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

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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

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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

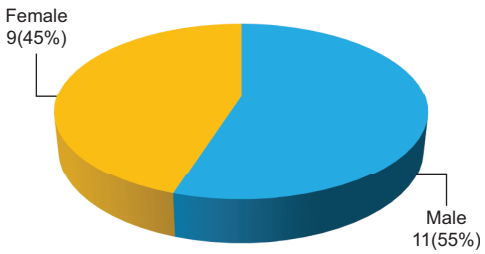

Fig.-1: *Distribution of patients by age at onset (n=20).*

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.

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