

Original Research Article

Relationship between cerebral blood flow velocities and sociodemographic characteristics of sickle cell anaemia children aged 2-16 years seen at federal teaching hospital Owerri

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ABSTRACT

Background: Sickle cell anaemia (SCA) is a chronic haemolytic state associated with recurrent blood transfusions, infections and its attendant complications. The study compared the relationship between cerebral artery blood flow velocities (CBFV) and socio-demographic parameters (age, sex, socioeconomic status and age at diagnosis) of male and female SCA children aged 2-16 years seen at Federal Teaching Hospital Owerri, Imo state.

Methods: Structured questionnaire were used to obtain relevant bio-sociodemographic information's from SCA children that attended the sickle cell specialist clinic of the hospital between April and September 2023. Later, Transcranial Doppler ultrasound scan was done for them.

Results: A total of 102 subjects were screened within the study period. CBFV decreases with increasing age, 100% of those with abnormal CBFV were aged 2-6 years and 75% females. Majority of children with abnormal CBFV belonged to lower and middle socioeconomic class. Abnormal CBFV was found in 17.6% of subjects

Conclusions: The prevalence of abnormal cerebral blood flow velocity in SCA children is 17.6% and majorily in younger age group. Identification of subjects at risk for a CVA helped in primary prevention by prompt therapy institution.

Keywords: Age at diagnosis, Cerebral artery blood flow velocities, Sickle cell anaemia, Socioeconomic status

INTRODUCTION

Sickle cell disease (SCD) is a genetic disorder resulting from a point mutation in Beta chain where hydrophilic glutamic acid is replaced by hydrophobic valine.¹ With almost 305,000 live births annually, SCD is the most common genetic haematological disorder worldwide.² Sickle cell disease affects 20-25 million people globally, with 75% of these residing in Africa; especially in malaria endemic areas like Nigeria, Senegal, Madagascar etc.³ Sickle cell anaemia (SCA) affects up to 2% of the global population, 90% of this global population reside in

Nigeria, India and the democratic republic of Congo.⁴ Complications of SCA are protean involving virtually every system of the body with neurologic complications being one of the most severe occurring in 25% or more of affected patients.⁵⁻⁷

These neurologic complications include ischemic and haemorrhagic strokes, transient ischemic attacks, silent cerebral infarction, seizures, headaches, visual loss.⁸⁻¹⁰ Stroke resulting from cerebrovascular accidents (CVA) is devastating and potentially fatal. CVA could be overt typically due to large artery vasculopathy involving the

intracranial internal carotid arteries and proximal middle cerebral arteries or silent involving penetrating arteries of the major arteries. Approximately 11% of SCA patients have a CVA before the age of 20 years which are usually ischemic.¹¹ Prevention of CVA is thus an important part of comprehensive care for sickle cell disease children especially those aged 2-16 years. This is routinely carried out in most developed countries through the use of Transcranial Doppler (TCD) ultrasonography however, this service is scarce in developing countries.

In the 1990s, Robert Adams and associates demonstrated the efficacy and significance of TCD scanning by identifying children who were at a high risk of cerebrovascular accidents.¹² The Doppler scan evaluates the blood flow velocity in the main arteries of the brain. The values obtained from this procedure are categorized as abnormal (≥ 200 cm/s), conditional (170-199 cm/s) and normal or standard risk (< 170 cm/s). Children with abnormal blood velocities are at high risk for CVA while children whose velocities fall within the conditional range are at moderate risk for CVAs.

Taking into consideration the fact that Transcranial Doppler ultrasonography has become routine in the management of children with SCA to prevent CVA and the fact that some children may present with CVA even before their first TCD this study aimed to describe the blood flow velocities of major arteries of the brain in SCA children aged 2-16 years, determine its relationship with sociodemographic characteristics (age, gender, socioeconomic status).

Additionally, it is hoped that the results of this study will help advance our understanding of this crucial topic, as well as add to the already existing knowledge on cerebral blood flow velocities.

METHODS

One hundred and two children with SCA between the ages of 2 and 16 were enrolled in the study. The participants were recruited from the Paediatric Sickle Cell clinic of Federal Teaching Hospital Owerri, Imo state Nigeria. Approval was obtained from the hospital's Research and ethics Committee. Informed written consent and assent were obtained from the parents/caregivers and patients before enrollment into the study.

Inclusion criteria

Patients aged 2 to 16 years were consecutively enrolled in the study during routine visits to the clinics. These include eligible patients who were previously diagnosed SCA as homozygous haemoglobin S disease using cellulose acetate electrophoresis at alkaline pH. All patients were in steady state defined as the absence of an acute illness (pain crisis, fever or other SCA-related

acute complications) or transfusion in the preceding four weeks.

Exclusion criteria

Patients with acute illness such as fever, central nervous infection, major head injury, previous cerebrovascular accidents, epilepsy requiring anticonvulsants were excluded from this study. Other exclusion criteria include children less than two years of age and above 16 years, those receiving hydroxyurea and recipients of chronic blood transfusion, those with genotype Haemoglobin SC.

Data collection

Sociodemographic Data: A structured questionnaire was used to obtain basic bio-demographic data such as age, sex, socioeconomic status, past medical, neurological and blood transfusion history.

The socioeconomic classification

This was determined using the revised scoring scheme proposed by Oyedele.¹⁵ The classification was based on occupation and educational attainments of both parents/caregivers which were graded on a scale of I-V, with highly skilled and highly educated being I and unemployed and uneducated being V. The mean of four scores (two for occupation and education for father and two for same for mother) approximated to the nearest whole number was assigned to each child. For this study, subjects were divided into 5 socioeconomic classes I-V, with I&II, III, IV&V as upper, middle and lower socioeconomic classes respectively.

Non-imaging TCD

The cerebral blood flow velocities of all enrolled patients were measured in line with the Stroke Prevention in Sickle Cell Disease protocol using a 2-MHz hand-held probe connected to a Doppler box. The test measured and assessed the blood flow velocity in arteries, referred to as the Willis circle. When TCD hits a wave in the MCA (middle cerebral artery) and ACA (anterior cerebral artery) that can be heard and recorded, it produces audible noises. The procedure was performed utilizing a non-imaging PMD model 150 by Spencer Technology in Washington. During the procedure, the patient lay down on a bed and was conscious.

A transducer was positioned directly on the patient's temporal area (transtemporal window). The transducer was moved differently so that the ultrasound waves were pointed towards the blood vessels under investigation. For each vessel, several measurements were made between 40 and 60 mm on both sides. The TAMMV was used to capture the maximum velocity in the left and right cerebral arteries used. Values greater than 170 cm/sec but less than 200 cm/sec were regarded as conditional risks, while a velocity of ≥ 200 cm/sec was regarded as abnormal

(high risk). A TAMMV of less than 170 cm/sec was considered normal (standard risk). For the purpose of this study conditional risk and high risk were considered abnormal velocity while standard risk was considered as normal velocity.

Statistical analysis

The data were collated and entered into the Excel spreadsheet. IBM Statistical Package for Social Sciences (SPSS) version 26.0 was used to analyse the data. As needed, frequency tables and figures were utilised to summarise the variables. The data was subjected to normalcy testing and was normally distributed.

Quantitative variables with a normal distribution were summarized using the mean and standard deviation. For categorical variables, percentages and frequencies were generated. Differences between mean of two groups was tested using independent t test. Differences in proportions was tested using Chi square. A p value of <0.05 was considered statistically significant.

RESULTS

A total of 102 SCA children aged between 2 and 16 years old were studied. The mean age of the study participants was 7.7 ± 4.4 years. Amongst the study participants, 55.9% were males, while 44.1% were females. Majority of the participants (60.8%) belonged to the middle socioeconomic class.

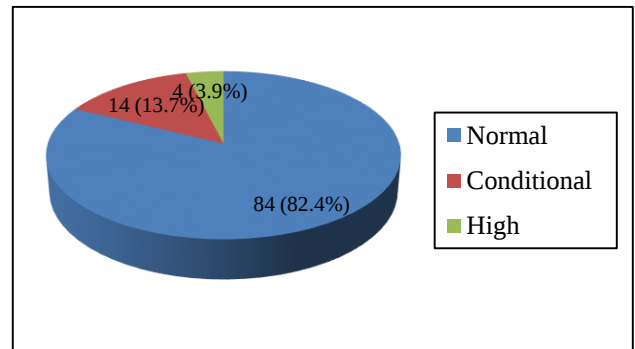


Figure 1: Pattern of the cerebral blood flow velocities.

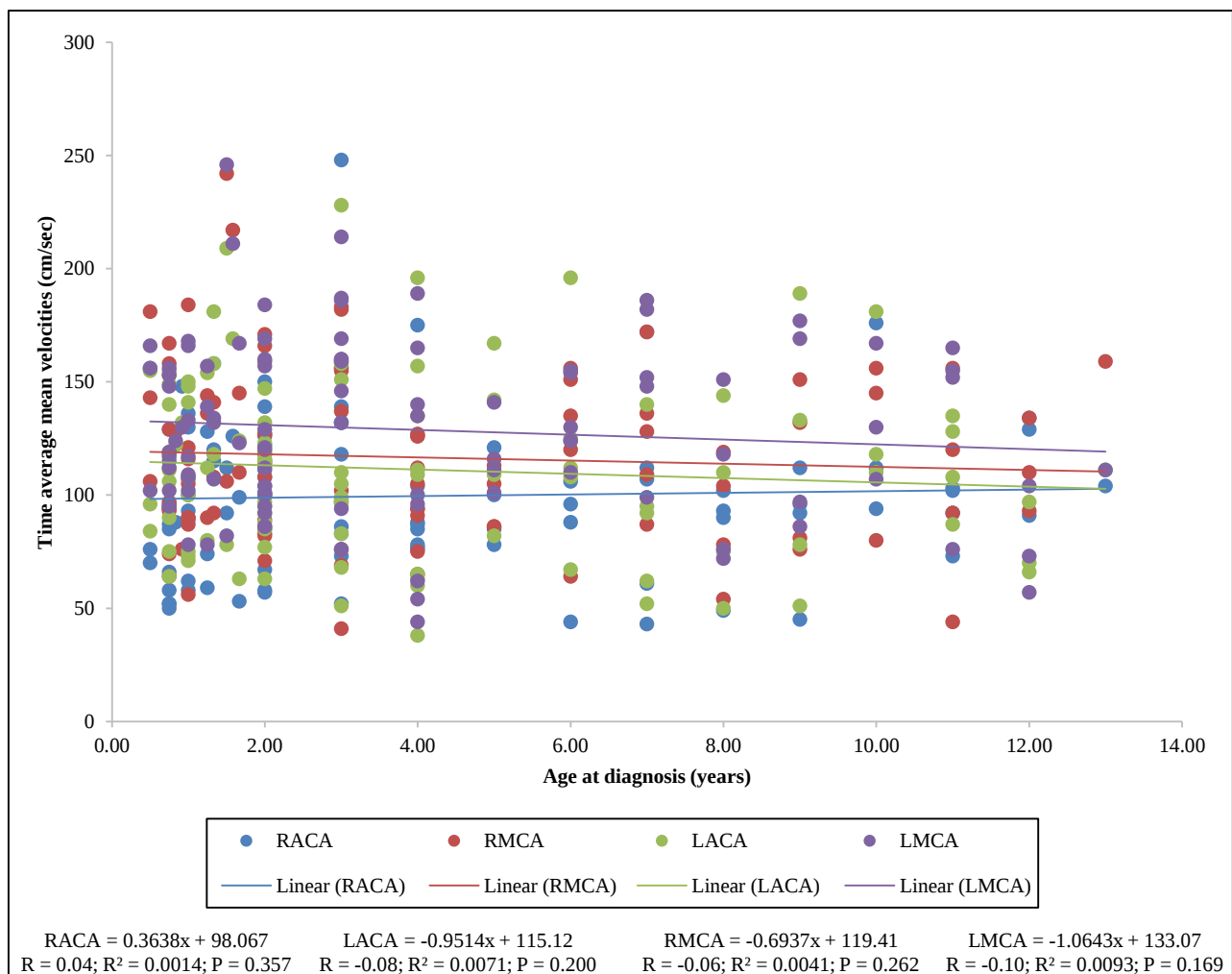


Figure 2: Relationship between age at diagnosis and CBFV.

TAMMV in the anterior and middle cerebral arteries in the study participants

The time average mean maximum velocities ranged between 38.0 and 248.0 cm/sec. The minimum, maximum, mean velocities and standard deviation in the RACA, LACA, RMCA and LMCA are as shown in table 2. The lowest velocity was found in the left anterior cerebral artery and the highest in the right anterior cerebral artery. The highest mean velocity was found in the left middle cerebral artery.

Table 1: Sociodemographic and anthropometric characteristics of study participants.

Variables	Frequency, N (%)
Age group (in years)	
2- 6	46 (45.1)
7-11	31 (30.4)
12-16	25 (24.5)
Gender	
Males	57 (55.9)
Females	45 (44.1)
Parent's social class	
Lower	29 (28.4)
Middle	62 (60.8)
Upper	11 (10.8)

Table 2: TAMMV In the anterior and middle cerebral arteries in the study participants.

	Minimum velocities (cm/sec)	Maximum velocities (cm/sec)	Mean velocities (cm/sec)	Standard deviation cm/sec
RA CA	43.0	248.0	99.4	33.7
LA CA	38.0	228.0	111.1	38.6
RM CA	41.0	242.0	116.4	37.1
LM CA	44.0	246.0	128.5	38.0

RACA-Right anterior cerebral artery, LACA-Left anterior cerebral artery, RMCA-Right middle cerebral artery, LMCA-Left middle cerebral artery

Pattern of cerebral blood flow

Majority of the participants had standard risk with prevalence of 82.4%, while prevalence of abnormal blood flow velocity (conditional and high risk) was (17.6%) see Figure 1.

Relationship between cerebral blood flow and age

Ninety two percent (23/25) of children aged 12 -16 years had normal velocities compared to the 80.4% (37/46) and 77.6% (24/31) seen in children aged 2-6 years and 7-11

years respectively. While abnormal flow was seen in only 8% compared to the 19.6% and 22.6% of those aged 12-16 years, 2-6 years and 7-11 years respectively. This difference was however not significant ($\chi^2=2.236$ and $p=0.327$) Table 3.

Relationship between cerebral blood flow and gender

The blood flow pattern was similar in both males and females Table 4.

Table 3: Cerebral blood flow pattern and age.

Age (in years)	Cerebral blood flow pattern		χ^2	P value
	Normal N (%)	Abnormal N (%)		
2-6 (n=46)	37 (80.4)	9 (19.6)	2.236	0.327
7-11 (n=31)	24 (77.4)	7 (22.6)		
12-16 (n=25)	23 (92.0)	2 (8.0)		

Table 4: Relationship between cerebral blood flow and gender.

Cerebral blood flow pattern				
Gender	Normal N (%)	Abnormal N (%)	χ^2	P value
Male	47 (82.5)	10 (17.5)	0.000	0.975
Female	37 (82.2)	8 (17.8)		

Relationship between age at diagnosis and CBFV

There were no statistically significant correlations between time average velocities in all the arteries and age at diagnosis ($p=0.357, 0.200, 0.262, 0.169$). Coefficient of correlation (R), coefficient of determination (R^2) and probabilities are shown in the Figure 4 for the various arteries.

Table 5: Relationship between socioeconomic status and CBFV.

SES	Frequency, N (%)		χ^2	P value
	Normal n=84	Abnormal n=18		
Lower	23 (79.3)	6 (20.7)	0.739	0.691
Middle	51 (82.3)	11 (17.8)		
Upper	10 (90.9)	1 (9.1)		

Table 6: Ages at diagnosis.

Age at diagnosis (in years)	Males (n=57)	Females (n=45)
<1	8 (14.0%)	8 (17.8%)
1-2	20 (35.1%)	13 (28.9%)
3-4	13 (22.8%)	7 (15.5%)
>4	16 (28.1%)	17 (37.8%)

Table 7: Cerebral blood flow pattern and age categories at diagnosis.

Age at diagnosis (in years)	Normal (n=84)		Abnormal (n=18)	
	Males (n=47)	Females (n=37)	Males (n=10)	Females (n=8)
<1	8 (9.6)	7 (8.3)	0 (0.0)	1 (5.6)
1-2	18 (21.4)	10 (11.9)	2 (11.1)	3 (16.7)
3-4	8 (9.6)	6 (7.1)	5 (27.7)	1 (5.6%)
>4	13 (15.5%)	14 (16.7%)	3 (16.7%)	3 (16.7%)

Table 8: Oyedeji socioeconomic classification.

Parents level of education	Score	Father	Mother
No formal education	5		
Primary	4		
SSCE/GCE/Grade 2 teachers training	3		
SSCE/GCE/professional training	2		
University graduate/equivalent	1		
Senior Public Servant/contractor/Professional manager/large scale traders	1		
Intermediate grade public servants/senior secondary school teachers	2		
Junior secondary school teachers/driver/artisan/clerks/typists	3		
Petty trader/labourer/messenger	4		
Unemployed/Full Time House wife/Student/Subsistence Farmer	5		

Relationship between socioeconomic status (SES) and CBFV

Majority of the study participants belonged to middle socioeconomic class. Majority of those with abnormal velocity were from the middle and lower (17/18) SEC. only one child from the upper class had abnormal velocity. This difference was however not statistically significant ($p=0.691$).

Ages at diagnosis

Sixteen of the 102 (15.7%) children were diagnosed with SCA before the age of 1 year. Thirty-three (32.4%), 20 (19.6%) and 33 (32.4%) were diagnosed at the age of 1-2 years, 3-4 years and >4 years respectively. Their gender distribution is shown in Table 6.

Cerebral blood flow pattern and age categories at diagnosis

Males with abnormal CBFV were diagnosed at age 3-4 years in 50.0%. Females are diagnosed equally at 1-2 years and more than 4 years.

DISCUSSION

This was a hospital based descriptive cross-sectional study. In this study, 102 SCA children aged two to

sixteen years were recruited, 45.1% of study participants were 2-6 years with mean age of 7.7 ± 4.4 years. The male to female ratio was 1.3:1. This is similar to that reported by Adekunle et al and Lagunju et al, who also studies ages two to sixteen years with mean age of 7.66 ± 4.2 years, M:F ratio was 1:1.4 and 9.22 ± 4.0 years, M:F 1.5:1 respectively.^{13,14} Majority of the study participants (60.8%) belonged to middle socioeconomic class. This is similar to that reported by Animasahun et al, in Lagos. Conversely, Aliu et al, in Gombe reported that 75.8% of their participants belonged to low socioeconomic class.^{16,17} Although all these studies were hospital based, the findings documented by Aliu et al, may be explained by the location and degree of literacy.

In this study, the TAMMV ranged from 38.0 to 248.0 cm/sec. The highest velocity was recorded in right anterior cerebral artery (RACA) followed by left middle cerebral artery (LMCA). The lowest velocity was found in the left anterior cerebral artery (LACA). This is in contrast to that documented by Lagunju et al, where the maximum velocity was recorded in left middle cerebral artery (LMCA) followed by left internal carotid artery (LICA) and the lowest velocity was recorded in right and left anterior cerebral arteries.¹⁴

Furthermore, Adekunle et al and Ismail et al, both documented maximum velocity in the right MCA.^{13,18} However, while Adekunle et al, documented minimum

velocity in the left ACA (similar to the current study), Ismail et al, documented minimum velocity in the left terminal internal carotid artery (different from this study). Although the same age group and methodology were used in all the studies, no immediate explanation can be provided for the difference in the affected arteries. In this present study, majority of SCA patients had standard risk CBFV. This is the same as previously documented by different authors both within and outside the country.^{13,14,18} This does not negate the fact that screening and interventions is important in the comprehensive management of SCA patients. The prevalence of abnormal CBFV documented in this study was 17.6% out of which 13.7% was conditional risk (CR) and 3.9% was high risk for CVA. All the children with high risk CBFV were aged 2-6 years and majority of those with CR were aged 7-11 years. The prevalence of high risk CBFV in this study is similar to 4.0% reported from the Cooperative Study of Sickle Cell Disease (CSSCD).¹³ In contrast however, the prevalence for high risk CVA in this study is lower than previous reports of 7.8% and 11.5% from a Jamaican and Dallas cohort study respectively.^{13,19}

In Nigeria, the prevalence reported in this study is similar to the 3% reported by Ismail et al, in Kano but lower than reports the 5.4% from Ahmed et al, in Abuja and Fatunde et al, in Ibadan, the 6.3%, 8.4%, 10.8% by Kehinde et al, in Lagos, Lagunju et al, in Ibadan, Adekunle et al, in Lagos respectively.^{10,14,18,20-22}

Younger subjects had a higher prevalence of abnormal CBF velocities. All (100%) of subjects with high CBF velocities were between 2-6 years age group. In this study, the prevalence of abnormal pattern reduced with increase in age suggesting that high CBF has a negative correlation with age. This is similar to the findings by Lagunju et al, where the researchers documented that with decreasing age there is higher CBF velocities. This was different from that found by Adekunle et al, who also studied children aged 2 -16 years but noted that ages 5-10 years had the highest prevalence of abnormal CBF velocities.^{14,22} This would suggest that children with SCA in the first 10 years of life should be priority target for routine TCD examinations in settings of limited resources.

In addition, this study found a prevalence of conditional risk (CR) to be 13.7%. This is similar to the 11% documented by Ismail et al.¹⁸ Conversely, it is lower than the prevalence of 21.9% found by Lagunju et al and 25.8% by Adekunle et al.^{14,22} This may be attributed to a larger sample size used compared to the present study.

Majority (92%) of participants with normal CBFV belonged to age 12-16 years corroborating the 87% documented by Adekunle et al. However, there was no statistical significance between CBFV and age. The current study showed that majority (75%) of participants with high risk CBF velocities were females and 64.3% of

those with CR were males. However, there was no statistical significance between CBFV and gender. This is similar to the study by Lagunju et al, but different from the study by Chhadi et al, in India who reported a higher prevalence (70.6%) in males.^{14,23} This difference may be explained by the fact that majority of the recruited study participants in the study by Chhadi et al, were males. In this study, majority of the participants were in the middle socioeconomic class (60.8%) and in addition, all those with high risk CBF velocities were in the middle socioeconomic class. Seventeen out of 18 children with abnormal velocity were from the lower and middle SEC however, the study did not show any significant relationship between socioeconomic status and abnormal CBFV. There is presently to the best of the researcher's knowledge, no available studies for comparison with the current study.

In this study, the age at diagnosis ranged from 6 months to 13 years. Only 15% of children were diagnosed with SCA before the age of 1 year with a mean age of diagnosis of 48 months. On the contrary, Chukwu et al, in Enugu, Brown et al, in Ibadan and Akodu et al, in Lagos documented age at diagnosis to range from 2 months to 14.7 years, 2.5 months to 14 years and 3 months to 12 years with mean age of 24 months, 24 months and 18 months respectively.²⁴⁻²⁶ Fifty percent of males with abnormal CBFV were diagnosed at age 3-4 years and 16.7% of females were diagnosed equally at ages of 1-2 years and more than 4 years. There was no statistically significant correlation between TAMMV in the arteries and age at diagnosis. There was dearth of literature to compare with the present study.

CONCLUSION

The prevalence of abnormal CBFV in SCA children aged 2-16 years in FUTHO was 17.6%. All the children with high risk CBFV were in the age group 2-6 years. There was no relationship between age, gender, socioeconomic status and abnormal CBFV. The age at diagnosis was not associated with abnormal CBFV.

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