Original Article

Acute chest syndrome in pediatric sickle cell disease: A 19-year tertiary center experience

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Abstract:

INTRODUCTION: The most common cause of death among sickle cell disease (SCD) patients is acute chest syndrome (ACS). Since SCD is a common condition in the Eastern province of the Kingdom of Saudi Arabia (KSA), we aimed to provide a detailed description of the clinical characteristics and ACS management.

METHODS: We retrospectively studied pediatric (<14 years) patients with SCD diagnosis who were admitted with ACS or developed ACS after admission from January 2002 to December 2020. The absence of chest X-ray or hemoglobin electrophoresis was the reason to exclude patients from the study. The primary objective of the study was to evaluate and report the clinical, laboratory, and management characteristics of ACS.

RESULTS: Ninety-one ACS episodes (42 patients) were included, with a mean diagnosis age of 7.18 ± 3.38 years. Twenty-two (52.4%) patients were male. Twenty-five patients had recurrent ACS episodes. The median absolute number of ACS was 3.5 (interquartile range [IQR], 2–9), with maximum ACS episodes of 13/1 year and a minimum of 1 ACS episode per year. At the first ACS episode, the mean age was 6.62 ± 3.38 years, while the overall mean age at ACS episode diagnosis was 7.18 ± 3.38 years. The most common antecedent events were vaso-occlusive crisis (12 episodes, 13.2%) and upper respiratory tract infections (8 episodes, 8.8%). The most frequently encountered presenting symptoms were fever (70.3%) and cough (70.3%). The most common antibiotics used were azithromycin (82.4%) and ceftriaxone (75.8%). Nine patients (9.9%) required pediatric intensive care unit (PICU) admission. Of the 91 ACS episodes, there was no in-hospital mortality. The median hospital and PICU length of stay were 8 days (IQR, 5–10.25) and 4 days (IQR, 3–5.5), respectively.

CONCLUSION: This study has reported the most common clinical characteristics and management of ACS among pediatric SCD patients in the Eastern province of KSA.

Keywords:

Acute chest syndrome, hemoglobinopathy, pediatrics, pulmonary complications, Saudi Arabia, sickle cell disease

Sickle cell disease (SCD) is the most common inherited hemoglobinopathy worldwide.[1] It is a common condition in the eastern and southwestern provinces of the Kingdom of Saudi Arabia (KSA).[2] Acute chest syndrome (ACS) is a common cause of mortality and morbidity among SCD patients. ACS is only second to vaso-occlusive crisis (VOC) as a cause of hospital admissions.[3,4] ACS is defined as a new lung infiltration on chest X-ray (CXR) in conjunction with fever or respiratory symptoms.[5]

ACS risk factors include younger age, male gender, respiratory diseases, hospitalization

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during the winter season, high white blood cell (WBC) count, high hemoglobin, and low fetal hemoglobin.[6] Moreover, Buchanan *et al*. found that the use of opioids in children with painful crises increased the likelihood of developing ACS during hospitalization.[7] Furthermore, a single ACS episode in early life is a risk factor for developing ACS in the future.[8]

SCD patients are prone to ACS because the sickled red blood cells (RBCs) can clump together, bind to leukocytes, and attach to the endothelium leading to pulmonary hypoxia, thereby precipitating the occurrence of pneumonia and pulmonary infarction.[9] Nonetheless, infections can precipitate ACS.[10] Therefore, it is difficult to differentiate between pneumonia and ACS on clinical grounds.

Given the prevalence of SCD and ACS among Saudi patients in the Eastern province, the previous studies did not present a detailed description of the clinical characteristic, laboratory findings, and management of ACS among SCD in the Eastern province in KSA. To gain a better understanding and improve the patients' outcomes, the present study was conducted to evaluate the laboratory, clinical characteristics, and management of ACS among SCD patients admitted to a tertiary university hospital.

Methods

This was a retrospective cohort study conducted at a tertiary hospital at Al-Khobar, Saudi Arabia. It was approved by the Ethics Committee of the Institutional Review Board (IRB) with the following registration number (IRB-UGS-2020-01-294).

All patients with SCD <14 years of age who were diagnosed with ACS between January 2002 and December 2020 were included. ACS was defined as new pulmonary infiltrates on CXRs associated with respiratory symptoms such as cough, tachypnea, wheezing, shortness of breath, chest pain, or fever of >38.5°C.[5] Patients with no reported confirmed diagnosis of SCD by hemoglobin electrophoresis, equivocal diagnosis of ACS, or incomplete data of patients were excluded.

The data were collected from the hospital's electronic medical record system using a predetermined set of variables. The collected information was divided into baseline data, ACS episodes data, and outcomes data. The baseline data include patients' demographics, age at SCD diagnosis, SCD genotype, comorbidities, laboratory data, medications including hydroxyurea, and SCD-related adverse events. Data about each ACS episode were the age at the episode, season, presenting symptoms, vital signs, laboratory results at several intervals, and radiological findings. Furthermore, management data were collected, including intravenous fluids, analgesics, antibiotics, bronchodilators, blood transfusion, maximum oxygen therapy required, and chest physiotherapy. Blood transfusion was classified into simple transfusion and exchange transfusion. Simple transfusion was defined as intravenous administration of packed RBC of any volume (without removal of patient's blood). Exchange transfusion was defined as exchanging the patient's sickle RBCs with exogenous normal RBCs (i.e., erythrocytapheresis) using an automated apheresis machine. Outcome data were collected, including hospital length of stay (LOS), need for pediatric intensive care unit (PICU) admission, PICU LOS, need for endotracheal intubation, and mortality.

The data were analyzed by the IBM Statistical Package for the Social Sciences (SPSS) version 26 (IBM, Armonk, NY, USA). Kolmogorov–Smirnov test was used to test the data normality, in which $P < 0.05$ was considered skewed data. Metric data were presented as mean and standard deviation or median with 25th–75th interquartile range (IQR), as appropriate measures of the data central of tendency. The categorical data were presented as frequencies and percentages. The missing data were handled by exclusion (pairwise deletion).

Results

During the 19 years, 361 patients diagnosed with SCD were admitted, with a total of 1636 admissions. There were 106 admissions with the diagnosis labeled as ACS. There were 15 admissions that were excluded. Figure 1 illustrates the inclusion and exclusion processes.

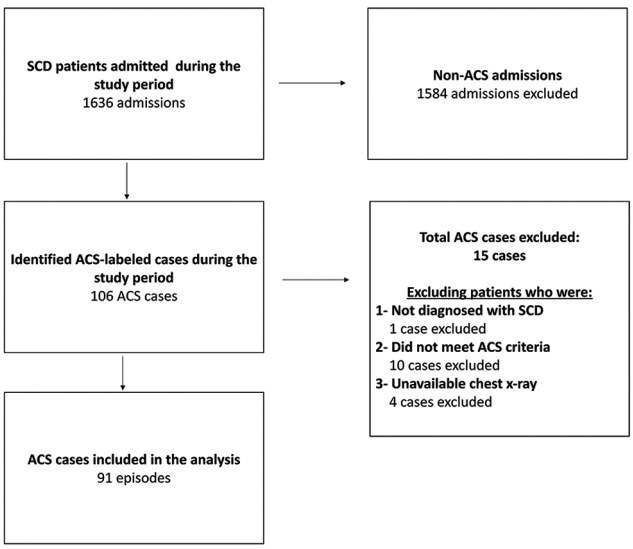

Figure 1: Flow chart showing the screening, inclusion, and exclusion processes. SCD = Sickle cell disease, ACS = Acute chest syndrome

ACS constituted 5.6% of all SCD-related admissions, with a median of 3.5 (IQR, 2–9) admissions per year. These were a total of 91 ACS episodes diagnosed in 42 patients. Twenty-five patients had recurrent ACS episodes.

Of the 42 patients admitted with ACS, 22 (52.4%) were male with a male: female ratio of 1.1. The mean age at ACS episode diagnosis was 7.18 ± 3.38 years, with the mean age at the first ACS episode of 6.62 ± 3.38 years. The genotypes of the patients in the present study include hemoglobin SS (69%), hemoglobin Sβ^0 thalassemia (21.4%), and hemoglobin Sα thalassemia (21.4%). There was no hemoglobin Sβ+ thalassemia nor hemoglobin SC disease in this cohort. The demographics and baseline characteristics are displayed in Table 1.

There were 22 patients (52.4%) that were found to have one or more comorbidities, most commonly asthma (26.2%) and glucose-6-phosphate dehydrogenase deficiency (21.4%). Of the 9 patients who were diagnosed with three or more episodes of ACS, 8 (88.9%) had at least one comorbidity. Most patients were on folic acid (92.9%) and penicillin (66.7%) at home. There was only one patient (1%) on hydroxyurea before the first ACS episode. There were 2 (4.8%) patients on simple blood transfusion.

Most ACS episodes occurred during fall (37.4%) and winter (31.9%) seasons. VOC was found to be an anticipating event in 12 episodes (13.2%), upper respiratory tract infections in 8 episodes (8.8%), trauma in 2 episodes (2.2%), and morphine use in 2 episodes (2.2%). None of the episodes were seen postoperatively (i.e., within 2 weeks of surgery).

There were 61 (67%) ACS episodes diagnosed in the emergency department when the patient presented with symptoms for a median of 2 days (IQR, 1–3), while the remaining were diagnosed during the admission for other indications. The patients diagnosed in the in-patient ward were admitted for a median of 3.5 (IQR, 2–4) days until ACS diagnosis was made. Table 2 displays the characteristics, clinical features, and physical examination findings of ACS episodes.

The WBC was notably higher on hospital admission (median, 19.2 [IQR, 13.36–26] k/μL), ACS diagnosis (median, 18.2 [IQR, 13.4–24.48] k/μL), and PICU admission (median, 23.3 [IQR, 12.45–39.35] k/μL) in comparison to the baseline value (median, 12 [IQR, 9.75–17.75] k/μL). From white blood cells linage, the neutrophil count was dominantly elevated. Baseline neutrophil percentage was 40.59% ± 14.56%; in contrast, neutrophil was 59.72% ± 16.39% at hospital admission, 60.44% ± 16.57% at ACS diagnosis, and 72.36% ± 15.63% at PICU admission. Nonetheless, neutrophil percentage

Table 1: Demographics and baseline characteristics of the included patients (*n*=42)

Study variables	Total population (*n*=42), *n* (%)
Demographics	
Gender	
Male: female	22:20 (52.4:47.6)
Nationality	
Saudi	41 (97.6)
Genotype	
Hgb SS	29 (69)
Hgb Sβ0 thalassemia	9 (21.4)
Hgb Sα thalassemia	4 (9.5)
Age at the time of first ACS diagnosis, mean±SD	6.62±3.38
Age grouping at the time of first ACS diagnosis	
Infants (≤1 year)	2 (4.8)
Toddlers (1–3 years)	8 (19)
Children (4–14 years)	32 (76.2)
Electrophoresis at SCD diagnosis (mean±SD)*	
HbS	71.69±12.57
HbF	24.94±12.6
HbA2	2.16±1.19
Number of VOC admissions (years), median (IQR)	2 (1–3)
SCD-related hospitalizations (years), median (IQR)	3 (2–4)
SCD-related adverse events encountered throughout their pediatric follow-up	
Splenic sequestration	8 (19)
Cholecystitis	1 (2.4)
Osteomyelitis	8 (19)
Hemolytic crisis	5 (11.9)
Aplastic crisis	6 (14.3)
Thromboembolic events	3 (7.1)
AVN	1 (2.4)
VOC	32 (76.2)
Sepsis	1 (2.4)
Comorbidities	
G6PD deficiency	9 (21.4)
Asthma	11 (26.2)
CVS diseases[d]	2 (4.8)
Endocrine diseases[e]	3 (7.1)
Developmental delay	2 (4.8)
OSA	1 (2.4)
Miscellaneous[f]	4 (9.52)
Having ≥1 comorbidities	22 (52.4)
Medications before ACS episodes	
Hydroxyurea therapy at baseline	1 (2.4)
Folic acid	39 (92.9)
Penicillin V*	28 (66.7)
Simple transfusion*	2 (4.8)
Albuterol*	5 (11.9)

*Missing details were excluded, [d]HTN and CHD, [e]Type-1 DM, rickets, and SIADH, [f]Epilepsy, achalasia, autism, and eczema. ACS=Acute chest syndrome, SCD=Sickle cell disease, VOC=Vaso-occlusive crisis, AVN=Avascular necrosis, G6PD=Glucose-6-phosphate dehydrogenase, CVS=Cardiovascular system, OSA=Obstructive sleep apnea, IQR=Interquartile range, SD=Standard deviation, HTN=Hypertension, CHD=Coronary heart disease, DM=Diabetes mellitus, SIADH=Syndrome of inappropriate secretion of antidiuretic hormone

Table 2: Acute chest syndrome episodes' characteristics, clinical features, and physical examination (*n*=91)

Study variables	Total population (*n*=91), *n* (%)
Age at time of all ACS episodes' diagnoses, mean±SD	7.18±3.38
Days from symptom onset to hospital presentation, median (IQR)*	2 (1–3)
ACS episodes diagnosed in ER	61 (67)
ACS episodes diagnosed after admission	30 (33)
ACS episodes required PICU admission	9 (9.9)
Time from hospital presentation to inpatient diagnosis of ACS (days), median (IQR)*	3.5 (2–4)
Seasons	
Winter	29 (31.9)
Spring	16 (17.6)
Summer	12 (13.2)
Fall	34 (37.4)
Clinical features at hospital presentation	
SOB	47 (51.6)
Fever	64 (70.3)
Cough	64 (70.3)
Chest pain	30 (33)
Extremity pain	18 (19.8)
Back pain	15 (16.5)
URTI symptoms	20 (22)
GI symptoms	15 (16.5)
Others[d]	6 (6.6)
SpO2 (%), median (IQR)	96 (89–99)
Chest examination	
Wheezing	10 (11)
Crackles	44 (48.4)
Reduced breath sound	33 (36.3)
Respiratory distress[e]	17 (18.7)

*Missing details were excluded, [d]Others include generalized edema, decreased feeding and decreased activity, and headache, [e]Respiratory distress was defined as the presence of ≥1 of the following: use of accessory muscles, increased work of breathing, intercostal retraction, and grunting. ACS=Acute chest syndrome, SD=Standard deviation, IQR=Interquartile range, ER=Emergency room, PICU=Pediatric intensive care unit, SOB=Shortness of breath, URTI=Upper respiratory tract infection, GI=Gastrointestinal, SpO_2=Oxygen saturation

returns to near baseline 24-h before hospital discharge with 41.52% ± 16.41%. Notably, 74 cases had a qualitative C-reactive protein test that showed positive in 66 ACS episodes (89.2%) at hospital admission. Prior to antibiotic initiation, blood cultures were ordered in 81 cases, in which only 5 (6%) cases resulted in positive growth. Table 3 displays the baseline and admission laboratory findings.

Antibiotics that were used included azithromycin (82.4%), ceftriaxone (75.8%), vancomycin (47.3%), and cefuroxime (23.1%). Analgesia used in the management of ACS included paracetamol in 75 episodes (82.4%), nonsteroidal anti-inflammatory drugs in 36 episodes (39.6%), and morphine in 2 episodes only (2.2%). Most episodes that required bronchodilators were managed with albuterol (84.6%). Two patients needed an escalation of oxygen therapy: one patient (1.1%) was escalated to bilevel positive airway pressure, whereas the other (1.1%) required intubation due to clinical deterioration. Seventy-three (80.2%) ACS episodes required blood transfusion, with the most common transfusion type being simple transfusion (73.6%). Only 1 (1.1%) episode required exchange transfusion, and 1 episode required both exchange and simple transfusion (1.1%). The management of ACS episodes is shown in Table 4.

Seventeen patients were found to be using hydroxyurea. Only one was started on hydroxyurea before experiencing an ACS episode. Sixteen patients had at least one ACS episode before starting hydroxyurea. Ten ACS episodes occurred in six patients who have been using hydroxyurea. Eleven patients had no subsequent ACS after initiating hydroxyurea therapy.

Nine patients (9.9%) required PICU admission. The indications for PICU admission were clinical deterioration (3 patients), hypoxemia (2 patients), acute respiratory distress syndrome (1 patient), sepsis (1 patient), shock (1 patient), and the need for exchange transfusion (1 patient). The median hospital and PICU LOS were 8 days (IQR, 5–10.25) and 4 days (IQR, 3–5.5), respectively. Of the 91 ACS episodes, there was no inhospital mortality.

Discussion

In this retrospective descriptive study, we determined the prevalence of ACS episodes among SCD patients that were admitted. In addition, we reported the baseline laboratory data, which are laboratory values that were obtained within 1 year prior to the first ACS episode. Moreover, the antecedent events, seasonal frequency, clinical features, physical findings, radiological findings, treatment and hospital course, and the outcomes for each ACS episode were described in this study.

The ACS episodes in this study account for 5.6% of all SCD-related hospitalizations. In our cohort, the reported ACS incidence is lower than the 7.7% reported from Qatif Central Hospital in the Eastern province of Saudi Arabia, which is in the same region as our hospital.[11] Moreover, this is lower than the 6.2% reported in a study that was conducted outside KSA.[12] However, the results of this study can underestimate the actual incidence of ACS for two reasons. First, the number of ACS episodes may be higher than what has been reported in this study as we cannot confirm if our patients were admitted to another hospital due to ACS episodes. Second, some ACS episodes might be missed and not enrolled in the study because they were not labeled as ACS in the admission note.

Table 3: Baseline and admission laboratory and microbiology data

Study variables	Baseline (*n*=42)	At hospital admission (*n*=91)	At ACS diagnosis (*n*=91)	At PICU admission (*n*=9)	24 h prior to hospital discharge (*n*=91)
WBC (k/μL), median (IQR)*	12 (9.75–17.75) (*n*=29)	19.2 (13.36–26) (*n*=90)	18.2 (13.4–24.48) (*n*=86)	23.3 (12.45–39.35) (*n*=9)	10.95 (7.95–14.85) (*n*=34)
Neutrophil (%), mean±SD*	40.59±14.56 (*n*=23)	59.72±16.39 (*n*=66)	60.44±16.57 (*n*=64)	72.36±15.63 (*n*=7)	41.52±16.41 (*n*=23)
Lymphocyte (%), mean±SD*	43.69±16.24 (*n*=27)	26.35±13.12 (*n*=85)	25.93±13.43 (*n*=82)	18.97±10.92 (*n*=7)	41.04±16.67 (*n*=25)
Hemoglobin (g/dL), mean±SD*	8.28±0.88 (*n*=31)	7.56±1.37 (*n*=88)	7.50±1.42 (*n*=84)	7.57±2.56 (*n*=9)	9.28±0.94 (*n*=35)
Reticulocyte (%), median (IQR)*	9 (6.5–13) (*n*=31)	9.6 (6.4–12.5) (*n*=83)	8.5 (6.05–12.4) (*n*=77)	6.3 (1.9–14.3) (*n*=7)	4.4 (1.75–8.9) (*n*=21)
Platelets (k/μL), mean±SD*	410.9±184.15 (*n*=30)	369.75±173.24 (*n*=88)	355.47±172.34 (*n*=85)	311.78±151.41 (*n*=9)	534.18±316.23 (*n*=34)
LDH (U/L), mean±SD*	519.5±184.55 (*n*=12)	543.3±165.75 (*n*=46)	554.3±187.45 (*n*=43)	619.2±335.42 (*n*=5)	480.75±217.61 (*n*=4)
Positive CRP-qualitative, *n* (%)*	N/A	66 (89.2) (*n*=74)	68 (95.8) (*n*=71)	6 (85.7) (*n*=7)	7 (100) (*n*=7)
Blood culture, *n* (%)*	N/A	Positive: 5 *N*egative: 76 Missi*n*g: 10	N/A	N/A	N/A
Hb S (%), median (IQR)*	77.45 (69.8–84.025) (*n*=6)	73.3 (57.7–82.025) (*n*=20)	N/A	N/A	N/A
Hb F (%), median (IQR)*	16.45 (8.2–21.1) (*n*=6)	8 (5.5–18.8) (*n*=19)	N/A	N/A	N/A

*Missing details were excluded. ACS=Acute chest syndrome, PICU=Pediatric intensive care unit, WBC=White blood cells, IQR=Interquartile range, SD=Standard deviation, LDH=Lactate dehydrogenase, CRP=C-reactive protein, N/A=Not applicable

Regarding associated events with ACS, VOC was recognized in 13.2% of patients admitted with ACS. This proportion is lower than the 50%, the 71%, and the 83% that, respectively, reported by Al-Dabbous, Jaiyesimi and Kasem, and Al-Hawsawi.[11,13,14] The association between ACS and VOC can be attributed to two reasons: first, ACS can be secondary to a fat embolus and bone spicules which are contents that originated from the necrosis of the bone marrow due to VOC. These contents migrate to the lung, causing lung inflammation, hypoxemia, and acute-onset pulmonary hypertension.[15-17] Second, the use of opiates to manage VOC can lead to hypoventilation, which can result in the formation of ACS.[18]

Jaiyesimi and Kasem did not observe seasonal variation in Oman when they compared the hot months of March–August and the cold months of September–February.[13] In contrast, the present study has observed a seasonal variation in ACS patterns. ACS was most prevalent during the fall months in Saudi Arabia; however, it was least prevalent during the summer.

Regarding the clinical features, the most prevalent symptoms in the current study were fever (70.3%) and cough (70.3%). The reported findings are similar to what have been reported by Nansseu *et al*. and Al-Hawsawi.[12,14] Moreover, Taylor *et al*. reported similar findings of the most common symptoms in children below the age of 13 years. However, above the age of 13 years, cough and chest pain were more prevalent.[19] Moreover, 100% of the patients in the present study have lung infiltration as per ACS definition.

The high WBC count at the time of admission and diagnosis of ACS observed in our cohort is consistent with similar studies, such as the Ochaya *et al*.'s study, which reported a median WBC count of 24.9 k/μL (IQR, 18.1–29.8 k/μL).[20] Besides, Jaiyesimi and Kasem reported a mean value of WBC at ACS of 15.37 ± 8.39 k/μL (compared to 10.73 ± 3.00 k/μL at steady-state), and Al-Dabbous reported a mean WBC count of 17.8 k/μL at the time of ACS (compared to 11.4 k/μL at baseline).[13] The observed elevated level of WBC count can be attributed to infections being the common causes of ACS, especially among children.[10]

Regarding hemoglobin, Jaiyesimi and Kasem reported a decrease in the mean hemoglobin from 8.48 ± 0.83 g/dL during a steady state to 7.37 ± 1.12 g/dL at the time of ACS.[13] Srair *et al*. reported an average hemoglobin level of 8.3 g/dL.[21] Moreover, Al-Dabbous reported a mean baseline hemoglobin of 8.6 g/dL that dropped into 7.8 g/dL at ACS diagnosis.[11] Similarly, our study demonstrated a mean baseline hemoglobin of 8.28 ± 0.88 g/dL that dropped at the time of admission to 7.56 ± 1.37 g/dL. Nonetheless, Nansseu *et al*. reported a lower mean hemoglobin value at ACS than most of the literature, which was 6.48 ± 1.15 g/dL.[12] The observed

Table 4: Management of acute chest syndrome episodes

Study variables	Total population (*n*=91), *n* (%)
Crystalloid fluid	91 (100)
Morphine	2 (2.2)
Paracetamol	75 (82.4)
NSAIDs	36 (39.6)
Antibiotics	91 (100)
Macrolides	79 (86.8)
Third generation cephalosporin	70 (76.9)
Second generation cephalosporin	21 (23.1)
Vancomycin	43 (47.3)
Meropenem	8 (8.8)
Cloxacillin	4 (4.4)
Piperacillin/tazobactam	1 (1.1)
Cefixime	1 (1.1)
Gentamicin	1 (1.1)
Change in antibiotic during hospitalization course	18 (19.8)
Bronchodilators	77 (84.6)
Blood transfusion	
Transfusion	73 (80.2)
Type of transfusion*	
Simple	67 (91.8)
Exchange	1 (1.4)
Both	1 (1.4)

*Missing details were excluded. NSAIDs=Nonsteroidal anti-inflammatory drugs

drop in hemoglobin and rise in WBC count during ACS that is observed in our study is consistent with multiple reports.[11,13,19]

Poncz *et al*. reported an average hemoglobin drop from the baseline of 11% and an increase in the reticulocyte count from the baseline of 15%.[22] This reported reticulocytosis suggests increased hemolysis. However, we found no notable increase in the reticulocyte count at the time of hospital admission (9.6 [IQR, 6.4–12.5]%), ACS diagnosis (8.5 [IQR, 6.05–12.4]%), and PICU admission (6.3 [IQR, 1.9–14.3]%) in comparison to the baseline (9 [IQR, 6.5–13]%). This unexpected observation might be due to a greater marrow suppression in our cohort.

In addition, Poncz *et al*. reported a rebound increase in platelet count observed after 1 week of illness.[22] Similarly, we observed a rebound thrombocytosis in the blood samples collected 24-h prior to hospital discharge, which showed 534.18 ± 316.23 k/μL compared to 410.9 ± 184.15 k/μL at baseline and 369.75 ± 173.24 k/μL at hospital admission.

Similar trends of decreased hemoglobin and leukocytosis can be observed in the adult population. Al-Suleiman *et al*. reported mean hemoglobin at ACS of 7.1 ± 1.5 g/dL compared to a baseline of 9.3 ± 1.6 g/dL and a mean WBC of 18.6 ± 7 k/μL compared to a baseline of 11.3 ± 4.8 k/μL.[23] Moreover, Maitre *et al*. reported a range of hemoglobin level drop of 1.6–2.25 g/dL (based on the genotype), WBC count level of 20.3 ± 8.5 k/μL (an increase of 9.2 ± 8.3 k/μL from baseline), and platelet count of 384 ± 202 k/μL at ACS diagnosis (an increase of 67 ± 209 k/μL from baseline).[24]

In our study, all performed urine cultures were sterile, which is similar to the findings reported by Jaiyesimi and Kasem.[13]

The management of our patients included the use of oxygen, broad-spectrum antibiotics, hydration with crystalloid fluid, analgesics, and simple blood transfusion to most of the patients in addition to bronchodilators and chest physiotherapy. This comes in line with the management of ACS in the literature.[12,25]

In the current study, seventeen patients were found to be using hydroxyurea. Of these seventeen, eleven patients did not develop subsequent ACS episodes following the initiation of hydroxyurea therapy. Hankins *et al*. examined the long-term effect of hydroxyurea on infants with SCD, and they observed a threefold reduction of incidence of ACS among those treated with hydroxyurea compared to those who did not receive it.[26] One of the reasons that can explain the development of ACS in our patients despite prescribing hydroxyurea is poor medication compliance, as reported by some of our patients.

Vaccination of SCD patients is a simple measure that can be done to reduce ACS incidence by decreasing the rate of infection.[27] Regular vaccination with pneumococcal vaccine (PCV 23) and annual influenza vaccine are recommended to potentially reduce the risk of ACS secondary to infection by these organisms.[28] The Ministry of Health in Saudi Arabia provides guidelines regarding SCD vaccinations that are highly recommended.[29] Furthermore, the Ministry of Health's recommendation for PCVs is similar to the Saudi Thoracic Society Guidelines.[30] In our center, we followed the Ministry of Health recommendations, in which most likely, our patients have been vaccinated as per the schedule. However, the vaccination status of our population was not a part of the data collection because the vaccination occurred in primary health-care centers, which was not well documented in the hospital archives.

In the current study, the average duration of hospitalization was 8 days. This is more than the 6.8 days and 6.5 days, respectively, reported by Nansseu *et al*. and Poncz *et al*.[12,22] Moreover, this duration is higher than both narcotic recipients (7 days) and those who did not receive narcotics (4 days) that was reported in a retrospective study by Sprinkle *et al*.[31] On the contrary,

the observed length of stray in our cohort was lower than the 10 days LOS reported by Vichinsky *et al*.[10]

A Saudi study examined the prevalence and effect of consanguinity on SCD and its complications in pediatric SCD patients. They found that 44% of SCD patients ($n = 120$) and 38.5% of patients with ACS ($n = 39$) were products of consanguineous marriage.[32] However, we could not examine the consanguinity factor in our cohort because of the unavailability of these data in our electronic medical charts.

Limitations and strengths

The present study possesses several points of strength. First, it included patients who were admitted with the diagnosis of ACS in an 18-year period. Second, rigorous inclusion and exclusion criteria were used for patients' selection. Third, having four independent pediatric consultants reviewing the data has ensured further accuracy. Finally, the collected variables were extracted rigorously using a predetermined protocol to minimize extraction errors and missing values.

Despite the previously mentioned points of strength of the current study, some limitations deserve to be considered. First, this is a single-center study with a small sample size; therefore, the results of this might have limited generalizability to other health-care facilities. Second, we could not confirm or include possible ACS episodes of our patients treated in another hospital. Third, potential bias due to the limited spectrum of case and control cannot be ruled out.

Conclusion

This study has reported the prevalence of ACS, the clinical history and features, seasonal variation, laboratory data, and radiological findings. Moreover, treatment and hospital outcomes were reported. The observed findings might be considered when developing future research with a superior study design to find how to implement these observations in the improvement of patients' care.

Ethical approval

This study's ethical approval was obtained from the ethics committee of the IRB and was licensed with the following registration number (IRB-UGS-2020-01-294). The requirement of written informed consent was waived by the IRB.

Disclosure

A substudy was generated from this dataset that was published prior to this study.[33] The aim of the substudy was to examine predictors of recurrent ACS in pediatric patients with SCD. The same dataset was utilized in both studies with different research question, objectives, analyses, and outcomes.

Data availability statement

The analyzed datasets used in this study and all analysis output reports are available upon reasonable request from the corresponding author. The data do not contain any identifiable data, and the confidentiality of the included patients is fully maintained.

Guarantor statement

All authors agreed to be responsible for the accuracy of the present study's content and hold accountable for any raised questions or concerns related to the accuracy or integrity of any part of the work.

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Conflicts of interest

There are no conflicts of interest.

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