Research Article

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First and Common Clinical Presentation of Sickle Cell Disease in Children

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ABSTRACT

Background: *sickle cell disease (SCD) is the most common inherited blood disease worldwide with the vast majority of cases occurring in sub-Saharan Africa. In Sudan, sickle cell anemia is one of the commonest chronic hemolytic anemias with high mortality and morbidity.*

Objective: *the objective of this study is to determine the first and common presentation of sickle cell in children to assist early diagnosis, prevent complications and decrease morbidity and mortality of sickle cell disease in children.*

Methodology and Results: *the study represented a combined descriptive study (hospital-based) and analytic study (cross-sectional observational) at Mohamed El-Amin Hamed Pediatric Emergency Hospital for Children in Omdurman, Khartoum State where 50 children diagnosed with sickle cell anemia, for the first time, aged 4 months – 17 years were included during period of six months (January – June 2016). The commonest first presentation of SCD was sickle cell crises in 46%, features of infection in 18% and the rest 36% presented with combined symptoms. 62% of children presented with pallor as a feature of anemia, 32% with jaundice, 14% with fatigability, 14% with shortness of breathing and 6% presented with other symptoms related to anemia.*

Conclusion and Recommendations: *It is clear that features of vaso-occlusive crises were the first presenting clinical features of sickle cell disease followed by features of infections and anemia. We believe that starting premarital screening, neonatal screening, expand and support SCD clinics and stablishing social support networks will help in decreasing morbidity and mortality from SCD.*

Keywords

First presentation, Children, Sickle cell disease.

Introduction

Sickle cell disease (SCD) is the most common inherited blood disease worldwide, with the vast majority of cases occurring in sub-Saharan Africa. The condition derives from a point mutation of the β-globin gene found on the short arm of chromosome 11 through which the hydrophilic amino acid glutamic acid is substituted with the hydrophobic amino acid valine at the sixth position. The result is a change in the structure and dynamics of hemoglobin such that certain conditions including deoxygenation and acidosis predispose to hemoglobin polymerization. When this occurs, erythrocytes assume a misshapen and rigid form that promotes pathological

processes leading to intravascular inflammation and occlusion of small blood vessels [1]. It is recessive autosomal disease caused by SS, CC and SC homozygotic genotypes. Patients with the SS genotype have the most severe form of SCD [2].

Sickle cell disease (SCD) affects many people throughout the globe, particularly those descending from Sub-Saharan Africa, the Middle East and South Asia. In general, SCD exists in the malarial regions of tropical areas. However, migration from a malarial area increases the number of children with SCD in Europe and North America. In the United States, SCD affects 1 in 500 African Americans. It is estimated that the population of sickle cell disease is approximately 4.4 million people, whereas 43 million are estimated to have sickle cell trait [3]. In a recent review of cross-sectional population surveys and cohort studies of SCD in Africa, it was estimated that between 50 and 90% of SCA children died before age 5 years. This extrapolates to 150,000–300,000 annual SCA child deaths, potentially accounting for 5–10% of the region's total child mortality [4].

In Sudan, Archibald first reported sickle cell anaemia in 1926. Three foci of the disease have been described: Western Sudan, southern Sudan among the southern nilotes and in the Blue Nile Province, central Sudan [5]. The available data revealed the wide range of sickle cell disease frequencies in different areas of Sudan ranging from 0.8% in central Sudan to 30.4% in Western Sudan. The Messeryia tribe (a branch of the Baggara tribes) in Kordofan and Darfur showed the highest rate of sickle cell disease where it is estimated that one in every 123 children born is at risk of having SCD. Gedarif State in Eastern Sudan also showed high rate of sickle cell gene among the population that migrated from Western Africa and Sudan [6]. Sickle cell anemia is one of the commonest chronic hemolytic anaemias with high mortality and morbidity in Sudan [7].

The major symptoms of SCD are mild to severe anaemia, painful crises, frequent infections, hand and foot syndrome and stroke. Some patients require frequent blood transfusion, while others may never need a single transfusion during their lifetime. In severe form of SCD, the patients have retarded growth, bone defects, multiple organ dysfunction and other complications due to frequent transfusion requirements, while patients with a mild disease may reach average height and have no multiple organ abnormalities [8].

Patients with sickle cell disease have an increased susceptibility to bacterial infections, particularly to *Streptococcus pneumoniae, Haeniophilus injluenzae*, which cause fulminant meningitis and septicemia. Other complications are the sequelae of vaso-occlusion and anaemia. Essentially every organ in the body can be affected. Splenic sequestration is an acute medical emergency requiring urgent management with blood transfusion. The liver has been reported to show abnormal function tests due to sickling and infarctive phenomena. Gall stones were reported in more than 30% of patients over 10 years of age. The thromboembolic features of the disease may involve the brain and other parts of the nervous system producing different neurological deficits [5].

SCD clinics can help bridge distance and other barriers to care by supporting a family's primary Health Care Practitioners. Preventive and supportive strategies should be offered. New-born screening inclusion has not only helped reduce SCD-related infant mortality rates, but allows for earlier referral, parent education, preventive strategies, and genetic counselling. Children with SCD should receive the 13-valent pneumococcal conjugate *and* polysaccharide vaccines against *Streptococcus pneumoniae*, and both conjugated quadrivalent meningococcal (A, C, W, Y) *and* serogroup B vaccines targeting *Neisseria meningitidis*. Daily prophylactic penicillin VK or amoxicillin should be prescribed for all children with SCD from 2 months to 5 years of age. Duration of prophylaxis may be extended. High quality studies have shown that hydroxyurea use can significantly reduce risk for acute chest syndrome (ACS), vaso-occlusive episodes (VOE), transfusions, hospitalization, and mortality [9]. The only intervention that may be curative is stem cell transplantation (SCT), but this comes at considerable cost and requires expertise. Gene therapy is experimental and if successful would overcome some of the hurdles of SCT [10].

Patients with sickle cell anaemia were known not to survive beyond their 20th birthday. However, improved understanding of the disease and more effective use of penicillin and antimalarial prophylaxis at an early age have made a remarkable improvement in the survival of patients with sickle cell disease. It has been reported that 50% of children with sickle cell anaemia in Zambia died before three years of age and only 10% of affected individuals in Zimbabwe were over ten years of age. In the United States, where infections and acute splenic sequestration crisis could be controlled, the patients still die during young adult life due to progressive vasculopathy. The improvement of this situation depends on the early identification of these individuals at increased risk of organ damage and giving them the appropriate management [5].

Methodology and Results

Methodology

The study represented a combined descriptive study (hospital-based) and analytic study (cross-sectional observational) at Mohamed El-Amin Hamed Pediatric Emergency Hospital for Children in Omdurman, Khartoum State where all children included in the study were diagnosed with sickle cell anemia for the first-time during period of 6 months from January – June 2016.

Objective

The objective of this study is to determine the first and the common presentation of sickle cell in children to assist early diagnosis, prevent complications and decrease morbidity and mortality of sickle cell disease in children.

Sample

Inclusion criteria: all children presented to emergency department and diagnosed with SCD for the first time aged 0-17 years.

Exclusion criteria: all children known to have SCD.

Consent

All children and their parents or care takers in the study were told briefly about the importance of this research and the aims of this study. Consent was obtained from care takers, head of emergency department and hospital administration.

Study Technique

Emergency doctor interviewed all children included. Detailed medical history and thorough clinical examination was performed. The diagnosis of SCD was confirmed by laboratory tests and hemoglobin electrophoresis.

Results

It was found that children diagnosed with sickle cell anemia for the first time aged less than 5 years were 27 (54%) and those more than 5 years were 23 (46%). The male: female ratio was 3:1 as males were 37 and females were 13. It was found that the majority of children included had no family history of SCD (54%) where there was no history of consanguinity and the rest (46%) had positive family history of SCD and consanguinity. The first presentation of SCD was sickle cell crises in 46%, infection in 18% and the rest 36% presented with combined symptoms (Figure 1). 62% of children presented with pallor as a feature of anemia, 32% with jaundice, 14% with fatigability, 14% with shortness of breathing and 6% presented with other symptoms related to anemia (Table1). 48% of children presented with fever as a feature of infections, 20% with cough, 2% with skin infection, 2% with urinary tract infection, 4% with gastroenteritis (diarrhea) and 14% presented with other symptoms related to infections (Table2). The patients presented with vaso-occlusive crisis 64% of them presented with hand-foot syndrome as a feature of vaso-occlusive crisis, 12% with abdominal pain, 10% with long bones pain, 2% with back pain, 2% with chest pain and 12% with other features related to vaso-occlusion (Figure 2). No other sickle cell crises detected on presentation (splenic sequestration, hemolytic or aplastic crises). 48.3% of children had admission with vaso-occlusive crisis, 18.3% with pneumonia, 6.67% with gastroenteritis and blood transfusion for each, 11.6% with infections, 5% with hemolytic crisis and 3.3% with osteomyelitis (Figure 3).

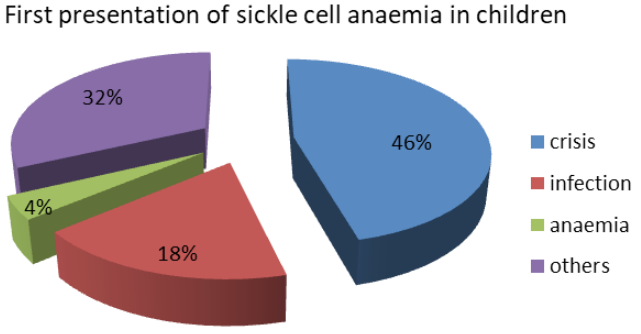

Figure 1: Showed the First Presentation of Sickle Cell Anemia in Children.

Table 1: Showed the Presenting Symptoms of Anemia.

Symptom	Frequency	Percent %
Pallor	31	62%
Jaundice	17	34%
Fatigability	7	14%
Shortness of breathing	6	12%
Others	3	6%
Total	50	100%

Table 2: Showed the Presenting Symptoms of Infection.

Symptoms	Frequency	Percentage (%)
Fever	24	48%
Cough	10	20%
Skin infection	2	4%
Urinary tract infection	2	4%
Diarrhea	4	8%
Others	8	16%
Total	50	100%

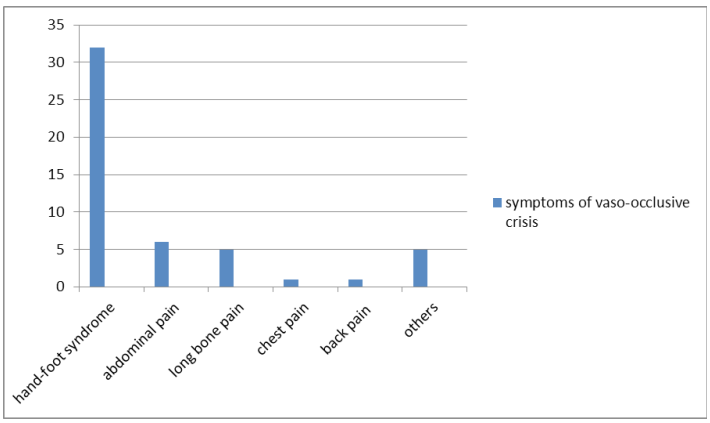

Figure 2: Showed Symptoms of Vaso-Occlusive Crisis.

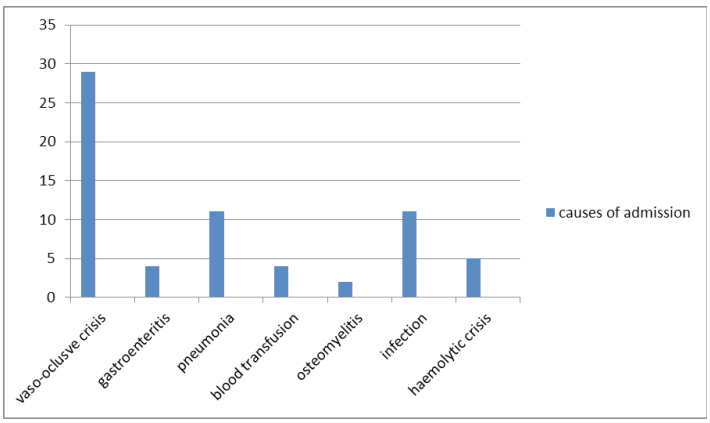

Figure 3: Showed the Causes of Admission of Children with SCA to Hospital.

Discussion

This study represented a combined descriptive study (hospital-based) and analytic study (cross-sectional observational) at Mohamed El-Amin Hamed Pediatric Emergency Hospital for Children in Omdurman, Khartoum State where 50 children aged 4 months – 17 years included in the study were diagnosed with sickle cell anemia for the first-time during period of 6 months

from January – June 2016. It was found that children aged less than 5-years were 27 (54%) and more than 5-years were 23 (46%). Males were found to be 37 (74%) and females were 13 (26%) and male: female ratio was 3:1. Unlike the study by Meysaa et al. 2022, Osama Atiat Alla et al. 2018 and Adam et al. 2019 where the female were the majority of the studied group [3,11,12].

In our study we found that the first presentation of SCD was sickle cell crises due to vaso-occlusion in 46%. Children presented with infection were 18% constituted the second common presenting feature of SCD. This was similar to the report by Meysaa et al. 2022 [3] and Abdelrahim 1997 [5] where they found the most common presentation was vaso-occlusive crises followed by infection and fever. On the other hand, Abdelrahim 1997 reported features of anemia among the commonest presenting features. In Jamaica, a prospective study of 314 patients followed from birth showed that dactylitis was the most common initial symptom found in 40% of all patients, followed by painful crises in more than one fourth of the study group. Trowel1 and co-workers reviewed the natural history of sickle cell disease in Uganda and found that pallor, jaundice and painful crises were among the most persistent features in all ages. It was found in Kenyan children with sickle cell anaemia that 25% presented with hand-foot syndrome, bone and abdominal pain, anaemia and hepatosplenomegaly, which were among the commonest features. The same type of presentation has been reported in eastern Nigeria [5].

Surprisingly, the clinical phenotype of SCD in Saudi Arabia has two major forms. Clinically, the disease has a different spectrum of disease with its acquired problems. For example, SCD patients from the Eastern province have a 27% risk of avascular necrosis of the femoral head compared with 8% to 12% in the African type. Late persistent splenomegaly is reported in 50% to 80% of patients, resulting in a higher risk of splenic complications such as sequestration crisis, chronic hypersplenism, splenic infarction and abscess, trauma, and rupture, and 20% required splenectomy. In the Western province, the frequency of splenomegaly is significantly less frequent. Acute chest syndrome in SCD children less than 12 years of age occurs less commonly in the East compared with the West (7.7– 13.4% vs 22.6%, respectively) and recurrence rate is significantly lower in patients from the Eastern province [13].

Interestingly, M Pedram, from Iran reported a 3.5-year-old girl first presentation of sickle cell anemia was acute splenic sequestration crisis which was associated with acute chest syndrome treated with wide spectrum antibiotic and transfusion exchange. The patient was discharged with stable clinical state after 8 days [14]. Emily Meier & Miler 2012 in the USA reported splenic sequestration occurs in as many as 30% of SCD patients at less than 6 years of age. Acute splenic sequestration (ASS) may be classified as major or minor episodes. Major episodes are life threatening, with rapid enlargement of the spleen and circulatory collapse requiring transfusion. Minor episodes also involve rapid enlargement of the spleen, but the haemoglobin reduction is less severe (absolute values remaining above 6 g/dL) [15].

Moreover, Alexis Claeys et al. 2021 from Belgium reported 2 cases; first case was 20 months boy, the first child of healthy, nonconsanguineous parents from Angola. the family history did not reveal any relevant information except that the mother is a carrier of sickle cell anemia (HbAS), which was denied to the father. The other child was 3-years old boy, the first child of healthy, nonconsanguineous parents from Guinea. The family history did not reveal any relevant information. Both children presented with limping and inability to walk for some time and finally they found that limping is pain due to vaso-occlusive crises (VOC), and the presence of a high HbF, the diagnose of sickle cell anemia was delayed [16].

We concluded that sickle cell anemia is one of the major health problems in Sudan with high morbidity and mortality. It is crucial is to detect the early features of sickle cell in children to assist early diagnosis, prevent complications and decrease morbidity and mortality in affected children.

Conclusion

Sickle cell anemia is one of the commonest chronic hemolytic anaemias with high mortality and morbidity in Sudan. It was clear that the first presenting clinical features of sickle cell disease were features of vaso-occlusive crises followed by features of infections and anemia.

Recommendations

- Establish premarital screening program nationwide.
- Start neonatal screening program to all new-borns.
- Encourage and maintain the specialized sickle cell clinics.
- Increase awareness of health workers about common presenting features of SCD for early diagnosis and prevention of morbidity and mortality.
- Stablish social support networks.

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Consent

Informed consent was obtained from caretakers, head of emergency department and hospital administration.

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