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CONTENTS

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ORIGINAL ARTICLES

Serum Creatine Kinase Concentration & Its Association with Severity in Acute Ischemic Stroke Patients: A Cross-Sectional Analytical Study

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Abstract:

Background: *The diagnosis of ischemic stroke remains a clinical one, with confirmatory evidence obtained through neuroimaging. Analogous to the role that the creatine kinase (CK), a biochemical test may be useful in diagnosis as well as detect severity which ultimately helps in the management of acute ischemic stroke.*

Objective: *To evaluate serum creatine kinase level and its association with severity in acute ischemic stroke patients.*

Methods: *This cross-sectional analytic study was carried out in the Department of Neurology, BSMMU, Dhaka from January 2014 to December 2014.In this study 50 acute ischemic stroke patients were enrolled as cases.*

Result: *In this study, 42.0% patients were female and 58% were male and their mean age was 55.96±10.93 years. According to classification by NIH Stroke score, 32% patients was found in minor stroke, 28% in moderate stroke, 26% in moderate to severe stroke and 14% in severe stroke. 80.0% patients had increased level of serum creatine kinase. In this study there is a positive correlation between NIH Stroke Score and Serum creatine kinase level ($r= 0.869$, $p < 0.0001$).*

Conclusion: *Increase severity of acute ischaemic stroke causes increased level of serum creatine kinase.*

Keywords: *Acute ischemic stroke, Serum creatine kinase; NIH stroke score; Bangladesh.*

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 focal higher cerebral dysfunction (such as aphasia), hemi sensory loss, and visual field defect or brain-stem deficit.[1] The neurovascular syndromes enable the physician to localize the lesion—sometimes so precisely that even the affected arterial branch can be specified[1-]3. Most embolic strokes characteristically occur suddenly, and the deficit reaches its peak almost at once. Thrombotic strokes may have an abrupt onset, but they evolve somewhat more slowly over a period of several minutes or hours and occasionally days; in the latter case, the stroke usually progresses in a series of steps rather than smoothly. In hypertensive cerebral hemorrhage the deficit may be virtually static or steadily progressive over a period of minutes or hours, while subarachnoid hemorrhage is almost instantaneous[1-3].

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An analogous example would be cerebrovascular thrombosis. About two thirds of patients with cerebrovascular thrombosis develop increase in serum creatine phosphokinase(CPK) levels, maximum at 48 to 72 hours after the stroke. Values as high as 2,900 units per ml. have been reported. The CPK slowly returns to normal over a two week period[4,5]. The level of CPK activity in the serum and spinal fluid are quite independent of each other, since neither isoenzyme crosses the blood brain barrier in significant amounts[6].

Creatine kinase(CK) is a dimeric globular protein consisting of two subunits with a molecular mass of 43 kDa. It buffers cellular ATP and ADP concentrations by catalysing the reversible exchange of high-energy phosphate bonds between phosphocreatine and ADP produced during contraction. At least five isoforms of CK exist: three isoenzymes in cytoplasm (CK-MM, CK-MB and CK-BB) and two isoenzymes (non-sarcomeric and sarcomeric) in mitochondria[7].

CK-MM is found in several domains of the myofibre where ATP consumption is high and is a marker of muscle disease[8]. CK-MB increases in acute myocardial infarction[9] and CK-BB increases in brain damage[10]. Patients with neurological conditions such as acute cerebrovascular accidents[11]and proximal spinal muscular atrophy[12] show marked elevation of CK-BB. Brain is a rich source of a variety of enzymes and any injury (e.g. stroke) to brain tissue could similarly result in an increase in activity of these enzymes in cerebrospinal fluid. A simultaneous increase in serum levels will probably depend on integrity of blood brain barrier. If injury is severe enough to disrupt the blood brain barrier there might be some rise in enzymatic activity in serum. As the stroke syndrome is usually clearly delineated clinically but in some patients laboratory evidence of the presence of cerebral infarction may provide additional diagnostic and prognostic information. Determinations of serum enzyme activity have the advantage of permitting repeated sampling without danger or inconvenience to the patient. The objective of the present study was to determine the variations in serum creatine kinase (CK) activity in patients presenting with acute ischemic stroke and to correlate these findings with the severity of disease.

Method:

This cross-sectional analytical study was conducted in the Department of Neurology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka over a period of one year from January 2014 to December 2014. Fifty diagnosed patients of acute ischaemic stroke within first 2 weeks of presentation age 18 years and above of any sexes were included in this study. The demographic information, relevant history, examination findings and investigation reports of all the study subjects were recorded in the data collection sheet. Any complication during the procedure and hospital admission if required was also recorded. All data were recorded systematically in preformed data collection form (questionnaire). Quantitative data were expressed as mean and standard deviation and qualitative data were expressed as frequency distribution and percentage. Statistical analysis was performed by using windows based computer software "Statistical Packages for Social Sciences" (SPSS-12). Associations between continuous variables were analyzed by Kruskal-Wallis test. Correlation was done by Spearman correlation coefficient test. For all statistical tests, it was considered p value <0.05 as statistically significant.

Result:

Table-I

Demographic profile of the study population (n=50)

	Frequency (n)	Percentage (%)
Age (years)		
≤50	16	32
51 -60	20	40
>70	14	28
Mean ± SD	55.96± 10.93	
Min - Max	32.00 - 75.00	
Gender		
Male	29	58
Female	21	42
Male: female ratio	1.38 : 1	

Out of 50 acute ischaemic stroke patients, females were 42% and males were 58%. Male and female ratio was 1.38: 1. Mean age of the patients was 55.96±10.93 years with range of 32 to 75 years. The most frequent age group was 51-60 years.

Table-II

Serum creatine kinase level in different groups of acute ischaemic patients (NIH stroke score).

Group	Serum Creatine Kinase (u/L)	P value*
Minor Stroke(16)	194.6 ± 79.0	<0.0001[s]
Moderate Stroke(14)	699.5 ± 250.2	
Moderate to Severe Stroke (13)	1414.3 ± 444.8	Severe (7)
3204.2 ± 753.2		
Total	1074.4 ±1052.6	

The highest increased value of Serum CK was recorded in severe stroke which was 3204.28 (753.23) u/L. It was decreased step by step by moderate to severe stroke accounted 1414.31(444.83) u/L, 699.57 (250.23) u/L in moderate stroke and 194.62 (79.02) u/L in minor stroke.This increasing trend of serum CK level from minor stroke to severe stroke i.e. severity was tested by Kruskal-Wallis test which was statistically highly significant (p value <0.001).

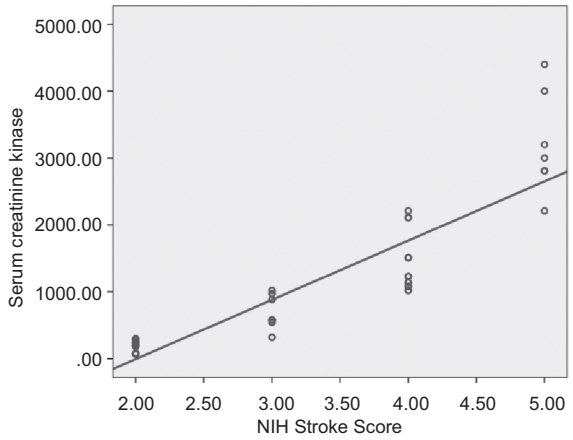

Fig.-1: *Correlation between NIH Stroke Score and Serum creatine kinase level of the study population*

NIH Stroke Score had a positive correlation with serum creatine kinase level of the study population (r= 0.960; p<0.0001).

Discussion:

In this study, male to female ratio was 1.38: 1. Mean age of the patients was 55.96±10.93 years with range of 32 to 75 years. The most frequent age group was 51-60 years. In correspond of these study findings, Elyaset al.[13]also found male predominance in their study (63.33%). A study at Bangabandhu Sheikh Mujib Medical University, Bangladesh revealed male to female ratio 2.75:1. In that same study, it was reported that age range from 35 to 79 years with mean 59.45 years and majority of patients were in 7th decade (n=20, 33%) and 6th decade (n=16, 27%).[14]

According to classification by NIH Stoke score in this study, more patients were found in minor stroke (32%) which was followed by moderate (28%), moderate to severe (26%) and severe stroke (14%).

The mean serum creatine kinase level was found 1074.4±1052.6u/L in the range of minimum 67.0 to maximum 4400.00 u/L. Ay et al.[15] estimated total CK level in 32 patients of stroke. They found elevated CK level among 62.5% patients. Another study done by Norris et al.[16] found 101 patients had raised total CK values among 224 patients with stroke which stands for 46%. Myers et al.[17] found 15 stroke patients out of 100 patients with abnormally high CK values.

The highest increased value of Serum CK was recorded in severe stroke patients which was 3204.2±753.2 u/L. It was decreased step by step, moderate to severe stroke accounted 1414.3±444.8 u/L, 699.5±250.2 u/L in moderate stroke and 194.6±78.0 u/L in minor stroke. Increasing trend of serum CK level from normal to severe stroke i.e. severity was tested by multiple comparison test which was statistically highly significant (p <0.0001). There was a positive correlation between NIH Stroke Score and serum creatine kinase level of the study population (r=0.960; p<0.001), which indicates that increase severity of stroke causes increase level of serum creatine kinase. Capocchiet al.[18] also correlated with severity of brain damage in acute ischemic stroke patients with serum CK-BB level. In stroke patients they found a statistically significant correlation between severity of brain damageand serum values of CK-BB. Eisenet al.[6] also

suggested that the presence of high peak activities and an early rise in serum CPK may indicate increase severity as well as a poor prognosis. All these study findings correspond with this study.

Conclusion:

It can be concluded that serum creatine kinase level has association with severity in acute ischemic stroke patients.Serum creatine kinase in this regard can be an important tool in understanding the severity of acute ischemic stroke.

References:

1. Bradley WG, Daroff RB, Fenichel GM, Jankovic J, (2004) *Neurology in clinical practice. Principles of diagnosis and management,* 4th edn. Philadelphia: Butterworth-Heinemann.
2. Victor M, Ropper AH. (2005) Adams and Victor's principles of Neurology, 8th edn, New York; McGraw-Hill
3. Aminoff MJ, (2001) Neurology and General medicine, 3rd edn, Philadelphia, Churchill Livingstone, pp. 1060-1067
4. Acheson J, James DC, Hutchinson EC, Westhead R. Serum-creatine-kinase levels in cerebral vascular disease. The Lancet. 1965 Jun 19;285(7399):1306-7.
5. Wolintz AH, Jacobs LD, Christoff N, Solomon M, Chernik N. Serum and cerebrospinal fluid enzymes in cerebrovascular disease: Creatine phosphokinase, aldolase, and lactic dehydrogenase. Archives of neurology. 1969 Jan 1;20(1):54-61.
6. Eisen AA, Sherwin AL. Serum creatine phosphokinase activity in cerebral infarction. Neurology. 1968 Mar 1;18(3):263-263.
7. Takagi Y, Yasuhara T, Gomi K. Creatine kinase and its isozymes. Rinshobyori. The Japanese journal of clinical pathology. 2001 Nov:52-61.
8. Nigro G, Comi LI, Limongelli FM, Giugliano MA, Politano L, Petretta V, Passamano L, Stefanelli S. Prospective study of X linked progressive muscular dystrophy in campania. Muscle & nerve. 1983 May 1;6(4):253-62.
9. Borrayo-Sanchez G, Sosa-Jarero F, Borja-Teran B, Isordia-Salas I, Argüero-Sánchez R. Qualitative determination of markers for myocardiac necrosis during pre-hospital admission for acute coronary syndrome. Cirugia y cirujanos. 2006;74(4):231-5.
10. Pfeiffer FE, Homburger HA, Yanagihara T. Creatine kinase BB isoenzyme in CSF in neurologic diseases: measurement by radioimmunoassay. Archives of neurology. 1983 Mar 1;40(3):169-72.
11. Bell RD, Rosenberg RN, Ting R, Mukherjee A, Stone MJ, Willerson JT. Creatine kinase BB isoenzyme levels by radioimmunoassay in patients with neurological disease. Annals of neurology. 1978 Jan 1;3(1):52-9.
12. Rudnik-Schöneborn S, Lützenrath S, Borkowska J, Karwanska A, Hausmanowa-Petrusewicz I, Zerres K. Analysis of creatine kinase activity in 504 patients with proximal spinal muscular atrophy types I–III from the point of view of progression and severity. European neurology. 1998;39(3):154-62.
13. Elyas DM, Rahman A, Mohammad QD, Mondol BA, Hossain S, Islam SS, Shahi MS, Baki M, Sarker MA. Comparative Study of Risk Factors Between Lacunar and Non-lacunar Ischemic Strokes. Bangladesh Journal of Neuroscience. 2013 Nov 30;28(2):88-95.
14. Das BK and Anwarullah, AKM. Association of serum triglyceride with ischaemic stroke. MD (neurology thesis), Bangabandhu Sheikh Mujib Medical University, Dhaka, 2013 July.
15. Ay H, Arsava EM, Sarýbaþ O. Creatine Kinase-MB elevation after stroke is not cardiac in origin. Stroke. 2002 Jan 1;33(1):286-9.
16. Norris JW, Hachinski VC, Myers MG, Callow J, Wong T, Moore RW. Serum cardiac enzymes in stroke. Stroke. 1979 Sep 1;10(5):548-53.
17. Myers MG, Norris JW, Hachinski VC, Weingert ME, Sole MJ. Cardiac sequelae of acute stroke. Stroke. 1982 Nov 1;13(6): 838-42.
18. Capocchi G, Tassi C, Ricci S, Zampolini M, Fausti R, Rossi A. Creatine kinase BB activity in serum of patients with acute stroke: correlation with the severity of brain damage. The Italian Journal of Neurological Sciences. 1987 Dec 10;8(6):567-70.

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Cerebral Angiographic Study of Anatomical Variations of Anterior Cerebral Artery Complex in Bangladeshi Population

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Abstract:

Background: *Anterior cerebral artery is an important terminal branch of internal carotid artery. It forms the anterior component of circle of Willis along with the anterior communicating artery. It is known for the frequent variations. The knowledge of anatomical variations in anterior cerebral artery is of considerable help to clinicians and interventionists.* Method: *Morphology and variations of the anterior cerebral arteries and the anterior communicating artery were studied in 90 patients undergone digital subtraction angiography (DSA).* ***Results:*** *Variations were found in 33% (n=30). Variations of the segments in relation with size, course, communications and terminations of the anterior cerebral artery (ACA) were noted. These were divided into different groups like hypoplasia, aplasia, duplication and fenestrations. Hypoplasia/Aplasia of proximal anterior cerebral artery (A1) was 24.5% in right side and 9% in left side. Anterior communicating artery (AComA) was found absent in 9% and fenestration in 9%. Callosomarginal artery was found absent in 2.2% in right side and 4.5% in left side. In right callosomarginal artery 6% had abnormal origin and 3.5% abnormal in left side.Pericallosal artery was present 100% on both sides.* Conclusion: *Variations of anterior cerebral artery complex anatomy is found common in Bangladeshi population.*

Key words: *Anterior cerebral artery complex, variations, hypoplasia, aplasia, fenestration.*

Introduction:

The anterior cerebral artery complex consists of two anterior cerebral arteries (ACA), one anterior communicating artery (AComA) and two recurrent arteries of Heubner. The anatomy of theanterior cerebral artery (ACA) is variable and the description of the ACA and its branches is complicated[1]. Segmentation and branching of the ACA is mostly described similarly bydifferent authors, although the relationship of the pericallosal(PrcA) and callosomarginal arteries (CmA) is not agreed upon[2].Different branches of ACA are also variable inorigin[3]. Different authors have described thesegments of the ACA differently. It can be divided into proximal or pre-communicatingand distal or post-communicatingsegments. The pericallosal artery is distal to the A1 segment and consists of several segments that can be divided according to its relationship with the corpus callosum[4]. The A2 segment(infracallosal section) runs vertically from the AComA to the genu of the corpus callosum. The A3 segment (precallosal part) curves around the genu, and the A4 segment(supracallosal section) usually runs in the callosal sulcus and almost reaches the splenium[5]. The A5 segment (cortical branches) varies considerably; for this reason it is difficult to describe a standard arterial pattern.The two basic configurations of the ACA are determined by the presence or absence of the CmA[6]. The different segments of the ACA are

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illustrated in Figure 1.Few authors only described three separate segments, namely the A1 segment (also referred to as the horizontal proximal segment or pre-communicating part), the A2 segment(vertical proximal segment or post-communicating part) and the A3 segment (the distal segments and cortical branches). The A2 and A3 segments have collectively been referred toas the ascending (or vertical) segment and the A4 and the A5segments as the horizontal segment. The ACA have also been divided into a basal (from the origin to the rostrum of the corpus callosum) and a distal part (runs around genu and above corpus callosum)[7]. Some authors refer to the A1 segment as the ACA and the artery distal to the AComA as the pericallosal artery. A few authors have also referred to the A1 and A2 segments as the ACA, and the artery distal to the origin of the callosomarginal artery, the pericallosal artery[8]. Since the origin of the callosomarginal artery can vary, this terminology can be problematic. The CmA is also not always present and therefore it is preferable to classify the pericallosal artery as the segment distal to the AComA. Presence of the CmA artery has been observed in 40.0% to 93.4% of specimens.[9]TheCmA can be due to the different definitions used for this artery. The variability of the absence or presence of the CmA can be due to the different definitions used for this artery. The ACA complex has a strong clinical importance. It is the most common site of intracranial aneurysm[10]. Despite its considerable significance, little is known about the anatomical variations of the ACA complex[11, 13, 14]. Many anomalies such as aplasia, hypoplasia, duplication or fenestration of ACA segments and AComA have been described[15, 16]. Authors used various methods such as digital subtraction angiography (DSA), computed tomography angiography (CTA), Magnetic resonance angiography (MRA), cadaveric dissection or intraoperative observations to study the anterior cerebral circulation of brain. However those studies have a number of limitations. Firstly, they are focused on patients with intracranial aneurysms, and not healthy subjects[17,18,19]. Secondly, the authors base their conclusions on a relatively small study group, rarely exceeding 100 patients. Thirdly, their observations are often limited to the anomalies of the A1 segment (most commonly associated with AComA aneurysms) regardless of AComA and A2 and other segment anomalies[1]. Complete study of anterior cerebral artery complex is lacking in the population of our country. Digital subtraction angiography is now-a-days becoming popular minimally invasive angiographic study method for cerebral vessels[20,21]. Most of the pathologies of cerebral vasculature can be explored and treated by Neurointervention methods. The development of Neurointervention is progressively increasing in the field of management of vascular pathologies in brain. So complete understanding by the help of digital subtraction angiography of ACA complex is very important for this population of Bangladesh.

Comparatively few studies describe the anatomy of the ACA complex in subjects without intracranial aneurysms. These are mainly cadaveric studies[26, 27]. There is still a need for further study to explore the anatomy of the anterior cerebral circulation. The results of such studies would be useful when planning neurointerventional procedures and surgical approaches [25], and would allow avoiding any unexpected anatomical variations during treatment of AComA aneurysms. Such anatomical problems may include double fenestrations of the A2 segment mimicking an aneurysm neck [12] or mistaking a duplicated A1 segment for an AComA aneurysm [19]. The aim of this study was to see the common variations of ACA complex configurations by using digital subtraction angiography (DSA).

Materials and Methods:

This retrospective observational study was conducted in the department of Neurointervention of National Institute of Neurosciences Hospital, Dhaka, Bangladesh during January 2015 to December 2015. All collected data were collected from digital database, checked, edited and analyzed by using computer based SPSS software version 16.0. Data were presented by frequency distribution and percentage.

A total of 90patientsreffered in the Neuro-intervention department for digital subtraction

angiography (DSA)were included in this study. Sampling technique was purposive. The angiogram machine was SIEMENS Artis Zee system and framing rate was 4f/sec. Angiograms with gross pathology like arteriovenous malformations (AVM) in anterior circulation were excluded from this study. Anterior part of the circle of Willis was studied. Morphological variations, branching pattern and course of the ACA and AComAwere observed. Variations of the size, course, segments, communications and terminations of the anterior cerebral artery complex were noted. These variations were divided into different groups like hypoplasia, aplasia, and duplication of pre-communicating segment of ACA (A1), double AComA, fenestrations, azygos ACA and variation in the A2 segment of ACA in its terminal branches. Origin of callosomarginal artery and the course of pericallosal artery were noted and pictures were drawn in data collection sheet.

Results:

Out of the 90 patients, majority 63(70%) were belonged to over the age 40 years. And 40 or less than40 years were 27 (30%) (Table I). It was observed 50(55.5%) were male and 40(44.5%) were female. Male to female ratio was 5:4 (Table I). Morphologic variationseg. Aplasia/hypoplasia/ fenestration in A1 or AcomA or absent/abnormal origin of callosomarginalartery were present in 30(33%) of cases. Variations related with the A1 segment of ACA are agenesis, hypoplasia and duplication. Hypo- plastic/ under-developed A1/ Aplastic segment were present in 30 cases. It was seen in 22 (24.5%) on the right and 8 (9%) on the left A1 segment. (Table II).

Table-I

Socio-demographic characteristics of the study patients (n=90)

Characteristics		No. of respondents	Percentage
Sex	Male	50	55.5
	Female	40	44.5
Age	≤40	27	30
	>40	63	70

Table-II

Morphologic variation of A1 segment of ACA on both sides (n=90)

Right A1	Number of patients	Percentage
Normal	68	75.5
Hypoplasia/Aplasia	22	24.5
Left A1		
Normal	82	91
Hypoplasia/Aplasia	8	9

All possible forms of abnormalities of AComA were present in 22 (24.5%) of cases and normal in 68 (75.5%) cases. Fenestration of AcomA was seen in 8 (9%) cases, Hypoplastic/ Absent AComA was seen in 8 (9%) cases. Other abnormalities like duplication were present 6 (6.5%) cases. (Table III)

Table-III

Morphologic variation of AComA of ACA complexs (n=90)

AComA	Number of patients	Percentage
Normal	68	75.5
Fenestration	8	9
Hypoplasia/Aplasia	8	9
Others	6	6.5

Azygos anterior cerebral artery was found in 2 (2.2%) cases. Triple A2 segment was found in 1 (1.1%) case. Callosomarginal artery was absent in 2 (2.2%) in right side and4 (4.5%) in left side. Out of them 5 (6%) in right side and 3 (3.5%) in left sidewere abnormal in origin. (Table IVA, IVB)

Pericallosal artery was found in all cases on both sides in this study.

Table IVA

Morphologic variation of origin of Right Callosomarginal artery (n=90)

Right Callosomargina Artery	Number of patients	Percentage
Present	88	97.8
Absent	2	2.2
Origin		
Normal	83	94
Abnormal	5	6

Table-IVB

Morphologic variation of origin of Left Callosomarginal artery (n=90)

Left Callosomargina Artery	Number of patients	Percentage
Present	86	95.5
Absent	4	4.5
Origin		
Normal	83	96.5
Abnormal	3	3.5

Discussion:

Multiple variations in anatomy of anterior cerebral artery complex like agenesis, hypoplasia, fenestrations etc resulting in defective circulation has been reported in the different publications[1,8]. If the artery on one side is narrowed, the vascular insufficiency is compensated by crossing over by opposite side artery, or by giving branches that cross over to the other side. It indicates that the circle of Willis offers a potential shunt in abnormal conditions such as occlusions and spasms. In normal circumstances it is not an equalizer and distributer of blood from different sources. Majority (70%) of the study subject wasover 40 years of age, and less than 40 years is 30%. Among them male were 55.5% and female were 44.5%, and male to female ratio were5:4. Morphological variations eg. Aplasia/hypoplasia/fenestration in A1 or AcomA or absent/abnormal origin of callosomarginalartery was present in 30 (33%) of cases. In Text book of Practical Neuroangiography by Pearse Morris, third edition showed the range of variation between 11% to 43%[2]. In a cadaveric study Gunnal et al found total variation up to 31.3%[30]. Variations related with the A1 segment of ACA are agenesis, hypoplasia and duplication. Hypo- plastic/ under-developed A1/Aplastic segment were present in 30 cases. It was seen in 22 (24.5%) on the right and 8 (9%) on the left A1 segment. In previous cadaveric study by Riggs and Rupshowed 7% A1 hypoplasia[4]. Pai et alfound no hypoplasia or aplasia.[5] ButPiganiol et al found 2.1% and Macchi et al found it 0.7%[6,7]. In a 3DCTA study Niederberger et al showed 10% hypoplasia/apasia in a series.In general, our study shows a higher percentage of variations. Hypoplasia/Aplasia are more common in right side than the left side (24.5% vs8%).

All possible forms of abnormalities of AComA were present in 22 (24.5%) of cases and normal in 68 (75.5%) cases. Fenestration of AcomA was seen in 8 (9%) cases, Hypoplastic/ Absent AComA was seen in 8 (9%) cases. Other abnormalities like duplication were present 6 (6.5%) cases. Autopsy studies described the frequency of fenestrations in the anterior circulation in up to 64.4 %[25]. Investigations that used three-dimensional digital subtraction angiography (DSA) found a greater incidence of fenestrations in the anterior cerebral circulation, which was 27 % for aneurysm patients and 22 % for patients without aneurysm[18]. On the other hand, Sanders et al. studying 5,190 cerebral angiograms found only 3 fenestrations in the AComA complex.[23] A study by Bozÿek et al. using CTA described the incidence of AComA complex fenestrations to be 1.75 %[3]. Zhao et al, Uchino et aland Saidi et al in cadaveric study found fenestration 0,8%, 1.2% and 26% respectively[13, 15, 28], These findings emphasis the fact that two-dimensional imaging is not a suitable tool for detecting intracranial arterial fenestrations.The most common anomaly of the anterior cerebral circulation wasfenestratedAComA. Again Cadaveric studies show a vast range of AComA hypoplasia frequency from 9.15 to 30 %[1, 4, 7]. In addition, aplastic AComA is a rare autopsy finding, found only in 1.8 % of studied subjects[9]. This phenomenon can be explained by the fact that hypoplastic arteries may notbe hemodynamically efficient, therefore are not visible in angiographic studies and thus are considered to be aplastic. On the other hand, autopsy findings always visualize the artery trunk, even when contrast flow would not be possible. Li et al. using CTA found aplastic AComA's in 9.38 % of study subjects[8]. AComA 3D imaging provides the excellent quality data, but unfortunately it is rarely available in everyday clinical practice[20]. Paiet alshowed 20% aplastic/ hypoplastic AComA[5].

Azygos anterior cerebral artery was found in 2 (2.2%) cases. In text book Practical Neuroangiography by Pearse Morrisshowed that incidence of azygos ACA is only0.3%[2]. Schik et al,

Dietrich et al, Baptista et aland Kakau et alfound 1.1%, 0.5-5%, 0-5% and 0.1-5% respectively[17, 18, 22]. But some study like Osborn et alshowed this value very high (10%).[24] In thisstudy we found one (1.3%) case of a triple A2 segment. Most authors identify the triple A2 segment as a persistent median artery of corpus callosum, a remnant of embryological cerebral circulation[11]. MRA studies show that the frequency of a triple A2 segment ranges between 0.4 and 3.03 %[14, 28]. Usually a triple A2 is an incidental finding. Sun et al. reported a very interesting case of a triple A2 segment associated with the presence of an aneurysm[16]. We have not found such pathology in our study.

Callosomarginal artery was absent in 2 (2.2%) in right side and 4 (4.5%) in left side. Out of them 5 (6%) from right sideand 3 (3.5%) from left side wereabnormal in origin. Callosomarginal artery usually originates at the top of the knee of corpus callosum. But very early origin or late origin are also seen. Abnormal origin may be associate with aneurysm formation. The CmA is also not always present and therefore it is preferable to classify the pericallosal artery as the segment distal to the AComA[17, 25]. The CmA has been observed in 40.0% to 93.4% of specimens[6, 11, 17, 21, 25, 27, 26, 29]. The variability of the absence or presence ofthe CmAis due to the different definitions used for this artery by different authors. The CmAis the largest branch of the pericallosal artery that has been defined as the artery that runs near the cingulate sulcus and gives off two or more cortical branches[2]. But this is problematic since there can occasionally be more than one artery that arises from the pericallosal artery, run in the cingulate sulcus and give rise to a number of cortical branches .Ugur et al. proposed a new classification system[29]. The CmA was either defined as typical, atypical or absent. Anatypical CmA was observed when there was only a very shortartery coursing in the cingulate sulcus. Two symmetricalcallosomarginal arteries can also be present in the samehemisphere. A typical CmA has a longer course comparedto the two symmetrical atypical callosomarginal arteries andusually originates from the A3 segment .Ugur et al.observed typical, atypical or absent CmA's in 49%, 34%and 17% respectively[29].

Conclusion

Anterior cerebral artery complex is a common place for anatomical variations and this has a relation with aneurysm formations. The knowledge of these variations will help the clinicians to understand pathophysiology, angioarchitecture and hemodynamics of the lesions in anterior circulation. Morphology and variations of the anterior cerebral artery complex were studied in 90 patients undergone digital subtraction angiography (DSA). Among them 33.3% (n=30) had different forms ofvariations. Variations of the segments in relation with size, course, communications, origin of callosomarginal arteries, course of pericallosal arteries were noted. These were divided into different groups like hypoplasia, aplasia, duplication and fenestrations. Hypoplasia/Aplasia of proximal anterior cerebral artery (A1) was 24.5% in right side and 9% in left side. Anterior communicating artery (AComA) was found absent in 9% and fenestration in 9%. Callosomarginal artery was absent in 2.2% in right side and 4.5% in left side.Whereas,in right callosomarginal artery 6% had abnormal origin and 3.5% in left side.Pericallosal arteries were present 100% on both sides.This study was performed in a small number of subjects. Multicenter studies are necessary to reach a satisfactory conclusion about the complete understanding of anatomy of anterior cerebral artery complex in this population.

References:

1. Krayenbuhl HA, Yasargil MG. Cerebral angiography. 2nd Ed. New York: Thieme Medical Publishers Inc, 1982:91-3.
2. Morris P. Practical Neuroangiography. 3rd Ed. Philadelphia: Lippincott Williams & Wilkins, 2013:161-74
3. Bozÿek P, Pilch-Kowalczyk J, Kluczewska E, Zymon-ZagórskaA .Detection of cerebral artery fenestrations by computed tomography angiography. *NeurolNeurochir Pol.* 2012;46:239–244
4. Riggs HE, Rupp C. Variations in form of Circle of Willis. *Arch Neurol*1963; 8(1):8-14.
5. Pai SB, Kulkarni RN, Varma RG.

Microsurgical anatomy of the anterior cerebral artery—Anterior communicating artery complex: An Indian study. *Neurol Asia* 2005; 10:21-8.

6. Piganiol G, Toga M, Paillas J. L'arterecommuni-canteanterieure, Etude embriologiqueetanatomique. *Neurochirurgie* 1960; 6:3-19.
7. 7.Macchi C, Catini C, Federico C, Gulisano M, Pacini P, Cecchi F. Magnetic resonance angiographic evaluation of circulusarterio-suscerebri (circle of Willis): a morphologic study in 100 human healthy subjects. *Ital J AnatEmbryol*1996; 101:115-23.
8. Li Q, Li J, Lv F, Li K, Luo T, Xie P.A multidetector CT angiography study of variations in the circle of Willis in a Chinese population.*J ClinNeurosci.*2011;18:379–383
9. Maga P, Tomaszewski KA, Pasternak A, Zawilin´ski J, Tomaszewska R, Gregorczyk-Maga I et al. Extra- and intracerebral course of the recurrent artery of Heubner. *Folia Morphol (Warsz)*2013;72:94–99
10. Maga P, Tomaszewski KA, Skrzat J, Tomaszewska IM, Iskra T, Pasternak A et al.Microanatomical study of the recurrent artery of Heubner. *Ann Anat*2013;195:342–350
11. Gomes FB, Dujovny M, Umansky F, Berman SK, Diaz FG, Ausman JI, Mirchandani HG, Ray WJ.Microanatomy of the anterior cerebral artery.*SurgNeurol* 1986; 26(2):129-141
12. Compton MR. The pathology of ruptured ACA aneurysms. *Lancet* 1962; 2:421-38.
13. Zhao HW, Fu J, Lu ZL, Lü HJ. Fenestration of the anterior cerebral artery detected by magnetic resonance angiography.*Chin Med J (Engl)* 2009; 259
14. Parmar H, Sitoh YY, Hui F. Normal variants of the intracranial circulation demonstrated by MR angiography at 3 T. *Eur J Radiol*2005;56:220–228.
15. Saidi H, Kitunguu P, Ogengo JA. Variant anatomy of the anterior cerebral artery in Adult Kenyans.*Afr J NeurolSci*2008; 27:97-105.
16. Sun C, Xv ZD, Yuan ZG, Wang XM, Wang LJ, Liu C. MSCT diagnosis of aneurysms associated with an unusual variant: atypical triplication anterior cerebral artery. *SurgRadiolAnat* 2012; 34:777–780.
17. Kakou M, Destrieux C, Velut S. Microanatomy of the pericallosal arterial complex. *J Neurosurg*2000;93:667–675
18. 18.Dietrich W, Reinprecht A, Gruber A, Czech T. De novo formation and rupture of an azygospericallosal artery aneurysm. Case report.*J Neurosurg*2000; 93:1062-4
19. Stefani MA, Schneider FL, Marrone AC, Severino AG, Jackowski AP, Wallace MC. Anatomic variations of anterior cerebral artery cortical branches. *ClinAnat*2000; 13:231-6.
20. Zurada A, Gielecki J, Shane Tubbs R, Loukas M, Maksymowicz W, Chlebiej M. Detailed 3D-morphometry of the anteriorcommunicating artery: potential clinical and neurosurgical implications. *SurgRadiolAnat*2011;33:531–538
21. Kedia S, Daisy S, Mukherjee KK, Salunke P, Srinivasa R, Narain MS. Microsurgical anatomy of the anterior cerebral artery in Indian cadavers. *Neurol India*2013; 61(2):117-121
22. Baptista AG. Studies on the arteries of the brain. II. The anterior cerebral artery: Some anatomic features and their clinical implications. *Neurology* 1963; 13:825-35.
23. Sanders WP, Sorek PA, Mehta BA. Fenestration of intracranial arteries with special attention to associated aneurysms andother anomalies. AJNR Am *J Neuroradiol*1993;14:675–680
24. Osborn AG. Diagnostic Cerebral Angiography. 2nd Ed. Philadelphia, PA: Lippincott Williams & Wilkins. Neurology 1999:34-9.
25. Perlmutter D, Rhoton AL. Microsurgical anatomy of the distal anterior cerebral artery. *J Neurosurg*1978; 49:204-228
26. Ring BA, Waddington MM: Roentgenographic anatomy of the pericallosal arteries. Am J

Roentgenol Radium *TheNuclMed* 1968; 104:109-118

27. Saidi H, Kitunguu PK, Ogeng'OJA.Variant anatomy of the anterior cerebral artery in adult brains. *Afr J NeurolSci*2008; 27(1):97-105
28. Uchino A, Takase Y,Nomiyama K, Egashira R, Kudo S. Fenestration of the middle cerebral artery detected by MR angiography. *MagnReson Med Sci*2006; 5(1):51-55,
29. Ugur HC, Kahilogullari G, Esmer AF, Combert A, Kanpolat Y. A neurosurgical view of anatomical variations of the distal anterior cerebral artery: An anatomical study. *J Neurosurg*2006; 104:1-7,
30. Gunnal SA, Wabale RN, FarooquiMS : Variations of anterior cerebral artery in human cadavers: *Neurology A*sia 2013 ; 18(3): 249-259

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Frequency of EEG Changes In Different Types of Clinically Diagnosed Epileptic Patients

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Abstract:

Background: *Diagnosis of epilepsy is based mainly on clinical history and examination. EEG constitutes the single most valuable laboratory test in the evaluation of patients with epilepsy. Objective: The objective of the present study was to find out the frequency of EEG abnormality among different types of clinically diagnosed epileptic patients.* ***Methods:*** *This cross-sectional study was carried out in the Department of Neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka. A total of 152 epileptic patients attended in the Epilepsy Clinic, General OPD and EEG room of the Department of Neurology were enrolled for this study. Information on socio-demographic and seizure characteristics was obtained. The records from patients were obtained using the standard data collection form.* ***Result:*** *Out of 152 epileptic patients male were 62.5% and female were 37.5%, mean age was 20.69 ± 11.83 years. Abnormal EEG was found in 81 (53.3%) patients. Most of the patients 64 (79.0%) had generalized epileptic discharge and 17 (21.0%) had focal epileptic discharge. Out of 81 patients with abnormal EEG wave, 31 (38.3%) patients had spike and wave, 26 (32.1%) patients had sharp wave and 24 (29.6%) patients had multiple types of EEG wave.****Conclusion:*** *The EEG is an important tool for diagnosing an epilepsy syndrome, knowledge of which aids in planning treatment and determining prognosis.*

Introduction:

Epilepsy is a common chronic neurological disorder. More than half a century before the discovery of the human EEG, Hughlings Jackson offered a definition of epilepsy based on patho-physiology[1]. Though Gibbs and his colleagues[2] discovered the pattern of epileptic discharges in 1935, the first description of an Epileptic crisis dates back to 3000 BC. Since the introduction, Electroencephalogram (EEG) has been used to diagnose and manage epilepsy. A seizure is any clinical event caused by abnormal electrical discharge in the brain whilst epilepsy is tendency to have recurrent seizures.[3]. In other words the term "Epilepsy" refers to recurrent and unprovoked seizures. About 50 million people worldwide have epilepsy, with almost 90% of these people being in developing countries[4]. There is a wide variation of incidence of epilepsy worldwide due to variation in classification system of epilepsy and methodology adopted in different studies[5]. The life time incidence of epilepsy varies from 2% to 5%. With the incidence of 2-10 per thousand for South East Asian countries, it is estimated that there are 1.5-2 million people suffering from epilepsy in Bangladesh. Epilepsy is more likely to occur in young children or people over the age of 65 years, however it can occur at any time[7]. Broadly, epilepsies are classified as either generalized or partial with several subcategories in each class[8]. Most primary epilepsies are thought to have a genetic basis and their mode of inheritance is polygenic[9]. Its etiology and pathogenesis depends on multiple factors i.e. idiopathic, genetics, environmental, metabolic and various structural lesions in the brain. Epilepsy is mostly diagnosed

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clinically, but EEG remains central to the diagnosis of epilepsy[10]. Even with the tremendous advances in Neurodiagnostic procedure, the role of EEG is not abolished[9].

Methods:

This cross-sectional descriptive study was carried out in Epilepsy Clinic, General OPD and EEG room in the Department of Neurology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka over a period of two and half years from January 2014 to June 2016. A total of 152 clinically diagnosed epileptic patients attended in Epilepsy Clinic, General OPD and EEG were enrolled in this study. Epileptic patients having metabolic disturbances were excluded. In all cases single EEG was done following standard procedure by expert EEG technician using 10/20 channel EEG machine with photic stimulation, sleep deprivation and hyperventilation and EEG was done for at least 20-30 minutes. The demographic information, relevant history, examination findings and investigation reports of all the study subjects were recorded in the data collection sheet. Result was done by using Microsoft Excel.

Results and Observation:

In this study, mean age of the patients was 20.69±11.83 years within the range of 1.5-75 years. Male (62.5%) were predominant than female (37.5%). Male female ratio was 1.67:1. In this study, 102 (67.1%) cases were generalized seizure and 50 (32.9%) cases were focal seizure. Among generalized seizure patients most common clinical features were generalized convulsion 63.2%, frothy mouth 61.8%, loss of consciousness 59.9% and tongue bite 57.2 % in case of generalized seizure and in focal seizure most common was abnormal movement (20.4%). According to clinical diagnosis, most of the patients (50.7%) had GTCS followed by 19 (12.5%), 18 (11.8%), 13 (8.6%), 13 (8.6%) and 12 (7.9%) patients had focal seizure without impairment of consciousness, focal seizure with secondary generalization, absence seizure, focal seizure with impairment of consciousness and myoclonic seizure respectively. Abnormal EEG was found in 81 (53.3%) patients, of them most of the patients (65.3%) had generalized epileptic discharge and 25 (34.7%) had focal epileptic discharge. Among focal epileptic discharge, 9 (52.9%) patients had temporal focal seizure followed by 5 (29.4%) and 3 (17.7%) patients had frontal focal seizure and parietal focal seizure respectively. Among generalized seizures, 56 (87.5%) patients had generalized epileptic discharge and 8 (12.5%) patients had typical absence seizure. Out of 81 patients with abnormal EEG wave, 31 (38.3%) patients had spike and wave, 26 (32.1%) patients had sharp wave and 24 (29.6%) patients had multiple types of EEG wave.

Table-I

Distribution of patients according to age (n=152)

	Frequency	Percentage
Age		
Mean ± SD	20.69 ± 11.83	
Range (min-max)	1.5 -75	
Gender		
Male	95	62.5
Female	57	37.5

Table-II

Distribution of patients according to common presenting features (n=152)

Presenting features	Frequency	Percentage
Generalized seizure	102	67.1
Generalized convulsion	96	63.2
Frothy mouth	94	61.8
Loss of consciousness	91	59.9
Tongue bite	87	57.2
Post ictal confusion/ Headache	77	50.7
Urinary incontinence	60	39.5
Nocturnal attack	34	22.4
Focal seizure	50	32.9
Abnormal movement	31	20.4
Impairment of consciousness and abnormal mannerism	21	13.8
Convulsion starts on one side then generalized	11	7.2
Psychiatric symptoms	8	5.3

Table-III

Distribution of patients according to clinical diagnosis (n=152)

Clinical	Frequency	Percentage
GTCS	77	50.7
Focal seizure without impairment of consciousness	19	12.5
Focal seizure with secondary generalization	18	11.8
Typical absence seizure	13	8.6
Focal seizure with impairment of consciousness	13	8.6
Myoclonic seizure	12	7.9

Table-IV

Distribution of patients according to clinical diagnosis and their EEG findings (n=152)

Clinical diagnosis	Total (n=152)	EEG	
		Normal(n=71)	Abnormal(n=81)
GTCS	77	44.2% (34/77)	55.8% (43/77)
Focal seizure without impairment of consciousness	19	42.1% (8/19)	57.9% (11/19)
Focal seizure with secondary generalization	18	55.6% (10/18)	44.4% (8/18)
Typical absence seizure	13	38.5% (5/13)	61.5% (8/13)
Focal seizure with impairment of consciousness	13	53.8% (7/13)	46.2% (6/13)
Myoclonic seizure	12	58.3% (7/12)	41.7% (5/12)
Total	152	46.7% (71/152)	53.3 (81/152)

Table V

Distribution of abnormal EEG findings in patients according to seizure type (n=81)

Abnormal	Frequency	Percentage
Focal epileptic discharge	17	21.0
Temporal	9	52.9
Frontal	5	29.4
Parietal	3	17.7
Generalized epileptic discharge	64	79.0
Generalized epileptic discharge	56	87.5
Typical absence seizure	8	12.5

Table-VI

Distribution of abnormal EEG wave (n=81)

Abnormal activity	Frequency	Percentage
Spike and wave	31	38.3
• Generalized epileptic discharge	14	17.3
• Focal epileptic discharge	9	11.1
• Typical absence seizure	8	9.9
Sharp and wave	26	32.1
• Generalized epileptic discharge	23	28.4
• Focal epileptic discharge	3	3.7
Multiple	24	29.6
• Generalized epileptic discharge	19	23.5
• Focal epileptic discharge	5	6.2

Discussion:

Diagnosis of epilepsy is based mainly on clinical history and examination. EEG constitutes the single most valuable laboratory test in the evaluation of patients with epilepsy. It is a safe, non-invasive procedure for evaluation of electrophysiological state of patients with epilepsy in the ictal or interictal period.

Marino et al[6] showed that the incidence of epilepsy is highest at both extreme of ages, especially in neonatal period and after 6th decade. It varies among different age groups and forms a U-shape curve, which shows the lowest incidence for people between the age of 30 and 40 years. The highest incidence of epilepsy is seen in the first year of life as well as among the elderly[11]. In this study 84.2% patients were below or equal to 30 years of age. Chowdhury et al[11] found 85.8% patients below 31 years and Owolabi et al[12] found 74.5% of epilepsy were <31 years old. Most of the patients in this study were children and young adult.

This study showed that males (62.5%) were more prone to epilepsy than females (37.5%), this may be due to some of the risk factors, like trauma, are more common among males. In the study of Owolabi et al.[12], male was 61.2% and female was 38.8%. Similar result was seen in the study of Sidig et al.[13] [Male was 54.1% and female was 45.9%].

In this study, out of 152 patients most common clinical features were generalized convulsion 63.2%, frothy mouth 61.8%, loss of consciousness 59.9% and tongue bite 57.2% in case of generalized seizure and in focal seizure most common was abnormal movement (20.4%). Almost similar result was found in the study of Sidig et al[13].

In our study, among the clinically diagnosed epileptic patients most of them (50.7%) had GTCS followed by 19 (12.5%), 18 (11.8%), 13 (8.6%), 13 (8.6%) and 12 (7.9%) patients had focal seizure without impairment of consciousness, focal seizure with secondary generalization, absence seizure, focal seizure with impairment of consciousness and myoclonic seizure respectively in clinical diagnosis. Sidig et al. [13] found that 86.4% had generalized epilepsy, while 13.6% had focal epilepsy clinically. Most of our epileptic patients had generalized epilepsy, may be due to the fact that generalized epilepsy is dramatic in its presentation. So that affected people are interested to seek medical treatment, unlike focal seizures which may go unnoticed.

In this study abnormal EEG was found in 53.3% patients. Abnormal EEG was seen in 57.1%, 62.7% and 65.0% epileptic patients in the study of Owolabi et al.[12], Chowdhury et al.[12]and Sidig et al. [13] respectively.

Most of the patients (79.0%) had generalized epileptic discharge and 17 (21.0%) had focal epileptic discharge in abnormal EEG. Sidig et al.[13] reveled abnormal EEG in 64.8% cases, of them 86.4% had generalized discharges while 13.6% had focal discharge. Owolabi et al.[12] found 51.5% generalized and 48.5% partial among abnormal EEG patients.

Among patients with focal seizure 9 (52.9%) patients had temporal focal seizure followed by 5 (29.4%) and 3 (17.7%) patients had frontal focal seizure and parietal focal seizure respectively. Among the patients with Focal seizure, most common focus was temporal lobe. Temporal lobe was the most vulnerable part in focal seizure[14].

Out of 81 patients with abnormal EEG wave, 31(38.3%) patients had spike and wave, 26 (32.1%) patients had sharp and wave and 24 (29.6%) patients had multiple types of EEG wave. Among patients with epileptiform activity, generalized sharp and wave complexes and focal sharp and slow wave complexes were the most common finding[13]. In contrast to our findings Chowdhury et al.[11] found 74% spike and wave, 11% sharp and wave 6% poly spikes and 2% slow waves, which probably accounts for the difference in age group of sample population.

Conclusion:

Based on the above study it can be concluded that diagnosis of epilepsy is based on clinical history and examination. EEG may constitute as one of the most valuable laboratory test in the evaluation of patients with epilepsy. The presence of an interictal spike/sharp wave helps to confirm a clinical diagnosis of epilepsy, aids in defining the

epilepsy syndrome, provides information that assists in planning drug management and determining prognosis.

References:

1. Hughlings Jackson, J. On the anatomical, physiological and pathological investigation of epilepsies.West Riding Lunatic Asylum Medical Reports. 1873;3:315

1. 2 Gibbs FA, Davis H, Lennox WG. The electro encephalogram in epilepsy and in conditions of impaired consciousness. American Journal of EEG Technology. 1968 Jun 1;8(2):59-73.

2. Allen CMC, Lueck CJ, Dennis M. Neurologic disease. In: Colledge NR,Walker BR, Ralston SH (eds) Davidson's Principles and Practice of Medicine, 21st edn. USA: Elsevier Limited. 2010.1172

3. Palmini A, Andermann F, Olivier A, Tampieri D, Robitaille Y, Andermann E, Wright G. Focal neuronal migration disorders and intractable partial epilepsy: a study of 30 patients. Annals of neurology. 1991 Dec 1;30(6):741-9.

4. Yacubian 2000. Yacubian EMT: Epilepsia: o conceito atual. In Epilepsia da Antiguidade ao Segundo Milênio. Edited by: Yacubian EMT. Lemos, São Paulo; 2000:82-8.

5. WHO 2015. Report on Epilepsy in South East Asia 'Some facts and figures in Epilepsy', Accessed on: 02-10-2015

6. Marino Jr RA, Cukiert A, Pinho E, Pinho E. Aspectos epidemiológicos da epilepsia em São Paulo. Arq Neuropsiquiatr. 1986;44(2):243-54.

7. King MA, Newton MR, Jackson GD, Fitt GJ, Mitchell LA, Silvapulle MJ, Berkovic SF. Epileptology of the first-seizure presentation: a clinical, electroencephalographic, and magnetic resonance imaging study of 300 consecutive patients. The Lancet. 1998;352(9133):1007-11.

8. Adams RD, Victor M, Rooper AH. (eds) Epilepsy and other seizure disorder, Principles of Neurology, 8th edn, New York, USA: Mc Graw Hill Book Company. 2005. 271-95

9. Cascino GD. Use of routine and video electroencephalography. Neurologic clinics. 2001 May 1;19(2):271-87.

10. Forsgren L. and Hesdorffer D. Epidemiology and prognosis of epilepsy. In Shorvon S, Perucca E and Engel J, (eds), *The Treatment of Epilepsy*, 3rd edn. London, UK: Wiley-Blackwell, 2009. 21–31.

11. Chowdhury RN, Hasan AH, Rahman KM, Mondol BA, Deb SR, Mohammad QD. Interictal EEG changes in patients with seizure disorder: experience in Bangladesh. SpringerPlus. 2013 Jan 29;2(1):1.

12. Owolabi LF, Shehu S, Owolabi SD, Umar M. Interictal electroencephalography in patients with epilepsy in northwestern Nigeria. Annals of Nigerian Medicine. 2013 Jul 1;7(2):48.

13. Sidig A, Hussein A, Yassien F, Hamad A, el-Adil O, Saad M, Mubark B, Aldar MM. The pattern of clinical presentation of epilepsy among adolescence Sudanese epileptic patients. Journal of Neuroscience and Behavioral Health. 2011 Jan 31;3(1):1-7.

14. Aneesh P, Mohan M, Varma SC. The Study of Interictal Electro Encephalographic (EEG) patterns in different types of Seizures. International Journal of Scientific and Research Publications. 2013; 3(9), 1-2.

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

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Abstract:

Background: Recent studies have provided evidence that uric acid (UA) is suspected to play a neuro-protective role in Parkinson's disease (PD). Uric acid is a natural antioxidant that may reduce oxidative stress, a mechanism thought to play a role in the pathogenesis of PD. This study aimed to evaluate whether the serum UA level was associated with PD in a relatively small population of Bangladeshi patients.

Materials and methods: *An observational prospective case control Study was conducted in Neurology of Sir Salimullah Medical College & Mitford Hospital including both the male and female wards during July 2012 to December 2013. Serum uric acid were determined from 40 PD patients and compared with 70 age and sex matched control; following the uric acid colorimetric method, the serum creatinine (Scr) levels were also measured to reduce the bias caused by possible differences in renal excretion function. Data were analyzed with software SPSS 16 and statistical descriptive methods (mean percentage, SD) and* t*-test.*

Result: *In this study, 22 men (55%) and 18 women (45%) with PD were evaluated. The mean serum uric acid in patients was 3.7±0.97 and in the control group was 5.32±0.44. This difference was statistically significant (p=0.001). Also, the mean serum uric acid in both men (3.48±0.98) and women (4.1±1.17) in patients group was statistically lower than both men (5.39±0.46) and women (5.17±0.35) in control group.(p=0.001).*

Conclusion: This present study showed a positive association between low serum UA and PD .

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

Introduction:

PD is the second commonest neurodegenerative disease, clinically characterized by rest tremor, rigidity, bradykinesia, gait impairment and pathologically, there are degeneration of dopaminergic neurons in the substantia nigra pars compacta, reduced striatal dopamine, and intracytoplasmic proteinaceous inclusions known as Lewy bodies[1]. UA is the final oxidation product of purine metabolism and is excreted in urine. It is a marker of oxidative stress, and may have a potential therapeutic role as an antioxidant [2,3]. It is reported that uric acid could suppress oxidative stress and prevent dopaminergic cell death in animal models of Parkinson's disease. Reduced UA levels have been found not only in the substantia nigra but also in the cerebrospinal fluid and serum of PD patients[4-6] .The association between UA and risk of PD has been investigated in several previous prospective studies and higher

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serum uric acid levels might have been correlated to a significantly reduced risk of PD[7,8]. There is also evidence that higher uric acid levels could slow the clinical progression of PD[9.10] . Some recent studies show that UA can decrease the onset of the disease or its intensity, because of having the antioxidant effects and this effect must be considered in the therapeutic process of the disease [11]. Some other studies indicate that high uric acid levels lead to the decrease of the free radicals and subsequently the onset of the disease[3]. Another 14 years period research in America revealed that the risk of onset of PD in people with higher dietary intake of uric acid index was much lower than others; instead, the onset of Gout and renal stones was higher than other people [11,12]. Some studies also show that the risk of PD is much lower in patients suffering from Gout [13,14]. Despite the above researches, results of the recent researches are not yet adequate for a general conclusion, so yet there are many studies indicating the need for more investigations[5,15-17]. Here, with considering the above studies, we would like to embark on measuring the serum UA levels in PD patients in Bangladesh to find out their association, so that the study result might open new era of future research regarding alternative management of PD.

Materials and Methods:

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

Result:

In this study, the age distribution of study population in case group the mean age was found 69.15±10.08 years. In control group, the mean age was 67.14±10.25 years. The mean age difference was not statistically significant (p>0.05) between two groups.(Table I).

Table-I

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

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

ns= not significant

P value reached from unpaired t-test

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

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

In Table IV shows serum uric acid level with sex. It was observed that in male, serum uric acid was found 3.48±0.98 mg/dl in case group and 5.39±0.46 mg/dl in control group. In female serum uric acid was found 4.1±1.17 mg/dl in case group and 5.17±0.35 mg/dl in control group.

Table-II

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

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

ns= not significant

P value reached from chi square test

Table-III

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

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

s= significant

P value reached from unpaired t-test

Tabl-IV

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

	Serum Uric Acid				P value
	Case (n=40)		Control (n=70)		
	Mean	±SD	Mean	±SD	
Male	3.48	±0.98	5.39	±0.46	0.001s
Range (min,max)	2.5	5.2	4.8	6.2	
Female	4.1	1.17	5.17	±0.35	
Range (min,max)	1.8	5.8	4.5	5.8	

s= significant

P value reached from unpaired t-test

Discussion:

This observational prospective case control study was carried out with an aim to determine the relation of serum UA level with prevalence of PD and also to find out the correlation of UA with severity of PD. In this study it was observed that in case group 37.5% patients were in 8th decade and their mean age was 69.15±10.08 years, varied 48 – 100 years. In control, 38.6% patients were in 6th decade and their mean age was 67.14±10.25 years, varied 50 – 90 years. The mean age was almost alike between two groups. In a recent research showed that the mean age of male patients of the control group was 64.7±6.4 years and the mean age of the female patients of the control group was 63.2±5.6 years [18]. There were no statistical differences between the mean ages of the estimated groups. 20 % of patients were under 60, 18% between 61–65, 28% were between 66–70 and 34% were more than 70 years old, which is consistent with the current study[18]. Another researcher mentioned in his study that one in seven patients with PD is under the age of 50 years, and there is an increase in prevalence with increasing age [19]. In this study only 5% of patients were 50 years or below which is much lower than that of previous study. The prevalence of PD in industrialized countries is thought to be approximately 0.3% [20]. This rises to 1.0% in people over the age of 60 and 3% in people over 80 years [22]. In the UK, PD is estimated to affect 100–180 per 100,000 of the population and has an annual incidence of 4–20 per 100,000[22]. Finding of present study regarding age also consistent with these previous studies.

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

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

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

There was no relationship between the uric acid and the duration of illness (Table II), and this was

in line with other studies. More researches still deem necessary in this area[25-17]. The main limitation of the research was the lack of comparison between the serum uric acid levels and the severity of illness which has to be considered in future studies [28-30].

Conclusion:

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

References:

1. Longlo, DL, Kasper, DL, Jameson, IJ, Fauci, AS, Mauser, SL & Loscalzo, J 2012, 'Harrison's principles of internal medicine', 18th ed. *New York McGraw Hill.* pp. 3317-35.
2. Becker, BF 1993, 'Towards the physiological function of uric acid', *Free Radical Biology & Medicine*. Vol. 14, no. 6, pp. 615–31.
3. Glantzounis, GK, Tsimoyiannis ,EC, Kappas, AM & Galaris, DA 2005, 'Uric acid and oxidative stress', *Curr Pharm Des,* vol.11, no. 32, pp. 4145-51.
4. Church, WH & Ward, VL 1994, 'Uric acid is reduced in the substantia nigra in Parkinson's disease: effect on dopamine oxidation', *Brain Res Bull,* vol. 33, pp. 419-425.
5. Davis, JW, Grandinetti, A, Waslien, CI, Ross, GW, White, LR & Morens, DM 1996, 'Observations on serum uric acid levels and the risk of idiopathic Parkinson's disease', *Am J Epidemiol,* vol. 144, no. 5, pp. 480-484.
6. Ascherio, A, LeWitt, PA, Xu, K, Eberly, S, Watts, A & Matson, WR et al. 2009, 'Urate as a predictor of the rate of clinical decline in Parkinson disease', *Arch Neurol,* vol. 66, No. 12, pp. 1460-1468.
7. Gao, X, Chen, H, Choi, HK, Curhan, G, Schwarzschild, MA & Ascherio, A 2008, 'Diet, urate and Parkinson's disease risk in men', *Am J Epidemiol*. vol. 167, no. 7, pp. 831-838.
8. de Lau, LM, Koudstaal, PJ, Hofman, A & Breteler, MM 2005, 'Serum uric acid levels and the risk of Parkinson disease', *Ann Neurol,* vol. 58, pp. 797-800.
9. Schiess, M & Oh, I 2008, 'Serum uric acid and clinical progression in Parkinson disease: potential biomarker for nigrostriatal failure', *Arch Neurol,* vol. 65, pp. 698-699.
10. Schwarzschild, MA, Schwid, SR, Marek, K, Watts, A, Lang, AE & Oakes, D et al. 2008, 'Serum urate as a predictor of clinical and radiographic progression in Parkinson disease', *Arch Neurol,* vol. 65, pp. 716-723.
11. Andreadou, E, Nikolaou, C & Gournaras, F 2009, 'Serum uric acid levels in patients with Parkinson's disease: Their relationship to treatment and disease duration', *Clin Neurol Neurosurg,* vol. 111, no. 9, pp. 724-8.
12. de Lau, LM, Koudstaal, PJ & Hofman, A 2008, 'Serum uric acid levels and the risk in men', *Am J Epidemiol,* vol. 167, no. 7, pp. 831-8.
13. De Vera, M, Rahman, MM & Rankin, J 2008, 'Gout and risk of Parkinson's disease: A cohort study', *Arthritis Rheum,* vol. 59, no. 11, pp. 1549-54.
14. Schlesinger, I & Schlesinger, N 2008, 'Uric acid in Parkinson's disease', *Mov Disord,* vol. 23, no. 12, p. 16.
15. Prasad, KN, Cole, WC & Kumar, B 1999, 'Multiple antioxidants in the prevention and treatment of Parkinson's disease', *J Am Coll Nutr,* vol. 18, no. 5, pp. 413-23.
16. Frasier, M, Chowdhury, S, Eberling, J & Sherer, T 2010, 'Biomarkers in Parkinson's disease: A funder's perspective', *Biomark Med* vol. 4, no. 5, pp. 723-9.
17. Tanner, CM 2010, 'Advances in environmental epidemiology', *Mov Disord,* vol. 25 Suppl 1, pp. S58-62.
18. Iranmanesh, F, Gadri, F, Bakhshi, H & Sarhadi, S 2012, 'Serum Uric Acid Level in Patients with Parkinson Disease', *Zahedan*

Journal of Research in Medical Sciences, pp. 1-3

19. Findley, LJ 2007, 'The economic impact of Parkinson's disease', *Parkinsonism Relat. Disord.* Vol. 13, pp. S8–S12.
20. de Lau, LM & Breteler, MM 2006, 'Epidemiology of Parkinson's disease', *Lancet Neurol*, vol. 5, no. 6, pp. 525–35.
21. Nussbaum, RL & Ellis, CE 2003, 'Alzheimer's disease and Parkinson's disease', *N Engl J Med*, vol. 348, no. 14, pp.1356–64.
22. The National Collaborating Centre for Chronic Conditions (2006). Parkinson's disease: national clinical guideline for diagnosis and management in primary and secondary care. London: Royal College of Physicians.
23. Tan, LCS, Tan, AKY & Tjia, HT 1998, 'The Profile of Hospitalised Patients with Parkinson's Disease', *Ann Acad Med Singapore*, vol.27, pp.808-12.
24. Hau,JG, Eugene C 'Correlation of serum uric acid levels with Parkinson's Disease symptom severity', Parkinson's Disease research education and clinical centre.
25. Annanmaki T, Muuronen A, Murros K. Low plasma uric
26. acid level in Parkinson's disease. Mov Disord 2007; 22(8): 1133-7.
27. Schlesinger I, Schlesinger N. Uric acid in Parkinson's
28. disease. Mov Disord 2008; 23(12): 16.
29. Shoulson I, Lasagna LC. Therapeutic directions for Parkinson's Disease. Mov Disord 2010; 25(Suppl 1): S152–S154.
30. Weisskopf MG, O'Reilly E, Chen H, et al. Plasma urate and risk of Parkinson's disease. Am J Epidemiol 2007; 166(5): 561-7.
31. Chen H, Mosley TH, Alonso A, et al. Plasma urate and Parkinson's disease in the Atherosclerosis Risk in Communities (ARIC) study. Am J Epidemiol 2009; 169(9): 1064–1069.
32. Winquist A, Steenland K, Shankar A. Higher serum uric acid associated with decreased Parkinson's disease
33. prevalence in a large community-based survey. Mov Disord 2010; 25(7): 932–936.

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Frequency and Risk Factors of Pneumonia and Urinary Tract Infection during Hospitalization in Acute Stroke Patients.

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Abstract:

Background: *Acute stroke Patients are at risk of developing a wide range of complications. Among these medical complications the most common are infections, including pneumonia and urinary tract infection (UTI). This study was designed to see the frequency and risk factors of pneumonia and UTI after acute stroke in hospitalized patients.*

Methods : *This prospective observational study was done in the Department of Neurology and Department of Medicine, Sylhet M.A.G Osmani Medical College Hospital, from May 2014 to November 2014. After hospitalization, a total number of 80 acute stroke patients were enrolled in this study. All patients of both sexes, presented with acute stroke, were confirmed by CT scan of head; vascular risk factors were recorded and relevant investigations were done.*

Results: *Among the study subjects Urinary tract infection was found in 23 (28.8%) patients. Statistically significant risk factors for UTI were : > 65 years age (OR=2.926; 95% of CI=1.044-8.202; p=0.037). Female gender (OR=0.327; 95% of CI=0.120-0.889; p=0.026), diabetes (OR=2.015; 95% of CI=1.019-7.780; p=0.042), Severe stroke (OR=3.331; 95% of CI=1.217-9.116; p=0.017), Foley tube catheterization (OR=4.229; 95% of CI=1.492-11.982; p=0.005). Pneumonia developed in 17 (21.2%) patients and no pneumonia in 63 (78.8%) patients.*

Conclusion : *UTI and pneumonia are common occurrence after acute stroke during stroke hospitalization. Older age, female gender, diabetes mellitus, severe stroke at presentation and urinary catheterization were found the risk factors of UTI; whereas older age, severe stroke at presentation, nasogastric tube feeding, oropharyngeal suction and difficulty in swallowing were found the risk factors of pneumonia in acute stroke.*

Keywords : *Acute Stroke, Hospitalization, Pneumonia, Urinary tract infection.*

Introduction:

Stroke is a crisis in cerebrovascular circulation and central nervous system function with focal neurologic dysfunction[1]. Stroke is the leading cause of major long-term disability in adults and the third leading cause of death after heart disease and cancer[2,3]. The annual incidence of stroke in the community is about 2 per 1,000 population, [4] and it remains a tremendous public heath burden. Patients who have had an acute stroke are at risk of developing a wide range of complications, including pneumonia, urinary tract infection (UTI), pressure ulcer, falls, venous thromboembolism (VTE), and severe constipation[5,-7]. These complications are important because they may cause death,[8-10] or can extend the hospital length of stay[11-12] worsen stroke outcomes, and increase cost of care[13]. Among these medical complications the most common are infections, including pneumonia and urinary tract infection (UTI) [14].

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A prospective cohort study (n=609) showed that 59% of patients had a complication during the mean hospital stay of 37 days[14] infectious complications were the third most common (after falls and skin breaks) and were predominantly urinary tract infections (UTI) (16%) and chest infections (12%). A multicentre study (n=1386) confirmed that amongst infectious complications at 7 days after the acute ischemic stroke onset, pneumonia (7.4%) and UTI (6.3%) are the most frequent[13].

Aslanyan et al.[15] reported that higher baseline National Institute of Health Stroke Scale (NIHSS) and age, male gender, history of diabetes and stroke subtype predicted pneumonia, which occurred in 13.6% of patients. Female gender and higher baseline NIHSS and age predicted UTI, which occurred in 17.2% of patients. Pneumonia was associated with poor outcome by mortality (hazard ratio, 2.2; 95% confidence interval, 1.5–3.3), Barthel index (<60) (odds ratio, 3.8; 2.2–6.7), NIHSS (4.9; 1.7–14) and Rankin scale (e”2) (3.4; 1.4–8.3). UTI was associated with Barthel index (1.9; 1.2–2.9), NIHSS (2.2; 1.2–4.0) and Rankin scale (3.1; 1.6–4.9). Pneumonia and UTI are independently associated with stroke poor outcome[15]. Therefore, prevention and prompt treatment of these infections in stroke patients might improve outcome[16].

So, this study is designed to see the Frequency and Risk Factors of pneumonia and UTI after acute stroke.

Materials and Methods:

It was a hospital based prospective observational study. The sudy was done in the Department of Neurology and Department of Medicine, Sylhet M.A.G Osmani Medical College Hospital, Sylhet. Consecutive admitted acute stroke patients in different Medicine and Neurology units of Sylhet M.A.G Osmani Medical College Hospital, Sylhet, during the study period and fulfilling the inclusion criteria, the study was done from May 2014 to November 2014.

Sampling technique:

Purposive sampling was employed as sampling technique in this study.

Data Collection Procedure:

Immediately after admission of a patient of suspected acute stroke, a proper diagnostic work up by taking detail history and clinical examination were done. A CT scan of brain was done to confirm acute stroke. Those, who met the inclusion criteria, were taken as sample

Informed written consent was obtained from the patients or guardians after full explanation of the details of the disease process and purpose of the study.

Past medical and personal history for cigarette smoking, arterial hypertension, diabetes mellitus, and ischaemic heart disease and other associated disease condition were also sought. All the data were recorded in a standard and pretested structured questionnaire.

Stroke severity at admission was determined using the modified National Institutes of Health Stroke Scale[17] and stroke was classified as mild (score 0-5), moderate (score 6-14) and severe (score 15-31) on mNIHSS scale (Appendix-II) [18].

Pneumonia was diagnosed by the attending clinician and based on the presence of e”3 of the following variables: fever (>38°C), productive cough with purulent sputum, abnormal respiratory examination (tachypnea [>22/min], tachycardia, inspiratory crackles, bronchial breathing), abnormal chest radiograph, arterial hypoxemia (PO_2 <70 mm Hg), and isolation of a relevant pathogen (positive gram stain and culture) [19].

UTI was diagnosed if patients presenting with (a) any of the following symptoms: dysuria, frequency, urgency, gross hematuria, or hypogastric pains with positive urine culture. In the absence of a urine culture, the laboratory diagnosis of UTI can be determined by the presence of significant pyuria defined as: (a) 8 or more pus cells/ mm^3 of uncentrifuged urine; or (b) 5 or more pus cells/hpf of centrifuged urine[20]. CA-UTI was diagnosed as “the presence of symptoms or signs compatible with UTI with no other identified source of infection along with e”10^3 colony-forming units (cfu)/mL of e”1 bacterial species” from a catheterized or previously catheterized (d”48 hours) urine sample[21].

Results:

The outcome of the study was as follows: Urinary tract infection was found in 23 (28.8%) patients. Distribution of patients by frequency of urinary tract infection was shown in figure 1.

Pneumonia developed in 17 (21.2%) patients. Distribution of patients by frequency of pneumonia in stroke patients was shown in figure-2.

The mean age of the patients of UTI was significantly higher than that of no UTI (t=2.075; p=0.041). Relationship between age and development of UTI was shown in table I. The age of the patient 65 years or higher significantly increased the risk of development of UTI compared to those aged under 65 years (OR=2.926; 95% of CI=1.044-8.202; X^2=4.334; p=0.037).

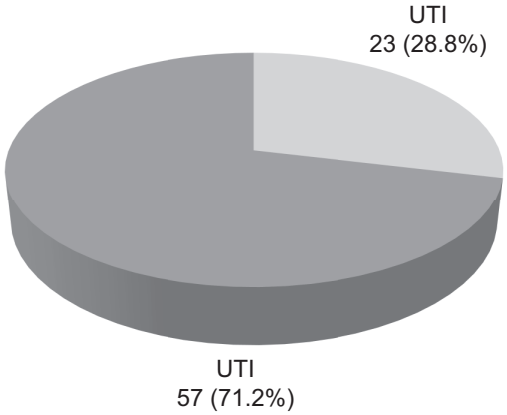

Fig.-1: *Distribution of patients by frequency of urinary tract infection (n=80)*

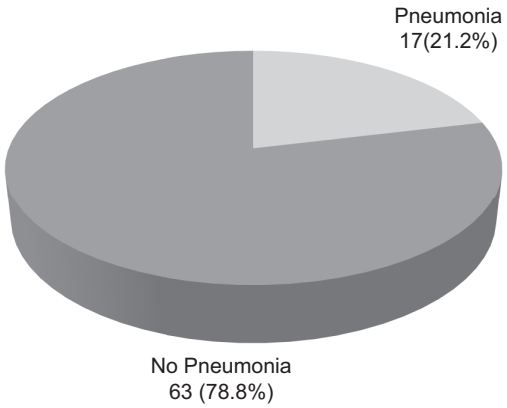

Fig.-2: *Distribution of patients by frequency of pneumonia in stroke patients (n=80)*

Table-I

Relationship between age and development of UTI

Age	UTI group (n=23)	No UTI group (n=57)	Odds Ratio (95% of CI)	p value
e"65 years	16 (69.6)	25 (43.9)	2.926 (1.044-8.202)	*p=0.037
<65 years	7 (30.4)	32 (56.1)		
Mean ± SD	70.96 ± 19.93	62.53 ±14.86		†p=0.041

*Chi-Square (χ^2) Test and †unpaired't' test were applied to analyze the data. Figure in the parenthesis indicates corresponding percentage. CI= confident interval, SD=standard deviation. Relationship between gender and development of UTI was shown in table-II. Development of UTI was significantly reduced in male gender compared to that female gender (OR=0.327; 95% of CI=0.120-0.889; X^2=4.334; p=0.026).

Table-II

Relationship between gender and development of UTI

Gender	UTI group (n=23)	No UTI group (n=57)	Odds Ratio (95% of CI)	p value
Male	10 (43.5)	40 (70.2)	0.327 (0.120-0.889)	*p=0.026
Female	13 (56.5)	17 (29.8)		
Total	23 (100.0)	57 (100.0)		

*Chi-Square (χ^2) Test was applied to analyze the data. Figure in the parenthesis indicates corresponding percentage. CI= confident interval, SD=standard deviation. Relationship between type of stroke and development of UTI was shown in table-III. There was no significant relationship between type of stroke and development of UTI (OR=2.234; 95% of CI=0.450-11.098; X^2=1.008; p=0.316).

Table-III

Relationship between type of stroke and development of UTI

Type of stroke	UTI group (n=23)	No UTI group (n=57)	Odds Ratio (95% of CI)	p value
Ischaemic	21 (91.3)	47 (82.5)	2.234 (0.450-11.098)	*p=0.316
Haemorrhagic	2 (8.7)	10 (17.5)		
Total	23 (100.0)	57 (100.0)		

*Chi-Square (χ^2) Test was applied to analyze the data. Figure in the parenthesis indicates corresponding percentage. CI= confident interval, SD=standard deviation.

Relationship between common risk factors of stroke and development of UTI shown in table-IV. Risk factors did not have significant role in the development of UTI.

Table-IV

Relationship between risk factors of stroke and development of UTI

Common risk factors of stroke	UTI group (n=23)	No UTI group (n=57)	Odds Ratio (95% of CI)	p value
Current smoker	14 (60.95)	27 (47.4)	1.278 (0.645-4.631)	p=0.274
Hypertension	14 (60.9)	31 (54.4)	1.305 (0.487-3.498)	p=0.597
Diabetes mellitus	11 (47.8)	14 (24.6)	2.015 (1.019-7.780)	p=0.042
Atrial fibrillation	4 (17.4)	3 (5.3)	3.789 (0.776-18.501)	p=0.082
IHD	4 (17.4)	6 (10.5)	1.789 (0.455-7.045)	p=0.401
Dyslipidaemia	12 (52.2)	29 (50.9)	1.053 (0.400-2.776)	p=0.916

*Chi-Square (χ^2) Test was applied to analyze the data. Figure in the parenthesis indicates corresponding percentage. CI= confident interval, SD=standard deviation.

Relationship between severity of stroke and development of UTI was shown in table-V. In UTI group, 13 (56.5%) patients had severe stroke; while in no UTI group 16 (28.1%) patients had severe stroke. Severe stroke significantly increased the risk of development of UTI (OR=3.331; 95% of CI=1.217-9.116; X^2=5.740; p=0.017).

Table-V

Relationship between severity of stroke and development of UTI

Severity of stroke	UTI group (n=23)	No UTI group (n=57)	Odds Ratio (95% of CI)	p value
Severe	13 (56.5)	16 (28.1)	3.331 (1.217-9.116)	*p=0.017
Mild to moderate	10 (43.5)	41 (71.9)		
Total	23 (100.0)	57 (100.0)		

*Chi-Square (χ^2) Test was applied to analyze the data. Figure in the parenthesis indicates corresponding percentage. CI= confident interval, SD=standard deviation.

Relationship between catheterization and development of UTI was shown in table-VI. In UTI group, 16 (69.6%) patients had Foley tube catheterization; while in no UTI group 20 (35.1%) patients. Foley tube catheterization significantly increased the risk of development of UTI (OR=4.229; 95% of CI=1.492-11.982; X^2=7.178; p=0.005).

Table-VI

Relationship between catheterization and development of UTI

Foley tube catheterization	UTI group (n=23)	No UTI group (n=57)	Odds Ratio (95% of CI)	p value
Yes	16 (69.6)	20 (35.1)	4.229 (1.492-11.982)	*p=0.005
No	7 (30.4)	37 (64.9)		
Total	23 (100.0)	57 (100.0)		

*Chi-Square (χ^2) Test was applied to analyze the data. Figure in the parenthesis indicates corresponding percentage. CI= confident interval, SD=standard deviation.

Table VII shows the age of the patient 65 years or higher significantly increased the risk of development of pneumonia compared to those aged under 65 years (OR=4.062; 95% of CI=1.192-13.842; X^2=5.496; p=0.019).

Table-VII

Relationship between age and development of pneumonia

Age	Pneumonia group (n=17)	No pneumonia group (n=63)	Odds Ratio (95% of CI)	p value
≥65 years	13 (76.5)	28 (44.4)	4.062 (1.192-13.842)	*p=0.019
<65 years	4 (23.5)	32 (55.6)		
Mean ± SD	71.82 ± 13.33	63.10 ± 13.41		†p=0.020

*Chi-Square (χ^2) Test and †unpaired 't' test were applied to analyze the data. Figure in the parenthesis indicates corresponding percentage. CI= confident interval, SD=standard deviation.

Relationship between gender and development of pneumonia was shown in table-VIII. In pneumonia group, 13 (76.5%) patients were male; while in no pneumonia 37 (58.7%) patients were male. There was no gender variation in the development of pneumonia (OR=2.284; 95% of CI=0.669-7.796; X^2=1.798; p=0.180).

Table-VIII

Relationship between gender and development of pneumonia

Gender	Pneumonia group (n=17)	No pneumonia group (n=63)	Odds Ratio (95% of CI)	p value
Male	13 (76.5)	37 (58.7)	2.284 (0.669-7.796)	p=0.180
Female	4 (23.5)	26 (41.3)		
Total	17 (100.0)	63 (100.0)		

*Chi-Square (χ^2) Test was applied to analyze the data. Figure in the parenthesis indicates corresponding percentage. CI= confident interval, SD=standard deviation.

Relationship between type of stroke and development of pneumonia shown in Table-IX.There was no significant relationship between type of stroke and development of pneumonia (OR=1.415; 95% of CI=0.279-7.171; X^2=0.177; p=0.674).

Table-IX

Relationship between type of stroke and development of pneumonia

Type of stroke	Pneumonia group (n=17)	No pneumonia group (n=63)	Odds Ratio (95% of CI)	p value
Ischaemic	15 (88.2)	53 (84.1)	1.415 (0.279-7.171)	p=0.674
Haemorrhagic	2 (11.8)	10 (15.9)		
Total	17 (100.0)	63 (100.0)		

*Chi-Square (χ^2) Test was applied to analyze the data. Figure in the parenthesis indicates corresponding percentage. CI= confident interval, SD=standard deviation

Relationship between common risk factors of stroke and development of pneumonia was shown in table-X. Rrisk factors did not have significant role in the development of pneumonia.

Table-X

Relationship between risk factors of stroke and development of pneumonia

Common risk factors of stroke	Pneumonia group (n=17)	No pneumonia group (n=63)	Odds Ratio (95% of CI)	p value
Smoker	13 (76.5)	28 (44.4)	1.22 (0.41-3.61)	p=0.721
Hypertension	11 (64.7)	34 (54.0)	1.56 (0.51-4.75)	p=0.428
Diabetes mellitus	7 (42.2)	18 (28.6)	1.75 (0.58-5.31)	p=0.320
Atrial fibrillation	3 (17.6)	4 (6.3)	3.16 (0.63-15.75)	p=0.143
IHD	3 (17.6)	7 (11.1)	1.71 (0.39-7.48)	p=0.470
Dyslipidaemia	11 (64.7)	30 (47.6)	2.02 (0.66-6.12)	p=0.211

*Chi-Square (χ^2) Test was applied to analyze the data. Figure in the parenthesis indicates corresponding percentage. CI= confident interval, SD=standard deviation

Relationship between severity of stroke and development of pneumonia was shown in table-XI. Severe stroke significantly increased the risk of development of pneumonia (OR=3.308; 95% of CI=1.095-9.995; X^2=4.760; p=0.017).

Table-XI

Relationship between severity of stroke and development of pneumonia

Severity of stroke	Pneumonia group (n=17)	No pneumonia group (n=63)	Odds Ratio (95% of CI)	p value
Severe	10 (58.8)	19 (30.2)	3.308 (1.095-9.995)	*p=0.029
Mild to moderate	7 (41.2)	44 (69.8)		
Total	17 (100.0)	63 (100.0)		

*Chi-Square (χ^2) Test was applied to analyze the data. Figure in the parenthesis indicates corresponding percentage. CI= confident interval, SD=standard deviation

Relationship between nasogastric (NG) tube feeding and development of pneumonia was shown in table-XII. Nasogastric tube feeding significantly increased the risk of development of pneumonia (OR=4.062; 95% of CI=1.192-13.842; X^2=5.496; p=0.019).

Table-XII

Relationship between nasogastric tube feeding and development of pneumonia

NG tube feeding	Pneumonia group (n=17)	No pneumonia group (n=63)	Odds Ratio (95% of CI)		p value
Yes	13 (76.5)	28 (44.4)	4.062	(1.192-13.842)	p=0.019
No	4 (23.5)	35 (55.6)			
Total	17 (100.0)	63 (100.0)			

*Chi-Square (χ^2) Test was applied to analyze the data. Figure in the parenthesis indicates corresponding percentage. CI= confident interval, SD=standard deviation

Relationship between oropharyngeal suction and development of pneumonia was shown in table-XIII. Oropharyngeal suction significantly increased the risk of development of pneumonia (OR=3.778; 95% of CI=1.207-11.827; X^2=5.602; p=0.018).

Table-XIII

Relationship between oropharyngeal suction and development of pneumonia

Oropharyngeal suction	Pneumonia group (n=17)	No pneumonia group (n=63)	Odds Ratio (95% of CI)		p value
Yes	8 (47.1)	12 (19.0)	3.778	(1.207-11.827)	p=0.018
No	9 (52.9)	51 (81.0)			
Total	17 (100.0)	63 (100.0)			

*Chi-Square (χ^2) Test was applied to analyze the data. Figure in the parenthesis indicates corresponding percentage. CI= confident interval, SD=standard deviation

Relationship between difficulty in swallowing and development of pneumonia was shown in table-XIV,difficulty in swallowing significantly increased the risk of development of pneumonia (OR=3.942; 95% of CI=1.277-12.170; X^2=6.128; p=0.013).

Table-XIV

Relationship between difficulty in swallowing suction and development of pneumonia

Difficulty in swallowing	Pneumonia group (n=17)	No pneumonia group (n=63)	Odds Ratio (95% of CI)		p value
Yes	11 (64.7)	20 (31.7)	3.942	(1.277-12.170)	p=0.013
No	6 (35.3)	43 (68.3)			
Total	17 (100.0)	63 (100.0)			

*Chi-Square (χ^2) Test was applied to analyze the data. Figure in the parenthesis indicates corresponding percentage. CI= confident interval, SD=standard deviation

Discussion :

A total 80 patients with acute stroke of first attack were selected according to inclusion and exclusion criteria. Urinary tract infection (UTI) was found in 23 (28.8%) patients . This result was supported by Roth et al.[22] and Ersoz et al.[23] Roth et al.[22] found that frequency of UTI among their stroke patients was 30.5% and Ersoz et al.[23] observed the frequency of symptomatic UTI in 27.3% of their stroke patients.

In the present study ,the mean age of the patients of UTI was significantly higher than that of no UTI (t=2.075; p=0.041). This result was correlated with the study of Stott et al.[16] that the mean age of the patients with UTI was significantly higher than that of with no UTI [75.7 (SD 10.5) vs 66.4 (SD 14.0)

years; p<0.001)]. But Chen et al.[24] did not find significant difference between the patient of UTI and that of no UTI [73.5 (SD 6.3) vs 73.2 (SD 5.8); p>0.05].

In the current study,the age of the patient 65 years or higher significantly increased the risk of development of UTI compared to those aged under 65 years (OR=2.926; 95% of CI=1.044-8.202; p=0.037). This results was nearly correlated with the study of Ovbiagele et al.[25] that older aged patients with stroke significantly increased the risk of development of UTI (OR=1.20; 95% of CI=1.01-1.43; p=00.04). Ersoz et al.[23] that 19.6% patients were aged under 65 years and 35.2% patients aged 65 years or higher developed UTI (p=0.067).

This study showed development of UTI was significantly reduced in male gender compared to that female gender (OR=0.327; 95% of CI=0.120-0.889; p=0.026). This result was in line with the study of Ovbiagele et al.[25] that male patients with stroke decreased the risk of UTI (OR=0.50; 95% of CI = 0.33, 0.74; p=0.0006). But this result was different from the study of Chen et al.[24] and Stott et al.[16] Chen et al.[24] found that 43.3% of UTI patients were male and 50.3% of patients with no UTI were male (p>0.05). Stott et al.[16] reported that 41.5% of UTI patients were male and 51.3% of patients were male in patients with no UTI (p=0.149).

There was no significant relationship between type of stroke and development of UTI (OR=2.234; 95% of CI=0.450-11.098; p=0.316). Similar result was observed in the study of Stott et al.[16] that type of stroke did not differ between UTI group and non-UTI group (p=0.847).

The difference between diabetic and non-diabetic was statistically significant (OR=2.015; 95% of CI=1.019-7.780; p=0.042). Chen et al.[24] and Stott et al.[16] supported this result.

In the current study 13 (56.5%) patients had severe stroke in UTI group; while in no UTI group 16 (28.1%) patients had severe stroke. Severe stroke significantly increased the risk of development of UTI (OR=3.331; 95% of CI=1.217-9.116; p=0.017). In this regards previous studies[9, 10] reported that baseline mNIHSS score was significantly higher in UTI group than that of group with no UTI,[9,10] and higher baseline NIHSS score was a predictor of UTI in acute stroke patients.

In this study 16 (69.6%) patients had Foley tube catheterization in UTI group; while in no UTI group 20 (35.1%) patients had Foley tube catheterization. Foley tube catheterization significantly increased the risk of development of UTI (OR=4.229; 95% of CI=1.492-11.982; p=0.005). This result was correlated with the study of Chen et al.[24] that indwelling catheter in 87.1% of patients of UTI group and 42.3% of patients of non-UTI group (p<0.05). Ersoz et al.[23] also supported this result (p=0.041)

In the present study pneumonia developed in 17 (21.2%) patients and no pneumonia in 63 (78.8%) patients. This result was supported by other studies[24, 26] . Chen et al. [24] observed the frequency of pneumonia in acute ward was 23.8% and Sellars et al. [26] found frequency of pneumonia among their stroke patients was 18.9%. But others reported lower frequency of pneumonia among their stroke patients. Ovbiagele et al.[25] found pneumonia in 10% of stroke patients during stroke hospitalization and Aslanyan et al. [15] found pneumonia in 10.9% in first week of stroke.

In the current study the mean age of the patients of pneumonia was 71.82 ± 13.33 years and that of no pneumonia was 63.10 ±13.41 years. The mean age of the patients of pneumonia was significantly higher than that of no pneumonia (p=0.020). Sellars et al.[26] supported this result that the mean age of the patients of pneumonia was significantly higher than that of no pneumonia (75.9 ± 11.4 years versus 64.9 ± 13.9 years; p<0.001). Ovbiagele et al.[25] also supported this result. But Chen et al.[24] did not find significant difference between the mean age of the patients of pneumonia and that of no pneumonia.

In this study 13 (76.5%) patients were aged 65 years or higher in pneumonia group; while in no pneumonia 28 (44.4%) patients were aged 65 years or higher. The age of the patient 65 years or higher significantly increased the risk of development of pneumonia compared to those aged under 65 years (OR=4.062; 95% of CI=1.192-13.842; p=0.019). in this regards Ovbiagele et al.[25] found

that increasing age per decade increased the risk of development of pneumonia (OR=1.35; 95% of CI=1.35 (1.20-1.52; p<0.0001).

In this study 13 (76.5%) patients were male in pneumonia group; while in no pneumonia 37 (58.7%) patients were male. There was no gender variation in the development of pneumonia (OR=2.284; 95% of CI=0.669-7.796; p=0.180). This result was consistent with the study of Ovbiagele et al.[25] that there was no gender variation in the development of pneumonia (OR=1.11; 95% of CI=0.66-1.87; p=0.70). Chen et al.[24] and Sellars et al.[26] also supported this result.

In the current study 15 (88.2%) patients had ischemic and 2 (11.8%) had hemorrhagic stroke in pneumonia group, while in no pneumonia group 53 (84.1%) patients had ischemic and 10 (15.9%) had hemorrhagic stroke. There was no significant relationship between type of stroke and development of pneumonia (OR=1.415; 95% of CI=0.279-7.171; p=0.674). Chen et al.[24] supported this result that there was no significant relationship between type of stroke and development of pneumonia.

This study showed that 7 (42.2%) patients had diabetes mellitus in pneumonia group; while 18 (28.6%) patients had diabetes mellitus in no pneumonia group. The difference between the two groups was statistically not significant (OR=1.75; 95% of CI=0.58-5.31; p=0.320). Ovbiagele et al.[25] supported this result that diabetes mellitus did not increase the risk of development of pneumonia (OR=1.56; 95% of CI=0.83- 2.95; p=0.17). Chen et al.[24] and Sellars et al.[26] also supported this result.

This study showed that 13 (76.5%) patients were current smoker in pneumonia group; while 28 (44.4%) patients were current smoker in no pneumonia group. The difference between the two groups was statistically not significant (OR=4.062; 95% of CI=0.41-3.61; p=0.721).

In this study severe stroke significantly increased the risk of development of pneumonia (OR=3.308; 95% of CI=1.095-9.995; p=0.017). In this regards previous study by Sellars et al.[26] reported that baseline mNIHSS score was significantly higher in pneumonia group than that of no pneumonia group.

Nasogastric tube feeding significantly increased the risk of development of pneumonia (OR=4.062; 95% of CI=1.192-13.842; p=0.019). Chen et al.[24] supported this result that nasogastric tube feeding was significantly higher in pneumonia group than that of no pneumonia group.

Oropharyngeal suction significantly increased the risk of development of pneumonia (OR=3.778; 95% of CI=1.207-11.827; p=0.018). Other available studies did not report the relationship between current smoker and development of UTI. But oropharyngeal suction was required in those patients who had difficulty in swallowing and thereby increases the risk of aspiration.

Difficulty in swallowing significantly increased the risk of development of pneumonia (OR=3.942; 95% of CI=1.277-12.170; p=0.013). Sellars et al.[26] supported this result that dysphagia was significantly higher in pneumonia group than that of no pneumonia group.

Conclusion

UTI and pneumonia are common occurrence after acute stroke during stroke hospitalization. Older age, female gender, diabetes mellitus, severe stroke at presentation and urinary catheterization are the risk factors of UTI; whereas older age, severe stroke at presentation, nasogastric tube feeding, oropharyngeal suction and difficulty in swallowing are risk factors of pneumonia in acute stroke.

References:

1. Alajbegovic A, Alajbegovic S. stroke in Diabetic patients in cantonal Hospital Zenica. Med Arh. 2009; 63(4):194-6.
2. Strong K, Mathers C, Bonita R. Preventing stroke: saving lives around the world. Lancet Neurol. 2007; 6:182–7.
3. Bonita R, Beaglehole R. Stroke prevention in poor countries. Time for action. Stroke. 2007; 38:2871–2.
4. Hamidon BB, Raymond AA, Norlinah MI, Jefferelli SB. The predictors of early infection

after an acute ischaemic stroke. Singapore Med J. 2003; 44:344–6.

5. Govan L, Langhorne P, Weir CJ. Does the prevention of complications explain the survival benefit of organized inpatient (stroke unit) care?: further analysis of a systematic review. Stroke. 2007;38:2536–40.
6. Indredavik B, Rohweder G, Naalsund E, Lydersen S. Medical complications in a comprehensive stroke unit and an early supported discharge service. Stroke. 2008;39:414–20.
7. Ingeman A, Andersen G, Hundborg HH, Svendsen ML, Johnston SP. In-Hospital Medical Complications, Length of Stay, and Mortality Among Stroke Unit Patients. Stroke. 2011;42:3214-8.
8. Bae HJ, Yoon DS, Lee J, Kim BK, Koo JS, Kwon O, et al. In-hospital medical complications and long-term mortality after ischemic stroke. Stroke. 2005;36:2441–5.
9. Cavallini A, Micieli G, Marcheselli S, Quaglini S. Role of monitoring inmanagement of acute ischemic stroke patients. Stroke. 2003;34: 2599–2603.
10. Heuschmann PU, Kolominsky-Rabas PL, Misselwitz B, Hermanek P, Leffmann C, Janzen RW, et al. Predictors of in-hospital mortality and attributable risks of death after ischemic stroke: the German Stroke Registers Study Group. Arch Intern Med. 2004;13:164:1761–8.
11. Saxena SK, Ng TP, Yong D, Fong NP, Gerald K. Total direct cost, length of hospital stay, institutional discharges and their determinants from rehabilitation settings in stroke patients. Acta Neurol Scand. 2006;114: 307–14.
12. Saxena SK, Koh GC, Ng TP, Fong NP, Yong D. Determinants of length of stay during post-stroke rehabilitation in community hospitals. Singapore Med J. 2007;48:400–7
13. Weimar C, Roth MP, Zillessen G, Glahn J, Wimmer ML, Busse O, et al. German Stroke Date Bank Collaborators. Complications following acute ischemic stroke. Eur Neurol. 2002;48: 133–40.
14. Davenport RJ, Dennis MS, Wellwood I, Warlow CP. Complications after acute stroke. Stroke. 1996; 27:415–20.
15. Aslanyan S, Weir CJ, Diener HC, Kaste M, Lees KR; GAIN International Steering Committee and Investigators. Pneumonia and urinary tract infection after acute ischaemic stroke: A tertiary analysis of the gain international trial. Eur J Neurol. 2004;11:49–53.
16. Stott DJ, Falconer A, Miller H, Tilston JC, Langhorne P. Urinary tract infection after stroke. QJM. 2009; 102: 243–9.
17. Lyden PD, Lu M, Levine SR, Brott TG, Broderick J. NINDS rtPA Stroke Study Group. A modified National Institutes of Health Stroke Scale for use in stroke clinical trials: preliminary reliability and validity. Stroke. 2001;32:1310–7.
18. Govan L, Langhorne P, Weir CJ. Categorizing stroke prognosis using different stroke scales. Stroke. 2009;40(10):3396-9.
19. Mann G, Hankey GJ, Cameron D. Swallowing function after stroke: prognosis and prognostic factors at 6 months. Stroke. 1999;30:744–8.
20. Report of the Task Force on Urinary Tract Infections 1998. The Philippine Clinical Practice Guideline on the Diagnosis and Management of Urinary Tract Infections: A Quick Reference Guide for Clinicians. Phil J Microbiol Infect Dis. 2002; 31(1):27-44
21. Hooton TM, Bradley SF, Cardenas DD, Colgan R, Geerlings SE, Rice JC, et al; Infectious Diseases Society of America. Diagnosis, prevention, and treatment of catheter-associated urinary tract infection in adults: 2009 International Clinical Practice Guidelines from the Infectious Diseases Society of America. Clin Infect Dis. 2010;50:625-63.

22. Roth E, Lovell L, Harvey R, Heinemann A, Semik P and Diaz S. Incidence of and risk factors for medical complications during stroke rehabilitation. Stroke. 2001; 32: 523–9.

23. Ersoz M, Ulusoy H, Oktar MA, Akyuz M. Urinary tract infection and bacteriurua in stroke patients: frequencies, pathogen microorganisms, and risk factors. Am J Phys Med Rehabil. 2007;86:734–41.

24. Chen C-M, Hsu H-C, Tsai W-S, Chang C-H, Chen K-H, Hong C-Z. Infections in acute older stroke in patients undergoing rehabilitation. Am J Phys Med Rehabil. 2012;91:211-9.

25. Ovbiagele B, Hills NK, Saver JL, Johnston SC, For the CASPR Investigators. Incidence & Risk Factors of pneumonia and urinary tract infection during stroke hospitalization. J Stroke Cerebrovasc Dis. 2006; 15(5): 209–13.

26. Sellars C, Bowie L, Bagg J, Sweeney MP, Miller H, Tilston J, et al. Risk Factors for Chest Infection in Acute Stroke: A Prospective Cohort Study. Stroke. 2007; 38:2284-91.

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Etiological Pattern of Dementia in Bangladesh

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Abstract:

Background: *Dementia is a chronic & progressive neurodegenerative disorder affecting usually older people of more than 65 years in which there are disturbances of multiple higher cortical functions including memory, thinking, orientation & others. Dementia patients are increasing in number as the population of older age group is increasing. All types of dementia are treatable, at least with psychosocial interventions. So, accurate diagnosis and evaluation of etiological pattern is essential.* ***Methods:*** *This cross sectional study was carried out in the Department of Neurology, Bangabandu Sheikh Mujib Medical University, Dhaka, Bangladesh from January 2012 to December 2012 on 88 patients with dementia diagnosed on the basis of mini mental state examination and DSM-IV criteria.* ***Results:*** *Vascular dementia was the underlying diagnosis in most of the cases (43.3 %) followed by Alzheimers Disease (20.2%) and Parkinson Disease (9%). Other causes were Mixed Dementia, Intracranial Space Occupying Lesion, Post Encephalitic, Hypoxic Encephalitic, Chronic Subdural Haematoma and Tubercular Meningitis.* ***Conclusion:*** *Vascular dementia is more than Alzheimer's Dementia in Bangladesh. Multiple vascular risk factors contribute to this.*

Key words: *Dementia, Alzheimer's disease, elderly people*

Introduction

Dementia is a syndrome due to disease of the brain - usually of a chronic or progressive in nature in which there are disturbances of multiple higher cortical functions, including memory, thinking, orientation, comprehension, calculation, learning capacity, language, and judgment. Consciousness is not clouded[1,2]. The impairments of cognitive function are commonly accompanied, and occasionally preceded, by deterioration in emotional control, social behavior, or motivation[2]. Dementia is typically diagnosed when acquired cognitive impairment has become severe enough to compromise social and/or occupational functioning.[2,3] Mild cognitive impairment (MCI) is a state intermediate between normal cognition and dementia, with essentially preserved functional abilities[1-4].

Dementia mainly affects older people, more than 65 year of age. The prevalence doubles with every five-year increment in age after 65 There is a fourfold variation in prevalence overall, from 2.07% in West Sub-Saharan Africa to 8.50% in Latin America among persons aged >60 years[5,6]. However, most of the estimated age-standardized prevalence figures lie in a band between 5% and 7%[6]. The prevalence is estimated to be 6.38% in South East Asia[6]. Life expectancy is increasing across the world, with population aging increasing the most rapidly in low-income and middle-income countries, where the prevalence of dementia is therefore expected to increase[5].

Dementia occurs in a large number of conditions primarily or secondarily affecting the brain. Alzheimer's disease is the most common form of dementia, irreversible and possibly contributes to 60-70% of cases[2,7] Vascular dementia, either in the form of multi-infarct dementia or post-stroke dementia, is the second most common cause of dementia, accounting for as many as 40% of

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cases[2-4]. Dementia may develop late in Parkinson's disease[4]. Dementia with Lewy bodies, and a group of diseases that contribute to fronto-temporal dementia are important but rare causes. The boundaries between subtypes are indistinct and mixed forms often co-exist[2]. Infections of brain structures, such as meningitis and encephalitis due to tuberculosis or other infections, such as HIV/ AIDS and syphilis, can affect the brain permanently in later stages and can be primary causes of dementia[2-6]. Chronic Subdural Haematoma or other causes of intracranial space occupying lesion may lead to dementia[5]. Sudden, severe hypoxia may also cause brain damage and symptoms of dementia[2.4-7]. Dementia in people with chronic alcoholism is believed to result from other complications such as liver disease and nutritional deficiencies[2.4-7].

Age may be a risk factor in itself or may reflect the effect of increasing time during which other factors can exert their influence. Cardiovascular risk factors are smoking, high blood pressure, diabetes and hyperlipidaemia[8]. All of these are independent risk factors for the development of vascular dementia and predispose to the development of atherosclerosis, which is associated with dementia of all clinical types. These risk factors also predispose to acute stroke, which is well established as a risk factor for the development of dementia[8,9]. Current literature suggests that there is a causal relation between vascular mechanisms and the development of non-genetic AD. Smoking, high blood pressure and diabetes mellitus are all independent risk factors for the development of AD[10-12]. Life expectancy in Bangladesh in 2012 was 69 years for male and 71 years for female. Above 65 years population is 7.6million (4.8% of total population) [13].

Number of population in older age group is increasing. So, patients of neurodegenerative disorder including dementia is increasing. Because all types of dementia are treatable, at least with psychosocial interventions, accurate diagnosis and evaluation of etiological pattern is essential to determine the appropriate treatment and to provide information about prognosis, possible genetic risks, and health care planning to the patient and family. With this intention this study was carried out to explore the etiological pattern of dementia in a tertiary care hospital.

Methods:

This cross sectional study was carried out in the department of Neurology, Bangabandu Sheikh Mujib Medical University, Dhaka, Bangladesh from January 2012 to December 2012. Consecutive 106 patients of any age with history suggestive of dementia from the Neurology outpatient department of BSMMU were initially enrolled.

The history and findings of general and neurological examinations were recorded in a semi-structured data sheet. Neuropsychological assessments were done by mini mental state examination (MMSE)[1,14] and 88 patients with MMSE score 24 or less were diagnosed as dementia. Patients complaining of loss of memory but score obtaining 25 or more were diagnosed as minimal cognitive impairment (MCI) and were excluded from the study. Patients with post-traumatic amnesic state and acute confusional state were also excluded.

Neuro-imaging, either computed tomography (CT) or magnetic resonance imaging (MR1) was done for all patients. Laboratory tests including complete blood count, blood sugar, serum creatinine, serum electrolytes, liver function tests, thyroid function tests and serum vitamin B12 assay were also done for all patients. Venereal diseases research laboratory (VDRL) test was done in selected cases. Alzheimer's disease and vascular dementia (VD) were diagnosed on the basis of DSM-IV criteria[1,15].

Written informed consent was obtained from each patient. The study protocol was approved by the ethical committee and institutional review board (IRB) of BSMMU.

Results:

Among 88 patients diagnosed to have dementia, 57 (65%) were male and 31 (35%) were female. Age range was 32-85 years with mean age of 67.9. Most of the patients (40, 45.5%) belonged to 70-74 years age group followed by 65-69(24, 27.2 %) years age group.

Among the demented patients, 38 (43.2%) were retired from their profession. Housewives (29, 33%)

were also of significant number. Most (35, 33.7 %) were illiterate and only 14(13.5%) completed graduation. (Table-I & Table-II)

Table I

Socio-demographical status of the patients

	n	%
Gender (n=88)		
Male	54	70.2
Female	34	29.8
Education (n=88)		
Illiterate	29	33.7
Primary	33	30.8
Secondary	14	19.2
HigherSecondary	6	2.9
Graduate andAbove	6	13.5
Marital status (n=88)		
Married	73	86.0
Single	1	1.0
Widow	14	13.0
Occupation (n=88)		
Day laborer	5	5.7
Service	9	10.2
Housewife	29	33.0
Business	2	2.3
Retired	38	43.2
Farmer	5	5.7

Table-II

Age distribution of demented patient

Age	Number of patient
30-49	4 (4.54 %)
50-54	4 (4.54 %)
55-59	7 (7.95 %)
60-64	13 (14.77 %)
65-69	14 (15.90 %)
70-74	20(22.72 %)
75 -79	6 (6.81 %)
80-84	13(14.77%)
85 – 89	7 (7.95 %)

In our study 52 patients had history of stroke, 43 patients were hypertensive, 21 patients were diabetic, 8 patients were suffering from ischemic heart disease and 5 patients were suffering from dyslipidaemia. (Table-III)

Table-III

Distribution of patients according to diseases accompanying dementia

Diseases accompanying dementia	Number ofpatients
DM	21
HTN	43
Dyslipidaemia	5
IHD	8
Stroke	52

Vascular dementia was the underlying diagnosis in most of the case i.e. 45 patients(43.3%) followed by Alzheimers Disease(21,20.2%) and Parkinsons Disease (8.7,9%). Other causes were Mixed Dementia (4), Intracranial space occupying lesion(3), Post Encephalitic(1), Hypoxic encephalitic (1), Chronic Subdural Haematoma (1) and Tubercular Meningitis(1). (Table-IV)

Table-IV

Distribution of dementia patients by underlying diseases

Diagnosis	Frequency	Percentage
Alzheimers Disease	21	20.2
Vuscular Dementia	45	43.3
Mixed Dementia	4	3.8
Parkinsons disease	9	8.7
Post Encephalitic	1	1.0
ICSOL	3	2.9
Hypoxic encephalitic	1	1.0
Chronic Subdural Haematoma	1	1.0
Tubercular Meningitis	1	1.0

Discussion:

Male were predominant (65%) in this study. Ratio between male and female was 1.8:1. A similar study carried out in BSMMU by Islam MN et al was also dominated by male (62.4%)[16].Hoffman et al[17] found that the prevalence of dementia was slightly higher in men then in women among subjects under 75 years. On the contrary, Kukull et al reported that sex did not affect dementia, which is not consistent with the present study although the occurrence of non-AD dementia was found significantly less frequent in women than in men[18]. In the present

study, cases were enrolled from Neurology department of BSMMU, both inpatient and outpatient, where most of the patients were male. In Bangladesh, due to socio-cultural practice, female patients are less likely to seek medical help for their illness than male. This may be the reason of the inconsistency of the distribution of sex in this study.

In this study, most of the patients (45.5%) belonged to 70-74 years age group and most were retired from their profession. Dementia mainly affects older people, more than 65 year of age. The prevalence doubles with every five-year increment in age after 65.6 McDowell et al[19] and Nunes B et al[20] showed that prevalence of dementia was increasing steeply with age.

Most of the patients (33.7%) in this study were illiterate and only 13.5% completed graduation. Qiu C et al, 2001 observed in the Kungsholmen Project that, the association between a low level of education (<8 years) and an increased incidence of AD or dementia was present independently of age, sex, baseline cognitive performance, vascular disease, and socioeconomic status[21]. Letenneur L et al also found low educational attainment to be associated with a higher risk of Alzheimer's disease[22]. Kukull WA et al stated that a higher educational level is associated with decreased risk of both AD and non-AD dementia, or, conversely, a lower educational level is associated with an increased risk. Subjects who have more than 15 years of education were at nearly half the risk of subjects with less than 12 years of education.[18] Similar result was reported by Monorey JT et al[8].

The distribution of major categories of dementia was recorded in this study. Vascular dementia was found the highest number (43%), followed by Alzheimer's disease (20%), Parkinson's disease (8.7%), mixed dementia (3.8%). In developed countries, Alzheimer's disease is the main cause of dementia. Alzheimer's Research Trust states that in England, Alzheimer's disease is the most common cause of dementia, accounting for about 60% of all cases, followed by vascular dementia and dementia with Lewy bodies which together account for 15-20% cases[23-25]. Suh et al mentioned that Alzheimer's disease (AD) has become nearly twice as prevalent as vascular dementia (VaD) in Korea, Japan, and China since transition in early 1990s. Prior to this, in the 1980s, VaD was more prevalent than AD in these countries. In Nigeria, the prevalence of dementia was low. Indian studies were contradictory, with both AD and VaD being more prevalent in different studies.

Stroke, HTN, DM, IHD and Dyslipidaemia (52, 43, 21, 8 and 5 patients respectively) were the diseases accompanying dementia in this study. There were frequent overlap e.g. same patient were suffering from stroke, DM and Dyslipidaemia. HTN, DM, IHD and Dyslipidaemia are recognized risk factor of stroke and stroke may lead to vascular dementia which was found to be 43.3% in this study.

Conclusion:

In Bangladesh, Vascular dementia is more than Alzheimer's Dementia. Multiple vascular risk factors contribute to this. Patients should have regular cardiovascular risk factors screening to prevent this dementia.

Limitations of study. Prevalence of dementia could not be known as only demented patients from a tertiary care hospital were included. Community and population-based studies are required to obtain accurate epidemiological data on dementia in Bangladesh. The diagnostic criteria used to diagnose and differentiate dementia subtypes have less than ideal sensitivity and specificity and syndromes overlaps & multiple pathologies could be present. Moreover validation and adaptation of many western neuro-cognitive, behavioral, functional scales and questionnaires are required for diagnosis of dementia in our socio-cultural perspective.

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References:

1. The ICD-10 classification of mental and behavioural disorders. Clinical descriptions

and diagnostic guidelines. Geneva, World Health Organization, 1992.

2. Dekosky ST, KauferDI, Hamilton RL, Wolk DA, Lopez OL. Dementia. In: Bradley WG, daroffRB, Fenichel GM, Jancovic J (eds). Neurology in clinical practice: 5th ed. Philadelphia: Elsevier; 2008. p.1856.
3. Bird ID, Miller BL. Dementia. In :Fauci AS, Kasper DL, Longo DL, Braunwald E, Hauser SL, Jameson JL. Harrisons's principles of internal medicine. 17th ed. Newyork : McGraw-Hill; 2008. p. 2536
4. Hugo J, Ganguli M. Dementia and Cognitive Impairment Epidemiology, Diagnosis and Treatment. Clin Geriatr Med. 2014; 30 : 421-42.
5. Prince M, Prina M, Guerchet M. World Alzheimer report 2013. Journey of caring: An analysis of long term care for dementia. Alzheimer's Disease International. Available at: http://www. alz.co. ukiresearch/world-report-2013.
6. Prince M, Bryce R, Albanese E, Wimo A, Ribeiro W, Ferri CP. The global prevalence of dementia: A systematic review and metaanalysis. Alzheimer's &Dementia. 2013; 9: 63-75
7. Shelley B P, Khabouri J A. The Spectrum of Dementia : Frequency, Causes and Clinical Profile. Dement Geriatr Cogn Disord. 2007; 24:280-287.
8. Monorey JT, Tang MS, BergkindL, Scott M, Merchant C, Bell K, Stern Y, Mayeux R. Low density lipoprotein cholesterol and the risk factor of dementia with stroke. JAMA. 1999; 282(3):254-260.
9. Catriona D, McCullagh, Craig D, Stephen P, Passmore PP. Risk factors of dementia. Advances in Psychiatry Treatment. 2001; 7: 24 — 31.
10. Masellis M, Sherborn K, Neto PR, Sadovnick DA, Hsiung GR, Black SE. Early-onset dementias: diagnostic and etiological Considerations. Alzheimer's Research & Therapy. 2013; 5 (Suppl 1):S7.
11. Makin. SDJ, Turpin S, Dennis MS, Wardlaw JM. Cognitive impairment after lacunar stroke: systematic review and meta-analysis of incidence, prevalence and comparison with other stroke subtypes. J Neurol Neurosurg Psychiatry. 2013; 84: 893-90.
12. De la Tone JC. Is Alzheimer's disease a neuro-degenerative or a vascular disorder? Data, dogma, and dialectics. Lancet Neurol. 2004; 3: 184-190.
13. Health statistics of Bangladesh. World health organization, 2012. Available from: www.who.int/countries/bgdien.
14. Folstein, M., Folstein, S. and McHughs, P. The Mini-mental state: a practical method for grading the cognitive state of patients for the clinician. Journal of Psychiatric Research.1975; 12:189-98.
15. American Psychiatric Association. Diagnostic and statistical manual of mental disorders, 4thed (DSM-IV). Washington DC: American Psychiatric Association, 1994.
16. Islam MN, Khan RK, Rahman MM, Hayee MA, Jahan ME, Bhuiya MM. Etiological pattern of demented patients attending a tertiary care hospital. Mymensingh Med J. 2013 Jul; 22(3):496-503.
17. Hofman A, Rocca WA, Brayne C, BretelerMmb, Clarke M, Cooper B. International Journal of Epidemiology. The Prevalence of Dementia in Europe: A Collaborative Study of 1980— 1990 Findings. 1991;20(3):736-48
18. Kulull WA, Higdon R, Bowen JD, McCormick WC, Teri L, Schellenberg GD. Dementia and Alzheimer disease incidence: a prospective cohort study. Arch Neurology. 200; 59(11):1737-46.
19. McDowell I. Canadian study of health and aging : study methods and prevalence of dementia. CMAJ. 1994;150(6):899-9
20. Nunes B, Silva RD, Cruz VT, Roriz JM, Pais J, Silva M. Prevalence and pattern of cognitive

impairment in rural and urban population from Northern Portugal. BMC Neurology 2010;10:42

21. Qiu C, Backman L, Winblad B, Agitero-Torres H, Fratiglioni L. The influence of education on clinically diagnosed dementia incidence and mortality data from the. Arch Neurol. 2001 Dec;58(12):2034-9.

22. Letenneur L, Gilleron V, Commenges D, Helmer C, Orgogozo JM, Dartigues JF. Are sex and educational level independent predictors of dementia and Alzheimer's disease? Incidence data from the PAQUID project. J NeurolNeurosurg Psychiatry. 1999 Feb;66(2):177-83.

23. Luengo-Fernandez R, Leal J, Gray A. Dementia 2010. Health Economics Research Centre, University of Oxford for the Alzheimer's Research Trust. Available from : www.dementia2010.org

24. Ravaglia G, FortiP, Maioli F, Martelli M, Servadei L, Brunetti N. Incidence and etiology of dementia in a large elderly Italian population. Neurology. 2005:64(9):1525-30

25. Prencipe M, Casini AR, Ferretti C, Lattanzio MT, Fiorelli M, Culasso F. Prevalence of dementia in an elderly rural population: effects of age, sex and education. J Neurol Neurosurg Psychiatry. 1996; 60(6):628-33.

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Adapting Bangla Mini-Mental State Examination (MMSE-B) among Healthy Elderly in Bangladesh

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Abstract

Background: *The aim of our study was to determine whether modified Bangla version (MMSE-B) is as effective as mini mental state examination (MMSE) tool for use in Bangladeshi people.*

Methods: *This descriptive observational study was carried out in Department of Neurology, DMCH from January 2013 to December 2013. A total 200 healthy adults (patient attendants at the clinic) who met the inclusion criteria, were interviewed using a structured questionnaire containing information on age, sex, residence, educational backgrounds and questions set at MMSE English version (MMSE-E) and modified Bangla version for MMSE-B (Figure-1). MMSE and MMSE-B both were applied in 1:1 ration. The literate people were asked whether they are comfortable to answer in English (MMSE-E) or they would like the translated form and we applied the form of MMSE (MMSE-T) according to their wish. But in other group of people the modified Bangla version (MMSE-B) was used irrespective of level of education.*

Result: *The mean age at presentation was 58.1±7.8 and 94% were within 50-70 years of age. Male were more common (80, 66) in both the groups and most of them belonging to rural areas. MMSE-B were mostly employed on people having only primary level of education (up to class five,* n=*80) or no education (*n=*2), whereas MMSE-E were employed up on people having a level of education higher than class five (*n=*96). Every question in each item of cognitive domain correlated well (correlation co-efficient range from 0.801- 0.971) except the 7th (correlation co-efficient 0.418) which had higher mean score for MMSE-B than those of MMSE-E (0.90 versus 0.54). The mean score of MMSE-B was greater than the mean score of MMSE-E for most of questions except the 1st question that is related to orientation of time. The mean of total score in MMSE-E and MMSE-B were 24.04 and 24.91 respectively with a correlation co-efficient of 0.940.* Conclusion: *MMSE-B is adaptable for use in Bangladeshi people irrespective of level of education.*

Introduction:

The global life expectancy of individuals in Bangladesh has significantly increased over the past fifty years and this has led to an increased risk of ageing associated disability in mental and neurological functions. With the increase of elderly population in Bangladesh[1], as in most Western countries, the detailed examination and assessment of cognitive function have become a necessary one. But the exact evaluation of cognitive impairment is often difficult, especially among the elderly. Among the battery of screening tools available, mini mental state examination (MMSE) had been most widely used[2-4]. It has been modified and translated into many languages, including Chinese and Finnish[5], Korean[6] ,

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Japanese[7], Spanish[8], Hindi[9] etc. Though MMSE had been universally used as screening instrument, it has limitations in terms of its sensitivity and confounding biases with regard to education,[10] and culture and language[11,12]. In 1988, Jorm and colleagues[13] published an analysis addressing MMSE bias by level of education among a sample of elderly population using methods outlined in Berk's Handbook of Methods for Detecting Test Bias. So there has been an increasing need for development of a neuropsychiatric tool that effectively identifies the cognitive deficit among Bangladeshi adult population. MMSE have been extensively studied for their reliability, validity and correlation with other psychometric tests. It has a higher interrater reliability[14] and sensitivity and scores correlating well with the degree of cortical atrophy observed on the brain CT scan[15] and also with results of other tests[16,17]. However, there are a number of intrinsic problems which make it difficult to use with people from non western social and cultural backgrounds. The illiterate cannot perform two of the test items (eg 'write a sentence' and 'close your eyes') and in some languages there are no phrases or words such as 'no ifs, ands or buts' and 'WORLD', which makes translation from English difficult. Test performance is also influenced by demographic factors[18,19]. The literacy rate in Bangladesh[1] is only 59.82% (including those who can just write their names). It is therefore often difficult to apply MMSE appropriately in such group of people. Many of them cannot calculate up to 100, do not follow English calendar, can't make sentences or spell the words backward. These limitations led us to develop a modified Bangla version of MMSE for our people.

Materials and Methods:

Study sample:

This is a descriptive type of observational study carried out in weekly neurology outdoor clinic of Department of Neurology, DMCH from January 2013 to December 2013. During this period a total of 200 healthy adults (patient attendants at the clinic) who met the inclusion criteria, were interviewed using a structured questionnaire containing information on age, sex, residence, educational backgrounds and questions set at MMSE-E and modified Bangla questions for MMSE-B (Figure-1). The literate people we asked whether they were comfortable to answer in English or they would like the translated form (MMSE-T) and we applied the form of MMSE according to their wish. But in other group of people the modified Bangla version (MMSE-B) was used irrespective of level of education.

The inclusion criteria:

(1) Both the male and female, above 50 years of age;

(2) Willing to cooperate;

(3) Able to give informed consent;

(4) No evidence of any diagnosed psychiatric disorder (past or present);

(5) No problem suggestive of organic pathology (due to head injury, seizure, mental retardation or substance abuse);

(6) No problems with speech, hearing or vision, which would impede the conduct of examination.

Exclusion criteria

(1) Uncooperative persons;

(2) Diagnosed case of psychiatric disorder or comorbid condition;

(3) Having any significant organic pathology like head injury, seizure, mental retardation, substance abuse, etc., or having physical health problems which affects activities of daily living during past one year;

(4) Having problems with speech, hearing, and vision, which can impede the interview.

The tests were performed by experienced neurologists, from consultants up to the level of professors.

Consent to participate:

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

Ethical approval:

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

Tools:
The MMSE-E and MMSE-B were applied to 200 different healthy adults. For systemic application the MMSE was translated to Bangla from the English version and then retranslated back to English for the check of consistency by atleast three experts. The Bangla Modification of MMSE was done by the "Technical Committee for the Development of MMSE in Bangladesh" and approved by the "Committee for the Development of MMSE in Bangladesh." Lastly the best translated form of MMSE and the modified Bangla MMSE was applied and pre-tested.

Test Modifications: Item by Item description

Orientation to time:
In the English MMSE, a point each is given for correctly named day, date, month, year and season, for a total of five points. But elderly Bangladeshi people usually do not know or keep track of years in the Roman calendar. So keeping the option open for Bengali calendar, we have included seasons like summer, winter and rainy season etc. as an alternative. Thus, the five final items are: day, date, month, year and season.

Orientation to place:
In MMSE-E, five questions are asked, which could include 'name of this place/building', floor (storey), street address, city, county, state and country. It was difficult to identify five appropriate spatial orientation questions for our sample. Buildings in the villages neither have street numbers nor do the streets have names. So we have finally selected 'country', 'district', 'city', 'name of interview place' and 'floor'.

Registration:
In the MMSE-E, the names of three objects are given. We opted for words equivalent in familiarity to 'apple, table, and penny' used in the MoVIES[20,21] project. But tables are not ubiquitous pieces of furniture in the rural setting. So we simplified the words to 'Banana', 'a bird' and 'taka'. In bangle Taka means the currency or the penny.

Attention:
The MMSE-E has two alternative attention subtests: (i) backwards spelling of WORLD and (ii) serial subtractions of seven starting at 100. These two tasks require that the subject be able to keep his attention on a specific problem for a period of time, maintain a set of response and have sufficient working memory to hold and manipulate few pieces of information in mind while solving a multistep problem. As most of our people are illiterate, spelling either forwards or backwards is never an option. We also have changed the mental arithmetic to a deduction of seven from thirty. We gave the subtraction task in the form of a story: A man has 30 cows, if he sells seven of those, how many will remain and if he sells seven in the next month, how many will be there, in the farm and so on.

Recall:
The subject is asked to recall the three objects (banana, bird and taka) named earlier.

Naming:
As in the English version, the subjects are shown a wristwatch and asked to name it. As a second object we used a pen rather than a pencil. Because, the ball-point pens are the more familiar objects than pencil and there was chance of confusion between a pen and pencil.

Repetition:
In English, the standard phrase for repetition is 'No ifs, ands or buts'. This is also a test of fluency. Patients with non-fluent aphasia find repetition particularly difficult as it requires connecting the words with preposition and making appropriate word without grammatical errors. Our technical committee came to a consensus about a Bangla phrase ' ek maghe shit jai na' meaning 'One swallow does not make a summer'.

Visual command (read and follows command):
In the English version, the subject is shown a written command 'Close your eyes' and asked to do as it says. For our mostly illiterate subjects, we have excluded the written part of the test. Here the examiner says 'Look at me and do exactly what I do' and then closes his own eyes for 2 seconds (follow example), while the co-examiner observes and records the subject's response.

Three-step task:
We haven't changed this task at all. As in the English version, the subject is asked to pick up (or take) a given piece of paper with his right hand, fold it in half with both hands and give the paper back to the examiner, with a point being given for each step remembered and correctly executed.

Making a sentence:
This is a task with immense difficulty for most of our subjects. In the English version, the subject is asked to write a complete sentence and is given a full point if the sentence has a subject and a predicate, regardless of spelling, grammar and syntax. We asked them to tell us something about the surroundings. In some cases we had to give some clues.

Copying a figure:
We knew that any task involving paper and pencil would be unfamiliar and intimidating to our population. In the original MMSE, the subject is asked to copy a figure consisting of two intersecting pentagons. A point is awarded only if there are 10 angles and two of them intersect. We thought that the intersecting pentagons will be too difficult for these subjects to copy and therefore substituted with a simpler figure (three circles connecting one another).

Result:

Subject Characteristics:
The demographic characteristics of both groups of study subjects are shown in table-1. There was no significant difference (Chi-Square value= 3.383, *p* value >0.05) in study subjects between these two groups except for the level of education (*p* value <0.05). In subjects older than 50 years, the mean age at presentation was 58.1±7.8 and 94% were within 50-70 years of age. Male were more common (80, 66) in both the groups and most belongs to rural areas (72, 62). The subjects up on whom MMSE were employed had higher level of education than those of MMSE-B. MMSE-B were mostly employed on people having only primary level of education (up to class five, *n*=80) or no education (*n*=2), whereas MMSE were employed up on people having a level of education higher than class five (*n*=96).

Table-I

Demographic profile of the respondents (N=200).

Profile		English (n)	Bangla (n)	*p* value
Age (years)	51-60	64	66	>0.05
	61-70	28	30	
	71-80	6	0	
	>80	2	4	
Sex	Male	80	66	>0.05
	Female	20	34	
Residence	Rural	72	62	>0.05
	Urban	28	38	
Level of education	None	0	2	<0.05
	~ Class 5	4	78	
	Class 5-10	36	16	
	HSC	20	0	
	Honors	24	4	
	Masters	16	0	

Consistency of questions:
The mean score of each question in every item of MMSE and MMSE-B along with their correlation co-efficient are shown in Table-2. Every question in each item of cognitive domain was correlated well (correlation co-efficient range from 0.801-0.971) except the 7th (correlation co-efficient 0.418).

Table-II

Correlation of each question in English and Bangla version of MMSE

Question number	Mean score-English	Mean score-Bangla	Correlation co-efficient
1	4.56	3.98	0.902
2	4.48	4.56	0.939
3	3.00	3.04	0.992
4	3.36	3.60	0.820
5	2.26	2.60	0.889
6	1.76	1.88	0.835
7	0.54	0.90	0.418
8	1.80	1.86	0.881
9	0.52	0.62	0.951
10	0.94	0.99	0.801
11	0.84	0.88	0.971
Total	24.04	24.91	0.940

The mean score for this question was higher among subjects answering MMSE-B than those of MMSE (0.90 versus 0.54). The mean score of

MMSE-B was greater than the mean score of MMSE for most of questions except the 1st question that is related to orientation of time. The mean of total score in MMSE-E and MMSE-B were 24.04 and 24.91 respectively with a correlation co-efficient of 0.940.

Discussion:

It is of immense importance that the MMSE applied should be appropriate in regard to its subjects and items studied in a specified segment of population in relation to their language and socio-cultural background. Henceforth, MMSE had been translated and or modified in different languages. Our endeavor was also to test the applicability of Bangla version of MMSE. Our study result has both qualitative and quantitative implications. Our data suggests that carefully modified Bangla version i.e, MMSE-B is not only effective as MMSE for most of the cognitive domain assessed but also even better in some segments. Irrespective of level of literacy our subjects were also more comfortable with MMSE-B.

In this study, MMSE was adapted into MMSE-B in order to meet two goals: (1) to be consistent with Bangladeshi cultural contexts and (2) feasible for use in illiterate and less educated elderly. The original MMSE[2] contains 12 items with a possible score ranging from 0 to 30. Two items are reading and writing dependent: reading and following command 'Close your eyes' and writing a sentence, both of which are not possible to perform among illiterate or less educated. These two literacy dependant items were replaced by saying something about the surroundings. Also the calculation segment was simplified by serial subtraction of 7 from 30.

In this study subjects answering MMSE-E scored better in the 1st question related to orientation of time. This is probably due to the fact that English calendar much frequently and commonly used by the people in general in Bangladesh than the local Bengali calendar that is relatively more used by the farmers.

All the other questions correlated well with MMSE except the 7th questions which was even better in MMSE-B. This is due to the fact that in the seventh question the English phrase "No Ifs, and, or buts were replaced by familiar Bangla phrase that has helped in understanding and repeating. Irrespective of level of literacy, the questions in MMSE and MMSE-B correlated well individually and also with the mean of total score. Interestingly in this study, subjects scored better in all other questions (except the 1st one) while answering MMSE-B than MMSE. This is consistent with the study of Tiwari et al[22], Ganguli et al[9], Das et al[12]. All these studies were done among Hindi speaking people either in India or abroad. The modification done was also similar to our study and they also modified the questions in relation to local cultural context and adapting to illiterate people either in rural or urban areas. Geographically Bangladesh share common border with India except in the south and also share a similar socio-cultural background with the people of India. So it is not unlikely to get similar results of these study findings. Xu G et al[23] conducted a study in China with Chinese adapted MMSE (CAMSE) up on both literate and illiterate people with dementia and without dementia. They showed that CAMSE was feasible to use in clinical dementia screening. Similarly Jeong SK et al[24] showed that Korean version of MMSE (KmMMSE) was useful and reliable. These results prove the usefulness of developing culturally adaptable version of MMSE in ASIA.

Literatures[25,26] suggest that lower levels of education are associated with higher prevalence of dementia and that lack of education may be a risk factor for Alzheimer's disease. If there is a genuine difference in risk, one would expect to find higher prevalence rates of Alzheimer's diseases in societies with lower educational levels, perhaps in pandemic proportions in subgroups with no education. It is therefore a methodological challenge to develop appropriate cognitive tests for uneducated and illiterate populations. Our endeavor was to simplify the test as far as possible in context of Bangladesh as well as to keep this modified version at least as effective as MMSE for use in screening purpose.

We had several limitations in the study. First of all, the number of subjects is small. Secondly, this is a single centre experience which may not represent

the whole country. However the issue of representativeness is a bit minimized by using Dhaka Medical College Hospital which is the largest tertiary level hospital in the country and receives people from all over the country. Finally, there is chance of inter observer variability in assessing the MMSE.

Conclusion:

MMSE-B correlates well with MMSE-E as per individual question and also in total score. The test results are even better in MMSE-B. So MMSE-B is adaptable for use in Bangladeshi people irrespective of level of literacy.

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Competing interest: None.

Authors Contribution:

SKG was involved in planning the study, setting the methodology, consultation and data collection for this study. ATM HH and MZRK were involved in data analysis, data interpretation and writing the manuscript. The rest were involved in consultation and data collection. All the authors have read and approved the final version of the manuscript.

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References:

1. Rahman NM, Kamal GM, editor. Socio-economic and Demographic Report: Population and Housing Census 2011. Bangladesh Bureau of Statistics 2011. National Series, Vol 4.
2. Folstein, M. F., Folstein, S. E. and McHugh, P. R. 'Mini-mental state': A practical method of grading the cognitive state of patients for the clinician. J Psychiutr. Res 1975; 12: 189-198.
3. Diniz, B. S. O., Yassuda, M. S., Nunes, P. V., Radanovic, M. and Forlennza, O. V. Mini-mental State Examination performance in mild cognitive impairment subtypes. International Psychogeriatrics 2007; 19: 647–656.
4. Nakasujja, N., Musisi, S., Walugembe, J. and Wallace, D. Psychiatric disorders among the elderly on non-psychiatric wards in an African setting. International Psychogeriatrics 2007; 19: 691–704.
5. Salmon, D. P., Riekkinen, P. J., Katzman, R., Zhang, M., Jin, H. and Yu, E. Cross-cultural studies of dementia: a comparison of MMSE performance in Finland and China. Archive Neurology 1989; 46: 769–772.
6. Park, J. H. and Kevon, Y. C. Modification of the MMSE for use in the elderly in a non-Western society. Part I. Development of Korean version of MMSE. International Journal of Geriatric Psychiatry 1990; 5: 381–387.
7. Larson, E. The Ni-Hon-Sea Project: an overview. In J. D. Curb and A. B. Graves (eds.), Multi-national Epidemiological Studies of Dementia (symposium abstract). Gerontologist 1992 ; 32 (Suppl. 2): 219.
8. Loewonstein, D. A., Arguelles, T., Barker, W. W., and Duara, R. A comparative analysis of neuropsychological test performance of Spanish-speaking and English-speaking patients with Alzheimer's disease. Journal of Gerontology 1993; 48: 142–149.
9. Ganguli, M, Ratclif G, Chandra V. A Hindi version of the MMSE: the development of a cognitive screening instrument for a largely illiterate rural elderly population in India. International Journal of Geriatric Psychiatry 1995; 10: 367– 377.
10. Jones, R. N., and Gallo, J. J. Education bias in the Mini-mental State Examination. International Psychogeriatrics 2001; 13: 299–310.
11. Shulman, K. I. et al. IPA survey of brief cognitive screening instruments. International Psychogeriatrics 2006; 18: 281–294.
12. Das, S. K. et al. An urban community-based study of cognitive function among non-demented elderly populations in India. Neurology Asia 2006; 6 (11): 37–48.

13. Berk, R. A. Handbook of Methods for Detecting Test Bias. Baltimore: Johns Hopkins University Press, 1982.

14. Anthony, J. C., LeResche, L., Niaz, U., Von Korff, M. R. and Folstein, M. F. Limits of the 'minimental state' as a screening test for dementia and delirium among hospital patients. Psycho Med.1982; 12: 397- 408.

15. Tsai, L. and Tsuang, M. T. The mini-mental state test and computerized tomography. Am. J. Psychiut. 1979; 136:436-438.

16. Thal, L. J., Grundman, M. and Golden, R. Alzheimer's disease: A correlational analysis of the Blessed information-memory-concentration test and the mini-mental state exam. Neurology 1986; 36: 262- 264.

17. Fillenbaum, G. G., Heyman, A., Wilkinson, W. E. and Hayness, C. S. Comparison of two screening tests in Alzheimer's disease: The correlation and reliability of the mini-mental state examination and the modified Blessed test. Arch. Neurol. 1987; 44: 924-8.

18. Escobar, J. I., Burnam, A, Karno, M., Forsythe, A. Landsverk, J. and Golding, J. M. Use of the mini-mental state examination (MMSE) in a community population of mixed ethnicity: Cultural and linguistic artifacts. J. Nerv. Ment. Dis.1986; 174: 607-614.

19. Fillenbaum, G. G., Hughes, D. C., Heyman, A., George, L. K. and Blazer, D. G. Relationship of health and demographic characteristics to Mini-Mental State Examination score among community residents. Psychol. Med. 1988; 18: 719-726.

20. Ganguli, M., Belle, S., Ratcliff, G., Seaberg, E., Huff, F. J., von der Porten, K. and Kuller, L. H. Sensitivity and specificity for dementia of population based criteria for cognitive impairment: The MOVIES Project. J. Gerontol. Med. Sci.1993; 48 (4): 152-l61.

21. Ganguli, M., Seaberg, E., Belle, S., Fischer, L. and Kuller, L. H. Cognitive impairment and the use of health services in an elderly rural population: The Mo- VIES project. J. Am. Geriatr. Soc 1993;. 41 (l0): 1065-1070.

22. Tiwari SC, Tripathi RK, Kumar A. Applicability of the Mini-mental State Examination (MMSE) and the Hindi Mental State Examination (HMSE) to the urban elderly in India: a pilot study. International Psychogeriatrics (2009), 21:1, 123–128

23. XU G, Meyer GS, Huang Y et al. Adapting Mini-Mental State Examination for dementia screening among illiterate or minimally educated elderly Chinese. Int J Geriatr Psychiatry 2003; 18: 609–616.

24. Jeong SK, Cho KH, Kim JM. The usefulness of the Korean version of modified Mini-Mental State Examination (K-mMMSE) for dementia screening in community dwelling elderly people. BMC Public Health 2004, 4:31.

25. Mortimer, J. A. and Graves, A. B. (1993) Education and socioeconomic determinants of dementia and Alzheimer's disease. Neurology 43, Suppl. 4, S3944.

26. Katzman. R. (1993) Education and the prevalence of dementia and Alzheimer's disease. Neurology 43: 13-20.

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Electrophysiological Grading to Assess the Severity of Carpal Tunnel Syndrome in Symptomatic Diabetic Patients

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Abstract:

Background: *Carpal tunnel syndrome (CTS) is the most frequent compressive focal mononeuropathy found in clinical practice. Patients mostly experience pain, paresthesia, and less commonly, weakness in the median nerve distribution which badly affects dexterity and grip. Common risk factors include repetitive wrist movements, metabolic and degenerative diseases, connective tissue disease and pregnancy. Nerve conduction study is one of the most sensitive and specific tools to diagnose CTS. This study was aimed to grade the CTS cases according to the severity based on electrophysiological findings and explore its association with clinical presentation of diabetic patients had nerve conduction study at BIRDEM General Hospital.* Materials and Methods: *This observational study was done in the electro diagnostic clinic of Neurology department, BIRDEM during the period Sept 2015 to Feb 2016. The study included 100 hands of 84 patients suffering from CTS consecutively attending the clinic. All the patients were interviewed and clinically examined. Demographic data including age, gender, occupation, affected hand and hand dominance along with duration of disease were recorded. Patients were graded according to clinical history and objective findings and again based on the Canterbury NCS Severity Scale.* ***Results:*** *Of these 84 diabetic patients presenting with impression of CTS 96% were females. Mean age of the study subjects was 49.6±10.1 (28-85). Most of the female patients were housewives. Clinical grading of CTS was as follows: mild symptoms in 54.76%, moderate symptoms in 23.8% and severe symptoms in 28.58% patients. According to The Canterbury NCS Severity Scale out of total 100 hands,3.5% had Grade 2 (Mild) 30.5%had Grade 3 (Moderate) ,29.4 % had Grade 4 (Severe), 34.1% had Grade 5 (Very severe) disease. Only 2 patients had Grade 6 (extremely severe) lesion. Of the study subjects 22 (26.19%) had bilateral and rest (73.81%) had unilateral disease.* ***Conclusion:*** *Data demonstrated female preponderance of the diabetic CTS cases of middle age. Proportional graded deterioration of electrophysiological parameters along with the clinical severity grades highlights the fact that NCS provide additional and independent objective evidence in the diagnosis and severity assessment of CTS and plausibly has important role in prioritizing treatment plan.*

Keywords: *Carpal Tunnel Syndrome, Nerve Conduction Studies, Canterbury NCS Severity Scale, Diabetes Mellitus*

Introduction:

Carpal Tunnel Syndrome (CTS) is the entrapment of the median nerve within the carpal tunnel. In the carpal tunnel the median nerve lies immediately beneath the Palmaris Longus tendon and anterior to the flexor tendons[1]. Certain conditions, such as diabetes mellitus, amyloidosis, hypothyroidism, and rheumatoid arthritis, obesity, pregnancy can predispose to CTS. [2]. CTS is the most frequent entrapment neuropathy causing

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numbness, tingling, discomfort, pain and weakness in hands ranging from mild to debilitating extent, especially for those whose work or recreational activities require extensive use of hands[3].

Electro diagnostic (EDx) studies are a valid and reliable means of confirming the clinical diagnosis of CTS . The amplitudes along with the conduction velocities of the sensory nerve action potential and motor nerve action potential reflect the functional state of axons, and are useful parameters and complement the clinical grading in the assessment of severity of CTS[4]. The management of patients diagnosed with CTS is based upon the acuity and severity of clinical symptoms and the degree of neurogenic injury as assessed by electro diagnostic studies and this leads to better management of disease whether by ergonomic modifications, conservative methods or surgical interventions [5,6].

An audit carried out on records and notes of electrophysiological lab of National Institute of Neurosciences and Hospital (NINS) from January to December 2013 showedCarpal tunnel syndrome (CTS) was the most common condition (19.2%) observed at the lab[6].Common risk factors associated with carpal tunnel syndrome in Bangladesh were identified[7].Another randomized controlled trial evaluated the efficacy of local corticosteroid in idiopathic carpal tunnel syndrome among 60 idiopathic CTS patients[8].But assessing the severity of CTS in diabetic patients and grading it on the basis of electro diagnostic studies has not yet been conducted in Bangladesh.

The current study looks at the demographic profile, clinical presentation and the pattern of severity of Carpal Tunnel Syndrome (CTS) in diabetic patients referred for electro diagnostic studies (NCS) at BIRDEM General Hospital, Dhaka.

Methods:

This is a retrospective analytic electrophyisologic study performed in 100 hands of 85 diabetic patients clinically diagnosed with CTS at a referral hospital in Dhaka. Adult patients aged e" 18 years of both sexes were consecutively and purposively selected from between September, 2015 and February , 2016 for a period of Six (6) months. A thorough medical record review was applied and patients with traumatic median nerve injury, poly-neuropathy, history of malignancy, pregnancy, obesity ,hypothyroidism ,rheumatoid arthritis and those who have been previously operated for CTS were excluded. The exclusion criteria also included cervical spine related problem. Demographic data including age, gender, occupation ,affected hand and hand dominance along with duration of disease were recorded. Patients were graded according to clinical history and objective findings and again based on the Canterbury electrophysiological grading scale.

Clinical grading of CTS severity:

•CTS is considered mild if there is numbness, tingling, or discomfort in the median nerve distribution but no sensory loss or weakness, no sleep disruption, and no difficulty with hand function or interference with activities of daily living (ADLs).

•CTS is considered moderate if there is sensory loss in the median distribution, or if nocturnal symptoms occasionally disrupt sleep. Symptoms (sensory loss or pain) may interfere slightly with hand function but the patient should be able to perform all ADLs.

•CTS is considered severe if there is weakness in the median distribution, or if symptoms are disabling and prevent the patient from carrying out one or more ADLs, or if nocturnal symptoms routinely disrupt sleep.

NCS was performed by the neurologist with standard surface stimulation and recording techniques. Motor and sensory studies were performed for the ulnar and median nerves. The Sensory component of each nerve was stimulated antidromically while the motor part was stimulated orthodromically and the F wave was recorded. The action potentials was recorded as sensory nerve action potential (SNAP) and compound muscle action potential (CMAP) for sensory and the motor nerves respectively. The parameters obtained were;onset latency, amplitude of CMAP, duration, area, distance and nerve conduction velocity (CV).If the median nerve sensory NCS results were normal,a comparison test was performed to compare sensory conduction values of the median nerve and ulnar nerve between the wrist and ring finger.

CTS was classified into six grades based on the Canterbury electrophysiologic grading scale. The scale grades neurophysiological severity of CTS from 0 - no abnormality, to 6 - extremely severe CTS.

Electro diagnostic grading of CTS is as follows: normal (grade 0)

very mild (grade 1): CTS demonstrable only with most sensitive tests;

mild (grade 2): sensory nerve conduction velocity slow on finger/wrist measurement, normal terminal motor latency;

moderate (grade 3): sensory potential preserved with motor slowing, distal motor latency to abductor pollicisbrevis (APB) < 6.5 ms;

severe (grade 4): sensory potentials absent but motor response preserved, distal motor latency to APB < 6. 5 ms;

very severe (grade 5): terminal latency to APB > 6.5 ms;

extremely severe (grade 6): sensory and motor potentials effectively unrecordable (surface motor potential from APB < 0.2 mV amplitude).

Approval from hospital ethical committee was taken. Verbal informed consent was taken after explaining the purpose of study and use of data for research and publication. A statistical software (SPSS Inc, version 20) was used for analysis. Frequencies and descriptive statistics were calculated for various variables. Descriptive statistics were used to calculate mean and SD for age. The data are presented as tables and figures.

Results:

This is retrospective analytic study in 100 hands of 84 diabetic patients presented with symptoms and signs of CTS confirmed by NCS. Female preponderance (male 3 vs female 82) was present among the 84 study subjects .

Table-I

Age distribution of study population (N=85)

Age groups	Frequency	Percentage
15-24	1	1.19
25-34	3	3.57
35-44	20	23.8
45-54	37	44
55-64	17	20.2
>65	6	7.14

Table I shows the age distribution of study population.Mean age of our study group was 49.6 ± 10.1 (28-85). Distribution of subjects on the basis of age group showed 57 (67.8%) fell between 35-54 years. Only 6 (7.14%) had age more than 65 and 1 (1.19%) below 35 years.

Table-II

Occupational distribution of study population (N=85)

Occupation	Frequency	Percent
Housewife	58	69
Manual worker /Trader	5	5.9
Teacher	6	7.14
Writer /clerk	4	4.76
Driver	2	2.38
Student	1	1.19
Nurse	7	8.33

Of the total 85 subjects 58 (69%) were housewife. Teacher and nurse constituted 6 (7.14%) and 7 (8.33%) respectively of the subjects of the total . Other patients were white-collar workers having clerical work, computer job, trader and driver. Table II depicts the occupational distribution of study population.

Table-III

Clinical grading of CTS severity of study population (N=85)

Clinical grading of CTS severity	Clinical history and objective findings	Frequency	Percent
Mild	Paresthesia	46	54.56
Moderate	Sensory loss	14	16.66
Severe	Disruption of sleep due to pain	20	28.58
	Thenar muscles atrophy and/or weakness	4	

Table III shows the clinical grading based on associated clinical history and objective finding as per Mackinnson's classification.burden of CTS symptoms of study population. 54.56% patients were categorized as mild CTS with Paresthesia and 16.66 % had moderate CTS with sensory loss

in median nerve distribution clinically. 28.58 % patients experienced symptoms of severe CTS with frequent disruption of sleep due to pain and Thenar muscles atrophy and/or weakness in 4% cases.

The diagnosis of CTS was confirmed and study subjects were graded according to the severity on the basis of The Canterbury NCS electrophysologic grading scale. Grading on the basis of The Canterbury NCS electrophysologic grading scale was shown in Table IV. Eighty-two (96.5%) out of 85 had moderate to severe grade of CTS. But grade 3 ,4and 5 constituted the major bulk of it 80 (94.14%). Of the 3 (3.6%) male 1 (one) each had grade 3, 4 and 5 CTS according to the Canterbury NCS electrophysologic grading scale.

Table-IV

Distribution of different grades of severity of CTS on the basis of The Canterbury NCS electrophysologic grading scale in study population (N=85)

Grade	Number	Percent
Grade 0 (normal)	0	0
Grade 1 (very mild)	0	0
Grade 2 (Mild)	3	3.5
Grade 3 (Moderate)	26	30.5
Grade 4 (Severe)	25	29.4
Grade 5 (Very severe)	29	34.1
Grade 6 (Extremely severe)	2	2.39

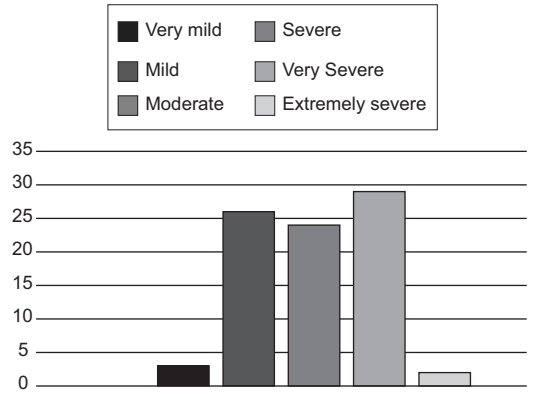

Fig.-1: *Distribution of different grades of severity of carpal tunnel syndrome (CTS) in 100 hands*

Figure1 shows percentages and number of hands placed in different grades of severity according to electro diagnostic criteria. Grade V (Very severe) CTS was the most frequent one (34.1%) followed by Grade 3 (moderate) in 30.5 % of hands.

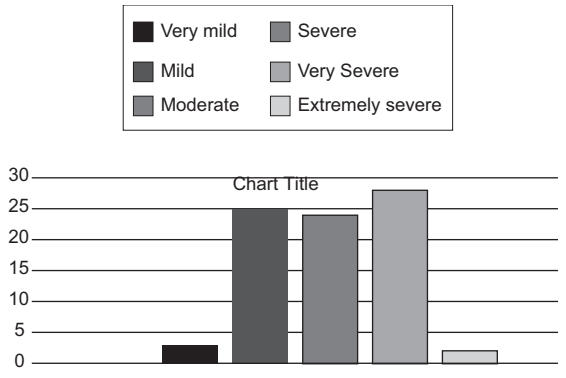

Fig.-2: *Frequency of different grades of severity of CTS in female patients*

Figure2 shows the frequency of different grades of CTS among female population of our study group.

Involvement of hands with CTS of the study subjects was shown in Table 5. In our study population 22 (26.19%) had bilateral disease and rest (73.81%) had unilateral disease. Right hand (dominant) was more frequently involved (n=68) compared to left (n=13) with ratio of 5:1 Twenty two cases showed involvement of both hands. Right and left hand was involved in 65 and 13 cases respectively. Grade 3 damage according to the Canterbury NCS electrophysiological grading scale was present in19, 4 and 7 in right, left and both hands respectively. Grade 4 damage was present in 18, 2 and 5 hand respectively. Grade 5 damage was present in 24, 7 and 8 hand respectively.

Table-V

Distribution of unilateral (right /left) or bilateral disease in 100 hands

Grade	Number of hands	Right hand	Left hand	Both hands
Grade 0 (normal)	0	0		
Grade 1 (very mild)	0	0	0	0
Grade 2 (Mild)	3	3	0	0
Grade 3 (Moderate)	30	19	4	7
Grade 4 (Severe)	25	18	2	5
Grade 5 (Very severe)	38	24	7	8
Grade 6 (Extremely severe)	2	2	0	0
	100	65	13	22

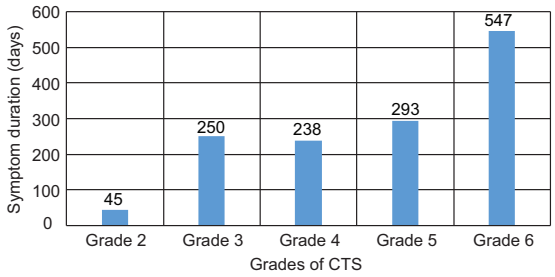

Fig.-3: *Distribution of different grades of CTS in study population (N=84) according to duration of symptoms*

Correlation between duration symptoms of CTS and different grades of CTS according to electrodiagnostic criteria was sought and in this study and is shown in Figure 3 . The mean duration of symptoms was 45 days in case of mild disease, 250 days in case of moderate disease, 238 days in case of severe disease, 293 days in case of very severe and 547 days in case of extremely severe disease.

Discussion:

Carpal tunnel syndrome is a common disorder among adults. Depending on its definition, the estimated prevalence of CTS in the general population is 1 to 5 percent[9]. CTS is more frequent in women (0.7 to 9.2 percent) than in men (0.4 to 2.1 percent) [10]. In a larger study , the female to male ratio for CTS prevalence was approximately 3 to 1[11]. A marked female predominance was observed in this current study group of diabetic patients with CTS . But again these results are based on single centre study, further multi-centered studies in this could suggestthe actual prevalence and female to male ratio.

Mean age of this study group was 49.6 ± 10.1years. The mean age at diagnosis was 46 (range 16–96) years in large case–control study using the UK General Practice Research Database[12]. In the current study it was observed that incidence of carpal tunnel syndrome in diabetic population showed a positive correlation with increasing age of the patient,as71.34% of our patients were above the age of 45.Similar results were observed in other studies [13] .

There is increasing evidence suggesting that several occupational and biomechanical factors are associated with CTS. Occupational factors that have been proposed to cause or aggravate CTS include repetitive hand and wrist use, forceful hand and wrist use, work with vibrating tools, sustained wrist or palm pressure, prolonged wrist extension and flexion and use of hands in cold temperatures. In our study that majority of sufferers were housewives. This result is in favour of some other study results [14]. whereas some studies showed Carpal tunnel syndrome may be present in up to 42% in workers in certain occupations (e.g., poultry processing) and has annual incidence of 193 per 100,000 in all women[15]. Other high –risk occupations are computer professionals[16], assembly line workers, concert pianists and construction workers with vibrating power tools[17].

CTS is a clinical diagnosis that is suspected when the characteristic symptoms of tingling or numbness affects the first 3 fingers and the radial aspect of the 4 th finger and specific provocative tests of the hand such as Phalen's sign and , Tinel's signs are found . Weakened grip and difficulty performing fine motor tasks may occur in more advanced carpal tunnel syndrome. On physical examination, careful observation may reveal sensory loss of median nerve innervated area , mild flattening of the thenar eminence or frank atrophy[18]. The current study population was clinically diagnosed and categorized into 3 grades of severity. Other studies observed correlation of clinical severity with functional disability by The Quick Disabilities of Arm, Shoulder and Hand (QDASH) scale and found a statistically significant positive relationship between QDASH results and clinical severity ($r = 0.43$; $p = 0.0001$) [19].

NCS is one of the most sensitive and specific tools for diagnosing CTS. Optional testing includes needle EMG of C5 toT1 muscles (to exclude cervical radiculopathyas a contributing factor) [20].

Though there are different ways of expressing the severity of carpal tunnel syndrome (CTS) we used the Canterbury NCS Severity Scale for CTS; which are largely independent of the exact normal values used in any given laboratory and demonstrate a highly significant linear relationship between the

neurophysiological grading and a numerical score derived from the clinical history[21].The comparison with symptom score reveals a strong linear relationship and shows that the neurophysiological ranking does correspond to a clinical variable, in agreement with other studies[22].

In the current study dominant hand was frequently involved however frequency of bilateral lesion in electrophysiological studies was 26.19% .In other studies bilateral manifestation is more common than unilateral (60%), but significantly more often begins or is more strongly expressed in the dominant hand[23]. Our results were influenced by impression of the referring physician and not entirely by patients complaints.

The current study showed a trend towards more severe electrophysiologic CTS than in those reported in the literature[24,25]Yazdanpanah P et al[26] in their study conducted on both pregnant and non-pregnant females found that out of sixty-one non-pregnant women who had CTS, 73.6% had mild, 20.8% had moderate and 5.6% had severe CTS. In our observation of 100 hands , 3% had mild ,30% moderate ,25% severe ,38% very severe and 2% had extremely severe CTS as classified electro physiologically. The high frequency of moderate to very severe grade CTS might be due to the fact that we recruited our patients who were referred for electro diagnostic studies for their symptoms, while in Iranian study the study sample was from general population.

A positive correlation between age and severity of nerve conduction abnormality, was noted by many authors [27], and might be contributory factor in our study too. Several mechanisms including mechanical compression and microvascular insufficiency may be suggested to cause severer CTS in diabetic patients[28].

This observational study showed duration of disease influences electrophysiological severity of CTS. A study to find relation of symptom severity and functional status of CTS patients with electrophysiological findings using The Quick Disabilities of the Arm, Shoulder, and Hand (QuickDASH) questionnaire concluded that QDASH results were high in patients whose duration of the disease was >6 years and in patients with severe clinic symptoms. Also, in a correlation analysis, a positive correlation between disease duration and clinical severity with QDASH results. However, no relationship between the electrophysiological level and QDASH results was found[20].

In this current observation nerve conduction studies have been used as a quantitative measure of severity of CTS and can be considerable assistance to anyone attempting to compare different studies on CTS. Our study also has some limitations. The natural history of CTS in Diabetic population is not well defined. Study including more patients with CTS, with baseline and follow-up data on symptoms and neurophysiologic parameters are needed to predict prognostic factors. Multicentre based studies in general population are required to know about the prevalence of disease and health cost burden in Bangladesh.

Conclusion:

Data demonstrated female preponderance of the diabetic CTS cases of middle aged housewives. Proportional graded deterioration of electrophysiological parameters along with the clinical severity grades highlights the fact that NCS provide additional and independent objective evidence in the diagnosis and severity assessment of CTS and plausibly has important role in prioritizing treatment plan. Study also shows that diabetic patients with CTS become symptomatic within short duration of disease ;so early recognition of symptoms and prompt referral for electrophysiological testing is recommended.

References:

1. Alfonso C, Jann S, Massa R, Torreggiani A. Diagnosis treatment andfollow-up of the carpal tunnel syndrome: a review. Neurolog Sci. 2010;31(3): 243–52.
2. Becker J, Nora DB, Gomes I, Stringari FF, Seitensus R, Panosso JS, et al.An evaluation of gender, obesity, age and diabetes mellitus as riskfactors for carpal tunnel syndrome. Clin Neurophysiol 2002; 113 :1429-34.

3. Palmer K. Carpal tunnel syndrome: The role of occupational factors.BestPract Res Clin Rheumatol. 2011; 25(1): 15–29.

4. Srikanteswara PK, Cheluvaiah JD, Agadi JB, Nagaraj K. The Relationship between Nerve Conduction Study and Clinical Grading of Carpal Tunnel Syndrome.J Clin Diagn Res. 2016 Jul;10(7):OC13-8.

5. Jarvik JG, Comstock BA, Kliot M, Turner JA, Chan L, Heagerty PJetal. Surgery versus non-surgical therapy for carpal tunnel syndrome: a randomised parallel-group trial. Lancet 2009;374(9695):1074

6. Huisstede BM, Fride´n J, Coert JH, et al. Carpaltunnel syndrome: hand surgeons, hand therapists, and physical medicine andrehabilitation physicians agree on amultidisciplinary treatment guideline Vresultsfrom the European HANDGUIDE Study. ArchPhys Med Rehab 2014;95(12): 2253Y2263.

7. Chowdhury RN , Hussain ME, Islam MN, Hosen M, Khan AFMA M, MdFerdousMian.An audit of patients referred for nerve conduction study in a tertiary care hospital in Bangladesh.J Dhaka Med Coll. 2014; 23(1): 102-108.

8. Islam MN, Chowdhury MSJH,Chowdhury MTI,Chowdhury AH, Islam M, Hossain E etal .Identification of common risk factors associated with Carpal tunnel Syndrome. Bangladesh J Neuroscience 2013;Vol 29(2):70-78

9. *AhmedA, IslamM R, RahmanHZ, BhuiyanMM.* Efficacy of Local Corticosteroid in Idiopathic Carpal Tunnel Syndrome: A Randomized Controlled Trial. Bangladesh J Neuroscience 2012; Vol. 28 (1): 10-15

10. Atorshi I, Gummenson C, Johnsson R, Ornstein E, Ranstam J, Rosen I etal. Prevalence of carpal tunnel syndrome in a general population.JAMA 1999; 282(2): 153–8.

11. Stevens JC, Witt JC, Smith BE, Weaver AL. The frequency of carpal tunnel syndrome in computer users at a medical facility. Neurology 2001; 56:1568.

12. Latinovic R, Gulliford MC, Hughes RA. Incidence of common compressive neuropathies in primary care. J N e u r o l N e u r o s u r g Psychiatry. 2006;77(2):263–265.

13. Claire BurtonLinda S Chesterton ,Graham Davenport .Diagnosing and managing carpal tunnel syndrome in primary careBr J Gen Pract. 2014 May; 64(622): 262–263.

14. Kouyoumdjian JA, Zanetta DM, Morita MP. Evaluation of age, body mass index, and wrist index as risk factors for carpal tunnel syndrome severity. Muscle Nerve 2002; 25:93.

15. Nehete SR, Raut BB, Hiremath AS, Thatte RM. A study the various clinical and electrophysiological parameters of severity of carpal tunnel syndrome, their correlation with post-operative recovery. Indian J Plast Surg. 2017 Sep-Dec;50(3):260-265.

16. Musolin K, Ramsey JG, Wassell JT, Hard DL. Prevalence of carpal tunnel syndrome among employees at a poultry processing plant. ApplErgon 2014; 45(6):1377Y1383.

17. Ali KM, Sathiyasekaran BWC. Computer professionals and carpal tunnel syndrome (CTS). Int J OccupSafErgon 2006; 12: 319–25.

18. Kozak A, Schedlbauer G, Wirth T, et al. Association between work-related biomechanical risk factors and the occurrence of carpal tunnel syndrome: an overview of systematic reviews and a meta-analysis of current research. BMC Musculoskelet Disord 2015; 16:231.

19. Kaplan SJ, Glickel SZ, Eaton RG .Predictive factors in the non-surgical treatment of carpal tunnel syndrome.J Hand Surg Br. 1990;15(1):106

20. Yasemin E, Ne_e G Y, , Selim S C. The relationship between QDASH scale and

clinical, electrophysiological findings in carpal tunnel syndrome . Advances in Clinical and Experimental Medicine 2018;27(1):71–75

21. American Association of Electro diagnostic Medicine, American Academy of Neurolog and American Academy of Physical Medicineand Rehabilitation. Practice parameter Forelectrodiagnostic studies in carpal tunnelsyndrome: summary statement. MuscleNerve 2002;25(6):918Y922.
22. You H, Simmons Z, Freivalds A, Kothari MJ, Naidu SH. Relationshipsbetween clinical symptom severity scales and nerve conduction measures in carpal tunnel syndrome. Muscle Nerve 1999;22:497–501.
23. Dec P, Zyluk A .Bilateral carpal tunnel syndrome - A review. NeurolNeurochir Pol. 2018 Jan - Feb;52(1):79-83.
24. Ali Z, Khan A, Shah SM, Zafar A . Clinical and electro-diagnostic quantification of the severity of carpal tunnel syndrome. Ann Pak Inst Med2012Sci 8: 207-212.
25. Padua L, LoMonaco M, Gregori B, Valente EM, Padua R, et al). Neurophysiological classification and sensitivity in 500 carpal tunnel syndrome hands. Acta Neurol Scand 1997; 96: 211-217.
26. Yazdanpanah P, Aramesh S, Mousavizadeh A, Ghaffari P, KhosraviZ, KhademiA et al. Prevalence and severity of carpal tunnel syndromein women. Iran J Public Health. 2012; 41: 105–110.
27. Kouyoumdjian JA. Carpal tunnel syndrome. Age, nerve conductionseverity and duration of symptomatology. ArqNeuropsiquiatr 1999;57:382–386.
28. Yoo Hwan Kim,Kyung-Sook Yang, Hanjun Kim, Hung YoulSeok, Jung Hun Lee, Myeong Hun Son et al. Does Diabetes Mellitus Influence Carpal Tunnel Syndrome?J Clin Neurol. 2017 Jul; 13(3): 243–249.

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CASE REPORT

A Rare Case Report on Distal Spinal Muscular Atrophy (SMA)

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Abstract:

Spinal muscular atrophies (SMA) are heterogeneous group of motor system disorders of alpha motor neuron clinically characterized by progressive lower motor neuron features. The distal form of SMA is an extremely rare disorder, which usually presents in the young adults and has a relatively slow progression with almost normal life-span. Differential diagnosis of this syndrome includes hereditary motor sensory neuropathy-Charcot-Marie-Tooth disease (CMT) and distal myopathies, which should be excluded before confirming this rare entity. As distal form of SMA is a very extremely rare condition so we would like to present a young male with this disorder and a short discussion of the theoretical aspects.

Key words: *Spinal muscular atrophies (SMA), Distal, Peroneo-muscular Atrophy, and Hereditary.*

Introduction:

Spinal muscular atrophy (SMA) is a relatively less frequent group of degenerative anterior horn cell disorder clinically characterized by proximal muscle weakness, muscle wasting, muscle twitching and areflexia in varying combinations. Almost all cases are genetically determined, with most being autosomal recessive due to homozygous deletions or mutation of the survival motor neuron (SMN) gene on chromosome[5]. Traditionally, SMA is classified as one of the four types based on the age at onset: SMA type 1 (infantile SMA or Werdnig-Hoffmann syndrome), SMA type 2 (intermediate SMA), SMA type

3 (juvenile SMA or Kugelberg-Welander disease), and SMA type 4 (adult-onset SMA, pseudomyopathic SMA. SMA type 1 begins within the first few months of life; children with this disease are never able to sit without support. Symptoms include severe hypotonia, limb weakness is severe, generalized, and worse proximally, a weak cry, and respiratory distress. Death from respiratory failure, pneumonia, and malnutrition usually occurs before age 2 years. The signs and symptoms of SMA type 2 usually begin between the ages of 6 and 18 months. Delayed motor milestones are often the first clue to neurological impairment, with more prominent leg weakness then arm weakness. The onset of the juvenile form of SMA is usually between 5 and 15 years presenting with slowly progressive limb-girdle weakness difficulty in walking. Adult onset SMA type 4 presents with slowly progressive limb-girdle weakness leading to difficulty in walking, climbing stairs, and rising from a chair or the floor. Fasciculations are an important finding. A new class of adult-onset SMA has recently emerged and is sometimes referred to as *SMA-5* distinguished by a distal rather than proximal pattern of slowly progressive muscular atrophy.[1]

The distal form of SMA is an extremely rare form of this entity, which presents in the young adults with predominantly distal muscle involvement in the lower limbs, which progressively involve the distal upper limbs and very slowly progressive and having almost a normal life-span.[2,3] It is inherited as both autosomal dominant and autosomal recessive form of inheritance.[3,4] Other neuromuscular disorders presenting with peroneal muscular atrophy like hereditary motor sensory neuropathy (CMT 2) and

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distal myopathies need to be excluded before this rare entity is confirmed which can be done by physical examination, investigating muscle enzyme(S. CPK, Aldolase), NCS & EMG, CSF study, Muscle biopsy & genetic study.Physiotherapy, rehabilitation and education to the patient and parents, genetic counseling are helpful in managing these patients and preventing this disorder.

Case Report:

A 22 years male, a right-handed, first year Honors student, visited us in the outpatient department, department of neurology, Bangabandhu Sheikh Mujib Medical University, presented with insidious onset progressive weakness of all limbs with distal wasting for two years. He states that he was alright two years ago when he developed progressive distal weakness with wasting of his legs and difficulty in walking and running. Over the last six months, the weakness in his lower limbs progressed to involve the proximal lower limbs and he noted similar weakness and wasting of hand muscles. He has also history of occasional muscle cramp in leg muscles. He denied any muscle twitching in his arms and legs. He has no stiffness of limbs, muscle pain, tingling or numbness sensations, difficulty in swallowing, neck or back pain. There was no bowel or bladder dysfunction. There was no history of parental consanguinity. He has normal developmental milestones. There was no similar case in the family. On general examination, he had pes cavus deformity, normal vital parameters, no high arched palate. Neurological assessment revealed normal higher mental function, speech and cranial nerves. There was wasting of the intrinsic muscles of hands and feet with bilateral foot drop, also wasting of distal forearm and legs with relatively preserved proximal muscle groups, no fasciculation observed. There was distal hypotonia, muscle power proximally grade-4/5 and distally grade-2/5, areflexia, bilateral non responsive plantar reflexes and a high stepping gait. There was no sign of cerebellar, sensory or autonomic dysfunction. There was no abnormal spinal curvature or thickened nerves. Investigations revealed a normal hematological and biochemical profile. Muscle enzymes levels, serum creatinine phosphokinase (159 IU/L). Nerve conduction studies on the sensory and motor nerves of upper and lower limbs were within normal limits. Electromyography studies revealed features of chronic denervation with reinervation in form of increased insertional and spontaneous activity and long duration, high amplitude, polyphasic MUAP) Fig. 1,2,3,4.CMT was excluded by having no sensory complaint or findings, no nerve thickening & normal NCS findings. Distal myopathy was

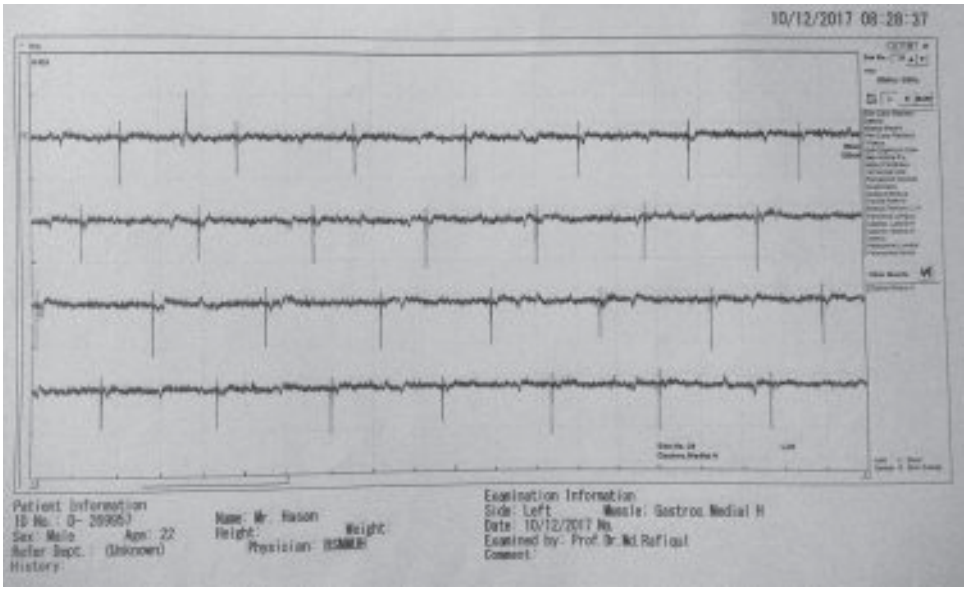

Fig.-1:

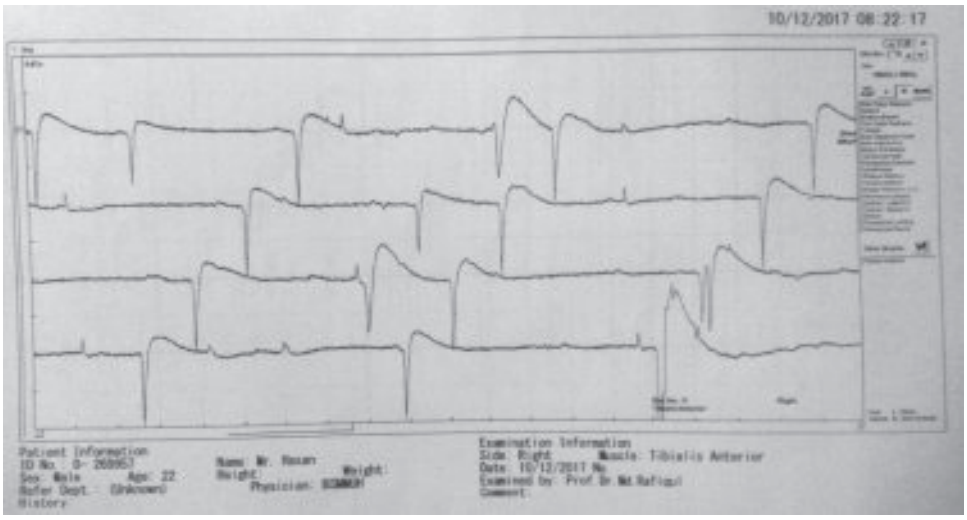

Fig.-2:

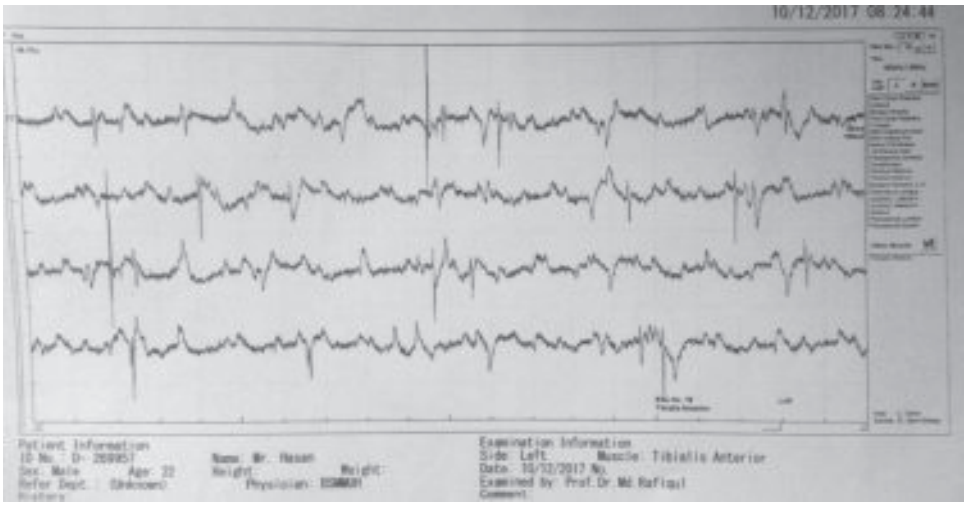

Fig.-3:

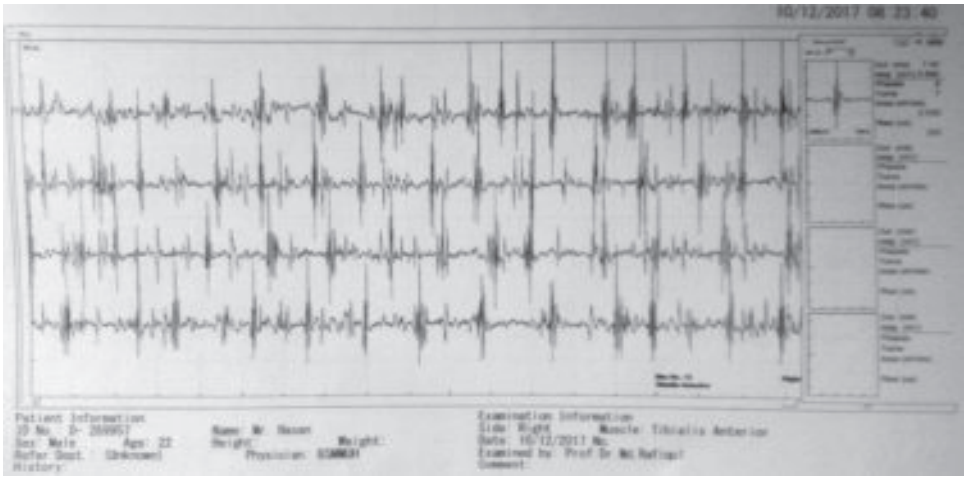

Fig.-4:

excluded by normal muscle enzyme & neuropathic EMG findings. But muscle biopsy, genetic study not done. Parents and siblings were not available for neurological assessment.

Fig 1, 2, 3 showing features of chronic denervation: (1) Fibrillation potential (2) Positive sharp wave (3) Fibrillation, positive sharp wave & fasciculation

Figure: 4 showing features of chronic active reinervation; polyphasic, high amplitude, long duration

MUAP with reduced recruitment.Discussion:
Motor system disease is a group of disorders characterized by progressive degeneration of motor neurons in the spinal cord, brainstem and motor cortex. Patient usually presents with various combinations of upper and lower motor neuron features. Progressive spinal muscular atrophy is a group of degenerative neuromuscular disorder characterized by lower motor neuron involvement features with varying combinations of weakness, muscle wasting, areflexia and muscle twitching which gradually involves the proximal muscles of the lower limbs, upper limbs, later distal part of limbs and variable neck, trunk and respiratory muscle involvement. A form of progressive spinal muscular atrophy with predominantly distal involvement (Distal SMA) is a rare subgroup of this disorder 2, 3 Distal SMA is an inherited form of SMA with autosomal recessive or dominant form of inheritance (Table 1).

Autosomal recessive form distal SMA is the more common form and occurs with a greater frequency in products of consanguineous marriages but parental consanguinity and similar illness in other siblings was not found in our patients .4, 5. It manifests as a very gradually progressive distal muscular weakness with slow clinical progression and having an almost normal life-span. Lower limbs are preferentially involved and below-knee atrophy with foot drop is commonly seen, as in our patient. Hands and proximal limbs are involved much later and to a lesser degree which was also found in our patient. However there is a type of distal SMA where upper limb predominance is seen (Type V).6 Carriers of the disease may be clinically normal though subtle EMG abnormalities may be the evident. The importantdifferential diagnosis of this peroneal muscular atrophy syndrome is peripheral neuropathies like HMSN (Charcot-Marie-Tooth II), where there is axonal type of involvement with almost normal conduction velocities. Chronic inflammatory demyelinating polyneuropathy (CIDP) and distal myopathies should be considered in the differential diagnosis.5 Differentiation from CMT is possible as there is always some degree of clinical or electrophysiological sensory nerve involvement in CMT. Distal myopathies can be differentiated by presence of high CPK and LDH levels and EMG findigns of myopathy. Muscle biopsy is conclusive evidence of the nature of muscular involvement. In neurogenic disorders, there is evidence of "group atrophy" with intervening muscle fibres normal or at times hypertrophic. In extreme forms of neurogenic atrophy, the muscle fibres may be

Table-I

World Federation of Neurology Classification of Hereditary Motor Neuropathies (Distal Spinal Muscular atrophy) 5

Type	Inheritance	Age of onset	Gene	Age of unableto walk	Life expectancy
Type I (Juvenileonset)	AD	2-20 yr	Unknown	Rare	Normal
Type I I(Adultonset)	AD	20-40 yr	*HSP22*,*HSP27*	Rare	Normal
Type III (Mildjuvenile)	AR	2-10 yr	Unknown	Rare	Normal
Type IV (Severejuvenile)	AR	4m-20yr	Unknown	30yr	?
Type V (Upperlimb predominant)	AD/ sporadic	5-20yr	*GARS*,*BSCL2*	Never	Normal
Type VI (Severeinfantile)	AR	infancy	*IGHMBP2*	Unable to walk	<1 yr
Type VII (Withvocal cord palsy)	AD	10-20yr	Unknown	Rare	Normal

replaced by fibrocollagenous tissue. The distal form of SMA has a relatively better prognosis compared to other forms of this disorder. Though the initial progression is rapid, the disease stabilizes in the later stages with patients remaining ambulant and having a normal life span. Since genetic inheritance is well known, genetic counseling of the carriers helps in preventing the disease. There is no definitive therapeutic modality available. Management of this disorder involves active multi-disciplinary approach with neurologist, occupational and physical therapist and rehabilitation experts. Respiratory support and care of the bed-ridden is seldom required in the natural course of distal SMA. Patient education about the natural course of the disease and its prognosis is important to involve the patient in the management process. Recent advances in gene therapy can pave way for a possible genetic treatment for this untreatable entity.

In conclusion, distal SMA is an extremely rare form of motor system disease. Other common causes of similar presentation of peroneo-muscular syndrome can be excluded by clinical, electrophysiological, and biochemical methods. Prognosis of this entity is relatively better than other forms of SMA. Patient education with multi-disciplinary approach to rehabilitate these patients is pertinent in managing these patients.

References:

1. Russman B S, Spinal Muscular Atrophy: Clinical Classification and Disease Heterogeneity. Journal of child Neurology, 2007, 946-951.
2. Harding AE, Thomas PK. Hereditary distal spinal muscular atrophy. A report of 14 cases and a review of literature. J Neurol Sci 1980; 45:337-48.
3. Pearn J, Hudgson P. Distal spinal muscular atrophy. A clinical and genetic study of 8 kindreds. J Neurol

Sci 1979;43:183-91.

4. Viollet L, et al. Mappjng of autosoma recessive chronic distal spinal muscular atrophy to chromosome 11q13. Ann Neurol 2002;51:585-92.
5. Boylan KB, Cornblath DR. Werdnig-Hoffmann disease and chronic distal spinal muscular atrophy with apparent autosomal dominant inheritance. Ann Neurol 1992; 32:404-7.
6. Dyck T, Thomas PK. Peripheral Neuropathies. III Ed WB Saunders. 1990:1058-59.