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# Acute Respiratory Distress and Major Sickle Cell Syndrome at the Albert Royer National Children's Hospital in Dakar

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## Abstract

**Introduction:** Respiratory distress is a frequent reason for consultation in children with sickle cell disease and can lead to complications that can sometimes be life-threatening. In Senegal, there are few pediatric studies on respiratory distress in children with sickle cell disease. Our objective was to study the epidemiological, diagnostic, and evolutionary characteristics of acute respiratory distress in the context of major sickle cell syndrome. **Methodology:** This was a retrospective, descriptive study of sickle cell patients hospitalized in the Emergency Department and Pediatric Pulmonology and Intensive Care Unit of CHNEAR for respiratory distress between January 1, 2021, and September 30, 2022. All hospitalized patients with respiratory distress due to severe sickle cell disease whose medical records were available and usable were included. All incomplete records were excluded. The collected data were entered into Google Forms and analyzed using Excel 2019. **Results:** A total of 2828 patients were hospitalized, including 67 for respiratory distress in patients with severe sickle cell disease, representing a prevalence of 2.37%. The mean age of the patients was 9.5 years. The male-to-female ratio was 1.91. The genotypic profile was SS in all patients. The main reasons for consultation were fever (56.7%), chest pain (49.3%), cough (47.8%), and respiratory difficulties (35.8%). Among our patients, 82.09% presented with hypoxemia. Mild respiratory distress was found in 44.78%, moderate in 52.24%, and severe in 4.78%. Pulmonary consolidation syndrome was found in 56.72% of patients. Nasopharyngeal swabs were performed in 14.92% of cases, with two positive results isolating SARS-CoV-2 and influenza A virus. Chest X-rays were abnormal in 89.40% of cases. The main causes of respiratory distress were acute

chest syndrome (ACS) in 61.19% of cases, pneumonia in 47.76%, and asthma attack in 10.45%. Severe acute anemia (7.46%) and decompensated heart disease (4.48%) were the two extra-respiratory causes. Antibiotic therapy was administered in 94.03% of cases. The outcome was favorable in 98.5% of cases. One death was due to cardiac arrest. The average length of hospital stay was 8 days. **Conclusion:** Respiratory distress can be life-threatening in children with sickle cell disease. Clinicians must be trained to manage any respiratory symptoms in sickle cell patients quickly and effectively to prevent the resulting consequences.

## Keywords

Acute Respiratory Distress, Major Sickle Cell Syndrome, Children, Senegal

## 1. Introduction

Sickle cell disease is a clinically recessive, biologically codominant, autosomal dominant hereditary disorder characterized by the presence of an abnormal hemoglobin called hemoglobin S in red blood cells. Approximately 1700 children are born with sickle cell disease each year in Senegal [1]. The causes of acute respiratory distress in children with sickle cell disease are dominated by pneumonia and acute chest syndrome. The lack of previous studies on respiratory distress in children with severe sickle cell disease, and its frequent cause of hospitalization in pediatric settings in Senegal, motivated this study, whose overall objective was to describe the epidemiological, diagnostic, and evolutionary aspects of acute respiratory distress in children with severe sickle cell syndrome hospitalized in the Emergency Department and the Pediatric Pulmonology Department of Albert Royer Hospital in Dakar. The specific objectives were to determine the frequency of acute respiratory distress in children with major sickle cell disease; to determine the sociodemographic and clinical aspects; to identify the main etiologies of this acute respiratory distress and to specify the management methods.

## 2. Methodology

This was a retrospective and descriptive study of sickle cell patients hospitalized in the Emergency Department and Pediatric Pulmonology Department of CHNEAR for respiratory distress between January 1, 2021, and September 30, 2022. All sickle cell patients with a major form of the disease hospitalized for respiratory distress whose medical records were available and usable were included. Incomplete records were excluded. The collected data were entered into Google Forms and analyzed using Excel 2019. The operational variables were defined as follows: Respiratory distress was classified according to the CRS score (Clinical Respiratory Syndrome). Respiratory Score), mild (<3), moderate (4 - 7), severe (8 - 12). The score takes into account respiratory rate, auscultation, use of accessory muscles, mental status, oxygen saturation on room air, and color.

Hypoxemia was defined as a pulse oximetry saturation below 95% on room air. Leukocytosis was considered significant if the white blood cell count was greater than 20,000. CRP was considered elevated if the threshold was greater than 20 mg/L.

## 3. Results

### 3.1. Epidemiological Aspects

Of the 2828 patients hospitalized, 67 were admitted for respiratory distress related to severe sickle cell disease, representing a prevalence of 2.37%. The average age of the patients was 9.5 years. The male-to-female ratio was 1.91. Among our patients, 52% came from the suburbs of Dakar and 36% from central Dakar. In our study, 72% of the patients were educated, with 51% attending primary school. In our study, forty-one (41) of the patients had a low socioeconomic status, representing 61%.

### 3.2. Clinical Aspects

All our patients had a genotypic profile of the SS type. Sickle cell disease was diagnosed during hospitalization in 2 patients (3%), and 87.9% of patients were followed up regularly. Eight (8) of these patients (12.1%) were poorly monitored, and 94% of patients were taking folic acid. No information regarding hydroxyurea was found for our patients, and 3 (4.5%) were receiving oral penicillin prophylaxis. Among our patients, 98.5% had up-to-date vaccination status according to the Expanded Program on Immunization (EPI), and 13.4% had received the additional vaccines recommended for individuals with sickle cell disease. The main reasons for consultation were fever (56.7%), chest pain (49.3%), cough (47.8%), and respiratory distress (35.8%), as shown in Figure 1.

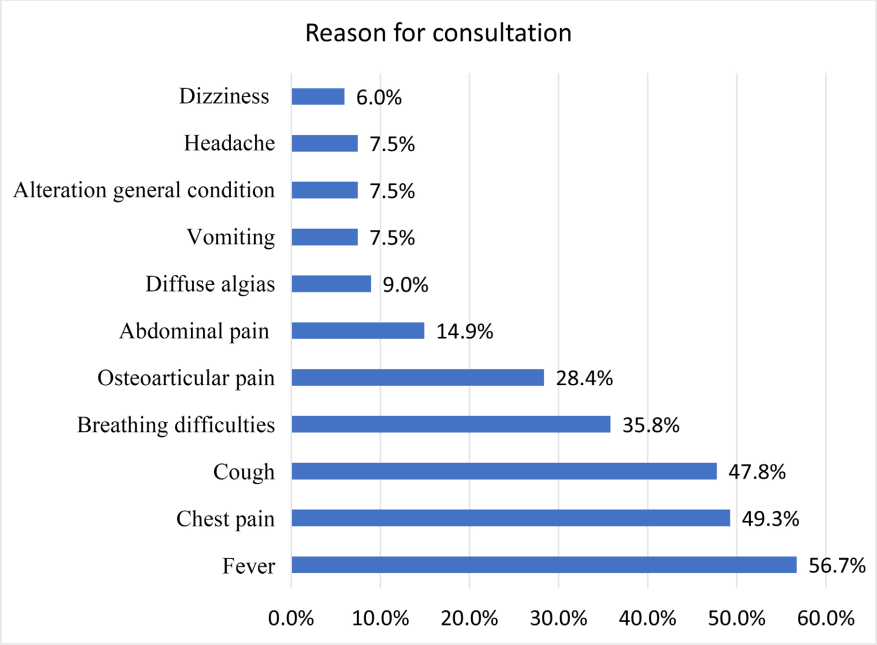


Figure 1. Distribution of children according to reasons for consultation.

The general examination revealed hypoxemia in 55 patients, representing a rate of 82.09% of cases.

On physical examination, we found mild respiratory distress in 30 of our patients (44.78%), moderate in 35 patients (52.24%), and severe in 3 patients (4.78%).

During the pleuropulmonary examination, pulmonary consolidation syndrome was found in 38 patients (56.72%), bronchial syndrome in 16 patients (23.88%), and pleural effusion syndrome in 2 patients (2.99%). The respiratory system examination was normal in 16.41%.

### 3.3. Paraclinical Aspects

Leukocytosis was found in 45 patients (67.16%), with a mean white blood cell count of 20,000/mm$^3$. Reticulocyte counts, performed in 9 patients, revealed one patient with aregenerative anemia (a count below 80,000). The mean hemoglobin level was 6.83 g/L, with a range of 2.2 to 9 g/L. C-reactive protein (CRP) testing was performed in 66 patients (98.95%). It was positive in 51 patients (77.27%), with a mean level of 147.75 mg/L and a range of 7.89 mg/L to 368 mg/L.

Pleural tap was performed in 5 of our patients (7.46%). Bacteriological results in 3 patients were consistent with pleurisy caused by common bacteria, including 1 with Staphylococcus aureus. Nasopharyngeal PCR was performed in 10 of our patients (14.92%). Two of these tests were positive, with SARS-CoV-2 and influenza A virus isolated.

Sixty-six patients (66) had an X-ray, *i.e.* 98.5%, the results of the chest X-ray are recorded in Table 1.

Table 1. Chest X-ray results.

| Chest X-ray | Anomaly | Frequency (n) | Percentage (%) |
|---|---|---|---|
| **normal** | | 7 | 10.60 |
| **abnormal** | Alveolar syndrome | 49 | 74.24 |
| | Interstitial syndrome | 13 | 19.69 |
| | Fluid effusion | 5 | 7.57 |
| | Thoracic distension | 4 | 6.06 |
| | Atelectasis | 1 | 1.51 |
| | Cardiomegaly | 8 | 12.12 |

A chest CT scan was performed in one (1) of our patients, *i.e.* 1.49%, and was in favor of a post-COVID fibrosing sequela.

A transthoracic echocardiogram was performed in 5 of our patients, *i.e.* 7.46%, and showed 4 cases of rheumatic heart disease with mitral and aortic insufficiency associated with pulmonary arterial hypertension and 1 case of heart disease with systolic dysfunction and dilation of the cardiac chambers.

### 3.4. Etiological Aspects

In our study, the causes of acute respiratory distress in our patients were acute chest syndrome (61.19%), pneumonia (47.76%), which can coexist in the same patient, and asthma attacks (10.45%). Severe anemia and decompensated heart disease accounted for 7.46% and 4.48%, respectively.

### 3.5. Therapeutic Aspects

Oxygen therapy and hydration were administered in 100% of cases, an analgesic-antipyretic in 98.51% of cases and antibiotic therapy in 94.03% of cases as shown in Figure 2.

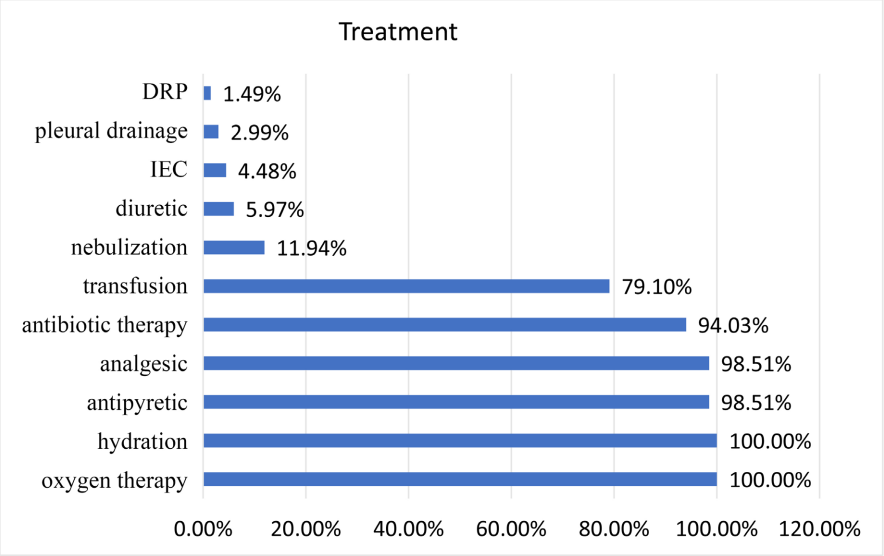


Figure 2. Distribution according to treatments administered.

### 3.6. Evolutionary Aspects

The outcome was favorable in 98.5% of cases (66 patients). One child (1.5%) with acute chest syndrome (ACS) associated with pleuropneumonia had an unfavorable outcome, dying from cardiorespiratory arrest. The average length of hospital stay was 8 days, ranging from 2 to 53 days.

## 4. Discussion

### 4.1. Limitations of the Study

The retrospective nature of our study constituted a limitation, the single-center study and its potential for incomplete records.

### 4.2. Epidemiological Data

The average age of the patients was 114 months (9.5 years), with a range of 30 to 240 months. The 5 - 10 year age group was the most represented, accounting for 38.81%.

Our results are close to those of Dème/ly *et al.* [2], who found a median age of 98 months with a range of 15 months to 20 years and a predominance of the 5 - 10 year age group. Camara Emanuel *et al.* [3] from Conakry found similar results, with a mean age of 9.6 years and the 5 - 10 year age group being the most represented. However, Innocent *et al.* [4] in Nigeria reported a relatively higher rate, with 53.3% of their patients under 5 years old. Thus, the lack of early screening for hemoglobinopathies, particularly sickle cell disease (especially in the neonatal period), would explain the relative rarity of diagnoses of major sickle cell syndromes [3]. In Senegal, sickle cell disease is rarely diagnosed before the age of 2, and neonatal screening is not systematic. [1]

In our study, we observed a male predominance (66%) with a sex ratio of 1.9. Our results are close to those of Edwige Tine [5] who observed a male predominance (69%) with a sex ratio of 1.11. Berthold S *et al.* [6] and Méllouki N [7] had respective sex ratios of 2.12 and 1.34. The male predominance observed in our work could be partly explained by the fact that fetal hemoglobin production is lower in boys, with consequently greater expressivity of the disease according to Labie *et al.* [8].

The patients predominantly had a low socioeconomic status (61%). Diagne *et al.* [9] noted that 30% of fathers had low and irregular or no income. Belala A *et al.* [10] in Morocco found that 94.33% of patients came from families where the father had a low and irregular income. In the absence of health insurance, the average cost of caring for a child with sickle cell disease is estimated at five hundred thousand (500,000) francs per year in Senegal [9].

### 4.3. Clinical Data

The genotypic profile of sickle cell disease was SS in all our patients (100%). Alpha Seydi, in his study in Senegal, also showed a predominance of the homozygous form with a rate of 94.8% against 4% for the compound heterozygous form SC [11]. This predominance could be explained by the fact that the homozygous SS form is the most frequent in Senegal.

87.9% of patients were followed up regularly and 12.1% were poorly followed up. In Yaoundé, Nansseu *et al.* [12] reported that 1.1% of their patients were poorly followed up.

Among our patients, 94% were taking folic acid. Boiro *et al.* [13] found similar results with 98.6% of their patients receiving folic acid supplementation, which is necessary to boost red blood cell production and prevent anemia.

Patients were vaccinated according to the EPI in 98.5%. In sub-Saharan Africa, the vaccination coverage rate of children with sickle cell disease is satisfactory, ranging from 87 to 99% [14] [15].

These results are achieved thanks to vaccination campaigns carried out in Senegal for several years for all children from birth and also the free provision of vaccines.

Oral antibiotic prophylaxis was administered to only three (3) of our patients,

or 4.5%, which is slightly higher than the rate reported by Mpemba-Loufoua *et al.*, who showed in their study that penicillin chemoprophylaxis was observed in only 0.4% of patients. Expanded Program on Immunization (EPI) boosters, recommended sickle cell vaccines, and oral penicillin prophylaxis are not being administered correctly to sickle cell patients as recommended by the WHO. This is due to the high cost of vaccines and also to a low socioeconomic level in most households [16].

The main reasons for consultation were: Fever, at 56.7%. Nansseu *et al.* [17] in Cameroon found a much higher rate in their patients, at 90.5%. Conversely, Lebouc *et al.* [18] noted a lower rate of 49.3%. This frequency of fever is thought to be linked to the extreme susceptibility of sickle cell patients to infections.

Chest pain was reported in 49.3% of cases, while Bertholdt *et al.* [19] found a rate of 67%. Cissé *et al.* [20] and Nansseu *et al.* [17] found lower rates of 24% and 28.6%, respectively.

Cough was reported in 47.8% of cases, although Nansseu *et al.* in Cameroon [17] observed a higher rate of 81%. Carole Lebouc *et al.* [18] noted a lower rate of 37.1%. Fever, cough, and chest pain are the main symptoms, consistent with previous reports, these symptoms being primarily indicative of pulmonary infections [21] [22].

Respiratory difficulties were reported in 35.8% of cases. Lebouc *et al.* [18] observed more or less similar results with a rate of 35.7% in their study. Cissé *et al.* [20] observed higher rates of 71.11%. This may be due to the delays in seeking medical attention observed in our settings.

Hypoxemia was found in 55 patients, representing a rate of 82.09%. The majority of our hypoxemic patients had an oxygen saturation between 80 and 90%. Bertholdt S [19] found that 50% of patients had a saturation <95%. Innocent *et al.* in Nigeria [4] found that 100% of patients had a pulse oximetry saturation below 95%. Hypoxemia reflects the severity of the distress and is often explained by the frequency of acute chest syndrome.

### 4.4. Paraclinical Data

In 70.31% of cases, leukocytosis greater than 20,000/mm$^3$ was found. Cissé *et al.* [20] in Mali found leukocytosis in 97.77% of patients. Indeed, leukocytosis is physiological in sickle cell disease and is thought to be due to bone marrow hyperactivity and inflammatory processes. Similar results are found in the literature [23]-[25]. However, in the presence of a clinical infectious syndrome, a leukocyte count above 20,000 leukocytes/mm$^3$ is a strong indicator of infection [26]. The mean hemoglobin level was 6.83 g/L, with a range of 2.2 to 9 g/L. Our results are comparable to those of Doumbia S *et al.* [27], who, in their study in Burkina Faso, found a mean hemoglobin level of 6.7 g/dL. Nansseu *et al.* [17] had similar results with a mean of 6.48 g/dL. Indeed, anemia is a constant feature in sickle cell patients due to chronic hemolysis, which can worsen in acute situations. CRP was positive in 51 patients (77.27%), with a mean level of 147.75 mg/L and a range of

7.89 to 368 mg/L. Nansseu *et al.* [17] found results that were higher, with a mean CRP value of 228.4 mg/dL and extremes ranging from 4.5 to 432 mg/dL, but lower than those of Lebouc *et al.* [18], who had a mean CRP of 88 mg/dL. Elevated CRP most often indicates infection. However, in sickle cell disease, CRP can be positive due to inflammation occurring during vaso-occlusive events.

The main causes of respiratory distress in our patients were acute chest syndrome (61.19%), pneumonia (47.76%), and asthma attacks (10.45%). Acute chest syndrome (ACS) was most often associated with pneumonia. Therefore, in our study, the majority of ACS cases had an infectious origin. In Gabon, pneumonia is also the leading cause of infection in sickle cell patients, primarily affecting younger children [28]. ACS is a frequent emergency in underdiagnosed children and is sometimes confused with pulmonary infection or thoracic vaso-occlusion, which are the main causes [6] [29]. Microbial infection with local inflammation, as well as vaso-occlusion, are among the pathophysiological events that trigger the vicious cycle of ACS [6]. Asthma is not more common in children with sickle cell disease but may be associated with the occurrence of CVO, STA [30].

### 4.5. Therapeutic Data

Oxygen therapy was used in all patients (100%), of which 63 patients (84%) received nasal cannula oxygen therapy, 4% received a high concentration mask, and 1% received a simple mask.

Lebouc *et al.* [18] noted a lower rate of 94.1% in their patients, whereas Cissé *et al.* [9] found significantly lower results, with oxygen use in 68.89% of patients. Oxygen use is mandatory for any patient with respiratory distress , the goal being to achieve a saturation level above 95%.

Analgesics were administered to the majority of patients (98.51%). Step 1 analgesics were used in 66 patients (98.51%), with 32 patients (48%) receiving them without any other analgesics. Thirty-four (34) patients (52%) also used Step 2 analgesics in addition to Step 1. Lebouc *et al.* [18] found similar results, with Step 1 analgesics used in 100% of patients, Step 2 in 47%, and morphine used in 69%. Bertholdt *et al.* [6] used morphine in 33.33% of patients for pain relief. This could be explained by the intensity of pain in sickle cell patients. In our setting, the availability and ease of administration of morphine explain the use of Step 1 and Step 2 analgesics. All patients received hydration (100%). Cissé *et al.* [9] observed almost identical results with intravenous (IV) hydration in 91.11% of patients. Lebouc *et al.* [18] in Guadeloupe noted that 100% of their patients were hydrated. Our results align with the literature, which recommends intravenous hydration, taking into account the child's needs and the risks of pulmonary congestion [31] [32]. Antibiotics were administered to the majority of patients (94.03%). Third-generation cephalosporins (3GCs) were used in 51 patients (76.12%), macrolides in 43 patients (64.18%), and aminoglycosides in 17 patients (25.37%). Third-generation cephalosporins and macrolides were the most frequently used, and both were administered in combination in 65.07% of patients. Aminoglycosides were used in 25.37% of cases, vancomycin in 4.48%, and quinolones and imipenem in

5.97% and 4.48%, respectively. Our results are similar to those of Lebouc *et al.* [18], who observed that beta-lactam antibiotic therapy, often combined with macrolides, was initiated in the majority of cases (82.9%). Cissé *et al.* [9] noted that 77.33% of patients were treated with third-generation cephalosporins, but a higher rate was used with vancomycin (55.56%) and the amoxicillin-clavulanic acid combination (55.56%). Indeed, in cases of acute streptococcal tuberculosis (AST), broad-spectrum antibiotic therapy active against intracellular bacteria and pneumococci (macrolides and cefotaxime) should be adopted [29] [33]. Fifty-three patients (53), or 73.53%, received simple transfusions. Carole Lebouc *et al.* [18] noted a higher rate, with 81.4% of their patients receiving transfusions, but Cissé *et al.* [9] in Mali found a lower rate of 31.31%. Early transfusion of patients should be encouraged, particularly transfusion of packed red blood cells [17], but it must also adhere to very strict rules to limit the risks of alloimmunization, the consequences of which can be dramatic in patients with a disease that may require transfusions [34].

### 4.6. Evolving Data

Almost all patients (98.5%) (n = 66) had a favorable outcome. One child (1.51%) had an unfavorable outcome, dying from cardiorespiratory arrest following acute chest syndrome associated with pleuropneumonia. Bertholdt *et al.* [6] in Brussels reported a rate of 4%. Nansseu *et al.* [17] in Cameroon noted similar results with a mortality rate of 4.8%. The mean length of hospital stay was 8 days, with a range of 2 to 53 days. The mode and median were 7 and 8 days, respectively. These results are comparable to the 7-day duration reported by Bertholdt *et al.* [6] but slightly longer than the results of Vychinski *et al.* (5.4 days) [21]. Hunald *et al.* [22] reported superior results with a mean length of hospital stay of 10 days.

## 5. Conclusion

In patients with major sickle cell syndrome, respiratory distress is often due to acute chest syndrome and pneumonia. Treatment is necessary to prevent factors associated with an unfavorable prognosis**.** The implementation of neonatal screening programs would promote early diagnosis and improved management of sickle cell disease.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this article.

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