Causes of hospitalization in sickle cell diseased children in western region of Saudi Arabia. *A single center study*

Abeer A. Abd Elmoneim, MD,
Zakaria M. Al Hawsawi, MD, Badr Z. Mahmoud, MBBCh,
Abdullah A. Bukhari, MBBCh,
Abdulmalik A. Almulla, MBBCh,
Abdullah M. Sonbol, MBBCh, Anas M. Makhdoum, MBBCh.

ABSTRACT

Objectives: To highlight the causes of hospitalization among sickle cell diseased (SCD) children in Al-Madinah Al-Munawarah, Saudi Arabia.

Methods: A retrospective study conducted at the Maternity and Children's Hospital, Al-Madinah Al-Munawarah, Saudi Arabia. A data of 739 SCD children admitted to the hematology/oncology unit between October 2010 and September 2015 were collected. The collected data were analyzed using an independent t test and a Chi square test as appropriate.

Results: Approximately 49% of the studied children were presented by acute painful crisis. Acute chest syndrome was reported in 20.9%. Infection was the cause of admission in 17.5%, and acute anemia was reported in 8.1% of the studied patients. No significant difference of the reported clinical manifestations by patients' gender. Children aged <12 years showed significantly high frequency of acute chest syndrome (ACS) (26.5%), while acute painful crisis (66.4%) was significantly more frequent among children aged ≥12 years.

Conclusion: This study revealed high rate of hospitalization of SCD children because of acute painful crisis, ACS, infection, and anemia. These admissions causes could potentially be continuously assessed to minimize the rate of hospitalization.

Saudi Med J 2019; Vol. 40 (4): 401-404
doi: 10.15537/smj.2019.4.24049

The prevalence of sickle cell anemia (SCA) in Saudi Arabia shows marked regional variation, with the highest prevalence in the Eastern (0.17%) and Southern provinces (0.10%).[1] In Al Madinah, the Western province, the estimated prevalence of sickle cell homozygosity (Hb SS) was 0.01%, and that of the carrier state (Hb AS) was 0.09%.[2] Patients with SCA suffer from life-threatening complications caused by acute sickling of red blood cells resulting in acute pain and organ dysfunction. Complications of SCA mostly require hospitalization, which constitutes a significant burden on caregivers.[3] Causes of hospitalization in SCD children vary but still infection is the main cause, particularly in developing countries.[4]

In the previous Saudi studies, acute chest syndrome (ACS) and infections were the main causes for hospital admission;[1,2] ACS was more frequent in patients <12 years old (13.5%) than in older patients (5.1%). In a previous study, carried out on 53 patients aged 6 months to 12 years in Al Madinah, the main causes of hospitalization were vaso-occlusive crisis (77.3%), infection (67.9%), ACS (22.6%), anemia (12.6%), and cerebrovascular accident (9.4%).[2] No other studies have investigated the causes of hospitalization of SCD children in Al Madinah region. The present retrospective study aimed to identify the main causes of hospitalization in recent years among SCD children in Al Madinah and to compare the results obtained with the previously published data.

Methods. This is a retrospective study of 739 SCD children's medical records. The sample studied included all patients admitted with SCA to the Hematology/Oncology Center at Maternal and Children's Hospital (MCH) over a 6-year period between October 2010 and September 2015. Located in the western region, Al Madinah is the fourth largest city in the Kingdom of Saudi Arabia (KSA). It is the capital of Al Madinah province, with a total population of 1.7 million in the province. The MCH, a tertiary health care center located in Al Madinah city, forms part of the national health system and is a referral center for the treatment of SCD children.

Patient records during the study period were identified according to diagnosis, which was obtained from the hospital's electronic records. Selected records were those bearing D57 codes (sickle cell disease) according to the International Classification of Diseases, 10th Revision (ICD-10).[5]

Patients who were not admitted to the hospital during the study period or those diagnosed with sickle-cell trait were excluded from this study. Every readmission of each patient was considered for analysis, regardless of the time elapsed between readmissions.

A data collection sheet was developed on the basis of similar study data to guide the extraction of information from patient records. The sheet included sociodemographic data (age, gender, residency, and nationality), as well as variables related to clinical

presentation of SCA, including vaso-occlusive crisis, ACS and bacterial infection.

Data from the studied cases, including their clinical presentations and laboratory findings, were tabulated and presented as frequency number, percent or mean ± SD. Comparison of clinical presentation and laboratory findings by gender of the studied cases was performed using an independent t test and Chi square test, as appropriate. A $p<0.05$ was used as an indicator of statistically significant differences. An internet-based search through Pubmed web site was used to find prior related study. This study proposal was approved by the local Ethics Committee of the Hematology/Oncology Center at MCH in Al Madinah. Ethical guidelines according to principles of Helsinki Declaration were followed to ensure privacy and confidentiality of the collected data. Data were analyzed using the Statistical Analysis System software package, version 8.2 (SAS Institute, USA).[6]

Results. This study analyzed data from 739 cases with SCA admitted to MCH in Al Madinah, KSA, during the period from 2010 to 2015.

Table 1 shows the distribution of the studied cases according to their age, gender, nationality, and laboratory findings. **Table 2** shows the distribution of the studied cases according to their clinical presentation.

Although there was no statistically significant difference between the studied males and females in terms of their clinical presentation ($p=0.66$), acute painful crisis (50.2%), acute chest pain (21.5%), and stroke (2.2%) were more frequent among female patients. Infection (18.1%) and anemia (8.7%) were the most frequent clinical presentations among male patients. Four male patients (0.97%) presented with priapism.

Table 3 presents the comparison of the studied cases by their clinical presentation and age groups.

Discussion. Sickle cell anemia is one of the most significant health problems among children in the Eastern, Western, and Southern provinces of KSA, where the gene frequency of this disease is prevalent. Previous study documented the genetic variants and its relation to severity of SCA in these areas.[7] However, relatively few studies have reported the main causes of hospitalization among these patients. In our retrospective study, we enrolled data from 739 SCA patients hospitalized in MCH in Al Madinah city over a 6-year period to identify the main causes of hospital admission among Saudi children with SCA.

The study findings indicate that approximately half of the studied children presented with acute painful crisis (49.7%). In a previous Saudi study, acute painful crisis and dactylitis were significantly more common among Eastern province patients than Western province patients; moreover, the onset was significantly later in Eastern province patients.[8] Similar findings were reported previously, as the main causes of hospitalization were vaso-occlusive crisis (77.3%), infection (67.9%), ACS (22.6%), and anemia (12.6%).[2] Severe abdominal pain usually is similar to acute abdomen, which may be a referred pain from either intra-abdominal soft tissue or organ infarction.[9] Bone aches result from infarction of bone marrow (BM). Bone aches usually involve bones where the BM is mostly active. The areas of BM activity is changeable with age, consequently, the pattern of bone aches are easy to predict. For example, metatarsals and metacarpals are the most bone to be affect by bone aches in the first 18 months of life resulting in hand foot syndrome presentation.[9]

In the present study, infection was the third most frequent presenting manifestation among the studied SCA children (17.5%). In a previously published data,

Table 1 - Patients' characteristics (n=739).

Characteristic	n (%)
Age in years; mean±sd	14.2 ± 2.1
Age in years	
<12	340 (46.0)
≥12	399 (54.0)
Gender	
Male	414 (56.0)
Female	325 (44.0)
Hb (g/dL)	8.1 ± 2.1
WBCs (x10^6)	17.2 ± 8.8
Platelets count (x10^9)	411.5 ± 212.6

Hb - hemoglobin, WBC - white blood cells

Table 2 - Distribution of the studied cases according to their clinical presentation.

Clinical presentation	n (%)
Acute painful crisis	367 (49.7)
Acute chest syndrome	155 (20.9)
Infections	129 (17.5)
Acute anemia	60 (8.1)
Hand foot syndrome	14 (2.0)
Stroke	10 (1.3)
Priapism	4 (0.5)

Disclosure. Authors have no conflict of interests, and the work was not supported or funded by any drug company.

Table 3 - Comparison of clinical presentation of the studied case by their age.

Clinical presentation	<12 years n=340	≥12 years n=399	*P*-value
Acute painful crisis	102 (30.0)	265 (66.4)	
Acute chest syndrome	90 (26.5)	65 (16.3)	
Infections	84 (24.7)	45 (11.3)	
Acute Anemia	50 (14.7)	10 (2.5)	
Hand foot syndrome	8 (2.4)	6 (1.5)	
Stroke	6 (1.8)	4 (0.01)	
Priapism	0 (0.0)	4 (0.01)	0.01*

Values are presented as number and percentage (%).
*p-value are significant

however, infection was the second most frequent cause of hospital admission in SCD children in Al Madinah as reported previously.[2] The regression of infection from second most frequent cause of hospitalization to the third one in the present study can be attributed to the improvement in environmental sanitation and growth of health care services in KSA during the last 2 decades.[10] Consequently, the incidence of infection has declined. However, increased susceptibility to bacterial infection remains the main cause of morbidity and mortality in patients with SCA, particularly in early childhood. Infection rates showed some variation across KSA regions. In the southern area, the reported infection rate among SCA patients was 21.2%, and in the eastern region of KSA it was 8.6%.[11] The difference in the incidence of infection among current study and previous KSA studies may be attributable to the presence of two different genetic types of SCA in the country.[12]

In the present study, acute anemia was present in 8.1% of the studied SCA children. The mean Hb (hemoglobin) concentration was 8.1 ± 2.1 gm/dL. A much higher rate of presentation was reported in the previously in SCD children in Al Madinah,[2] where severe anemia (Hb < 5 gm/dL) was present in 18.9% of patients. Cerebrovascular stroke in this study was reported in 10 of the studied children (1.3%) while in the previous Al Madinah Study,[2] cerebrovascular stroke was reported in 5 patients (9.43%), aged 12 years and younger, and none of them died. A similar finding to this study was observed in southern KSA, where stroke was reported in 2% of patients. The incidence of stroke,was much higher in Western countries.[9] However, with the introduction of brain MRI/magnetic resonance angiogram (MRA), silent cerebral has been reported in with a prevalence of 35-40%.[13] Stroke affects 30% of SCD children and 11% by the age of 20 years. It is usually ischemic in children and hemorrhagic in adults.[9] The STOP (Stroke Prevention in SCA) study showed that annual routine screening can minimize the rate of stroke from 10% to 1% in SCD children.[14]

Statistical analyses of the reported data according to sex and age (<12 years versus ≥12 years) have revealed no significant differences (p=0.66) in the reported clinical manifestations among the studied males and females. However, acute painful crisis (50.2%), acute chest pain (21.5%) and stroke (2.2%) were more frequent among female patients. Infection and anemia were more frequent among male patients, representing 18.1% and 8.7% of cases, respectively. Children aged <12 years showed a significant higher (p=0.01) frequency of ACS (26.5%), infection (24.7%,) and anemia (14.7%), while acute painful crisis (66.4%) and priapism were significantly (p=0.01) more frequent among children aged ≥12 years. Consistent with these findings, Hawsawi et al.[2] reported a similar prevalence of ACS (26.6%) among their studied 53 children aged <12 years. In the Eastern province, however, the rate of hospital admission because of ACS was as low as 7%. The authors attributed this to the theory that SCA patients in Eastern province generally have a milder form of the disease with less frequent acute chest crises, most likely due to the high prevalence of the Asian haplotype among SCA patients in this area, coexisting alpha-thalassemia, persistence of high Hb-F levels, hematological characteristics, social circumstances, and geographical and climatic variation. In the present study, priapism was reported in 4 male patients, all of whom were aged ≥12 years. According to a previous study, the mean age at which priapism occurs is 12 years, and by the age of 20 years, as many as 89% of males with sickle cell disease have experienced one or more episodes of priapism.[15]

The strength of this study is that it is the first study in this millennium to evaluate the clinical manifestations of SCA as causes of hospitalization among children with the disease in Al Madinah, Saudi Arabia. Like other retrospective studies, the potential risk of omitted data in the present study could not be avoided, and thus, the study analysis did not extend to comparisons of the studied clinical manifestations by SCA genotype. However, the main aim of this study was to update the Saudi literature with the main causes of hospitalization among SCA-diseased children, irrespective of its genotype.

In conclusion, advances in the medical and supportive care of SCA patients has resulted in changes in the causes of hospital admission for these patients. This study confirms that causes of hospitalization in SCD children have changed over time.

Future studies should focus on outcomes of hospitalized SCA-diseased children in Al Madinah, as well as in other Saudi provinces, taking into consideration the management of these patients during hospitalization.

Acknowledgment. *The authors would like to thank SAGE languages services (www.Sagepub.com) for English language editing.*

Received 12th December 2018. Accepted 28th February 2019.

From the Pediatric Department, Taibah University, Al-Madinah Al-Munawarah, Kingdom of Saudi Arabia.

Address correspondence and reprints request to: Dr. Abeer A. Abd Elmoneim, Pediatric Department, Taibah University, Al-Madinah Al-Munawarah, Kingdom of Saudi Arabia. E-mail: abeeraaa6@gmx.de ORCID ID: orcid.org/0000-0002-1614-9067

References

1. Memish ZA, Owaidah TM, Saeedi MY. Marked regional variations in the prevalence of sickle cell disease and β-thalassemia in Saudi Arabia: findings from the premarital screening and genetic counseling program. ***J Epid and Global Health*** 2011; 1: 61-68.
2. Hawasawi ZM, Nabi G, Al Magamci MS, Awad KS. Sickle cell anemia in childhood in Madina. ***Annals Saudi Medical*** 1998; 18: 293-295.
3. Brandow AM, Liem RI. Sickle cell disease in the emergency department: atypical complications and management. ***Clin Pediatr Emerg Med*** 2011;12: 202-212.
4. Brown BJ, Jacob NA, Lagunju IA, Jarrett OO. Morbidity and mortality pattern in hospitalized children with sickle cell disorders at the University College Hospital, Ibadan, Nigeria. ***Nigerian Journal Paediatrics*** 2013; 40: 34-39.
5. World Health Organization. International classification of diseases, 10th revision (ICD-10); 2018. [cited 2017 January 20] Available at: http://www.who.int/classifications/icd/en/
6. SAS Institute Inc. Proprietary Software Release 8.2. Cary, NC, SAS Institute Inc., 1999. Available at: https://www.sas.com/en_ae/home.html?utm_source=google&utm_medium=cpc&utm_campaign=brand-global&utm_content=GMS-40252&gclid=EAIaIQobChMItK3qjMiB4QIVjp3tCh0fWANtEAAYASAAEgI0JvD_BwE
7. El-Hazmi MA, Warsy AS, Bashir N, Beshlawi A, Hussain IR, Temtamy S, et al. Haplotypes of the beta-globin gene as prognostic factors in sickle-cell disease. ***East Mediterr Health J*** 1999; 5: 1154-1158.
8. Padmos MA, Roberts GT, Sackey K, Kulozik A, Bail S, Morris JS, et al. Two different forms of homozygous sickle cell disease occur in Saudi Arabia. ***Br J Haematol*** 1991; 79: 93-98.
9. Telfer P, Coen P, Chakravorty S, Wilkey O, Evans J, Newell H. Clinical outcomes in children with sickle cell disease living in England: a neonatal cohort in East London. ***Haematologica*** 2007; 92: 905-912.
10. Yousef AA, Al-Shamrani AS, Al-Haider SA, Said YS, Al Harbi S, Al-Harbi AS. Pediatric pulmonary services in Saudi Arabia. ***Ann of Thoracic Med*** 2013; 8: 224-228.
11. Abu-Srair HA, El-Bashir AM, Al-Dabous IS, Al-Khater M. Incidence of major infection in sickle cell pediatric patients at Qatif Central Hospital. ***Ann Saudi Med*** 1991; 11: 267-270.
12. El Mouzan MI, Al Awamy BH, Al Turki MT, Niazi GA. Variability of sickle cell disease in the Eastern province of Saudi Arabia. ***J Pediatr*** 1989; 114: 973-976.
13. Musallam KM, Khoury R, Abboud MR. Cerebral infarction in children with sickle cell disease: a concise overview. ***Hemoglobin*** 2011; 31: 618-624.
14. Wang WC, Pavlakis SG, Helton KJ. MRI abnormalities of the brain in one-year-old children with sickle cell anemia. ***Pediatr Blood Cancer*** 2008; 51: 643-646.
15. Rogers ZR. Priapism in sickle cell disease. ***Hematol Oncol Clin North Am*** 2005; 19: 917-928.