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HAEMOGLOBIN PHENOTYPES OF PATIENTS ADMITTED TO THE CHILDREN EMERGENCY ROOM OF THE UNIVERSITY OF BENIN TEACHING HOSPITAL, BENIN CITY, EDO STATE, NIGERIA.

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Abstract
Sickle cell anaemia (SCA) is the most common inherited haemoglobinopathy in Blacks. In Nigeria with high burden of SCA, there are relatively few programmes for the disease management and there is no focus on comprehensive care of the diagnosed child. In an effort to detect early the disease condition so as to foster a decline in mortality and morbidity for this group, we screened all admitted cases into the Children Emergency Room (CHER) of the University of Benin Teaching Hospital (UBTH), Benin City for their haemoglobin phenotypes and computed the contribution of SCA related morbidities to paediatric admissions. This descriptive and cross-sectional study was conducted between April and September 2011. It involved 589 children aged six months to 17 years admitted during the study period. Haemoglobin SS (SCA) contributed 5.8% (34/589) of the admissions. Haemoglobin AA made up 73.7% (434/589). The others were haemoglobin AS(20.0%) and haemoglobin AC (0.5 %). The related morbidities in children with SCA were infections (44.1%), vaso-occlusive crisis (29.4%), severe anaemia (20.6%) and cerebrovascular accident [CVA](5.9%). Among those with HbSS, 17.6% were newly diagnosed while 82.4% were known HbSS patients. All the newly diagnosed HbSS cases were less than 24 months of age and presented with acute problems. Furthermore, all children with CVA were newly diagnosed HbSS. It is concluded that sickle cell anaemia related morbidities contribute significantly to paediatric admissions. A strong case is made for the initiation of Sickle Cell Disease screening programmes in all health institutions in Nigeria.

Introduction

Sickle cell disease (SCD) is an inherited structural haemoglobinopathy which causes chronic haemolytic anaemia.[1] SCD is the most common inherited disorder in blacks.[2] It is inherited as an autosomal recessive disorder and occurs when a child is homozygous for the sickle haemoglobin (HbSS) or is heterozygous for the sickle haemoglobin and another abnormal haemoglobin for example, β-thalasaemia (HbSβ?) and haemoglobin C (HbSC).[3,4] The homozygous state (HbSS) or sickle cell anaemia (SCA) is the most common and severe form of SCD.[4]

Sickle cell anaemia is common in Africa, Saudi Arabia and Mediterranean countries.[3,5] Sixty to 70 percent of the world's burden of SCD fall on Africa. Between 200,000 and 230,000 children are

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thought to be born with SCA in Africa every year.[3] In Nigeria, the prevalence of SCA is 20 per 1000 births[3,6]and about 150,000 children are born with it every year.[3]

Sickle cell disease is a problem of major public health significance as it is a major cause of morbidity and mortality.[3] It contributes an equivalent of five percent of under-five deaths in Africa with more than nine percent of such deaths in West Africa.[3,5] More than half of children with SCD would have died before their fifth birthday from malaria, bacterial infections and anaemia.[3,5]In Nigeria with high burden of SCA, there are relatively few programmes for the disease management and there is no emphasis on comprehensive care of the diagnosed child. Systematic screening like chorionic villous sampling for prenatal diagnosis and newborn screening are not routinely done.[3] The management of these children remains inadequate as simple, cheap and cost effective interventions are not widely practiced.[3,6] In an effort to detect early the disease condition so as to foster decline in mortality and morbidity, we screened all admitted cases into the Children Emergency Room (CHER) of the University of Benin Teaching Hospital (UBTH), Benin City for their haemoglobin phenotypes and computed the contribution of SCA related morbidities to paediatric admissions.

Subjects and Methods

This prospective and cross-sectional study consisted of children admitted into CHER, UBTH from April to September 2011. The CHER of the hospital is a 15-bed ward which provides emergency care to children in Edo and neighbouring States. All children aged six months to 17 years admitted into CHER were consecutively recruited for the study. The ages, gender and diagnoses warranting admissions were recorded.

The haemoglobin phenotypes of the subjects were determined by cellulose acetate electrophoresis at pH 8.6.[7,8] Children less than six months of age were excluded from the study because the method of determining patients' haemoglobin phenotype available to us (cellulose acetate electrophoresis), is not a particularly sensitive method for screening in the newborn and early infancy.[8]

Ethical approval was obtained from the Ethics Committee of UBTH and written informed consent obtained from parents/caregivers of subjects.

Data analysis was done using the Statistical Package for Social Sciences (SPSS) version 16.0 (SPSS Inc. Chicago IL). Measures of statistical location like mean and standard deviation of continuous variables were computed and frequency tables generated as required with p values less than 0.05 considered as significant.

Results

A total of 589 children were recruited. They consisted of 337 (57.2%) males and 252 (42.8%) females, giving a male: female ratio of 1.3: 1. Of the 589 children studied; a high proportion (80.3%) were aged 6 months to 5 years (Table I). The mean age of the study population was 39.33 ± 44.79 months. The mean age at presentation of children with SCA (71.98 ± 50.82 months) was significantly higher than the mean age of children with haemoglobin AA (38.23 ± 44.69 months) ($p = 0.00$, $t = -3.84$, 95% C.I. = -51.02 to -16.48). The mean age for the newly diagnosed children with SCA (16.00 ± 5.20 months) was significantly lower than the mean age of children with Hb AA (38.23 ± 44.69 months). ($p = 0.01$, $t = 2.66$, 95% C.I. = 13.17 to 98.80).

The children with SCA made up 5.8% (34/589) of the admitted cases. Four

Table I: Age and gender distribution of the study population.

Age (years)	Male (%)	Female (%)	Total (%)
≤ 5	266 (56.2)	207 (43.8)	473 (100.0)
6-9	42 (58.3)	30 (41.7)	72 (100.0)
10-13	20 (58.8)	14 (41.2)	34 (100.0)
14-17	9 (90.0)	1 (10.0)	10 (100.0)
Total	337 (57.2)	252 (42.8)	589 (100)

Table II: Haemoglobin phenotype distribution of the study population according to gender.

Genotype	Male (%)	Female (%)	Total (%)
AA	251 (57.8)	183 (42.2)	434 (100.0)
AS	63 (53.4)	55 (46.6)	118 (100.0)
SS	20 (58.8)	14 (41.2)	34 (100.0)
AC	3 (100.0)	0 (0.0)	3 (100.0)
Total	337 (57.2)	252 (42.8)	589 (100.0)

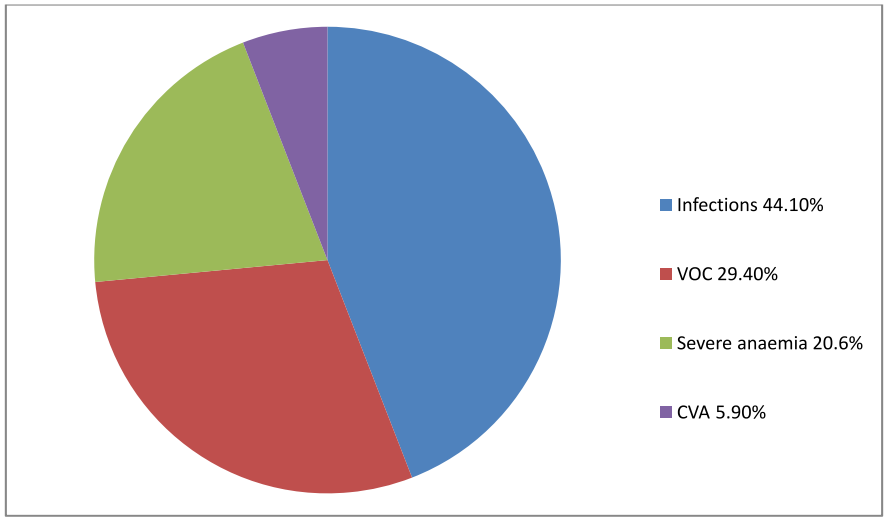

Figure 1: Reasons for Admission inchildren with Sickle Cell Anaemia.

hundred and thirty four (73.7%) of the study subjects had haemoglobin AA, 118 (20.0%) had haemoglobin AS and three (0.5%) had haemoglobin AC (Table II). Of the 34 children with HbSS, six (17.6%) were newly diagnosed, while the remaining 28 (82.4%) were known HbSS patients. Of the 34 children with SCA identified, 18 (53.0%) were aged six months to 5 years, 13 (38.2%) were aged 6-10 years, two (5.9%) were aged 11-15 years while one (2.9%) was aged 16-17 years. All newly diagnosed children with HbSS were in the age group 6 months to 24 months.

The main reason for admission among children with SCA was infectious diseases (44.1%) including malaria, pneumonia, gastroenteritis, meningitis. Other reasons for admission include vaso-occlusive crisis, severe anaemia and cerebrovascular accident (Figure 1). All the children with cerebrovascular accidents (CVAs) were newly diagnosed HbSS.

Discussion

The high prevalence of HbSS observed in the current study relative to the HbSS prevalence in the general population attests to the morbidities associated with the disease. One would have expected the mean age at presentation of children with HbSS to be less than that of those with HbAA. The plausible explanation for this finding is that majority of the patients with HbSS were known cases as opposed to the newly diagnosed. While those with HbAA would have less reasons to be admitted as they grow older because of the maturation of their immune system, the children with HbSS on the contrary develop functional asplenia.[9] Functional asplenia results in increased susceptibility of the individual to infections with encapsulated organisms like Streptococcus pneumoniae, Haemophilus influenzae and Salmonella typhi.[9]

The clinical course of SCA varies.[7] While some patients are asymptomatic and are detected only during population screening, others develop frequent painful episodes of vaso-occlusive crises. Most patients fall between these extremes and have relatively long asymptomatic periods interspersed by occasional clinical crises.[9] Although the disease can be diagnosed at birth, clinical abnormalities usually do not occur before the age of 6 months mainly because the predominant haemoglobin prior to this time is fetal haemoglobin (HbF) as against HbS. The S haemoglobin is adult type haemoglobin and does not reach maximum production in early life.[9] Nevertheless, the diagnosis of SCA is often delayed until the disease becomes clinically manifest.

Newly diagnosed children with SCA are likely to present with acute problems like vaso-occlusive crises (VOC), bacterial infections and severe anaemia that could necessitate presentation in the emergency room as revealed by present study. Early diagnosis facilitated by newborn screening[10,11] may have picked these children earlier because it has the capability of reaching infants who would otherwise be lost to the health care system.

In a Saudi Arabian study conducted to document the morbidities in sickle cell patients presenting in hospital and the burden of delivering care to these patients, the authors documented the mean age at first admission as 3.8 years.[12] The older age of presentation in Saudi Arabia compared with the mean age of the newly diagnosed children with SCA in the current study may be attributed to higher standard of living, availability of comprehensive health care and better housing and sanitary conditions and that exist in Saudi Arabia. Also, a major problem among patients with SCA in tropical Africa is the fact that the

natural history of the disease is somewhat complicated with recurrent episodes of malaria infection, thus necessitating presentation for other reasons apart from SCA .[13-14]In consonance with present study, the Saudi Arabian study[12] alluded to earlier recorded same causes of admission; however, in varying frequencies. They documented the most frequent causes of admissions in order of frequency as pain crisis (VOC), haemolysis, infectious diseases and anaemia.

The prevalence of cerebrovascular accident (CVA) found in the current study was comparable to that of 5.4% found in children with SCD by Fatunde et al[15] in 2005 in Ibadan, Nigeria. However, Lagunju et al[16] recorded a higher prevalence of 6.8% in 2011 also in Ibadan. Central nervous system complications, particularly cerebrovascular thrombosis and haemorrhage, occurring in young patients with SCD can cause severe disability.[17] Children who survive CVA are also at increased risk of motor disabilities, learning difficulties and epilepsy. Studies have shown that episodes of CVA are lethal,[17] emphasizing the importance of the institution of early diagnostic and treatment procedures whenever they are suspected.

In conclusion, sickle cell anaemia and related morbidities contribute significantly to paediatric admissions. Infections are the major cause of admission and cerebrovascular accident is a serious burden especially in the newly diagnosed children. A strong case for the initiation of SCD programmes in all health institutions in Nigeria is made.

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