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Transcranial Doppler Screening In Children with Sickle Cell Disease of South Gujarat Population

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ABSTRACT

Background: TCD (Transcranial Doppler) is a well-established study to predict Cerebrovascular stroke in SCD (Sickle cell disease). We aim to establish baseline TCD findings in Indian children with SCD and compare the results with the available STOP (Stroke prevention trial in Sickle Cell Anemia) protocol. We would also compare TCD findings in homozygous sickle cell disease and heterozygous sickle cell trait.

Material and Methods: Seventy nine children with SCD were included in this study for one year period. TCD was performed and TAMMV (time-averaged maximum mean) velocity in the middle cerebral, anterior cerebral, posterior cerebral and internal carotid arteries was measured. Children were divided into two groups. Group I (56 homozygos–70.88%) and group II (23 heterozygos–29.11%).

Results: In group I, 50 children fall in normal range with average TAMM velocity of 127.59 ± 17.48 cm/s. There was 1 (1.78%) abnormal result and 5 (8.9%) conditional results in group I. All results were normal in group II with average TAMM velocity of 116.33 ± 12.412 cm/sec. Middle cerebral artery was the only affected vessels amongst all.

Conclusions: In our study, there was low prevalence of abnormal TCD results as compared to STOP protocol. The difference was significant in TAMM velocity between two groups, with all children being within normal range in group II. Result of this study differs from previous studies, done in western countries probably due to difference in haplotype.

Key Words: Transcranial Doppler, Cerebrovascular stroke, Sickle cell disease

INTRODUCTION

Sickle cell disease (SCD) is one of the most common genetic diseases worldwide and its highest prevalence occurs in Middle East, Mediterranean regions, Southeast Asia, and sub-Saharan Africa. It is caused by a mutation in beta globin gene which is expressed on hemoglobin S resulting in haemoglobinopathy.[1-3]

Sickle cell gene is mainly restricted to tribal population in India, in states like Gujarat, Madhya Pradesh, Orissa, Chhattisgarh, Jharkhand, Andhra Pradesh etc. Based on the 1981 census and prevalence of Hb S invarious populations studied, Rao (1988) estimated the expected number of sickle homozygotes as 1,31,375 in our country while expected number of sickle cell heterozygotes was 24,34,170. At that time the sickle cell gene was detected in 75 districts from various states of India. Based on several hospital based & epidemiological surveys in various ethnic groups done in last 54 years, prevalence of sickle gene is found to be 0-18% in north eastern India, 0-33.5% in western India, 22.5-44.4% in central India and 1-40% in southern India and the gene frequency of Hb-S varies between 0.031- 0.41.[4]

In developing countries, detection of sickle cell disease is very difficult due to lack of awareness and

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sensitization amongst people. Prevention of adverse outcome of disease is an even bigger challenge. In developed countries, survival is no longer a major problem, due to timely detection of the disease and good standards of care. Nevertheless, morbidity remains high with a stroke risk which is the major complication of sickle cell disease. In the absence of intervention, it accounts for nearly 11% before the age of 18 years.[1,5]

Most strokes are due to a macro-angiopathy affecting the terminal internal carotid arteries and proximal middle and anterior cerebral arteries, with smooth muscle hyperplasia and intimal fibrosis that led to progressive stenosis and occlusion with moyamoya-like collateral development.[1,6]

Chronic transfusions are effective in reducing the risk of (1) recurrent ischaemic stroke, and (2) a first stroke in children with HbSS who have abnormally high velocities on TCD.[1,7]

Transcranial Doppler (TCD) is an essential investigation in the prediction of stroke in sickle cell disease and therefore very helpful for preventive interventional measures like prophylactic blood transfusion. Transcranial Doppler is noninvasive, repeatable, cost-effective investigation which provides real time hemodynamic information of cerebral vasculatures. Transcranial Doppler study can measures flow velocity in the large intracranial arteries, narrowing of which leads to cerebral infarction. So increased flow velocity in middle cerebral artery is noted on TCD in case of cerebral ischemia.

According to the French and U.S. guidelines &Adams et al. children with SCD may be categorized in risk zones according to velocities as mentioned below [1,8]: (Table 1)

Table 1: risk zones according to velocities

Velocity (cm/s)	Risk zone	Prognosis
<170	Normal	Good
170 - 199	Low (conditional)	Moderate
>200	High	Poor

Chronic blood transfusions, if implemented in a timely fashion in those with flow velocity >200 cm/s, can reduce the risk of stroke by as much as 92%.[9]

METHODS AND MATERIAL

This was prospective observational study, conducted in department of Radiodiagnosis of SMIMER (Surat Municipal Institute of Medical Education and Research) hospital for the duration of 12 months. Children with sickle cell disease without a prior history of stroke and aged between 2 to 16 years were included, after getting written informed consent from parents. Uncooperative patients, patients on hydroxyurea treatment or history of recent blood transfusion were excluded from the study.

Approval from the Human Research Ethical Committee was acquired. Detailed history, hemoglobin, hematocrit values and other relevant information were documented in a pre-designed performa.

All transcranial doppler examinations were performed using GE logic P9 ultrasound machine with dedicated 1-5 MHz transducer.

TCD was carried out on middle cerebral, terminal internal carotid; anterior cerebral, posterior cerebral and vertebral arteries on either side or TAMM velocity were recorded. According to STOP criteria, TAMMV were further divided into normal (TAMMV < 170 cm/sec), conditional (TAMMV 170 - 199 cm/sec) and abnormal (TAMMV >= 200 cm/sec).

Patients were divided into two groups on basis of hematological differences. Group I was composed of patients with homozygous form and group II with patients having heterozygous form.

RESULTS

A total of 79 children with sickle cell disease were evaluated in our study. Group I was composed of 56 patients (70.88%) with homozygous form and group II was composed of 23 (29.11%) patients with heterozygous form. There were no statistically significant differences between the groups in regards to sex and age.

Table 3 shows the velocities in both groups. In group II all children were having TAMMV within normal range with average TAMMV of 116.33 ± 12.412 cm/sec. In group I, 50 (89.28 %) patients had TAMMV within normal range with average TAMMV of 127.59 ±17.48 cm/sec. In group II, 5 (8.9%) patients were falling into conditional zone with average TAMMV of 188.36±6.23cm/sec. and 1 (1.78 %) patient had abnormal velocity with TAMMV 224.0 cm/sec.

Table 2: mentions sex distribution in both groups

Sex	Group I	Group II	Total
Female	28 (50)	10 (43.5)	38 (48.1)
Male	28 (50)	13 (56.5)	41 (51.9)
Total	56 (100)	23 (100)	79 (100)

p- Value =0.598 (chi-square applied) no association in between the sex and group.

Table 3: Age and velocity distribution between two groups

Group	N	Mean ± SD	P- Value
Age			
I	56	7.63 ± 3.46	0.392
II	23	6.87 ± 3.88	
MCA velocity			
I	50	127.59 ± 17.48	0.01
II	23	116.33 ± 12.41	

SD= Standard deviation; *independent t-test applied for comparison of two independent group mean.

Statistically significant difference was observed in velocities of MCA between the two groups (P –value is 0.01).

DISCUSSION

Use of TCD has increased as main screening tool in predicting risk of stroke in both asymptomatic and symptomatic patients with SCD since STOP criteria was established.[10]

We conducted this study in Indian tribal population with high endemicity of sickle cell disease and compared our results with STOP criteria.

STOP study was first and the biggest study on transcranial Doppler in paediatric patients with sickle cell anemia with abnormal results in MCA as high as 9.7%.[11]

The result of our present study significantly differs with that of the STOP study as we noticed an abnormal result in only one patient (1.78 %). However similar results have been observed in two different studies conducted in Brazilian and Iranian children, which shows conditional velocity 8.1% & 3% and an abnormal result in 1.6% & 3 % respectively.[12,13]

Also in our study, we noticed high TAMMV in MCA only, whereas TAMMV in terminal internal carotid, anterior cerebral, posterior cerebral and vertebral arteries were within normal range. In previous study about TCD in SCD conducted by Adams in 1992internal carotid and anterior cerebral arteries also were affected with middle cerebral artery.[14]

There were no abnormal or conditional results of TCD noted in group II, may be due to less severity of SCD in this group. Other studies carried out in Brazilian and Iranian children also observed similar results in group II. [12,13]

In our study, lower prevalence of abnormal TCD as compared to STOP criteria (conducted on African descendants) may be due to difference in B globin haplotype.

Studies show that in Indian SS patients Arab-Indian haplotype is more prevalent. This specific haplotype is associated with high HbF levels, which in turn is related to milder clinical course including cerebral stroke. This reason is well explained with lower abnormal results in our study as compared to STOP study and other studies from African continent where Bantu haplotype is prevalent which have the lowest HbF level and thus most severe clinical course.[15,16]

CONCLUSION

Prevalence of abnormal transcranial doppler results in Indian children with sickle cell disease is significantly low as compared to STOP criteria may be due to the difference of haplotype and ethnicity. These raise the need of similar and larger scale study, focusing on the same subject of different haplotypes and their effect on clinical severity.

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REFERANCES

1. Verlhac S. Transcranial Doppler in children. Pediatr Radiol. 2011 May;41 Suppl 1:S153-65. doi: 10.1007/s00247-011-2038-y. Epub 2011 Apr 27. PMID: 21523592.
2. Modell B., editor. *Guidelines for the Control of Haemoglobin Disorders*. Sardinia, Italy: WHO; 1989.
3. Serjeant G. R. Sickle-cell disease. *The Lancet*. 1997; 350 (9079):725–730. Doi: 10.1016/s0140-6736(97) 07330-3. [PubMed] [Cross Ref]
4. Ajit C. Gorakshakar, Regional Medical Research Centre for Tribals (RMRCT) Epidemiology of Sickle Hemoglobin in India, 103-106
5. Ohene-Frempong K, Weiner SJ, Sleeper LA et al (1998) Cerebrovascular accidents in sickle cell disease: rates and risk factors. Blood 91(1):288–294
6. Verlhac S, Bernaudin F, Tortrat D et al (1995) Detection of cerebrovascular disease in patients with sickle cell disease using transcranial Doppler sonography: correlation with MRI. MRA and conventional angiography. Pediatr Radiol 25(Suppl 1):S14–S19
7. Adams RJ, McKie VC, Carl EM et al (1997) Long-term stroke risk in children with sickle cell disease screened with transcranial Doppler. Ann Neurol 42:699–704
8. Mary Hokazono; Gisele Sampaio Silva; Edina Mariko Koga Silva; Josefina Aparecida Pellegrini Braga, Sao Paulo Med. J. vol.129 no.3 São Paulo May 2011
9. 9. M. Arkuszewskia,b, J. Krejzaa,c,d, R. Chena, Sickle Cell Disease: Reference Values and Interhemispheric Differences of Nonimaging Transcranial Doppler Blood Flow Parameters, AJNR, American journal of neuroradioloty*AJNR* 2011 32: 1444-1450
10. Armstrong-Wells J, Grimes B, Sidney S, Kronish D, Shiboski SC, Adams RJ, Fullerton HJ. Utilization of TCD screening for primary stroke prevention in children with sickle cell disease. Neurology. 2009;72:1316–1321
11. Adams RJ, McKie VC, Hsu L, et al. Prevention of a first stroke by transfusions in children with sickle cell anemia and abnormal results on transcranial Doppler ultrasonography. N Engl J Med. 1998;339(1):5-11.
12. Bavarsad Shahripour, R., Mortazavi, M. M., Barlinn, K., Keikhaei, B., Mousakhani, H., Azarpazhooh, M. R., Alexandrov, A. V. (2014). Can STOP Trial Velocity Criteria Be Applied to Iranian Children with Sickle Cell Disease? Journal of Stroke, 16(2), 97–101. http://doi.org/10.5853/jos.2014.16.2.97
13. Hokazono Mary, Silva Gisele Sampaio, Silva Edina Mariko Koga, Braga Josefina Aparecida Pellegrini. Results from

transcranial Doppler examination on children and adolescents with sickle cell disease and correlation between the time-averaged maximum mean velocity and hematological characteristics: a cross-sectional analytical study. Sao Paulo Med. J. [Internet]. 2011 May [cited 2017 Oct 03]; 129 (3): 134-138. Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid =S1516-31802011000300003&lng=en. http://dx. doi. org /10. 1590/S1516-31802011000300003.

14. Adams RJ, Nichols FT, Figueroa R, McKie V, Lott T. Transcranial Doppler correlation with cerebral angiography in sickle cell disease. Stroke. 1992;23(8):1073-7.

15. Mukherjee, M. B., Lu, C. Y., Ducrocq, R., Gangakhedkar, R. R., Colah, R. B., Kadam, M. D., Mohanty, D., Nagel, R. L. and Krishnamoorthy, R. (1997), Effect of α-thalassemia on sickle-cell anemia linked to the Arab-Indian haplotype in India. Am. J. Hematol., 55: 104–109. doi:10.1002/(SICI)1096-8652 (199706) 55:2<104:AID-AJH9>3.0.CO;2-X

16. Steinberg, M. H. (2005), Predicting clinical severity in sickle cell anaemia. British Journal of Haematology, 129: 465–481. doi:10.1111/j.1365-2141.2005.05411.x