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Acute Thoracic Syndrome in Children: Epidemiological, Diagnostic and Evolutionary Aspects at the Albert Royer National Children's Hospital in Dakar Senegal

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Abstract

Acute chest syndrome (ACS) is a serious pulmonary complication of sickle cell disease. It is estimated to be responsible for a quarter of deaths in the pediatric sickle cell population. In Senegal, there are not enough pediatric studies in this area. The objective of our study was to determine the epidemiological, diagnostic and evolutionary characteristics of ATS at the Albert Royer National Children's Hospital (CHNEAR) in Dakar. This was a retrospective study in patients hospitalized at CHNEAR for ATS from January 1, 2021 to March 31, 2022. We included patients hospitalized and diagnosed with ATS. We had collected 102 patients, *i.e.* a hospital incidence of 2.96%. The average age of the children was 9 years old; the sex ratio was 1.04. The main symptoms on admission were hypoxemia (97.06%), chest pain (77.45%), dyspnea (77.45%) and fever (65.69%). 52.94% of patients had an associated vaso-occlusive crisis (VOC). The chest x-ray was abnormal in 92 patients, a rate of 90.20% and showed images of pneumonia (71%); bronchitis (17.65%) and pleurisy (0.98%). None of the children benefited from a pulmonary ultrasound. The treatment associated with analgesics (100%), broad-spectrum antibiotics (100%), oxygen therapy (100%), hydration (95.09%), transfusion (73.53%), non-ventilation invasive (6.86%), intubation (2.94%) and beta 2 mimetics (12.75%). No patient benefited from incentive spirometry. Almost all of the patients 95.10% (n = 97) had a favorable clinical evolution. However, five children (4.90%) had an unfavorable outcome including one case of complication such as stroke (0.98%) and four (4) cases of death. The average hospital stay was 8 days. ATS is common in children with sickle cell disease in Senegal and its etiologies seem to be dominated by infectious causes in our context.

Keywords

Acute Chest Syndrome, Sickle Cell Disease, Children, Senegal

1. Introduction

Sickle cell disease is a hereditary disease with autosomal transmission, clinically recessive and biologically codominant, characterized by the presence in the red blood cells of an abnormal hemoglobin called hemoglobin S. The latter is responsible for the sickling of the red blood cells in a situation of hypoxia [1]. It is one of the most common genetic diseases in France [2]. Acute chest syndrome (ACS) is one of the major complications of sickle cell disease. It is defined by the occurrence in a sickle cell patient of an acute respiratory attack, febrile or not, painful or not, associated with new pulmonary infiltrates on the chest X-ray [3]. Hypoxemia is not present in the definition, but is a predictor of unfavorable outcome [4]. This pathology is more common in the pediatric population with a frequency that decreases with age, the peak incidence being between the ages of 2 and 4 years [5]. In Senegal, the absence of previous studies on the acute chest syndrome and the fact that it constitutes a frequent reason for hospitalization in a pediatric environment motivated the realization of this work in the pediatric pulmonology and continuing care department of the Albert Royer children's hospital in Dakar with the general objective: To describe the epidemiological, diagnostic and evolutionary aspects of ACS at the Albert Royer children's hospital in Senegal. The specific objectives were to determine the incidence of ACS at the CHNEAR in Dakar, to determine the major signs of STA and to specify the methods of management of ACS.

2. Methodology

The study was conducted at the Albert Royer National Children's Hospital (CHNEAR) in Dakar, Senegal. This was a retrospective study from January 1, 2021 to March 31, 2022, *i.e.* a duration of 15 months. It was descriptive and analytical in patients who were hospitalized for an acute chest syndrome. We included hospitalized patients in whom the diagnosis of acute chest syndrome (ACS) was made whether they were known to have sickle cell disease or not on admission, whose file was available and usable. Any incomplete file was excluded from the study. Sociodemographic, clinical, paraclinical and evolutionary data were collected using a pre-established survey form filled out from patient files. The data collected was entered into the Epi info V 7.2 software. The analysis was performed with Excel 2010 and SPSS version 22 software.

During the analysis, the qualitative variables were described by frequency tables and bar charts. Quantitative variables were described by their positional parameters.

Hypoxemia was defined by a pulsed oxygen saturation of less than 95% in

ambient air.

3. Results

3.1. Epidemiological Aspects

A total of 3451 children were hospitalized during the study, among them 102 patients were hospitalized for ACS, *i.e.* a hospital incidence of 2.96%. The average age of the patients was 110 ± 54.6 months and extremes of 12 and 204 months.

3.2. Clinical Aspects

93 patients were known to have sickle cell disease and were followed regularly. The baseline hemoglobin level was 7.59 ± 0.87 g/l.

Sickle cell disease was diagnosed during hospitalization in 2 patients, *i.e.* 1.96%.

A notion of corticosteroid therapy was found in 11.76% of patients (n = 12). Eighty-eight children (86.27%) had a history of familial sickle cell disease.

Chest pain was present in 79 patients and dyspnea in 79 patients.

Hypoxemia was found in 99 patients, a rate of 97.06% (Table 1).

Pulmonary condensation was found in 72 patients or 70.59% during the pleuropulmonary examination, bronchial syndrome in 17 patients (16.67%) and pleural effusion in 1 patient or 0.98%.

Abdominal pain was the main sign found during abdominal examination in 49 patients (48.04%) and splenomegaly in 14 patients or 13.73%.

The CVO was found in 53.94% (n = 54) of the patients during the osteo-articular examination.

3.3. Paraclinical Aspects

The average hemoglobin level was 6.97 ± 1.44 g/l with extremes of 2.2 and 10 g/l.

The mean leukocyte count was 27469 ± 21885 elements/mm^3. The mode and the median were respectively 24000 elements/mm^3 and 23950 elements/mm^3.

Ninety-two patients (90.20%) had a positive C-reactive protein (CRP) with an average rate of 113 ± 92.73 mg/l and extremes of 5.2 and 350.2 mg/l. Blood culture was performed in 12 patients (11.76%) of which 3 came back positive for staphylococcus aureus.

Table 1. Distribution of patients by general examination results. N = 102.

General review		Fréquency (n)	Pourcentage (%)
General state	Discoloured mucous	89	87.25
	AEG	69	67.65
Functional signs	Chest pain	79	77.45
	Dyspnea	79	77.45
	Cough	54	52.94
Constant	Hypoxémia	99	97.06
	Tachycardia	77	75.49
	Fever	67	65.69

The chest X-ray performed in all patients returned normal in 10 patients (9.80%) and abnormal in 92 (90.20%) and showed images of pneumonia (71%); bronchitis (17.65%) and pleurisy (0.98%).

The chest CT scan was performed in one patient (0.98%) and the results showed lesions in favor of SARS Cov2 infection.

None of the children benefited from a pulmonary ultrasound during their hospitalization.

3.4. Therapeutic Aspects

Analgesic treatment was prescribed in all patients as well as antibiotic therapy and oxygen therapy. Seventy-five patients (73.53%) were transfused, of which 97.33% (n = 73) simply and 2.67% (n = 2) in transfusion exchange (Figure 1).

Cefotaxime was used in 88 or 87.13% and macrolides were administered in 81 patients or 80.20% (Figure 2).

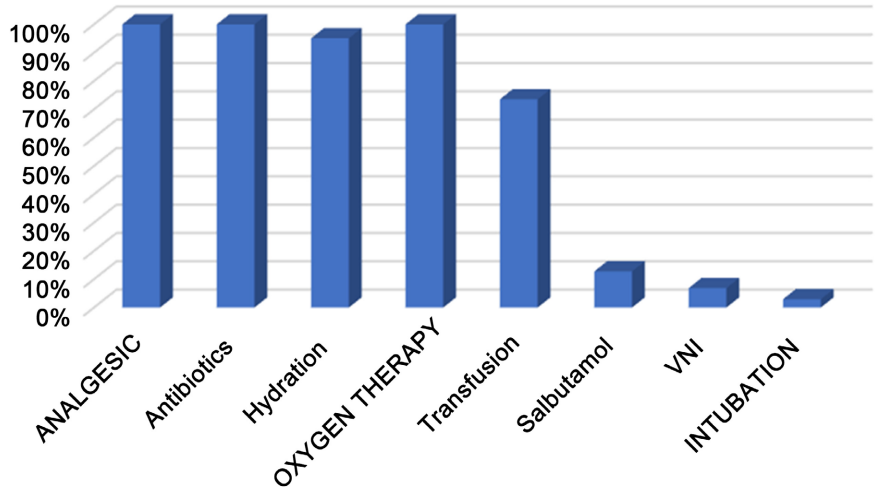

Figure 1. Distribution of patients according to treatment (N = 102).

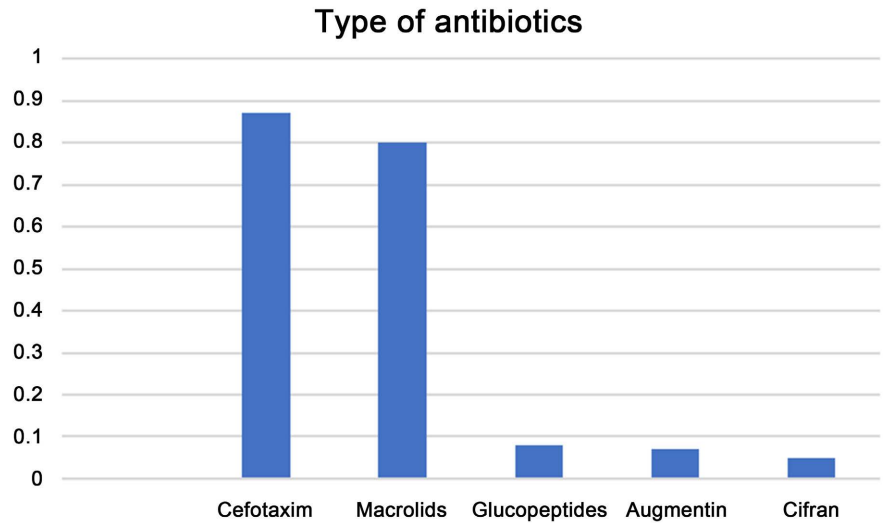

Figure 2. Distribution of patients by type of antibiotic (N = 102).

Incentive spirometry and preventive heparin therapy were not performed in patients.

3.5. Evolutionary Aspects

The evolution was favorable in 97 patients (95.10%). 5 children had an unfavorable outcome including 4 cases of death (3.92%) and one complication such as stroke (0.98%).

Causes of death:

- 2 of the deaths were due to severe acute respiratory distress syndrome followed by cardiopulmonary arrest.
- One death caused by septic shock with intravascular disseminated coagulation following sepsis with pulmonary localization due to SARS COVID 19.
- Death as a result of a stroke-type complication followed by a deep coma and then brain death: patient disconnected from the respirator.

The average length of hospitalization was 8 days and extremes of 3 and 31 days.

4. Discussion

4.1. Epidemiological Aspects

In our sample, 102 patients had ACS out of 3451 hospitalizations during the study period, an incidence of 2.96%. This rate is lower than the 10% - 20% rate of admissions reported by Miller and Gladwin in their study [6]. ATS is a frequent emergency in children but is underdiagnosed and is sometimes confused with a pulmonary infection or a thoracic vaso-occlusive crisis, which are the main causes [7]. Hemoglobin electrophoresis is not carried out systematically in Senegal, most parents do not know their status or that of their children and some patients have escaped enrolment. For financial constraints, we would also have missed all those whose chest X-ray was normal at the beginning but who subsequently developed an ACS since the radiological results can change over time [5]. While it is true that the presence of new pulmonary infiltrates on the chest X-ray is the key element in defining the disease [8], some have asserted that a single normal chest X-ray does not exclude the diagnosis [5].

In our cohort, the age groups 9 - 10 years and 13 - 14 years were the most represented with each a percentage of 10.78 (n = 11). The median age was 9 years old.

A study conducted in Brussels by Bertholdt al [7] reports similar results with a median of 8 years. The 0 - 5 age group represented 24.4% and that of more than 5 years 75.6% of the patients. Innocent *et al.* [9] in Nigeria report a relatively higher rate with 53.3% of their patients who were under 5 years old.

The American cooperative study found an incidence which decreases with age, the peak incidence being between the ages of 2 and 4 years (25 out of 100 persons/year in this age group, reaching 8.8/100 people/year for adults) [10].

This is not consistent with what we found in our study. This difference can be

explained by the fact that the diagnosis of sickle cell disease is often discovered late in our context and that the ACS, occurring in the population under 5 years old, is often confused with another pulmonary pathology, especially infectious, given the absence early detection and the frequency of infectious pathologies in sub-Saharan Africa.

Among the children, 6.86% (n = 7) were poorly followed. In Yaoundé Nansseu *et al.* [11] reported that only 1.1% of their patients were poorly followed.

In fact, patients who are not regularly monitored may have episodes of ACS and not come to consult at the Albert Royer hospital, which would underestimate the number during enrolment.

1.96% of patients (n = 2), did not know their status at the time of admission and the diagnosis of sickle cell disease was made during hospitalization. The ACS can sometimes be the circumstance of discovery of sickle cell disease and can quickly engage in this case the vital prognosis of the child [12].

4.2. Clinical Aspects

Hypoxemia was found in 99 patients, *i.e.* 97.06%. Innocent *et al.* in Nigeria [9] found that 100% of patients had pulse oxygen saturation below 95%. Hypoxemia is not present in the definition, but is a predictor of unfavorable outcome [4]. This strong finding of hypoxemia in our children hospitalized for STA is explained by the late consultation period. Hypoxemia is a criterion of severity of the acute chest syndrome and its rapid and adequate management can promote a better clinical course.

Fever was present in 67 patients on admission, a rate of 65.69%. Nansseu *et al.* [11] in Cameroon found a much higher rate in their patients, *i.e.* 90.5%. However Lebouc *et al.* [13] noted a lower rate of 49.3%. This frequency of fever would be linked to the extreme susceptibility of sickle cell patients to infections and especially to encapsulated germs.

Chest pain was observed in 77 patients or 77.45%. Bertholdt *et al.* [7] found a rate of 67%. On the other hand Cissé *et al.* [14] and Nansseu *et al.* [11] found respectively lower rates of 24% and 28.6%. Chest pain is a key element of the diagnosis and should prompt appropriate treatment to avoid serious complications.

Dyspnea was found in 79 patients in our series, *i.e.* 77.45%. Cissé *et al.* [14] observe more or less similar results with a rate of 71.11%. Lebouc *et al.* [13] found dyspnea in 35.7% in their study.

Respiratory distress and chest pain are part of the clinical picture of ATS, which explains the high frequency of dyspnea in our study.

The evaluation of respiratory distress must be strict in order to be able to classify it and allow its rapid management. The latter will consist of early oxygen therapy and an improvement in hemoglobin levels through transfusion, which will improve oxygen transport to the tissues.

Pulmonary auscultation was abnormal in 90 patients, a rate of 88.24%. Lebouc

et al. [13] in the West Indies found abnormal pulmonary auscultation in 79.4% of their patients.

Pulmonary condensation syndrome was found in 72 patients on admission, a rate of 70.59%. This was the main sign found during the pleuropulmonary examination.

Cissé *et al.* [14] had found a rate of 64.44% of pulmonary consolidation. Lebouc *et al.* [13] in the West Indies found a much higher rate of 82.4%.

A bronchial obstruction syndrome was noted in 17 patients or 16.67%. TINE *et al.* [15] in Senegal observed a rate of 13%. Indeed bronchospasm is sometimes present (13%) during the ACS [16].

Only one patient (0.98%) presented with pleural effusion syndrome. Indeed, it has been described that parenchymal involvement is sometimes associated with pleural involvement in severe forms [17].

4.3. Paraclinical Aspects

The average hemoglobin level was 6.97 ± 1.44 g/l with extremes of 2.2 and 10 g/l. The mode and median were 6.2 and 7 g/dl, respectively. Our results are comparable to those of Doumbia S *et al.* [16] who, in their study in Burkina Faso, found an average hemoglobin level of 6.7 g/dl with extremes ranging from 2.5 g/dl to 10 g/dl. Nansseu *et al.* [11] had similar results with an average of 6.48 g/dl but lower than those of Bertholdt S *et al.* [7] in whom the average rate was 8.3 g/dl. Indeed, anemia is constant in sickle cell patients due to chronic hemolysis which can worsen in acute situations. The management of anemia in case of ACS may be necessary for a good improvement in oxygen transport.

Hyperleukocytosis was noted in 98 patients, *i.e.* 96.08%. The mean number of leukocytes was 27469 ± 2185 elements/mm^3 with extremes of 6630 and 196,200 elements/mm^3. The mode and the median were respectively 24,000 elements/mm^3 and 23,950 elements/mm^3. Cissé *et al.* [14] in Mali had found the same results with hyperleukocytosis in 97.77% of patients and an average of 31,856/mm^3 of leukocytes and extremes ranging from 11,500 to 78,300/mm^3. Nansseu *et al.* [11] noted an average of 32479.4/mm^3 with extremes ranging from 10,600 to 73,900/mm^3.

This may suggest that infection can initiate or precipitate the development of ATS in our patients, thus validating previous reports [7] [10].

Ninety-two patients (90.20%) had a positive CRP with an average rate of 113 ± 92.73 and extremes of 4.10 and 350.2. Nansseu *et al.* [11] had found results that are superior to ours with an average 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.* [13] who found an average CRP of 88 mg/dl. The increase in CRP is therefore almost constant during ATS and is not synonymous with bacterial infection [17].

Blood cultures were performed in 12 patients (11.76%) and only 3 all came back positive for Staphylococcus aureus. Lebouc *et al.* [13] found similar results with positive blood cultures in 29.9% of cases. However Nansseu *et al.* [11] in

Cameroon, performed blood cultures in 47.6% of patients but no germ was identified.

The blood cultures carried out had isolated Staphylococcus Aureus on 3 occasions, being therefore the germ most frequently found in nosocomial infections, on catheter material and osteomyelitis in patients with sickle cell disease [18] [19]. Lebouc *et al.* [13] confirm by reporting in their study that the most common pathogen in their patients was coagulase-negative staphylococcus.

The chest x-ray was abnormal in 92 patients, a rate of 90.20%. LEBOUC *et al.* [13] noted superior results highlighting abnormal chest X-rays in 94.1%. Douamba *et al.* [16] in Burkina Faso, on the other hand, observed a lower rate with 76.5% of anomalies.

This difference could be explained by the lag of the radiological diagnosis compared to the clinic. Repetition of chest x-rays may be necessary, sometimes hampered by the lack of financial resources limiting their performance. A normal chest X-ray does not exclude the diagnosis of ACS [5].

No child benefited from a pulmonary ultrasound, although the latter remains very contributive in the early diagnosis of the acute chest syndrome. It can be performed at the patient's bedside, less irradiating than the chest X-ray and allows early signs to be sought, such as consolidation predominantly at the bases of the lungs with air bronchogram, pleural effusion can also be associated [20].

4.4. Therapeutic Aspects

In accordance with the literature, our management of ACS included careful hydration, respecting daily fluid needs, analgesics, broad-spectrum antibiotic therapy, oxygen supplementation and transfusion.

Antibiotic therapy was used in all patients, *i.e.* a rate of 100%. 3rd generation cephalosporins and macrolides being the most frequently used antibiotics, and are administered respectively in 88 patients, *i.e.* a rate of 87.13% and in 81 patients, *i.e.* 80.20%, the two are associated in 80.20% of patients.

In fact, in the case of ACS, a broad-spectrum antibiotic therapy active on intracellular germs and pneumococcus (macrolides and Cefotaxime) must be adopted [3]. In Senegal, the absence of 100% care in terms of medico-social coverage of children with sickle cell disease proves the fact that several children monitored do not have good vaccination coverage against encapsulated germs. Senegal's expanded immunization program does not cover non-compulsory vaccines.

Oxygen therapy was used in all patients, 13 of whom received oxygen therapy with glasses.

This is related to the fact that children arrive late in the emergency room at the stage of often profound hypoxemia. All this is linked to the low socio-economic level in most children followed for sickle cell disease.

None of our patients benefited from incentive spirometry. It should have been performed in all patients over 5 years hospitalized for CVO or for early ACS

in order to limit hypoventilation and worsening of severe forms. The absence of physiotherapists and the non-availability of this device justifies the non-prescription.

Seventy-five patients (n = 75) were transfused, a rate of 73.53%. 97.33% of these patients either (n = 73) in a simple way and 2.67% (n = 2) in transfusion exchange. This is explained by the fact that the majority of children arrive with a hemoglobin level having dropped by at least 2 points at the time of diagnosis. Transfusion can improve oxygen transport and is very beneficial in children hospitalized for ATS [21].

Almost all of the patients 95.10% (n = 97) had a favorable evolution. However, five children (4.90%) had an unfavorable outcome including 1 case of complication such as cerebrovascular accident (0.98%) and 4 cases of death, *i.e.* 3.92%, which is consistent with the percentage of 4% obtained by Bertholdt *et al.* [10] in Brussels. Nansseu *et al.* [11] in Cameroon note similar results with a mortality rate of 4.8%.

Two (2) patients died in a context of severe acute respiratory distress followed by cardiopulmonary arrest. The first death caused by septic shock with a CIVD following a sepsis with pulmonary localization to Sars cov 2. The second death following a stroke type complication followed by a deep coma and brain death.

The duration of hospitalization was on average 8 days and extremes ranging from 3 to 31 days which is comparable to the duration of 7 days reported by Bertholdt S *et al.* [7] but a little higher than the results of Vychinski *et al.* [22] which yields 5.4 days. Hunald *et al.* [23] reported superior results with an average hospital stay of 10 days.

The introduction of other supportive care in our practice such as incentive spirometry as elsewhere [6] as well as the systematic supply of oxygen and early blood transfusion could considerably reduce the hospital stay.

5. Conclusion

Acute chest syndrome is the second cause of hospitalization and the first cause of death among sickle cell patients in Senegal. Generalized neonatal screening must be implemented in order to allow early diagnosis and treatment of children with sickle cell disease. For better management adapted to our contexts, other multicenter studies would be necessary in order to be able to clearly describe the etiological factors associated with ATS in our populations.

Conflicts of Interest

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

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