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Correlation between Anthropometric Variables, Social Class, Age and Hematological Profile among Children with Sickle Cell Anemia in ENUGU South-East Nigeria

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Authors' contributions

This work was carried out in collaboration between all authors. Author KIA had primary responsibility for protocol development, patient screening, enrolment, outcome assessment, preliminary data analysis and writing of the manuscript. Authors OIO and JMC compiled and wrote the study. Authors KIA, OIO, JMC and ATC participated in writing of the manuscript. Author Elias Aniwada did the statistical analysis. All authors read and approved the final manuscript.

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ABSTRACT

Background: Sickle cell anaemia (SCA), a common haematological genetic disorder, could affect both the growth and haematological profile of the sufferer.
Objectives: This study aims at determining any correlation between anthropometric variables and haematological parameters among children with sickle cell anaemia (SCA).
It also determines the association between social class and haematological parameters of children with SCA.
Methods: A total of 80 subjects were recruited into the study, comprising 40 HbSS patients. This is cross sectional study of haematological indices and anthropometric measurement of children with sickle cell anaemia aged 6-20 years.
All data were coded, entered, and then analyzed using the Statistical Package for Social Sciences program (SPSS), version 20.
Results: There was statistical significant correlation between BSA and total white blood cell count (TWBC) (p=0.028) but not with Haemoglobin concentration (Hb) and Erythrocyte sedimentation rate (ESR). Hb: r=0.073, p=0.654 ESR: r=0.224, p=0.164 TWBC: r=0.348, p=0.028. The Haemoglobin concentration, TWBC and ESR values are 7.77 g/dl, 11.96×10^9, and 15.4 mm/hr There is also no statistical significant correlation between BMI and haematological variables: TWBC r= 0.100 p=0.51, Hb: r=0.118, p= 0.469 ESR: r= 0.033, p=0.841.
There is also no statistical significant correlation between chest circumference and haematological indices. TWBC r= 0.216 p=0.181, Hb: r=0.043, p= 0.793 ESR: r= 0.143, p=0.378.
There were no statistical differences in mean for all the variables studied among the social classes. Hb; p=0.373 ESR p=0.633. TWBC p= 0.451.
Conclusion: Infection is not the only cause of elevation in TWBCs. it is important to also consider the impact of surface area on white blood cell count of children with SCD before using antimicrobials for such infections.

Keywords: Sickle cell anemia; anthropometry; hematological; children; Enugu.

1. INTRODUCTION

Sickle-cell disease anaemia (SCA) is a hereditary disorder of the blood characterized by an abnormality in the oxygen-carrying haemoglobin molecule in red cells [1]. High prevalence of sickle gene is known in some part of the world especially in Africa [1].

Sickle cell anaemia is caused by a single point mutation where in the normal codon GAG is replaced by GUG in the β^6 chain and these results in substitution of valine for glutamic acid at this position [1]. It is also known that β globin gene is located in the short arm of chromosome 11 [1].

Sickle cell anaemia was originally found in the tropics and subtropics but is now common worldwide due to migration of people from tropical to temperate zones [2]. The prevalence of sickle cell anaemia in Nigeria ranges from 0.4%-3% affecting about 20 per thousand newborns [3].

Disease distribution varies greatly among different geographical regions. Studies indicate that hematological genetic diseases are highly distributed in agricultural areas which were endemic with malaria transferring mosquitoes [4-5]. Malaria has placed the strongest known selective pressure on the human genome since the origination of agriculture within the past 10,000 years [4-5]. The presence of the sickle cell gene gives carriers a relatively higher immunity against malaria infection. Consanguineous marriages are also common in these areas which lead to an increase in the prevalence of the disease [4-5]. This genetic disease has different ways of manifestation. It could be in form of a trait or a disease.

Sickle cell trait is a condition in which a person has one abnormal allele of the hemoglobin beta-gene but does not display the severe symptoms of the disease. Example of such trait is AS and Sc [6].

The features of sickle cell anaemia are numerous and any organ or system could be implicated [4]. Nevertheless, it is variable in severity, for instance, concurrent alpha-thalassemia is known as a modifier of sickle cell disease severity. Haplotypes could also modify or worsen severity.

For example, children with the Senegal haplotype, on average, have the best clinical outcome, while those with the Cameroun/Bantu haplotype, on average, have the most severe outcome. Children with Benin haplotype usually have a disease of intermediate severity [7].

Most sickle cell patients do not show clinical signs in early infancy mainly because of the predominance of HbF at this period [8].

However at the second half of the first year, most of them may show signs of the disease. At times, due to some predisposing factors such as dehydration and infection, they may develop acute exacerbations called crisis which in turn can lead to long term complications like cerebrovascular accidents and end organ failure [8].

Sickle cell anaemia is associated with a haematological disorder that may contribute to certain morbidities such as haemolysis, vaso-occlusion and cerebrovascular accidents [9]. For instance, elevated total white blood cell (WBC) counts are common in SCA patients and adhesion of (activated) neutrophils to endothelium in patients with SCA may lead to endothelial damage, which may contribute to cerebrovascular accidents and other diseases [10]. Moreover, platelet activation and aggregation are accentuated in children with SCD, which is worse in crisis [11]. The increased platelet count among children with sickle cell anaemia which is due to increased levels of β-thromboglobin, platelets factor 4 and decreases in amounts of thrombospondin could also lead to cerebrovascular accidents [11].

These hematological indices when low in SCD with malnutrition poses an additive effect [5]. It is a well known fact that disparity in nutritional intake in children with sickle cell anemia may affect the haemogram and physical development of SCA children [12].

There is paucity of data on studies that correlated haematological profiles with anthropometric variables among children with sickle cell anemia especially in the south east region. This study therefore aims at determining any correlation between anthropometric variables and haematological parameters in sickle cell anaemia. It also determines the association between social class and haematological parameters.The findings from this study may add to the increasing knowledge of this challenging disease and may help to improve management of children with SCD.

2. SUBJECTS AND METHODS

This study was carried out in the University of Nigeria Teaching Hospital (UNTH) Enugu, South-east, Nigeria. It is a referral centre for various health facilities in Enugu state and her environs. The subjects were children with haemoglobin genotype HbSS attending the paediatric sickle cell clinic at UNTH Enugu.

Ethical clearance for the study was obtained from the Research and Ethical Committee of the University of Nigeria Teaching Hospital Ituku Ozalla. Informed consent was sought from parents or care givers. A written consent was obtained from the parents/ caregivers of the subjects and controls after explaining to them, in detail, the objectives of the study as well as the specimen and method of collection. Those who cannot read or write were verbally informed and their consent obtained.

Patients aged 6 months to 20 years with haemoglobin genotype SS (diagnosed by cellulose acetate electrophoresis at P.H 8.6) are included in the study while any patient with recent blood transfusion during the preceding four months. (This is because, the red blood cell life span is about 120 days and the 4^{th} month may still contain significant haemoglobin AA red blood cell) were excluded.

Children with sickle cell anaemia who attended the sickle cell clinic or present at the children emergency ward and who fulfilled the inclusion criteria were consecutively recruited into the study.

2.1 Sample Size Determination

A minimum sample size that was representative of the study population was determined using a standardized method [12].

$$N = \frac{Z^2 P (I - P)}{D^2}$$

Where Z = 1.96 i.e. the level of significance P =1.6% i.e prevalence of sickle cell anaemia with an attribute from a previous study at the University of Nigeria Teaching Hospital Enugu D = Tolerable error (0.05).

This yielded a minimum sample size of 23. However to enhance the accuracy of the study results, a sample size of 40 was adopted.

A cross sectional study of haematological indices and anthropometry measurement of children with sickle cell anaemia aged 6-20 years was undertaken.

2.2 Hematological Profile

Measurements of the hematological profile (Packed cell volume, haemoglobin concentration, white cell count and ESR) were taken using the recommended methods [13].

2.3 Anthropometric Variables

Weight in kilograms was taken with subjects using a normal bathroom standing scale [*Deteco scales Inc. Brooklyn, New York, USA*]. Recordings were made to the nearest 0.5 kg. [14-15].

Standing height in centimeters (cm) was measured with a stadiometer [*CMS weighing equipment of 17 Campdem Road, London, NW1*]. The height in (cm) was read off. Recordings were made to the nearest 0.5cm. [14-15].

Chest circumference was recorded in the horizontal plane through the fourth sternocostal junction at the end of normal expiration using a standard tape measure made of non-irritant, non-elastic material. Measurements were made to the nearest 0.5 cm. The height and weight values for the subjects were used to compute the anthropometric variables of Body Mass Index (BMI) and Body Surface Area (BSA) [16-18].

In this study, considering our study population (Aged greater than 10 years) we grouped the BSA into greater than 1 m^2 (> 1 m^2) and less than 1 m^2 (< 1 m^2). The chest circumference values were computed with appropriate normogram for age and sex and grouped into normal, above normal and below normal.

The social classes of subjects were determined using the recommended method by Oyedeji [19].

2.4 Data Analysis

Data was analyzed by SPSS version 17 Chicago; an initial frequency count of all variables was done. Data presentation was in the form of tables. The mean, ranges and standard deviation of all values were computed. Correlation between anthropometric variables and haematological parameters among children with sickle cell anaemia (SCA) was done using the Pearson correlation variable. Association between social class and haematological parameters of children with SCA was calculated using t test and ANOVA. Level of significance was set at $P<0.05$.

3. RESULTS

3.1 Determinant of Socio-demographic Characteristics and Hematological Indices of Children with Sickle Cell Anemia

Table 1 shows that majority of respondents were aged 10 years and above. Their mean age was 13.23±.46. The subjects were also well matched for sex; male (50%), female (50%) giving a ratio of 1:1.

Table 1 also shows the haematological indices of children with Sickle cell anemia. The Haemoglobin concentration, total white blood count (TWBC) and erythrocyte sedimentation rate (ESR) values are 7.77 g/dl, 11.96×10^9, and 15.4 mm/hr. This is statistically significant .$p<0.01$.

3.2 Relationship of Body Surface Area (BSA), Body Mass Index (BMI) and Chest Circumference with Haemato-logical Indices

Table 2 shows statistical significant correlation between BSA and total white blood cell count (TWBC) ($p=0.028$) but not with Haemoglobin concentration (Hb) and Erythrocyte sedimentation rate (ESR). Hb: $r=0.073$, $p=0.654$ ESR: $r=0.224$,$p=0.164$ TWBC: $r=0.348$, $p=0.028$. There is also no statistical significant correlation between BMI and total white blood cell count (TWBC), Haemoglobin concentration (Hb) and Erythrocyte sedimentation rate (ESR): TWBC $r= 0.100$ $p=0.51$, Hb: $r=0.118$, $p= 0.469$ ESR: $r= 0.033$, $p=0.841$. There is no statistical significant correlation between chest circumference and total white blood cell count, Haemoglobin concentration (Hb) and Erythrocyte sedimentation rate (ESR).: TWBC $r= 0.216$ $p=0.181$, Hb: $r=0.043$, $p= 0.793$ ESR: $r= 0.143$, $p=0.378$. Table 2.

3.3 Comparison of Age and Social Class with Hematological Profile of Respondents

There were no statistical differences in mean for all the variables, Haemoglobin concentration, Erythrocyte sedimentation rate, and total white blood cell count (Hb, ESR and TWC) studied between those 10 years and below with 10 years and above. Hb; p=0.948 ESR p=0.928. TWBC p= 0.649 Table 3.

There were no statistical differences in mean for all the variables studied among the social classes. (Hb, ESR and TWC). Hb; p=0.373 ESR p=0.633. TWBC p= 0.451 Table 3.

Table 1. Socio-demographic characteristics of respondents and Haematological indices of children with sickle cell anemia compared with a reference range

Socio-demographic variable	Frequency	Percent	
	n= 40	100(%)	
Age (years)			
0-10	7	17.5	
10 and above	33	82.5	
Mean±SD	**13.23±3.46**		
Sex			
Male	20	54.0	
Female	20	46.0	
Social class			
High	35	87.5	
Middle	4	10.0	
Low	1	2.5	
Variable	**Mean**	**SD**	**Normal range**
Hb	7.77	1.21	13.83±1.32*
Twbc	11,960.00	4914.70	5.67±1.59*
ESR	15.45	4.26	3-10 mm/hr**

Table 2. Relationship of Body Surface Area (BSA), Body Mass Index (BMI) and chest circumference with haematological indices

Variable	n=40	Mean	Test statistics R	p value
	BSA	1.306	0.073	0.654
	Hb	7.772		
	BSA	1.306		
	ESR	15.450	0.224	0.164
	BSA	1.306		
	TWBC	11960.000	0.348	0.028
Variable	**n=40**	**Mean**	**Test statistics R**	**p value**
	BMI	33.750	0.118	0.469
	Hb	7.772		
	BMI	16.379	0.033	0.841
	ESR	15.450		
	BMI	16.379	0.100	0.541
	TWBC	11960.000		
Variable	**n=40**	**Mean**	**Test statistics R**	**p value**
	chest circumference	69.607	0.043	0.793
	Hb	7.772		
	chest circumference	69.607	0.143	0.378
	ESR	15.450		
	chest circumference	69.607	0.216	0.181
	TWBC	11960.000		

Table 3. Comparison of age and social class with hematological profile of respondents

Variables	Age in years	n=40	Mean	Test statistics t test	p value
Hb	10 below	7	7.800		
	11 and above	33	7.766	0.065	0.948
ESR	10 below	7	15.000		
	11 and above	33	15.545	0.091	0.928
TWBC	10 below	7	12742.857		
	11 and above	33	11793.939	0.459	0.649
	11 and above	33	1.489		
				F test (ANOVA)	
Hb	Upper class	35	7.860	1.073	0.373
	Middle class	4	7.050		
	Lower class	1	7.600		
ESR	Upper class	35	15.514	0.578	0.633
	Middle class	4	15.000		
	Lower class	1	15.000		
TWBC	Upper class	35	11674.285	0.900	0.451
	Middle class	4	14900.000		
	Lower class	1	10200.000		

The overall analysis (ANOVA) is not significant ($p > 0.05$). Difference is not significant ($p \leq 0.05$)

4. DISCUSSION

Body mass index among children with sickle cell anaemia is an important marker for malnutrition [20-21]. The impact of malnutrition on haematological variables among children with sickle cell anemia has remained a grey area in our environment. Haematological indices have shown to bear no impact on indices of malnutrition in this study. Nikhar et al. [22], in his study also corroborated the same finding. The reason for this could be that since sickle cell anemia is a chronic haematological disorder, it affects weight for age and not much on weight for height.BMI is a measure of weight for height and thus may not necessarily create much impact on haematological variables. A study on weight to age and ponderal index studies may make this picture clearer.

We noted no gender difference when we compared anthropometrical variables with haematological profiles of children with sickle cell anemia. Contrary reports were however documented by Zemel et al. [23] who noted female preponderance in his study. However Singhal et al. [24] reported increases among the male counterpart. These variations of results could be due to differences in geographical and racial construct. Other reasons could also be due to hormonal differences [25]. It has also been propounded that females had high increases of haematological indices with their anthropometry, probably because they have more tendency to release stress mediators. Stress can lead to neutrophilia which results from rise on plasma levels of cortisol [26].

The high values of Leucocyte count and ESR and lower mean values of haemoglobin concentration in females may be due to a transcription factor for haemoglobin F which has been linked to X chromosome [27]. This transcription factor enhances production of variable levels of HbF through globin gene modification and transcription factor programming [27]. Again neuro-hormonal factors could also explain this gender difference.

Expectedly, high levels of leucocyte count were noted among children with sickle cell anaemia. It is a well known fact that leucocytosis in sickle cell disease patients may due be to auto splenectomy resulting from recurrent splenic vessels occlusion, which make patients more vulnerable to overwhelming infections particularly, encapsulated organisms like *Streptococcus pneumonia* and *Haemophilus influenza* [28]. Furthermore, adhesion of (activated) neutrophils to endothelium in patients with SCD may lead4 to endothelial damage as described in other vascular diseases [24]. Sanjeev et al. [29] noted similar findings.

Children with sickle cell anaemia have significantly lower haemoglobin concentration. This may be due to premature haemolysis and reduced red blood cell lifespan in these subjects.

Other studies have also documented similar findings [30,31].

Increase in total white cell count (TWBC) with Body surface area of children with sickle cell anemia noted in this study could be due to elaboration of acute phase reactants in these individuals. C-reactive protein (CRP), serum amyloid A (SAA), fibrinogen, white blood cell count, secretary non pancreatic phospholipids 2-II (sPLA2-II), ferritin, and ceruloplasmin are acute phase reactants. It has been noted that increases in body surface area causes an elevation in basal metabolic rates which in turn will cause a rise in acute phase reactants [32].

5. CONCLUSION

Infection is not the only cause of elevation in TWBCs. It is important to also consider the impact of surface area on white blood cell count of children with SCD before using antimicrobials for such infections or any medical intervention.

The limitation of this study lies in the fact that a community base study with a higher sample size will make the study better.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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