Section: General Medicine

Original Research Article

CLINICAL PROFILE, RISK FACTORS, MANAGEMENT, AND OUTCOME OF ACUTE CHEST SYNDROME IN PATIENTS WITH SICKLE CELL DISEASE: A PROSPECTIVE OBSERVATIONAL STUDY AT A TERTIARY CARE CENTRE

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Received *: 05/05/2026*
Received in revised form *: 20/06/2026*
Accepted *: 05/07/2026*

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DOI: 10.70034/ijmedph.2026.3.92

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2026; 16 (3); 561-567

ABSTRACT

Background: Acute Chest Syndrome (ACS) is one of the most severe and life-threatening complications of Sickle Cell Disease (SCD), contributing significantly to morbidity, prolonged hospitalization, and mortality. Early identification of clinical features, laboratory abnormalities, and prognostic factors is essential for timely management and improved patient outcomes. The objective is to determine the clinical profile, risk factors, laboratory and radiological characteristics, management strategies, and outcomes of patients with Acute Chest Syndrome admitted with Sickle Cell Disease at a tertiary care centre.

Materials and Methods: A prospective longitudinal observational study was conducted among 60 patients with Sickle Cell Disease diagnosed with Acute Chest Syndrome admitted to the Department of Medicine, New Civil Hospital, Surat, over a 16-month period (May 2018–September 2019). Patients aged ≥12 years fulfilling the diagnostic criteria for ACS were included. Clinical history, physical examination, laboratory investigations, radiological findings, treatment modalities, and outcomes were recorded using a predesigned proforma. Data were analyzed using SPSS version 16.0. Descriptive statistics were expressed as mean ± standard deviation and percentages.

Results: Among the 60 patients, 40 (66.7%) were females and 20 (33.3%) were males. The majority (71.7%) belonged to the 19–30-year age group. Tachypnoea (91.7%), increased work of breathing (86.7%), chest pain (78.3%), and hypoxaemia (68.3%) were the predominant presenting features. The mean hemoglobin level was 7.03 ± 1.92 g/dL, and the mean white blood cell count was 21,935 ± 14,166/mm³. Bilateral lower-zone consolidation was the most common chest radiographic finding, whileultrasonography frequently demonstrated lung consolidation (85.0%) and splenomegaly (71.7%). Simple blood transfusion was administered to 91.7% of patients, exchange transfusion to 20.0%, and incentive spirometry to 76.7%. Overall, 52 (86.7%) patients were discharged, whereas 8 (13.3%) died. Higher leukocyte counts, elevated HbS levels, lower HbF levels, and the requirement for mechanical ventilation were associated with poorer outcomes.

Conclusion: Acute Chest Syndrome remains a major cause of morbidity and mortality among patients with Sickle Cell Disease. Early recognition, prompt supportive care, timely blood transfusion, and multidisciplinary management are essential to improve survival. Leukocytosis, high HbS levels, low HbF

levels, and severe respiratory involvement may serve as important prognostic indicators for adverse outcomes.
Keywords: Acute Chest Syndrome; Sickle Cell Disease; Hemoglobin S; Hemoglobin F; Blood Transfusion; Leukocytosis; Mechanical Ventilation; Pulmonary Complications; Outcome; Tertiary Care Centre.

INTRODUCTION

Sickle cell disease (SCD) is one of the most common inherited hemoglobinopathies worldwide and remains a major cause of morbidity and mortality, particularly in low- and middle-income countries. It results from a single point mutation in the β-globin gene, leading to the substitution of valine for glutamic acid at the sixth position of the β-globin chain and the production of abnormal hemoglobin S (HbS). Under conditions such as hypoxia, dehydration, acidosis, or infection, HbS polymerizes, causing erythrocyte sickling, chronic hemolysis, vaso-occlusion, endothelial dysfunction, and progressive multiorgan damage.[1,2]

Globally, more than 300,000 infants are born annually with SCD, and this number is expected to increase substantially over the coming decades. India has the second-highest burden of SCD after sub-Saharan Africa, with a high prevalence among tribal and scheduled caste populations in Gujarat, Maharashtra, Madhya Pradesh, Chhattisgarh, Odisha, and other central Indian states.[3,4] In Gujarat, SCD represents an important public health concern and contributes significantly to recurrent hospital admissions and healthcare utilization.

Acute chest syndrome (ACS) is one of the most severe complications of SCD and is a leading cause of hospitalization, intensive care admission, and mortality in affected patients.[5,6] ACS is defined as the presence of a new pulmonary infiltrate involving at least one lung segment on chest radiography accompanied by one or more new respiratory symptoms such as fever, cough, chest pain, tachypnoea, wheezing, or hypoxaemia.[7] The incidence of ACS varies with age, occurring more frequently in children but resulting in greater morbidity and mortality among adults.[6]

The pathophysiology of ACS is complex and multifactorial. Pulmonary infection, fat embolism secondary to bone marrow infarction, pulmonary vaso-occlusion, hypoventilation due to painful vaso-occlusive crises, and pulmonary thrombosis are recognized mechanisms contributing to disease development.[5,8] Infectious organisms such as Mycoplasma pneumoniae, Chlamydia pneumoniae, respiratory viruses, and bacterial pathogens have been implicated in triggering ACS episodes, although non-infectious mechanisms also play a significant role.[9,10]

Patients with ACS typically present with fever, chest pain, cough, dyspnoea, tachypnoea, hypoxaemia, and increased work of breathing. Clinical deterioration may occur rapidly, progressing to respiratory failure and the need for intensive care support if diagnosis and treatment are delayed.[6,7] Laboratory evaluation commonly demonstrates anemia, leukocytosis, elevated inflammatory markers, and hypoxaemia on arterial blood gas analysis, while chest radiography remains the cornerstone of diagnosis.[7,11]

Management of ACS is multidisciplinary and includes supplemental oxygen, adequate analgesia, careful intravenous hydration, broad-spectrum antibiotics with coverage for atypical pathogens, incentive spirometry, bronchodilator therapy when indicated, and blood transfusion in selected patients.[7,12] Exchange transfusion is recommended in severe cases with worsening hypoxaemia, multilobar pulmonary involvement, or progressive respiratory failure. Hydroxyurea therapy has also been shown to significantly reduce the frequency of ACS episodes and vaso-occlusive crises by increasing fetal hemoglobin levels and decreasing sickling of erythrocytes.[13,14]

Despite advances in supportive care and disease-modifying therapy, ACS remains associated with prolonged hospitalization, recurrent admissions, increased healthcare costs, and considerable mortality.[6,15] Furthermore, the clinical profile and outcomes of ACS differ across geographical regions because of variations in genetic background, environmental factors, infectious etiologies, and access to healthcare services. Data from western India, particularly Gujarat, remain limited, despite the high prevalence of SCD in this region.

A better understanding of the demographic characteristics, clinical presentation, laboratory profile, and outcomes of ACS is essential for early diagnosis, timely intervention, and improved patient care. Therefore, the present study was undertaken to evaluate the clinical profile and hospital outcomes of patients with acute chest syndrome associated with sickle cell disease admitted to a tertiary care centre in South Gujarat. The findings of this study may help optimize management strategies and improve outcomes in this high-risk population.

Aim: To evaluate the clinical profile, management, and outcomes of Acute Chest Syndrome in patients with Sickle Cell Disease.

Objectives

- To determine the proportion of Acute Chest Syndrome among hospitalized patients with Sickle Cell Disease.
- To identify the risk factors associated with Acute Chest Syndrome.
- To evaluate the management strategies used for Acute Chest Syndrome.
- •To assess the clinical outcomes of patients with Acute Chest Syndrome.

MATERIALS AND METHODS

Study Design and Setting: This prospective longitudinal observational study was conducted in the Department of General Medicine at New Civil Hospital, Surat, a tertiary care teaching hospital in South Gujarat, India, over a period of one year. All consecutive patients with sickle cell disease admitted to the medicine wards during the study period were screened for Acute Chest Syndrome (ACS) and enrolled if they fulfilled the eligibility criteria.

Study Population: Patients aged >12 years with confirmed sickle cell disease who fulfilled the diagnostic criteria for ACS were included in the study. ACS was defined as an acute illness characterized by fever and/or respiratory symptoms associated with a new pulmonary infiltrate on chest radiography. For patients aged 12–18 years, written informed consent was obtained from parents or legal guardians, along with assent from the adolescent participants.

Patients aged <12 years and those not fulfilling the diagnostic criteria for ACS were excluded from the study.

Data Collection: Detailed demographic characteristics, clinical history, smoking status, comorbidities, physical examination findings, laboratory investigations, and chest radiographic findings were recorded using a predesigned case record proforma. Laboratory investigations included complete blood count, hemoglobin level, leukocyte count, HbS and HbF levels, and other relevant investigations. Special investigations related to sickle cell disease were performed as indicated. Interdepartmental consultations were obtained whenever required. Information regarding treatment modalities, including oxygen therapy, antibiotic therapy, incentive spirometry, simple or exchange blood transfusion, ventilatory support, and clinical outcomes, was also documented.

Statistical Analysis: Data were entered into Microsoft Excel and analyzed using Statistical Package for the Social Sciences (SPSS) version 16.0. Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. The Chi-square test was used to assess the association between categorical variables, and the independent Student's t-test was applied to compare the means of continuous variables between groups. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 60 patients with Acute Chest Syndrome (ACS) associated with Sickle Cell Disease (SCD) were included in the study.

Table 1. Demographic Characteristics of Patients with Acute Chest Syndrome (N = 60)

Variable	Frequency (n)	Percentage (%)
Gender		
Female	40	66.7
Male	20	33.3
Age Group (years)		
12–18	15	25.0
19–30	43	71.7
31–40	2	3.3
>40	0	0.0

Among the 60 patients, 40 (66.7%) were females and 20 (33.3%) were males, with a female-to-male ratio of 2:1. The majority of patients belonged to the 19–30 years age group (71.7%), followed by 12–18 years (25.0%) and 31–40 years (3.3%). No patient was older than 40 years.

Table 2: Clinical Characteristics of Patients with Acute Chest Syndrome (N = 60)

Clinical Variable	Frequency (n)	Percentage (%)
Presenting symptoms		
Tachypnoea	55	91.7
Increased work of breathing	52	86.7
Chest pain	47	78.3
Hypoxaemia	41	68.3
Fever	26	43.3
Cough	11	18.3
Wheezing	4	6.7
Body ache	54	90.0
Myalgia	40	66.7
Jaundice	28	46.7
Abdominal pain	26	43.3
Arthralgia	22	36.7
Headache	19	31.7
Palpitations	16	26.7
Vomiting	9	15.0
Decreased urine output	5	8.3
Nausea	3	5.0

The most common presenting feature was tachypnoea (91.7%), followed by increased work of breathing (86.7%), chest pain (78.3%), hypoxaemia (68.3%), and fever (43.3%). Cough and wheezing were observed in 18.3% and 6.7% of patients, respectively.

Among the associated symptoms, body ache (90.0%) was the most frequent complaint, followed by myalgia (66.7%), jaundice (46.7%), abdominal pain (43.3%), arthralgia (36.7%), headache (31.7%), palpitations (26.7%), vomiting (15.0%), decreased urine output (8.3%), and nausea (5.0%).

These findings indicate that respiratory symptoms were the predominant clinical manifestations, accompanied by generalized musculoskeletal pain.

Table 3: Clinical Examination and Laboratory Findings (N = 60)

Variable	Mean ± SD / n (%)
Pulse rate (beats/min)	117.75 ± 18.93
Systolic BP (mmHg)	105.37 ± 15.11
Diastolic BP (mmHg)	74.13 ± 9.50
Respiratory rate (/min)	33.43 ± 9.70
Oxygen saturation (%)	88.53 ± 6.46
Body temperature (°F)	100.77 ± 0.71
PaO_2 (mmHg)	63.45 ± 13.16
Pallor	50 (83.3)
Icterus	38 (63.3)
Bilateral lower zone crepitations	32 (53.3)
Hemoglobin (g/dL)	7.03 ± 1.92
Total leukocyte count (/mm³)	21,935 ± 14,166
Platelet count (/mm³)	223,255 ± 159,090
ESR (mm/hr)	60.30 ± 34.62
LDH (U/L)	1588.77 ± 1729.22
CRP (mg/dL)	5.90 ± 5.26
HbS (%)	76.28 ± 5.98
HbF (%)	11.09 ± 3.92

The mean pulse rate was 117.75 ± 18.93 beats/min, while the mean respiratory rate was 33.43 ± 9.70 breaths/min. The mean oxygen saturation on room air was 88.53 ± 6.46%, indicating significant hypoxaemia. Pallor was present in 83.3% of patients, whereas 63.3% had icterus. Bilateral lower zone crepitations were the most common respiratory examination finding, observed in 53.3% of patients.

Laboratory evaluation demonstrated severe anemia with a mean hemoglobin level of 7.03 ± 1.92 g/dL. The mean total leukocyte count was 21,935 ± 14,166/mm³, while the mean platelet count was 223,255 ± 159,090/mm³. Elevated inflammatory and hemolytic markers were observed, with mean ESR, LDH, and CRP values of 60.30 ± 34.62 mm/hr, 1588.77 ± 1729.22 U/L, and 5.90 ± 5.26 mg/dL, respectively. The mean HbS and HbF levels were 76.28 ± 5.98% and 11.09 ± 3.92%, respectively.

Table 4: Imaging Findings in Patients with Acute Chest Syndrome (N = 60)

Imaging Findings	Frequency (n)	Percentage (%)
Chest X-ray		
Bilateral lower zone consolidation	27	45.0
Right lung consolidation	14	23.3
Left lung consolidation	6	10.0
Bilateral pleural effusion	4	6.7
Ultrasonography		
Lung consolidation	51	85.0
Splenomegaly	43	71.7
Hepatomegaly	38	63.3
Pleural effusion	18	30.0
Gall bladder calculi	9	15.0

Chest radiography most commonly demonstrated bilateral lower zone consolidation (45.0%), followed by right lung consolidation (23.3%) and left lung consolidation (10.0%). Ultrasonography revealed lung consolidation (85.0%), splenomegaly (71.7%), hepatomegaly (63.3%), pleural effusion (30.0%), and gall bladder calculi (15.0%).

Table 5: Treatment Modalities (N = 60)

Treatment	Frequency (n)	Percentage (%)
Oxygen therapy	60	100.0
Simple blood transfusion	55	91.7
Incentive spirometry	46	76.7
Mechanical ventilation	46	76.7
Exchange blood transfusion	12	20.0

Ceftriaxone	30	50.0
Azithromycin	17	28.3
Clindamycin	15	25.0
Meropenem	14	23.3

All patients received supportive treatment with oxygen therapy. Simple blood transfusion was administered to 91.7% of patients, while 20.0% required exchange transfusion. Incentive spirometry was used in 76.7% of patients, and the same proportion required mechanical ventilation during hospitalization.

Among the antibiotics prescribed, ceftriaxone (50.0%) was the most commonly used, followed by azithromycin (28.3%), clindamycin (25.0%), and meropenem (23.3%).

Table 6: Comparison of Clinical Outcomes (N = 60)

Variable	Discharged (n=52)	Expired (n=8)
Mean age (years)	21.67 ± 4.95	22.13 ± 8.20
Female	37	3
Male	15	5
Mean WBC (/mm³)	22,677 ± 13,354	31,645 ± 19,017
Mean HbS (%)	75.61 ± 6.12	80.65 ± 1.77
Mean HbF (%)	11.68 ± 3.87	7.30 ± 1.16
Overall outcome	52 (86.7%)	8 (13.3%)

Of the 60 patients included in the study, 52 (86.7%) were discharged, while 8 (13.3%) died during hospitalization. Mortality was higher among males (25.0%) than females (7.5%). Patients who died had higher mean total leukocyte counts (31,645/mm³ vs. 22,677/mm³), higher HbS levels (80.65% vs. 75.61%), and lower HbF levels (7.30% vs. 11.68%) compared with those who survived.

DISCUSSION

Acute Chest Syndrome (ACS) is one of the most serious pulmonary complications of Sickle Cell Disease (SCD) and remains a leading cause of hospitalization, intensive care admission, and mortality among affected individuals. The syndrome results from a combination of pulmonary infection, vaso-occlusion, fat embolism, and inflammatory injury, leading to progressive hypoxemia and respiratory failure if not recognized early. Despite advances in supportive care, ACS continues to contribute significantly to disease-related morbidity and mortality.[16-18]

In the present study, females constituted 66.7% of the study population, whereas males accounted for 33.3%. Although SCD is inherited as an autosomal recessive disorder and affects both sexes equally, hospital-based studies have reported variable gender distributions depending on regional demographics, healthcare-seeking behavior, and referral patterns. The predominance of female patients in our study may therefore represent the characteristics of the study population rather than a true biological difference.[16,19]

Most patients (71.7%) belonged to the 19–30-year age group, indicating that ACS predominantly affected young adults. Previous studies have shown that ACS occurs across all age groups; however, adults generally experience more severe episodes with increased risk of respiratory failure and mortality compared with children.[17,19]

Respiratory manifestations were the predominant clinical presentation in our study. Tachypnoea (91.7%), increased work of breathing (86.7%), chest pain (78.3%), and hypoxemia (68.3%) were the most frequent findings. These observations are consistent with the diagnostic criteria for ACS, which include new pulmonary infiltrates accompanied by respiratory symptoms such as chest pain, tachypnoea, fever, cough, wheezing, or hypoxemia. Early recognition of these manifestations is essential because rapid progression to respiratory failure may occur.[17,20]

Body ache, myalgia, abdominal pain, and arthralgia were common associated symptoms in the present study, reflecting the underlying vaso-occlusive process. Painful vaso-occlusive crises frequently precede ACS, resulting in hypoventilation, atelectasis, and pulmonary complications. Adequate analgesia and pulmonary care therefore remain essential components of management.[16,17]

Laboratory evaluation demonstrated severe anemia with a mean hemoglobin concentration of 7.03 ± 1.92 g/dL, accompanied by marked leukocytosis. Patients who died had substantially higher leukocyte counts than survivors, suggesting that leukocytosis may be an important marker of disease severity. Elevated leukocyte counts have consistently been associated with increased inflammation, pulmonary injury, and poor clinical outcomes in ACS.[17,21]

The mean HbS level was higher and HbF level was lower among patients with fatal outcomes. Increased HbS promotes erythrocyte sickling and vaso-occlusion, whereas HbF inhibits HbS polymerization and reduces the frequency and severity of vaso-occlusive complications. These findings support the established protective role of fetal hemoglobin and emphasize the importance of hydroxyurea therapy for long-term prevention of recurrent ACS.[16,17]

Radiological evaluation showed that bilateral lower-zone consolidation was the most frequent chest

radiographic abnormality, while ultrasonography commonly demonstrated pulmonary consolidation, splenomegaly, and hepatomegaly. Chest radiography remains the first-line imaging modality for diagnosing ACS, although lung ultrasonography has emerged as a valuable bedside tool with high diagnostic accuracy for pulmonary consolidation and pleural effusion.[18,19]

All patients received oxygen therapy and supportive treatment. Simple blood transfusion was administered to 91.7% of patients, whereas 20.0% underwent exchange transfusion. Blood transfusion improves oxygen delivery and reduces the proportion of circulating sickled erythrocytes. Exchange transfusion is particularly beneficial in severe or rapidly progressive ACS because it lowers HbS levels without significantly increasing blood viscosity. Current recommendations advocate individualized transfusion strategies based on disease severity and clinical progression.[16,17]

Broad-spectrum antibiotics formed an important component of therapy because distinguishing infectious from non-infectious ACS at presentation is often difficult. Ceftriaxone was the most frequently prescribed antibiotic in our study, followed by azithromycin. Current treatment recommendations support empirical administration of a third-generation cephalosporin together with a macrolide to provide coverage for both typical and atypical respiratory pathogens.[18-22]

Incentive spirometry was used in 76.7% of patients. Although evidence regarding its effectiveness continues to evolve, incentive spirometry remains widely recommended to reduce atelectasis, improve lung expansion, and decrease pulmonary complications in hospitalized patients with SCD. Recent systematic reviews suggest that larger randomized studies are required to define its precise benefit, but it continues to be incorporated into comprehensive supportive management.[25]

Mechanical ventilation was required in 76.7% of patients, reflecting the severity of illness among patients referred to this tertiary care centre. Patients requiring ventilatory support experienced poorer outcomes, highlighting respiratory failure as an important predictor of mortality. Similar findings have been reported in critically ill adults with ACS, where the need for invasive ventilation is associated with increased mortality.[17,25]

The overall in-hospital mortality rate in the present study was 13.3%, whereas 86.7% of patients were successfully discharged. Mortality was associated with higher leukocyte counts, higher HbS levels, lower HbF levels, and severe pulmonary involvement. These findings emphasize the importance of early diagnosis, close monitoring, prompt oxygen supplementation, appropriate antimicrobial therapy, timely transfusion, and multidisciplinary management to improve clinical outcomes.

Overall, the present study highlights that ACS remains a major cause of morbidity in young adults with SCD. Early identification of respiratory symptoms, aggressive supportive care, and appropriate transfusion therapy are essential for improving survival. Preventive strategies, including hydroxyurea therapy, vaccination, regular follow-up, and patient education, are likely to reduce the incidence of recurrent ACS and improve long-term outcomes.[16,26]

CONCLUSION

Acute Chest Syndrome (ACS) remains one of the most serious and potentially life-threatening complications of Sickle Cell Disease (SCD), particularly among young adults. In the present study, the majority of patients were aged 19–30 years, with respiratory symptoms such as tachypnoea, increased work of breathing, chest pain, and hypoxaemia being the predominant clinical manifestations. Severe anemia, leukocytosis, elevated inflammatory markers, and high HbS levels were common laboratory findings, while bilateral lower-zone consolidation was the most frequent radiological abnormality.

Most patients responded favorably to early supportive management, including oxygen therapy, broad-spectrum antibiotics, blood transfusion, and incentive spirometry. However, patients with higher leukocyte counts, higher HbS levels, lower HbF levels, extensive pulmonary involvement, and the need for mechanical ventilation had poorer clinical outcomes and a higher risk of mortality.

The findings of this study emphasize the importance of early recognition of ACS, prompt diagnosis, timely initiation of appropriate therapy, and close clinical monitoring to reduce morbidity and mortality. Identification of prognostic factors such as leukocytosis, HbS and HbF levels, and respiratory compromise may help clinicians stratify disease severity and optimize management.

Strengthening preventive strategies, including hydroxyurea therapy, vaccination, patient education, regular follow-up, and timely referral to specialized centers, may reduce recurrent episodes of ACS and improve the long-term outcomes and quality of life of patients with Sickle Cell Disease.

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