Original Article

Prevalence and Patterns of Sickle Cell Disease among Children Attending Tertiary and Non-Tertiary Health Care Institutions in a South Eastern State, Nigeria: A 10 year Survey

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ABSTRACT

Background: Sickle cell disease (SCD) is a global lifelong but preventable genetic blood disorder and it is most prevalent in sub-Saharan Africa within populations of very similar geographic distribution to malaria.

Objective: To determine the prevalence and patterns of sickle cell disease in children attending tertiary and non-tertiary hospitals in Imo State, Nigeria.

Methods: The study was a hospital based retrospective cross sectional survey from year 2004 to 2013 that identified all children with sickle cell disease that attended hospital. Data was collected using a proforma from patients' medical records. Descriptive analyses were done with frequencies and summary statistics. Chi square statistics were computed to determine significant relationships with the p set at<0.05.

Results: The prevalence rate of sickle cell disease was 5%. The most common symptom was fever (87.6%) followed by bone pain (45%) with the complaint of general body weakness appearing to be significantly associated with the type of health care institution attended. (p=0.000).The most common clinical sign was jaundice (59.8%), followed by pallor (51.1%); and the clinical complication experienced the most was infection (50.3%), followed by vaso-occlusive crises (36%). The occurrence of haemolytic crises appeared to be significantly associated with the type of health care institution attended (p=0.004).

Conclusion: Infection appears to be a leading complication and a trigger to subsequent sickle cell events within our environment. Therefore the management intervention should emphasis on infection prevention strategies within a framework of a preventive- interventional approach.

Keywords: Prevalence, Pattern, Sickle cell, hospital, survey

INTRODUCTION

Sickle cell disease (SCD) is a preventable but irreversible non communicable, genetically transmitted autosomal recessive blood disorder of significant public health concern in many parts of the world; South America, the Caribbean, Central America, Saudi Arabia, India, East Mediterranean and especially in sub Saharan Africa [1].

The three commonest forms of sickle cell disease in sub-Saharan Africa is Sickle cell anaemia (HbSS), Sickle haemoglobin C disease (HbSC) and Haemoglobin S beta Thalassemia disease (HbSBetaThal) which manifest when the mutant haemoglobin gene is inherited from both parents having sickle cell traits [2].This then produces abnormal haemoglobin that is less soluble than haemoglobin A which tends to crystallize out, resulting in sickle cell shaped deformation of the cells that block blood vessels and prematurely die.

In Africa, the sickle cell trait, also known as the carrier state, is most prevalent between latitudes 15°north and 20°south, ranging from 10% to 40% of the population with its geographical distribution very similar to malaria due to its partial protective effect against malaria [3]. Sickle cell disease affects nearly 100 million people globally with over 300,000 children with sickle cell disease born annually with mortality rates of over 50% [2].While sub Saharan Africa accommodates 75% of all SCD patients and 70% of all SCD births globally with majority dying before the age of 5 years, Nigeria is the most sickle cell endemic country in Africa with 2-3% of the total population affected, with an estimated 24%

prevalence of sickle cell trait, 100,000 annual SCD births and 100,000 annual SCD infant deaths [2, 4].
The public health implications of sickle-cell disease are significant, though an increasing proportion of affected children now survive past five years of age; they still remain at risk of premature death and chronic organ dysfunction in adulthood [5].
The pathophysiology of sickle cell disease is essentially similar globally although the frequency and severity of complications may vary between regions and people, as the spectrum of clinical expression is heterogeneous with some people having mild disease while others present with severe complications. This wide variation in the clinical manifestations and severity of SCD is probably due to the interaction of genetic and environmental factors such as infections, nutrition, geographic and climatic variation and socioeconomic status which influence and modify the sickle cell disease patterns [2, 6, 7]. Most of the morbidity of the disease arises from bone marrow necrosis, vaso-occlusive pain episodes or crises, and in later life, chronic ulcerations and end organ impairments. This leads to the interference of patient's education, work and psychosocial development thereby resulting in major social and economic impacts for the affected child and family [3, 6].
Thus, due to the unpredictable and variable clinical manifestations of SCD from haemolytic to vaso-occlusive related phenotypic characteristics which have been described [8], it is important to understand the patterns of sickle cell disease especially in poor resource settings in order to develop high index of suspicion and medical alertness; and also, to provide specific attention to the prevalent patterns within the geographical area that often are associated with substantial morbidity, decreased life span, and poor quality of life in children with SCD. This will ensure a more effective preventive- interventional approach to the management of SCD in our environment.

MATERIALS AND METHODS

Study Area

The study was conducted in three health care institutions in Imo State; a tertiary government hospital, a non- tertiary government hospital and a non- tertiary faith based private hospital namely, Imo State University Teaching Hospital in Orlu Local Government Area (LGA), a referral centre, Imo State Specialist Hospital, Umuguma in Owerri West LGA and Holy Rosary Hospital, Emekuku in Owerri North LGA respectively both secondary care centres. Imo State is in the South Eastern part of Nigeria; it had a total population of 3.93 million (2.03 million males and 1.9 million females) by 2006 census, with an expected population in 2013 of 4.95 million based on an annual growth rate of 3.2% between 2006 and 2013 [9]. The State occupies an area of 5289.49 square kilometres with a population density of about 707.9 per square kilometre [10].

Study Population/Study design

The study population comprised all cases of sickle cell disease in children less than 18 years of age that presented at the children's outpatient clinics of the three health care institutions from year 2004 to 2013. The study was a hospital based 10 year retrospective cross sectional survey that identified 356 children with sickle cell disease from 7324 children that presented at the children's outpatient clinic during that period.

Data Collection and Analysis

Data was collected using a proforma that included the age, sex, clinical symptoms, signs and complications from medical records. Medical students were recruited for data collection. Data was cleaned and validated manually, and analysed using SPSS v22. Descriptive statistics (frequency tables, graph and summary indices) were generated. Chi Square was used to test association between categorical variables. While p value was set at 0.05 significant level, a Bonferroni critical factor was used to identify significant associations.

Ethical Considerations

Ethical approval was obtained from the Ethics Committee of Imo State University Teaching Hospital (IMSUTHEC). All authors hereby declare that the study has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

RESULTS

Three hundred and fifty six children were identified with sickle cell disease out of the seven thousand three hundred and twenty four children attending the children's outpatient clinics from the identified health care institutions in Imo State over a 10 year period with a prevalence rate of 5%. (Fig 1).

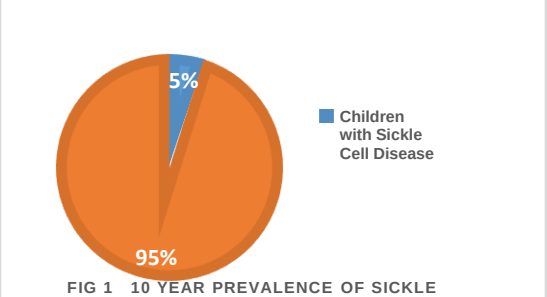

FIG 1 10 YEAR PREVALENCE OF SICKLE CELL DISEASE

The majority of children with sickle cell disease were male (58.4%) and there were no significant

preponderance of children with sickle cell disease in any particular age group. Gender appeared to be significantly associated with the type of health care institution attended. (p=0.007) (Table 1).

Table 1: Age and Sex distribution of Sickle Cell Disease in Health care Institutions

	Tertiary hospital (%)	Non tertiary hospital (%)	Non tertiary faith based hospital (%)	Total (%)	X^2	df	p value
	(n=187)	(n=50)	(n=119)	(N=356)			
Age (yrs)							
0-5	67(54.0)	17(13.7)	40(32.3)	124(100)	0.24	4	0.994
6-10	61(52.1)	16(13.7)	40(34.2)	117(100)			
11-15	59(51.3)	17(14.8)	39(33.9)	115(100)			
Gender							
Male	115(55.3)	19(9.1)	74(35.6)	208(100)	10	2	0.007*
Female	72(48.6)	31(20.9)	45(30.4)	148(100)			

*p<0.05, Statistically significant

Distribution of clinical symptoms of Sickle Cell Disease in Health Care Institutions

The most common symptom the children with sickle cell disease presented with was fever (87.6%), followed by bone pain (45%) and the least symptoms were foot ulcer (4.5%), chest pain (4.8%) and blood in urine (3.7%) categorised as 'others' (12.9%). General body weakness appeared to be significantly associated with the type of health care institution attended. (p=0.000) (Table 2).

Table 2: Distribution of clinical symptoms of Sickle Cell disease in Health care Institutions

Clinical symptoms	Tertiary hospital (%)	Non tertiary hospital (%)	Non tertiary faith based hospital (%)	Total (%)	X2	df	p value
	(n=187)	(n=50)	(n=119)	(N=356)			
Fever							
Present	162(51.9)	43(13.8)	107(34.3)	312(100)	0.87	2	0.648
Absent	25(56.8)	7(15.9)	12(27.3)	44(100)			
Bone pain							
Present	89(55.6)	24(15.0)	47(29.4)	160(100)	2.15	2	0.342
Absent	98(50.0)	26(13.3)	72(36.7)	196(100)			
Abdominal swelling							
Present	60(51.7)	23(19.8)	33(28.4)	116(100)	5.39	2	0.067
Absent	127(52.9)	27(11.3)	86(35.8)	240(100)			
Cough							
Present	45(58.4)	7(9.1)	25(32.5)	77(100)	2.4	2	0.301
Absent	142(50.9)	43(15.4)	94(33.7)	279(100)			
Vomiting							
Present	28(45.9)	6(9.8)	27(44.3)	61(100)	4.13	2	0.127
Absent	159(53.9)	44(14.9)	92(31.2)	295(100)			
General Body Weakness							
Present	12(24.0)	13(26.0)	25(50.0)	50(100)	19.71	2	0.000*
Absent	175(57.2)	37(12.1)	94(30.7)	306(100)			
Others							
Present	23(50.0)	7(15.2)	16(34.8)	46(100)	0.15	2	0.93
Absent	164(52.9)	43(13.9)	103(33.2)	310(100)			

***significant at p< 0.05 level, as value is less than the Bonferroni critical factor of 0.007**

Distribution of clinical signs of Sickle Cell Disease in Health Care Institutions

On examination, the most common clinical sign the children with sickle cell disease presented with was jaundice (59.8%), followed by pallor (51.1%) and the least clinical signs were dehydration (13.5%), gnathopathy (8.7%); and categorized as 'others' (14.0%) were asthenia (10.4%) and lethargy(3.6%).(Table 3).

Table 3: Distribution of clinical signs of Sickle Cell Disease in Health care Institutions

Clinical signs	Tertiary hospital (%)	Non tertiary hospital (%)	Non tertiary faith based hospital (%)	Total (%)	X2	df	p value
	(n=187)	(n=50)	(n=119)	(N=356)			
Jaundice							
Present	120(56.3)	24(11.3)	69(32.4)	213(100)	4.55	2	0.103
Absent	67(46.9)	26(18.2)	50(35.0)	143(100)			
Pallor							
Present	110(60.4)	21(11.5)	51(28.0)	182(100)	9.36	2	0.009**
Absent	77(44.3)	29(16.7)	68(39.1)	174(100)			
Hepato-Splenomegaly							
Present	60(45.8)	22(16.8)	49(37.4)	131(100)	3.88	2	0.144
bsent	127(56.4)	28(12.4)	70(31.1)	225(100)			
Frontal/Parietal Bossing							
Present	57(49.1)	13(11.2)	46(39.7)	116(100)	3.36	2	0.186
Absent	130(54.2)	37(15.4)	73(30.4)	240(100)			
Dehydration							
Present	24(50.0)	4(8.3)	20(41.7)	48(100)	2.48	2	0.289
Absent	163(52.9)	46(14.9)	99(32.1)	308(100)			
Gnathopathy							
Present	16(51.6)	4(12.9)	11(35.5)	31(100)	0.08	2	0.961
Absent	171(52.6)	46(14.2)	108(33.2)	325(100)			
Others							
Present	22(44.0)	3(6.0)	25(50.0)	50(100)	8.27	2	0.016**
Absent	165(53.9)	47(15.4)	94(30.7)	306(100)			

**** Not significant at p< 0.05 level, as value is greater than the Bonferroni critical factor of 0.007**

Distribution of clinical complications of Sickle Cell Disease in Health Care Institutions

The clinical complication experienced the most by the children with sickle cell disease was infection (50.3%), followed by vaso-occlusive crises (36%) and the least experienced were acute chest syndrome (4.8%), sequestration crises (4.5%), priapism (4.2%); and categorised as 'others'(9.0%) were megaloblastic crises (2.8%), stroke (0.3%), retinopathy (0.0%), nephropathy (0.8%), leg ulcer (2.5%) and hand and foot syndrome (2.5%).

The occurrence of haemolytic crises appeared to be significantly associated with the type of health care institution attended. (p=0.004) (Table 4).

DISCUSSION

The study determined the prevalence and patterns of sickle cell disease in children over a 10 year period and it was subsequently revealed that the prevalence rate of sickle cell disease was 5% with fever, jaundice and infection as the most common symptom, sign and complication associated with the sickle cell disease in children respectively. Also the pattern of disease of sickle cell among the children were generally similar across the tertiary and non-tertiary health care institutions studied except in the area of general body weakness as a presenting symptom (p<0.000) and haemolytic crises as a clinical complication (p<0.004).

The prevalence estimate in the present study could be explained by the fact that, the health care institutions involved in the study were referral centres and also, the estimate was not based on newborn screenings but on SCD children attending outpatient clinics and as such, may have been overestimated. Nevertheless previous studies in Nigeria generally reported prevalence rates between 2-3% with the exception of a study in Northern Nigeria that reported a prevalence rate of 11.9% [11-14].

It was observed in the present study that there were more male than female children (1.4:1) with SCD and this was similarly observed in a number of other studies [13, 15-18] though the study in Northern Nigeria reported a higher female to male ratio [14].It was also observed that, there was a significant gender distribution between the tertiary and non-tertiary hospitals ($p<0.007$) with more male children attending the tertiary health care institution. This could probably be due to the greater importance given to the male child culturally by parents; and as such are prepared to invest more resources to ensure that their male SCD childreceive supposedly better health care from the tertiary hospital. Also, the higher male to female ratio could be a reflection of the higher incidence of childhood illnesses occurring in males within our environment [13, 19].

Table 4: Distribution of clinical complications of Sickle Cell Disease in Health care Institutions

Clinical complications	Tertiary hospital (%)	Non tertiary hospital (%)	Non tertiary faith based hospital (%)	Total (%)	X2	df	p value
	(n=187)	(n=50)	(n=119)	(N=356)			
Infection							
Present	92(51.4)	27(15.1)	60(33.5)	179(100)	0.37	2	0.833
Absent	95(53.7)	23(13.0)	59(33.3)	177(100)			
Vaso-occlusive crises							
Present	74(57.8)	21(16.4)	33(25.8)	128(100)	5.35	2	0.069
Absent	113(49.6)	29(12.7)	86(37.7)	228(100)			
Haemolytic crises							
Present	33(70.2)	0(0.0)	14(29.8)	47(100)	11.04	2	0.004*
Absent	154(49.8)	50(16.2)	105(34.0)	309(100)			
Osteomyelitis							
Present	18(51.4)	6(17.1)	11(31.4)	35(100)	0.32	2	0.852
Absent	169(52.6)	44(13.7)	108(33.6)	321(100)			
Aplastic crises							
Present	8(38.1)	5(23.8)	8(38.1)	21(100)	2.55	2	0.28
Absent	179(53.4)	45(13.4)	111(33.1)	335(100)			
Acute chest syndrome							
Present	9(52.9)	4(23.5)	4(23.5)	17(100)	1.67	2	0.434
Absent	178(52.5)	46(13.6)	115(33.9)	339(100)			
Sequestration crises							
Present	5(31.3)	4(25.0)	7(43.8)	16(100)	3.41	2	0.182
Absent	182(53.5)	46(13.5)	112(32.9)	340(100)			
Priapism							
Present	8(53.3)	2(13.3)	5(33.3)	15(100)	0.01	2	0.996
Absent	179(52.5)	48(14.1)	114(33.4)	341(100)			
Others							
Present	21(65.6)	1(3.1)	10(31.3)	32(100)	4.18	2	0.123
Absent	166(51.2)	49(15.1)	109(33.6)	324(100)			

***significant at p=0.05 level, as value is less than the Bonferroni critical factor of 0.006**

In the present study, the age distribution of the children with SCD appeared to have similar proportions in the different age categories; 0-5, 6-10 and 11-17 year olds and this is contrary to reports from some studies that have observed a significantly higher proportion of sickle cell children between the ages of 0-5 years, as they tend not to survive beyond these ages due to increased mortality from frequent illnesses [13, 14, 17, 20]. Someother studies have also observed that SCD children are progressively living longer due to better and more effective management of SCD, even though they are now facing newer challenges of

chronic organ dysfunction in adulthood and associated premature death [5, 16]. Hence, this may probably explain the observation in the present study of a relatively high proportion of SCD children in the 6-10 and 11-17 year old categories.

Furthermore, in the present study, the general clinical picture for a majority of the SCD children comprised fever (87%) and bone pain (45%) with signs of jaundice (59.8%) and pallor (51.7%) associated with complications of infection (50.3%) and vaso-occlusive event (36%). On the contrary, a study in the South West of Nigeria had a clinical picture associated with vaso- occlusive crises and infection in 66.3% and 23.8% of the SCD children respectively [18]and similarly, studies in the South-South of Nigeria, observed vaso-occlusive crises in most of the patients [17, 20].

The hallmark of SCD is pain, with vaso-occlusion thought to be the underlying cause, but it appears that, the present study had more SCD children with the symptom offever than bone pain andwith the complication of infection than underlying vaso-occlusion. Fever in SCD is associated with infections which are thought to be the main causes precipitating sickle cell events and these infections may be related directly, indirectly or unrelated to the immune system [21]. Some of these infections may be the result of a complication such as splenic infarction or treatment of SCD itself e.g. blood transfusion transmissible infections or associated with the environmental conditions such as malaria, upper respiratory tract infection etc.

In our environment, malaria is endemic and it is the most commonly observed infection that can modify the clinical outlook and mortality risk in SCD by precipitating haemolytic and vaso-occlusive crises [13, 20, 22, 23]. Thus, malaria infection may explain the symptom of fever and some of the other clinical manifestations being observed in the present study amongst the majority of the SCD children.

The most common clinical signs observed in the present study were jaundice and pallor which was similarly observed in a study in the Southern part of Nigeria by George et al [13]although in that same study, bone pain, haemolytic crises, sequestration crises, acute chest syndrome, priapism and osteomyelitis were observed in 90%, 60.4%, 1.2%, 2.4%, 1.2% and 7.7% of SCD children respectively while in the present study, bone pain, haemolytic crises, sequestration crises, acute chest syndrome, priapism and osteomyelitis were observed in 45%, 13.2%, 4.5%, 4.8%, 4.2% and 9.8% respectively showing a variable and different clinical picture.

CONCLUSION

Sickle cell disease is a life-long illness and the pattern of disease and severity vary widely from person to person and from region to region depending on the haemoglobin variant and the prevailing socioeconomic and environmental conditions. Nevertheless, infection appears to be a leading complication and a trigger to subsequent sickle cell events within our environment thereby increasing the risk of morbidity and mortality among the SCD children.

The management intervention emphasis should be infection prevention within a framework of a preventive- interventional approach where premarital education, counselling and blood group screening should be the hallmark on one hand and on the other hand neonatal screening, family education and comprehensive care programmes that provide counselling, prompt treatment of acute sickle cell events and prophylactic treatments against other complications leading to better quality of life, care and improved survival.

LIMITATIONS

The prevalence of SCD was determined based on hospital data from children attending the outpatient clinics. Also the study faced the challenges of incomplete and missing data

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