy in recently diagnosed, untreated diabetic subjects of Bangladesh by electrodiagnosis and to explore whether abnormal $HbA_1C$ value, SGPT value and total cholesterol value relate to peripheral nerve dysfunction in diabetic patients.

The healthy controls and diabetic subjects were of comparable age and sex. Among the diabetic subjects, female predominated (56.7%) over males (43.3%) (Table I). Like the other previous studies, these subjects were severely hyperglycemic. This high glycaemic state can be explained by the fact that these patients were recently diagnosed and did not get any treatment. Moreover, one of the characteristic finding of these diabetic subjects in this region is moderate to severe hyperglycaemia[7].

Serum $HbA_1C$ (%) level was statistically significantly higher (P<0.001) in cases (7.01±0.80%) compared to control (5.51±0.65%) subjects (Table I). This high level of serum $HbA_1C$ (%) was frequently found in other previous studies. One finding in MIT (multiple insulin injection therapy) treated patients with mean diabetes duration of 8.2 years indicates that very low mean $HbA_1C$ values (about 6%) are required to prevent nerve dysfunction. On the other hand, mean $HbA_1C$ values over 9% invariably related to nerve dysfunction[8]. In electrophysiological investigation of diabetic patients, slowing of motor nerve conduction velocity has been found to be inversely correlated with the concentrations of $HbA_1C$. It has

been demonstrated that the control of blood glucose level protects against the development of neuropathy in type I diabetes.[9] In one study, somatic large motor fiber abnormalities of lower extremities correlated with only $HbA_1C$ concentration, which confirmed the assumption that hyperglycemia is an essential factor in the involvement of long nerves. However, the motor and sensory nerve conduction abnormalities of upper extremity were not found to be correlating with $HbA_1C$ concentration, age and diabetes duration[9].

We did not find any information regarding correlation between asymptomatic neuropathy and serum SGPT and serum total cholesterol in previous studies. We undertook these two variables (SGPT and total cholesterol) only for academic interest.

DML values of tibial nerve were slightly higher in diabetic subjects than control subjects but statistically not significant (P>0.10). CMAP values of tibial nerve were statistically significantly lower in diabetic subjects than control subjects (P<0.05). MCV values of tibial nerve were statistically significantly lower in diabetic subjects than control subjects (P<0.05). F latency values of tibial nerve were slightly higher in diabetic subjects than control subjects but statistically not significant (P>0.10) (Table II).

DML values of peroneal nerve were slightly higher in diabetic subjects than control subjects but statistically not significant (P>0.50). CMAP values were lower in diabetic subjects than control subjects but statistically not significant (P>0.05). MCV values were statistically significantly lower (P<0.10) in diabetic subjects than control subjects. F latency values were statistically significantly higher (P<0.001) in diabetic subjects than control subjects (Table II).

DML values of median nerve did not show statistically any significant difference (P>0.50). CMAP values were slight lower in diabetic subjects than control subjects but statistically not significant (P>0.10). MCV values were statistically significantly lower (P<0.05) in diabetic subjects than control subjects. F latency values showed statistically no significant difference (P>0.50). DSL values were slightly lower in diabetic subjects than control subjects. Those were statistically significant (P<0.05). SNAP and SCV values were slightly lower in diabetic subjects but statistically not significant (P>0.50) (Table II).

DML values of ulnar nerve were slightly lower in diabetic subjects but statistically significant (P<0.001). CMAP values were lower in diabetic subjects but statistically not significant (P>0.05). MCV values were statistically significantly lower (P<0.05) in diabetic subjects. F latency values showed statistically no significant difference (P>0.50). DSL values of ulnar nerve were slightly lower in diabetic subjects but statistically significant (P<0.001). SNAP values were slightly lower but statistically not significant (P>0.50). SCV values were slightly higher in diabetics but statistically not significant (P>0.10) (Table II).

DSL values of sural nerve were slightly lower in diabetic subjects but statistically significant (P<0.001). SNAP values were statistically significantly lower (P<0.05) in diabetic subjects. SCV values were lower in diabetic subjects but statistically not significant (P>0.10) (Table III).

Most of the nerve conduction parameters tended to differ statistically significantly in diabetic subjects from those of control subjects. Same dysfunction of peripheral nerves were reported previously in recently detected diabetic subjects[10]. Our findings provide supportive evidence for the existence of an acute metabolic component of diabetic neuropathy.[10] Findings of abnormalities of motor nerve function parameters support the hypothesis that abnormalities of motor nerve conduction velocities are related to their level of hyperglycemia in young diabetic subjects[11].

Some investigators suggested that sural nerve dysfunction is the most common indicator of peripheral nerve dysfunction, and it is the first to be affected, and correlates most closely with the neuropathological findings[9].

In previous study, correlation found between high serum $HbA_1C$ level and asymptomatic nerve dysfunction[8].Correlation did not found clearly between high serum SGPT, high total serum cholesterol and asymptomatic nerve dysfunction. These two variables (SGPT and total cholesterol) were taken into consideration only for academic

interest to find out relationship with asymptomatic neuropathy.

After evaluating the results, we suggest that the most useful and practical nerves for the electrophysiological study in diabetic patients are the motor and sensory nerves of lower extremity. The prominence of motor, sensory and autonomous nerve dysfunction in lower extremity must be correlated with the length of these nerves. All the necessary proteins which are synthesized in cell body are transmitted to distal parts of the nerves by axoplasmic flow and maintain the anatomic and functional integrity of the nerve. The interruption of axoplasmic flow in long nerves is more prominent than in short nerves. One data indicate that in early period, the axoplasmic flow might have been affected[10].

**Conclusion:**

Clinical spectrum of diabetic neuropathy is variable. It may be asymptomatic but once established as polyneuropathy, it is irreversible and may finally be disabling. Early detection of diabetic neuropathy is one of the major goals in the management of diabetes since timely intervention may substantially reduce mortality and morbidity.Metabolic peculiarities of young diabetics of Bangladesh have given the opportunity to see the influence of hyperglycemia on functional status of peripheral nerves in these subjects. To evaluate functional status of peripheral nerves, nerve conduction parameters and F wave latencies need to be studied. Motor nerve conduction parameters are affected more than sensory nerves and F-wave latencies are more frequently and early involved in these subjects.

**References:**


1. ADA [American Diabetic Association]. Consensus statement: standardized measures in diabetic neuropathy. Diabetic Care, vol. 18, suppl. 1.
2. Said G, Goulean G, Salma G, Tchobroutsky G. Severe early onset polyneuropathy in insulin dependent diabetes mellitus: a clinical pathological study. N Engl J Med.1992; 326(19):1251 63.
3. Douglas AG, Sima AAF, Stevens MJ, Feldman EL, Lattimar SA. Complications: neuropathy, pathologic considerations. Diabetes Care. 1992;15 (12):1902 25.
4. Malik RA.The pathology of human diabetic neuropathy. Diabetes. 1997; 46(2).S50 S53.
5. Gregerson G. Variations in motor conduction velocity produced by acute changes of the metabolic state in diabetic patients. Diabetologia. 1968; 4:273 77.
6. Pfeifer MA, Schumer MP. Perspectives in diabetes, clinical trials of diabetic neuropathy: past, present and future. Diabetes.1995; 44: 1355-61
7. Bajaj JS. Malnutrition related ketosis resistant diabetes mellitus: classification, causes and mechanism. In: Krall LP, editor. World book of diabetes in practice. Amsterdam: Elsevier,1986; 276 80.
8. Hyllienwark L, Brismar T, Ludvigsson J. Subclinical nerve dysfunction in children and adolescents with IDDM. Diabetologia. 1995; 38:.685 92.
9. Karsidag S, Morali S, Sargin M, Salman S, Karsidag K, Us O. 2005. The electro-physiological findings of subclinical neuropathy in patients with recently diagnosed type 1 diabetes mellitus. Diabet Res Clin Pract.2005;67:211 19.
10. Fraser DM, Campbell IW, Ewing DJ, Murray A, Neilson JM, Clarke BF. 1977. Peripheral and autonomic nerve function in newly diagnosed diabetes mellitus. Diabetes. 1977; 26:546 50.
11. Graff RJ, Jeffery B, Heller E, Pote D. Nerve conduction abnormalities in untreated maturity onset diabetes: relation to levels of fasting plasma glucose and glycosylated haemoglobin. Ann Intern Med.1979;.298 303.

Bangladesh Journal of Neuroscience 2014; Vol. 30 (1) : 23-26

# Pattern of ECG findings in Ischemic Stroke

SK MAHBUB ALAM[1], MD RAFIQUL ISLAM[2], HASAN ZAHIDUR RAHMAN[2],
MD REZAUL KARIM KHAN[2], MONIRUZZAMAN BHUIYAN[2]. ABDUL KADER SHAIKH[3]

**Abstract:**

***Background:*** *The diagnosis of ischemic stroke remains a clinical one, with confirmatory evidence obtained through neuroimaging. ECG changes are common in patients with ischemic stroke. Objective: The objective of this study was to see ECG findings among ischemic stroke patients.* ***Materials and Methods:*** *This study was carried out in the Department of Neurology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka from July 2006 to October 2008. A total of 36 patients with acute Ischemic stroke were selected by purposive sampling method and diagnosed by history, clinical findings ard was confirmed by CT scan of head. The clinical details, investigations of the respondents were reviewed. Data were recorded in a pre-designed data* collection sheet. ***Result:*** *Majority of the subjects were in 7th decade 12(33.3%) and 6th decade 9(25%) with the male to female ratio was 1.25:1. Among the patients with abnormal electrocardiographic findings, 7(19.4%) patients each had myocardial ischemia, 4(11.1%) had conduction block and ventricular arrhythmias, 7(19.4%) had atrial fibrillation, 5(13.9%) had ventricular hypertrophy, 7(19.4%) had myocardial infarction, 6(16.7%) patients had non-specific ST changes.* ***Conclusion:*** *Myocardial ischemia, atrial fibrillation and myocardial infarction are common electrocardiographic findings of ischemic stroke patients.*

## Introduction:

Acute stroke is characterized by the rapid appearance (usually over minutes) of a non-convulsive, non-traumatic focal deficit of brain function, most commonly a hemiplegia with or without signs of higher cerebral dysfunction (such as aphasia), hemisensory loss, and visual field defect or brain-stem deficit. Provided that there is a clear history of a rapid onset focal deficit, the chance of the brain lesion being anything other than vascular is 5% or less. Stroke is the third commonest cause of death after ischemic heart disease and cancer in developed countries and is responsible for a large proportion of physical disability[1]. It is also the commonest cause of morbidity and mortality among adult population, one year case fatality being 42 percent[2].The main types of stroke and their relative occurrences are: Ischemic stroke - 85% and Hemorrhagic stroke -15%[3]. Coronary heart disease and ischemic stroke share the same risk factors and may co-exist in the same patient and in most of the patients with ischemic stroke, the mortality may be related to the underlying coronary heart disease[4].ECG changes are common in-patients with ischemic stroke. Studies have shown that the frontal lobe, insular cortex and amygdale play an important role in the regulation of heart via the sympathetic and parasympathetic systems and cardiac involvement is more common in patients with cerebral lesion involving these areas[5,6] In financial terms, stroke represents 6% of hospital running costs and 4.6% of all National Health Service costs. About 40-50% of beds are occupied by stroke patients in neurology ward which is reported in a developing country like ours[7]. Ischemic stroke, which is perhaps the commonest subtype of stroke, is associated with ECG changes; some of these changes have been thought to be due either to the stroke itself or pre-existing heart disease. Because ECG is rapid, noninvasive and low cost, successful detection of cardiac complications early in the course of acute ischemic stroke could have an impact on clinical management.

1. Assistant Professor, Department of Neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka.
2. Professor, Department of Neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka.
3. Associate Professor, Department of Neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka.

**Aims and Objectives:**

Many studies are available from other countries, especially from Japan, India but there has been no such study from Bangladesh. The aims of the study was to see the normal and abnormal EGG findings among the ischemic stroke patients in Bangladeshi population.

**Materials and Methods:**

This was an observational study carried out in the Department of Neurology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka. Study subjects were collected from admitted patients in neurology ward in Bangabandhu Sheikh Mujib Medical University followed up to discharge in the neurology ward and subsequent follow up were done in stroke clinic of neurology OPD from July 2006 to October 2008. A total of 36 patients with acute ischemic stroke with abnormal EEC were selected by purposive sampling method and diagnosed by history, clinical findings and was confirmed by CT scan of head and ECG were selected from among the patients admitted in neurology ward, Department of Neurology, BSMMU, during the study period. Chi-square test and unpaired students 't' test has been done in this study.

**Results:**

A total number of 36 ischemic stroke patients with abnormal electrocardiographic findings were taken in this study(Table-I). The age range were between 42 to 84 years and mean age was 62.39±10.64.

**Table-I**

*Age distribution of ischemic stroke patients with abnormal ECG findings.*

| Age (years) | (N-36) | Percentage % |
|---|---|---|
| 40-49 | 5 | 13.9 |
| 50-59 | 9 | 25.0 |
| 60-69 | 12 | 33.3 |
| 70-79 | 8 | 22.2 |
| >80 | 2 | 5.6 |
| Total | 36 | 100 |
| Mean±SDRange | 62.39±10.64 | |

**Table-II**

*Sex distribution of study subject*

| Diabetes mellitus | (N-36) | Percentage % |
|---|---|---|
| Present | 12 | 33.3 |
| Absent | 24 | 66.7 |
| Total | 36 | 100 |

Table-II showed sex distribution of ischemic stroke patients with abnormal ECG findings where 55.6% were male and 44.4% were female.

**Table-III**

*Distribution of diabetes mellitus among the study subjects*

| Diabetes mellitus | (N-36) | Percentage % |
|---|---|---|
| Present | 12 | 33.3 |
| Absent | 24 | 66.7 |
| Total | 36 | 100 |

Table-III showed that diabetes mellitus was present in 12 (33.3%) patients among the study subjects

**Table- IV**

*Distribution of dyslipidaemia among the study subjects*

| Dislipidaemia | (N-36) | Percentage % |
|---|---|---|
| Present | 13 | 36.1 |
| Absent | 23 | 63.9 |
| Total | 36 | 100 |

Table-IV showed the distribution of dyslipidemia was present among 13(36%) patients the study subject.

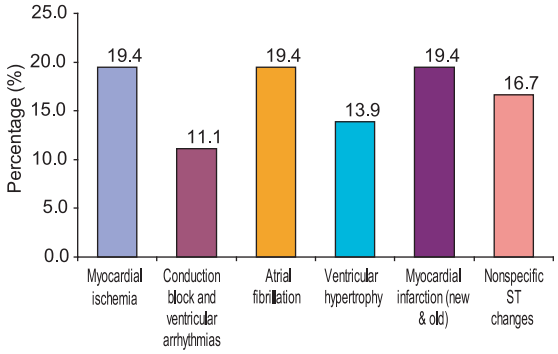


**Fig.-1:** *The EEG findings among the study subjects.*

Fig.-1 showed distribution of abnormal ECG findings among ischemic stroke patients, where 7(19.4%) patients had myocardial ischemia, 4(11.1%) had conduction block and ventricular arrhythmias, 7(19.4%) had atrial fibrillation, 5(13.9%) had ventricular hypertrophy, 7(19.4%) had myocardial infarction and 6(16.7%) patients had non-specific ST changes.

**Discussion:**

This was a hospital based observational study and was carried out to see the electrocardiographic findings of ischemic stroke patients. The study subjects were selected from the admitted patients of neurology ward, Department of Neurology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka with abnormal ECG findings. A total of 36 patients had been studied during the study period. In this study, majority of the subjects were in 7th decade 12(33.3%) and 6th decade 9(25%). Next common age group were 8th decade 8(22.2%) and 5th decade, 5(13.9%). In a previous study among 51 stroke patients majority of them were in the age group of 50-69 years[8]. In another study among 100 stroke patients, the age range was 18-84 years and most of his cases were between 50-70 years[9]. So, this study is consistent with other studies. In this study the mean (±SD) age of the patients 62.39±10.64 years. Similar past studies had comparable age statistics of the patients[10].

In this study, the male to female ratio was 1.25:1. Male involvement was 12.5% higher than that of female. In a previous study male to female ratio was 1.2:1 which is similar to this study[11].

In this study among patients 12 (33.3%) patients were diabetic. In a study carried out in Dutch community on stroke patients where 29% patients were diabetic[12]. In another study among ischemic stroke patients 30% were diabetic[13].Independent of age, coronary heart diseases (i.e. angina pectoris or myocardial infarction) are clearly associated with ischemic stroke. The evidences are available in postmortem[14,15], case control[16] and cohort studies[17].

In a previous study it was found that atrial fibrillation was present in 19.5% of cases[11]. In this study, 19.4% of patients with abnormal ECG had atrial fibrillation and 11.1% had ventricular arrhythmias. Therefore the present study is consistent with the findings of previous studies.

In this study, myocardial ischemia was one of the common (19.4%) ECG findings. In some previous studies it was also found that myocardial ischemia was a common ECG finding in stroke patients[11,18,19]. Therefore this study was consistent with many of the previous studies.

Considering all the above observations, it is established that this study showed a close relationship between abnormal electrocardiographic findings with ischemic stroke patients.

**Conclusion:**

From the statistical analysis of the results obtained in this study, it has been seen that myocardial ischemia, myocardial infarction and atrial fibrillation has a close relationship with ischemic stroke patients. Many patients has non-specific ST changes. Multi centered prospective study with large sample size could be done for better evaluation .

**References:**


1. Allen CMC,Luek CJ. Disease of the nervous system, In: Hastel C, Chilves ER, Hunter J AA, Boon NA. eds. Davidson's Principles of Medicine: 18th ed. Cerebrovascular disease.UK. Charchil livingstone; 1999: 974
2. Hasanuzzamman MA, Ullah AKMA, Haque A, Mohammad QD, Shahnaz S. 'Relationship of protein C deficiency to ischaemic stroke in young patients'. *Bangladesh Journal of Neuroscience* 2004; 20:16-23.
3. Brown MM. 'Cerebrovascular disease, Epidemiology, history, examination and differential diagnosis'. *Medicine International 1996;* 10(34):35-41.
4. Oppenheimer SM. 'Neurogenic cardiac effects of cerebrovascular disease'.Curr Opin *Neurol* 1994; 20-4.
5. Hachinski VC. The clinical problem of brain and heart. Stroke 1993; 24: 1-2.

6. Oppenheimer SM, Cechetto DF. & Hachinski VC. Cerebrogenic cardiac arrhythmias, Cerebral electro-cardiographic influences and their role in sudden death rate. *Neurology* 1990:47:513-9.

7. Ullah AKMA, Miah GA, Islam KN.'Pattern of admission in the department of neurology, IPGMR-A one year study'. *Bangladesh Journal of Neuroscience* 1992; 8:17-23.

8. Timble M,Bell DA, Brien W, Vladimar H, Keefe BO. 'Antiphospholipid syndrome: Prevalence among patients with stroke and transient ischemic attack.*Am J Med* 1990; 88: 593-7.

9. Chowdhury SGM. 'Third Ibrahim Memorial lecture presented at the scientific seminar of APB' 1990; 21: 8-13.

10. Akbar MA, Awan MM, Taseer IH, Qureshi A, Chaudhary GM. *Electro-cardiographic predictors of mortality in acute stroke'* PMRC Research Centre, Multan. 2005; 2.

11. Bozluolcay M, Ince B, Celik Y, Harmanci H, Ilerigelen B, Pelin Z. 'Electrocardiographic findings and prognosis in ischaemic stroke'. *Neurol India* 2003; 51: 500-2.

12. Herman B, Leyten ACM, Van Luijk ST, Frenken CWGM, Opde, Schulle BPM. 'Increase risk factors for stroke in a Duch community'.*Stroke* 1982; 13:334-9.

13. Haque A and Mannan MA. 'Study on cerebrovascular disease: Report of the study of 410 cases of acute cerebro-vascular disease', In: Proceedings of Japan-Bangladesh Conference on Cardiology, 1984; 46-53.

14. Kogan A. 'Atherosclerosis and myocardial lesions in subjects dying from fresh cerebrovascular disease'.Bull World Health Organ. 1976; 53:597-609.

15. Stemmerman GN, Hayshi T, Resch, JA. 'Riskfactors related to ischaemic and haemorrhagic cerebrovascular disease at autopsy: The Honolulu heart study', *Stroke* 1984; 15: 23-8.

16. Friedman GD, Loveland DB & Ehrlich SP. 'Relationship of stroke to other cardiovascular disease'. *Circulation* 1984; 38: 533-46.

17. Kannel WB, Wolf P. 'Epidemiology of cerebrovascular disease', In: vascular disease of the central nervous system. 2nd ed. Churchill Livingstone, Edinburgh 1983; 1-24.

18. Korpelainen JT, Sotaniemi KA, Huikuri HV, Myllya VV. 'Abnormal heart rate variability as a manifestation of autonomic dysfunction in hemispheric brain infarction'. *Stroke* 1996; 2059-63.

19. Broderic JP.'Heartdisease and stroke'.*Stroke* 1993; 2: 355-9.

Bangladesh Journal of Neuroscience 2014; Vol. 30 (1) : 27-34

# Effect of Long Term Use of Carbamazepine on Lipid Profile in Adult Epileptic Patients

MD KHAIRUL KABIR PATWARY[1], SHAKILA SULTANA[2], MD SALAHUDDIN[3], ABU JAFOR MD SALAHUDDIN[4], MOHAMMED SAYEED HASSAN[4], MD KABIRUZZAMAN[5], MD ABDUL ALIM[5], RASHED IMAM ZAHID[5], NURUDDIN MD EUSUF[6], SUBASH KANTI DEY[7], AHSAN HABIB[7], BAHADUR ALI MIAH[8], KANUJ KUMAR BARMAN[8], MD RAFIQUL ISLAM[9].

**Abstract:**

***Objective:*** *To evaluate the effect of long term use of carbamazepine on lipid profile in adult epileptic patients*

***Methodology:*** *The study was conducted in the Department of Neurology at BSMMU, Dhaka over a period of 2 years from January 2010 to December 2011. Adult epileptic patients taking carbamazepine as anticonvulsant and attending the Epilepsy Clinic and Neurology OPD of BSMMU, Dhaka were the study population. A total of 107 cases and 107 controls were included in the study. Data were collected by interview of the patients, clinical examination and laboratory investigations using the research instrument*

***Result:*** *The mean age of case and control groups were almost identical (23.3 ± 6.8 vs. 23.8 ± 6.4 years, p = 0.972). The proportion of male and female patients was similar in both the study groups. Of the 107 cases, more than 70% had generalized epilepsy and the rest (29%) focal epilepsy. Of the 107 cases, 8% had family history of epilepsy. The prevalence of raised triglycerides and raised LDL were observed to be significantly higher in the case group than those in the control group (35.5% vs. 23.4%, p = 0.049 and 15% vs. 0.9%, p < 0.001 respectively). The prevalence of low HDL was also significantly higher in the former group than that in the latter group (43.9% vs. 18.7%, p < 0.001). The mean serum triglyceride and LDL were higher and mean HDL was lower in the case group than those in the control group. Over half (51.4%) of the case group exhibited dyslipidemia compared to the control group (27.1%). The risk of developing dyslipidemia in epileptic patients receiving carbamazepine for longer duration was nearly three-fold (95% of CI = 1.6 – 5.0) higher than that in the control group (p < 0.001). There*

*is positive correlation between duration of carbamazepine treatment and lipid profile. Serum total cholesterol and triglycerides bear linear relationship with duration of treatment with carbamazepine (r = 0.201, p = 0.038 and r = 0.223, p = 0.021 respectively). The association of dyslipidemia with sex in epileptic patients receiving carbamazepine for more than 2 years. The proportion of dyslipdemia was considerably higher in the female patients than their male counterparts, although the difference was not statistically significant (55.3% vs. 41.9%, p < 0.211).*

***Conclusion:*** *A conclusion can be made from the above mentioned result that long-term use of carbamazepine in epileptic patients may cause dyslipidemia and the risk of having dyslipidemia in such patients is 3 times greater than the normal healthy population.*

***Key words:*** *Carbamazepine, lipid profile and Epilepsy.*

---

1. Assistant Professor, National Institute of Neurosciences & Hospital (NINS), Dhaka.
2. Resident, Department of Paediatrics, Bangabondhu Sheikh Mujib Medical University (BSMMU), Dhaka.
3. Registrar, Department of Medicine, Chittagong Medical College, Chittagong.
4. Junior Consultant, National Institute of Neurosciences & Hospital (NINS), Dhaka.
5. Medical Officer, National Institute of Neurosciences & Hospital (NINS), Dhaka.
6. Upazilla Health &Family Planning Officer , Morelgonj, Bagerhat.
7. Assistant Professor, Department of Neurology, Bangabondhu Sheikh Mujib Medical University, Dhaka.
8. Associate Professor, Department of Neurology, Bangabondhu Sheikh Mujib Medical University , Dhaka.
9. Professor, Department of Neurology, Bangabondhu Sheikh Mujib Medical University (BSMMU), Dhaka.

**Introduction:**

Epilepsy is a common chronic neurological disorder characterized by recurrent unprovoked seizures[1,2]. These seizures are transient signs and/or symptoms of abnormal, excessive or synchronous neuronal activity in the brain[2]. About 50 million people worldwide have epilepsy, with almost 90% of these people being in developing countries[3] . Epilepsy is more likely to occur in young children or people over the age of 65 years; however, it can occur at any time[4].

Epilepsy is usually controlled, but cannot be cured with medication. However, over 30% of people with epilepsy do not have seizure control even with the best available medications [5,6]. The mainstay of treatment of epilepsy is anticonvulsant medications. Often, anticonvulsant medication may continue for life-long and can have major effects on quality of life. The choice among anticonvulsants and their effectiveness differs by epilepsy syndrome. Mechanisms, effectiveness for particular epilepsy syndromes, and side effects differ among the individual anticonvulsant medications.

Currently there are 20 medications approved by the Food and Drug Administration for the treatment of epileptic seizures: carbamazepine, clorazepate, clonazepam, ethosuximide, felbamate, fosphenytoin, gabapentin, lacosamide, lamotrigine, levetiracetam, oxcarbazepine, phenobarbital, phenytoin, pregabalin, primidone, tiagabine, topiramate, valproate semisodium, valproic acid, and zonisamide. Most of these drugs are available in Bangladesh but carbamazepine, valproic acid, lamotrigine, clonazepam, phenobarbital, phenytoin are commonly used.

Although there is scarcity of data regarding the side-effects of anticonvulsants on Bangladeshi population, 88% of patients with epilepsy, in a European survey reported at least one anticonvulsant related side effect[8]. Most side effects are mild and "dose-related" and can often be avoided or minimized by the use of the smallest effective dose. Some examples include mood changes, sleepiness, or unsteadiness in gait. When anticonvulsant drugs are used in large quantities during long-term antiepileptic therapy, it may be associated with various metabolic abnormalities in connective tissues, endocrine system and the liver[9]. Anticonvulsants may alter liver function and increase the activity of hepatic microsomal enzyme system. This enzyme induction phenomenon is associated with an altered metabolism of various substances such as drugs and lipids[9, 10]. This anomaly has focused attention on changes in lipid profile during long-term anticonvulsant therapy especially by alter liver function and increase the activity of the hepatic microsomal enzyme system[10, 11].

The effect of anti-epileptic drugs (AEDs) on serum lipid profile is controversial. Eiris and associates (2000)[12] found that the effects of long-term AED therapy on lipid profile and, particularly, on apolipoprotein serum levels increase risk of atherosclerosis-related disease. On the other hand, Tegkul and associates (2006)[13] opposed such association. They suggested that 2 years AED monotherapy with VPA, CBZ or PB did not cause a significant level of concern for an atherogenic effect in children with epilepsy.

Carbamazepine elevates total cholesterol levels by 0 to 15% and HDL-cholesterol levels by 0 to 30%. These effects are dosage independent and seem to be more pronounced in women[14]. However, one study[15] showed levels of HDL-cholesterol decreased by almost 40%. Although the effects of phenobarbital and phenytoin on serum lipid levels have been studied less frequently, reports[14] indicate that they both elevate total cholesterol levels by 5 to 15%. However, reported changes in HDL-cholesterol levels vary from a 40% decrease to a 45% increase. Triglyceride levels are not affected by any of the anticonvulsants[15,16]. They found that, carbamazepine treatment alters the serum lipid profile of the children in such a way that it facilitates the development of atherosclerosis[16].

The influences of Carbamazepine on lipid profile of epileptic patients in Bangladesh have not been investigated. Therefore, a case-control study to investigate the effect of this drug on serum levels of lipids (triglyceride, total cholesterol, HDL and LDL) deemed essential.

**Methodology:**

Study design:A case control study was considered suitable for the study.

Place and period of Study:The study was conducted in the Department of Neurology at BSMMU, Dhaka over a period of 2 years from January 2010 to December 2011.

**Study population:**
Adult epileptic patients taking carbamazepine as anticonvulsant and attending the Epilepsy Clinic and Neurology OPD of BSMMU, Dhaka were the study population.

Sample size:A total of 107 cases and 107 controls were included in the study.

Sampling procedure:The required number of cases and controls were selected consecutively.

**Inclusion criteria of cases:**
- Epileptic patients from 18 years onwards
- Patients who were taking carbamazepine for at least 2 years

**Exclusion criteria for cases:**
- Epileptic patients taking more than one anticonvulsant drugs
- Patients with diabetes mellitus, nephrotic syndrome, myxoedema which might affect the blood lipid.
- Any other chronic clinical conditions which can alter lipid profile.
- Patients taking carbamazepine for less than two years.
- Patients taking lipid lowering drugs.

Data processing and statistical analysis:Data were processed and analyzed using software SPSS (Statistical Package for Social Sciences) version 11.5.The test statistics used to analyze the data were descriptive statistics, Chi-square ($c^2$) test and Student's t Test. For all analytical tests, the level of significance was set at 0.05 and $p < 0.05$ was considered significant.

**Results:**
A total of 214 adult participants were included in the study. Of them 107 were epileptic patients and considered as cases and another 107 apparently healthy subjects or non- epileptic patients were taken as controls. The mean age of case and control groups( Table-I) were almost identical (23.3 ± 6.8 vs. 23.8 ± 6.4 years, p = 0.972). The proportion of male and female patients was similar in both the study groups. Of the 107 cases, more than 70% had generalized epilepsy and the rest (29%) focal epilepsy. Of the 107 cases, 8% had positive family history of epilepsy.

The prevalence of raised triglycerides and raised LDL were observed to be significantly higher in the case group than those in the control group (35.5% vs. 23.4%, p = 0.049 and 15% vs. 0.9%, p < 0.001 respectively)( Fif-3). The prevalence of low HDL was also significantly higher in the former group than that in the latter group (43.9% vs. 18.7%, p < 0.001) (Fif-4). The mean serum triglyceride and LDL were higher and mean HDL was lower in the case group than those in the control group (Table II).

Over half (51.4%) of the case group exhibited dyslipidemia compared to the control group(27.1%)(Table-III). The risk of developing dyslipidemia in epileptic patients receiving carbamazepine for longer duration was nearly three-fold (95% of CI = 1.6 – 5.0) higher than that in the control group (p < 0.001) (Fig-1).

**Table-I**
*Comparison of age between two groups*

| Age (years) | Group | | p-value |
|---|---|---|---|
| | Case (n = 107) | Control(n = 107) | |
| 18-25 | 77(72.0) | 69(64.5) | |
| 25 – 30 | 15(14.0) | 25(23.4) | |
| e" 30 | 15(14.0) | 13(12.1) | |
| Mean ± SD | 23.3 ± 6.8 | 23.8 ± 6.4 | 0.972 |

* Figures in the parenthesis denote corresponding %;

**Table-II**

*Comparison of lipid profiles between two groups*

| Lipid profile# | Group | | p-value |
|---|---|---|---|
| | Case (n = 107) | Control (n = 107) | |
| Total cholesterol | 85(79.4) | 93(86.9) | |
| Normal (< 200 mg/dl) | 22(20.6) | 14(13.1) | 0.144 |
| Raised (>200 mg/dl)Mean ± SD | 175.3 ± 30.6 | 174.4 ± 32.4 | |
| Triglyceride | 69(64.5) | 82(76.6) | |
| Normal (< 150 mg/dl) | 38(35.5) | 25(23.4) | 0.049 |
| Raised (>150 mg/dl) | 157.4 ± 63.2 | 133.1 ± 68.1 | |
| Mean ± SD | | | |
| LDL | 91(85.0) | 106(99.1) | |
| Normal (<130 mg/dl) | 16(15.0) | 1(0.9) | < 0.001 |
| Raised (>130 mg/dl) | 112.4 ± 23.2 | 96.9 ± 16.9 | |
| Mean ± SD | | | |
| HDL | 47(43.9) | 20(18.7) | |
| Low (<40 mg/dl) | 60(56.1) | 87(81.3) | < 0.001 |
| Normal (e”40 mg/dl) | 39.6 ± 8.9 | 43.3 ± 10.6 | |
| Mean ± SD | | | |

Figures in the parentheses indicate corresponding percentage;

# Data were analysed using Chi-square ($\div^2$) Test.

**Table-III**

*Association between carbamazepine use in epileptic patients and dyslipidemia*

| Dyslipidemia | Group | | Odds Ratio | p-value |
|---|---|---|---|---|
| | Case(n = 107) | Control(n = 107) | (95% CI of OR) | |
| Present | 55(51.4) | 29(27.1) | 2.8(1.6 – 5.0) | < 0.001 |
| Absent | 52(48.6) | 78 (72.9) | | |

Figures in the parentheses indicate corresponding percentage;

# Data were analysed using Chi-square ($\div^2$) Test.

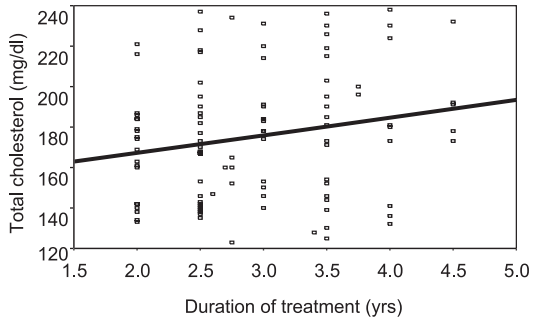


**Fig.-1:** *Correlation between duration of treatment and total cholesterol (n = 107)*

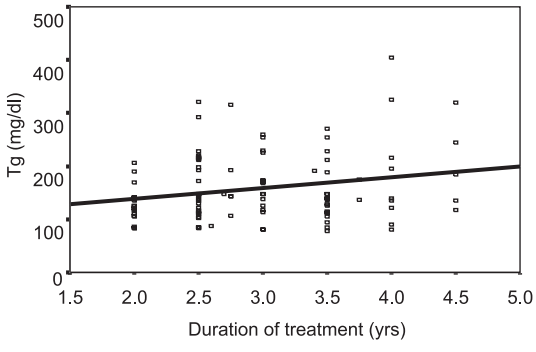


**Fig.-2:** *Correlation between duration of treatment and triglycerides (n = 107)*

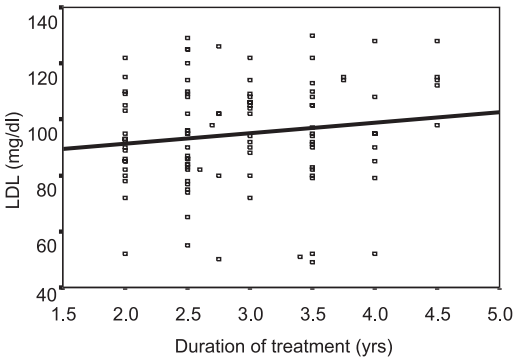


**Fig.-3:** *Correlation between duration of treatment and LDL cholesterol (n = 107)*

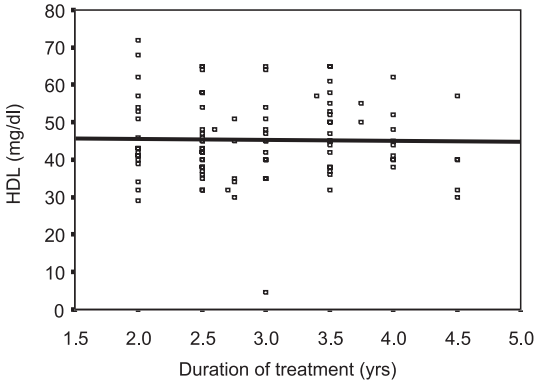


**Fig.-4:** *Correlation between duration of treatment and HDL cholesterol (n = 107)*

**Table IV**

*Comparison of dyslipidemia between sexes among case group*

| Dyslipidemia# | Sex | | p-value |
|---|---|---|---|
| | Male(n = 31) | Female(n = 76) | |
| Present | 13(41.9) | 42(55.3) | 0.211 |
| Absent | 18(58.1) | 34(44.7) | |
| Lipid profiles | | | |
| Total cholesterol (mg/dl) | 167.2 ± 28.9 | 178.6 ± 30.9 | |
| Triglyceride (mg/dl) | 154.4 ± 71.2 | 158.7 ± 60.2 | |
| LDL (mg/dl) | 111.8 ± 15.8 | 113.4 ± 17.3 | |
| HDL (mg/dl) | 42.0 ± 11.0 | 46.7 ± 10.1 | |

Figures in the parentheses indicate corresponding percentage;

# Data were analysed using Chi-square ($\div^2$) Test.

There is positive correlation between duration of carbamazepine treatment and lipid profile( Fig.1). Serum total cholesterol and triglycerides bear linear relationship with duration of treatment of carbamazepine (r = 0.201, p = 0.038 and r = 0.223, p = 0.021 respectively).

The association of dyslipidemia differs with sex in epileptic patients receiving carbamazepine for more than 2 years. The proportion of dyslipdemia was considerably higher in the female patients than their male counterparts, although the difference was not statistically significant (55.3% vs. 41.9%, p < 0.211).

The mean serum creatinine and serum TSH were somewhat higher in the case group than those in the control group (0.8 ± 0.1 vs. 0.7 ± 0.2 mg/dl, p < 0.001 and 3.2 ± 0.5 vs. 3.1 ± 0.5 mIU/L, p = 0.318 respectively). However, random blood sugar was almost similar and within normal range in both the groups (5.3 ± 0.4 vs. 5.2 ± 0.8 mmol/L; p = 0.138). The purpose of the study was to evaluate the long-term effect of carbamazepine on serum lipids.

**Discussion:**

The present study was carried out in BSMMU to find the effect of long-term use of carbamazepine on serum lipids of adult epileptic patients. The study included a total of 214 subjects with equal number of cases (n = 107) and controls (n = 107). The controls were selected from the epileptic patients receiving

antiepileptic drugs other than carbamazepine. The study found that long-term use of carbamazepine alters the serum lipid components in patients with epilepsy and lead to dyslipidemia. The study also explored whether dyslipidemia can be caused by other factors including diabetes, renal impairment and thyroid disorders and concluded that dyslipidemia in epileptic patients could primarily be considered as due to long-term use of carbamazepine. Carbamazepine is one of the most frequently used antiepileptic drugs. There are at least 20 antiepileptic drugs that are currently being used.

The study results revealed that less participants in between 18-25 years were somewhat higher in case group compared to that in control group. However, the mean age of case and control groups were almost identical (23.3 ± 6.8 vs. 23.8 ± 6.4 years, p = 0.972). The proportions of male and female patients were similar in both the study groups.

In the study all the lipid components, except total cholesterol were significantly abnormal in the case group compared to their control counterpart (Total cholesterol- 20.6% vs 13.1%, p-0.144, Triglyceride-35.5% vs 23.4%, p-0.049, LDL-15% vs 0.9%, p-<0.001, HDL-43.9% vs 18.7%, p- <0.001). The study findings are consistent with the results from a study carried out by Pankaj K et al. (2004)[17].

In the present study the number of patients with elevated triglycerides and LDL were significantly higher in patients receiving carbamazepine than those in the control group (35.5% vs. 23.4%, p = 0.049 and 15% vs. 0.9%, p < 0.001 respectively). The number of patients of low HDL was also significantly higher in the former group than that in the latter group (43.9% vs. 18.7%, p < 0.001). Nikolas T et al.[18]revealed that compared with controls, epileptic patients on carbamazepine showed significantly higher serum TC, HDL-c, and LDL-c and non-significantly higher TG values which are not consistent with findings of the present study . Eiris and collegues[19] also reported higher mean total cholesterol, HDL cholesterol and LDL cholesterol in patients receiving carbamazepine for a mean duration of 5.8 years .

Linvingston S (1976)[20] also reported an increase in triglycerides in 35 epileptics on long-term treatment with Carbamazepine, which is consistent with this study. An increase in tryglycerides and cholesterol was observed by Reynolds *et al* (1976)[21] in epileptic patients with long-term treatment of anticonvulsant drugs. In this study, the findings are partially compatible with the findings of their study.

The risk of developing dyslipidemia in epileptic patients receiving carbamazepine for at least 2 years or more was observed to be nearly three-fold (95% of CI = 1.6 – 5.0) higher than that in the control group (p < 0.001). Hamed SA and Nabeshima T also reported that prolonged use of antiepileptic drugs (AEDs) are associated with multiple risk factors that are critically implicated in pathobiology and dysfunction of the vessel wall[22] .

The duration of treatment with carbamazepine was found to bear a linear relationship with total cholesterol and triglycerides (r = 0.201, p = 0.038 and r = 0.223, p = 0.021 respectively). Verrotti A et al,[23] assessed the effect of long-term treatment of (at least 2.5 years) phenobarbital, carbamazepine and sodium valproate on serum lipids and lipoproteins in epileptic patients and found that patients treated with carbamazepine had high levels of total cholesterol, triglycerides, LDL after long-term treatment .

The proportion of dyslipidemia was considerably higher in female epileptics than that in male epileptics which bears consistency with findings from Sudhop et. al. (1999) [24] who observed HDL and LDL differences to be more pronounced in women treated with carbamazepine than those in men when compared with their controls.

Therefore, the findings of the present study are consistent with the results from similar studies i.e., long-term use of carbamazepine alters the serum lipid components in patients with epilepsy and lead to dyslipidemia. As the epileptic patients participated in the study were younger with mean age being 23 years, there is less possibility that dyslipidemia was influenced by age.

**Conclusion:**

A conclusion can be made from the above mentioned result that long-term use of carbamazepine in epileptic patients may cause dyslipidemia and the

risk of having dyslipidemia in such patients is 3 times greater than the normal healthy population.

**References:**


1. Commission on Epidemiology and Prognosis, International League Against Epilepsy, 'Guidelines for epidemiologic studies on epilepsy Commission on Epidemiology and Prognosis, International League Against Epilepsy". *Epilepsia* 1993: 34; 592–96.
2. Blume W, Lüders H, Mizrahi E, Tassinari C, van Emde Boas W & Engel J. 'Glossary of descriptive terminology for ictal semiology: report of the ILAE task force on classification and terminology', *Epilepsia* 2001; 42 (9); 1212–18.
3. Fisher R, van Emde Boas W, Blume W, Elger C, Genton P, 'Epileptic seizures and epilepsy: definitions proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE)', *Epilepsia* 2005;46 ( 4): 470–72.
4. Epilepsy: aetiogy, epidemiology and prognosis. World Health Organization. February 2001.Archived from the original on 2007-05-18. http://web.archive.org/web/20070518073641/http://www.who.int/mediacentre/factsheets/fs165/en/. Retrieved 2007-06-14.
5. The National Society for Epilepsy, 2009, *what is Epilepsy?* Available at: http://www.epilepsynse.org.uk/AboutEpilepsy/Whatisepilepsy.
6. Cascino GD. 'Epilepsy: contemporary perspectives on evaluation and treatment', *Mayo Clinic Proc* 1994;69:1199–1211.
7. Engel J Jr. 'Surgery for seizures', N Engl J Med 1996;334(10): 647–52.
8. Baker GA, Camfield C, Camfield P, Cramer JA, Elger CE, Johson LA et al. 'Commission on Outcome Measurement in Epilepsy – 1994-97: Final Report', Epilepsia 1998; 39( 2): 213-31.
9. Engel J, 2001, 'A Proposed Diagnostic Scheme for People with Epileptic Seizures And With Epilepsy: Report Of The Ilae Task Force On Classification And Terminology', *Epilepsia* 2001;42( 6):796-803.
10. Olson D 2008, 'Differentiating Epileptic Seizures From Nonepileptic Spells', Available at: http://www.consultantlive.com/consultant-for-pediatricians/article/1145470/1404577
11. The National Society for Epilepsy, 2009, *what is Epilepsy?* Available at: http://www.epilepsynse.org.uk/AboutEpilepsy/Whatisepilepsy.
12. Eiris JM, Lojo S & Del Rio MC.Effects of long-term treatment with antiepileptic drugs on serum lipid levels in children with epilepsy'. *Neurology* 1995; 45:1155-57.
13. Tekgul H, Demir N,Gokben S. 'Serum lipid profile in children receiving anti-epileptic drug monotherapy: is it atherogenic'. *J Pediatr Endocrinol Metab* 2006; 19( 9): 1151-55.
14. Mantel-Teeuwisse AK, Kloosterman JME ,Maitland-van der Zee AH , 'Drug-induced lipid changes: a review of the unintended effects of some commonly used drugs on serum lipid levels'. *Drug Saf* 2001; 24:443-56
15. Zeitlhofer J, Doppelbauer A, Tribl G.'Changes of serum lipid patterns during long-term anticonvulsive treatment'. *Clin Invest* 1993;71: 574-78.
16. Demircioðlu S, Soylu A & Dirik E. 'Carbamazepine and valproic acid: effects on the serum lipids and liver functions in children', *Pediatr Neurol* 2000; 23(2)142-46.
17. Pankaj K, Manoj T, Yogesh K, Tyagi AK, Ajay K, Yogesh KR. 'Effect Of Anticonvulsant Drugs On Lipid Profile In Epileptic Patients', *Journal of Neurology* 2004;3(1): 2-4.
18. Nikolaos T, Stylianos G, Chryssoula N, Irini P, Christos M ,Dimitrios T, 'The effect of long-term antiepileptic treatment on serum cholesterol (TC, HDL, LDL) and triglyceride levels in adult epileptic patients on monotherapy'. Med Sci Monit.2004; 10(4):50-52.

19. Eiris JM, Lojo S, Del Rio MC , 'Effects of long-term treatment with antiepileptic drugs on serum lipid levels in children with epilepsy'.*Neurology,* 1995; 45:1155–7.

20. Livingston S, 'Pheytoin and serum cholesterol'. Br Med J 1976;1:586-88.

21. Reynolds EH, Chadwick D , Galbraith AW . 'One drug (Pheytoin) in the treatment of epilepsy' *Lancet*,1976;1:923-26.

22. Hamed SA and Toshitaka N. 'The High Atherosclerotic Risk among Epileptic: the Atheroprotective Role of Multivitamins.' Journal J Pharmacol Sci 2005; 98(4): 340-53.

23. Verrotti A, Domizio S, Angelozzi B, Sabatino G, Morgese Giarelli F. 'Changes in serum lipids and lipoproteins in epileptic children treated with anticonvulsants'. J Paediatr Child Health 1997; 33(3): 242-45.

24. Sudhop T, Bauer J, Elger CE , Von Bergmann K.'Increased high-density lipoprotein cholesterol in patients with epilepsy treated with carbamazepine: a gender-related study', *Epilepsia* 1999; 40:480–84.

Bangladesh Journal of Neuroscience 2014; Vol. 30 (1) : 35-44

# Association of Dementia in Ischemic Stroke: A Case Control Study

DR. ABU JAFOR MD SALAHUDDIN[1], MD REZAUL KARIM KHAN[2], MD MUNIRUZZAMAN BHUIYAN[2], NURUDDIN MD EUSUF[3], RASED IMAM ZAHID[4], KHAIRUL KABIR PATWARY[5], MUHAMMAD SALAHUDDIN[6], MD SAYEED HASSAN[1], MD ABDUL ALIM[4], SUKUMAR MAJUMDER[7], MD MASUD RANA[8]

**Abstract:**

***Objectives:*** *To evaluate the association of dementia in ischemic stroke.* ***Methodology:*** *This case control study was carried out in the department of Neurology at BSMMU, Dhaka from 1st January 2010 to 31st December 2011 for duration of two years to evaluate the association of dementia in ischemic stroke. The target population for this study include all patients presented with ischemic stroke at the range of 3 to 6 months after stroke with the age group of 40 to 70 years are included in this study and patients of dementia other than ischemic stroke like Alzhiemer's disease, vit-B12 deficiency, thyroid dysfunction were excluded from this study. A total number of 120 respondents were included in this study. Age & sex matched 60 patients of ischemic stroke were selected as cases and rest 60 people were taken as control group. Informed written consent was taken from each patient or his/ her attendant. All information regarding history and physical findings; and other risk factors for dementia were collected to fill up the preformed questionnaire. Relevant physical examinations like nervous system examination, selected general and systemic examination were recorded.* ***Result & Observation:*** *Dementia was present in case and control group 18(30.0%) and 2(3.3%) respectively. The difference was statistically significant (p=0.001). Present smoking habit was more in case (45.0%) than in control group (16.7%) which was statistically significant (p=0.001) with a OR of 4.07 with a 95% CI of 1.89-8.75. Past smoking habit was more in case (16.7%) than control group (11.7%). Non-smoker was more in control (71.7%) than case group (38.3%). Diabetes mellitus was more common in case group (38.3%) than control group 5(8.3%) which was statistically significant (p=0.001) with a 6.84 OR and 95% CI of 2.39-19.6.* ***Conclusion:*** *The study permit to conclude that dementia is directly associated with ischemic stroke. We found a correlation between age, family history of dementia, hypertension, diabetes mellitus and dyslipidemia with dementia.*

***Keywords:*** *Dementia, Ischemic Stroke.*

## Introduction:

Dementia is an acquired and persistent compromise in multiple cognitive domains that is severe enough to interfere with everyday functioning[1]. This definition stands in contrast with delirium or acute confusional state, which are distinguished primarily by prominent deficits or fluctuations in attentional processing. Although dementia syndromes tend to be chronic, progressive, and irreversible, and acute confusional states tend to be acute to subacute, fluctuating,

1. Junior Consultant, National Institute of Neurosciences & Hospital, Dhaka.
2. Professor,Department of Neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh
3. Thana Health & Family Planning Officer, Moralganj Health Complex, Bagerhat.
4. Medical officer, National Institute of Neurosciences & Hospital, Dhaka.
5. Assistant professor, National Institute of Neurosciences & Hospital, Dhaka.
6. Registrar, Department of Medicine, Chittagong Medical College Hospital,
7. Registrar, Department of Neurology, Rangpur Medical College Hospital, Rangpur.
8. MO, Department of Neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.

and reversible, these distinctions are more relative than absolute[2].

Dementia is a syndrome consisting of a loss of several separable but overlapping intellectual abilities and present in a number of different combinations[3]. Memory is the most common cognitive ability lost with dementia; 10% of persons >70 and 20–40% of individuals >85 years of age have clinically identifiable memory loss. In addition to memory, other mental faculties are also affected in dementia; these include language, visuospatial ability, calculation, judgment, and problem solving. Neuropsychiatric and social deficits also develop in many dementia syndromes, resulting in depression, withdrawal, hallucinations, delusions, agitation, insomnia, and disinhibition. The most common forms of dementia are progressive, but some are static and unchanging or fluctuate dramatically from day to day. Most diagnoses of dementia require some sort of memory deficit, although there are many dementias, such as frontotemporal dementia, where memory loss is not a presenting feature[4].

Dementia affects more than 4 million Americans and results in a total health care cost of >$100 billion annually. The reported frequency of dementia due to potentially reversible causes varies from 0 to 23%[5,6,7]. Historically, patients with dementia due to recurrent strokes were diagnosed with multi-infarct dementia termed as vascular dementia, since the disease can occur after a single vascular incident[8]. Vascular dementia is widely accepted as the second most common cause of cognitive impairment.

Stroke is clearly related to vascular dementia, the second-most-common type of dementia[9]. There has been a recent upsurge of interest in poststroke dementia (PSD), which is a subtype of vascular dementia. PSD is operationally defined as the presence of dementia identified at 3 months after an acute, either recurrent or first-ever, stroke[10]. The prevalence of PSD among recurrent or first-ever stroke patients varies from 6% to 31.8%[10-12].

Stroke is the major cause of physical disability in adults[13]. It is the second most common cause of dementia, and the third leading cause of death in developed countries[14]. In a population of 1 million inhabitants, 2400 patients will have a stroke every year, of whom fewer than 50% will be independent 1 year later[15]. Leys et al (2005)[13] reported that dementia is one of the major causes of dependency after stroke.

Poststroke dementia (PSD) is one of the main causes of dependency in survivors and includes any dementia after a stroke, irrespective of its cause like vascular, degenerative, or mixed[13]. A huge increase in prevalence and burden of PSD is likely to happen because of the decline in mortality after stroke and ageing of populations[16]. PSD includes all types of dementias that happen after stroke, irrespective of their cause[13]. In prevalence studies, PSD included both pre-existing dementia and new-onset dementia after stroke[3]. In community-based studies with adjustment for age, the prevalence of dementia in people with a history of stroke is about 30% [17]. In hospital-based studies, the prevalence of PSD ranges from 5·9 to 32%[13]. Stroke increases the risk of dementia up to 12 times[18,19]. The overall prevalence of dementia is estimated in India was 3.36%[20].

In Bangladesh there is no research and data about prevalence or incidence of post stroke dementia. Post stroke dementia is the most disabling of all the neurological diseases and in the context of our country it poses a huge burden both socially and economically. The treatment cost benefit is frustrating and rehabilitation is not expectedly available. So, we should concentrate more on prevention. As there is no local data on this topic, this study is therefore planned to identify the association of dementia with ischemic stroke and to find out the determinants of dementia in ischemic stroke.

**Methods:**

This study was a case control study, which was carried out in the department of Neurology at BSMMU, Dhaka, from 1st January 2010 to 31st December 2011 for a duration of two years. The target population for this study included all patients presented with ischemic stroke of 40-70 years of age in both sexes. Age and sex matched volunteer/ patients other than ischemic stroke were selected as the control group. Data collection was conducted

by researcher himself. All data were compiled and edited meticulously by thorough checking and rechecking. All omissions and inconsistencies were corrected and were removed methodically. All data were recorded systematically in preformed data collection form (questionnaire) and quantitative data was expressed as mean and standard deviation and qualitative data was expressed as frequency distribution and percentage. Statistical analysis was performed by using SPSS for windows version 15.0. 95% confidence limit was taken. Probability value <0.05 was considered as level of significance.

**Results and Observations:**

A total number of 120 respondents were included in this study of which 60 patients of ischemic stroke were selected as case and the rest 60 volunteer were selected as control.

The mean age of case and control group were 57.13 ± 7.39 and 57.37 ± 7.94 respectively (p=0.868). In both case and control groups male and female were equal in number which were 42(70.0%) and 18(30.0%) respectively. Smokers/ ex-smokers were more in case than control group which was 39(65.0%) and 15 (25.0%) respectively (p=0.001) with as OR of 5.57 with a 95% CI of 2.53-12.27. Non-smokers were more in case than control group which was 21 (35.0%) and 45(75.0%) respectively. Diabetes mellitus was more common in case group than control which was 30 (50.0%) and 5(8.3%) respectively. The difference was statistically significant (p=0.001) with 11.00 as OR and 95% CI of 3.87-31.31. Hypertension was more common in case group than control which was 45(75.0%) and 20(33.3%) respectively. The difference was statistically significant (p=0.001) with 6.84 as OR and 95% CI of 2.71-13.27. Dyslipidaemia was more common in case group than control which was 39(65.0%) and 26(43.3%) respectively. The difference was statistically significant (p=0.017) with 2.43 as OR and 95% CI of 1.16-5.07. Cardiac diseases were more common in control group than case which was 5(8.3%) and 4(6.7%) respectively. The difference was statistically not significant (p=0.729) with 0.79 as OR and 95% CI of 0.20-3.08. Family history of dementia was more common in case group than control which was 6 (10.0%) and 1 (1.7%) respectively. The difference was statistically not significant (p=0.051) with 6.56 as OR and 95% CI of 0.76-56.22. These are shown in Table I.

**Table-I**

*Respondents characteristics (n=120)*

| Variables | Group | | P value | OR (95%CI) |
|---|---|---|---|---|
| | Case (Stroke) n=60 | Control (non-stroke) n=60 | | |
| Age (y) | 57.13 ± 7.39 | 57.37 ± 7.94 | 0.868 | |
| Sex | | | | |
| Male | 42 (70.0)# | 42 (70.0) | 1.000 | |
| Female | 18 (30.0) | 18 (30.0) | | |
| Smoking | | | | |
| Smoker/ Ex-smoker | 39(65.0)# | 15 (25.0) | 0.001* | 5.57 (2.53-12.27) |
| Non smoker | 21 (35.0) | 45(75.0) | | |
| Diabetes mellitus | 30 (50.0) | 5(8.3) | 0.001* | 11.00 (3.87-31.31) |
| Hypertension | 45(75.0) | 20(33.3) | 0.001* | 6.00 (2.71-13.27) |
| Dyslipidaemia | 39(65.0) | 26(43.3) | 0.017 | 2.43 (1.16-5.07) |
| Cardiac disease | 4(6.7) | 5(8.3) | 0.729 | 0.79 (0.20-3.08) |
| Family history ofdementia | 6 (10.0) | 1 (1.7) | 0.051 | 6.56 (0.76-56.22) |

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

#Figure within parentheses indicates in percentage.

**Table-II**

*Distribution of the respondents by dementia (n=120)*

| Dementia | Group | | p value |
|---|---|---|---|
| | Case (n=60) | Control (n=60) | |
| Present | 18 (30.0) | 2 (3.3) | 0.001 |
| Absent | 42 (70.0) | 58 (96.7) | |
| Total | 60 (100.0) | 60 (100.0) | |

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

**Table-III**

*Distribution of the respondents by MMSE (n=120)*

| MMSE | Case (n=60) | | | Control (n=60) | | |
|---|---|---|---|---|---|---|
| | Dementia | Non-dementia | p value | Dementia | Non-dementia | p value |
| Severe | 01(5.55%) | 0 (0.0) | | 00 | 00 | |
| Moderate | 14 (77.77) # | 0 (0.0) | 0.001 | 1 (50.0) | 0 (0.0) | |
| Mild | 3 (16.68) | 0 (0.0) | | 1 (50.0) | 0 (0.0) | |
| Normal | 0 (0.0) | 42 (100.0) | | 0 (0.0) | 58 (100.0) | |
| Total | 18 (100.0) | 42 (100.0) | | 2 (100.0) | 58 (100.0) | |

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

#Figure within parentheses indicates in percentage.

(Scores on the MMSE ranges from 0 to 30, with scores of 24 or higher being traditionally considered normal. Scores less than 10 generally indicate severe impairment while scores between 10 and 19 indicate moderate dementia. Scores between 19-24 indicate MCI.)

Table II shows the distribution of the patients by dementia. In case and control group dementia was present in 18(30.0%) cases and 2(3.3%) in control respectively. Dementia was absent in 42(70.0%) cases and 58(96.7%) in control. The difference is statistically significant (p=0.001).

Table III shows the distribution of the patients by MMSE. In case group dementia was present with a severe, moderate and mild MMSE in 01(5.55%), 14 (77.77%) and 3(16.68%) cases respectively. In control group dementia was present with moderate and mild MMSE in only 1 (50.0%) case in each category.

**Table-IV**

*Distribution of the respondents by smoking habit.*

| Smoking habit | Group | | p value |
|---|---|---|---|
| | Case (n=18) | Control (n=02) | |
| Smoker | 14 (77.8) # | 0 (0.0) | 0.023 |
| Non-smoker | 4 (22.2) | 2 (100.0) | |
| Total | 18 (100.0) | 2 (100.0) | |

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

#Figure within parentheses indicates in percentage.

Table IV shows the distribution of the patients by smoking habit. In case group smoker and nonsmoker were 14 (77.8%) and 4 (22.2%) respectively. In control group no smoker was found and only 2 (100.0%) cases were non-smokers. The difference is statistically significant (p=0.023).

**Table-V**

*Distribution of the respondents by Hypertension.*

| Hypertension | Group | | p value |
|---|---|---|---|
| | Case (n=18) | Control (n=2) | |
| Present | 14 (77.8) # | 0 (0.0) | 0.023 |
| Absent | 4 (22.2) | 2 (100.0) | |
| Total | 18 (100.0) | 2 (100.0) | |

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

Table V shows the distribution of the patients by hypertension. In case group hypertension was present in 14 (77.8%) cases and absent in 4 (22.2%) cases. In control group hypertension was absent in all 2 (100.0%) cases. The difference is statistically significant (p=0.023).

**Table-VI**

*Distribution of the respondents by Diabetes mellitus.*

| Diabetes mellitus | Group | | p value |
|---|---|---|---|
| | Case (n=18) | Control (n=2) | |
| Present | 13 (72.2)# | 0 (0.0) | 0.042 |
| Absent | 5 (27.8) | 2 (100.0) | |
| Total | 18 (100.0) | 2 (100.0) | |

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

Table VI shows the distribution of the patients with dementia by diabetes mellitus. In case group diabetes mellitus was present in 13 (72.2%) cases and absent in 5 (27.8%) cases. In control group diabetes mellitus was absent in all 2 (100.0%) cases. The difference is statistically significant (p=0.042).

**Table-VII**

*Distribution of the respondents by dyslipidaemia.*

| Dyslipidaemia | Group | | p value |
|---|---|---|---|
| | Case (n=18) | Control (n=02) | |
| Present | 13 (72.2)# | 0 (0.0) | 0.042 |
| Absent | 5 (27.8) | 2 (100.0) | |
| Total | 18 (100.0) | 2 (100.0) | |

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

Table VII shows the distribution of the patients by dyslipidaemia. In case group dyslipidaemia was present in 13 (72.2%) cases and absent in 5 (27.8%) cases. In control group dyslipidaemia was absent in all 2 (100.0%) cases. The difference is statistically significant (p=0.042).

**Table-VIII**

*Distribution of the respondents by Cardiac disease*

| Cardiac disease | Group | | p value |
|---|---|---|---|
| | Case (n=18) | Control (n=02) | |
| Present | 1 (5.6)# | 1 (50.0) | 0.047 |
| Absent | 17 (94.4) | 1 (50.0) | |
| Total | 18 (100.0) | 2 (100.0) | |

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

Table VIII shows the distribution of the patients by cardiac disease. In case group cardiac disease was present in 1 (5.6%) case and absent in 17 (94.4%) cases. In control group cardiac disease was present only 1 (50.0%) case and absent in only 1 (50.0%) case. The difference is statistically significant (p=0.047).

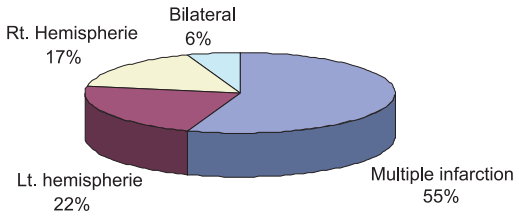


**Fig.-3:** *Distribution of respondents by CT/ MRI findings*

Figure 3 shows distribution of patients according to site of lesion by CT/MRI scan where multiple infraction in 10(55%), left hemispheric 4(22%), right hemispheric 3(17%) and bilateral 1(6%) were found.

**Table-IX**

*Distribution of the respondents by family history of dementia.*

| Family history of dementia | Group | | p value |
|---|---|---|---|
| | Case (n=18) | Control (n=02) | |
| Yes | 4 (22.2)# | 0 (0.0) | 0.456 |
| No | 14 (77.8) | 2 (100.0) | |
| Total | 18(100.0) | 2 (100.0) | |

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

Table IX shows the distribution of the patients by family history of dementia. In case group family history of dementia was present in 4 (22.2%) cases and absent in 14 (77.8%) cases. In control group no family history of dementia was found and absent in 2 (100.0%) cases. The difference is not statistically significant (p=0.456).

**Table-X**

*Distribution of the respondents by biochemical parameters (n=120)*

| Biochemical parameters | Group | | p value |
|---|---|---|---|
| | Case (Mean±SD) | Control (Mean±SD) | |
| Blood Sugar (Random) | 6.45±2.34 | 6.15±1.48 | 0.866 |
| Serum creatinine | 1.18±0.44 | 0.88± 0.02 | 0.381 |
| S. TSH | 2.24±1.31 | 2.92±1.19 | 0.496 |
| Vitamin $B_{12}$ | 665.07±277.55 | 796.50±112.43 | 0.121 |

*t test was done to measure the level of significance.

Table X shows the distribution of the patients by biochemica1l parameters. In case and control groups the mean blood sugar was 6.45 ± 2.34 and 6.15 ± 1.48 respectively (p=0.866). In case and control groups the mean serum creatinine was 1.18 ± 0.44 and 0.88 ± 0.02mg respectively (p=0.381). In case and control groups the mean S. TSH was 2.24 ± 1.31 and 2.92 ± 1.19mmol/L respectively (p=0.496). In case and control groups the mean vitamin $B_{12}$ was 665.07 ± 277.55 and 796.50 ± 112.43 respectively (p=0.121).

**Table-XI**

*Distribution of the respondents by serum lipid profile (n=120)*

| Serum lipid profile | Group | | p value |
|---|---|---|---|
| | Case (Mean±SD) | Control (Mean ± SD) | |
| Total cholesterol | 198.59±64.45 | 182.00±7.07 | .727 |
| LDL | 126.53±52.09 | 109.50±3.53 | .658 |
| HDL | 39.47±12.56 | 53.50±4.95 | .144 |
| TG | 149.41±77.82 | 96.00±43.84 | .362 |

*t test was done to measure the level of significance.

Table XI shows the distribution of the patients by serum lipid profile. In case and control groups the mean Total cholesterol was 198.59 ± 64.45 and 182.00± 7.07mg/L respectively (p=0.727). In case and control groups the mean LDL was 126.53±52.09 and 109.50±3.53mg/L respectively (p=0.658). In case and control groups the HDL was 39.47±12.56 and 53.50±4.95mg/L respectively (p=0.144). In case and control groups the mean TG was 149.41±77.82 and 96.00±43.84mg/L respectively (p=0.362).

**Table-XII**

*Distribution of the respondents by dementia and age*

| Age | Group | | p value* |
|---|---|---|---|
| | Dementia (n=20) | No dementia (n=100) | |
| Mean (±SD) | 61 (±7.62) | 56.4 (±7.4) | 0.007 |

*Unpaired t test was done to measure the level of significance

Table XII shows the distribution of the respondents by dementia and age. Out of all patients of dementia mean of age was 61 (±7.62) years. On the contrary among all respondents of non-dementia, mean of age was 56.4 (±7.4) years. This variation is statistically significant at p value less than 0.007 level.

**Table-XIII**

*Distribution of the respondents by dementia and stroke (n=120)*

| Respondents | Group | | p value* |
|---|---|---|---|
| | Dementia (n=20) | No dementia (n=100) | |
| Case (stroke) | 18 (90.0) | 42 (42.0) | |
| Control (Healthy adult) | 2 (10.0) | 58 (58.0) | <0.001 |
| Total | 20(100.0) | 100(100.0) | |

*Chi square test was done to measure the level of significance
OR (95% CI) = 12.43 (2.74-56.48)

Table XIII shows the distribution of the respondents by dementia. Out of all patients of ischemic stroke 18 had developed dementia. On the contrary among healthy control only 2 had dementia. This variation is statistically highly significant at p value less than 0.001 level. Patients with stroke had 12.43 times more chance to develop dementia than healthy controls.

**Table-XIV**

*Distribution of the respondents by dementia and smoking (n=120)*

| Smoking | Group | | p value* |
|---|---|---|---|
| | Dementia (n=20) | No dementia (n=100) | |
| Present | 14 (70.0) | 40 (40.0) | |
| Absent | 6 (30.0) | 60 (60.0) | 0.014 |
| Total | 20 (100.0) | 100(100.0) | |

*Chi square test was done to measure the level of significance
OR (95% CI) = 3.5 (1.24-9.87)

Table XIV shows the distribution of the respondents by dementia and smoking habit. Out of all patients of dementia 70.0% were smoker. On the contrary among all respondents of non-dementia 40.0% were smoker. This variation is statistically significant at p value less than 0.014 level. Smokers had 3.5 times more chance to develop dementia than that of non-smoker.

**Table-XV**

*Distribution of the respondents by dementia and hypertension (n=120)*

| Hypertension | Group | | p value* |
|---|---|---|---|
| | Dementia (n=20) | No dementia (n=100) | |
| Present | 14(70.0) | 51(51.0) | |
| Absent | 6(30.0) | 49 (49.0) | <0.12 |
| Total | 20 (100.0) | 100(100.0) | |

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

Table XV shows the distribution of the respondents by dementia and hypertension. Out of all patients of dementia 70% were hypertensive. On the contrary among all respondents of non-dementia 51% were hypertensive. This variation is statistically not significant at p value less than 0.012 level.

**Table-XVI**

*Distribution of the respondents by dementia and diabetes mellitus (n=120)*

| DM | Group | | p value* |
|---|---|---|---|
| | Dementia (n=20) | No dementia (n=100) | |
| Present | 13 (65.0) | 22 (22.0) | |
| Absent | 7 (35.0) | 78 (78.0) | <0.001 |
| Total | 20 (100.0) | 100(100.0) | |

*Chi square test was done to measure the level of significance
OR (95% CI) = 6.58 (2.34-18.51)

Table XVI shows the distribution of the respondents by dementia and diabetes mellitus. Out of all patients of dementia 65% were diabetic. On the contrary among all respondents of non-dementia 35% were non diabetic. This variation is statistically significant at p value less than 0.001 level. Diabetic patients had 6.58 times more chance to develop dementia than that of non-diabetic patients.

**Table-XVII**

*Distribution of the respondents by dementia and dyslipidaemia (n=120)*

| Dyslipidaemia | Group | | p value* |
|---|---|---|---|
| | Dementia (n=20) | No dementia (n=100) | |
| Present | 13(65.0) | 52(52.0) | |
| Absent | 7(35.0) | 48(48.0) | <0.287 |
| Total | 20(100.0) | 100(100.0) | |

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

Table XVII shows the distribution of the respondents by dementia and dyslipidaemia. Out of all patients of dementia 65% had dyslipidaemia. On the contrary among all respondents of non-dementia 52% had dyslipidaemia. This variation is statistically not significant at p value less than 0.287 level.

**Table-XVIII**

*Distribution of the respondents by dementia and family history of dementia (n=120)*

| Family history of dementia | Group | | p value* |
|---|---|---|---|
| | Dementia (n=20) | No dementia (n=100) | |
| Present | 4 (20.0) | 4 (4.0) | |
| Absent | 16 (80.0) | 96 (96.0) | 0.033 |
| Total | 20(100.0) | 100(100.0) | |

*Chi square (after Yates correction) test was done to measure the level of significance

OR (95% CI) = 6.00 (1.36-26.45)

Table XVIII shows the distribution of the respondents by dementia and family history of dementia. Out of all patients of dementia 20% had family history of dementia. On the contrary among all respondents of non-dementia 4% had family history of dementia. This variation is statistically significant at p value less than 0.033 level. Family history of dementia had 6 times more chance to develop dementia than that of no family history of dementia.

**Table-XIX**

*Distribution of the respondents by dementia and different risk factors (n=120)*

| Variables | Group | | Unadjusted OR | Adjusted OR |
|---|---|---|---|---|
| | Dementia (n=20) | No dementia (n=100) | | |
| Stroke | 18 (90.0) | 42 (42.0) | 12.43 | 8.49** (1.42-50.64) |
| Smoker | 14 (70.0) | 40 (40.0) | 3.5 | 1.28 (0.35-4.68) |
| DM | 13 (65.0) | 22 (22.0) | 6.58 | 4.91** (1.35-17.82) |
| Family history of dementia | 4 (20.0) | 4 (4.0) | 6.0 | 2.3 (0.42-12.62) |
| Age (y) | 61 (±7.62) | 56.4 (±7.4) | | 1.14** (1.04-1.25) |

*Significant

Table XIX shows in bivariate analysis we got ischemic stroke, smoking habit, diabetes mellitus, family history of dementia and age as significant risk factors for dementia. In binary logistic regression model we entered these variables as predictors for dementia to draw the conclusion about the significant risk factors for dementia. In this logistic model (enter method) we found ischemic stroke, diabetes mellitus and age as significant risk factors for dementia. Since age is a quantitative variable, an increase in one-year in age has a 14% (95% CI 4%-25%) increase in odds of having dementia. This 14% obtained by taking Odd of age-15. Discussion:

A total number of 120 respondents were included in this study of which 60 patients of ischemic stroke were selected as case and the rest 60 volunteers were selected as control.

The distribution of the patients by age was recorded in this study. In 40 – 49 years age group among cases dementia was present in 2 (11.1%) cases and absent in control group. In 50 – 59 years age group dementia was present in 5(27.8%) cases and absent in control group. In 60 years and above age group dementia was present in 11(61.1%) cases and 2 (100.0%) in control group. The mean age± SD is 60.50±7.44 and 70.00 ± 0.0 in case and control groups respectively (p=0.021). Similar result was recorded by Lis and Gaviria[21].

The distribution of the patients by sex was recorded in this study. In case group the presence of dimentia in male was predominant than female which was 13(72.2%) and 5(27.8%) respectively. In control group the presence of dimentia in male was 2 (100.0%) and no in female. The difference was statistically not significant (p=0.346). But the study done by Andersen et al (1999) mentioned that there was a gender differences in risk for vascular dementia. Similarly Launer et al (1999)[22] found that gender was a potential modifiers of risk of dementia which is consistent with the present study.

The distribution of the patients by presences of dementia was recorded. In case and control group dementia was present in 18(30.0%) cases and 2(3.3%) in controls respectively. Dementia was absent in case and control groups which was 42(70.0%) in cases and 58(96.7%) in controls respectively. The difference was statistically significant (p=0.001). Tatemichi et al (1992)[19] shows the frequency of dementia with acute ischemic stroke, based on examinations performed 3 months after stroke onset. They found dementia was present 26.3% in cases and 3.2% in controls. So, this study permit to conclude that dementia was directly associated with ischemic stroke.

The distribution of the patients by smoking habit is recorded in this study. In case group smoker and non-smoker were 14(77.8%) and 4(22.2%) respectively. In control group no smoker was found and only 2(100.0%) cases were non-smoker. The difference is statistically significant (p=0.023). Smokers have 3.17 times more chance to develop stroke than non-smokers. Similar result was reported by Posner et al(2000)[23] and mentioned that smoking increased the risk of dementia significantly.

The distribution of the patients by MMSE is recorded in this study. In case group dementia was present

with a severe, moderate and mild MMSE in 01(5.55%), 14(77.77%) and 3(16.68%) cases respectively. In control group dementia was present with a moderate and mild MMSE in only 1 (50.0%) case in each category.

The distribution of the patients with dementia by hypertension was recorded in this study. In case group hypertension is present in 14(77.8%) cases and absent in 4(22.2%) cases. In control group hypertension was absent in all 2 (100.0%) cases. The difference is statistically significant (p=0.023). Posner et al (2000)[23] mentioned that hypertension is directly affect memory, language, or general cognitive function. A history of hypertension may be an antecedent to VaD, particularly in the presence of heart disease or diabetes.

The distribution of the patients with dementia by diabetes mellitus was recorded in this study. In case group diabetes mellitus was present in 13(72.2%) cases and absent in 5(27.8%) cases. In control group diabetes mellitus was absent in all 2(100.0%) cases. The difference is statistically significant (p=0.042). Similar result was reported by Strachan et al[26].

The distribution of the patients with dementia by dyslipidaemia was recorded in this study. In case group dyslipidaemia was present in 13 (72.2%) cases and absent in 5 (27.8%) cases. In control group dyslipidaemia was absent in all 2 (100.0%) cases. The difference is statistically significant (p=0.042).

The distribution of the patients with dementia by cardiac disease was recorded in this study. In case group cardiac disease was present in 1 (5.6%) case and absent in 17 (94.4%) cases. In control group cardiac disease was present 1 (50.0%) case and absent in 1 (50.0%) case. The difference is statistically significant (p=0.047). Similar result was reported by Posner et al(2000)[23] and mentioned that a history of hypertension may be an antecedent to VaD, particularly in the presence of heart disease.

The distribution of the patients by family history of dementia was recorded. In case group family history of dementia was present in 4 (22.2%) cases and absent in 14 (77.8%) cases. In control group no family history of dementia was found i.e. absent in all 2 (100.0%) cases. The difference is not statistically significant (p=0.456). But Huang et al (2004)[27] mentioned that a family history of dementia continue to influence the occurrence of dementia. Launer et al (1999)[22] also reported a result correlating between family history of dementia and occurrence of dementia and found a result which is consistent with the present study.

**References:**


1. American Psychiatric Association. 'Diagnostic and Statistical Manual of Mental Disorders: DSM-IV, 4th ed.' Washington, DC: American Psychiatric Association 1994,
2. Bradley WG, Daroff RB, Fenichel GM, Jankovic J, editors. 'Neurology in clinical practice. 5th ed.' Philadelphia: Butterworth-Heinemann Elsevier 2008.
3. Ropper AH, Brown RH, editors. 'Adams and Victor's principles of neurology' 8th ed. New York The MacGraw-Hill Companies 2005.
4. Fauci AS, Kasper DL, Longo DL, Braunwald E, Hauser SL, Jameson JL, et al, editors, 'Harrison's principles of internal medicine' 17th ed. New York: The MacGraw-Hill Companies 2008.
5. Clarfield AM, 'The decreasing prevalence of reversible dementias: an updated meta-analysis' *Arch Intern Med*; 2003, 163:2219-2229.
6. Clarfield AM, 'The reversible dementias: do they reverse?' *Ann Intern Med* 1988;109:476-486.
7. Weytingh MD, Bossuyt PM, van Crevel H, 'Reversible dementia: more than 10% or less than 1%? A quantitative review' *J Neurol*; 1995, 242: 466-471.
8. Rojas-Fernandez CH, Moorhouse P, 'Current concepts in vascular cognitive impairment and pharmacotherapeutic implications' *Ann Pharmacother* . 2009;43:1310-23
9. Skoog I, Nilsson L, Palmertz B, Andreasson LA, Svanborg A, 'A population-based study of dementia in 85-year-olds' *N Engl J Med* 1993; 328: 153–8.

10. Pohjasvaara T, Erkinjuntti T, Yilkoski R, Hietanen M, Vataja R, Kaste M, 'Clinical determinants of poststroke dementia' *Stroke*1998;29:75–81.

11. Inzitari D, Carlo A, Pracucci G, Lamassa M, Vanni P, Romanelli M, 'Incidence and determinants of poststroke dementia as defined by an informant interview method in a hospital-based stroke registry' *Stroke* 1998; 29:2087–93.

12. Madureira S, Guerreiro M, Ferro JM, 'Dementia and cognitive impairment three month after stroke' *Eur J Neurol* 2001;8:621–27.

13. Leys D, Hénon H, Mackowiak-Cordoliani MA, FP, 'Poststroke dementia' Lancet Neurol 2005; 4: 752–59

14. Murray CJ, Lopez AD, 'Global mortality, disability, and the contribution of risk factors: Global Burden of Disease Study' Lancet 1997; 349: 1436-42

15. Hankey GJ, Warlow CP, 'Treatment and secondary prevention of stroke: evidence, costs, and effects on individuals and populations. Lancet' 1999, 354: 1457–63.

16. Rothwell PM, Coull AJ, Giles MF, 'Change in stroke incidence, mortality, case-fatality, severity, and risk factors in Oxfordshire' UK from 1981 to 2004: Oxford Vascular Study. Lancet 2004,363: 1925–33.

17. Zhu L, Fratiglioni L, Guo Z, Aguero-Torres H, Winblad B, Viitanen M, 'Association of stroke with dementia, cognitive impairment, and functional disability in the very old: a population based study' Stroke 1998; 29: 2094–99.

18. Liu CK, Lin RT, Chen YF, Tai CT, Yen YY, Howng SL, 'Prevalence of dementia in an urban area in Taiwan' J *Formos Med Assoc* 1996 ;95:762–68.

19. Tatemichi TK, Desomnd DW, Mayeux R, Paik M, Hier DB, Price TR, 'Dementia in stroke survivors in the Stroke Data Bank cohort prevalence, incidence, risks, and clinical features in a hospitalized cohort' *Neurology* 1992;42:1185–93.

20. Shaji S, Bose S and Verghese A, 'Prevalence of dementia in an urban population in Kerala, India' British Journal of Psychiatry 2005, 186:136-40.

21. Lis and Gaviria M. Vascular dementia, hypertension, and the brain. Neurol Res. 1997;19:471-80.

22. Launer LJ, Andersen K, Dewey ME, Letenneur L, Ott A, Amaducci LA, 'Rates and risk factors for dementia and Alzheimer's disease: results from EURODEM pooled analyses. EURODEM Incidence Research Group and Work Groups. European Studies of Dementia. Neurology'. 1999;52(1):78-84.

23. Posner HB,Tang MX, Luchsinger J, Lantigua R,Stern Y, Mayeux R, 'The relationship of hypertension in the elderly to AD, vascular dementia, and cognitive function' Neurology 2000;58: 1175-81

24. O'Bryant SE, Humphreys JD, Smith GE, Ivnik RJ, Graff-Radford NR, Petersen RC. 'Detecting Dementia with the Mini-Mental State Examination (MMSE) in Highly Educated Individuals' Arch Neurol. 2008 ; 65(7): 963–67

25. Strauss, E.; Sherman, EMS.; Spreen, O, 'A Compendium of Neuropsychological Tests: Administration, norms, and commentary' 3rd ed. Oxford University Press; Oxford: 2006.

26. Strachan MW, Deary IJ, Ewing FM, Frier BM, 'Is type II diabetes associated with an increased risk of cognitive dysfunction' A critical review of published studies. Diabetes Care; 1997, 20: 438-45

27. Huang W, Qiu C, von Strauss E, Winblad B, Fratiglioni L, 'APOE genotype, family history of dementia, and Alzheimer disease risk: a 6-year follow-up study' Arch Neurol. 2004;61(12):1930-1934

Bangladesh Journal of Neuroscience 2014; Vol. 30 (1) : 45-49

# Evaluation of C Reactive Protein in Acute Ischemic Stroke

KAZI GIASUDDIN AHMED[1], ABU SALEH MD BADRUL HASAN[2], BIPLOP KUMAR ROY[3], MD RAFIQUL ISLAM[4],MD. RUHUL QUDDUS[5]

**Abstract:**

*Background: Stroke is a dreadful health hazard all over the world as well as in our country. The relationship between serum C-reactive protein (CRP) level and acute ischaemic stroke is not well studied especially in Bangladesh. Aims and Objectives: To evaluate the association of C-reactive protein (CRP) in acute ischemic stroke .Materials and Methods: This case-control study was carried out in the Department of Neurology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka during the period from January 2006 to December 2007. A total of 30 acute ischaemic stroke patients were included in the case group. Another 30 age and sex matched and apparently healthy persons without any stroke were taken as controls. Results: The stroke patients [21 (70.0%) male; mean age, 56.3 (SD±13.7) years] and control subjects [25 (83.3%) male; mean age, 53.4 (SD ± 9.9) years] were similar in age and sex (p>0.05 each). CRP level was significantly higher in acute ischaemic stroke patients than that of control [42.06 (SD ± 21.26) mg/L; vs 4.30 (SD ± 0.072) mg/L; p<0.001]. CRP was found positive in 28 (93.7%) stroke patients and none of the control subjects. CRP was 16 times significantly higher in stroke patients than that of control subjects (OR=16.00; 95% CI=4.18-61.22; p<0.001).Conclusion: This study confirms that CRP is elevated in acute ischaemic stroke. More local studies are required regarding the significance of CRP as a risk factor for acute ischemic stroke.*

## Introduction:

World Health organization defined stroke as a clinical syndrome occurring due to sudden cerebral dysfunction, producing focal or global neurological deficit, persisting for more than 24 hours or the patient dies within 24 hours, vascular in origin, non-epileptic and non-traumatic in nature[1]. Stroke remains third leading cause of death after heart disease and cancer after the age of 40[2]. About 4 million deaths per year worldwide are due to stroke, three-quarters of them in developing countries[3].

Of all strokes, 85 percent are ischaemic infarction and 15 percent are haemorrhage; thus ischaemic cerebrovascular disease accounts for a substantial proportion of all strokes. Although the proximate cause of most brain infarcts is thrombus formation, atherosclerosis is the chief underlying cause[4]. C-reactive protein (CRP), one of the acute-phase reactants, is an indicator of underlying systemic inflammation and a novel plasma marker of atherothrombotic disease[5]. Furthermore, elevated plasma levels of C-reactive protein are not disease specific but are sensitive markers produced in response to tissue injury, infectious agents, immunologic stimuli, and inflammation[6].

Elevated blood levels of C-reactive protein (CRP) are associated with an increased risk of therosclerotic vascular disease including stroke[7].However the role of CRP in the etiology and prognosis of ischemic stroke remains to be clearly defined[8]. One hypothesis is that CRP plays a direct causal role in the pathogenesis of atherosclerosis by promoting endothelial cell adhesion molecule expression, monocyte recruitment or complement

1. Assistant Professor, Department of Neurology, National Institute of Neurosciences & Hospital, Dhaka.
2. Assistant Professor, Department of Neurology, Dinazpur Medical College & Hospital,Dinazpur.
3. Associate Professor, Department of Neurology, Sylhet MAG Medical College & Hospital,Sylhet
4. Professor , Department of Neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh
5. Assistant Professor, Department of Neurology, Shaheed Abu Naser Hospita, Khulna

activation, or by mediating low density lipoprotein cholesterol uptake by macrophages[9].

This "atherogenic hypothesis" is consistent with prospective observational studies of apparently healthy individuals as well as patients with established vascular disease, including stroke which have shown that elevated blood concentrations of CRP are a significant predictor of future cardiovascular events, independent of conventional vascular risk factors[10].

Elevated blood concentrations of CRP during the acute phase of ischaemic stroke event primarily reflect the extent of cerebral ischaemic injury and its complications[11]. Higher values of C-reactive protein (CRP) are significantly associated with large infarct size and worst outcome[12]. So C-reactive protein might indicate the inflammatory status during the acute phase of ischaemic stroke. Use of plasma CRP levels may aid indentifying a potentially large number of men and women who are at risk for cerebrovascular events[6].

As C-reactive protein is a marker of inflammation and if we target for intervention against inflammatory response in ischaemic stroke may halt the disease progression and improve outcome. The purpose of the study is to find out the association of C-reactive protein in ischemic stroke.

**Materials and Methods:**

This was an observational case control study carried out in the Department of Neurology in collaboration with the Department of Microbiology and Immunology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka during the period from January 2006 to December 2007.

A total of 30 patients were included in the study group whom met the inclusion and exclusion criteria. Inclusion were all acute ischaemic stroke (<4 weeks duration) proved clinically and confirmed by neuroimaging (CT/MRI of brain), aged more than 30 years and either sex. Patients with history of acute myocardial infarction, venous thrombosis, myeloproliferative diseases, malignancy, rheumatological diseases, connective tissue diseases, recent surgery (within one month) and recent infection (within one month) were excluded.

A total of 30 age and sex matched and apparently healthy persons were taken as controls. Controls never suffered from stroke and came in neurology outpatient department for nonspecific disorders and symptoms like anxiety neurosis, myalgia, burning limbs, tingling numbness, headache and somatoform disorders and had no clinically apparent infection or inflammation or sign of neurological deficit.

Written consent was taken after explaining the study procedure and aims of the study. Detail history was taken about age, sex, hypertension, diabetes, smoking habit, cardiac disease and oral contraceptive pills. They were also asked about febrile infection or productive cough, diarrhoea and dysuria. They were clinically evaluated for the presence of sinusitis, diabetes, hypertension, and tuberculosis, pneumonia, bronchitis. For detection of lymphadenopathy cervical, supraclavicular, axillary and inguinal groups of lymph nodes were searched for. They were also clinically evaluated for presence of any valvular and ischemic heart disease. All of them were investigated for serum C-reactive protein, complete blood count, serum creatinine, random brood sugar, serum lipid profile, ECG and chest X-ray P/A view.

Measurement of C-reactive protein in serum was estimated by Nephelometric System by using commercial kit (DADE BEHRING BN 100, USA) in the Department of Microbiology and Immunology of Bangabandhu Sheikh Mujib Medical University.

Data were processed and analyzed with the help SPSS (Statistical Package for Social Sciences) 11.0 version for windows. All quantitative data were expressed as mean and standard deviation; and comparisons between the groups of patients were performed by unpaired t test. Qualitative data were expressed as frequency and percentages; and comparison was done by the Chi-Square ($\div^2$) test or Fisher's Exact Test. Any probability value of less than 5% ($p < 0.05$) was considered statistically significant.

**Results:**

The age of the stroke patients ranged from 35 years to 80 years with the mean age of 56.3 (SD±13.7) years; while the age of the control subjects ranged

from 32 years to 71 years with the mean age of 53.4 (SD ± 9.9) years. There was no significant difference was observed between the mean age of case group and control group (p>0.05) (Table-I).

Among 30 stroke patients 19 (63.3%) were above 50 years of age and 11 (36.7%) were less than 50 years. Among control subjects 16 (53.3%) were above 50 years and 14(46.7%) patients were below 50 years. There was no significant difference of age group between case and control subjects (p>0.05) (Table-I).

There were 21 (70.0%) males and 9 (30.0%) females in stroke patients group; while 25 (83.3%) males and 5 (16.7%) females in control group. There was no significant difference of sex between the groups (p>0.05) (Table-I).

C-reactive protein (CRP) level of stroke patients ranged from 3.60 to 65.00 mg/L with the mean of 42.06 (SD ± 21.26) mg/L; while CRP level of the control subjects ranged from 3.20 to 5.60 mg/L with the mean of 4.30 (SD ± 0.072) mg/L. CRP level was significantly higherin stroke patients than that of control subjects (t=9.723; p<0.001) (Table-II).

CRP was positive in 28 (93.7%) stroke patients and none of the control subjects. CRP was positivity was 16 times significantly higher in stroke patients than that of control subjects (OR=16.00; 95% CI=4.18-61.22; p<0.001) (Table-II).

**Table-I**

*Distribution of study subjects by demographic features*

| Demographic features | Study Group | | p-value |
|---|---|---|---|
| | Case (n = 30) | Control (n = 30) | |
| Age | | | |
| Mean (SD) years | 56.3 (SD ± 13.7) | 53.4 (SD ± 9.9) | *p>0.05 |
| 31-40 years | 7 (23.3%) | 3 (10.0%) | |
| 41-50 years | 4 (13.3%) | 11 (36.7%) | †p>0.05 |
| 51-60 years | 6 (20.0%) | 10 (33.3%) | |
| 61-70 years | 10 (33.3%) | 5 (16.7%) | |
| 71-80 years | 3 (10.0%) | 1 (3.3%) | |
| Sex | | | |
| Male | 21 (70.0%) | 25 (83.3%) | ‡ p>0.05 |
| Female | 9 (30.0%) | 5 (16.7%) | |

* Unpaired t test, †Fisher's Exact test, and ‡Chi-Square ($\div^2$) test were employed to analyse the data.

**Table-II**

*Distribution of the patients by status of C-reactive protein*

| C-reactive protein | Study Group | | Odd ratio (95% CI) | *p-value |
|---|---|---|---|---|
| | Group-A (n=30) | Group-B (n=30) | | |
| Positive | 28 (93.7%) | 0 (0.0%) | 16.0 (4.2-61.2) | p<0.001 |
| Negative | 2 (6.7%) | 30 (100.0) | | |
| Mean (±SD) mg/L | 42.06 (SD ± 21.26) | 4.30 (SD ± 0.072) | | p<0.001 |

*Fisher's Exact test and †Unpaired t test were done analyse the data. SD=standard deviation; CI= confidence interval, OR=Odd ratio, CRP negative: <6 mg/L, CRP positive: e"6 mg/L

**Discussion:**

Several case-control studies with ischemic stroke patients have indicated that recent infections are a possible risk factor for ischemic stroke[13-16]. In particular; there is increasing evidence that inflammatory processes are involved in cerebral ischemia. There is growing evidence that C-reactive protein (CRP), a peripheral marker of inflammation, is also a marker of generalized atherosclerosis[15]. This relationship between inflammation and atherosclerosis make CRP a potential marker for prognosis after vascular events and a potential predictor of future vascular events. The present study was conducted in the Department of Neurology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka.

The present study showed that mean age of the cases was 56.3 (SD ±13.7). This finding is consistent with the findings of a previous study of Ropper and Brown[2] where the average age was 58 (SD±12) years. Eslami et al.[17] found that 55% of stroke patients were in the age group above 60 years, 35% of the patients were in the age group 40-60 years and 10% of stroke patients were in the age group below 40 years. Syed et al.[18] reported that 47.1% of stroke patients were in the age group 55-69 years, 24.9% of the patients were in the age group above 69 years, 21.6% of the patients were in the age group 40-54 years and 6.4 % of stroke patients were in the age group below 40 years.

Seventy percent of this study subjects were male and 30% were female. In this regards Syed et al.[18] found 62.6% of patients were male and 37.2% of patients were female; and Guerrero-Romero and Rodríguez-Morá[19] found 62.7% of patients were male and 37.3% of patients were female. Shaikh et al.[20] found 61% of patients were male and 39% of patients were female in their series. This difference found in the study may be due to the attitude of our society that the females are less frequently brought to the hospitals for treatment.

In this study serum CRP level was found to be elevated in 28 (93.3%) stroke patients with mean CRP value was 42.06 (SD± 21.26) mg/L; whereas among the control it was 4.30 (SD±0.72) mg/L. These findings are consistent with several studies[21-23]. The possible explanations are 1) CRP concentration may reflect the degree of stroke severity, correlating with the degree of inflammation directly consequent to cerebral infarction; 2) CRP concentration may indicate underlying unstable atherosclerotic disease; 3) CRP may be raised as a consequence of secondary complications of stroke at the time of sampling[22].

In this study 2 stroke patients were negative for C-reactive protein value. Grau [24] found about 25% of patients with first ever ischaemic stroke had normal levels of CRP after stroke. It might be due to the variability of the degree of inflammatory response to ischemic stroke[5].

This study was not without limitations. The limitations were 1) The study was not prospectively designed to assess the effect of CRP on long term outcome of ischaemic stroke; 2) This study was conducted in a tertiary care hospital.

Conclusion: This study confirms that C-reactive protein is elevated in acute ischaemic stroke. Further more local studies are required with higher sample size regarding the significance of CRP as a risk factor for acute ischemic stroke.

**References:**


1. Aho K, Harmsen P, Hatano S. Cerebrovascular disease in the community: results of a WHO collaborative study. Bull WHO 1980; 58: 113-30.
2. Ropper AH, Brown RH. Cerebrovascular Disease. In: Adams and Victor's Principles of Neurology, 8th edn. New York: McGraw-Hill Company. 2005; pp. 660-746.
3. Murray CJL, Lopez AD. Mortality by cause for eight regions of the world: global burden of disease study. Lancet 1997; 349:1269-76.
4. Ross R. Atherosclerosis, an inflammatory disease. N Eng J Med 1999; 340:115-26.
5. Gabbay C, Kushner I. Acute phase proteins and other systemic responses to inflammation. N Eng J Med 1999; 340: 448-54.
6. Rost NS, Wolf PA, Kase CS, Kelly HM, Silibershatz H, Massaro JM, et al. Plasma concentration of C-reactive protein and risk of

ischaemic stroke and transient ischaemic attack: The Framingham Study. Stroke 2001; 32: 2575-79.

7. Lagrand WK, Visser CA, Hermens WT. C-reactive protein as a cardiovascular risk factor. More than an epiphenomenonan. Circulation 1999; 100:96-102.
8. Yeh E, Anderson V, Pasari V. C-reactive protein. Linking inflammation to cardiovascular complications. Circulation 2001; 104: 974-5.
9. Zwaka TP, Hombach V, Torzewski J. C-reactive Protein mediated low density lipoprotein uptake by macrophages. Implications for atherosclerosis. Circulation 2001; 103: 1194-7.
10. Papa F, Di Napoli M, Bocola V. C-reactive protein in ischemic stroke: an independent prognostic factor. Stroke 2001; 32: 917-24.
11. Muir KW, Weir CJ, Alwan W. C-reactive protein and outcome after ischemic stroke. Stroke 1999; 30: 981-85.
12. Petty GW, Brown RD, Whisnant JP. Ischemic stroke subtypes: a population-based study of functional outcome, survival and recurrence. Stroke 2000; 31:1062-8.
13. Feigin VL, Lawes CM, Bennett DA, Anderson CS. Stroke epidemiology: a review of population-based studies of incidence, prevalence and case-fatality in the late 20th century. Lancet Neurol 2003; 2(1): 43-53.
14. Feigin VL. Stroke epidemiology in the developing world. Lancet 2005; 365: 2160-61.
15. Ridker PM, Danielson E, Fonseca FA, Genest J, Gotto AM, Kastelein JJ. Rosuvastatin to prevent vascular events in men and women with elevated C-reactive protein. N Engl J Med 2008; 359: 2195-207.
16. Petrea RE, Beiser AS, Seshadri S, Kelly-Hayes M, Kase CS, Wolf PA. Gender differences in stroke incidence and poststroke disability in the Framingham heart study. Stroke 2009; 40(4): 1032-37.
17. Eslami V, Sahraian MA, Gheini MR, Motamedi M, Yazdani T. Impaired glucose metabolism in nondiabetic patients with acute stroke. Iranian Journal of Neurology 2008;7(23):246-58.
18. Syed NA, Khealani BA, Ali S, Hasan A, Akhtar N, Brohi H, et al. Ischemic Stroke Subtypes in Pakistan: The Aga Khan University Stroke Data Bank. JPMA 2003; 53:584.
19. Guerrero-Romero F, Rodríguez-Morán M. Proteinuria Is an Independent Risk Factor for Ischemic Stroke in Non–Insulin-Dependent Diabetes Mellitus. Stroke 1999;30:1787-91.
20. Shaikh NA, Bhatty S, Irfan M, Khatri G, Vaswani AS, Jakhrani N. Frequency, characteristics and risk factors of Carotid Artery Stenosis in ischaemic stroke patients at Civil Hospital Karachi. JPMA 2010; 60:8-12.
21. Marquardt L, Ruf A, Mansmann U, Winter R, Buggle F, Kallenberg K, et al. C-reactive protein in ischaemic stroke. J Neurol Sci 2005; 236: 65-71.
22. Keith W, Cristopher J, Wafa A, Lain B, Kennedy R. C-reactive protein and outcome after ischaemic stroke. Stroke 1999; 30: 981-85.
23. Hsu KO, Chung J, Chia H, Chen KK, Jen HC, Farzaneh S, et al. Relation of C-reactive protein to stroke, cognitive disorders, and depression in the general population: systemic review and meta-analysis. Lancet Neurol 2005; 4: 371-80.
24. Grau AJ. Infection, inflammation, and cerebrovascular ischemia. Neurology 1997; 49:47-51.

Bangladesh Journal of Neuroscience 2014; Vol. 30 (1) : 50-52

***REVIEW ARTICLE***

# Role of Caregivers Training as Predictor of Outcome in Stroke Survivors – A Review

MD. SHAHIDUR RAHMAN

**Abstract:**

*There are many predictors of poor functional outcome in stroke survivors. Need of caregivers training to address the discharged patients for their home care management is often overlooked. Early discharge, lack of post-acute management facilities including home or community based services are other important predictors of poor functional outcome. Most of the patients are discharged home directly from hospital neurology unit after acute care management for inability to pay hospital costs. Rich patients who reside in the city can afford to receive treatment from trained nurse or physiotherapist at home but poor patients go home without any preparation for home care management of the patients. Hospital based rehabilitation management of stroke survivors are scarcely available in our country but thousands of inadequately treated patients are discharged home without any training to the caregivers. They come back to the outpatients department for next visit with multiple complications. This review article tried to find out the need and impact of caregivers training on outcome of stoke survivors.*

**Introduction:**

Stroke is the leading cause of adult disability in the world as well in Bangladesh. Many variables have an impact on disability and quality of life after stroke including age, comorbidities, severity of neurological deficit, state of mind and social risk [1]. Stroke rehabilitation in Bangladesh is inadequately addressed mostly due to resource constraints. Most patients go to their remote villages after acute care management in the hospital with incomplete recovery and profound disability. Care givers to manage the patient at home are usually not trained or briefed on physiotherapy or nursing care. Most of the patients return to next visit with many complications.

Stroke has a profound effect on the lives of patients, their spouses and family members. These effects include role and relationship changes, psychological distress and the challenge of coping with long-term disability[2,3].Family carers provide most post-discharge care to patients but often receive little preparation for this. Long-term caring can result in increased stress and burden for caregivers[2, 3,4.].

A single-center individually randomized trial reported by the London Stroke Carers Training Course (LSCTC), a structured competency-based training program, decreased caregiver burden and anxiety, and improved psychological outcomes for patients. Overall costs were reduced, due largely to earlier discharge in the LSCTC group compared with usual care[4,5].One of the most important interventions is the training of families and other caregivers in specific care techniques to prevent complications, perform physical functions, and encourage patients to perform any activities they are capable of doing. Training in problem-solving techniques can help family members provide effective support in the home environment. Additional teaching focuses on the dissemination of knowledge about strokes, their consequences, and use of medications, stroke prevention, and other care aspects[6].Evidence now exists that both education and counseling significantly improve caregiver knowledge and stabilize some aspects of family functioning. Family education has been found to contribute to the long term maintenance of rehabilitation gains[7,8,9].

Associate Professor, Physical Medicine and Rehabilitation, Bangabandhu Sheikh Mujib Medical University

Education of family and caregivers: Families and caregivers should be educated in the care of these patients. The family and caregiver education may include; preventing recurrent stroke, signs and symptoms of potential complications and psychological dysfunction, medication administration, assisted ADL tasks (e.g., transfers, bathing, positioning, dressing, feeding, toileting, and grooming), swallowing techniques, nutrition and hydration, care of an indwelling bladder catheter, skin care, contractures, use of a feeding tube, home exercises (range of motions) and sexual functioning[10].The patient and family/caregivers should be given information and provided with an opportunity to learn about the causes and consequences of stroke, potential complications, and the goals, process, and prognosis of rehabilitation. The presence and effectiveness of large social support networks can have a positive influence on the physical recovery and quality of life of the stroke survivor.

**Review of relevant studies:** A National Stroke Association survey in USA found that stroke survivors often do not reach their rehabilitation goals, and lack of information is a major barrier to continued recovery: 38% of 523 long-term stroke survivors reported a lack of information about community and rehabilitation resources[11].Inadequate provision of information is predictive of poor quality of life in stroke patients and their families [12].

Forster and colleagues reviewed nine studies of educational intervention. There is some evidence that combining information with educational sessions improves knowledge and is more effective than providing information alone [13]. As the patient progresses from hospital-based rehabilitation to the community, involvement of caregivers in rehabilitation becomes increasingly important. Formal training of caregivers in delivery of care reduces personal costs and improves quality of life [4].

The systematic review and one meta-analysis looked at caregiver support interventions and found that social support improved patient outcomes and family functioning. A comparison of passive versus active information intervention determined that there was no significant effect on the number of cases of anxiety or depression in patients, carer mood or satisfaction or death. A qualitative analysis found no strong evidence of an effect on other outcomes. Meta-analyses showed a significant effect from information therapy on patient and carer knowledge, one aspect of patient satisfaction, and patient depression scores[14,15].

An evidence-based educational program for stroke survivors after discharge home described 39 comprehensive educational guidelines. The program recommended that educational programs provided to stroke survivors and their families be interactive, interdisciplinary, and focused on identified needs[16].

The first few weeks after discharge from an inpatient stay after a stroke are difficult as the patient attempts to use newly learned skills without the support of the rehabilitation environment or team. Adequate support from family and caregivers is critical to a successful outcome. It is also important to ensure that all necessary equipment and support services are in place.

Evans et al after noting that rehabilitation services are effective in improving short-term survival, functional ability, and the most independent discharge location, have suggested that "the lack of long-term benefits of short-term rehabilitation may suggest that therapy should be extended to home or sub–acute care settings, rather than being discontinued at discharge. These services should be organized and in place at the time of discharge"[17].

Clinicians should work with the patient and caregivers to avoid negative effects, promote problem solving, and facilitate reintegration of the patient into valued family and social roles. Preexisting organizational and functional characteristics of the family may have important effects on a successful transition to community living. A caregiver is more likely to give adequate support if he/she is a spouse who is knowledgeable about stroke and its disabilities, is not depressed, and lives in an otherwise well-functioning family unit[18].

**Conclusion:**

Prognosis in stroke survivors depends on many factors. A home or community based management should be addressed timely and adequately. Caregivers training or briefing during hospital stay for home management are helpful and brings better outcome. Patients and caregivers should be educated throughout the rehabilitation process to address patient's rehabilitation needs, expected outcomes, procedures and treatment as well as

appropriate follow-up in the home/ community. Patient and caregiver education should be provided in both interactive and written formats. Caregivers should be provided with a variety of methods of training based on their specific needs, cognitive capability, and local resources; Training may be provided in individual or group format, and in community-based programs. Hospital based rehabilitation management of stroke survivors are scarcely available in our country but thousands of inadequately treated patients are discharged without any training to the caregivers. They come back to the outpatients department for next visit with multiple complications. This review article intends to highlight the importance of caregivers training to stroke survivors especially at low resource setting in Bangladesh.

**References:**


1. Pinedo S, Erazo P, Tejada P, Lizzaraga N, Ayacart J, Miranda L et al. Rehabilitation efficiency and destination on discharge after stroke. Eur J Phys Rehabihil Med 2014; 50: 323-33.
2. Alaszewski A, Alaszewski H, Potter J Risk, uncertainty and life threatening trauma: analysing's stroke survivors' accounts of life after stroke. Forum 2006;7:18, [Online].
3. Forster A, Brown L, Smith J, House A, Knapp P, Writt JJ et al. Information provision for stroke patients and their caregivers. Cochrane Database Syst Rev 2012;(11):CD001919.
4. Kalra L, Evans A, Perez I, Melbourn A, Patel A, Knapp M et al Training care givers of stroke patients: randomized controlled trial. Br Med J 2004;328:1099-101.
5. Patel A, Knapp M, Evans A, Perez I and Karla L. Training care givers of stroke patients: economic evaluation. BMJ 2004;328:1102.
6. Harvey RL, Roth EJ, Yu DT, Celnik P, Stroke Syndromes; In: Braddom RL editor. Physical Medicine and Rehabilitation; 4th edition Elsevier Saunders: 2011; P. 1177-222.
7. Evans RL, Matlock A-L, Bishop DS, et al: Family intervention after stroke: does counseling or education help? Stroke1988; 19:1243-249.
8. Friedland JF, McColl M: Social support intervention after stroke: results of a randomized trial, Arch Phys Med Rehabil 1992;73:573-81
9. Gresham GE, Duncan PW, Stason WB,: Post-stroke rehabilitation.Clinical practice guideline No. 16, US Department of Health and Human Services, Agency for Health care Policy and Research (AHPR); May 1995. AHPR Publication no. 95-0662.
10. Clinical Practice Guidelines for the management of stroke rehabilitation, American Heart Association/American Stroke Association (VA/DOD), The management of Stroke Rehabilitation working group,Version 2; 2010.
11. Jones F. Strategies to enhance chronic disease self-management: how can we apply this to stroke? Disabil Rehabil. 2006 Jul 15-30;28(13-14):841-7.
12. O'Mahoney, P. G., Rodgers, H. Thomson, R. G., Dobson, R. G., & James, O. W. Satisfaction with information and advice received by stroke patients. Clinical Rehabilitation 1997;11;168-72.
13. Forster A, Smith J, Young J, Knapp P, House A, Wright J. Information provision for stroke patients and their caregivers. Cochrane Database Syst Rev 2001:CD001919.
14. Bhogal SK, Teasell RW, Foley NC, Speechley MR. Community reintegration after stroke. Top Stroke Rehabil 2003; 10:107-29.
15. Smith J, Forster A, .,House A, Knapp P, Wright J, Young J. Information provision for stroke patients and their caregivers. Cochrane Database Syst Rev 2008:CD001919.
16. Ostwald, K., Davis, S., Hersch, G., Kellet C., Godwin K. Evidence-Based Educational Guidelines for Stroke Survivors After Discharge Home J Neurosci Nurs. 2008;40(3):173-179,191.
17. Evans RL, Connis RT, Hendricks RD, Haselkorn JK. Multidisciplinary rehabilitation versus medical care: a meta-analysis. Soc Sci Med. 1995; 40: 1699–1706.
18. Evans RL, Bishop DS, Ousley RT. Providing care to persons with physical disability: effect on family caregivers. Am J Phys Med Rehabil. 1992; 71(3): 140–44

Bangladesh Journal of Neuroscience 2014; Vol. 30 (1) : 53-56

## *CASE REPORTS*

# Clinical presentation of Mucopolysaccharidosis type II (Hunter syndrome): A Case Report

HAFIZUR RAHMAN[1], MD. RAFIQUL ISLAM[2], HASAN ZAHIDUR RAHAMAN[2], MD. ARIFFUJAMAN[3]

**Abstract:**

*Mucopolysaccharidosis (MPS) is a rare disease, caused by deficiency of lysosomal enzyme. MPS cases have been reported throughout the world. MPS patient typically appear normal at birth, but clinical features appear between two to four years of age. We report a case of 12-years-old boy presented with progressive deformity of multiple joints for eight years duration and gradual decline the cognitive function for the same period. On examination, his head was large, short stature, a coarse facial feature with depressed nasal bridge and stubby finger with flexion of distal interphalangeal joint. There was severe mental retardation. We diagnose the patients as Hunter Syndrome, on the basis of clinical findings, radiological features and positive for MPS screening test in urine. Although the golden standard for diagnosing the type of MPS is enzyme analysis. We could not do enzyme analysis as it is not available in Bangladesh.*

**Introduction:**

Mucopolysaccharidosis (MPS) is a group of autosomal recessive metabolic disorders caused by the absence or malfunctioning of the lysosomal enzymes needed to break down molecules called glycosaminoglycans (GAGs). GAGs are oligosaccharide components of proteoglycans which provide structural integrity to connective tissues. Accumulation of partially degraded GAGs causes thickening of tissue and compromise of cell and organ function. This results in permanent, progressive cellular damage which affects the appearance, physical abilities, organ and system functioning and, in most cases, mental development. Common clinical presentation includes facial dysmorphism, hepatosplenomegaly, joint stiffness and contractures, pulmonary dysfunction, myocardial enlargement and valvular dysfunction and neurological involvement. We report this case of MPS type II because of its rarity and the atypical features of severe mental retardation, macrocephalic head, no corneal clouding and all other features suggestive of MPS type II. The purpose of presenting this case is to highlight the distinctive manifestation of Hunter syndrome.

**Case presentation:**

A twelve-year-old boy was admitted in neurology department with progressive deformity of multiple

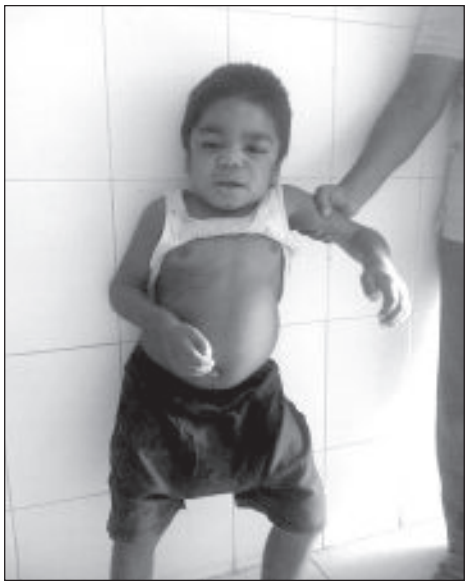

**Fig.-1:** *Male boy with mucopolysaccharidosis showing an macrocephalic head, coarse facial appearance with depressed nasal bridge and a protuberant abdomen.*

1. MD Phase B student, Department of neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka.
2. Professor, Department of neurology, Department of Neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka.
3. MD (thesis part) student, Department of neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka.

joints for eight years duration and gradual decline of cognitive function for the same period. Deformity initially started in right interphalangeal joint since he was four, without any history of trauma and joint pain. It was gradual and progressive, later involved in wrist, elbow, and knee joint bilaterally. Last two months, his deformity so severe that he was bed-ridden. At same period, his cognitive function showed gradual declining. He was second issue of a consangious parents. His birth history was uneventful and milestone of development was normal upto age four. He had no history of prolonged fever, unconsciousness, seizure, any focal neurological deficit.

On examination his head was macrocephalic in shape, with a head circumference of 53.5 cm. He had a depressed nasal bridge, a short neck, coarse facial appearence,and small stubby fingers with flexion of the distal interphalangeal joint, (Figure 1). Anthropometric examination showed him to be severely stunted growth (height 41.5 inch). His abdomen was soft and slightly distended with a protruding umbilicus. Fundoscopy revealed bilateral papilloedema .

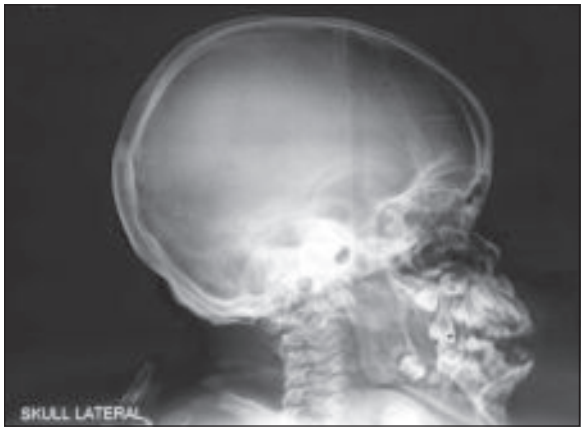


**Fig.-2:** *Lateral x-ray of the skull showing an enlarged skull.*

Suspecting MPS, we performed a skeletal survey. Anteroposterior and lateral X-rays of the skull showed an enlarged and normal sella turcica (Figure2). The bones of the skull and sutures appeared normal for his age.

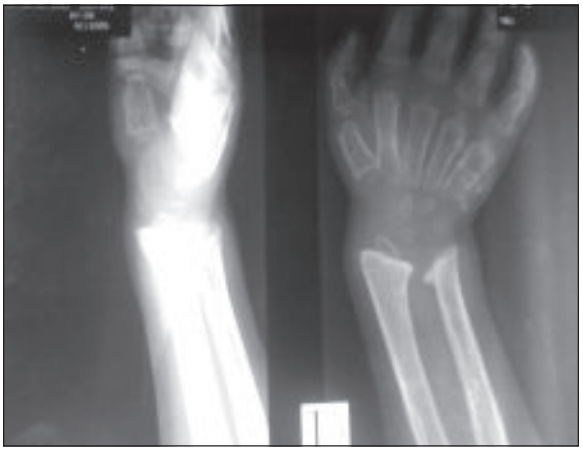

**Fig.-3:** *X-ray of wrist and hand showing pointing of metacarpal bones, with inferior breaking of radius and ulna.*

X-ray of wrist joint and hand showed pointing of metacarpal bones, inferior breaking of both radius and ulna, three carpal bones were ossified and epiphysis for lower ulna yet not appeared. (Figure 3). An antero-posterior chest X-ray view showed no parenchymal lesions were seen in visualized lung fluids and cardiac shadow also normal (Figure 4). CT scan of brain showing communicating hydrocephalus (Figure 5).

However in our patient there was atypical presentation such as an macrocephalic head, severe mental retardation, and no corneal clouding,

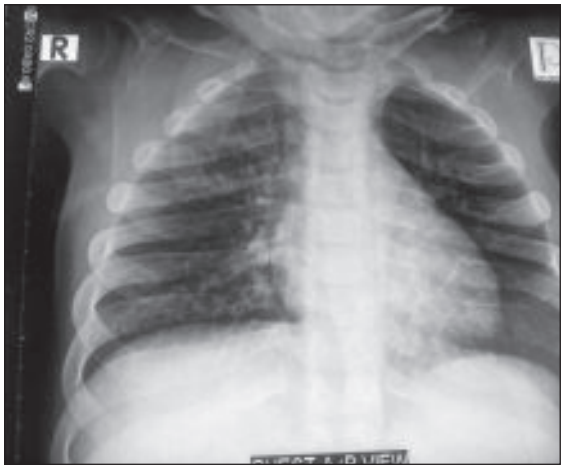


**Fig.-4:** X-ray of chest in P/A view showing normal findings.

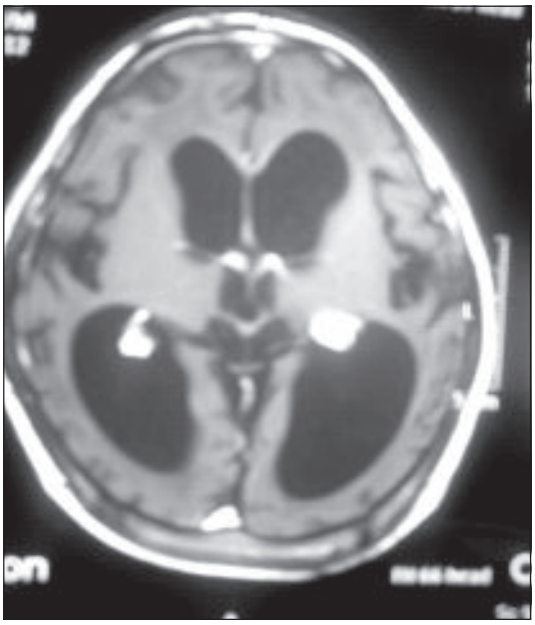

**Fig.-5:** *CT scan of brain showing communicating hydrocephalus.*

which are important features of MPS type II. We could perform measurement of GAG, keratan and heparan sulphates, in his urine and it was positive. Although the golden standard for diagnosing hunter syndrome is enzyme iduronate sulfatase analysis. We could not do enzyme analysis as it is not available in Bangladesh. Our diagnosis of MPS was confirmed from history, clinical examination, skeletal survey and urinary screening test positive.

Discussion:

Mucopolysaccharidosis was first described by Charles Hunter, a Canadian physician, who in 1917 described a rare disease found in two brothers[1-3]. Mucopolysaccharidoses are a group of inherited diseases characterized by defective lysosomal enzymes responsible for the degradation of mucopolysaccharides, which are major components of intercellular connective tissue. Hunter syndrome caused by deficiency of enzyme, iduronate- 2-sulphatase.[1] This leads to an accumulation of incompletely degraded mucopolysaccharides in the lysosomes which affect various body systems through enzymatic activity[4]. All MPS are autosomal recessive, except Hunter syndrome which is X-linked recessive. In affected individuals, undegraded or partially degraded GAG accumulates within the lysosomes and is excreted in excess in the urine. The accumulation of GAG within the lysosomes is responsible for the clinical manifestation of this disorder[5].

Mucopolysaccharidosis type II or Hunter syndrome is rare and is caused by a deficiency of iduronate-2-sulfatase. Hunter syndrome is one of the most common MPS with a prevalence of one in 170,000 male live births. MPS type II is classified into mild (type II, HB) and severe (type II, A) and this classification is based on the length of survival and the presence or absence of central nervous system (CNS) disease. Patients typically appear normal at birth in both types. In the severe form the clinical features appear between two and four years of age while in the mild form the clinical features appear in the second decade of life. In the severe form there is severe mental retardation and loss of skills. Death usually occurs in the first or second decade of life and the main cause of death is obstructive airway disease or cardiac failure. In the milder form there is mild mental retardation but intelligence is normal, stature is near normal, and clinical features are less obvious and progress very slowly. Diagnosis is usually made in the second decade of life. Death usually occurs in the fourth decade and the main cause of death is cardiac failure.

Diagnosis of the disease is usually made by clinical presentation and skeletal survey. The common clinical presentations are a large head (dolichocephalic), short stature, mental retardation, coarse facial features, a protuberant abdomen, a broad nose with flared nostrils, large jaws, hypotonia and a large tongue which becomes apparent between two and four years of age, and these clinical features were present in our case. Other clinical features include upper respiratory tract infection, valvular heart disease leading to right and left ventricular hypertrophy and heart failure, chronic diarrhea, enlarged liver and spleen, umbilical as well as inguinal hernia, corneal clouding with poor vision and hearing loss caused by both connective and sensorineural deficits. A communicating hydrocephalus is a common finding and can lead to severe manifestation of neurological signs which were not present in our case.

Analysis of GAGs (heparan and dermatan sulphates) is a screening test for MPS type II. The presence of excess heparin and dermatan sulphates in the urine is evidence of MPS type I, MPS type II or MPS type VII. Confirmatory diagnosis is by enzyme assay in leukocytes, fibroblasts or dried blood spots and plasma sample, using substrates specific for 12S. Absent or low 12S activity in males is diagnostic of Hunter syndrome, provided other sulfatase deficiency has been ruled out.

Enzyme replacement therapy using idursulfase (Elaprase), a recombinant human I2S produced in the human cell line, has been recently approved in the United States and the European Union for the management of MPS type II. Weekly intravenous infusion is given over three hours at a dose of 0.5 mg/kg diluted in saline. Bone marrow transplantation (BMT) and umbilical cord blood transplantation (UCBT) are definitive treatments for MPS. Apart from these, supportive management is very important. Physical therapy and daily exercise may improve mobility of joints. Blood transfusion, infection and nutritional management are also important in the management of MPS type II[6].

**Conclusion:**

Based on clinical findings and radiological features it is possible to diagnose a case of mucopolysaccharidosis. Urinary glycosaminoglycans (heparin and keratan sulphate) estimation and genetic studies confirms the diagnosis and its type, which will help in offering enzyme replacement therapy to the given individual.

**References:**


1. Wraith JE, Scarpa M, Beck M, Bodamer OA, Meirleir LD, Guffon N, Ploeg AT, Zemen J. Mucopolysaccharidosis Type II (Hunter syndrome): A clinical review and recommendations for treatment in the era of enzyme replacement therapy. Eur J Pediatr 2008;167: 267–77.
2. Martin R, Beck M, Eng C, Giugliani R, Harmatz P, Mufioz V, Muenzer J. Recognition and diagnosis of mucopolysaccharidosis II (Hunter syndrome) Pediatrics 2008;121: 377–86.
3. Hunter C. A rare disease in two brothers. Proc R Soc Med 1917;10:104-16.
4. Kliegman RM, Behrman RE, Jenson HB, Stanton FB. Nelson Textbook of Pediatrics. 18th ed. Philadelphia: Saunders; 2007. 620-26.
5. Tuschl K, Gal A, Paschke E, Kircher S, Bodamer OA. Mucopolysaccharidosis Type II in females: Case report and review of literature. Pediatr Neurol 2005;32:270-72.
6. Patil R, Waseka N , Jadhav SG, Zore R, Sangoi P, Vishwanath D. Clinical Presentation and Diagnosis of Mucopolysaccharidosis Type 2 (Hunter Syndrome). Journal of the association of physicians of india. 2013; 61: 54-56.

Bangladesh Journal of Neuroscience 2014; Vol. 30 (1) : 57-61

# Cauda Equina Syndrome due to Multiple Myeloma: A Case Report

MD. RASHEDUL ISLAM[1], TANBIN RAHMAN[2], RUMANA HABIB[3], AMINUR RAHMAN[4]
NIRMALENDU BIKASH BHOWMIC[5], MD. AMIRUL HAQUE[5]

**Abstract:**

*Cauda equina compression following vertebral compression fractures or vertebral plasmacytomas is relatively uncommon presentation of multiple myeloma. Here we describe a case of cauda equina syndrome due to multiple myeloma in an elderly Bangladeshi male who presented with difficulty in walking, urinary complaints & unexplained weight loss. CT guided FNAC from lesion of spine, bone marrow study, skeletal survey, MRI of spine & immune electrophoresis confirmed the diagnosis of multiple myeloma. We treated the patient with radiotherapy, dexamethasone, antimyeloma therapy, physiotherapy & bisphosphonates in collaboration with hematologists & neurosurgeons. He showed significant improvement both clinically & biochemically in the follow up.*

**Introduction:**

Multiple myeloma (MM) is a clonal B-cell disorder characterized by proliferation and accumulation of B-lymphocytes and plasma cells in the bone marrow and, more rarely, at extramedullary sites. Bone disease occurs in approximately 80% of patients with newly diagnosed MM, and in 70% of the cases bone pain is the first symptom to be reported at disease onset[1] Pathological fractures, osteolyses, osteoporosis or, in general, skeletal-related events (SRE), that include also the need for radiotherapy or surgery to the bone, can severely impair patients quality of life and reduce survival[2]. Spine is the bone site that is most frequently affected by MM related lesions[3].

Spinal cord compression (SCC) occurs in up to 20% of patients with MM at various disease stages[4]. The pathogenetic mechanisms are induced by displacement and compression of the spinal cord, and this can be caused by either epidural invasion by neoplastic tissue arising from a vertebral mass, or by osseous fragments protruding from a fractured vertebral body. Pain is the first and more common presenting symptom[5,6]. It is generally a mechanical pain caused by periosteal infiltration of the vertebrae, it becomes more intense in case of cough or labor, and it is further exacerbated when exerting pressure on the spinous processes. Radicular pain can also be present[5,6].This can be caused by nerve-root compression and it is perceived according to the dermatomal distribution of the nerve root. Motor dysfunction is the second more frequent symptom of SCC. Patients complain about weakness of lower limbs, in particular when walking or going up the stairs. Sensory symptoms such as paresthesias, tingling, or numbness can occur simultaneously or after motor dysfunction; they usually precede autonomic-sphinteric symptoms that are usually represented by bladder dysfunction.[5,6] Prompt recognition of these symptoms and subsequent intervention is mandatory as the picture invariably proceeds to paralysis that is frequently irreversible[7].

MRI is the most sensitive and specific imaging technique to evaluate spinal lesions, as it allows morphological detection of vertebral compression fractures together with spatial evaluation of neural damage or paraspinal masses. The most interesting feature, however, is the possibility to evaluate the characteristics of bone marrow infiltration by the disease. MM related vertebral focal lesions present with a diffusely reduced signal in T1-weighted images and enhanced in T2-weighted images; bone marrow infiltration can thus be defined as “focal” when a clear number of lesions can be identified in the

1. Registrar, Department of Neurology, BIRDEM General Hospital, Dhaka.
2. MD (Hematology) Student, Dhaka Medical College, Dhaka.
3. Assistant Professor, Department of Neurology, BIRDEM General Hospital, Dhaka.
4. Consultant, Department of Neurology, BIRDEM General Hospital, Dhaka.
5. Professor, Department of Neurology, BIRDEM General Hospital, Dhaka.

context of a normal background; “diffuse” when all the bone marrow shows an altered signal, and “mixed” when both focal lesions and diffuse alteration are present[8, 9].

Regarding therapeutic approaches, decompressive laminectomy was frequently performed in the past but its use is now abandoned due to the residual instability of the vertebral column, to the possible delay in the beginning of antimyeloma therapy after surgery and, above all, to the sensitivity of neoplastic cells to steroids and radiotherapy, that now represent the mainstay of the treatment of SCC[6]. High-dose steroids, such as Dexamethasone at doses of 40–60mg/day for 4–6 days must be soon initiated upon recognition of SCC, aiming at obtaining both a plasmacytolitic and an antioedema effect. Radiotherapy must be also administered early[10].

**Case report:**

A 65-year-old man presented to the Neurology department, BIREM for evaluation of two months of gradual onset of lower extremity weakness resulting in falls. He also reported a two day history of bladder retention. A systemic review of the patient was notable for dull but intense chronic back pain. He was no longer ambulatory, had left lower limb numbness and tingling, and had experienced an unintentional 10 kg of weight loss over the last six months. A systemic review of our patient was otherwise unremarkable.

On physical examination of our patient revealed anaemia, restricated spinal mobility & tenderness on lower spine. He had wasting, hypotonia, diminished muscle power (2/5 bilaterally), areflexia and absent plantar response in lower limbs. All modalities of sensation were diminished at L4/L5/S1 dermatomal distribution on left side along with saddle anaestheisa & reduced anal spincter tone. SLR was restricted on left side. Other findings on physical examination were unremarkable.

His hemoglobin of 8.1 g/dl, 4,800 /cu mm, Platelet-1, 70,000/cmm, ESR 120mm in 1$^{st}$ hour, PBF: Nonspecific morphology. Results for corrected serum calcium and coagulation studies were normal. His total protein level was 62 g/l and his albumin level was 25 g/l. His alkaline phosphatase was 395 iu/L.

Radiographic studies on admission included a normal chest radiograph and ECG. Magnetic resonance imaging (MRI) of his lumbar spine showed collapse with altered signal intensity in L5 & focal altered signal intensity in L1-L4, S1 vertebrae. Central & paracentral disc bulge causing thecal sac indentation & bilteral lateral recess narrowing at L5/S1 level. Common tumor markers (CEA, CA 19-9, and PSA) were found to be normal. Serum protein electrophoresis demonstrated hypoproteinemia with hypoalbuminemia and borderline low gamma globulins. Urine protein electrophoresis didn’t show Bence jones protein. Immuno electrophoresis revealed monoclonal light chains. X-ray lumbosacral spine revealed collapse L5 vertebrae (Fig.-1). X ray skull & pelvis showed multiple lytic lesions (Fig.-2).

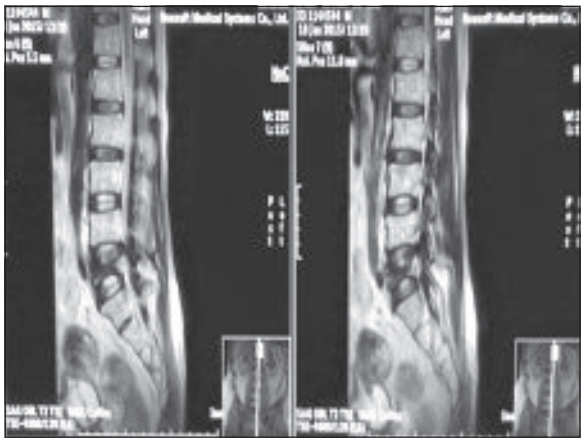

**Fig.-1:** *X-ray of lumbosacral spine showing collapse lumbar vertebrae.*

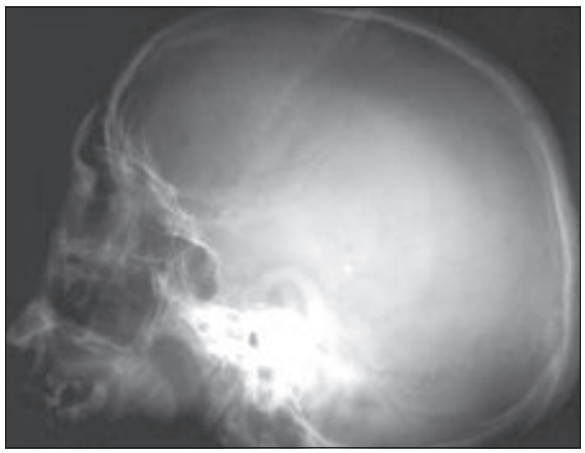

**Fig.-2:** *X-ray of skull showing lytic lesions.*

Tissue from lumbar vertebral body L5 showed adequate cellular material containing numerous mononuclear cells having eccentric nuclei with abundant cytoplasm. Some of those cells had multiple nucleu. Bone marrow examination revealed grossly increased plasma cells almost completely replacing normal haemopoeitic cells replacing more than 80% of existing marrow cells. The cells are distributed in sheets & clusters & include some immature forms (Fig.-3).

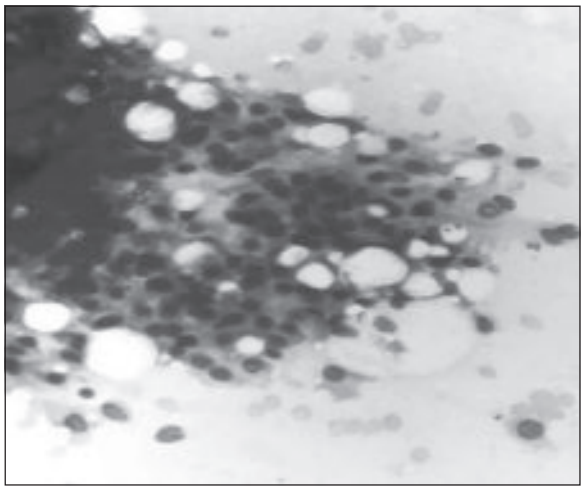

**Fig.-3:** *Bone marrow examinations showing plasma cell.*

**Discussion:**

This case presented a challenge in that our patient's initial presentation had a preponderance of lower extremity symptom. Thus, his pretest probability was highest for conditions affecting the lumbar spine, such as cauda equine syndrome from disc herniation or metastatic disease. The initial MRI of his lumbar spine in fact confirmed disc herniation with protrusion.

Our patient's history brings into consideration tuberculosis, particularly as an infection of the vertebral body (Pott's disease, tuberculous spondylitis, or tuberculoma), which most commonly manifests in adults[11,12]. The absence of tuberculosis in other locations does not exclude the diagnosis. Tuberculomas can have associated collapsed vertebrae and present with numbness, paraplegia and bladder disturbances similar to this presentation.

Other granulomatous diseases, such as sarcoidosis, were also considered as neurosarcoid lesions can resemble a tumor. Spinal cord involvement can occur as part of systemic sarcoidosis[13] .The lesion may have represented a benign tumor, such as osteoblastoma, giant cell tumor, hemangioma. It may have also represented a primary malignancy such as solitary plasmacytoma, chordoma, chondrosarcoma, lymphoma or malignant giant cell tumor[14]. MRI findings provided evidence against many of these diagnoses, as well as against primary intramedullary central nervous system neoplasms, such as ependymoma or astrocytoma, which are more common in children than in adults[15].

Primary bone neoplasms account for fewer than 10% of all cases of bone tumors, with metastatic lesions far more widespread in the adult population.[14] Bone metastases, including those to the spine, are a frequent complication of cancer (approximately 5%), occurring most commonly in prostate cancer (up to 70% of patients) and 15% to 30% of patients with cancer of the lung, colon, stomach, bladder, rectum, thyroid and kidney[16]. Both osteolytic and osteoblastic metastases can cause pathologic fractures and subsequent spinal cord compression[16].

With clinical features of cauda equina syndrome, anemia, high ESR, raised alkaline phosphatase, multiple myeloma with plasmacytoma formation was the most likely possibility. Magnetic resonance imaging (MRI) of his lumbar spine showed collapse with altered signal intensity in L5 & focal altered signal intensity L1-L4, S1 vertebrae led us to do CT guided FNAC from the lesion. We went for myeloma screen by skeletal survey, urinary Bence Jones protein, plasma protein electrophoresis, immune electrophoresis & bone marrow study. To rule out metastatic lesions, we went for common tumor markers as our patient's age, weight loss, metastatic prostate cancer was considered as one of our differential diagnosis. FNAC from vertebral lesion, bone marrow findings together with protein electrophoresis and radiographic images, confirmed the diagnosis of cauda equina syndrome due to multiple myeloma.

Making the diagnosis includes demonstrating these M-proteins in either serum or urine, proving the presence of more than 10% of these malignant plasma cells in the bone marrow and observing the clinical manifestations of the disease in our patient[17,18,20]. Spinal cord compression following vertebral compression fractures or vertebral plasmacytomas comprises 5% of the presentations of multiple myeloma[17, 18, 21].

Our review of recent articles revealed few case reports of plasmacytomas as initial presentations of multiple myeloma.[19,21,22] Despite identifying such a mass as plasmacytoma, additional tests are required to distinguish between a solitary plasmacytoma of the bone, an extramedullary plasmacytoma or the systemic disease multiple myeloma. Patients with solitary plasmacytoma of the bone are more likely to progress to multiple myeloma than those ith extramedullary plasmacytoma, but both conditions have a better overall prognosis than the systemic disease[19, 12, 23].

We treated the patient with radiotherapy, dexamethasone, antimyeloma therapy & rehabilitation in collaboration with hematologist & neurosurgeon. He showed significant improvement both clinically & biochemically in the follow up.

**Conclusion:**

Diagnosis of cauda equine syndrome must be rapid in order to avoid complication. The site and morphology of the lesion should be identified as precisely as possible. Compression of spinal cord or cauda equina is relatively uncommon presentation of multiple myeloma. Meticulous history taking, examination, biochemical parameters guide the right way further investigations. Prompt diagnosis, treatment, regular follow up in essential as these are the most important part deciding prognosis.

**References:**


1. Kyle RA, Gertz M. A, Witzig T. E et al., "Review of 1027 patients with newly diagnosed multiple myeloma," Mayo Clinic Proceedings, vol. 78, no. 1, pp. 21–33, 2003.
2. Croucher P I and J Apperley JF, "Bone disease in multiple myeloma," British Journal of Haematology. 1998; 103( 4)902–10
3. Lecouvet FE, Vande Berg BC,Maldague BE et al., "Vertebral compression fractures inmultiple myeloma. Part I. Distribution and appearance at MR imaging," Radiology 1997 ; 204(1) 195–99
4. Prasad D and Schiff D, "Malignant spinal-cord compression," The Lancet Oncology 2005;6( 1) 15–24
5. Bach F, B. H. Larsen BH, RohdeK et al, "Metastatic spinal cord compression," Acta Neurochirurgica, 1990;107(1-2)37–43
6. S. Helweg-Larsen and P. S. Sorensen, "Symptoms and signs in metastatic spinal cord compression: a study of progression from first symptom until diagnosis in 153 patients," European Journal of Cancer A 1994;30( 3): 396–98
7. Levack P, Graham J, Collie Det al. "Don't wait for a sensory level—Listen to the symptoms: a prospective audit of the delays in diagnosis ofmalignant cord compression," Clinical Oncology 2002; 14(6): 472–80
8. Lecouvetn FE, Vande Berg BC, Maldague B E et al. "Vertebral compression fractures inmultiplemyeloma. Part I. Distribution and appearance at MR imaging," Radiology 1997;204, pp. 195–99
9. A. Baur A, St¨abler A, Br¨uning R et al., "Diffusion-weighted MR imaging of bonemarrow: differentiation of benign versus pathologic compression fractures," Radiology 1998;207(2) 349–56
10. Flouzat-Lachaniette CH, Allain J, Roudot-Thoraval F, and Poignard A, "Treatment of spinal epidural compression due to hematological malignancies: a single institution's retrospective experience," European Spine Journal 2013;22: 548–55
11. Al-Deeb SM, Yaqub BA, Sharif HS, Motaery KR: Neurotuberculosis: a review. Clin Neurol Neurosurg 1992; 94(Suppl):S30-S33.
12. Bahemuka M, Murungi JH: Tuberculosis of the nervous system: a clinical, radiological and pathological study of 39 consecutive cases in Riyadh, Saudi Arabia. J Neurol Sci 1989; 90(1):67-76.

13, Saleh S, Saw C, Marzouk K, Sharma O: Sarcoidosis of the spinal cord: literature review and report of eight cases. J Natl Med Assoc 2006, 98(6):965-76.

14. Weinstein JN, McLain RF: Primary tumors of the spine. Spine 1987, 12(9):843-51.

15. Shrivastava RK, Epstein FJ, Perin NI, Post KD, Jallo GI: Intramedullary spinal cord tumors in patients older than 50 years of age: management and outcome analysis. J Neurosurg Spine 2005; 2(3):249-55.

16. Saleh S, Saw C, Marzouk K, Sharma O: Sarcoidosis of the spinal cord: literature review and report of eight cases. J Natl Med Assoc 2006; 98(6):965-76.

17. Roodman GD: Mechanisms of bone metastasis. N Engl J Med 2004; 350(16): 1655-64.

18. George ED, Sadovsky R: Multiple myeloma: recognition and management. Am Fam Physician 1999; 59(7):1885-94.

19. Kyle RA, Gertz MA, Witzig TE, Lust JA, Lacy MQ, Dispenzieri A et al. Review of 1027 patients with newly diagnosed multiple myeloma. Mayo Clin Proc 2003; 78(1):21-33.

20. Nofsinger YC, Mirza N, Rowan PT, Lanza D, Weinstein G: Head and neck manifestations of plasma cell neoplasms. Laryngoscope 1997; 107(6):741-746.

21. Wavre A, Baur AS, Betz M, Muhlematter D, Jotterand M, Zaman K et al.: Case study of intracerebral plasmacytoma as an initial presentation of multiple myeloma. Neuro Oncol 2007; 9(3):370-72.

22. Ustuner Z, Basaran M, Kiris T, Bilgic B, Sencer S, Sakar B et al. Skull base plasmacytoma in a patient with light chain myeloma. Skull Base 2003; 13(3):167-71.

23. Corwin J, Lindberg RD: Solitary plasmacytoma of bone versus extramedullary plasmacytoma and their relationship to multiple myeloma. Cancer 1979; 43(3):1007-13.