VOL. 33 NO. 1 ISSN 1023-4853 January 2017

BANGLADESH JOURNAL OF NEUROSCIENCE

CONTENTS

OFFICIAL ORGAN OF BANGLADESH SOCIETY OF NEUROSCIENCES

Bangladesh Journal of Neuroscience

INSTRUCTIONS FOR AUTHORS

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

Manuscript Submission

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

Permissions

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

Title Page

The title page should include:

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

Abstract

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

Keywords

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

Acknowledgments

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

Manuscript Submission

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

Permissions

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

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

Reference list

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

The entries in the list should be numbered consecutively.

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

Ethical approval:

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

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

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

Informed consent:

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

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

Bangladesh Journal of Neuroscience 2017; Vol. 33 (1): 1-5

ORIGINAL ARTICLES

Association between Age and New Onset Ischemic Stroke in Diabetic Patients

SINA H[1], ISLAM MR[2], HABIB M[3], GHOSE SK[4], AHMED KGU[5], CHOWDHURY AH[6], SAHA K[7], ARIFUZZAMAN M[8], ALAM I[9], MUSTARY T[10], DHALI SA[11]

Abstract

Background: *Ischemic stroke is the end result of occlusion of a blood vessel supplying the brain by a thrombus originating somewhere outside the brain or as a result of a thrombotic stenosis of a cerebral blood vessel itself. Older people have higher prevalence of ischemic stroke.* ***Objective:*** *To evaluate the association between higher age and new onset ischemic stroke in patient with diabetes mellitus.* ***Method:*** *This cross sectional study was conducted in the Department of Neurology, BSMMU, Dhaka from February 2013 to September 2014 on 50 DM patients with first attack of ischemic stroke. mRS was measured on 14th day of the stroke.* ***Result:*** *Majority of the patients (40.0%) were in age group 51-60 years. The mean age was 58.9 ± 9.6 years with a range from 30 to 75 years. Males were 52.0% and females were 48.0%. Male to female ratio was 1.08:1. It was observed that more than one third (36.0%) patients were current smoker, 9(18.0%) were ex-smoker and 23(46.0%) were non smoker. Majority of the patients, 29(58.0%), had hypertension. Mean systolic BP was found 129 ±16 mmHg with a range from 90 to 160 mmHg. The mean diastolic BP was found 81±11 mmHg with a range from 60 to 100 mmHg. Age has significant positive correlation with modified ranking scale on 14th day of stroke [r= 0.322 (p=0.023)].* ***Conclusion:*** *As per study result, it can be concluded that increasing age is associated with higher level of mRS.*

Keywords: *Ischemic stroke, diabetes mellitus, mRS, age.*

Introduction:

Ischemic stroke is characterized by the sudden loss of blood circulation to an area of the brain, resulting in a corresponding loss of neurologic function. Acute ischemic stroke is caused by thrombotic or embolic occlusion of a cerebral artery and is more common than hemorrhagic stroke.

Stroke is the third leading cause of death worldwide and the leading cause of acquired disability in adults in most regions. WHO estimated that there were over 2.1 million people who died of stroke in 1990 alone. In Asia, burden of stroke is likely to increase substantially in the near future because of the aging population[1]. In Bangladesh, stroke is the third leading cause of death[2]. Bangladesh is ranked 84 in the world in mortality rate due to stroke by the World Health Organization. The prevalence of stroke in Bangladesh is 0.3%. The high number of disability-adjusted life-years lost due to stroke (485 per 10,000 people) show that stroke severely impacts Bangladesh's economy[2].

1. Dr. Hashmi Sina, Assistant Professor, Neurology, Dhaka Medical College.
2. Prof. Md. Rafiqul Islam, Professor, Neurology, Bangabandhu Sheikh Mujib Medical University.
3. Prof. Mansur Habib, Professor & Head, Neurology, Dhaka Medical College.
4. Dr. Swapon Kumar Ghose, Associate Professor, Neurology, Dhaka Medical College.
5. Dr. Kazi Gias Uddin Ahmed, Associate Professor, Neurology, Dhaka Medical College.
6. Dr. Ahmed Hossain Chowdhury, Associate Professor, Neurology, Dhaka Medical College.
7. Dr. Kanol Saha , Associate Professor, Neurology, Dhaka Medical College.
8. Dr. Mohammad Arifuzzaman, Assistant Professor, Neurology, Dhaka Medical College.
9. Dr. Iftikher Alam, Junior Consultant, Neurology. Dhaka Medical College.
10. Dr. Tamanna Mustary, Thesis Part Student, Dermatology and Venereal Diseases, Dhaka Medical College.
11. Dr. Sabbir Ahmed Dhali, Registrar, Neurology, Dhaka Medical College.

Though the incidence and prevalence of stroke increase sharply with age it can affect at any age[3] Studies done in both western countries and Asia disclose a higher incidence of ischemic stroke in men than in women under 80, however, most elderly patients with stroke (aged >80 years) are women[4,5]. In addition, disparities exist in risk factors, clinical presentation, and outcomes of stroke among patients with different ages and genders[6-9].

Most ischemic stroke patients have multiple vascular risk factors. There are quite a few studies from developed countries concerning the age effect on the profile of vascular risk factors in ischemic stroke patients and the results are inconsistent[4,9-11]. Such studies are scarce in Bangladeshi population and whether the distribution pattern is different from that of developed countries remains to be elucidated. Thereby, we investigated the age specific prevalence of vascular risk factors in patients with first-ever ischemic stroke in Bangladesh.

Method:

This cross sectional study was conducted in the Department of Neurology, BSMMU, Dhaka, from February 2013 to September 2014. Fifty patients with first attack of ischemic stroke with DM were included in this study. Patient's mRS was done on the 14th day of stroke. During this period other relevant investigations were done and recorded. Correlation between age and mRS was confirmed using Pearson Correlation Test. Statistical software SPSS 12.0 was used for analysis. A p value of <0.05 was taken as level of significance.

Results:

It was observed that the mean age of the patients was 58.9 ± 9.6 years with a range from 30 to 75 years and majority of the patients (40.0%) were in age group 51-60 years in this study. Twenty six (52.0%) patients were male and 24(48.0%) were female. Male to female ratio was 1.08:1. It was also observed that more than one third (36.0%) of the patients were current smoker, 9(18.0%) were former smoker and 23(46.0%) were non smoker. More than half of the patients had hypertension. It was observed that mean systolic BP was found 129 ± 16 mmHg with a range from 90 to 160 mmHg and the mean diastolic BP was 81±11 mmHg with a range from 60 to 100 mmHg.

Significant positive correlation was found between age and modified ranking scale on 14th day of stroke [r= 0.504 (p<0.001)].

Age significantly positively correlated with mRS. The estimated odds ratio suggests that there is 1.11 times greater likelihood of facing severe disability for 1 year increase in age.

Table-I

Demographic and clinical profile of the study subjects (n=50)

	Frequency	Percentage
Age (years)		
≤40	4	8.0
41-50	5	10.0
51-60	20	40.0
61-70	19	38.0
>70	2	4.0
Mean ±SD	58.9 ± 9.6	
Range (min-max)	(30-75)	
Gender		
Male	26	52.0
Female	24	48.0
Smoking habit		
Current	18	36.0
Former	9	18.0
Non smoker	23	46.0
Hypertension	29	58.0
Systolic BP (mmHg) [Mean ±SD]	129 ± 16	
Diastolic BP (mmHg) [Mean ±SD]	81 ± 11	

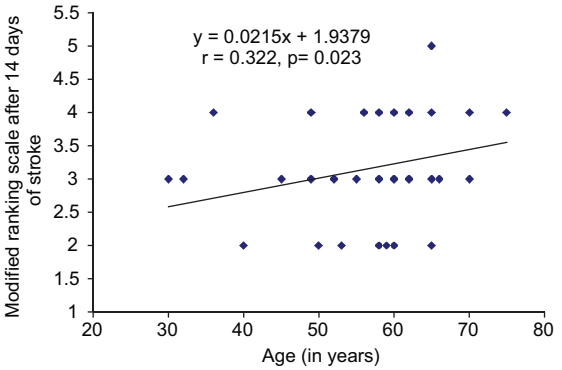


Fig.-1: *The scatter diagram shows significant positive relationship [r= 0.322 (p=0.023)] between age with modified ranking scale on 14th day of stroke.*

Table-II

Multivariate logistical regression analysis of modified ranking Scale for Stroke Severity (mRS) and the outcome variables

Independent variables	p value	OR	95% CI for OR	
			Lower	Upper
Age	0.020*	1.112	1.017	1.216
Sex	0.056	0.070	0.005	1.071
Smoking	0.115	0.254	0.046	1.399
Hypertension	0.192	0.373	0.085	1.641
HBA1c	0.014*	2.332	1.186	4.584

Discussion:

In this study 78.0% of the patients were in 6th and 7th decade and the mean age was 58.96±9.58 years with range from 30 to 75 years. Similar findings also found in the study of Shuangxi et al.[12], Basu et al.[13] and Doi et al.[14] where mean age was 60.5±8.65 years, 60.0 ±13 years and 58.0±10.0 years respectively. On the other hand, higher age was observed in the studies of Rathore et al.[15], Kamouchi et al.[16] and Sare et al.[17] where mean age was 64.8±9.4 years, 69.0±12.0 years and 68.9±12.1 years respectively. The higher mean age may be due to increased life expectancy, geographical variations, racial and ethnic differences may have significant impacts.

In this study it was observed that 52.0% patients were male and 48.0% female and male to female ratio was 1.08:1, which is closely resembled with Shuangxi et al.[12], Kamouchi et al.[16], Rathore et al.[15], Sare et al.[17], Basu et al.[13] and Yao et al.[18] series.

In the present study it was observed that more than one third (36.0%) of the patients were current smoker, 18.0% were former smoker and 46.0% were non smoker. Similar findings also seen in the studies of Shuangxi et al.[12], Kamouchi et al.[16] and Doi et al.[14] where current smoker was 38.9%, 46.0% and 50.1% respectively.

In this current study it was observed that 58.0% patients had hypertension. Similarly, 55.6% and 43.3% patients were found hypertensive in the studies of Shuangxi et al.[12] and Doi et al.[14] respectively. Hypertensive patient was 70.9%[16], 73.2%[10] and 74.0%[13].in some others studies which were higher than the current study.

Mean systolic BP was 129.25±15.98 mmHg and mean diastolic BP was 81±10.77 mmHg in our study. Doi et al.[14] found mean systolic blood pressure 134.0±20.0 mmHg and mean diastolic blood pressure 81.0±11 mmHg, which were similar to the current study. Kamouchi et al.[16] revealed mean systolic blood pressure 161.0±30.0 mmHg and mean diastolic blood pressure 88.0±18.0 mmHg which were higher than the current study. Similarly higher systolic and diastolic blood pressure was also revealed by Rathore et al.[15] and Sare et al.[17].

A significant positive correlation was observed between age and modified ranking scale on 14th day of stroke [r = +0.322; p=0.023]. The incidence and prevalence of stroke increase sharply with age[3]. Older patients had higher prevalence of classic vascular risk factors such as ischemic heart diseases, chronic heart failure, and atrial fibrillation[18]. The Framingham and other studies showed that advanced age in acute stroke was independently associated with high mortality (Kelly-Hayes et al. 1988) [19]. Advanced age with diabetes mellitus was also an independent predictor of 30-day mortality (Kasper et al. 2005) [20].

Conclusion:

Patients having new onset ischemic stroke with DM were predominant in above 5th decade and more common in male subjects. Finally it can be concluded that increased age is associated with higher mRS, so more stroke severity.

Acknowledgement: Mohammad Zahid Hasan, Office Assistant, Neurology, Dhaka Medical College Hospital

References:

01. Langhorne P. 'Stroke disease' In: Walker B, Colledge N, Ralton S, Penman I. 22nd ed. 2014. Davidson's Principles and Practice of Medicine, Elsevier, London.
02. Islam MN, Moniruzzaman M, Khalil MI, Basri R, Alam MK, Loo KW, Gan SH. Burden of stroke in Bangladesh. International journal of stroke. 2013 Apr; 8(3):211-13.
03. Marini C, Triggiani L, Cimini N, Ciancarelli I, De Santis F, Russo T, et al. Proportion of older people in the community as a predictor of increasing stroke incidence. Neuroepidemiology. 2001; 20(2):91-5.
04. Rojas JI, Zurrú MC, Romano M, Patrucco L, Cristiano E. Acute ischemic stroke and transient ischemic attack in the very old–risk factor profile and stroke subtype between patients older than 80 years and patients aged less than 80 years. European Journal of Neurology. 2007;14(8):895-99.
05. Wang D, Hao Z, Tao W, Kong F, Zhang S, Wu B, Lin S, Liu M. Acute ischemic stroke in the very elderly Chinese: risk factors, hospital management and one-year outcome. Clinical neurology and neurosurgery. 2011; 113(6):442-6.
06. Olindo S, Cabre P, Deschamps R, Chatot-Henry C, Rene-Corail P, Fournerie P, et al. Acute stroke in the very elderly: epidemiological features, stroke subtypes, management, and outcome in Martinique, French West Indies. Stroke. 2003; 34(7):1593-97.
07. Niewada M, Kobayashi A, Sandercock PA, KamiDski B, CzBonkowska A. Influence of gender on baseline features and clinical outcomes among 17,370 patients with confirmed ischaemic stroke in the international stroke trial. Neuroepidemiology. 2005; 24(3):123-28.
08. Ayala C, Croft JB, Greenlund KJ, Keenan NL, Donehoo RS, Malarcher AM, et al. Sex differences in US mortality rates for stroke and stroke subtypes by race/ethnicity and age, 1995–1998. Stroke. 2002; 33(5):1197-201.
09. Andersen KK, Andersen ZJ, Olsen TS. Age- and gender-specific prevalence of cardiovascular risk factors in 40 102 patients with first-ever ischemic stroke: a Nationwide Danish Study. Stroke. 2010; 41(12):2768-74.
10. Giralt D, Domingues Montanari S, Mendioroz M, Ortega L, Maisterra O, Perea Gainza M, et al. The gender gap in stroke: a meta analysis. Acta Neurologica Scandinavica. 2012 ; 125(2):83-90.
11. Roquer J, Campello AR, Gomis M. Sex differences in first-ever acute stroke. Stroke. 2003; 34(7):1581-85.
12. Shuangxi G, Song T, Bo S, Avinash C, Anna M, Hui F, et al. Study of the relationship of glycated hemoglobin levels and neurological impairment and three months prognosis in patients with acute ischemic stroke. Life Sci J. 2012; 9(2):119-21.
13. Basu S, Sanyal D, Roy K, Bhattacharya KB. Is post-stroke hyperglycemia a marker of stroke severity and prognosis: A pilot study. Neurology Asia. 2007 Jun; 12:13-19.
14. Doi Y, Ninomiya T, Hata J, Fukuhara M, Yonemoto K, Iwase M, et al. Impact of glucose tolerance status on development of ischemic stroke and coronary heart disease in a general Japanese population: the Hisayama study. Stroke. 2010; 41(2):203-9.
15. Rathore JA, Kango ZA, Mehraj A. Predictors of mortality after acute stroke a prospective

hospital based study. Journal of Ayub Medical College Abbottabad. 2011; 23(2):144-46.

16. Kamouchi M, Matsuki T, Hata J, Kuwashiro T, Ago T, Sambongi Y, et al. Prestroke glycemic control is associated with the functional outcome in acute ischemic stroke: the Fukuoka Stroke Registry. Stroke. 2011; 42(10):2788-94.
17. Sare GM, Ali M, Shuaib A, Bath PM. Relationship between hyperacute blood pressure and outcome after ischemic stroke: data from the VISTA collaboration. Stroke. 2009 ; 40(6):2098-103.
18. Yao XY, Lin Y, Geng JL, Sun YM, Chen Y, Shi GW, et al. Age-and gender-specific prevalence of risk factors in patients with first-ever ischemic stroke in China. Stroke research and treatment. 2012; 2012.
19. Kelly-Hayes M, Wolf PA, Kannel WB, Sytkowski P, D'Agostino RB, Gresham GE. Factors influencing survival and need for institutionalization following stroke: the Framingham Study. Arch Phys Med Rehabil 1988; 69:415–8.
20. Kasper DL, Braunwald E, Fauci AS, Hauser SL, Longo DL, Jameson JL, et al. editors. Harrison's Principles of Internal Medicine. 16th ed. New Delhi: McGraw-Hill, Medical Publishing Division; 2005; 2372–93

Bangladesh Journal of Neuroscience 2017; Vol. 33 (1): 6-12

Comparison of Carbamazipine and Amitryptyline for the Reduction of Diabetic Neuropathic Pain: A Randomized Clinical Trial

RAHMAN MM[1], KHAN RK[2], RIZVI A N[3], MD. ARIFUZZAMAN M[3], SHARIF A[4], KHANAM S [5]

Abstract

Background: D*iabetic neuropathy is very difficult to treat.* ***Objective:*** *The purpose of the present study was to compare the efficacy and safety of carbamazepine and amitryptyline for reduction of diabetic neuropathic pain.* ***Methodology:*** *This was a randomized controlled trial conducted in the department of Neurology including Neuropathy Clinic of BSMMU and in collaboration with department of Endocrinology, BSMMU, Dhaka from January 2012 to December 2013 for a period of two (2) years. Adult diabetic patients presented with neuropathic pain with symmetrical involvement of distal limbs from indoor and outpatient department of Neurology including Neuropathy clinic as well as indoor and outpatient department of Endocrinology, BSMMU were enrolled in the study population. The study population was divided into two groups named as group A and group B. The group A was experimental group. In this group, patients were treated with oral carbamazepine 400mg/day in two divided doses for initial 2 weeks, then 600mg/ day in three divided doses for further 4 weeks. The group B was control group. In this group, patients were treated with oral amitriptyline 25mg/ day at night for initial 2 weeks, then 50mg/day taking at night for further 4 weeks. During trial, three follow ups were taken at 2 weeks interval and encountered the clinical response by pain score (VAS) and the side effects. The first follow up after 2 weeks of treatment; the second follow up was after 4 weeks of treatment and the third follow up was after 6 weeks of treatment.* ***Result:*** *A total number of 110 cases clinically diagnosed as painful diabetic polyneuropathy, then 56 cases randomly selected for Group A and 54 cases randomly selected for Group B. During follow up of 6 weeks, 2 case of Group A developed skin rash for which they discontinued drug. From rest of cases, 2 from Group A and 4 from Group B were dropped out. Because they did not come for follow up. So finally 52 cases for Group A group and 50 cases for Group B group were studied. A total of 102 patients were included in the study. They were divided into four Groups according to their age. The mean age was found 52.17(±10.02) years in Group A and 53.41(±8.82) years in Group B. The mean (±SD) of percent improvement in Group A and Group B were 41.11(±11.29) vs. 31.76(±19.14) (P<0.05). Dizziness and Drowsiness were found in Group A as 33.3% and 37.0%. But in Group B dryness of mouth and constipation were found as 46.3% and 7.4%.* ***Conclusion:*** *In conclusion carbamazepine produced greater improvements than amitriptyline in relieving pain and paresthesia associated with diabetic neuropathy.*

Keywords: *Diabetic neuropathy; carbamazepine; amitriptyline; pain; paresthesia*

Introduction:

Diabetic neuropathic pain is difficult to treat and patients rarely experience complete pain relief. It is a frustrating problem for both providers and patients[1]. Drugs from several different pharmacological classes have been shown to be safe and effective in alleviating neuropathic pain. These include tricyclic antidepressants (TCAs), anticonvulsants, sodium-channel blockers, and topical agents[2].

1. Assistant Professor, Department of Neurology, Sheikh Sayera Khatun Medical College, Gopalgonj.
2. Professor, Department of Neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh..
3. Assistant Professor, Department of Neurology, Dhaka Medical College, Dhaka, Bangladesh
4. Assistant Professor, Department of ENT, Mugda Medical College, Dhaka, Bangladesh.
5. Medical Officer, National Institute of Mental health & Hospital, Dhaka, Bangladesh.

Carbamazepine (CBZ) produces significant pain reduction in patients suffering from painful diabetic neuropathy with a number needed to treat (NNT) of 3.3 based on several study[3]. The number needed to harm (NNH) for CBZ is 3.4 for minor side-effects and NNH of 24 for severe effects[4]. The common side-effects of CBZ are drowsiness, diplopia, blurred vision, nausea and vomiting. In treatment of the elderly population with this drug, one must be aware of possible cardiac disease, water retention, decreased osmolality and hyponatremia complications[5].

Tricyclic antidepressants (TCA) have been established to reduce pain independent of their effect on mood[6]. These drugs block the reuptake of norepinephrine and serotonin which are the two neurotransmitters that are implicated in nociceptive modulation; furthermore it also inhibits sodium channels. TCAs are effective for both constant and lancinating, paroxysmal pain[7]. Based on the evidence of several controlled studies in patients with painful diabetic neuropathy, these drugs are very effective[8-9]. In this context this present study was undertaken to compare the efficacy and safety of carbamazepine and amitryptyline for the reduction of diabetic neuropathy pain.

Methodology

Study Population and Setting: This study was designed as randomized controlled trial and was conducted from January 2012 to December 2013 for a period of two (2) years. This study was carried out in the department of Neurology including Neuropathy Clinic and in collaboration with department of Endocrinology at Banghabandhu Sheikh Mujib Medical University, Dhaka. Adult diabetic patients presented with neuropathic pain with symmetrical involvement of distal limbs from indoor and outpatient department of Neurology including Neuropathy clinic as well as indoor and outpatient department of Endocrinology were enrolled in the study population. Diabetic patients having neuropathic pain with symmetrical involvement of distal part of limbs for at least 6 months, pain score 4 or more using a visual analog scale (0 = no pain, 10 = worst pain possible) and all adult diabetic patients of both sexes between the age of 18-65 years. Patient with history of drug hypersensitivity reaction, impaired hepatic and renal function, pregnant women, lactating mother, patient treated by antidepressant, antiepileptic drugs within one month of commence of study, alcohol or substance abuser, patients with cognitive impairment, mood disorder, patients with cardiovascular disease like ischemic heart diseases, heart failure, heart block, arrhythmia, patients with urinary outflow obstruction, prostatism, glaucoma, known case of malignancy, connective tissue disease were excluded from this study.

Randomization and Blinding: The study population was included by purposive sampling technique after fulfilling the inclusion and exclusion criteria. Participants were randomized in two groups named as group A and group B by lottery. For unbiased randomization, two cards were provided. One marked with X and another marked with Y. Selected subjects were invited to draw a card blindly. Card drawn was marked with X, the subject was allocated for oral Carbamazepine and card drawn marked with Y was given oral amitriptyline. Carbamazepine receiver was fallen into group A and amitriptyline receiver was fallen into group B.

Allocation and Intervention: Before starting medication, it was sincerely explained about side effect of drug to each subject. Each subject in group A was treated with oral Carbamazepine. Starting dose was 400mg/day in two divided dose. After two weeks dose was increased to 600mg/day in three divided doses. Dose was not allowed to increase if intolerable side effect developed. Each subject in group B was treated with oral amitriptyline. Starting dose was 25mg/day, single dose given at night. After two weeks, dose increased to 50mg/day, single dose, given at night. Dose was not allowed to increase when intolerable side effect developed.

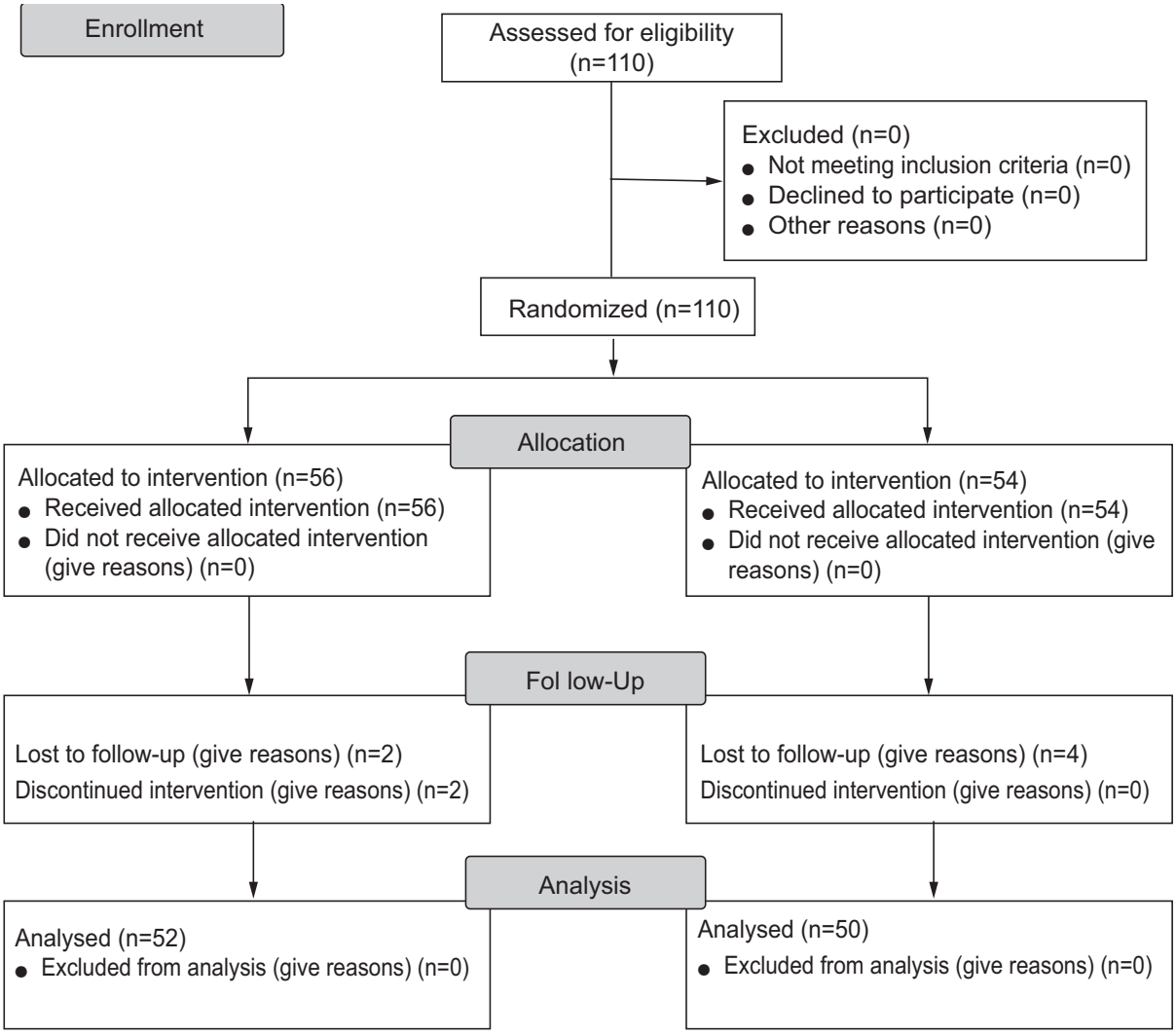


Fig.-1: *CONSORT Flow Chart*

Follow up and Outcome Measures: During the study period, three follow up were taken at 2 weeks interval and encountered the clinical response by pain score (VAS) and the side effects. The first follow up was after 2 weeks of treatment; the second follow up was after 4 weeks of treatment and the third follow up was after 6 weeks of treatment. Pain score was measured by using VAS (0-10) before starting medication and during follow up visit. Selected subject was asked to make a mark on VAS. Thus pain score was recorded in data information sheet. Dizziness, drowsiness, unsteadiness, nausea and vomiting, blurred vision and double vision, uncommon side effect include behavioral change, depression, unusual bleeding, anemia, jaundice, skin rash, itching, toxic epidermal necrolysis and Stevens-Johnson syndrome, water retention were recorded as common side effects of carbamazepine. Dry mouth, drowsiness, blurred vision, constipation, nausea, difficulty in passing urine, postural hypotension and confusion or delirium were the common side effect of amitriptyline.

Statistical Analysis: Data were analyzed by computer with the help of SPSS version 21.0 software package. All data was recorded systematically in a preformed data collection sheet and expressed the quantitative variables as mean+SD. It was analyzed for categorical variables by using chi-squared test and for continuous

variable t-test used. For all statistical tests, we considered p value <0.05 as statistically significant. Prior to the commencement of this study, the research protocol was approved by the Institutional Review Board (IRB) of BSMMU, Dhaka.

Results:

A total number of 110 cases clinically diagnosed as painful diabetic polyneuropathy, then 56 cases randomly selected for Group A and 54 cases randomly selected for Group B. During follow up of 6 weeks, 2 case of Group A developed skin rash for which they discontinued drug. From rest of cases, 2 from Group A and 4 from Group B were dropped out. Because they did not come for follow up. So finally 52 cases for Group A group and 50 cases for Group B group were studied. Table 1 shows the age distribution of both Groups. A total of 102 patients were included in the study. They were divided into four Groups according to their age. The mean age was found 52.17(10.02) years and range were (25-65) years in Group A and mean age was 53.41(8.82) years and range were (25-65) years in Group B. Most of the study patients were > 55 years age Group in both Group A and Group B (48.1% vs 60%). In this table shows no significant difference in age distribution among both Groups (Table 1).

Table-I

Distribution of the respondents by age Groups (n=102)

Age (years)	Group A (n=52)	Group B (n=50)	p value*
25-34 (n=5)	4(7.7%)#	1 (2.0%)	0.411[ns]
35-44 (n=12)	6(11.5%)	6(12.0%)	
45-54 (n=30)	17 (32.7%)	13 (26.0%)	
>55 (n=55)	25(48.1%)	30 (60.0%)	
Total	52(100%)	50(100%)	
Mean (±SD)	52.17±10.02	53.41±8.82	

ns=non significant; *Chi square test was done to measure the level of significance

Table II shows the response of Group A and Group B on DPN patients in term of pain. Before starting the medication pain Scales of both Groups were moderate and there was no significant difference (p>0.05) i.e 5.20 (0.86) vs 5.06 (0.82). But after trial from 1st follow up to 3rd follow up significant differences in pain reduction were observed in Group A than Group B. [1st follow up 4.40 (0.80) Vs 4.81 (0.85), p = 0.011; 2nd follow up 3.73 (0.86) Vs 4.07 (0.84), p = 0.041; 3rd follow up 3.00 (0.45) Vs. 3.41 (0.10), p =0.007] (Table 2).

Table-II

Distribution of the respondents by Visual Analog Scale (VAS) score in Both Groups during premedication and three Follow up (FU) in post-medication (n=102)

VAS	Group A (n=52)	Group B (n=50)	P value
Pre-Medication	5.20±0.86	5.06±0.82	0.361
Post-Medication 1st FU	4.40±0.80	4.81±0.85	0.011
Post-Medication 2nd FU	3.73±0.86	4.07±0.84	0.041
Post-Medication 3rd FU	3.00±0.45	3.41±0.10	0.007

mean (±SD); Independent Sample t test was done to measure the level of significance

The percent improvement of visual analog scale score of pre-medication and post-medication was measured. There was highly significant difference between Group A and Group B. The mean (±SD) of percent improvement in Group A and Group B were 41.11(±11.29) vs. 31.76(±19.14) and the median were 41.67 vs. 31.67 (Table III).

Table III

Distribution of the respondents by Percent Improvement of Visual Analog Scale score in Post-Medication (n=102)

Percent Improvement	Group A (n=52)	Group B (n=50)	p value
Mean (±SD)	41.11±11.29	31.76±19.14	0.0001
Median	41.67	31.67	

Mann-Whitney U test was done to measure the level of significance

Table IV shows the distribution of side effects in post-medication. There found dizziness, drowsiness, dryness of mouth, nausea and constipation as side effects. Dizziness and drowsiness were found in Group A as 33.3% and 37.0%. But in Group B dryness of mouth and constipation were found as 46.3% and 7.4%.

Table-IV

Distribution of Respondents by side effects in post-Medication periods in between two Groups (n=102)

Side Effects	Group A (n=52)	Group B (n=50)	p value
Dizziness			
Yes	18(33.3%)	0(0.0%)	0.0001[s]
No	34(66.7%)	50(100.0%)	
Drowsiness			
Yes	18(35.5%)	13(27.8%)	0.288[ns]
No	34(64.5%)	37(72.2%)	
Dryness of Mouth			
Yes	0(0.0%)	23(46.3%)	0.0001[s]
No	52(100.0%)	27(53.7%)	
Nausea			
Yes	3(7.4%)	2(5.6%)	0.647[ns]
No	49(92.6%)	48(94.4%)	
Constipation			
Yes	0(0.0%)	2(7.4%)	0.153[ns]
No	52(100.0%)	48(92.6%)	
Unsteadiness			
Yes	2(3.0%)	0(0%)	0.475[ns]
No	50(97.0%)	50(100.0%)	

s=significant, ns=not significant; P value reached from chi square test

Discussion:

Painful diabetic polyneuropathy significantly affect on the quality of life, sleep, mood, mobility, ability to motor activities and social behaviors of patients[6]. High prevalence of diabetes and consequently painful neuropathy limits the daily activities of the patients[9]. For a long time amitriptyline has been considered as a first line treatment for the pain management of diabetic neuropathic patients.

This randomized clinical trial was conducted in the departments of neurology including neuropathy clinic as well as Department of Endocrinology, BSMMU, Dhaka from January 2012 to December 2013. Total 110 adult diabetic patients who complain neuropathic pain with symmetrical involvement of distal limbs were enrolled in this study. In which 56 patients were treated with oral carbamazepine in Group A and 54 patients Group B were treated with oral amitriptyline. Two cases in group A withdrew from the study due to development of side effect. Another 2 cases from group A and 4 cases from group B failed to follow up. Finally analyzed the data of 52 patients from group A and 50 patients of group B. Detail information was collected by a data collection sheet and followed up the patients for 6 weeks to evaluate their clinical response and side effects.

There is no known study on such a type of clinical trial in painful diabetic neuropathic patients in Bangladesh. It is a little endeavor to evaluate the efficacy of carbamazepine and amitriptyline in the treatment of painful diabetic polyneuropathy in Bangladesh. Carbamazepine is the first anticonvulsant studied for the treatment of diabetic neuropathy[9]. In the present study it has given significant relief of neuropathic pain compared with amitriptyline on day 14, 28 and 42 ($P<0.001$). Mean percent reductions of pain are 15.1±9.53 and 4.9±7.01 in day 14, 28.19±13.0 and 19.6±11.9 in day 28 and 41.1±11.3 and 31.8±19.1 in day 42 in group A and group B respectively. In every follow up efficacy of carbamazepine has found more than that of amitriptyline ($p>0.001$); however, both drugs have ability to reduce pain. Wilton[10] has also found carbamazepine as a significant pain reliever in their clinical trial and has compared carbamazepine with placebo and has recorded pain score on day 10 and 14 and has found statistically significant improvement in carbamazepine group and the result is comparable with findings of this present study. A double blind, 6-wk, placebo-controlled, crossover trial of 30 patients has been conducted by Rull et al[11] and has found that carbamazepine relieves sensory symptoms in 93% with diabetic neuropathy which is superior to the results with placebo. In another double-blind, placebo-controlled, crossover trial conducted by Wilton[10], 40 patients have received either carbamazepine or placebo for 1 wk and have reported their pain using a 10-cm analog scale. Carbamazepine has provided significant relief of diabetic peripheral neuropathy pain compared with placebo on day 10 and day 14 ($P < 0.05$). Observers have also noted a statistically significant decrease in pain in favor of carbamazepine.

In Gomez-Perez et al[12] study 200 mg carbamazepine has been compared with 10 mg nortriptyline/ 0.5 mg fluphenazine in a double-blind, randomized, crossover, double-placebo trial involving 16 patients with diabetic peripheral neuropathy. Carbamazepine has reduced pain by 28.7% in the first 2 week and by 49% in the second 2 week compared with baseline values ($P < 0.001$ at week 4). Nortriptyline-fluphenazine has reduced pain by 38.2% in the first 2 week and by 66.6% in the second 2 week compared with baseline values ($P < 0.001$). However, there is no statistically significant difference between treatments. Adverse events are more common with nortriptyline/ fluphenazine than with carbamazepine.

In the present study dizziness, drowsiness, dryness of mouth, nausea and constipation were frequently reported side effects. In group A dizziness (33.3%) and drowsiness (37.0%) and in group B dryness of mouth (46.3%) and constipation (7.4%) were found as frequent complaints. Dizziness was found significantly common in carbamazepine ($P<0.001$) and dryness of mouth in amitriptyline ($P<0.001$) group. There are several limitations with use antiepileptic drugs. Carbamazepine did not gain popularity because of its adverse effects which ranged from somnolence, dizziness and gait disturbance. In earlier studies, hematopoietic issues were addressed but no patients were excluded because of them. Dizziness and somnolence were the most frequent tolerable adverse effects. Various side effects have been reported with the use of anticonvulsant drugs varying from dizziness, diplopia to life threatening rashes, blood dyscrasias and hepatotoxicity[9]. In the present study in carbamazepine group patients reported more dizziness (33.3%) and drowsiness (37.0%) and in amitriptyline group dryness of mouth (46.3%) and constipation (7.4%). Dizziness was found significantly common in carbamazepine ($P<0.001$) and dryness of mouth in amitriptyline ($P<0.001$) group.

In one retrospective cohort study of 143 patients with trigeminal neuralgia (TGN) in which long term effect over 16 years of CBZ was evaluated[13]. The drug was effective initially with few mild side effects in 99 patients (69%). Twenty five percent patients failed to respond to CBZ and 6% were intolerant to CBZ due to rash, nausea and thirst and water intoxication in 6, 1 and 1 patient respectively which necessitated cessation of the drug. This study has thus confirmed the efficacy of CBZ for the treatment of TN and proved that it may continue to be effective for many years.

Conclusion

It has been concluded that carbamazepine has produced greater improvements than amitriptyline in relieving pain and paresthesia associated with diabetic neuropathy. Additionally, carbamazepine has better tolerated than amitriptyline. These findings suggest that carbamazepine may be of benefit in treating the painful peripheral neuropathy associated with diabetes.

References:

1. Kamei J, Mizoguchi H, Narita M, Tseng LF. Therapeutic potential of PKC inhibitors in painful diabetic neuropathy. Expert Opin Investig Drugs 2001;10:1653–64
2. Galer BS. Neuropathic pain of peripheral origin advances in pharmacologic treatment. Neurology. 1995;45(12 Suppl 9):S17-25
3. McQuay HJ, Tramer M, Nye BA, Carroll D, Wiffen PJ, Moore RA. A systematic review of antidepressants in neuropathic pain. Pain. 1996;68(2):217-27
4. Wiffen PJ, Collins S, McQuay HJ, Carroll D, Jadad A, Moore RA. Anticonvulsant drugs for acute and chronic pain. The Cochrane Library. Clin J Pain 2005;15(4):313-25
5. Jensen PG, Larson JR. Management of painful diabetic neuropathy. Drugs & aging. 2001;18(10):737-49
6. Sindrup SH, Otto M, Finnerup NB, Jensen TS. Antidepressants in the treatment of neuropathic pain. Basic Clinical Pharmacology Toxicology 2005;96(6): 399-409
7. Galer BS, Gianas A, Jensen MP. Painful diabetic polyneuropathy: epidemiology, pain description, and quality of life. Diabetes research and clinical practice. 2000; 47(2):123-8

8. Woolf CJ. Pain: moving from symptom control toward mechanism-specific pharmacologic management. Annals of Internal Medicine. 2004;140(6):441-51

9. Hussain AM, Afshan G. Use of anticonvulsants drugs for neuropathic painful conditions. Journal of the Pakistan Medical Association. 2008;58(12):690

10. Wilton TD. Tegretol in the treatment of diabetic neuropathy. South African Medical Journal 1974;48(20):869-72

11. Rull JA, Quibrera R, Gonzalez-Millan H, Castaneda OL. Symptomatic treatment of peripheral diabetic neuropathy with carbamazepine (Tegretol®): double blind crossover trial. Diabetologia 1969;5(4): 215-18

12. Gómez-Pérez FJ, Choza R, Ríos JM, Reza A, Huerta E, Aguilar CA, Rull JA. Nortriptyline-fluphenazine vs. carbamazepine in the symptomatic treatment of diabetic neuropathy. Archives of Medical Research 1995;27(4):525-29

13. Taylor JC, Brauer S, Espir ML. Long-term treatment of trigeminal neuralgia with carbamazepine. Postgraduate Medical Journal 1981;57(663):16-18.

Bangladesh Journal of Neuroscience 2017; Vol. 33 (1): 13-17

Common Non-Neurological Medical Complications in Acute Ischemic Stroke Patients

HOSSAIN MA[1], HANNAN MA[2], BISWAS PK[3], JAHAN M[4], KHAN MAM[1]

Abstract:

Ischemic stroke patients suffer from different complications among which non-neurological medical complications are common along with stroke related neurological complications. This observational study was aimed to find out these non-neurological common medical complications of acute ischemic stroke patients admitted in hospital in this country. This study was conducted by every day observation of acute ischemic stroke patients admitted in the hospital. Medical complications were diagnosed on the basis of clinical features and laboratory findings. In acute ischemic stroke patients, development of medical complications is more common (60%). Among them infective complications were found more than non-infective complications. Urinary tract infections (17.8%), respiratory tract infection (17.8%), mixed complications (13.3%) were found commoner than other complications. Length of hospital stay (LOHS) was prolonged in those patients who developed these complications. These complications play a vital role in outcome of the patients.

Keywords: *acute ischemic stroke, complication, infection, length of hospital stay.*

Introduction:

Stroke is a major cause of death and disability worldwide[1]. Stroke is usually characterized by rapid onset of focal neurological deficit due to infarction or hemorrhage lasting more than 24 hours[2]. The definition of stroke is clinical and laboratory studies including brain imaging are used to support the diagnosis[3]. Countries of low and middle income have the largest burden of stroke, accounting for more than 85% of stroke mortality worldwide[4]. Cause of mortality and morbidity depends upon different neurological and non-neurological complications of acute ischemic stroke (AIS) patients. Most of the time we are concerned about the neurological complications only, but non-neurological medical complications also play devastating impact in outcome of stroke patients[5].

We have observed multiple medical complications like urinary tract infection, sepsis, respiratory tract infection, myocardial infarction etc in stroke patients. These complications cause deterioration of the patients. It is also strongly linked to a poor inpatient prognosis as well higher rate of complications lead to longer hospital stay and increase cost of care[6-9].

Such type of study was not previously performed in Bangladesh. It is important to identify the common complications in-hospital of AIS patients to provide necessary informations regarding proper management of AIS patients.

Materials and Methods:

This observational study was conducted in the department of Neurology of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh during January 2013 to December 2013 and received prior approval from Ethical Review Committee of BSMMU and all participants/ attendants gave informed written consent. All collected data were checked, edited and analyzed by using computer based SPSS software version 16.0. Data were presented by frequency distribution

1. Asstt. Professor of Neurology, NINS, Dhaka.
2. Professor, Department of Neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka
3. Associate Professor of Medicine, Dhaka Medical College, Dhaka.
4. Lecturer, Dhaka Medical College, Dhaka.
5. Assistant Professor of Neurology, National Institute of Neurosciences Hospital, Dhaka

and percentage. Parametric data was expressed in mean ± SD. Categorical data was evaluated by Chi square test. Significance was defined by p value < 0.05.

A total of 90 AIS patients admitted in the Neurology department of BSMMU were included in this study. Sampling technique was purposive. Patients presented with first ever AIS, confirmed by CT scan/ MRI of brain from 01 day to 02 weeks were enrolled in this study. Hemorrhagic stroke patients were excluded from this study.

After selection of subjects, detailed history, clinical examinations and all other information's were taken in a prescribed data collection form. Relevant baseline investigations (e.g. - complete blood count, urine R/M/E etc.) were performed. Imaging study (CT/MRI) was done for diagnosis and categorization of stroke. AIS subtype is defined by Oxford shire Community Stroke Project classification (OCSP) criteria. Cerebral infarctions were divided into the following clinical categories: total anterior circulation infarcts (TACI), partial anterior circulation infarcts (PACI), lacunar infarcts (LACI), and posterior circulation infarcts (POCI). Modified Rankin Scale (mRS) was measured to see functional outcomes at fourteenth day of stroke. Patients were followed up every day to see any in-hospital medical complications eg. Respiratory Tract Infection (RTI), Urinary Tract Infection (UTI), Bed sore, Electrolyte Imbalance (Sodium or Potassium abnormalities) and MI. Diagnosis of this complications were made by clinical findings, expert opinion and appropriate laboratory reports like Urine R/E and C/S for UTI, Chest X ray and Sputum C/S for RTI, ECG and/or Troponin I for MI, Serum Electrolytes, d-dimer, duplex study of lower limb vessels, Stool R/E etc. Length of hospital stay (LOHS) was measured from admission to discharge day of the patient.

Results:

Out of the 90 AIS patients, majority 36(40%) were belonged to age group of 61-70 years. The mean age was found 59 years with range from 30 to 75 years (Table I).

It was observed that more than half 49(54%) were male and 41(46%) were female. Male to female ratio was 1.2:1. It also showed that 49(54%) patients came from rural area and 41(46%) came from urban area (Table I).

Table-I

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

Characteristics		No. of respondents	Percentage
Sex	Male	49	54.4
	Female	41	45.6
Age	≤40	7	7.8
	41-50	9	10.0
	51-60	34	37.8
	61-70	36	40.0
	>70	4	4.4
Residence	Urban	41	45.6
	Rural	49	54.4

It was observed that non-smoker was found in 43(47.8%) patients, current smoker was 30(33.3%) and former smoker 17(18.9%).

It was observed that 52(57.8%) patients had hypertension and 38(42.2%) had no hypertension.

This study revealed that 32(35.6%) patients had diabetes mellitus (DM).

By Oxford shire Community Stroke Project classification (OCSP), It was observed that 4(4.4%) TAC, 15(16.7%) LAC, 51(56.7%) PAC, 14(15.6%) POC and 6(6.6%) syndromes.

It was observed that majority 38(42.2%) of patients had hospital stay of 11-15 days. The mean hospital stay was found in 13.68±6.6 days (Table II).

Table-II

Distribution of the patients by length of hospital stay (n=90)

Length of Hospital stay (days)	Number of patients	Percentage
≤5	3	3.3
6-10	23	25.6
11-15	38	42.2
16-20	4	4.4
21-25	18	20.0
>25	4	4.4
Mean ± SD	13.68±6.6	
Range (min, max)	(4, 31)	

Table II shows length of hospital stay of the patients. It was observed that majority 38(42.2%) of patients

had hospital stay of 11-15 days. The mean hospital stay was found in 13.68±6.6 days.

Medical complications were found in 54 (60%) patients. No complication was found in 36 (40%) patients. This present study results showed that UTI and RTI were found same, is 16 (17.8%) of patients. Bed sore was found in 3 (3.3%) patients. Electrolyte Imbalance was found in 2(2.2%) patients. Others/mixed complications were found in 12 (13.3%) patients. Gastroenteritis was 4 (4.4%) and myocardial infarction was 1 (1.11%) (Table IV).

Table-III

In-hospital medical complications in AIS patients (n=90)

Medical Complications	Number of (N) patients	Percentage
Complications	54	60
No complication	36	40

Table III Shows in-hospital medical complications were found in 54 (60%) patients, no complications in 36 (40%) patients.

Table-IV

Different in-hospital complications in AIS patients (n=90)

In-hospital complications	n	%
Gastroenteritis	4	4.4
UTI	16	17.8
RTI	16	17.8
Bed sore	3	3.3
Electrolyte Imbalance	2	2.2
MI	1	1.1
Others/Mixed complication	12	13.3

UTI- Urinary Tract Infection, RTI- Respiratory tract infection, MI- Myocardial infarction.

Discussion:

Frequency of stroke rises exponentially with increasing age[10]. Majority of the study subject (40%) were in seventh decade and the mean age was 59 years varied from 30 to 75 years (Table I). Similarly Hossain et al. in Faridpur Medical College showed highest incidence of stroke was between the sixth and seventh decade[11,12]. Kundu et al. in a Bangladeshi study showed 16% were young stroke (age<40years) and most patients (54%) were at and above 60 years of age[13]. Basu et al. obtained that median age was 60 years, mean age 60 ± 13 years varied from 25-88 years, which is closely resembled with the present study[14]. On the other hand, Gentile et al. showed the mean age was 65.7±13.6 years varied from 20 to 101 years. In another study conducted in University of south Carolina, USA, Bhatt and Rizvi found the average age of AIS patients was 67.8 years, which are higher with the current study, this may be due to increased life expectancy, and geographical influences may have significant impacts to developed AIS of their study patients[15].

In current study it was observed that AIS was predominant in male subjects, where 54% and 46% patients were male and female respectively and male to female ratio was 1.2:1. Similar observations regarding the sex incidence were also made by Basu et al. where they found 57.0% were male and 43.0% were female[14]. However, Gentile et al. and Bhatt and Rizvi were found 55.0% and 57.0% patients were female respectively.[15,3] More than a half (54%) of the patients attended from rural area and 46% came from urban. These findings are almost similar of the study done by Hossain et al[12]. The reason of higher percentage of AIS in rural patients might be that, lack of knowledge regarding risk factors due to low economical condition. It was observed that non-smoker was found in 47.8%patients, current smoker was 33.3% and former smoker 18.9%. In Stollberger et al. study showed 9.0% patients were current smoker. Hossain et al. showed 20.75% current smoker in a Bangladeshi study[12].

This study findings showed that more than one third (35.6%) of the patients had DM. Basu et al. from Kolkata and Bhatt and Rizvi from South Carolina showed 26.0% and 51.4% had a known history of DM respectively[14,15]. Stollberger et al. in 2005 found that 30% patients had a history of DM[20]. Gentile et al. obtained DM 39% in their study patients[3]. Hossain et al. showed 21% DM in stroke patients at Faridpur Medical College[12]. Kundu et al. showed DM is found in 99 (20%) patients[13]. And of these 99 patients only 57 (12%) patients

were known diabetic and the remaining patients were labeled as diabetic after admission.

In this study, it was observed that 57.8% patients had hypertension and 42.2% patients were normotensive. Similarly, Stollberger et al. found that 66.0% patients were hypertensive[20]. Basu et al. and Gentile et al. showed that 74.0% and 73.8% patients were known hypertensive respectively, which is higher with the current study[3,13]. In a study conducted at Faridpur Medical College showed 63% were hypertensive in stroke patients.[12] In the study by Kundu et al. hypertensive patients were found 69.60% (284) out of 500 patients[13].

In this present study it was observed that majority (42.2%) of patients had hospital stay of 11-15 days and the mean duration of hospital stay was 13.68±6.6 days varied from 4-31 days. Similarly, Stollberger et al. showed duration of hospitalization was 13 days varied from 9-20 days[20]. Gentile et al. and Bhatt and Rizvi (2010) observed the mean length of hospital stay were 7.40±8.15 days and 6.12±4.2 days respectively, which are lesser with the current study[3,15].

In this study, 54(60%) patients developed complications. This present study results showed that UTI and RTI were found same, is 16 (17.8%) of patients. Bed sore was found in 3 (3.3%) patients. Electrolyte Imbalance was found in 2 (2.2%) patients. Others/mixed complications were found in 12 (13.3%) patients. Gastroenteritis was 4 (4.4%) and myocardial infarction was 1 (1.11%). Stollberger et al. at Austria studied 992 patients of stroke where 12% had UTI, mixed complications in 29%, but RTI in stroke patients is 14%[20]. These findings are similar with current study.

Conclusion:

Ischemic stroke patients suffer from both neurological and non-neurological medical conditions. Our observation at a large urban teaching hospital showed non-neurological medical complications of acute ischemic stroke patients is very common in this country. Among them infective complications were found more common than non-infective complications. Urinary tract infections (17.8%), respiratory tract infection (17.8%), mixed complications (13.3%) were found more common than other complications. Length of hospital stay (LOHS) was prolonged in the patients who developed these complications. These complications play a vital role in outcome of acute ischemic stroke patients. This study should be conducted in a large scale in different hospitals for better understanding of different complications of so that proper steps can be taken to reduce mortality and morbidity of ischemic stroke patients.

References

1. Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL. Cerebrovascular disease. In: Harrison's Principles of Internal Medicine 17th Edition, McGraw Hill, New York. 2008.
2. Smith WS, Joey D, English S. Cerebro-vascular disease. In: Harrison's Principles of Internal Medicine 18th Edition, McGraw Hill, New York. 2011; 3270-94.
3. Gentile NT, Seftchick MW, Huynh T, Kruus LK, Gaughan J. 'Decreased mortality by normalizing Blood Glucose after Acute Ischemic Stroke'. *AcadEmerg Med*. 2006; 13: 174-80.
4. Williams LS, Rotich J, Fineberg N, Espay A, Bruno A, Fineberg SE, et al. Effects of admission hyperglycemia on mortality and costs in Acute Ischemic Stroke. *Neurology*.2002; 59: 67–71.
5. Frederic MW. Cerebrovascular disease. In: Cardiac and Vascular Disease Conn HLJR and Horwitzo (eds). Lea and Febiger, Philladelphia. 1971; 1473-99.
6. Wolf PA, Cobb JL, Agostine D. Epidemiology of stroke; Stroke 2nd Edition, Barnett HJM and Mohr JP (eds). Churchill Livingstone, Edinburgh. 1992; 3-27.
7. Houseley E. Definition of risk factors in stroke; Stroke Gillingam FJ and Mawdsley C (eds), Churchill Livingstone, New York. 1976; 251-60.
8. Grotta JC. Post-stroke management concerns and outcomes. *Geriatrics.* 1988; 43:40–48.

9. Sacco RL, Wolf PA, Kannel WB, McNamara PM. Survival and recurrence following stroke: the Framingham study. *Stroke.* 1982; 13: 290–295.

10. Silver FL, Norris JW, Lewis AJ, Hachinski VC. Early mortality following stroke: a prospective review. *Stroke.* 1984; 15:492–496.

11. Allen CM. Predicting the outcome of acute stroke: a prognostic score. *J NeurolNeurosurg Psychiatry.*1984; 47:475–480.

12. Hossain AM, Ahmed NU, Rahman M, Islam MR, Sadhya G, Fatema K. Analysis of sociodemographic and clinical factors associated with hospitalized stroke patients of Bangladesh. *Faridpur Med. Coll. J*. 2011; 1: 19-23.

13. Kundu NC, Ahmed Q, Sen M. 'Study of stroke and its risk factors among admitted patients in a tertiary level hospital'. *Bangladesh Journal of Neuroscience*. 2010; 26: 86-91.

14. Basu S, Sanyal*D*, Roy K, Bhattacharya K. 'Is post-stroke hyperglycemia a marker of stroke severity and prognosis: A pilot study'. *Neurology AISa.2007; 12: 13-19.*

15. Bhatt H, Rizvi AA. 'Average inpatient glucose levels during the first 72 hours Clinical Outcomes and Length of Hospital Stay in Patients with Acute Ischemic Stroke'. *Int J Diabetes &Metab*.2010; 18: 13-17.

16. Hart CL, Hole DJ, Smith GD. Influence of socioeconomic circumstance in early and later life on stroke risk among men in a Scottish cohort study. *Stroke*. 2000; 31(9): 2093-97.

17. Casper M, Wing S, Strogatz D. Variation in the magnitude of black- white differences in stroke mortality by community occupational structure. *J Epidemiol Community Health*.1991; 45: 02-307.

18. Shaper AG. Risk factors for stroke in middle age British men.*BMJ*.1991; 302: 1111-16.

19. Chapman J. Epidemiology of vascular lesions affecting the central nervous system: The occurrence of stroke in a sample population under observation for cardiovascular disease. *Am JPublic Health*.1966; 55: 191-01.

20. Stollberger C, Exner I, Finsterer J, Slany J, StegerC. 'Stroke in diabetic and non-diabetic patients: Course and prognostic value of admission serum glucose'. *Annals of Medicine*.2005; 37: 357–64.

Bangladesh Journal of Neuroscience 2017; Vol. 33 (1): 18-23

Sociodemographic and Clinical Factors of Acute Ischemic Stroke

HOSSAIN MA[1], HANNAN MA[2] , BARMAN KK[3], BISWAS PK[4], JAHAN M[5], KHAN MAM [6,]

Abstract:

An observational study was carried out to analyze prevalence of risk factors for ischemic stroke in hospitalized patient in a university hospital. Ninety patients were chosen by using purposive sampling technique. The mean age of patients was 59.01±9.87 years varied from 30 to 75 years and male to female ratio was 1.2:1. Highest incidence of stroke was between the 6th and 7th decade. Patients came from both rural 49 (54.4%) and urban 41 (45.6) area. Most of them belonged to the lower-middle group 70 (84.8%). Regarding education 47 (52.2%) patients had primary level education and 8 (8.9%) patients were illiterate. It was observed that among them current smoker were 30 (33.3%) and ex-smoker 17 (18.9%). It was also observed that 52 (57.8%) patients had hypertension and 32 (35.6%) had diabetes mellitus (DM). Ischemic heart disease was present in 14 (15.6%) patients. By Oxford shire classification of stroke, it was observed that PAC is common 51 (56.7%) among all forms. Majority 38 (42.2%) of patients had hospital stay of 11-15 days. The mean hospital stay was found 13.68±6.6 days. This study found that cigarette smoking, hypertension, diabetes mellitus and ischemic heart diseases are the major risk factors prevalent in our community while other risk factors demand further study.

Key words: *stroke, risk factors, hospitalized patients, Bangladesh.*

Introduction:

Stroke is usually characterized by rapid onset of focal neurological deficit due to infarction or hemorrhage lasting more than 24 hours[1]. The definition of stroke is clinical. Laboratory studies including brain imaging are used to support the diagnosis[2]. It is a major cause of death and disability worldwide[3]. Recently a study was published in Prothom Alo, a leading daily newspaper of Bangladesh which states that stroke is the first cause of adult death in Bangladesh. Countries of low and middle income have the largest burden of stroke, accounting for more than 85% of stroke mortality worldwide, but few reliable data are available to identify risk factors for stroke in most of these regions[4].

To reduce burden of stroke patients, modifiable risk factors should be identified and proper treatment could reduce the incidence of acute ischemic stroke (AIS). The incidence of stroke increases with age and affect many people in their golden years. It is third most common cause of death in developed countries. The age adjusted annual death rate from stroke is 116 per 100000 populations in the USA and some 200 per 100000 in UK[3]. Risk factors for ischemic stroke include irreversible or non modifiable factors like age, sex, heart disease and modifiable factors like

1. Dr. Md. Amir Hossain, MBBS, FCPS (Medicine), MD (Neurology), Assistant Professor of Neurology, National Institute of Neurosciences Hospital, Dhaka
2. Professor M. A. Hannan, MBBS, FCPS (Medicine), MD (Neurology), FRCP (Edin.) Chairman, Department of Neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka
3. Dr. Kanuj Kumar Barman, MBBS, MPH, MD (Neurology). Associate Professor, Department of Neurology, Bangabandhu Sheikh Mujib Medical University.
4. Dr. Prodip Kumar Biswas, MBBS, FCPS (Medicine), MD (Gastro). Associate Professor of Medicine, Dhaka Medical College, Dhaka.
5. Dr. Merina Jahan, FCPS (Obs & Gynae), Lecturer, Dhaka Medical College, Dhaka.
6. Dr Muhammad Abdul Momen Khan, MBBS, MD (Neurology). Assistant Professor of Neurology, National Institute of Neurosciences Hospital, Dhaka

hypertension, heart disease, diabetes mellitus, hyperlipidemia, smoking, excess alcohol, polycythemia and oral contraceptive[3]. The morbidity and mortality from cerebrovascular disease has been diminished in recent years largely due to better recognition and treatment of underlying arterial and cardiac disease including hypertension, diabetes and hyperlipidemia. There is no cure in management of stroke. But prevention is possible by early detection and reducing the modifiable risk factors. This is very much important in the concept of our country where medical facilities and resources are limited and most of the people lives below poverty level.

Materials and Methods:

This observational study was conducted in the department of Neurology of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh during January 2013 to December 2013 and received prior approval from Ethical Review Committee of BSMMU and all participants gave informed written consent. All collected data were checked, edited and analyzed by using computer based SPSS software version 16.0. Samples were collected purposively. Data were presented by frequency distribution and percentage. Parametric data was expressed in mean ± SD. Categorical data was evaluated by Chi square test. Significance was defined by p value <0.05.

A total of 90 AIS patients admitted in the Neurology department of BSMMU were included in this study. Sampling technique was purposive. Patients presented with first ever AIS, confirmed by CT scan/ MRI of brain from 01 day to 02 weeks were enrolled in this study. Hemorrhagic stroke were excluded from the study.

After selection of subjects, detailed history, clinical examinations and all other informations regarding sociodemographic and clinical factors of AIS were taken in a prescribed data collection form. Relevant baseline investigations (e.g- complete blood count, urine R/M/E etc.) were performed. Imaging study (CT/MRI) was done for diagnosis and categorization of stroke. AIS subtype is defined by Oxfordshire Community Stroke Project classification (OCSP) criteria. Cerebral infarctions were divided into the following clinical categories: total anterior circulation infarcts (TACI), partial anterior circulation infarcts (PACI), lacunar infarcts (LACI), and posterior circulation infarcts (POCI).

Length of hospital stay (LOHS) was measured in days from day of admission.

Results:

Out of the 90 AIS patients, majority 36 (40%) were belonged to age group of 61-70 years. The mean age was found 59 years with range from 30 to 75 years (Table I).

Table-I

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

Characteristics		No. of respondents	Percentage
Sex	Male	49	54.4
	Female	41	45.6
Age	d”40	7	7.8
	41-50	9	10.0
	51-60	34	37.8
	61-70	36	40.0
	>70	4	4.4
Residence	Urban	41	45.6
	Rural	49	54.4
Monthly family income (Taka)*	Low income	14	15.6
	Lower middle	70	77.7
	Upper middle	6	6.6
	Upper	0	0
Educational status	Illiterate	8	8.9
	Primary	47	52.2
	SSC	20	22.2
	HSC	10	11.1
	Graduate & above	5	5.6

*The state of the world’s children 2012
Low-income = <7000
Lower-middle income = 7000-27000
Upper-middle = 27000-84000
High income= >84000

It was observed that more than half (54%) were male and 41 (46%) were female. Male to female ratio was 1.2:1. It also showed that 49 (54%) patients came from rural area and 41 (46%) came from urban area (Table I). Regarding monthly family income of the patients it was observed that 14 (15.6%) patients came from low-income group, 70

(77.7%) came from lower-middle income group and 6 (6.6%) from upper-middle group (Table I).

It was observed that 8 (8.9%) patients were illiterate, 47 (52.2%) patients educated at primary level, 20 (22.2%) educated at SSC level, 10 (11.1%) educated at HSC level and 5(5.6%) educated at graduate & above in this study regarding educational status (Table I).

Regarding smoking status of the patients non-smoker was found in 43 (47.8%) of patients. But current smoker was 30 (33.3%) and ex-smoker was 17 (18.9%) (Table II). And 8 (8.9%) had habit of alcohol intake.

Table-II

Distribution of the study patients by smoking status (n=90)

Smoking status	Number of patients	Percentage
Non smoker	43	47.8
Current smoker	30	33.3
Ex-smoker	17	18.9

Table II shows smoking status of the patients. It was observed that non-smoker was found in 43(47.8%) patients, current smoker was 30(33.3%) and former smoker 17(18.9%).

This study revealed that 32 (35.6%) patients had diabetes mellitus (DM). Among the diabetic patients 20 (62.5%) had diabetes for less than 5 years and 12(37.5%) for ≥5 years (Table III)

Table-III

Distribution of the study patients by history of diabetes mellitus (n=90)

Diabetes Mellitus	Number of patients	Percentage
No	58	64.4
Yes	32	35.6
Duration of DM		
<5 years	20	62.5
≥5 years	12	37.5

Table III shows diabetes mellitus of the patients. It was observed that 32(35.6%) patients had diabetes mellitus. Among the diabetic patients 20(62.5%) had diabetes for less than 5 years and 12(37.5%) for ≥5 years.

Table-IV

Distribution of the study patients by history of hypertension (n=90)

Hypertension	Number of patients	Percentage
Yes	52	57.8
No	38	42.2

Table IV shows hypertension of the study patients. It was observed that 52(57.8%) patients had hypertension and 38(42.2%) had no hypertension.

It was observed that 52 (57.8%) patients were hypertensive and 38 (42.2%) had no history of hypertension (Table IV). Fourteen (15.6%) had a history of ischemic heart disease.

Table-V

Distribution of the study patients by presentation (n=90)

Presentation	Number of patients	Percentage
Hemiparesis/Monoparesis	71	78.9
Hemiparesis, cranial nerve involvement	5	5.6
Hemiparesis, Aphasia	10	11.1
Hemiparesis, Visual involvement	4	4.4
Duration (days)		
1-3	14	15.6
4-7	71	78.9
7-14	5	5.6

Table V shows presentation of the study patients. It was observed that 71(78.9%) patients had hemiparesis/monoparesis; 5(5.6%) had hemiparesis & cranial nerve involvement; 10(11.1%) had hemiparesis & aphasia and 4(4.4%) had hemiparesis & visual involvement.

Regarding presentation of illness it was found that 71 (78.9%) patients had hemiparesis/monoparesis; 5 (5.6%) had hemiparesis & cranial nerve involvement; 10 (11.1%) had hemiparesis & aphasia and 4 (4.4%) had hemiparesis & visual involvement (Table V).

Table-VI

Distribution of the study patients by Oxford shire Classification of Stroke (n=90)

CT/MRI of brain	Number of patients	Percentage
TACLAC	415	4.416.7
PAC	51	56.7
POC	14	15.6
Syndrome	6	6.6

Table VI shows Oxfordshire Classification of Stroke. It was observed that 4(4.4%) TAC, 15(16.7%) LAC, 51(56.7%) PAC, 14(15.6%) POC and 6(6.6%) syndromes.

According to Oxford shire Classification of Stroke it was observed that 4(4.4%) TAC, 15(16.7%) LAC, 51(56.7%) PAC, 14(15.6%) POC and 6(6.6%) were syndromes (Table VI).

Table-VII

Distribution of the patients by length of hospital stay (n=90)

Length of Hospital stay (days)	Number of patients	Percentage
≤5	3	3.3
6-10	23	25.6
11-15	38	42.2
16-20	4	4.4
21-25	18	20.0
>25	4	4.4
Mean ± SD	13.68 ±6.6	
Range (min, max)	(4, 31)	

Table VII shows length of hospital stay of the patients. It was observed that majority 38(42.2%) of patients had hospital stay of 11-15 days. The mean hospital stay was found in 13.68±6.6 days.

Majority 38 (42.2%) of patients had hospital stay of 11-15 days. The mean hospital stay was found in 13.68±6.6 days (Table VII).

Discussion:

Stroke frequency increases exponentially with increasing age[11]. Main bulk of the study subject (40%) were in seventh decade and the mean age was 59 years varied from 30 to 75 years (Table I). Similarly Hossain et al. in Faridpur Medical College showed highest incidence of stroke was between the sixth and seventh decade[12]. Kundu et al. in a Bangladeshi study showed 16% were young stroke (age<40years) and most patients (54%) were at and above 60 years of age[13]. Basu et al. at a study in Kolkata National Medical college obtained that median age was 60 years, mean age 60 ± 13 years varied from 25-88 years, which is closely resembled with the present study[14]. On the other hand, Gentile et al. showed the mean age was 65.7±13.6 years varied from 20 to 101 years[3].In another study conducted in University of South Carolina, USA, Bhatt and Rizvi found the average age of AIS patients was 67.8 years, which are higher with the current study, this may be due to increased life expectancy, and geographical influences may have significant impacts to developed AIS of their study patients[15].

In this current study it was observed that AIS was predominant in male subjects, where 54% and 46% patients were male and female respectively and male to female ratio was 1.2:1. Similar observations regarding the sex incidence were also made by Basu et al. where they found 57.0% were male and 43.0% were female[14]. However, Gentile et al. and Bhatt and Rizvi were found 55.0% and 57.0% patients were female respectively[3, 15]. More than a half (54%) of the patients attended from rural area and 46% came from urban. These findings are almost similar of the study done by Hossain et al.[12] The reason of higher percentage of AIS in rural patients may be due to lack of knowledge regarding risk factors of stroke management and due to low economical condition.

Considering socio-economic status, the lower-middle income group (monthly income BDT 7000-27000) comprised the majority (77.7%). This result correlated with the study by Hart CL et al. which concluded that poor socioeconomic circumstances were associated with greater risk of stroke, which was also found in other studies[16-18]. But this study disagreed with the study of Chapman et al. which showed the incidence of stroke was high among the high-income group[19].

Regarding educational status of the patients it was observed that 8.9% patients were illiterate, 52.2% patients educated at primary level, 22.2% educated at SSC level, 11.1% educated at HSC level and 5.6% educated at graduate & above. Hossain et al showed most of the study subjects were literate (63%)[12]. It represents the current increasing literacy rate in Bangladesh.

It was observed that non-smoker was found in 47.8% patients, current smoker was 33.3% and ex-smoker 18.9%. And 8.9% had habit of alcohol intake. In Stollberger et al. study showed 9.0% patients were current smoker and 75% were alcoholic. Hossain et al. showed 20.75% current smoker in a Bangladeshi study[12].

This study findings showed that more than one third (35.6%) of the patients had DM and among them 62.5% had DM for less than 5 years and 37.5% for e"5 years. Basu et al. and Bhatt and Rizvi showed 26.0% and 51.4% had a known history of DM respectively[14,15]. Stollberger et al. in 2005 found that 30% patients had a history of DM.[20] Gentile et al. obtained DM 39.0% in their study patients[3]. Hossain et al. showed 21% DM in stroke patients at Faridpur Medical College[12]. Kundu et al. showed DM is in 99 (20%) patients[13]. And of these 99 patients only 57 (12%) patients were known diabetic and the remaining patients were labeled as diabetic after admission.

In current study it was observed that 57.8% patients had hypertension and 42.2% patients were normotensive. Similarly, Stollberger et al. found that 66.0% patients were hypertensive[20]. But 15.6% had a history of ischemic heart disease. Basu et al. and Gentile et al. showed that 74.0% and 73.8% patients were known hypertensive respectively, which is higher than the current study[3,13]. In a study conducted at Faridpur Medical College showed 63% were hypertensive in stroke patients and 45.83% had history of ischemic heart disease. In the study of Kundu et al. hypertensive patients were 69.60% (284) out of 500 patients[13].

Regarding presentation of the study patients, it was observed that 78.9% patients had hemiparesis/ monoparesis; 5.6% had hemiparesis & cranial nerve involvement; 11.1% had hemiparesis & aphasia and 4.4% had hemiparesis & visual involvement.

Table VI shows distribution of the study patients according to Oxford shire Classification of Stroke. It was observed that 4.4% TAC, 16.7% LAC, 56.7% PAC, 15.6% POC and 6.6% syndromes.

In this present study it was observed that majority (42.2%) of patients had hospital stay of 11-15 days and the mean duration of hospital stay was 13.68±6.6 days varied from 4 – 31 days. Similarly, Stollberger et al. showed duration of hospitalization was 13 days varied from 9-20 days[20]. Gentile et al. and Bhatt and Rizvi (2010) observed the mean length of hospital stay were 7.40±8.15 days and 6.12±4.2 days respectively, which are lesser with the current study[3, 15].

Conclusion:

Stroke is one of the leading causes of mortality and morbidity and it is a socioeconomic challenge. And it is very true for a developing country like Bangladesh, where health care system including the stroke rehabilitation system is not within the reach of the general people. Stroke affects not only the patients but also their family. A stroke patient is a burden for the family, society as well as for the country. The objective of this hospital-based observational study was to identify the important risk factors for ischemic stroke prevalent in our society among the urban and rural population. This study may have not reflected the exact situation but gives an utmost picture of the disease. There are many risk factors for ischemic stroke, some are modifiable and some are not. In this study a number of modifiable risk factors were identified, of these diabetes and hypertension are two important factors. Others are smoking and ischemic heart disease. Prevention is better than cure. And it is very much true for ischemic stroke patients. In a developing country like ours the best policy for combating stroke is primary prevention. This study reveals that the major risk factors diabetes and hypertension need maximum attention for the prevention of stroke. Quitting of smoking and alcoholism are also important. By controlling diabetes and hypertension we can significantly reduce the incidence of ischemic

stroke. For this we need increase awareness among people regarding diabetes and hypertension and their complications.

References:

1. Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL. Cerebrovascular disease. In: Harrison's Principles of Internal Medicine 17th Edition, McGraw Hill, New York. 2008.
2. Smith WS, Joey D, English S. Cerebrovascular disease. In: Harrison's Principles of Internal Medicine 18th Edition, McGraw Hill, New York. 2011; 3270-94.
3. Gentile NT, Seftchick MW, Huynh T, Kruus LK, Gaughan J. 'Decreased mortality by normalising Blood Glucose after Acute Ischemic Stroke'. *Acad Emerg Med*. 2006; 13: 174-80.
4. Williams LS, Rotich J, Fineberg N, Espay A, Bruno A, Fineberg SE, et al. Effects of admission hyperglycemia on mortality and costs in Acute Ischemic Stroke. *Neurology*. 2002; 59: 67–71.
5. Frederic MW. Cerebrovascular disease. In: Cardiac and Vascular Disease Conn HLJR and Horwitzo (eds). Lea and Febiger, Philladelphia. 1971; 1473-99.
6. Wolf PA, Cobb JL, Agostine D. Epidemiology of stroke; Stroke 2nd Edition, Barnett HJM and Mohr JP (eds). Churchill Livingstone, Edinburgh. 1992; 3-27.
7. Houseley E. Definition of risk factors in stroke; Stroke Gillingam FJ and Mawdsley C (eds), Churchill Livingstone, New York. 1976; 251-60.
8. Grotta JC. Post-stroke management concerns and outcomes. Geriatrics. 1988;43:40–48..
9. Sacco RL, Wolf PA, Kannel WB, McNamara PM. Survival and recurrence following stroke: the Framingham study. *Stroke.* 1982;13: 290–95.
10. Silver FL, Norris JW, Lewis AJ, Hachinski VC. Early mortality following stroke: a prospective review. *Stroke.* 1984;15:492–96.
11. Allen CM. Predicting the outcome of acute stroke: a prognostic score. *J Neurol Neurosurg Psychiatry.*1984;47:475–80.
12. Hossain AM, Ahmed NU, Rahman M, Islam MR, Sadhya G, Fatema K. Analysis of sociodemographic and clinical factors associated with hospitalized stroke patients of Bangladesh. *Faridpur Med. Coll. J*. 2011; 1: 19-23.
13. Kundu NC, Ahmed Q, Sen M. 'Study of stroke and its risk Factors among admitted patients in a tertiary level hospital'. *Bangladesh Journal of Neuroscience*. 2010; 26: 86-91.
14. Basu S, Sanyal *D*, Roy K, Bhattacharya K. 'Is post-stroke hyperglycemia a marker of stroke severity and prognosis: A pilot study'. Neurology Asia. 2007; 12: 13-19.
15. Bhatt H, Rizvi AA. 'Average Inpatient Glucose Levels during the first 72 hours Clinical Outcomes, and length of hospital Stay in Patients with Acute Ischemic Stroke'. *Int J Diabetes & Metab*. 2010; 18: 13-17.
16. Hart CL, Hole DJ, Smith GD. Influence of socioeconomic circumstance in early and later life on stroke risk among men in a Scottish cohort study. *Stroke*. 2000; 31(9): 2093-97.
17. Casper M, Wing S, Strogatz D. Variation in the magnitude of black- white differences in stroke mortality by community occupational structure. *J Epidemiol Community Health*. 1991; 45: 02-307.
18. Shaper AG. Risk factors for stroke in middle age British men. *BMJ*. 1991; 302: 1111-16.
19. Chapman JM. Epidemiology of vascular lesions affecting the central nervous system: The occurrence of stroke in a sample population under observation for cardiovascular disease. *Am J Public Health*. 1966; 55: 191-20.
20. Stollberger C, Exner I, Finsterer J, Slany J, Steger C. 'Stroke in diabetic and non-diabetic patients: Course and prognostic value of admission serum glucose'. *Annals of Medicine*. 2005; 37: 357–64.

Bangladesh Journal of Neuroscience 2017; Vol. 33 (1): 24-29

Pattern of Presentation of Moyamoya Disease (MMD) Patients in Bangladesh: Experience from Tertiary Care Hospitals

KHAN SU[1], RAHMAN KM[2], HASAN ATM H[3], ISLAM SS[4], CHOWDHURY RN[5], PATWARY MKK[6], ELYAS DM[7], KHAN AM[8], HOSSAIN MA[9], AZAM MB[10], HASANAT MA[11]

Abstract:

Background: *Moyamoya disease is rare but not uncommon throughout the world. Clinical profile of childhood moyamoya (MMD) disease is not well delineated in Bangladesh.* ***Methods:*** *We conducted this cross sectional study in pediatrics and neurology department of Dhaka Medical College Hospital that involved 20 patients of MMD over a period of one year.* ***Result:*** *Among the cases about 2/3rd(65%) of the patients were within 8 years age at onset with mean age of the patients being 7.24(±3.34) years at onset with a male: female ratio of 1.2:1. Almost half of the patients had past history of intermittent episodes TIA which precipitated by hyperventilation and crying (p <0.05). Important history related to prothombotic conditions (Family History of stroke, MI, Hyperlipidemia, Obesity, Coagulation disorders) were also statistically significant (p<0.05). Sixteen patients in our series exhibited hemiparesis and out of them 4(25%) were alternating (p<0.05), followed by dysarthria at onest 13(65%). Convulsions and visual impairment were seen in 5 (25%) different patients, 3(15%) different patients had altered consciousness, involuntary movements, ataxia, headache and cognitive impairment at onset. We observed intellectual impairment in and psycho–motor retardation in two different patients. MRA abnormalities were found in 19 cases out of 20. Among 19 cases bilateral ICA stenosis with collaterals seen in 18 cases (90%), MCA stenosis along with bilateral ICA stenosis were seen in 16(80%) cases, ACA stenosis along with bilateral ICA stenosis were seen in 07(35%) cases, PCA stenosis along with bilateral ICA stenosis were observed in 05(25%) cases. No collaterals and without typical "puff of smoke" appearance was seen in 01(5%) and unilateral ICA stenosis with collaterals was seen in 01(5%) cases (probable MMD). Diagnostic Cerebral DSA was done in 07 (35%) patients and typical angiographic findings of Moyamoya disease were present in all of them.* ***Conclusion:*** *C-MMD may have various presentations. Stroke and TIA are most common presentation. MRA may well delineate the characteristics angrographic abnormality.*

Introduction:

Moyamoya disease is an uncommon chronic cerebral vasculopathy first described in 1957 by Takeuchi and Shimizu[1, 2]. It is characterized by progressive stenosis of the terminal portion of the internal carotid artery and its main branches, in

1. Dr. Sharif Uddin Khan, Associate Professor of Neurology, National Institute of Neurosciences & Hospital, Dhaka
2. Dr. Kazi Mohibur Rahman, Associate Professor of Interventional Neurology, National Institute of Neurosciences & Hospital, Dhaka
3. Dr A T M Hasibul Hasan, Registrar (Neurology), National Institute of Neurosciences & Hospital, Dhaka
4. Dr. Sirajee Shafiqul Islam. MBBS MD (Neurology). Associate Professor of Interventional Neurology, National Institute of Neurosciences & Hospital, Dhaka
5. Dr. Rajib Nayan Chowdhury, Associate Professor (Electrophysiology), National Institute of Neurosciences & Hospital, Dhaka
6. Dr. Md Khairul Kabir Patwary, Associate Professor of Neurology, National Institute of Neurosciences & Hospital, Dhaka
7. Dr. Dewan Mohammad Elyas, Assistant Professor of Neurology, National Institute of Neurosciences & Hospital, Dhaka
8. Dr. Abdul Momen Khan. MBBS MD (Neurology). Assistant Professor of Neurology, National Institute of Neurosciences & Hospital, Dhaka
9. Dr. Md Amir Hossain, Assistant Professor of Neurology, National Institute of Neurosciences & Hospital, Dhaka
10. Dr. Md Bokhtiar Azam, Assistant Professor of Neurology, National Institute of Neurosciences & Hospital, Dhaka
11. Dr. Md Amirul Hasanat, Assistant Professor of Anesthesiology, National Institute of Neurosciences & Hospital, Dhaka

association with the development of compensatory collateral vessels at the base of the brain[2, 3]. Suzuki and Takaku observed that the collateral vessels give the appearance of a "Puff of Smoke" on arteriography and given the name "moyamoya" (Puff of smoke in Japanese language) in 1969[2, 3]. Though Common among the Japanese population, Moyamoya has now been observed throughout the world in people of many ethnic backgrounds, including American and European populations[4, 5]. The incidence peaks in two age groups: children who are approximately 5 years of age and adults in their mid-40s[4, 5]. Incidence of moyamoya disease among females is 1.8 times more than that among males[6, 7]. Studies in the united states suggest an annual incidence of 0.086 per 100,000 (approximately one per million)[6, 7] and the European incidence is estimated at approximately 10% of that in Japan[5, 8]. The condition accounts for approximately 6% of childhood strokes in western countries, and half of these are in children aged less than 10 years[8].

Now-a-days, moyamoya disease is increasingly diagnosed throughout the world, and represents an important cause of 6% of childhood strokes and half of these are in children aged less than 10 years. So in any case of young stroke with undetected cause, searching for intracranial vessels abnormality by doing angiography is of paramount importance. A prompt diagnosis and early surgical revascularization can make the prognosis, much better. Without treatment, repeated strokes, transient ischemic attacks, brain hemorrhages, or seizures can lead to serious cognitive impairment, physical disability, or death. This study is therefore under taken to focus on the clinical presentation of the moyamoya diseases in Bangladesh. So, that physician's awareness will be increased and appropriate early diagnosis coupled with the expeditious intervention can be adopted to protect our child and young age groups from this morbid condition and therefore will promote the growth and productivity in life.

Materials and Methods

This was a cross sectional study conducted from July'2013 to June" 2014 in Department of Neurology and Department of Paediatrics in Dhaka Medical College Hospital (DMCH) and Paediatric neurology division of National Institute of Neurosciences and Hospital (NINS&H). Study population included stroke patients of both sexes attended in stroke clinic of neurology department and paediatric neurology clinic as well as admitted in Paediatrics and Neurology Department of Dhaka Medical College Hospital. Purposive convenient sampling technique was used. Since, it is a very rare disease, the statistical formula for sample size detection ($n=z^2pq/e^2$) is not applicable for this study. So, from the observation of different previous study, we have determined the sample size to be 40.

Inclusion criteria: Children presented with the following:

1) Focal neurological deficits of acute onset lasting greater than 24 hours

And

CT or MRI showing infarct in location consistent with neurological signs and symptoms.

and usually associated with head-ache, vomiting and clouding of consciousness to coma

And

CT or MRI showing heamorrhage in location consistent with neurological signs and symptoms.

2) Focal neurological deficits of acute onset which recovers completely within 24 hours with no visible (new) infarct on neuroimaging i.e. transient ischemic attack (TIA).

Exclusion criteria:

1) Patients with H/O recent trauma or injury to the head and neck area, Irradiation to the head, H/O recent cardiac surgery.
2) Clinical findings and Lab. findings suggestive of intracerebral SOLs and CNS infections.
3) Possible underlying diseases that can lead to Moyamoya syndrome (excluded by history and clinical examination).

Operational definition:

- Moyamoya disease:

o Moyamoya vasculopathy without any known risk factors.

o Must have bilateral disease

Moyamoya syndrome: is a phenomenon caused by an olegaemic state similar in presentation like moyamoya disease but caused by various disease entities, like a) Genetic disorders: Neurofibromatosis, Down's syndrome, Turner syndrome. (b) Hematological disorders: Sickle cell anaemia, Thalassemia, Aplastic anaemic. (c) Infectious disease: Tubercular meningitis, Leptospirosis. (d) Neoplasms: craniopharyngioma, wilm's Tumour. (e) Drug abuse: Phenobarbital (f) Irradiation for head neck tumour. (g) Other: Polycystic Kidney disease, Trauma.

Procedure of data analysis and interpretation

All the data was collected and recorded systematically in a questionnaire and analyzed by using SPSS version 17 and all the qualitative data was presented in terms of proportion or percentage at 95% CI (confidence interval). Qualitative data was compared in between different age groups and sex by chi-square test.

Ethical implications

Voluntary informed written consent was taken from the parents before collecting data. Privacy, anonymity and confidentiality were maintained during the procedures. Ethical clearance was taken from the ethical committee to perform the investigations and study.

Result:

This cross sectional analytical study was done in department of paediatrics and neurology, Dhaka Medical Collage Hospital for a period of 12 month. Total 20 patients diagnosed as a moyamoya disease were enrolled in this study. Among the cases about 2/3rd(65%) of the patients were within 8 years age at onset with mean age of the patients being 7.24(±3.34) years at onset, minimum age was 03 and maximum age was 14 (Table-1). Among them male were 11(55%) and female were 9(45%) with a male: female ratio of 1.2:1 (Figure-1).

Table-I

Distribution of patients by age at onset (n=20)

Age group	Frequency	Percentage
3-5 years	07	35.0
5-8 years	06	30.0
8-12 years	05	25.0
12-15 years	02	10.0
Mean (±SD)	7.24(±3.34)	3-14 years

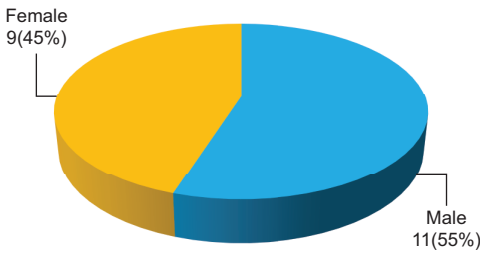


Fig.-1: *Distribution of patients by age at onset (n=20).*

Almost half of the patients had past history of intermittent episodes TIA which precipitated by hyperventilation and crying ($p < 0.05$). Important history related to prothombotic conditions (Family History of stroke, MI, Hyperlipidemia, Obesity, Coagulation disorders) were also statistically significant ($p<0.05$). Past H/O meningitis, otitis media and head neck trauma were present in 2 (10%) different patients and one (5%) patients had Familial occurrence of moyamoya disease (FMMD) (Table-2). Sixteen patients in our series exhibited

hemiparesis and out of them 4(25%) were alternating ($p<0.05$), followed by dysarthria at onest 13(65%). Convulsions and visual impairment were seen in 5 (25%) different patients, 3(15%) different patients had altered consciousness, involuntary movements, ataxia, headache and cognitive impairment at onset. Signs of meningeal irritations and papilloedema were present in 2(100%) same patients with haemorrhagic disease type ($p<0.05$). We observed intellectual impairment in and psycho–motor retardation in two different patients (Table-2).

In present study, MRA abnormalities were found in 19 cases out of 20. Among 19 cases bilateral ICA stenosis with collaterals seen in 18 cases (90%), MCA stenosis along with bilateral ICA stenosis were seen in 16(80%) cases, ACA stenosis along with bilateral ICA stenosis were seen in 07(35%) cases, PCA stenosis along with bilateral ICA stenosis were observed in 05(25%) cases, No collaterals and without typical "puff of smoke" appearance was seen in 01(5%) and unilateral ICA stenosis with collaterals was seen in 01(5%) cases (probable MMD). This one patient, who had no collaterals, not "puff of smoke" appearance and this patient was diagnosed by cerebral DSA (Table-3). Diagnostic Cerebral DSA was done in 07 (35%) patients and typical angiographic findings of Moyamoya disease were present in all of them (Table-4).

Table-II

Association between relevant clinical history and age group.

Clinical history	Age group		Total			P value
	≤5 years N=8	>5 years N=12		OR	95%CI	
H/O prematurity & any other perinatal complications	01	05	06(30%)	0.20	0.01-2.18	0.32
Family History of stroke, MI, Hyperlipidemia, Obesity, Coagulation disorders	04	01	05(25%)	11.0	0.92-130.32	0.03*
Familial occurrence of moyamoya disease (parent-offspring)	00	01	01(5%)	1.72	1.17-2.53	1.0
Significant Past History (meningitis, otitis media)	01	00	01(5%)	—	—	0.40
Past history of TIA(intermittent episodes)	01	09	10(50%)	0.05	0.0-0.74	0.01*
TIA precipitated by hyperventilation, crying	01	09	10(50%)	0.05	0.0-0.74	0.01*
Developmental delay	01	00	01(5%)	—	—-	0.33
H/O any hematologic diseases	0	01	01(5%)	00	0.0-28.99	1.0
H/O any CNS(TBM) or systemic infections	1	0	1(5%)	—	—	1.0
H/O autoimmune vasculitis like SLE & others	0	01	1(5%)	—	—-	1.0
presence of any childhood cancer, metabolic disorders like homocystinuria, hyperlipidemia	0	01	1(5%)	—	—	1.0
H/O any Head-Neck trauma & others associated conditions	0	1	1(5%)	—	—	1.0

Table-III

MRA findings of the study population

MRA findings	Number	Percentage
Bilateral ICA stenosis with collaterals (1)	18	90
(1)+MCA stenosis with collaterals	16	80
(1)+ACA stenosis with collaterals	07	35
(1)+PCA stenosis with collaterals	05	25
No collaterals and without typical "puff of smoke" appearance	01	5
unilateral ICA stenosis with collaterals	01	5

Table-IV

Findings of the Cerebral DSA

Findings of the Cerebral DSA	Frequency	Percent
Typical angiographic findings of Moyamoya disease(stenosis) present	07	35.0
Not done	13	65.0
Total	20	100.0

Discussion:

In this study , we selected only definite and probable cases which were diagnosed by the diagnostic criteria of the Research Committee on Moyamoya disease (spontaneous occlusion of the circle of Willis) of the Ministry of Health and Welfare of Japan (RCMJ) and excluded patient with systemic disease (moyamoya syndrome). Among 20 cases, 2/3rd(65%) of the patients were within 8 years with mean age of the patients being 7.24(±3.34) years at onset, minimum age was 03 and maximum age was 14. Male were 11(55.5%) and female were 9(45%). Male: Female ratio1.2:1. Ikezaki et al.[9] reported that, the patients under 10 years of age showed the first highest peak and constituted approximately 36% and 55% of all Korean and Japanese cases, respectively. A significant female predominance was seen in both countries. The familial occurrence rates were 1.8% and 6% in South Korea and Japan, respectively. Guzman et al.[10] reported that, pediatric patients with a mean age of 10.1 years (range 1–17.9 years) showed highest peak. A typical bimodal age distribution was observed. There was a 1:1 female/male distribution in the young children, which changed to 3:1 in the second decade of life and thereafter.

In this study, patients presented with hemiparesis, dysarthria, convulsions (generalized and focal/febrile and afebrile) and visual impairment, abnormal vital signs, altered consciousness, involuntary choreiform movements, ataxia, headache and cognitive impairment, intellectual impairment and psycho–motor retardation. The clinical features of patients with Moyamoya disease reflect the anatomic territory of the brain affected by the diseased vessel. In the Annual Report for the special working group of Welfare Ministry for Moyamoya in 1979, Yamaguchi et al. described four major types of Moyamoya disease according to clinical manifestations; the hemorrhagic type, the infarction type, TIA type, and epileptic type; the last three types being the most common in paediatric age group[11].

In present study, clinical manifestations were similar to those reported earlier in the literature including ischemic and hemorrhagic stroke, TIAs, headache, and seizure. Ischemic events were the most common presenting symptom in pediatric (51%) patients in R. Guzman et al.[10] series, a finding described in other large series as well. The incidence of hemorrhagic presentation in pediatric patients is known to be rare. Guzman et al.[10] reported that, 2.1% paediatric patients presenting with intracerebral hemorrhages, which was similar to present study. Headache has been described as a symptom in up to 49% of patients, and it can be associated with a hemorrhagic presentation of MMD or as an independent presenting symptom in children.

In present study, MRA abnormalities were found in 19 cases out of 20 which include bilateral ICA stenosis with collaterals, MCA stenosis along with bilateral ICA stenosis, ACA stenosis along with bilateral ICA stenosis, PCA stenosis along with bilateral ICA stenosis, etc. No collaterals and without typical “puff of smoke” appearance was seen in 01(5%) cases and unilateral ICA stenosis with collaterals was seen in 01(5%) cases(probable MMD). In South Korea, infarction is also higher in children than adults (*P*=.0024). Approximately 80% of the children had disease of the ischemic type in both countries. In a multivariate analysis of age at onset, sex, and angiographic stage, the age at onset (childhood onset) again showed the highest correlation with the presentation of ischemic type (odds ratio=0.0902 with confidential intervals from

0.0503 to 0.162; *P*<.0001) were similar to present study[9]. In this study, out of 20 patients, cerebral DSA was done in 07(35%) patients and found typical angiographic findings of Moyamoya disease (stenosis) were present.

We had some limitations in this study. First of all, the sample size was small. Secondly, data was collected from three tertiary hospitals only which may not reflect the total scenario in the country.

CONCLUSION

From the findings of the present study and discussion therefore, it can be concluded that paediatric patients with moyamoya disease usually present with TIAs or ischemic stroke in Bangladesh, Hemiparesis was the most common clinical presentation at onset, in our study, but it's alternating nature can lead to diagnostic challenges. Involuntary chorei-form movements and ataxia, migraine like headache, afebrile focal seizures, sudden visual impairment can also be the initial sign of the moyamoya disease without hemiparesis. MRA is a nice tool to delineate the vascular changes of the disease.

Reference:

1. Takeuchi K, Shimizu K. Hypogenesis of bilateral internal carotid arteries. No To Shinkei. 1957; 9: 37- 43.
2. Suzuki J, Takaku A. Cerebrovascular 'moyamoya' disease: disease showing abnormal net-like vessels in base of brain. Arch Neurol 1969; 20:288-99.
3. Fukui M, Guidelines for the diagnosis and treatment of spontanceous occlusion of the circle of Willis ("moyamoya" disease). Research Committee on Spontaneous Occlusion of the Circle of Willis (Moyamoya Disease) of the Health and Welfare, Japan. Clin Neurol Neurosurg 1997;99(Suppl. 2):S238-40.
4. Baba T, Houkin K, Kuroda S. Novel epidemiological features of moyamoya disease. J Neurol Neurosurg Psychiatry 2008; 79:900-904.
5. Wakai K, Tamakoshi A, Ikezaki K, et al. Epidemiological features of moyamoya disease in Japan: findings from a nationwide survey. Clin Neurol Neurosurg 1997; 99:Suppl 2:S1-S5.
6. Han DH, Nam DH, Oh CW. Moyamoya disease in adults: characteristics of clinical presentation and outcome after encephalo-duro-arterio-synangiosis. Clin Neurol Neurosurg 1997; 99:Suppl 2:151-55.
7. Han DH, Kwon OK, Byun BJ, et al. A co-operative study: clinical characteristics of 334 Korean patients with moyamoya disease treated at neurosurgical institutes (1976-1994). Acta Neurochir (Wien) 2000; 142:1263-73.
8. Epidemiological features of moyamoya disease in Japan: findings from a nationwide survey. Kenji wakai, Akiko Tomakoshi, Kiyonobu Ikezaki, Masashi Fukui, Takashi Kawamura, Rie Aoki, Masayo Koima, Yingsonglin, Yoshiyuki Ohnon. Clinical neurology & neurosurgery, Oct. 1997; vol-99, supplement 2, page S1-35.
9. Ikezaki K, Han DH, Kawano T, Kinukawa N, Fukui M. A Clinical Comparison of Definite Moyamoya Disease between South Korea and Japan, *Stroke. 1997; 28: 2513-17*
10. Guzman R, Lee M, Achrol A, Teresa Bell-Stephens T RN, Kelly M, Huy M, et al. Clinical outcome after 450 revascularization procedures for moyamoya disease, *J. Neurosurg. 2009;22:1-9*
11. Hayashi K, Uyama KS, and Izumi Nagata I. Clinical Features of Unilateral Moyamoya Disease, Neurol Med Chir (Tokyo) 2010; 50:378-85.

Bangladesh Journal of Neuroscience 2017; Vol. 33 (1): 30-33

Cerebral Venous Sinus Thrombosis- A Study of 4 Cases

SHEIKH AK[1], BISWAS R[2], ROY A[3], TUQAN S[4], SARKER M[5], BHUIYAN MM[6]

Abstract:

Cerebral venous sinus thrombosis is an uncommon but important cause of stroke, especially in young-aged woman. Clinical presentation is variable, usually in the form of focal neurological deficit, seizure, headache and other features of raised intracranial pressure, leading to misdiagnosis or delay in treatment. Here we report 4 cases of venous sinus thrombosis with variable presentation. Diagnosis is confirmed by neuroimaging including magnetic resonance imaging with magnetic resonance venography of brain. Treatment consists of anticoagulation along with supportive management.

Key words: *Cerebral venous sinus thrombosis, Stroke, Magnetic resonance venography*

Introduction:

Cerebral venous sinus thrombosis (CVST) is a rare disorder accounting for less than 1% of all strokes[1]. In the adult population, the incidence of CVST is estimated to be around 3-4 cases per one million people and most commonly occurs between the ages of 20-40 years with a mean age of 38.7 years[2]. Its epidemiology has changed over past few decades with increasing prevalence that may be attributed to not only greater awareness among the physicians, but also of greater availability of noninvasive radio diagnostic modalities like MRI with MRV[3]. Presenting symptoms are variable; therefore it is important for clinicians to consider CVST when evaluating patients, especially those at increased risk of thrombosis.

Case 1: A 39 year old lady presented with headache for 7days, 2 episodes of convulsion and irregular per vaginal bleeding for 2 months for which she took tab norethisterone acetate for 2 cycles. She denied any history of fever, blurred vision, ear discharge, speech abnormality, sphincter disturbance or head injury. On examination, she was afebrile with pulse 84/min, regular, BP-140/80 mm of Hg, respiratory rate-18/min. Neurological examination revealed only bilateral papilledema. Examination of other systems was normal. Investigation revealed normal biochemical, coagulation and vasculitic profile. Ultrasound showed bulky uterus and she was diagnosed as dysfunctional uterine bleeding. CT head was normal. MRI of the brain showed infarct in left parietal lobe and MRV revealed thrombosed venous sinuses (figure 1). She was managed with low molecular weight heparin 40 mg twice daily for 7 days followed by tab rivaroxaban 20 mg daily and tab levetiracetam 500 mg twice daily. During active bleeding, she was treated with low dose heparin along with tranexamic acid and there was no complication. She was discharged on day 14 of her illness and advised to continue anticoagulation for 6 months.

Case 2: A 37 year old male presented with occipital headache with blurring of vision for 2 weeks. He denied history of fever, vomiting, seizure or altered sensorium. On examination, he was afebrile with hemodynamically stable. Neurological examination revealed bilateral papilledema. Biochemical, coagulation and vasculitic profile were within normal limit. CT head & MRI brain was normal.

1. Dr. Abdul Kader Sheikh MBBS, FCPS, MD. Associate Professor of Neurology, Bangabandhu Sheikh Mujib Medical University & Consultant, Neurology, Square Hospitals Limited
2. Dr. Rama Biswas MBBS, FCPS, MD. Associate Consultant, Neurology, Square Hospitals Limited
3. Dr. Anindita Roy MBBS, MRCP. Specislist , Medicine, Square Hospitals Limited
4. Dr. Sadiqa Tuqan MBBS, FCPS. Specislist , Medicine, Square Hospitals Limited
5. Dr. Mallika Sarker MBBS, MRCP. Specislist , Medicine, Square Hospitals Limited
6. Prof. Md. Moniruzzaman Bhuiyan, Professor Neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.

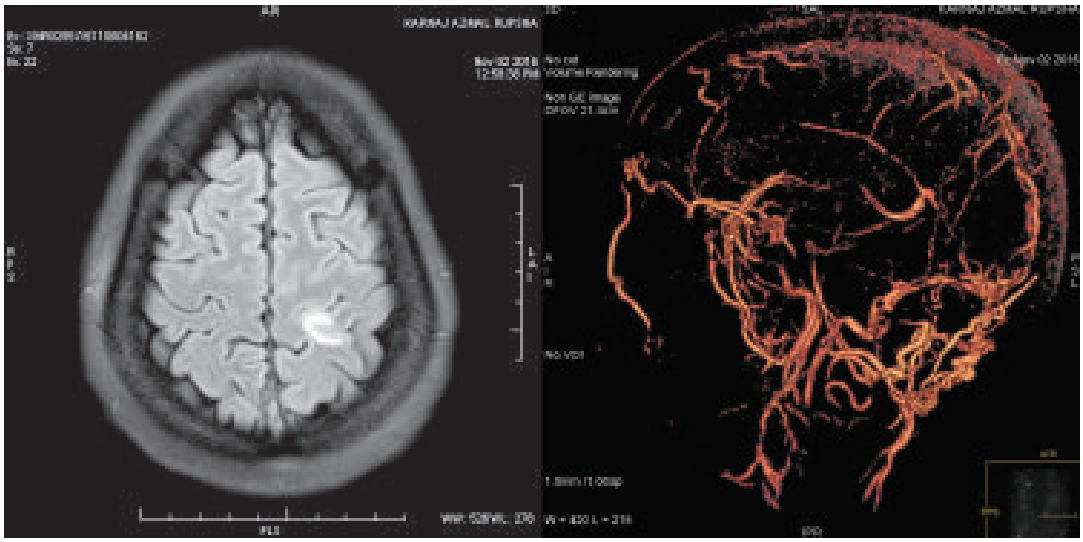


Fig.-1: *MRI brain showing left parietal lobe infarct and MRV showing thrombosed venous sinuses*

MRV showed evidence of superior sagittal sinus thrombosis (figure 2). He was treated with low molecular weight heparin 60 mg twice daily for 10 days followed by tab rivaroxaban 20 mg daily for 6 months.

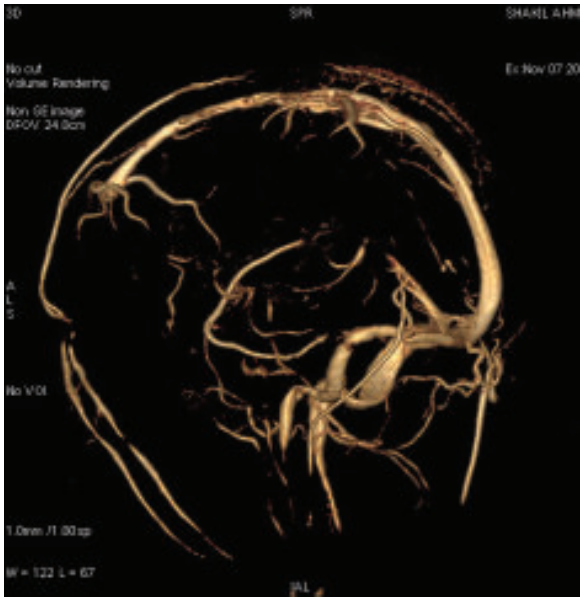


Fig.-2: *MRV of brain showing thrombosis of superior sagittal sinus*

Case 3: A 42 year old hypertensive male presented with headache, vomiting for 7-8 times and blurring of vision for 1 day. He denied any history of fever, convulsion, altered sensorium, speech abnormality or head injury. On examination, he was afebrile, pulse-94/min, BP-150/85 mm of Hg. Neurological examination revealed bilateral 6th cranial nerve palsy with 1mm pupil in both eye. CT head was normal. MRI brain showed pontine infarct and MRV showed evidence of superior sagittal sinus thrombosis (figure 3). He was started low molecular weight heparin 60 mg twice daily followed by tab rivaroxaban 20 mg daily for 6months.

Case 4: A 73 year old male presented with abdominal distension with vomiting for 10 days, hiccup for 7 days and drowsiness for 3 days. On examination, he was drowsy, dehydrated, pulse-98/min, BP-100/70 mm of Hg, respiratory rate-22/min. Abdomen was distended with sluggish bowel sound. Neurological examination showed GCS-12 (E3V4M5), pupil-2mm in both eye, absence of papilledema and focal neurological deficit. Among biochemical profile, serum sodium -129 mmol/L. Plain X-Ray abdomen revealed distended bowel loop. Upper GIT endoscopy reported pyloric stenosis. CT head & MRI brain was normal. MRV showed left transverse sinus thrombosis (figure 4). He was treated conservatively for subacute intestinal obstruction along with low molecular weight heparin 60 mg twice daily. He was gradually improving and discharged on 20 day of his illness with continuation of oral anticoagution for 6 months

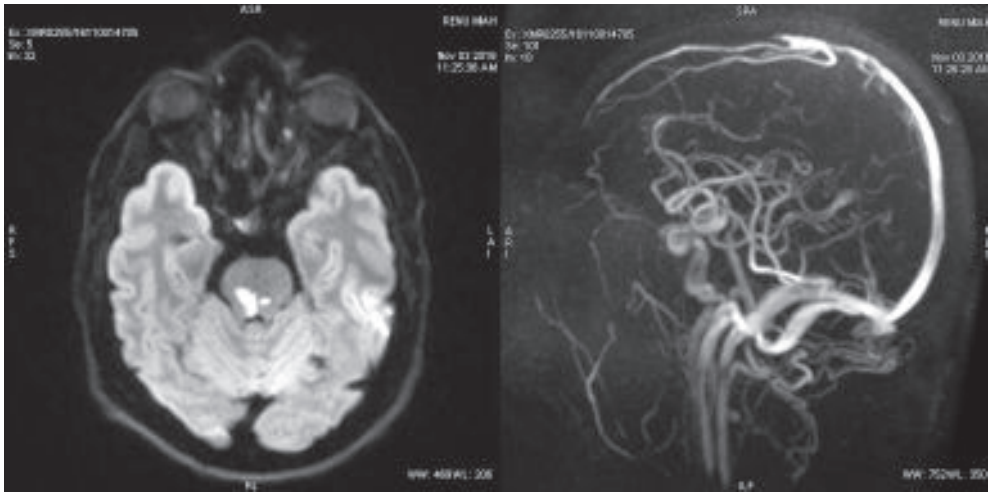


Fig.-3: *MRI of brain showing pontine infarct and MRV showing thrombosis of superior sagittal sinus*

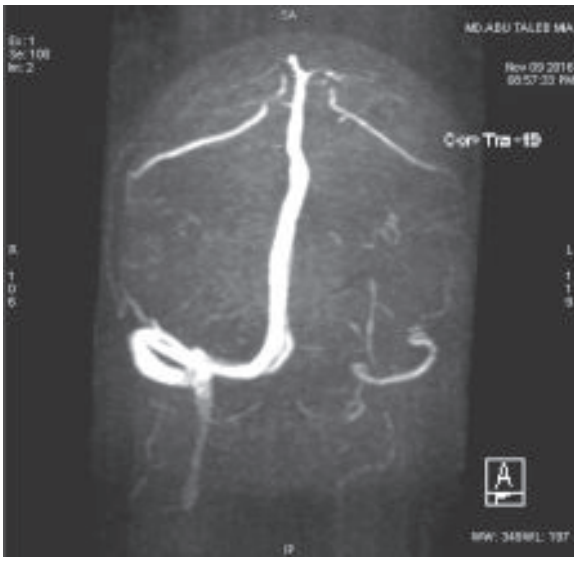


Fig.-4: *MRV of brain showing thrombosis of left transverse sinus*

Discussion:

Cerebral venous sinus thrombosis is a potential life threatening condition that requires rapid diagnosis and urgent treatment. The main causes of CVST are dehydration, puerperium, antiphospholipid antibody syndrome, malignancy, infection, polycythemic state, paraproteinemia, factor V Leiden & protein C resistance, hyperhomocysteinemia, drugs like oral contraceptive. No risk factor can be discovered after extensive investigation in 25% of cases[4]. In the 4 cases, only 1 had history of taking oral pill.

CVST most commonly involves superior sagittal sinus (72%) followed by lateral sinus (70%). More than one sinus involved in 30-40% of cases[5]. The sinuses involved in our cases were superior sagittal sinus in case 2& 3, transverse sinus in case 4 and multiple sinuses in case 1. So superior sagittal sinus was commonly involved in this study which was similar to Ashjadadeh N[6]. Clinical presentations are headache, seizure, focal neurological deficit and papilledema. Unusually patients present with thunderclap headache mimicking subarachnoid hemorrhage[4]. Among the cases, 3 patients presented with headache, 1 with seizure and 2 with papilledema.

Neuroimaging modalities of choice in CVST are computerized tomographic (CT) scan and MRI with MRV. Classically, CT scan depicts a hyperatenuating thrombus in the occluded sinuses; however, this sign is only present in 25% of patients. While CT scan is quick test to obtain in emergency room to assess extent of parenchymal injury. CT and MR angiography are also helpful to demonstrate the extent of thrombosis[7]. MRI with MRV is the investigation of choice which shows absence of flow void in the thrombosed sinuses. New modalities for diagnosis include 2D time-of-flight and phase contrast MRV[8]. In all of our cases, conclusive evidence was found on MRI with MRV. Work up for thrombophilic state such as Protein C, Protein S, antithromboin III, antiphospholpid antibody was done which was normal in this study.

Anticoagulation is the mainstay of treatment in CVST. Patients can be treated effectively with both forms of heparin .Oral anticoagulation should be initiated following acute treatment with heparin and continued for at least 3-6months if no procoagulant state was found or lifelong if there is an irreversible procoagulant state[9]. In all 4 cases, they were treated with low molecular weight heparin followed by oral anticoagulation (rivaroxaban) for 6 months. Warfarin was used as oral anticoagulant in most studies[10, 11]. But we treated with rivaroxaban and there was no complication. Outcome was good in all cases.

Conclusion:

CVST is a rare cause of stroke that presents with variable symptoms that can mimic other neurologic pathologies. Prompt verification of thrombus with neuroimaging is necessary to provide adequate treatment in a timely manner. Treatment outcome was good by using rivaroxaban.

References:

1. Ferro JM, Canhao P, Bousser MG, Barinagarrementeria F. Prognosis of cerebral vein and dural vein thrombosis: Results of the International Study of Cerebral Vein and Dural Vein thrombosis (ISCVT).*Stroke: A Journal of Cerebral circulation*. 2004; 35:664-70.
2. Ehtisham A, Stern BJ. Cerebral venous sinus thrombosis: A review. *The neurologist,* 2006;12: 32-8.
3. Siddiqui FM, Kamal AK. Incidence and epidemiology of cerebral venous thrombosis. *J Pak Med Assoc*.2006;56:485-7.
4. Mehta SR, Swammy AJ, Gutta A. A clinical profile of cortical venous thrombosis- A report of 20 cases. *JAPI.* 2002;50:76-7.
5. Brousser MG, Barnett HJM. Cerebral Venous Thrombosis. In: Stroke: pathophysiology, diagnosis and management. 2nd edition. New York. Churchill Livingstone. 1992; 517-37.
6. Ashjazadeh N, Haghighi AB, Poursadeghfard M, Azin H. Cerebral venous sinus thrombosis: A case series analysis. *IJMS*. 2011; 36(3): 178-82.
7. Khandelwal, N, Agarwal, A, Kochhar, R, Bapuraj, J.R., Singh P, Prabhakar S, Suri S. Comparison of CT venography with MR venography in cerebral sinovenous thrombosis. AJR. *American Journal of Roentgenology*, 2006; 187; 1637-43.
8. Wang AM. MRA of Venous sinus thrombosis. *Clin Neurosci, 1997; 4:158-64*
9. Coutinho JM, Stam J. How to treat cerebral venous sinus thrombosis. *Journal of Thrombosis and Haemostasis: JTH*.2010; 8:877-83.
10. Sultana N, Chowdhury MH, Mahbub S, Alam B. Cerebral venous sinus thrombosis: A rare presentation of headache mimicking subarachnoid haemorrhage. J Medicine, 2009; 10:115-18.
11. Mehta B, Muthukrishnan SM, VaradarajuluVSM, GuptaMA. Cerebral venous sinus thrombosis: A great masquerader. *MJAFI*, 2004; 60:299-301.

Bangladesh Journal of Neuroscience 2017; Vol. 33 (1): 34-38

REVIEW ARTICLE

Role of occupational therapy in improving quality of life of physically challenged persons

RAHMAN MS

Abstract:

Occupational therapy is a branch of medicine which uses different methods to help physically and mentally ill people to develop, maintain, and recover skills needed to function in day to day life, as well as in workplace environments. Thus lives of millions of disabled all over the world are enhanced to a meaningful quality of life. Occupational therapists also focus much of their work on identifying and eliminating environmental barriers to independence and participation in daily activities. This is a client-centered practice that places emphasis on the progress towards the client's goals. The interventions are made on adapting the environment, modifying the task, teaching the skill, and educating the client/family in order to increase participation in and performance of daily activities, particularly those that are meaningful to the client. They often find it challenging to implement client-centered and occupation-based assessment tools into practice. This part of rehabilitation medicine is neglected in our country. More work is needed to understand how best practices can be incorporated into a changing occupational therapy daily practice. The aim of this review article is to highlight the importance of occupational therapy and its application in improving the quality of life and quality adjusted life years in physically challenged persons.

Introduction:

Occupational science, the study of occupation, was created in 1989 as a tool for providing evidence-based research to support and advance the practice of occupational therapy, as well as offer a basic science to study topics surrounding "occupation"[1]. Occupational therapists have during many decades used a wide range of formalized assessment tools, including tools borrowed from other disciplines, in order to provide relevant services to clients[2]. During the last 20 years, the profession has seen a steady increase in the development and validation of assessment tools that more distinctly reflect occupational therapy domains of practice such as quality of occupational performance,[2,3] occupational gaps[4], and quality of social interaction[5]. Occupational therapists use assessment tools with an intended purpose to better guide intervention planning and to provide baseline and outcome measures in order to track progress and/or change among clients. Occupation-focused assessment refers to keeping the focus on occupation, with an immediate impact on occupational performance[6].

Practicing occupational therapy:

The role of occupational therapy allows occupational therapists to work in many different settings, work with many different populations and acquire many different specialties. This broad spectrum of practice lends itself to difficulty categorizing the areas of practice that exist, especially considering the many countries and different health care systems. In America the Occupational Therapy Practice Framework (OTPF) is the core competency of occupational therapy. The OTPF framework is divided into two sections: domain and process. The domain includes environment, client factors, such as the individual's motivation, health status, and status of performing occupational tasks. The domain looks at the contextual picture to help the occupational therapist understand how to diagnose and treat the patient. The process is the actions taken by the therapist

Prof. Md. Shahidur Rahman, Professor of Physical Medicine and Rehabilitation, Bangabandhu Sheikh Mujib Medical University

to implement a plan and strategy to treat the patient[7].

Studies show that contributions from occupational science are also reflected in clinical reasoning. Clinical reasoning is regarded as core element in health professional's practice and provides a link between research and practice[8].

Promotion of health and quality of life:

The practice area of Health and Wellness is emerging steadily due to the increasing need for wellness-related services in occupational therapy in order to improve the quality of life and quality adjusted life years. A connection between wellness and physical health, as well as mental health, has been found; consequently, helping to improve the physical and mental health of clients can lead to a general increase in wellness. Prevention of disease and injury, prevention of secondary conditions, promotion of the well-being of those with chronic illnesses, reduction of health care disparities, and enhancement of factors that impact quality of life, promotion of healthy living practices, social participation, and occupational justice should be focused in the practice area[9]. There must also be a shift from performance to participation in daily life, with evidence supporting the link between *participation* and a person's health status. A paradigm shift is imperative to reorganize the profession and make a dramatic shift[10].

The quality of life (QOL) concept was introduced in healthcare research to complement the traditional medical outcomes, such as mortality and morbidity[11]. Nowadays, this concept constitutes the highest level of health outcomes. The literature suggests that the factors that contribute to improve QOL level in older adults are maintenance of independence, autonomy, adaptability, social participation, social role functioning and others.[12] Those factors remain an important topic of study because of a need to clarify the specific influence of each factor on QOL.

Rehabilitation need:

Occupational therapists address the needs of rehabilitation, disability and participation. Occupational therapists provide treatment for adults with disabilities in a variety of settings including hospitals (acute rehabilitation, in-patient rehabilitation, and out-patient rehabilitation), home health, skilled nursing facilities, and day rehabilitation programs. When planning treatment, occupational therapists address the physical, cognitive, psychosocial, and environmental needs involved in adult populations across a variety of settings such as improving of life with assistive devices and telehealth[13]. One study showed that fall risk is closely related to ADL capability, and that the frequency of leaving the house is very important for reducing fall risk[14].

Mental health

Mental health and the moral treatment movement have been recognized as the root of occupational therapy[15]. According to the World Health Organization, mental illness is one of the fastest growing forms of disability. There is a focus on prevention and treatment of mental illness in populations including children, youth, the aging, and those with severe and persistent mental health issues[16]. More specifically, military personnel and veterans are populations that can benefit from occupational therapy but currently, there is a lack of focus on these populations regarding mental health care.[44] Occupational therapists provide mental health services in a variety of settings including hospitals, day programs, and long-term-care facilities[17].

Quality of life in physically challenged persons

To enable independence of older adults at home, occupational therapists perform fall screens and evaluate older adults functioning in their homes and recommend specific home modifications. When addressing low vision, occupational therapists modify tasks and the environment. While working with individuals with Alzheimer's Disease (AD), occupational therapists focus on maintaining quality of life, ensure safety, promote independence, and utilize retained abilities. The evidence for the effect of interventions should be appropriately designed to establish, modify, and maintain activities of daily living (ADLs), instrumental activities of daily living (IADLs), leisure, and social participation on quality of life (QOL), health and wellness, and client and caregiver satisfaction for people with Alzheimer's disease and related dementias[18].

A retrospective study done by Elisie and her colleagues determined whether the multicomponent rehabilitation program of a memory clinic had positive outcomes on ameliorating everyday functioning, quality of life, mood and behavioral disturbances of persons with dementia and reducing distress and burden of caregivers. For persons with dementia (n = 22), participating in the program did not improve everyday functioning and cognition but ameliorated quality of life significantly (Z=–2.7, p=0.006, 95% CI (.003–.005)) and stabilized mood, emotional and behavioral disturbances for 60% or more of them. This program appears to be promising and valuable, and might reduce institutionalization rates.[19]

Adults with cerebral palsy need assistance to maximize their capabilities, interact with others, and achieve independence. They experience difficulty communicating their needs to successfully obtain medical/rehabilitation and independent living services, which are necessary to achieve independent living. Knowledge of the experience of such clients can help occupational therapists to better serve them[20]. Following a six-week 3 hours per week clinical upper extremity functional training, study participants demonstrated significant and clinically meaningful functional improvements measured by motor activity log, Canadian occupational performance measure and wolf motor function test time scale. In contrast, the task oriented approach failed to demonstrate significant improvements on the wolf motor function test quality scale or on the impairment measures, upper extremity active range of motion and strength measures[21].

Occupational therapy and ICF

The International Classification of Functioning, Disability and Health (ICF) is a framework to measure health and ability by illustrating how these components impact one's function. This relates very closely to the Occupational Therapy Practice Framework, as it is stated that "The profession's core beliefs are in the positive relationship between occupation and health and its view of people as occupational beings[22]. The ICF is also built into the second edition of the practice framework. Activities and participation examples from the ICF overlap Areas of Occupation, Performance Skills, and Performance Patterns in the framework. The ICF also includes contextual factors (environmental and personal factors) that relate to the context in the framework. In order to enhance occupational therapy reasoning in clinical practice, different elements such as client-centered approach, evidence-based care and interdisciplinary work should be taken into account, but is a challenge[23].

Although the ICF can be very useful for occupational therapists, it is noted in the literature that occupational therapists should use specific occupational therapy vocabulary along with the ICF in order to ensure correct communication about specific concepts[24]. The ICF might lack certain categories to describe what occupational therapists need to communicate to clients and colleagues. It also may not be possible to exactly match the connotations of the ICF categories to occupational therapy terms. The ICF is not an assessment and specialized occupational therapy vocabulary should not be replaced with ICF terminology[25]. As the health care system continues to evolve toward one based on quality not quantity, demonstrating the value of occupational therapy has never been more important. Providing high-quality services, achieving optimal outcomes and identifying and promoting occupational therapy's distinct value are the responsibilities of all practitioners[26].

Conclusion: Physically challenged persons face widespread barriers in accessing services such as those for health care (including rehabilitation), education, employment, social services including housing and transport. Occupational therapists can assess and treat to develop, recover, or maintain the daily living and work skills of people with a physical, mental, or cognitive disorder. Occupational therapy is well known as part of recovery for people who've had a stroke or surgery: it helps them relearn everyday activities and adjust to doing them differently. But occupational therapy can also make a difference for people struggling with the physical changes that accompany aging, such as hand arthritis or hip or knee problems that cause pain and problems with mobility. Creating links among occupation, occupational participation,

and health in ways that are understandable to the general public, other health professionals, policy makers, and society must be occupational therapy's mission. The profession must continue to strategize how occupational therapy becomes the leader, in the promotion of health, well-being, and quality of life. Ultimate goal is to bring these physically challenged persons into mainstream of development so that they can contribute to the national economy.

References:

1. Yerxa, EJ, Clark, F, Jackson, J, Pierce, D, Zemke, R. An introduction to occupational science, a foundation for occupational therapy in the 21st century. OccupTher Health Care 1989; 6: 4.
2. Eric Asaba, Mio Nakamura, AkieAsaba, and Anders Kottorp, "Integrating Occupational Therapy Specific Assessments in Practice: Exploring Practitioner Experiences," Occupational Therapy International, vol. 2017, 2017.
3. M. Law, S. Baptiste, M. A. McColl, A. Opzoomer, H. Polatajko, and N. Pollock, "The Canadian occupational performance measure: an outcome measure for occupational therapy," Canadian Journal of Occupational Therapy, 1990; vol. 57, no. 2, pp. 82–87.
4. Fisher, A. G., & Jones, K. B., Assessment of Motor and Process Skills; Development, standardization, and administration manual 7th ed. 2012, Vol. 1 Fort Collins, CO: Three Star Press.
5. G. Eriksson, K. Tham, and J. Borg, "Occupational gaps in everyday life 1–4 years after acquired brain injury," Journal of Rehabilitation Medicine, 2006, vol. 38, no. 3, pp. 159–65.
6. A. G. Fisher, "Occupation-centered, occupation-based, occupation-focused: Same, same or different?" Scandinavian Journal of Occupational Therapy, 2013; vol. 20, no. 3, pp. 162–73,
7. Occupational Therapy Practice Framework: Domain and Process (3rd Edition)". *American Journal of Occupational Therapy*. 2014; 68 (Suppl. 1): S1–S48.
8. 8. Kristensen HK & Petersen KS, Occupational science, a contributor to occupational therapists Clinical reasoning, Scandinavian J of occupational therapy, 2016, vol 23 issue 3, p- 240-43.
9. Brownson, C. A.; Scaffa, M. E. "Occupational therapy in the promotion of health and the prevention of disease and disability statement". *American Journal of Occupational Therapy*2001; 55 (6): 656–60.
10. Michael A. Pizzi; Lorie Gage Richards. Promoting Health, Well-Being, and Quality of Life in Occupational Therapy: A Commitment to a Paradigm Shift for the Next 100 Years. American Journal of Occupational Therapy, 2017;71: p1-7.
11. Paskulin LMG, Molzahn A (2007). Quality of life of older adults in Canada and Brazil. *Western Journal of Nursing Research*29(1): 10–26.
12. Walker A. A European perspective on quality of life in old age. *European Journal of Ageing 2005;* 2(1): 2–12
13. Radomski, M.V.Occupational function, definition process and history, planning guiding and documenting practice In*Occupational Therapy for Physical Dysfunction*6th ed. 2008;edtrs. Baltimore, MD: Lippincott Williams & Wilkins p 40-60.
14. Yokoya T, Demura S, Sato S; Relationships between physical activity, ADL, capability and fall risk in community-dwelling Japanese elderly population. Environmental Health and Preventive Medicine 2007; 12: 25–32.
15. Brown, C & Stoffel V. Occupational Therapy in Mental Health.A Vision for Participation.1st ed. FA Davis Company, Philadelphia. 2010.ISBN-13: 978.
16. World Health Organization. "Mental Health Atlas 2011". Retrieved 19 April 2012.
17. Cogan, A M. Supporting our military families: a case for a larger role for occupational

therapy in prevention and mental health care". American Journal of Occupational Therapy 2014; 64 (8): 478 – 83.

18. Lori Letts; Mary Edwards; Julie Berenyi; Kathy Moros; Colleen O'Neill; Colleen O'Toole; et al; Using Occupations to Improve Quality of Life, Health and Wellness, and Client and Caregiver Satisfaction for People With Alzheimer's Disease and Related Dementias; American Journal of Occupational Therapy, September/October 2011, Vol. 65, 497-504.
19. Elise Cornelis, Ellen Gorus, Ingo Beyer, Katrien Van Puyvelde, Siddhartha Lieten, et al; A retrospective study of a multicomponent rehabilitation program for community-dwelling persons with dementia and their caregivers British Journal of Occupational therapy; 2018Vol. 81, no. 1,p. 5–14
20. Alice Kibele. Occupational Therapy's Role in Improving the Quality of Life for Persons With Cerebral Palsy. American Journal of Occupational Therapy, June 1989, Vol. 43, 371-77.
21. Khader A. Almhdawi, Virgil G. Mathiowetz, Matthew White,Robert C delMas.Efficacy of Occupational Therapy Task-oriented Approach in Upper Extremity Post-stroke RehabilitationOccupational therapy International 2016 Vol 23 No. 4, p-444-56.
22. Roley SS, DeLany JV, Barrows CJ, Brownrigg S, Honaker D, Sava DI,et al ; Occupational therapy practice framework: domain & practice, Am J OccupTher. 2008 Nov-Dec;62(6):625-83.
23. R. Ghysels,E. Vanroye,M. Westhovens &A. Spooren. A tool to enhance occupational therapy reasoning from ICF perspective: The Hasselt Occupational Performance Profile (H-OPP)Scandinavian Journal of Occupational Therapy . 2017, Volume 24; 2, p-126-35.
24. Stamm, T.A., Cieza, A., Machold, K., Smolen, J.S., &Stucki, G. Exploration of the link between conceptual occupational therapy models and the International Classification of Functioning, Disability and Health. Australian Occupational Therapy Journal, 2006, vol- 53, p- 9-17.
25. Haglund, L., &Henriksson, C. Concepts in occupational therapy. Occupational Therapy International, 2003, vol- 10, p- 253-268
26. Sandhu S, Furniss J and Metzler C; Using the New Post-acute Care Quality Measures to Demonstrate the Value of Occupational Therapy; The American journal of occupational therapy; 2018 vol 72, no. 2 p- 1-6.

Bangladesh Journal of Neuroscience 2017; Vol. 33 (1): 39-43

Role of Calcitonin Gene Related Peptide (CGRP) in Migraine

ALI M A[1], RAHAMAN H[2]

Abstract:

Migraine is the second most primary headache. The prevalence of Migraine is 12% in the general population, including 18% in women and 6% in men. Migraine can start in childhood and adolescence and continue throughout lifespan. It is most prevalent among people in their 30s and 40s. Migraine is a debilitating hemicranial headache that is pulsating, aggravated by movement, nausea, vomiting and having sensitivity to light and sound, with or without aura. It can affect all aspects of life as work and school, parenting and family relationships and personal and leisure time. There are some theory regarding pathogenesis of migraine which includes cortical spreading depression, cortical spreading oligemia, activation of trigeminocervical complex leading to neuroinflammation & release of vasodialating neuropeptides which include calcitonin gene related peptide (CGRP), substance P, vasoactive intestinal polypeptide (VIP), nitric oxide (NO), and pituitary adenylate cyclase activating peptide (PACAP) & genetic factor. CGRP is a potent vasodilator and causes perivascular plasma protein extravasation and nociceptive pain. Newer medications target CGRP both for acute and preventive treatment of migraine.

Keywords: *CGRP, Gepants, mAbs.*

Overview:

Migraine is a debilitating headache that is pulsating, aggravated by movement, nausea, vomiting and sensitivity to light and sound, all of these with or without aura[1]. A stable pattern (at least 6 months) of episodic disabling headache is usually migraine[2]. About 18% of adult women and 6% of men meet criteria for migraine[3]. Migraine can start in childhood and adolescence and continue throughout lifespan. It is most prevalent among people in their 30s and 40s, when they are busy with multiple roles and responsibilities[4]. It can affect all aspects of life as work and school, parenting and family relationships and personal and leisure time[5]. Two and half percent of episodic migraine cases convert to chronic migraine in 1 year. The modifiable risk factors are obesity, caffeine overuse, stressful life events, sleep disorders as snoring, poor acute treatment efficacy, allodynia, anxiety and depression. The nonmodifiable risk factors are female sex, low socioeconomic status, genetics[5].

Diagnosing migraine:

ICHD-3 (International Classification of Headache Disorder-3rd edition) Diagnostic criteria[6]:

A. At least five attacks fulfilling criteria B–D

B. Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated)

C. Headache has at least two of the following four characteristics:

1. Unilateral location
2. Pulsating quality
3. Moderate or severe pain intensity
4. Aggravation by or causing avoidance of routine physical activity (e.g. walking or climbing stairs)

D. During headache at least one of the following:

1. Nausea and/or vomiting
2. Photophobia and phonophobia

E. Not better accounted for by another ICHD-3 diagnosis.

1. Prof. Md. Ashraf Ali, Professor and Senior Consultant, Department of Neurology. Labaid Specialized Hospital, Dhaka, Bangladesh.
2. Dr. Habibur Rahaman, Phase B (MD Neurology), BSMMU, Dhaka, Bangladesh.

Brief screeners for diagnosing migraine—
ID migraine: 3 questions examining:

Presence or absence of nausea.

Presence or absence of photophobia.

Presence or absence of impact or disability.

Single criterion diagnosis——

Patient with episodic recurrent stable headache and nausea associated with

Headaches[3].

ICHD-3 (International Classification of Headache Disorder-3rd edition) Diagnostic Criteria for Episodic VS Chronic migraine.
Frequency determines subtypes—

Episodic migraine—Fewer than 15 headache days per month.

Chronic migraine— 15 or more headache days per month for at least 3 months.

Pathophysiology of Migraine:
There are some theory regarding pathogenesis of migraine which includes cortical spreading depression, cortical spreading oligemia, activation of trigeminocervical complex leading to neuroinflammation & release of vasodialating neuropeptides which include calcitonin gene related peptide (CGRP), substance P, vasoactive intestinal polypeptide (VIP), nitric oxide (NO), and pituitary adenylate cyclase activating peptide (PACAP), genetic contribution[7]. Some sorts of central generator or switch which turns on pathways that go out to the meninges. In the meninges, there are peripheral pain mechanisms that actually are the source of migraine pain. What happens in meninges—— Release of neuroinflammatory and vasodilating peptides and that combination of neurogenic inflammation and vasodilation activate and sensitize nociceptive afferents that carries signal back into the brain for integration. CGRP is released from trigeminovascular afferents. It is a potent vasodilator and causes perivascular plasma protein extravasation and nociceptive pain. It also enhances transmission of pain signals in the central nervous system. CGRP levels are elevated in migraineurs. So the target for migraine treatment involve reversal or prevention of some of those mechanisms. Acute treatment could reverse the vasodilation by vasoconstriction or prevent the release of neuro inflammatory and vasodilating peptides.

There are two ways to doing now——one can activate serotonin 1B receptor to vasoconstrict and another activate serotonin 1D receptor to prevent the release of neuroinflammatory peptide or prevent the return of signal back to the brain stem. In addition, primary most potent vasodilating peptide is CGRP. Triptans prevent the release of CGRP while they vasoconstrict and reverse the vasodilation of CGRP. Newer medications target CGRP both for acute and preventive treatment of migraine [8,9.]

Migraine Treatment:
The goal of acute migraine treatment is to terminate an attack of migraine and decrease the risk of episodic migraine becoming chronic migraine. Ideally this is a one and done response, pain free within 2 hours, with minimal adverse events and a low likelihood of headache recurrence[10].

First line Acute Treatments[11].
Level A evidence for the following classes
Triptans
NSAIDs
Ergots
Consensus clinical recommendations are for use
Specific medications—
Triptans.
Ergots (Dihydroergotamine)
Nonspecific medications—
NSAIDs

Combination of Triptan + NSAID (Sumatriptan-Naproxen).

Antiemetics in management of acute migraine:

Antiemetic drugs— Metoclopramide, Prochloperazine. Available in oral and parenteral forms. Parenteral form more effective in reducing headache. Effective for nausea as well headache pain. Consider in patients who cannot tolerate or do not respond to NSAIDs/ triptans. Antiemetics may result in sedation and extra pyramidal adverse effects[12].

Current evidenced based migraine prevention treatments—

Recommendation level based on evidence	Recommended drug classes
Level A, Established efficacy	Beta blockers- propranolol, metoprolol Antiepileptic drugs- divalproex sodium, sodium valproate, topiramate.
Level B, Probably effective	Antidepressants- Amitriptyline, Venlafaxine.Beta blockers — Atenolol, Nadolol.
Level C, Possibly effective	Angiotensin receptor blockers Candesartan.Antiepileptic drugs- Carbamazepine.Antihistamine -Cyproheptadine.

Migraine prevention guideline varies by country[13].

When to consider prevention

Attack frequency >1/ week or >2/ months.

Significant interference with routine activities despite use of acute treatment and uncommon subtypes are present as hemiplegic migraine, migraine with prolonged aura or migrainous infarction[14].

Migraine prevention: Treatment principles

Start low, go slow- titrate to avoid adverse effects. Choose treatments based on comorbidity and adverse effect profiles. Reevaluate treatment at regular intervals. Most preventive medications take at least 2 to 12 weeks before an effect is seen.

Introduction to CGRP as a treatment target in migraine prevention——

CGRP is a specific treatment target for prevention of migraine. mAbs are in late phase clinical studies for prevention of migraine. Small molecules gepants are in trials for migraine prevention. These are the first modern preventive treatments developed specifically for migraine[15].

In 1983, it was discovered that the Calcitonin gene produced Calcitonin gene related peptide (CGRP) in neural tissue. In early 1985, a review article described the CGRP containing nerves are found in cranial blood vessels and the trigeminal ganglion. CGRP is released from trigeminovascular afferents. It is a potent vasodilator and causes perivascular plasma protein extravasation and nociceptive pain. It also enhances transmission of pain signals in the central nervous system. CGRP levels are elevated in migraineurs[16].

In cluster headache there is significant increase in both VIP and CGRP level.

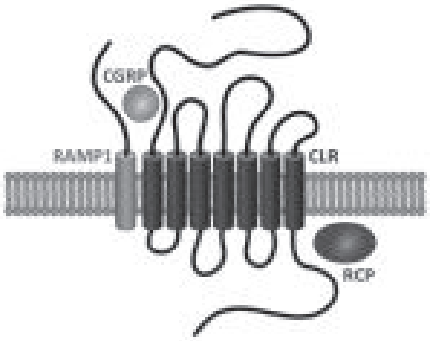
In chronic paroxysmal headache there is significant increase in both VIP and CGRP level. In cluster and chronic paroxysmal headache, all patients had CGRP release which normalized after treatment with Triptan[17].

It is found in two major forms—— alpha and beta.

Alpha CGRP is found in the brain and nervous system. Beta CGRP is found in the rest of the body[18].

CGRP receptor mechanism:

CGRP receptor complex



The CGRP receptor is a G-protein coupled receptor of the B type. This means that it contains 1 aspect, a 7- transmembrane G protein coupled receptor—the calcitonin like receptor (CLR). To work, CLR needs an associated receptor amplifying peptide (RAMP1). When RAMP1 and CLR meet via stimulation by CGRP, the receptor is activated and the G protein and the intercellular process continues[19].

CGRP receptors and migraine pathogenesis— CGRP receptors are found at every area concerned with migraine pathogenesis. They are found centrally in the brain stem, in trigeminal ganglion, in the cortex, in the meninges and dura matter, around the vessels within the meninges. Activation of CGRP and release of CGRP results in meningeal vasodilation and neurogenic inflammation. That is really one of the reason why CGRP is such an attractive target for migraine prevention[20].

First group of medicine that antagonizes CGRP were small molecule CGRP receptor antagonists or Gepants. They have been tested in numerous studies for acute treatment of migraine. They antagonize CGRP receptor and they terminate migraine attack. At least 6 of them have been studied in humans for acute migraine treatment. However when they are transferred to daily preventive therapy, hepatotoxicity occurred. Specifically occurred with Telcagepant, also with MK-3207. A new set of gepants has been developed for both acute and preventive treatment of episodic migraine. Two of them are Atogepant and BHV- 3500 are currently in phase 2 with daily dosing for the prevention of migraine[21].

Gepants VS Triptans :

Triptans and gepants have similar efficacy in clinical trials. Major benefit with gepants is that they do not carry cardiovascular risk. When developed, gepants are more likely to be used for triptan non responders and patients with cardiovascular disease. Gepants take longer to work and have greater tolerability[22]. Another approach is monoclonal antibody to CGRP or the CGRP receptor (mAbs) and they are big molecules. They do not cross blood brain barrier. They are eliminated by reticuloendothelial system. Since mAbs are not metabolized in the liver, they are not hepatotoxic. Because they do not penetrate the brain, peripheral anti CGRP action is sufficient to prevent migraine. They are working either at dura matter and meninges or in the trigeminal ganglion, both of which are external to blood brain barrier. They also have no CNS adverse effects. Four mAbs have been studied in phase 2 trials of the prevention of migraine. All four have similar very good efficacy, low rate of adverse events and very good tolerability[23].

	CGRP mAbs	Target administration	Route of
1)	Eptinezumab	CGRP ligand	Intravenous
2)	Galcanezumab	CGRP ligand	SC
3)	Fremanezumab	CGRP ligand	SC
4)	Erenumab	CGRP receptor	SC

All mAbs look remarkably effective in preventing both episodic and chronic migraine. Sometimes patients are taking mAbs and doing very well and get a breakthrough headache. At that time Triptan may be added. Triptans may work better in the presence of a mAbs.

As CGRP is a reactive vasodilator and acts as safeguard during cerebral and cardiac ischemia. mAbs are CGRP blockers and transform mild ischemic events into full blown infarctions. So disadvantage of mAbs is that putting the susceptible patients at high risk of myocardial infarction or stroke[24].

Conclusion:

CGRP provides a new target in migraine. CGRP antagonists— gepants and mAbs have the potential to really change the treatment landscape for migraine. mAbs are effective in migraine prophylaxis and gepants are effective in migraine prophylaxis and also to treat individual migraine attacks.

References:

1. Headache Classification Committee of the International Headache Society(IHS). The International classification of Headache Diorders, 3rd edition(beta version) Cephalalgia. 2013; 33:629-808.
2. Dodic D. Diagnosing headache: clinical clues and clinical rules. Adv Stud Med. 2003; 3:5550-55.
3. Lipton RB, D Dodic, R Sadovsky et al. A self administered screener for migraine in primary care. Neurology. 2003; 61:375-82.

4. Martin V, Donald P, Timothy T et al. The predictive value of abbreviated migraine diagnostic criteria. Headache. 2005; 45: 1102-12.

5. Diamon S, Bigal ME, Silberstein S et al. Patterns of diagnosis and acute and preventive treatment for migraine in the United States. Headache. 2007; 47: 355-63.

6. Headache classification committee of the International Headache Society (IHS).The International classification of Headache Disorders, 3rd edition (beta version) Cephalalgia. 2013; 33:629-808.

7. Burstein et al., 2012. Migraine: Multiple Processes, Complex Pathophysiology J Neurosci. 2015 Apr 29; 35(17): 6619–6629.

8. Goadsby PJ, Lipton RB, Ferrari MD. Migraine—current understanding and treatment. N Engl J Med. 2002; 346: 257-70.

9. Hargreaves RJ, Shepheard SL . Pathophysiology of migraine-new insights. Can J Neurol Sci. 1999; 26 suppl 3:S12-9.

10. LiptonRB, Fanning KM, Serran D et al.Ineffective acute treatment of episodic migraine is associated with new onset chronic migraine. Neurology. 2015;84:688-95.

11. Marmura MJ,Silberstein SD, Schwedt TJ. The Acute Treatment of Migraine in Adults : The American Headache Society Evidence Assessment of Migraine Pharmacotherapies. Headache. 2015;55:3-20.

12. Orr SL, Friedman BW,Christie S et al.Management of adults with acute migraine in the emergency department: The American Headache Society Evidence Assessment of parenteral pharmacotherapies. Headache. 2016; 56:911-40.

13. Silberstein SD, Holland S,Freitag F.Pharmacologic treatment for episodic migraine prevention in adults. Neurology. 2012; 78:1337-45.

14. Silberstein SD.Practice parameter: evidence based guidelines foe migraine headache (an evidence based review):report of the quality standards subcommittee of the American Academy of Neurology. Neurology. 2000; 55:754-62.

15. Tso AR,Goadsby PJ. Anti-CGRP monoclonal Antibodies : the next era of migraine prevention? Curr Treat Options Neurol. 2017;19:27.

16. Iyengar S, Ossipov MH, Johnson KW. The role of calcitonin gene-related peptide in peripheral and central pain mechanisms including migraine. Pain. 2017;158:543-59.

17. Edvinsson L, Ho TW.CGRP Receptor Antagonism and Migraine. Neurotherapeutics. 2010;7:164-175.

18. Russel FA,King R, Smillie SJ et al.Calcitonin gene-related peptide: physiology and pathophysiology. Physiol Rev. 2014;94: 1099-1142.

19. Ho TW, Edvinsson L, Goadsby PJ. CGRP and its receptor provide new insights into migraine pathophysiology. Nat Rev Neurol. 2010; 6:573-82.

20. Hargreaves RJ, Shepheard SL. Pathophysiology of migraine—new insights. Can J Neurol Sci. 1999;26(Suppl 3):S12-9.

21. Diener HC,Charles A, Goadsby PJ et al.New therapeutic approaches for the prevention and treatment of migraine. Lancet Neurol. 2015;14: 1010-1022.

22. Silberstein S, Lenz R, Xu C.Therapeutic monoclonal antibodies: what headache specialists need to know. Headache. 2015; 55: 1171-82.

23. Oakes TM. CGRP monoclonal antibody for the prevention of migraine. Poster presented at AHS 2016. Abstract PS42.

24. Maassen Van de Brink A,Meijer J, Villalon CM et al. Wiping out CGRP : potential cardiovascular risks.Trends Pharmacol Sci. 2016;37: 779-88.

25. Cephalalgia. 2013 Jul;33(9):629-808. The International Classification of Headache Disorders, 3rd edition (beta version). Headache Classification Committee of the International Headache Society (IHS). Comment in Cephalalgia. 2013 Jul;33(9):627-8. Cephalalgia. 2015 Apr;35(4): 368-9.

Bangladesh Journal of Neuroscience 2017; Vol. 33 (1): 44-46

CASE REPORT

A Case of Paroxysmal Kinesigenic Dystonia : Epilepsy Mimic

UDDIN M N[1], RAHAMAN H[2], HABIB A[3], RIZVI A N[4], BHUIYAN MM[5], ISLAM MR[6]

Abstract:

Background: *We report a rare case of movement disorder Paroxysmal kinesigenic dystonia who was misdiagnosed as Epilepsy and Conversion disorder.* ***Case report:*** *A 35 -year female presented with episodic painful twisting of her Right hand and arm only when she is awake. These events were triggered by sudden movements and would last several seconds to minutes. Her symptoms were unilateral and her physical and neurological examinations were normal. Treatment with anticonvulsants Oxcarbazepine improved her symptoms.* ***Conclusion:*** *Although an uncommon movement disorder, it is important to recognize the clinical presentation of Paroxysmal kinesigenic dystonia as most patients respond very well to medical treatment.*

Key Words: *Anticonvulsants; Oxcarbazepine; Movement disorder; Paroxysmal Nonkinesigenic dystonia; Medical treatment.*

Introduction:

Paroxysmal dyskinesias (PDs) are a rare heterogeneous group of disorders characterized by sudden attacks of involuntary movements like chorea, athetosis, dystonia, hemiballismus or combination of them. Paroxysmal kinesigenic dyskinesia (PKD) involves sudden attack of dyskinesias induced by voluntary movement. PKD most commonly occurs sporadically or as an autosomal dominant trait with variable penetrance. The exact pathophysiology of PKD is unknown although basal ganglia dysfunction appears to play a major role. Although the precise gene remains unknown, genetic linkage studies have isolated loci on chromosome 16. The episodic nature of PKD and its relationship with other episodic disease, such as Migraine, epilepsy & episodic ataxia, suggests channelopathy as a possible underlying pathology. PKD may remit spontaneously, but it also responds well to anti-convulsants as well as other agents[1, 2,3].

PD subtypes include

1) Paroxysmal kinesigenic dyskinesia (PKD) which induced by sudden voluntary movements;
2) Paroxysmal nonkinesigenic dyskinesia (PNKD) which occurs at rest: PKND is characterized by spontaneous attack that tends to be more dystonic in nature. Attacks tend to be longer & less frequent than PKD lasting 10 minutes to 6 hours. Attacks are precipitated by alcohol, caffeine, stress & less responsive to anti consultants.
3) Paroxysmal exertion-induced dyskinesia (PED) triggered by prolonged exercise: PED involves attacks provoked by ongoing exertion & lasting for 5-30 minutes, attacks occurs 10-15 minutes after exercise whereas attack of PKD occurs immediately on movements. In PED attacks are dystonic & involve the exercised body parts, they stop within 10-15 minutes of rest. Anticonvulsants have not proved useful in PED.
4) Paroxysmal hypnogenic dyskinesia (PHD) which occur in sleep. It is characterized by the patient suddenly awakening with cry alongwith involuntary dystonic & ballistic movements lasting upto 45 seconds[1, 2, 3].

Most cases of PKD are primary, categorized as either familial (usually autosomal dominant) or

1. Dr. Mohammad Najim Uddin, Assistant Professor (Neurology), CMOSH Medical College, Chittagong
2. Dr Habibur Rahaman, MD (Neurology) Student Phase B.
3. Dr. Ahsan Habib, Associate Professor (Neurology), Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh
4. Prof . (Dr.) Abu Nasir Rizvi, Professor (Neurology), Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh
5. Prof. Md. Moniruzzaman Bhuiyan, Professor Neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.
6. Prof. Md. Rafiqul Islam, Professor Neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.

idiopathic. Primary PKD usually has its onset in childhood between 6-16 years with a range of 4 months to 57 yrs. Males are more affected than females having ratio 2:1 to 4:1. The condition may be sporadic. It is inherited as autosomal dominant trait with variable penetrance. The clinical features is quiet distinctive of sudden onset involuntary movement precipitated by sudden movement. Attacks are usually unilateral followed bilateral attack. Extremities are more affected than face, neck & trunk. There is no alteration or loss of consciousness. However, in some cases a specific cause for the PKD has been identified, such as multiple sclerosis (MS), vascular lesions, trauma, or acquired metabolic abnormalities. Primary PKD is short lasting < 5 min, occurs in childhood whereas secondary PKD are tends to be longer in duration > 5 min & frequent in adult. Both children and adults are affected by PDs, which often cause diagnostic delays or an incorrect diagnosis due to a normal neurological examination between attacks and lack of familiarity with these movement disorders. Since most patients with PDs respond very well to medical treatment, it is important to recognize their clinical presentation [4, 6, 7].

Here in we report a case of PKD in a patient which is diagnosed as a focal epilepsy and Conversion disorder.

Case Report:

A 35-year-old female was admitted in our department with history of episodes of painful twisting of her right hand and arm for last 6 months. These abnormal events would last anywhere between several seconds to minutes and were triggered by sudden movements and also by when she was abruptly asked to do something. Her symptoms were unilateral and she denied any aura, post ictal confusion, changes in her level of consciousness, visual or speech problems, tongue biting, or bowel and bladder incontinence. It is for first time & no family history. Both her general physical and neurological examinations were normal in between attack. And during attack there was painful dystonic limb posturing with intact consciousness. Magnetic resonance imaging of the brain was also unremarkable. She was started on phenytoin but this was changed to Oxcarbazepine when she admitted in Department of neurology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. Her symptoms significantly improved with Oxcarbazepine treatment. Secondary causes of PNKD were ruled out.

Discussion:

PKD is a rare neurologic condition that has an estimated prevalence of 1 in 150,000 [4]. The onset of PKD is typically between 6-months to 40-years of age, with males more commonly affected than females [1, 2, 5]. Although the Pathophysiology of PKD remains unknown, several familial cases have been linked to a peri-centromeric chromosome 16 locus [8].

Diagnostic criteria include[6,7]

1. An identified kinesigenic trigger for the attacks, short duration of attacks (< 1 minute),
2. No pain or loss of consciousness during attacks,
3. Exclusion of other organic diseases,
4. Normal neurologic examination between attacks,
5. Age at onset between 1-20 years if no family history of PKD, and
6. Control of attacks with phenytoin or carbamazepine

A startle, sudden movement, hyperventilation, or continuous exercise can precipitate attacks, which typically last between a few seconds to 5 minutes [2]. The frequency of attacks can range from as many as 100 per day to fewer than 1 per month, with the extremities more often affected than the face, neck, or trunk. Symptoms are often unilateral, but can become bilateral, and there is usually a short refractory period before another attack can be triggered[9]. With PKD patients responding well to pharmacotherapy, it is important that an early diagnosis is made. Carbamazepine is the drug of choice, but a beneficial response has also been reported for other anticonvulsants such as phenytoin, oxcarbazepine, and barbiturates[10]. A careful differentiation from other movement disorders can also help avoid years of anguish and uncertainty for both patients and their families.

References:

1. Weber YG, Lerche H. Genetics of paroxysmal dyskinesias. CurrNeurolNeurosci Rep. 2009; 9:206-11.
2. Bhatia KP. The paroxysmal dyskinesias. J Neurol. 1999; 246:149-55.
3. Demirkiran M ,Jankovic J. Paroxysmal dyskinesia's: clinical features and classification,Ann Neurol. 1995 Oct; 38(4):571-9.
4. Lotze T, Jankovic J: Seminars in pediatric Neurology, volume 10, Issue 1, March 2003, pages: 68-79
5. Mehta SH, Morgan JC, SethiKD. Paroxysmal dyskinesias.Curr Treat Options Neurol. 2009; 11:170-8.
6. Van Rootselaar AF, Van Westrum SS, Velis DN, TijssenMA.The paroxysmal dyskinesias. Pract Neurol. 2009; 9:102-9.
7. Bruno MK, Hallett M, Gwinn-Hardy K, Sorensen B, Considine E. et al. Clinical evaluation of idiopathic. paroxysmal-kinesigenic dyskinesia: new diagnostic criteria. Neurology.2004; 63:2280-7.
8. Swoboda KJ, Soong B, McKenna C, Brunt ER, Litt M. et al. Paroxysmal kinesigenic dyskinesia and infantile convulsions: clinical and linkage studies. Neurology.2000; 55: 224-30.
9. Sethi KD. Paroxysmal dyskinesias. In: "Parkinson's Disease and Movement Disorders". Lippincott, Williams & Wilkins.4eds., Philadelphia; 2002: 430-7.
10. Mehta SH, Sethi KD. Therapeutics of paroxysmal dyskinesias. In: "Therapeutics of Parkinson's Diseaseand Other Movement Disorders. WileyBlackwell. 1 eds., West Sussex; 2008:91-120.