Original Article

Frequency of Childhood Ischemic Stroke in Children Presenting with Sickle Cell Anemia

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ABSTRACT

Objective: Frequency of Childhood Ischemic Stroke in children presenting with Sickle Cell Anemia
Study Design: Descriptive / cross-sectional study.
Place and Duration of Study: This study was conducted at the Pediatric Department, DHQ Teaching Hospital, Gomal Medical College, Dera Ismail Khan from November 2015 to May 2016.
Materials and Methods: All children under 18 years with Sickle Cell Anemia were enrolled. Children with stroke were investigated by performing Peripheral Smear and Hb Electrophoresis. Informed written consent was taken from parents. Confounding factors were identified and controlled by exclusion criteria.
Sample size of 105 was calculated by using WHO software based on confidence interval 95%, margin of error 6% and prevalence of Childhood Ischemic Stroke 11%.
Sampling technique was Non-probability consecutive sampling.
Results: A total of 105 patients presenting with sickle cell anemia presenting with highly suspicion of stroke were included in the study. There were 54 (51.43%) males and 51 (48.57%) females. Average age of the patients was 5.90 + 3.96, with range 6 months - 18 years. The Childhood Ischemic Stroke was found in 16(15.2%) patients.
Conclusion: Our findings provide novel information about ischemic stroke among children of sickle-cell disease. Sickle Cell Anemia is the most common genetic and hematologic risk factor for ischemic stroke in children. Implementation of an effective strategy is required for children with sickle cell disease to prevent Ischemic Stroke & prompt action to be taken for its management.
Key Words: Frequency, childhood ischemic stroke, sickle cell anemia

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INTRODUCTION

Hemoglobin S (HbS) is the result of a single base-pair change, thymine for adenine, at the sixth codon of the β globin gene. This change encodes valine instead of glutamine in the sixth position in the β globin molecule. Sickle Cell Anemia, homozygous Hb S, occurs when the both β globin genes have the Sickle cell mutation. In sickle cell anemia, Hb S is commonly as high as 90% of the total hemoglobin. In 2006, the World Health Organization (WHO) recognized Sickle Cell Anemia as a global public health problem[1]. In 2010, the 63rd World Health Assembly adopted a resolution on the prevention and management of birth defects, including sickle cell disease and the thalassemia. Finally, haemoglobinopathies have been included in the most recent Global Burden of Diseases, Injuries, and Risk Factors Study (the GBD 2010 study), which aims at providing a comprehensive and systematic evidence-based assessment of the burden of major diseases and injuries[2].

Neurological complications associated with Sickle Cell Anemia are varied and complex. Approximately 11% and 20% of children with Sickle cell anemia will have overt or silent strokes, respectively, before their 18th birth day[3]. The most common hematologic risk factor for stroke is Sickle Cell Anemia[4]

We present here the most recent practical directions on how to diagnose and manage arterial stroke in children, according to different international guidelines on the subject.[5]

The World Health Organization (WHO) defines stroke as "a clinical syndrome of rapidly developing focal or global disturbance of brain function lasting >24 hours or leading to death with no obvious nonvascular cause" [6]. A modern definition could be "a clinical syndrome characterized by (1) a neurological deficit related to the

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perfusion territory of a cerebral artery and (2) neuroradiological evidence of an ischemic lesion" [7,8].

In childhood, on the contrary, even in the presence of transient symptoms, imaging often shows a cerebral infarction [9].

Strokes are classically divided in primarily ischemic or hemorrhagic. While adult strokes are prevalently ischemic (80%) and due to atherosclerosis, in childhood up to 45% of strokes are hemorrhagic and are associated with a wide spectrum of risk factors [10].

The estimated incidence of ischemic stroke in children older than 28 days of life is variable [11,12] but, according to a large prospective, population study, it averages 13/100 for all strokes, 7.9/100 for ischemic strokes, and 5.1/100 for hemorrhagic strokes [12]. Approximately 20% of children die after an ischemic stroke while more than 50% of those surviving present neurological sequelae, most commonly hemiparesis [13]. The cumulative stroke recurrence rate has been reported to be 15% at 1 year, and 19% at 5 years [14] and up to 41% at 5 years [15]

In preparing this work we followed the most recent guidelines on arterial stroke in childhood.

MATERIALS AND METHODS

This Cross-sectional descriptive study was carried out in Pediatric Department, DHQ Teaching Hospital, Gomal Medical college, Dera Ismail Khan in 6 months duration from November 26, 2015 to May 25, 2016.

Sample size of 105 is calculated by using WHO software based on confidence interval 95%, margin of error 6% and prevalence of Childhood Ischemic Stroke 11%.

Sampling Technique: Consecutive non-probability sampling.

Inclusion Criteria: All children of both gender from the age of 6 months - 18 years.

• Children with sickle cell anemia having high suspicion of stroke.

Exclusion Criteria: Children having steroid therapy on medical records.

• Children with intake of anticoagulants at least in the last one month.

• Children having central nervous system infection such as meningitis or encephalitis.

• Children with history of head trauma.

Data Collection Procedure: Permission from hospital ethical committee was taken before starting study. Primary data was collected by using questionnaire. All children under 18 years with Sickle Cell Anemia were enrolled in study. Children admitted with stroke were investigated for evidence of Sickle Cell Anemia by performing Peripheral Smear and Hb Electrophoresis. Informed written consent had taken from parents. Physical examination including GCS and diagnostic investigations like CT scan brain had done. Confounding factors had identified and controlled by exclusion criteria.

Data Analysis: Data had analyzed by using SPSS version 10. Quantitative variables like age and GCS level were described in terms of means ± standard deviation. Categorical data like CT scan finding of infarction, gender and childhood ischemic stroke were described in terms of frequency and percentages. Childhood Ischemic stroke were stratified among age, gender and GCS level to see effect modifiers. Post stratification chi-square test had applied keeping P-value ≤ 0.05 as significant. All the results had presented as tables.

RESULTS

A total of 105 patients with sickle cell anemia & highly suspicion of stroke were included in the study. Average age of the patients was 5.90 $\pm$ 3.96 with range 6 months -18 years. Patient's age was divided in four categories, out of which most common age group with sickle cell anemia presenting with highly suspicion of stroke was 6 - 10 years. There were 32(35.9%) patients of the age 6 to 10 years, 27(25.7%) were < 5 years, 25(23.8%) were in the range of 11 - 15 years, 21(20.0%) patients were > 15 years of age. (Table 1).

The Childhood Ischemic Stroke was found in 16(15.2%) patients. (Table 2)

In total 105 patients mean GCS was 8.50 $\pm$ 3.2. Most of the patients i.e 53(50.5%) presented with GCS score of 6 - 10, followed by 36 (34.2%) with GCS of 11 - 15, followed by 16(15.2%) with GCS < 5 scores. (Table 3).

While stratifying Childhood Ischemic Stroke with regards to age wise distribution, in the age group < 5 years; Childhood Ischemic Stroke was present in 16 patients.

Table No. 1: Age wise distribution of the patients with sickle cell anemia.

	Frequency	**Percent**	**Cumulative Percent**
<5 years	27	25.7	25.7
6 – 10	32	30.5	56.2
11 – 15	25	23.8	80.0
15+	21	20.0	100.0
Total	**105**	**100.0**	

Table No. 2: Distribution of childhood ischemic stroke

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	16	15.2	15.2	15.2
	No	89	84.8	84.8	100.0
	Total	105	100.0	100.0	

In other age groups i.e. 6-10, 11-15 & >15 years no Childhood Ischemic Stroke was found. (Table 4). While stratifying Childhood Ischemic Stroke

with regards to gender, 16 male patients had Childhood Ischemic Stroke and there was no Childhood Ischemic Stroke among female gender (Table 5).

While stratifying Childhood Ischemic Stroke with regards to GCS there were 16 patients with GCS less the 5. (Table 6).

Table No. 3. Distribution of GCS among patients

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	< 5	16	15.2	15.2	15.2
	5 -10	53	50.5	50.5	65.7
	11-15	36	34.3	34.3	100.0
	Total	105	100.0	100.0	

Table No.4: Stratification of ischemic stroke with age

		Age				Total
		<5 Years	6-10	11-15	15>	
Stroke	Yes	16	0	0	0	16
	No	11	32	25	21	89
Total		27	32	25	21	105

Table No.5: Stratification of ischemic stroke with gender

		Gender		
		Male	Female	
Stroke	Yes	16	0	16
	No	38	51	89
Total		54	51	105

Table No. 6: Stratification of ischemic stroke with GCS

		GCS			Total
		< 5	5 -10	11-15	
Stroke	Yes	16	0	0	16
	No	0	53	36	89
Total		16	53	36	105

DISCUSSION

Sickle cell disease is an autosomal recessive inherited disorder with cerebrovascular accident (CVA) as one of its major complications [16].

Nearly 800,000 people suffer strokes each year in the United States; 82-92% of these strokes are ischemic.[17] Stroke occurs by the age of 20 in about 11 percent of patients with sickle cell anemia.[18-20]

The remarkable improvement in mental state and motor function in our patient gives credence to the efficacy of exchange blood transfusion. In preventing stroke recurrence in SCD patients, chronic blood transfusion program (CBT) is more widely employed. Our patient was offered CBT but mother declined. CBT is practically difficult in most developing countries for infrastructural and socio-economic reasons including sourcing donor blood and preventing or tackling hemosiderosis if and when it occurs.[21]

A study with 3647 patients with SCD it was found a predominance of ischemic cerebral events in individuals under 20 and above 29 years old and of hemorrhagic events in the group between 20 and 29 years of age, which determined a larger number of deaths (26%) in the latter.[22].

Despite the low number of individuals evaluated, findings are in accordance with data of references, evidencing patients with SCD and stroke in early age, all with ischemic event. There was bilateral hemisphere involvement by stroke in six patients, with recurrence in two and a single event in four patients.[23]

Neuropsychomotor development in SCD children was considered normal until three years of age with progressive performance decay in neuropsychological and motor function tests due to ischemic cerebral insults and/or silent infarct[24]. Similar findings was observed in this present study.

Most of our patients presented vascular event after four years of age and had apparently adequate neuropsychomotor development until the stroke. The present neurological exam evidenced important neurological sequelae: motor deficit in eight patients; mental deficiency in four; aphasia and visual deficit in two patients. Throughout the assessment, we observed lack of initiative, difficulty to understand the clinical neurologic assessment and slowness in motor and speech responses.

CONCLUSION

Our findings provide novel information about ischemic stroke among children of sickle-cell disease Sickle Cell Anemia is the most common genetic disease and the most common hematologic risk factor for ischemic stroke in children. Implementation of an effective ischemic stroke prevention strategy for children with sickle cell disease Prompt action to be taken for its management.

Author's Contribution:

Concept & Design of Study:	Sami ul Haq
Drafting:	Tosif Ahmad
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Revisiting Critically:	Sami ul Haq, Tosif Ahmad
Final Approval of version:	Sami ul Haq

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