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A Clinical and Hematological Study on the Sickle Cell Anemia among Children in El Obeid Hospitals, Sudan

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ABSTRACT

Background: *Sickle cell disease (SCD) is considered as one of the major types of anemia in Sudan, especially the western part of the country. We studied clinical and hematological findings to obtain an initial baseline data on sickle cell anemia in children in North Kordofan in general.* ***Materials and Methods:*** *Total 75 children were enrolled in the study prospectively using a questionnaire. Clinical data, as well as hematological parameters of full blood count (FBC) for each patient, were carefully obtained.* ***Results:*** *About 80% of the children were initially diagnosed at age less than 5 years. The study showed high frequencies of sickle cell disease among Falatah (13.3% vs 16%) and Jawama (12% vs 13.3%) for fathers and mothers, respectively. Total 80% of children's parents were relatives or from the same tribe. The most frequent clinical presentations were fever (84%), pallor (79%), and bone pain (62%). While common clinical findings were hepatomegaly (44%), joint swelling (35%), and bone swelling (31%). The overall mean hemoglobin concentration was 8.0 ± 2.4 g/dl, packed cell volume was 24.5 ± 7.0 percent, total white blood cells count was 14257 ± 7302 cells/ µL, platelets count was 470821 ± 162245 cells/ µL and reticulocytes count was 12.1 ± 9.8 percent.* ***Conclusion:*** *Epidemiological surveys are needed to determine exactly the magnitude of this problem at least in the region as well as designing a strategic plan to address urgent and long-term interventions in control of sickle cell disease.*

Keywords: Sickle cell anemia, Children, Hematological, Hospital, Sudan

INTRODUCTION

It has been a century since the first description of abnormally elongated red blood cells in an anemic patient and the link with the clinical symptoms of what is now called sickle cell anemia (SCA) was published [1]. Sickle cell anemia is an inherited blood disorder due to the substitution of valine to glutamic acid in position number 6 in the β-globin chain, this will cause deoxygenated sickle hemoglobin to form polymers that ultimately destroy red blood cells [2].

The valine residues occupy a position on the outer surface of the hemoglobin and cause intra-molecular hydrophobic attraction which results in reduced solubility and stability of the deoxygenated hemoglobin S (HbS) [3,4]. Heterozygous persons are asymptomatic carriers and homozygosity causes sickle cell anemia [5].

The prevalence of the sickle-cell disease is highest in sub-Saharan Africa. Although the scarcity of diagnostic facilities means that precise data are not available, a recent estimate suggests that more than 230,000 affected children are born in this region every year (0.74% of the births in sub-Saharan Africa), which is about 80% of the global total. By comparison, the yearly estimate of affected births in North America is 2600 and 1300 in Europe [6]. In Africa, sickle cell disease (SCD) is reported to be associated with a very high rate of childhood mortality, 50%-90%, yet there is a lack of reliable, up-to-date information [7]. Little is known about sickle-cell disease in Africa. Generally, diagnostic facilities are poor, routine screening is absent, and, despite the fact that most patients would survive if provided with a simple package of inexpensive interventions, most die undiagnosed in early childhood [8].

In Sudan, sickle cell disease was first reported in 1926 by Archibald [9]. The disease is considered one of the major

types of anemia especially in western Sudan where the sickle cell gene is frequent [10]. A study on hemoglobinopathies in Sudan showed that hemoglobin "S" is the most common abnormal hemoglobin in western Sudanese ancestry [11].

SCA was found to be predominant among the Afro-Asiatic speaking groups including nomadic groups of Arab and non-Arab descent that migrated to Sudan in various historical epochs. Those patients were clustered in western Sudan (Kordofan and Darfur) [10], where HbS is a natural extension of the West African HbS belt [12]. Still, there are no available updated data concerning the burden of sickle disease in Kordofan region, in spite of this area is considered as the highest endemic area in Sudan [13].

The presence of HbS is already well documented among the Albagara, an Afro-Arab constellation of tribes with a predominantly African descent. In a subgroup of Albagara (Misseria) studies showed the prevalence of sickle cell disease (SCD) to be 30%, 16% among immigrants from the province of Blue Nile [14].

Infants with HbS have complications only rarely in the early months of life, while HbF concentrations remain high. The disease is manifest clinically from the 3rd month onwards where the earliest presentation is frequently the 'hand-foot' syndrome of painful swelling of the dorsum of the hands or feet, often symmetrical, resulting from infarctions into the small bones. Patients suffer from chronic ill health interspersed with acute anemic, infarctive, and infective crises [15].

The aim of this study was to obtain an initial clinical and hematological baseline data on sickle cell anemia in children in North Kordofan in general.

MATERIALS AND METHODS

This study was conducted in El Obeid, North Kordofan State during the period November 2012 to December 2013. The state is located in the center of Sudan and covers a land area of 221,900 km squire with an estimated population of about 2,920,992 (2008 Population Census).

Participants were selected from those who attended El Obeid hospitals that are supplied with pediatric wards and admit children with sickle cell anemia during the study period. The inclusion criterion was all children aged (0-15) year and was diagnosed by their physicians as sickle cell disease patient. Total 75 sickle cell children were enrolled in the study.

The study protocol was approved by the ethical committee, Ministry of Health, North Kordofan State. An informed consent was obtained from each child guardian or parents before obtaining the sample and a questionnaire for each participant was filled by the clinician prior carrying out investigations. Sickling test and full blood count were performed from EDTA anticoagulated venous blood and results were then recorded. All data were entered to the computer and analyzed using the SPSS program.

RESULTS

There were 75 children among the study group, 34 (45%) were girls and 41 (55%) were boys. Their age range was 3 months up to 15 years, 1-5 years age group constituted the majority, 39 (52%). Mean weight was 15.8 ± 11.0 kg, while heights mean was 93.3 ± 8.0 cm. Total 80% of the children were initially diagnosed at age less than 5 years.

The majority of the children (80%) had completed the routine vaccination according to their age. The study demonstrated that 57% of them were in long-term use of folic acid.

The study showed high frequencies of sickle cell disease among Falatah (13.3% vs 16.0%) and Jawama (12.0% vs 13.3%) for fathers and mothers, respectively. Total 80% of children parents were relatives or from the same tribe. Table 1 shows the frequency of SCD among different tribes as well as parents' relation among the study group. Our findings demonstrate that only 37% had a family history for sickle cell disease.

Table 1 Tribes and parents' relation of children with SCD, El Obeid 2013

Variables	Frequencies	Percentages (%)
Father' s tribe	(n=75)	
Jawama	9	12%
Meseria	7	9%
Dar Hamid	3	4%
Hawazma	3	4%

Falatah	10	13%
Others	43	58%
Mother' s tribe	(n=75)	
Jawama	10	14%
Meseria	7	9%
Dar Hamid	1	1%
Hawazma	3	4%
Falatah	12	16%
Others	42	56%
Blood relation of parents	(n=75)	
1st degree	39	52%
2nd degree	8	10%
Same tribe	13	17%
Unrelated	15	20%

On studying clinical presentations, fever was the major feature (84%), followed by pallor, bone pain (Figure 1).

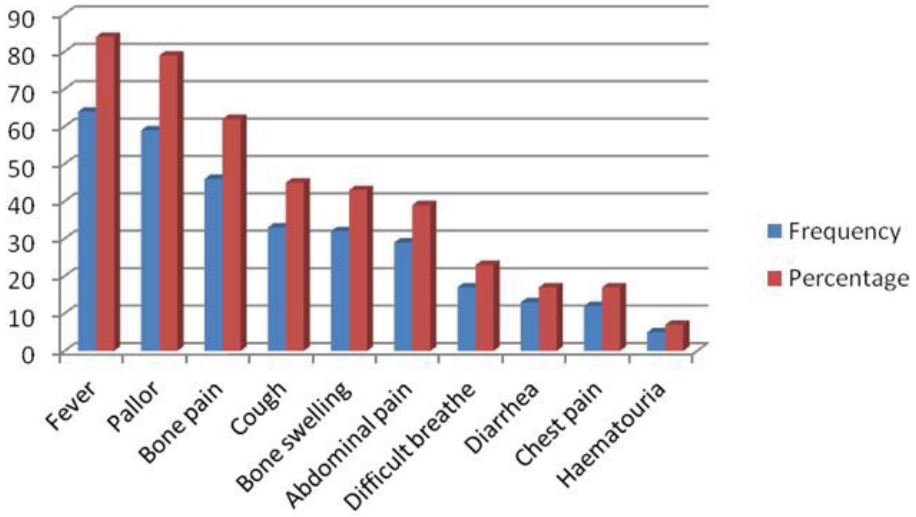

Figure 1 The major presenting symptoms of admitted children with SCD, El Obeid 2013

The common clinical findings were hepatomegaly (44%), joint swelling (35%), and bone swelling (31%) (Figure 2).

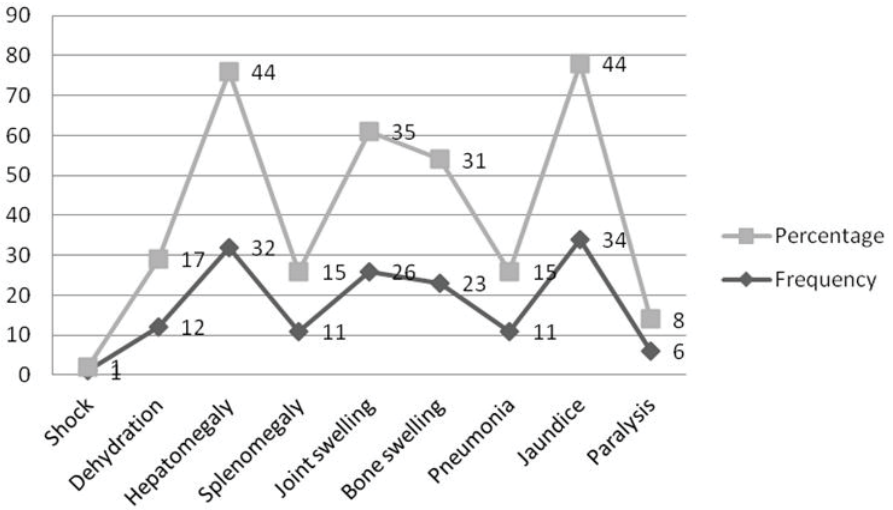

Figure 2 The major signs seen in admitted children with SCD, El Obeid 2013

Due to unavailability of Hb electrophoresis test during the study period, laboratory diagnosis of all cases was based on clinical grounds and sickling test, 84% demonstrated positive sickling test. The overall mean hemoglobin concentration was 8.0 ± 2.4 g/dl, packed cell volume 24.5 ± 7.0 percent, total white blood cells count 14257 ± 7302 cells/µL, platelets count 470821 ± 162245 cells/µL and reticulocytes count 12.1 ± 9.8 percent.

When hematological parameters were categorized, results among patients under study were: 39% had hemoglobin concentration 6-8 g/dl, 32% had packed cell volume, 20-25% had total white blood cells count (WBC<8000 cells/µL), 36% with WBC>15000 cells/µL. Total 59% of patients showed elevated platelets count, above 600,000. Reticulocytes count was high (above 5%) in 65% of patients.

DISCUSSION AND CONCLUSION

HbS has been suggested to be more common in populations from Kordofan and Darfur. Although many studies were conducted in the Kordofan region, most of the data remain unpublished. In this paper, we tried as much as possible to provide baseline data for clinical, hematological as well as ethical issues associated with sickle cell disease.

Falatah tribe showed the highest frequencies of HbS (16%), in this study, agreeing with that mentioned by Munsoor, et al., who reported similar findings in a study conducted in the same area [16]. Osman, et al., reported the highest frequency in Masaleet tribe study in Algadaref State [17]. Ahmed, et al., recognized Misseria tribe in West Kordofan, as the most frequent tribe with HbS, the prevalence of sickle cell disease (SCD) was up to 30% [14]. The same findings were documented in a study conducted by Nimir, et al., [18].

The study revealed that the majority of parents were relatives or from the same tribe, this high frequency of consanguineous marriage has a deep root in their traditions and customs. Consanguineous marriages have also been linked with the numerous abnormal Hb subtypes. Consequently, there was also the increased risk of continuing Hb abnormalities to future generation [11]. Designing control measures in such communities is challenging.

Total 84% of participants were diagnosed as sickle cell patients but only 37% had a family history for sickle cell disease according to their parents. This is because many families deny having this disorder so as not to be stigmatized. Confirmation of having HbS gene sometimes leads to family conflicts and social problems. On assessing presenting symptoms, fever was the major feature (84%), followed by pallor, bone pain. This is consistent with that reported by Bayoumi, et al., and Mohamed, et al., who mentioned that "generally in Sudan patients usually present with severe anemia, hand-foot syndrome, fever, jaundice and vaso-occlusive crises" [12,19].

Interestingly, some cases (10%) presented with hand-foot syndrome but had negative sickling test and their hematological parameters were unlike that of sickle cell patients. Further investigations were needed to accurately diagnose such cases.

The common clinical findings on examination were pallor (79%), hepatomegaly and jaundice both (44%), joint swelling (35%), bone swelling (31%), while only 15% demonstrated splenomegaly. Relatively similar findings were mentioned by Osman, et al., [19]. Among studied patients, they found that pallor (97%), jaundice (32%), palpable liver (60%), palpable spleen (6%), cardiac signs (27%), hand-foot syndrome (16%), and pneumonia (8%).

This study demonstrated that 88% had no cardiac abnormality, inconsistent with that reported by Bayoumi, et al., in a study conducted in Khartoum [12]. In their study all patients had mild to moderate cardiac enlargement; 42% had a moderately enlarged spleen but only 10% had an enlarged liver.

The overall mean of hemoglobin concentration and PCV were 8.0 g/dl and 24.5%, respectively. While mean reticulocytes count was 12.1%. Similarly, Bayoumi, et al., reported a mean hemoglobin concentration of 7.3 g/dl and mean reticulocyte count of 15.1% [12].

Almost 80% of patients showed elevation in the white blood cells (above 8000 cells/µL) with a mean count of 14257 cells/µL. Due to the re-distribution of the white cells between the marginal and circulating pools, pain, nausea and vomiting and anxiety have been reported to cause leukocytosis in the absence of infection [20]. Leucocytosis in sickle cell disease patients may be due to auto-splenectomy resulting from recurrent splenic vessels occlusion, which makes patients more vulnerable to overwhelming infections particularly, encapsulated organisms like *Streptococcus pneumonia* and *Haemophilus influenzae* [21].

Undoubtedly, leucocytosis is associated with poor prognosis, while reducing neutrophil count is associated with good prognosis [22]. Most patients showed relatively to marked elevated platelets count, above 600,000. It is as the same as that revealed by Osman, et al., [19]. A negative feedback effect on erythropoietin production in subjects as a result of the anemia could be responsible for the thrombocytosis. Erythropoietin has a structural homology with thrombopoietin, although the latter is considerably larger than the former but roughly half of thrombopoietin has an identity with or similarity to erythropoietin at the N-terminal region. It is, therefore, well recognized that thrombocytosis is associated with anemia of chronic disease and several types of anemia. Reduced or absent splenic sequestration of platelets as a result of hyposplenism in sickle cell disease which also contributes significantly to higher mean platelet counts in sickle cell disease [22].

Recommendations

In conclusion, the above findings have highlighted the urgent need for sickle cell control work plan. This plan should be comprehensive taking into account; raising community awareness, early identification of cases, updated sickle cell disease management protocols, genetic counseling services, advocacy, and multilateral partnership, intensive research on different aspects of SCD in this region. Sickle Cell Anemia Centre that recently established in this area could be the first step towards addressing effective control activities.

DECLARATIONS

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Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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