



Research Article

ASSESSMENT OF THE DIRECT COST ASSOCIATED WITH THE MANAGEMENT OF MAJOR SICKLE CELL SYNDROMES IN THE PEDIATRIC DEPARTMENT OF THE YALGADO OUÉDRAOGO UNIVERSITY HOSPITAL

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ABSTRACT

Background: Sickle-cell anemia is currently recognized as a major public health problem due to its high mortality and morbidity. Despite its well codified management, the occurrence of acute complications contributes significantly to the rising costs of health care. In Africa, where health coverage is limited, the study aimed at assessing the direct cost associated with the management of sickle-cell anemia in the pediatric department.

Methods: It was a prospective study of children followed regularly for major sickle cell syndrome in one pediatric ward. After the inclusion of the children through a verbal consent of the parents following an interview, the parents were asked to carefully keep any documentary evidence of the health-related spending and to maintain a telephone contact with the medical follow-up team. The second step consisted of the follow-up of the patients and the collection of all supporting documents.

Results: A total of 117 children with sickle-cell anemia were included in the study. The average length of hospital stay was 4.5 days for vaso-occlusive crises (VOCs) and 7.5 days for infections. The cost of vaccination was €25.5 per patient. The average amount spent for the management of infections was 120 Euros per inpatient versus 21 Euros per outpatient ($p < 0,005$). The average cost for the management of simple malaria was 8 Euros per outpatient.

Conclusion: The cost of treatment resulting from the complications of this chronic condition is high. There is no doubt that prevention is more economical than a purely curative attitude.

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INTRODUCTION

Sickle-cell anemia is an abnormality of the hemoglobin. It is the most common hereditary disease in the world. The WHO estimates that about 300,000 children are born worldwide each year with a major hemoglobin anomaly (WHO, 2006). The WHO also estimates that there are 200,000 people suffering from sickle-cell anemia in Africa (Labie, 2010). Sickle-cell anemia is currently recognized as a major public health problem due to its high mortality and morbidity. In industrialized countries, patient life expectancy has improved due to early diagnosis and treatment. Indeed, the neonatal screening implemented in the northern countries currently allows the implementation of international recommendations.

In developed countries, the economic impact of major sickle cell syndromes (MSCSs) on the populations is currently well established (Piel *et al.*, 2013). Overall, studies point out that sickle-cell anemia contributes significantly to higher health care costs (Pizzo *et al.*, 2015). However, in developed countries, care is subsidized for reasons of public health.

In Sub-Saharan Africa, specific national programs for the management of sickle-cell anemia are non-existent or at best limited. In the absence of optimal management, acute complications such as bacterial infections, malaria, vaso-occlusive crises and acute anemia are the common causes of consultation in emergency and in-patient departments. In African countries, health and social insurance systems are

lacking, costs associated with health care are entirely borne by families, thus exacerbating the existing poverty. Few studies have been carried out to estimate the financial burden induced by sickle-cell anemia. The study aimed at assessing the direct cost associated with the management of major sickle cell syndromes in one pediatric ward.

METHODS

This was a six-month prospective study on sickle-cell patients. The children were received on an outpatient basis as part of their regular medical follow-up in the pediatric ward of the Yalgado Ouédraogo University Hospital in Ouagadougou. The first step of the study consisted of the inclusion of the children after verbal consent of the parents following an interview. As a result of this consent, the parents were asked:

- To keep carefully any documentary evidence of health-related spending and to require the recording in writing of the results of additional examinations of any medical consultation or hospitalization;
- To maintain telephone contact with the medical follow-up team in order to either receive care in case of complication, or to inform the team of any critical episode that has occurred and already managed.

The second step was the follow-up of the patients and the collection of any documentary evidence of expenditure.

Follow-up

Recruitment was done during clinic appointments by the patients. In the absence of any complications, the follow-up period was as follows: every two months for children under 2; every three months for children under 5 and every 6 months for children ≥ 5 years of age. The median follow-up was estimated at 6 months (3 to 12 months).

At the follow-up consultation, the pneumococcal vaccine was considered a first line vaccine. The hepatitis B vaccine and the *type b Hemophilus influenzae* vaccine have been included in the Expanded Program on Immunization (EPI) since 2006.

Acute complications

The management of acute complications was carried out either through outpatient care or during hospitalization. The management of acute anemia through blood transfusion is free of charge in our context. The acute complications observed were classified into vaso-occlusive crises, infectious bacterial complications (broncho-pneumopathy, cutaneous staphylococcus, gastroenteritis, ENT infection, and bacteremia) and malaria.

Direct Cost

The cost of prevention focused on the cost of vaccines, folic acid supplementation, Antibiotic prophylaxis and seasonal anti-malarial prophylaxis. In addition to the cost of medicines, the cost of morbid episodes (malaria, vaso-occlusive crises, infections, etc.) in ambulatory care and during hospitalizations included the costs of consultation, hospitalization and the cost of complementary examinations. A list of all prescriptions for the prevention of acute complications and the management of morbid episodes was prepared. All the prices of drugs bought were documented. The amount spent on drugs corresponded to the cost of drugs. Drugs have been grouped into analgesics, antibiotics,

antipyretics, and adjuvant therapy. The cost of additional examinations was calculated from the cash receipts. For the costs of consultation and hospitalization, the tariffs in force in the facility where the patient was consulted and/or hospitalized were taken into account. The direct cost was the monetary value of expenditures for the prevention and treatment of a morbid episode. The cost in CFA francs was converted into Euros.

Statistical analysis

The quantitative variables are expressed on average. The materiality threshold was set at 5% for all analyzes.

RESULTS

Table I shows the characteristics of the patients. A total of 117 children aged 6 months to 14 years with sickle-cell anemia were included over a three month period. The MSCSs consisted of 38 homozygotes SS, 56 compound heterozygotes SC and 3 S⁺ thalassemia. Sixteen patients were lost to follow-up, four had incomplete data. The study therefore covered the 97 patients.

Table 1 General Characteristics of Patients

| Demographic data | N (%) |
|---|----------------------|
| Male | 49 (50.5) |
| Female | 48 (49.5) |
| Age (years) ^a | 7,9 (10 months - 14) |
| Type of hemoglobin | |
| Homozygote SS | 38 (39.2) |
| Compound heterozygote SC | 56 (57.8) |
| Compound heterozygote S ⁺ thalassemia | 3 (3.0) |
| Clinical data | |
| Pneumococcal immunization coverage | 93 (96) |
| Length of follow-up (months) ^a | 6 months |
| Length of hospital stay for VOCs (days) ^a | 4.5 |
| Length of hospital stay for infection (days) ^a | 7.5 |

a: Average value

A total of 179 morbid events were treated in ambulatory care, i.e. 2.26 events per child. The respective frequency of patients who developed acute complications was 57.8% (n = 56) for vaso-occlusive crises (VOCs), 47.2% (n = 46) for malaria and 22.1% (n=21) for broncho-pneumopathy. The hospitalization rate was 10.3% (10/97) including 2 cases for VOCs and 8 cases for infections (broncho-pneumopathy, septicemia, gastroenteritis). The average hospital stay for the VOCs was 4.5 days and for infections of 7.5 days. The acute complications treated in an outpatient setting are shown in Figure 1.

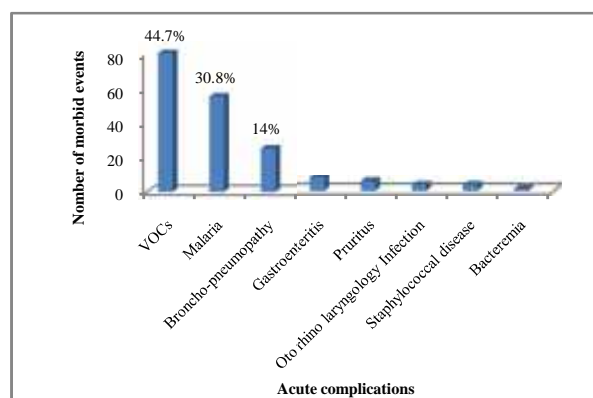


Figure 1 Acute complications managed in outpatient setting.

Table 2 shows the cost of major sickle cell syndrome management depending on the type of treatment

Table 2 Cost of MSCS management per treatment

| Care | Prevention cost* | Acute complications cost* | | p |
|---|------------------|---------------------------|---------------|-------|
| | | Outpatient | Inpatient | |
| Vaccines ^a | 25.5 (15 - 330) | - | - | |
| Folic acid prophylaxis ^a | 4 (0.5 - 25.5) | - | - | |
| Penicillin therapy ^a | 3 (2.3 - 4) | - | - | |
| Consultation / hospitalization ^a | Free | 4 (1 - 9) | 3 (0.3 - 6) | - |
| Antimalarial ^a | 7 (1 - 30) | 8 (0.6 - 25) | - | |
| Analgesic ^a | - | 6 (1 - 19) | 45 (34 - 56) | 0.005 |
| Antibiotic ^a | - | 21 (1.5- 160) | 120 (32- 229) | 0.005 |
| Adjuvant therapy ^a | - | 4 (0.5 - 25.5) | 9 (2- 25) | - |
| Additional examinations | 8.5 (0.5 - 25.5) | 5 (1 - 10) | 14.5 (6 - 26) | 0.05 |

a: Average cost (minimum/maximum value); * Euros; P: materiality threshold 0.05; - : immaterial

The average cost associated with the management of infections, vaso-occlusive crises and malaria is shown in Table 3.

Table 3 Cost of complications depending on the mode of care

| Complications cost* | Outpatient | Inpatient | P |
|-------------------------|---------------|---------------|-------|
| Infections ^a | 21 (1.5- 160) | 120 (32- 229) | 0.005 |
| VOCs ^a | 8 (2 - 39) | 45 (34 - 56) | 0.005 |
| Malaria ^a | 8 (0.6 - 25) | - | |

a: Average cost (minimum/maximum value); * Euros; P: materiality threshold 0.05; - : immaterial

DISCUSSION

Limitations of the Study

This first study assessed the direct cost of major sickle cell syndromes management in Burkina Faso. However, there are some limitations described as follows: the reduced number of our sample; the mechanism of recruitment of our patients which does not provide a true follow-up cohort; the restriction of the scope of the study to the pediatric department of CHU YO. These limitations do not make it possible to generalize the results nationally. In addition, the low income of patients limited the prescription of complementary examinations. The phenomenon of patients lost to follow-up (16/117) could be due to financial difficulties, which hinders medical follow-up. However, it should be noted that patients with low socioeconomic status and affected with chronic diseases are those having the most serious health problems and mostly using health resources (Ellison *et al.*, 2007).

Prevention and Cost

The anti-infectious prophylaxis of the MSCSs forms a crucial part of sickle cell disease control. A recommendation for this prophylaxis is the introduction of vaccines in the treatment of sickle-cell anemia, including pneumococcal vaccination (de Montalembert, 2008; Hardie, 2009). The occurrence of bacterial infections, particularly pneumococcal infections, is a significant cause of morbidity and mortality in infancy (Trends 2009). The cost of vaccination was €25.5/patient (€15 - €330). The Expanded Program on Immunization (EPI) aimed at ensuring total immunization of children under one is in place in Sub-Saharan Africa. Besides, the usual vaccines (tuberculosis, diphtheria, tetanus, poliomyelitis, measles, yellow fever, hepatitis B and *type b Haemophilus influenzae*) are available and free of charge until the age of 9 months.

However, the cost of booster doses shall be borne by the families. Conjugate vaccines for the immunization of infants under 2 are not yet commercialized in Burkina Faso. However, these conjugate vaccines represent - particularly in children - a major advance in infectious prophylaxis. The vaccine recommended in Africa for sickle-cell anemia is the pneumococcal vaccine of polysaccharide vaccine (Pneumo 23®). The latter, although available, is expensive at the price of €14.5 which is entirely borne by patients.

In addition to vaccination, antibiotic prophylaxis with oral penicillin should be instituted in children under 5. The reduction in the incidence of pneumococcal infections in children with sickle-cell anemia receiving penicillin antibiotic prophylaxis is no longer to be demonstrated (Hirst *et al.*, 2012). The average cost of penicillin therapy was €3/patient/6 months. Available and listed as a generic essential drug in Burkina Faso, and compared to the cost of vaccination and poor immunization coverage (Nacoulma *et al.*, 2006), treatment with phenoxymethylpenicillin should be the best therapeutic choice in terms of antibiotic prophylaxis in Africa. Malaria is a significant factor in sickle cell disease comorbidity. Seasonal anti-malarial prophylaxis should be instituted in sickle cell patients. Indeed, infection with *Plasmodium falciparum* is an aggravating factor of anemia (Ambe, 2001, Serjeant, 2003, Booth, 2010). This prevention has been systematic in our series. Intermittent preventive treatment of malaria (IPTp) is part of malaria control strategies in Sub-Saharan Africa. The WHO (WHO, 2010) now advocates a new intervention against *Plasmodium falciparum* malaria which is the *intermittent preventive treatment in infants (IPTi)* exposed to malaria. Malaria is a preventable disease; 7.50 Euros is enough to buy and distribute an insecticide-treated mosquito net and explain how it should be used. The cost of anti-malarial prophylaxis was €7 per patient/3 months. Africa, particularly Sub-Saharan Africa, has received significant support from the major international donors. Nevertheless, the financing of the prevention and treatment of malaria must continue in order to take advantage of the progress made in recent years.

Complications and Cost

The main acute complications of sickle cell disease in children are infections, vaso-occlusive crises and acute anemia. These various complications depending on their severity can be managed either in outpatient or in-patient settings.

Bacterial Infections

The incidence of bronchopneumonia was 14% and 8/10 of hospital admissions were due to infections. Infections account for a significant proportion of sickle cell disease morbidity and mortality, causing about 20% to 50% deaths (Booth, 2010). The average amount spent for the treatment of infection was 120 Euros per inpatient versus 21 Euros per outpatient. For a febrile episode, the cost of this ambulatory approach was US \$ 30 per outpatient versus US \$ 140 per inpatient [Rahimy *et al.*, 1999]. During hospitalization, rapid administration of intravenous antibiotic therapy is recommended in the management of febrile episodes in children (Vichinsky, 1991). Indeed, bacterial infection is one of the common occurrences in early childhood. The risk of infection is highest in children under five years of age. The bacteria causing such infection are pneumococcus, *type b*

Haemophilus influenzae, meningococcus, salmonella and staphylococcus aureus (Williams *et al.*, 2009) and are responsible for pneumonia, meningitis, septicemia, and osteomyelitis. The severity and rapid progression of these infections, especially for Pneumococcal infections, make it a vital emergency and require care in hospital setting. In Africa, in the absence of identification of the pathogen, the antibiotic treatment instituted must be bactericidal, adapted to the infectious site, active on the pneumococcus and having a broad spectrum.

Malaria

Sub-Saharan Africa is a hyperendemic zone for *Plasmodium Falciparum*. Any febrile illness is considered to be associated with malaria. The average cost of simple outpatient malarial care was 8 Euros (0.6 -25). For countries in Sub-Saharan Africa, this still high amount can be due to the prescription of specialty antimalarial drugs. In addition, most patients have access to antimalarial treatment through the private sector. However, for people infected with malaria, treatments costing € 1.50 exist and are very effective and can dramatically reduce morbidity and mortality (Cibulskis *et al.*, 2016). This amount represents the price of first-line treatment for malaria. The Global Fund has spent about US \$ 2 billion on malaria control in Sub-Saharan African countries (Morel *et al.*, 2006). This international initiative contributed to lower treatment costs. Despite affordable prices, the main challenge will consist in making effective anti-malarial medicines available to the most economically vulnerable people by strengthening the public drug sector.

Vaso-Occlusive Crises

Vaso-occlusive crises (VOC) due to tissue ischemia are one of the most common acute manifestations of the disease and the leading cause of hospitalization (Giro, 2007; Fosdal, 2007). The average cost for the treatment of VOCs was 8 Euros per outpatient and 45 Euros per in-patient. The treatment of VOCs is most often performed on an outpatient basis and is based on bed rest, hydration and analgesic I or II therapy. The treatment of any single VOC must be effective. Indeed, if the treatment is incorrect, the complication may lead to much more severe crises requiring hospitalization and the use of level III analgesics. Indeed, according to some recommendations (Rees *et al.*, 2003), a severe VOC requires hospitalization and it should be ideally treated with intravenous morphine. In our context, due to financial reasons and availability of treatment, it is therefore not uncommon to see a simple VOC evolving into complicated VOCs resulting in days of hospitalization.

CONCLUSION

Children with sickle cell anemia receive regular care that improves the overall prognosis and quality of life of patients. The treatment of sickle-cell anemia has been well codified in recent years. In Burkina Faso, there is a conventional treatment, but it must be based essentially on the prevention of acute complications. The cost of treatment resulting from the complications of this chronic condition is high. There is no doubt that prevention is more economical than a purely curative attitude. This preventive care will focus on regular medical follow-up and parental education.

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