Clinical and hematoloical complications in children with sickle-cell disease at Assuit University Children Hospital

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Background and aim
Sickle-cell disease (SCD) is a hereditary hemoglobinopathy with significant morbidity and potentially a fatal disease that has many associated acute and chronic complications. This study aims at identifying the most common complications associated with SCD, their risk factors, and to assess the quality of care and management of these cases at Assuit University Children Hospital.

Study type and setting
Cross-sectional descriptive study. It was conducted at Assuit University Children Hospital, including all cases of SCD, who were admitted at the hematology unit or who attended the outpatient hematology clinic during the period of the last 2 years.

Patients and methods
The study included 56 patients with SCD who attended the hematology unit or clinic for routine follow-up care or emergency services. We collected the medical data of our patients in standardized form by checking their medical records in our hospital. This form was designed to include personal characteristics, the reason for their hospitalization, family history, treatment protocols, and follow-up.

Statistical analysis
Microsoft Excel was used to analyze the entered data. Quantitative variables were expressed as means, while qualitative variables were expressed as numbers and percentages.

Results
Among the 56 (53.5%) participants were male. About (53%) of participants presented with vaso-occlusive episodes that were considered the most common complications of SCD, sequestration crisis (10.7%), and stroke (7%), while the prevalence of fever and infection was (5.3%).

Conclusion
Children with SCD in Egypt have a high prevalence of complications related to SCD. Through this study, we would like to improve the quality of care and management of these cases.

Keywords:
children, complications, sickle-cell disease, vaso-occlusive crisis

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Introduction

Sickle-cell disease (SCD) is a hereditary hemoglobinopathy resulting from hereditary mutation of beta-globin gene on chromosome 11. That results in production of hemoglobin S, which has changes in molecular stability and solubility, also, hemoglobin S polymerizes under deoxy conditions. These physical changes are responsible for the clinical presentation of SCD [1]. SCD is considered potentially fatal with significant morbidity affecting patient's health, so regular follow-up and proper care of the patients may improve their life [2]. Clinical manifestations of SCD usually occur early in childhood. Vaso-occlusive crisis, anemic crisis, acute chest syndrome, severe bacterial infections, and stroke are considered the five mean clinical features in SCD patients. Other manifestations such as avascular necrosis of femur, nephropathy, priapism, gallstone, and chronic leg ulcers are not commonly seen [3]. Management of SCD includes control of symptoms, treatment of complications, and prevention of various organ damages associated with the disease [4]. Here we intended to identify the most common complications associated with SCD, their risk factors, and to assess the quality of care and management of these cases at Assuit University Children Hospital.

Patients and methods

The study is a cross-sectional descriptive study that included 56 patients with SCD registered in the hematology unit and outpatient clinic at Assuit

University Children Hospital who had been diagnosed on the basis of history, examination, and hemoglobin electrophoresis.

Inclusion criteria

(1) Children and adolescents with SCD or combined with other hemoglobinopathies who attended for routine follow-up care or emergency services.
(2) Both genders were included.
(3) The age of our patients is less than 16 years.

Exclusion criteria

(1) Patients of other diseases rather than SCD.

Sample-size calculation

(1) SCD patients who were admitted over the last 2 years.

Clinical and hematological data were collected in standardized form by checking the medical records of patients in our hospital. This form was designed to include personal characteristics: name, age, gender, demographic information, age at first presentation, the reason for hospitalization, family history, treatment protocols during hospitalization, and interventions at the hematology clinic (including described medication, prophylactic vaccination, and regular laboratory tests to assess other organ affection, such as complete blood count, liver-function test, renal chemistry, urine analysis, screening for blood-borne infections, serum ferritin, and transcranial Doppler) in addition to routine-visit attendance for follow-up.

Microsoft Excel was used to analyze the entered data. Quantitative variables were expressed as means, while qualitative variables were expressed as numbers and percentages.

A written informed consent was obtained from parents of all subjects of the study. They informed that refusing participation in our study had no effect on the medical service provided to the child.

This study was approved by the Institutional Review Board of the Faculty of Medicine in Assuit University, Egypt. IRB local approval number 17101390.

Results

Baseline characteristics

The study included 56 participants, 30 males and 26 females. Different age groups were represented, about 21.4% were under 3 years old and the mean age of our patients was 6.5 years (Table 1).

Age at diagnosis

The mean age at diagnosis in our hospital was 1.5 years. Fifty percent of cases were diagnosed during infancy before the age of 12 months (Table 2).

Frequency of hospitalizations

About 96.5% of our patients were previously hospitalized at least once for management of SCD-related complications within the last 12 months (Table 3). The frequency of hospitalizations was higher in patients with older age and does not differ according to their gender.

Table 1 The characteristics of 56 children with sickle cell anemia at Assuit University Children Hospital

	n (%)
Gender	
Male	30 (53.5)
Female	26 (46.5)
Age (years)	
0-2	12 (21.4)
3-5	11 (19.6)
6-8	12 (21.4)
≥9	21 (37.5)
Governorate	
Assuit	21 (37.5)
New Valley	15 (26.7)
Sohag	11 (19.6)
Minya	5 (8.9)
Qena	4 (7)
Hb electrophoresis	
SCD	44 (78.5)
SCD with other hemoglobinopathies	10 (17.8)
Sickle cell trait	2 (3.5)
Family history of SCD	
Positive	40 (71.4)
Negative	16 (28.5)

SCD, sickle-cell disease.

Table 2 Recorded data about age at diagnosis in the studied cases

Age at diagnosis	*n* (%)
6-12 months	28 (49.9)
1-2 years	19 (33.9)
3 years	7 (12.5)
≥4 years	2 (3.5)

Table 3 Recorded data about frequency of hospitalization

Hospitalization	*n* (%)
0	2 (3.5)
1	8 (14.3)
2	18 (32)
3	18 (32)
4 or more	10 (17.8)

Prevalence of complications

Table 4 most common complication of SCD was a vaso-occlusive crisis. It had been diagnosed in 41 (53%) patients.

Treatment received during hospitalization

As shown in Fig. 1, 89% of participants needed blood transfusion according to the severity of anemia in our hospitalized patients with SCD. Intravenous fluids were received by 76.7 of our cases, analgesics 75%, and antibiotics received by 61.8%.

Interventions at the hematology clinic

Fig. 2 shows that folic acid and hydroxyurea intake were frequently provided. Pneumococcal vaccination was only given to 13 (23.2%) subjects and prophylactic oral penicillin was given to 10 (17.8%) subjects, despite their effectiveness in improving mortality.

Regular laboratory tests in our outpatient clinic were done only for a few number of cases during the routine visits, which is very defective. As shown in Table 5, transcranial Doppler was not done for any case.

Routine-visit attendance to the outpatient clinic

Table 6 shows that only 39.2% of participants came for follow-up routine visits at the hematology clinic in Assuit University Children Hospital.

Psychotherapy

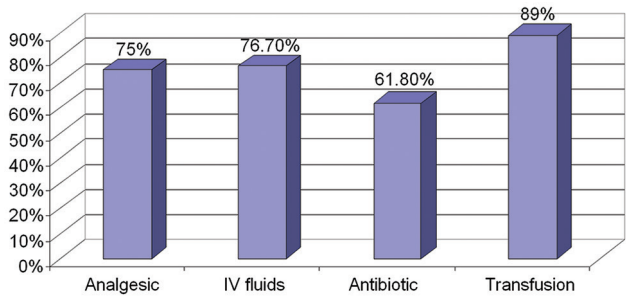
Table 7 shows that none of our cases had the chance to be evaluated by a psychotherapist.

Discussion

The purpose of this descriptive study is to provide a satisfactory attitude toward SCD in our locality and its management. We tried to give attention to identify the local clinical manifestations, phenotypes, and complications related to SCD, the practical challenges for diagnosis. Also, we aim at improving our current management guidelines and providing recommendations for SCD care program in our hospital. This is the first study to be done in our department regarding SCD. The primary outcome of this study was identifying the prevalence of complications related to SCD. The secondary outcomes included improving health services received by our patients during hospitalization and at our outpatient hematology clinic to reduce morbidity and mortality.

As regards the characteristics of SCD children seen at our hospital, there were 56 patients comprising 30 males and 26 females. The age presentation of children ranges from 1 to 16 years old with the mean age of 6.5 years. School-age patients were more frequently represented being 69.6% followed by preschool age 30.3%. Gender did not statistically influence disease severity. Almost the same age distribution was described among SCD

Figure 1



Recorded data about treatment received during hospitalization in the studied cases.

Table 4 Recorded data about prevalence of complications of sickle-cell disease

Clinical finding at presentation	*n* (%)
Acute painful episode	24 (42.8)
Acute chest syndrome	9 (16)
Hand–foot syndrome	8 (14.2)
Sequestration crisis	6 (10.7)
CNS complication	4 (7)
Fever and infection	3 (5.3)
Aplastic crisis	2 (3.5)

CNS, central nervous system.

Table 5 Regular follow up of laboratory and imaging parameters for sickle-cell disease cases at our hematology clinic

Regular laboratory tests and imaging in outpatient clinic	*n* (%)
CBC	22 (39.2)
LFT	17 (30.3)
Renal chemistry	14 (25)
Urine analysis	6 (10.7)
Screening for blood born infections (HCV, HIV)	5 (8.9)
Serum ferritin	3 (5.3)
TCD	0

CBC, complete blood count; LFT, liver-function test; TCD, transcranial Doppler.

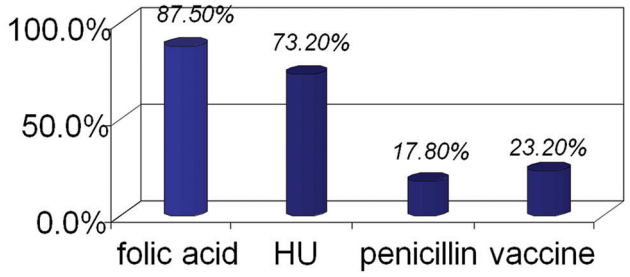
Table 6 Attendance of SCD cases to our outpatient hematology clinic for follow up routine visits

Routine visits	*n* (%)
Yes	22 (39.2)
No	34 (60.7)

Table 7 Recorded data about evaluation of our SCD cases by a psychotherapist

Psychotherapy	*n* (%)
Yes	0
No	56 (100)

Figure 2



Drug therapy received by children of SCD at the outpatient clinic in the studied cases. SCD, sickle-cell disease.

children in other countries. In Nigeria, Adegoke *et al.*[5] reported that the median age was 5.9 years, while the number of SCD cases that had been diagnosed under the age of 1 year was higher than our cases diagnosed at the same age. The contributed causes for older age of diagnosis are absence of a newborn screening program in our locality, and poor awareness of our community about the early symptoms of SCD.

The mean age of diagnosis of SCD was 1.5 years old for patients in our hospital. Half of our cases (50%) were diagnosed in infancy (before the age of 12 months). Many other countries that have no screening for newborns report an age of diagnosis at or more than 1-year-old. For example, in Brazil, Fernandes *et al.*[6] reported that the mean age of diagnosis was 2 years old.

Regarding the demographic distribution of SCD in our locality, Assuit was the most prevalent (37.5%) in the participants, followed by New Valley (26.7%) with increased frequency of cases admitted to our hematology unit in the last few years. Data from Egypt about SCD are very scarce. Previous studies revealed that the prevalence of the disease was found to be (1.6%), and most of the cases were from Seiwa, as reported by El-Beshlawy *et al.* [7].

Regarding hemoglobin electrophoresis, 78.5% of our cases had hemoglobin S only, while 17.8% present hemoglobin S associated with other hemoglobinopathies. Adegoke and Kuti [8] found that many factors may affect the clinical presentation and the severity of SCD, such as the polymorphisms of beta-globin haplotypes in SCD cases, in addition to other abnormal variants of hemoglobin. Most of the cases with SCD that were seen at Assuit University Children Hospital (71.4%) had a positive family history of that disease, however, their mean age of diagnosis was not different from those who had no family history. This disagrees with Aloni and Nkee [9], who found that having a family member affected with SCD increases awareness of the disease clinical presentation and improves quality of care provided for subsequent children. This depends on proper family education and access of good healthcare services. Identifying individuals with a high risk for serious SCD complications may be done through their positive family history for the disease.

About 96.5% of patients included in this study had been hospitalized in the last 12 months for management of their disease. Painful episodes were the most common cause for hospitalization they represented in 42.8% of our cases, acute chest syndrome (16%), hand–foot syndrome (14.2%), sequestration crisis (10.7%), and central nervous system complications (7%). The patients whose ages were less than 1 year at the first presentation had the highest frequency of hospitalization. These findings reveal that the earlier the symptoms appear, the higher the severity is. These results almost go with Adegoke and Kuti [8], findings that revealed a positive correlation between age and severity score.

Regarding the prevalence of complications related to SCD, vaso-occlusive crisis was the commonest that had been diagnosed in almost (53%) of the participants, regardless of age, and this matches with Teoh *et al.* [10]. Hand–foot syndrome was presented by 14.2% of cases. It is a vascular obstruction affecting the bone marrow of small bones. It usually occurs in infants and young children. Ballas [11] reported that children with SCD who develop dactylitis during the first year of age are at high risk for more severe course of illness and may develop cerebrovascular complications and tend to have more serious outcome. Stroke had been diagnosed in four (7%) participants, while acute chest syndrome represented by 16% of the cases. Several factors were found to be a risk for stroke and ACS among SCD in our patients. Family history had the strongest association, higher number of hospitalizations and increasing age were also associated.

During hospitalization of our SCD patients, about 89% of them needed blood transfusion according to the severity of anemia. In the United States, only 28.8% of SCD cases needed transfusion as reported by Raphael *et al.* [12]. About 61.8% of our cases received antibiotics. Bacterial infections precipitate painful crisis in children with SCD, so prophylactic penicillin and vaccination are important for those patients. Unfortunately, a few number of our cases received proper prophylaxis. Antibiotics were usually prescribed for patients with fever-associating vaso-occlusive crisis.

Interventions at the hematology clinic: For our cases, supportive treatment, which is the main regimen (as treatment was given only at the time of acute crisis) for all cases, was found to be defective, despite the continuous recommendation for their importance.

Lack of pneumococcal vaccination and prophylactic penicillin may be explained in our developing country by deficiency of resources. They are considered of high value in management of SCD as they reduce the frequency of complications and improve patients' life quality. Hydroxyurea was prescribed to 41 (73.2%) children. It is the main SCD-modifying drug. Powars *et al*. [4] found that using of hydroxyurea eliminates the frequency of vaso-occlusive episodes and disease mortality.

SCD management includes regular follow-up of the patient when established as a case of SCD. We found that regular laboratory tests were done only for a few number of cases who attended the routine visits in our outpatient hematology clinic. Screening transcranial Doppler had never been done for children with SCD in our hospital, although it has a significant importance in identifying patients at high risk for stroke. Galadanci *et al*. [13] reported that this screening program provides a chance for those children to start chronic blood transfusion that is used to protect high-risk individuals and to prevent further occurrence of stroke in patients with previous attack.

Screening for infectious diseases (HIV, HBV, and HCV) in our cases was done in only five cases from a total number of 56 cases with a percentage of 8.9% that is very defective as all cases receive frequent administration of blood transfusion that may carry the risk of transmission of viral infection. Lane [14] recommend that all people with SCD should be screened for HCV, HBV, and HIV at least every 6–12 months.

In our study, it was found that there is a major defect in the management of SCD according to a comprehensive care program and we lack the teamwork in its management as consultation was done only when complications occur not as a routine to regularly assess for early detection of any problem; psychotherapy was also defective as none of our cases had the chance to be evaluated by a psychotherapist. Only a few of our cases attend for follow-up and most of them come only when they develop a major health problem.

Conclusion

Children with sickle-cell anemia in Egypt are diagnosed late. The prevalence of complications and hospitalization is high among them. Vaso-occlusive crisis is the most common presentation of the disease. Blood transfusion and antibiotics are commonly used. Providing comprehensive care of those children, as well as using preventive therapies, such as hydroxyurea, prophylaxis with penicillin, and vaccination. Psychological support and proper family education, in addition to regular attendance of follow-up visits for cases, will result in a better outcome of SCD. The only curative treatment for SCD is hematopoietic stem cell transplantation from HLA-identical siblings. Other therapeutic lines such as hydroxyurea and supportive treatments are used when transplantation is not available.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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