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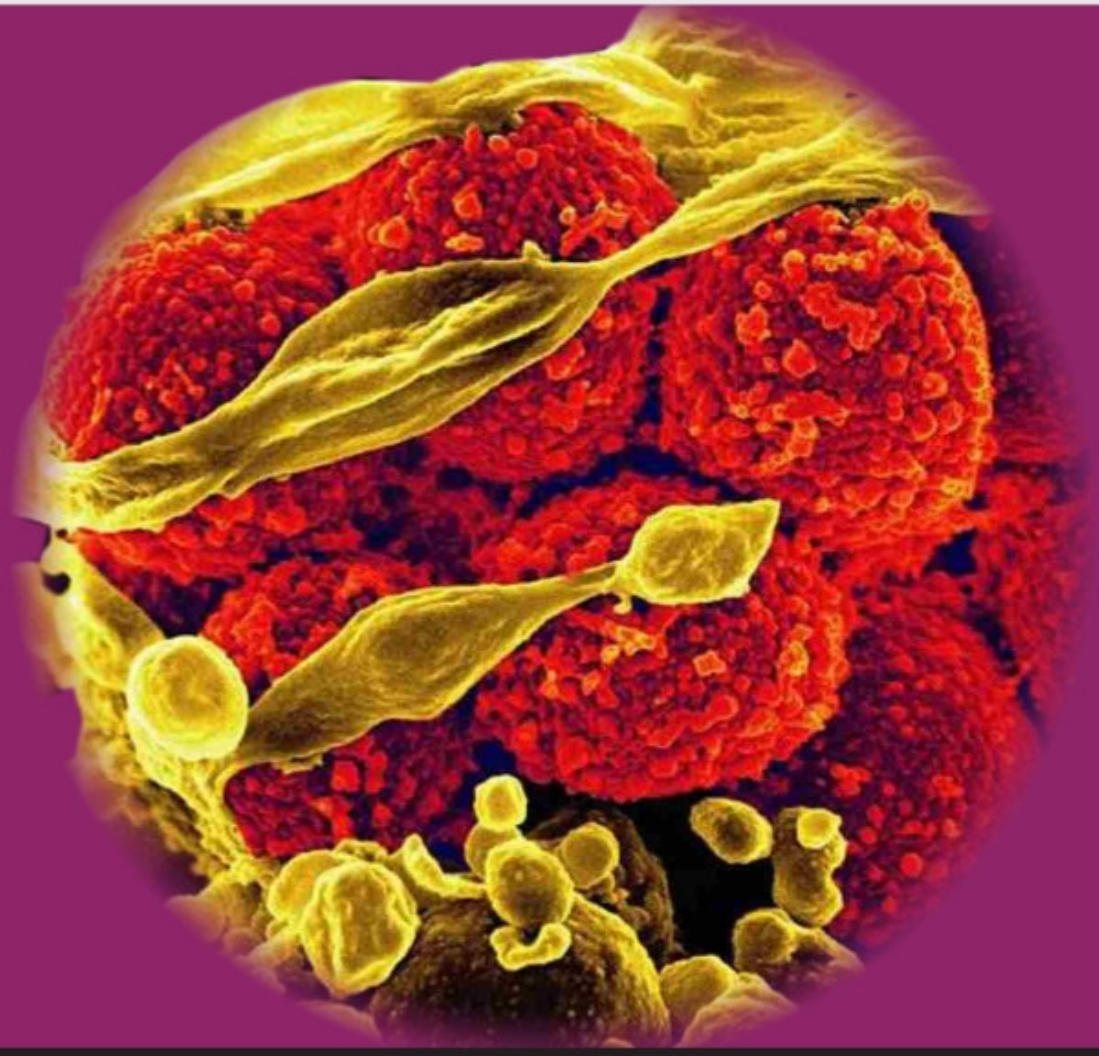

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ORIGINAL RESEARCH ARTICLE

Impact of Biosocial Factors on the Neuro-Cognitive Functions of School Children with Sickle Cell Anaemia

[1]Adegoke SA, [1]Oke OJ, [2]Akinlosotu MA, [3]Adeyemo MA, [4]Mohammed LO, [4]Fawale OO, [4]Adeniji EO, [1]Adeodu OO

[1]Department of Paediatrics and Child Health, Obafemi Awolowo University (OAU), Ile-Ife, Nigeria; [2]Department of Paediatrics, University of Medical Sciences, Ondo, Nigeria; [3]Department of Haematology and Blood Transfusion, Ladoke Akintola University Teaching Hospital, Osogbo, Nigeria.; [4]Department of Paediatrics, OAU Teaching Hospitals Complex, Ile-Ife, Nigeria.

Corresponding Author:
Adegoke Samuel A.,
Department of Paediatrics and Child Health,
Obafemi Awolowo University, Ile-Ife, Nigeria.
E-mail: adegoke2samade@yahoo.com

ABSTRACT

Background:

Sickle cell anaemia (SCA) may impair attention, memory, intelligence and academic performance. This study assessed cognitive function (academic performance and intelligent quotients, (IQ) of children with SCA and determined association between biosocial factors and neurocognition.

Materials and Methods:

Cognitive function of 120 children with SCA and 104 matched controls was assessed with Ziler's Draw-A-Person test, academic performance questionnaire (APQ) and average annual academic report. Association with disease severity, sociodemographic, nutritional and clinico-haematological factors was assessed using multivariate analyses.

Results:

More controls than subjects obtained high scores in the APQ, p=0.003. The mean annual academic score was also higher in the controls, p=0.028. However, there was no difference in their mean IQ scores, p=0.831. Disease severity scores, duration of school absenteeism, age and class of SCA children had negative correlation with average annual academic scores (p=0.004, 0.009, 0.031 and 0.038 respectively). IQ scores however positively correlated with average annual scores, p=0.007. Sex distribution, social class, nutritional status and haematological data had no influence on academic performance or IQ. Although, school absenteeism (OR=4.1, 95%CI =2.2–8.4, p=0.003) and IQ (OR=2.9, 95%CI =1.3–7.7, p=0.024) independently predicted academic performance, none of the factors predicted IQ.

Conclusion:

Children with SCA had poorer academic performance, although their IQs were comparable to controls. Age, school type, class, disease severity and duration of school absenteeism influences cognition of children with SCA.

Keywords: academic performance, intelligence, neurocognition, sickle cell disease

INTRODUCTION

Sickle cell disease (SCD) have both clinical and psychosocial effects . The clinical manifestations in children varies and include recurrent painful episodes, anaemia, infections and multiorgan dysfunctions.[1,2] Patients and caregivers also experience various psychosocial burdens which have been classified into three main objective domains (financial burden, disruption of family interactions and disruption of routine family activities); and some subjective domains such as feeling of depression, sorrow and anger towards the child and the inability of the family to cope with the disease.[3-5] On the other

hand, the psychosocial impacts of the disease on the affected child include cognitive dysfunction such as impairment in executive functions, attention, memory and sensori-motor skills.[6] They may have reduction in Intelligent Quotient (IQ), lower academic school performance, feelings of anxiety, self-hate and depressive symptoms such as low self-esteem and feeling of hopelessness.[7]

Cognitive function is the intellectual process by which an individual becomes aware of, perceives, or comprehends ideas. It encompasses all aspects of perception, thinking, reasoning and remembering.[8] Cognitive functioning affects job, behaviour and academic performances, especially among school children. Assessment of cognitive functions in children may therefore help in identifying academic strengths and weaknesses, and allow teachers and parents to identify and help those with learning disability and attention-deficiency and/or hyperactivity disorders.[8]

Several studies, particularly in developed countries with easy access to magnetic resonance imaging (MRI) have linked stroke and silent cerebral infarct (SCI) in children with sickle cell anaemia (SCA) to cognitive dysfunction and reduced intelligence quotient (IQ).[9-12] Some studies have however shown that some of these children with no evidence of brain abnormalities on conventional MRI may also have cognitive impairment, lower IQ and poor academic school performance.[13-15] Biologic and social factors such as chronic anaemic state and associated hypoxia, the level of foetal haemoglobin, SCD severity, school absences from recurrent hospitalisation, nutritional deficiencies such as low iron and zinc levels, socioeconomic status and SCA severity may be contributory factors.[16]

In sub-Saharan Africa with approximately 75% of global SCD burden [17], data on the relationship between cognitive function of children with SCA and sociobiologic factors are scanty. This study, therefore sought to assess cognitive function (measured by academic performance and intelligent quotients) of children with SCA and determine association with sociological and biological factors.

MATERIALS AND METHODS

Study Design, Location and Population

This was a comparative cross-sectional study in which sociodemographic, clinical, laboratory and neurocognitive data of primary school pupils aged 5 – 12 years with SCA in steady state and age- and sex distribution-matched apparently healthy haemoglobin AA controls were collected. Over the six-month study period, all 120 children with SCA who met inclusion criteria were recruited consecutively from the Paediatric Haematology Clinic, Wesley Guild Hospital Ilesa Unit, Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), Ile-Ife, Nigeria. The controls were 104 children who accompanied their siblings to the Paediatric Haematology Clinic, but without SCA or those seen at the Children General Outpatient Clinic of the hospital for school-entry medical tests. They were also selected consecutively over the study period. Steady state was defined as a period during which a child with SCA was free of crisis (pain or haemolytic), infection and any other acute illness for at least four weeks after the last event and at least three months after the last blood transfusion.[1] Those on chronic blood transfusion (CBT) program, those with significant neurodevelopmental disorders such as cerebral palsy, mental retardation or Down's syndrome were excluded. Permission for the study was obtained from the Ethics and Research Committee of the Institute of Public Health, College of Health Sciences, Obafemi Awolowo University, Ile-Ife, Nigeria (IPH/OAU/12/828). The participants were informed about the study both verbally and with the use of patient's information sheet. For each child recruited, written informed consent and assent were also obtained from the parents/caregivers and patients as appropriate. All participants were identified using codes and all information obtained were kept confidential.

Data Collection

Sociodemographic Characteristics

Data on the socio-demographics (age, sex, educational level and socioeconomic status) were obtained from both patients and caregivers using a proforma specifically designed for the study. Socioeconomic status was determined using the occupation of the father and the highest academic qualification of the mother according to Olusanya *et al* (1985).[18] The father's occupation has scores ranging from 1 to 3, while the mother's educational qualification has scores from 0 to 2. The total score was then calculated for each patient. The minimum and maximum possible scores were 1 and 5 respectively. Those with a total score of 1 or 2 were in the upper social class (i.e., social class 1); total score of 3 for middle social class (social class 2) and score of 4 or 5 for lower social class (social class 3).

Type of School: The type of school attended by the participants was categorised as private or public.

Clinical Data: Data on the clinical history and physical findings were obtained with a proforma and by review of relevant medical charts and documented. Complications SCD were as defined by Ballas *et al* (2010).[1] The clinical severity of SCD was determined based on the number of admissions, blood transfusions and significant painful crises in the previous 12 months and presence of lifetime complications using a validated scoring system described by Adegoke and Kuti (2013) among children with SCA in southwest Nigeria.[19] The total obtainable score using this disease severity scoring index ranged from 0 to 34. Patients with score of <8 were classified as having mild disease, 8 – 17 as moderate disease and >17 as severe disease.

Nutritional Data: Weight was measured to the nearest 0.1 kg by digital electronic scale (Scaletronix, White Plains, NY) and height to the nearest 0.1 cm with a stadiometer (Holtain, Crymych, UK). Weight, height and body mass index (BMI, weight/height^2) were transformed into z scores for height/age (HAZ), weight/height (WHZ) and BMI (BMI-Z). These were then compared to the reference values using WHO child growth standards [20] for children younger than five years, and National Center for Health Statistics (NCHS)/Centers for Disease Control and Prevention 2000 reference standards for those older than five years.[21] Underweight was defined as BMI-Z < -2 SD from the mean, overweight BMI-Z was > 2 SD but ≤ +3 SD from the mean and obese if BMI-Z was > +3 SD and normal when BMI-Z score for age and sex was between ± 2 SD from the mean. Stunting and wasting were defined as HAZ and WHZ < -2 SD respectively.

Haematological Parameters: Steady state haematocrits, leucocyte and platelet counts were determined using auto-hemoanalyser Pentra 60, Horiba® machines. Foetal haemoglobin percentage was measured using BIO-RAD® D10 high performance liquid chromatography (HPLC).

Assessment of Cognitive Function: Cognitive function of the study participants was measured using academic performance index and intelligence quotient scores.

Academic Performance

Academic performance was assessed with parental reports, previous session school report card and academic performance questionnaire (APQ).[22] Parents were requested to provide information on the total number of possible school days in the previous academic year (three terms), number of days the child was absent from school in the previous academic year and information on whether or not the child has ever repeated a grade. Other information included whether the child had a learning problem (i.e. whether the child had experienced increased difficulties at school when compared to their siblings or other classmates) and whether the child had ever

received special education services to cope academically. In this study, we considered absence from school for at least 10% of the total three-term school days of about 195 days (equivalent of at least 20 days) as significant enough to affect academic performance of primary school pupils. Previous studies for secondary school students considered 15% absence or more, as high or problematic absence, based on Kearney's criteria.[23,24]

Although parental information had been found to be reliable from the previous assessment among Nigerian and Saudi-Arabian children with SCD, in order to prevent information bias, data on number of school days, absences and average academic scores for the previous session (three terms) in percentage were verified from the child's previous session report card.[16,25] Average annual scores <50% were categorised as low, 50-69% as average while scores ≥ 70% were taken as high.

In addition to parental reports and report cards, APQ was also completed by the class teacher. A total of 240 questionnaires were sent out (120 for each arm of the study population), however, 224 were correctly filled and returned appropriately. These comprised of all the 120 sent to teachers of children with SCA and 104 to teachers of children without SCA. Retrieval was facilitated by the use of individual teacher's telephone number.

This validated questionnaire was given to the caregivers to present at school. After getting an informed consent from each teacher, he/she was required to complete the questionnaire for each child. The questionnaire was a ten-item questionnaire that assessed the child's skills in reading (item 1), comprehension (item 2), mathematics (items 3-6), writing (items 7-9) and percentage of homework completed on time (item 10) when compared with the average students in the class.[22] For each item, the scores ranged from 1 to 5: 1. indicates that the child is 90 - 100% comparable to the average students; 2 represents 80 - 89%; 3 is 70 - 79%; 4 is 60 - 69%; and 5 is 0 - 59%.

Measurement of Intelligent Quotient (IQ)

Intelligence was determined with Ziler Draw-A-Person test (DAPT), which has been standardised and validated in Nigerian children.[26] Each child was instructed to draw a complete person and no further instruction was given. Four points count as 1 'Draw –a –person' year equivalence. Hence, to derive the maturation age (MA), the total number of points scored was divided by 4, and thereafter 3 extra points were added. This was done because DAPT is only effective for children after the age of 3 years, i.e. MA = Points scored/4 + 3. i.e. The draw-a-person quotient = IQ = percentage of maturation age/chronological age. Scores above 75% suggested normal intelligence, scores between 50 and 75% indicated mild mental retardation and scores <50% moderate to severe mental retardation.[26,27]The DAPT has a correlation of 0.62 with Stanford-Binet Scale ,[28] moderate to good correlation (0.64–0.78) with Raven scale of intelligence in children,[29,30] a good correlation (0.81) with Weschler intelligence scale of children. The DAPT is a non-verbal test that is easy to use and is widely culturally acceptable.[31] It tests the cognitive maturity and knowledge of the child on how to reproduce his concept of the human figure by drawing parts of the body, placing them correctly in relation to each other proportionally.[31] The DAPT has no cultural limitations like other psychometric tests and the drawing of human figures has also been found interesting to children irrespective of their cultural background.[31,32]

Data Analysis

Both descriptive and inferential statistics were used for statistical analysis. The outcome variable was the cognitive function (academic performance score and IQ), while the study factors included sociodemographic and clinico-haematological data. Pearson's correlation and chi-square test were employed, as appropriate, to examine the influence of the study factors on the outcome at the level of bivariate analysis. A logistic regression model was used to test for

potential predictors of impaired cognitive function (poor academic performance and subnormal intelligence). Probability (*p*) values < 0.05 was accepted as significant values at 95% confidence interval.

RESULTS

Sociodemographic Data of Children with SCA and the Controls

A total of 224 children were studied, with 120 in SCA group and 104 apparently healthy haemoglobin AA children. One hundred and thirty-three (59.4%) of the 224 children, comprising of 76 (63.3%) of the 120 with SCA and 57 (54.8%) of the 104 controls were males (p = 0.195). Also, there was no significant difference in the mean ages of the subjects (9.13 ± 2.16 years) and controls, (9.72 ± 2.48 years; t = -1.896; p = 0.059). One hundred and fifty-four were aged 5 – 9 years comprising of 81 subjects and 73 controls. The remaining 70 (39 subjects and 31 controls) were adolescents aged 10 - 12 years. Social class distribution was also similar (χ^2 = 0.761; p = 0.683). One hundred and twenty-three (54.9%) of the total 224 children comprising 67 (55.8%) subjects and 56 (53.8%) controls were from middle social class.

Type of School

Majority, 192 (85.7%) of the participants were attending private schools. These included 98 (81.7%) subjects and 94 (90.4%) controls. There was however no significant difference in the type of schools attended by the subjects and the controls (χ^2 = 3.458; p = 0.063).

School Absenteeism

The number of missing days from school during the whole year ranged from 0 to 120 days, with a median (interquartile range, IQR) of 11.2 (6.9 – 17.6) days. The range was 0 – 120 days among SCA and 0 – 14 days among the controls. For subjects with SCA, three (2.5%) children absent for more than three months (>60 school days), 19 (15.8%) for between 1 and 3 months (20 – 60 school days) and 37 (30.8%) for less than 1 month (<20 school days). For the controls, all the 52 (50.0%) that were absent from school reported being absent for less than 1 month (<20 school days). In all, 64 of the 120 (53.3%) subjects with SCA and 52 (50.0%) of the 104 controls were absent for varying periods during the year. Using a cut-off of 20 school days, 27 (22.5%) of the 120 subjects with SCA as against none of the 104 controls were absent for more than 20 days (χ^2 = 26.607; p < 0.001).

Clinical Data of Subjects with SCA

The minimum and maximum sickle cell disease severity scores were 0 and 21 respectively with median (IQR) score of 8.8 (5.5 - 11.3). Sixty-two (51.7%) of the 120 subjects with SCA had mild disease, 49 (40.8%) had moderate disease, while 9 (7.5%) had severe disease including the three with prior history of stroke. Within 12 months preceding recruitment into the study, 72 (60.0%), 52 (43.3%) and 30 (25.0%) had at least one episode of significant pain necessitating hospital visit and analgesia use, SCD-related hospitalisation and transfusion respectively. None of the children had an overt stroke.

Nutritional data of Children with SCA and the Controls

Subjects with SCA had significantly lower median BMI-Z and HAZ scores than the controls (BMI-Z scores -0.88 vs. -0.21, p <0.001; and HA-Z scores -0.34 vs. 0.26, p <0.001). The prevalence rates of underweight (23.3% vs. 14.6%, p = 0.032) and stunting (11.7% vs. 0%, p = 0.003) were higher among subjects with SCA.

Haematological Data of Subjects with SCA:

The mean haemoglobin concentration of the 120 subjects with SCA was 7.3 ± 1.6 g/dl (range = 4.3 - 10.4g/dl), leucocyte counts was 22.3 ± 2.7 x10^9/L (range 4.8 – 29.5 ×10^9/L) while the mean platelet counts was 387.4 ± 152.5 ×10^9 /L (range from 80.0 – 842.0 ×10^9 /L).

Comparison of Academic Performance Score, Average Annual Academic Score and IQ in Subjects and Controls

Table 1 shows that significantly higher proportion of controls than children with SCA (55.8% versus 36.7%) were scored 90 – 100% in the APQ by their respective teachers in reading, comprehension, writing and mathematics (p = 0.003). More subjects with SCA (20.0%) than the controls (5.8%) were, however, scored average (i.e. APQ score of 60 - 69%; p = 0.002). No significant difference in the proportions of subjects with SCA and the controls who had low APQ scores.

The mean average annual academic score was higher in the controls (73.9 ± 20.2%) than SCA (63.4 ± 26.1%), p = 0.028. While more controls than subjects with SCA (59.6% against 40.8% respectively) had high average annual scores (i.e. scores ≥ 70%; p = 0.005), higher proportion of SCA (22.5% vs. 4.8%) had low annual score (scores <50%; p < 0.001). There was no difference in the mean IQ scores between the two groups, 71.3 ± 14.6% for the controls and 70.8 ± 19.6% for SCA (t = 0.21; Odd ratio (95% CI) = 1.0 (0.9 – 1.3); p = 0.831). Also, the proportion of children with either moderate or severe learning disability was similar (Table 1). The proportion of subjects with SCA (38.3%) who had normal intelligence was however higher than that of controls (25.0%; p = 0.033).

Factors Affecting Academic Performance of Subjects with SCA

Using average annual academic score of≥ 70% as good performance and score <70% as poor academic performance, 49 (40.8%) of the 120 subjects with SCA had good academic performance, while 71 (59.2%) had poor performance.

Effect of Age: There was no significant difference in the proportions of preadolescents or adolescents with good academic performance, 34 (42.0%) of 81 vs. 15 (38.5%) of 39 respectively (χ^2 = 0.135; p = 0.714). There was however a weak negative correlation between age and the average annual academic scores (r = – 0.4; p = 0.004).

Table 1. Comparison of academic performance score, average annual academic score and intelligence quotient in subjects with SCA and controls.

Variables		SCD n = 120 n (%)	Controls n = 104 n (%)	Test statistics	p-value
APQ scores					
	(90 – 100%)	44 (36.7)	58 (55.8)	9.055	0.003*
High(≥ 70)	(80 – 89%)	25 (20.8)	17 (16.3)	0.736	0.391
	(70 – 79%)	19 (15.8)	12 (11.5)	0.862	0.353
Average	(60 – 69%)	24 (20.0)	6 (5.8)	9.727	0.002*
Low	(0 – 59%)	8 (6.7)	11 (10.6)	1.097	0.295
Average Annual Academic Score (Mean ± SD)		63.4 (26.1)	73.9 (20.2)	-2.221	0.028*
High (≥ 70%)		49 (40.8)	62 (59.6)	7.827	0.005*
Average (50 – 69%)		44 (36.7)	37 (35.6)	0.029	0.866
Low (<50%)		27 (22.5)	5 (4.8)	12.834	<0.001*
Intelligence Quotient IQ (Mean ± SD)		71.3 (14.6)	70.8 (19.6)	-0.210	0.831
Normal intelligence (>75%)		46 (38.3)	26 (25.0)	4.541	0.033*
Mild MR (50 - 75%)		54 (45.0)	60 (57.7)	3.591	0.058
Moderate – severe MR (<50%)		20 (16.7)	18 (17.3)	0.016	0.899

*statistically significant

APS – Academic Performance Score; IQ - Intelligence Quotient, MR – Mental retardation

Effect of Type of Schools: Significantly higher proportion of children in private schools, 46 (46.9%) of 98 than those attending public schools, 3 (13.6%) of 22 had good academic performance (χ^2 = 6.927; p = 0.008).

Effect of Class: The present class of the subjects had a weak negative correlation with the average annual academic scores (r = - 0.3; p = 0.031). Although, higher proportion of children in Basic 1 – 3 than those in Basic 4 – 6 had good academic performance (45.6% vs. 26.6% respectively), it was not significant statistically (p = 0.068).

Effect of Duration of Absenteeism: As shown in table 2, more children who were absent for at least 20 days, 25 (92.6%) of 27, performed poorly academically compared to 46 (49.5%) of the remaining 93 (χ^2 = 14.764; p < 0.001). Duration of school absenteeism also negatively correlated with average annual academic scores (r = -0.6; p = 0.009).

Effect of Disease Severity: SCD severity score had a moderate negative correlation with average annual academic score; (r = -0.6, p = 0.038). Also, the proportion of the nine children with severe disease who performed poorly academically (88.9%, i.e. 8 of 9) was significantly higher than 63 (56.8%) of 111 with mild or moderate disease who performed poorly (p <0.001; Table 3). Disease severity score was also observed to have significant positive correlation with the duration of school absenteeism (r = 0.4; p = 0.026). Other factors such as sex distribution, socioeconomic class, nutritional status and haematological data did not significantly affect the academic performance of subjects with SCA (Tables 2-4).

Factors Affecting IQ of Subjects with SCA

Forty-six (38.3%) children with SCA had normal IQ while the remaining 74 (61.7%) had subnormal intelligence.

Effect of Age: The mean (SD) IQ was significantly lower among adolescents than preadolescents, 63.5 (7.7%) vs. 71.2 (12.8%), t = -3.46, p = 0.001.

Effect of Duration of School Absences: Similarly, the mean (SD) IQ of children with longer school absenteeism (at least 20 days) was lower, 60.9 (24.8%) than those with short school absenteeism, 69.3 (6.2%; t = -2.99; p = 0.003). There was also a moderate negative correlation between duration of school absence and IQ of children with SCA (r = -0.54; p = 0.001).

Effect of Disease Severity: The IQ of the 9 children with severe SCA (including the three with stroke) was lower than that of those without severe disease, 58.6 (3.9%) vs. 67.0 (1.7%; t = -12.56, p < 0.001). Other factors such as sex distribution, socioeconomic class, type of school, class of the child, nutritional status and haematological indices did not show significantly influence on the IQ (Table 2 - 4).

IQ and Academic Performance

Intelligence Quotient scores positively correlated with average annual academic score (r = 0.72; p = 0.007). More children with subnormal IQ than those with normal IQ performed poorly academically, 65 (87.8%) of 74 versus 6 (13.0%) of 46 respectively (χ^2 = 65.683; p < 0.001).

Logistic Regression: Binary logistic regression analysis was undertaken to demonstrate the influence of sociodemographic, clinical, nutritional and haematological factors on impairment of IQ and academic performance. Duration of school absenteeism (OR = 4.1; 95% CI = 2.2 – 8.4; p = 0.003) and IQ (OR = 2.9; 95% CI = 1.3 – 7.7; p = 0.024) independently predicted academic performance of children with SCA. However, although age, duration of school absences and disease severity were associated with IQ, none of these factors was found to be an independent predictor on regression analysis.

Table 2: Association between sociodemographic and types of schools and cognitive function among subjects with SCA.

Variable	Academic Performance Good n = 49 (%)	Intelligence Quotients Poor n = 71 (%)	P-value	Normal n = 46 (%)	Subnormal n = 74 (%)	P-value
Age (years) (Mean ± SD)						
Preadolescents (n =81)	34 (69.4)	47 (66.2)	0.714	39(84.8)	42 (56.8)	0.007*
Adolescents (n = 39)	15 (30.6)	24 (33.8)		7 (15.2)	32 (43.2)	
Sex Distribution						
Male (n =76)	31 (63.3)	45 (63.4)	0.990	29(63.0)	47 (63.5)	0.959
Female (n =44)	18 (36.7)	26 (36.6)		17(37.0)	27 (36.5)	
Social Class						
Upper (n =19)	8 (16.3)	11 (15.5)		10(21.7)	9 (12.2)	
Middle (n =67)	31 (63.3)	36 (50.7)	0.263	28(60.9)	39 (52.7)	0.077
Lower (n =34)	10 (20.4)	24 (33.8)		8 (17.4)	26 (35.1)	
Type of school						
Private (n =98)	46 (93.9)	52 (73.2)	0.008	40(87.0)	58 (78.4)	0.238
Public (n =22)	3 (6.1)	19 (26.8)		6 (13.0)	16 (21.6)	
Class						
Basic 1-3 (n =90)	41 (83.7)	49 (69.0)	0.068	36(78.3)	54 (73.0)	0.515
Basic 4-6 (n =30)	8 (16.3)	22 (31.0)		10(21.7)	20 (27.0)	
Number of School Absences						
<20 school days n =93	47 (95.9)	46 (64.8)	<0.001	44(95.7)	49 (66.2)	<0.001*
≥ 20school days n = 27	2 (4.1)	25 (35.2)		2 (4.3)	25 (33.8)	

*statistically significant

Table 3: Association between nutritional and clinical data including SCD severity and cognitive function among subjects with SCA.

Anthropometric and clinical data	Academic Performance			Intelligence Quotient		
	Good n = 49 (%)	Poor n = 71 (%)	P-value	Normal n = 46 (%)	Subnormal n = 74 (%)	P-value
BMI for age						
Underweight (n = 28)	7 (14.3)	21 (29.6)	0.113	8 (17.3)	20 (27.0)	
Normal BMI for age (n = 85)	38 (77.5)	47 (66.2)		35(76.1)	50 (67.6)	0.477
Overweight/obesity (n=7)	4 (8.2)	3 (4.2)		3 (6.6)	4 (5.4)	
Height for age						
Stunting (n = 14)	4 (8.2)	10 (14.1)	0.505	3 (6.6)	11 (14.9)	
Normal stature (n = 97)	42 (85.7)	55 (77.5)		41(89.1)	56 (75.7)	0.191
Tall for age (n = 9)	3 (6.1)	6 (8.4)		2 (4.3)	7 (9.4)	
Disease severity						
Mild (n = 62)	38 (77.6)	24 (33.8)	<0.001	34(73.9)	28 (37.8)	
Moderate (n = 49)	10 (20.4)	39 (54.9)		11(14.9)	38 (51.4)	<0.001*
Severe (n = 9)	1 (2.1)	8 (11.3)		1 (2.2)	8 (10.8)	

*statistically significant

Key: Overweight = BMI-Z > 2 SD but ≤ +3 SD from the mean; Obesity = BMI-Z > +3 SD; Normal = BMI-Z score between -2 SD and +2 SD from the mean. Stunting = HAZ < -2 SD. Mild disease = score of <8; Moderate disease = score 8 – 17; Severe disease = score >17.

Table 4: Correlation between haematological variables and academic performance/ Intelligence quotient scores among subjects with SCA.

Haematological variables	Average Annual Academic Scores Correlation coefficient (r)	P-value	Intelligence Quotient Scores Correlation coefficient (r)	P-value
Haemoglobin (g/dl)	0.28	0.053	0.46	0.051
Haematocrit (%)	0.40	0.059	0.54	0.052
MCV (fL)	0.11	0.074	0.35	0.294
MCH (pg)	- 0.45	0.083	- 0.35	0.094
MCHC (g/dl)	- 0.15	0.159	- 0.57	0.380
RDW (%)	- 0.32	0.325	- 0.62	0.711
Foetal haemoglobin (%)	- 0.31	0.211	- 0.35	0.103
WBC ($\times 10^9$/L)	- 0.72	0.061	- 0.44	0.271
Lymphocyte (%)	0.25	0.210	0.24	0.299
Granulocyte (%)	0.22	0.243	0.28	0.270
Monocyte (%)	- 0.47	0.084	- 0.72	0.063
Platelet count ($\times 10^9$/L)	- 0.08	0.704	- 0.03	0.518
MPV (fL)	0.53	0.315	0.55	0.726

DISCUSSION

Information on the association between biosocial factors, especially disease severity, on IQ and academic performance is lacking in children with SCD in many developing countries including Nigeria, a country with disproportionately high burden of the disease globally.[17,33] The patients had lower cognitive scores than the controls in the teachers-applied academic performance questionnaire scores and scores from annual academic report sheet. The IQ was however found to be comparable. This study demonstrates a high rate of school absenteeism among SCA cohorts. About half of the population experienced absenteeism during the academic year, with some up to 120 days and one of every five for more than 20 days. This is possibly because of high rate of SCD-related acute and chronic events as seen among our patients. Almost half had either moderate or severe disease. Also, within 12 months preceding recruitment into the study, 60% had at least one episode of significant pain, the leading cause of both out-patient treatment and hospitalisation among children with SCA.[34,35] Higher proportion of controls than children with SCA were scored 90 – 100% in the Academic Performance Questionnaire (APQ) by their respective teachers in reading, comprehension, writing and mathematics. The mean annual academic score was higher in controls than SCA. That is, more controls than subjects with SCA had high scores while more SCA had low annual academic score. Low APQ and average annual academic scores show that children with SCA are lagging behind their non-sickle cell counterparts. Indeed, only about two of every five children with SCA in this study scored high academically.

This study also showed that children with SCA and the healthy controls had no significant difference in mean IQ scores. This is contrary to the finding of Kawadler *et al (2016)* and that of Castro and Viana (2018) that IQ is lower among individuals with SCA.[36,37] Our findings may be attributed to a very small percentage of the study participants with severe disease.[36] In agreement with a previous study, patients with severe SCA had lower IQ than the ones without severe disease. Children with severe disease are more likely to have had stroke or SCI with subsequent lowering of intelligence.[37] Stroke and SCI (clinically silent area of hyperintensity

seen on T2-weighted MRI in the absence of overt stroke, or neurological symptoms lasting more than 24 hour) have been linked to neurocognitive impairment in individuals with SCA.[38] In childhood, the risk of stroke is highest in those with SCA, with approximately 11%, 15% and 25% of the affected children developing stroke by the end of second, third and fourth decade of life respectively.[38] The risk of stroke recurrence also ranges from 3 to 17%.[38,39] In addition, about one-third of children with SCA develop at least one SCI during their first decade of life.[36] Age, school absenteeism, severity of disease, type of school and class of the child influenced academic performance. In addition, the first three factors, influenced IQ. Children with SCA who have severe disease are more likely to be absent from school frequently and this may adversely affect their academic performance, as corroborated by this study.[40] The association of school absenteeism and poor academic performance in this study was also observed by Schatz (2004) and Moonie *et al (2008)*.[41,42] However, Ezenwosu *et al*(2013) found no association between academic performance and school absence.[27] School absenteeism can interfere with the acquisition of knowledge and other school activities hence causing poor academic performance.[43] It is advocated that in situations where prolonged hospitalization is anticipated, educational services should be provided to such children while in the hospital.

The observation that children attending private schools had better academic performance compared to the ones attending public schools, agrees with previous studies. [44,45] Better supervision of teachers and the pupils in the privately owned schools has been reported. This could result from prompt payment of teachers' salaries and allowances, maintenance of standard teacher pupil ratio and absence of industrial actions by the teachers hence ensuring continuity in the academic curriculum with fewer interruptions. [44] This study also observed that IQ scores positively correlated with average annual academic score and more children with subnormal IQ than those with normal IQ performed poorly academically. This is similar to what was found previously.[27] Intelligent quotient is an important determinant of academic performance in children and may help to determine proper class placement in children.[26] There was no association between IQ or academic performance and factors such as sex distribution, socioeconomic class, nutritional status and haematological data in the present study. Previous studies have shown that socioeconomic class correlated well with cognitive functioning in SCA.[37] Parents from upper social class are more likely to be able to afford private schools for their children compared to the ones from low social class. The potential debilitating effects of chronic anaemia on neurocognition have been previously studied.[16,37] Surprisingly haematocrit was not found to significantly influence cognition in this study and this could probably be because only a few of the children had severe disease. Severe SCA is associated with lower haemoglobin concentration, more hospital admissions and blood transfusions. [45]

This study has some limitations. Firstly, MRI which could have helped to determine the role of SCI on neurocognition could not be done because it was not available for use during the study. Secondly, the effects of oxygen saturation on cognitive function were not studied.

CONCLUSION

In conclusion, children with SCA had lower academic performance, although they had comparable IQs with matched controls. Age, type of school, the class, disease severity scores and duration of school absenteeism were associated with cognition of children with SCA. Physicians should, therefore, organise regular cognitive assessment and SCD-targeted programs to improve IQ and more importantly, academic performance to enable individuals with the disease maximize their potentials and achieve life goals.

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Author's Contributions:

SAA, OOA, OJO - study conception and design; SAA, MAA, MAA, OLM, OOF, EOA data acquisition; SAA, OJO - data analysis and interpretation of data; SAA – wrote the initial draft of the manuscript; all authors provided critical revision for important intellectual content; all authors approved of the final version to be published.

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