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Case Report

Observation of Causes of Death from Sickle Cell Anemia in Niger

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Abstract

Purpose: Improve the management of Major Sickle Cell Syndromes (SDM) by studying the circumstances in which patients affected by this disease die in Niger.

Methods: This was a retrospective study of descriptive and analytical type in sickle cell patients followed at the National Sickle Cell Reference Center (CNRD) in Niamey with a follow-up file, who died during our study period, which was 9 years (January 1, 2010 to December 31, 2018).

Results: During the study period, 6,465 sickle cell patients were followed up at the CNRD, 249 deaths were recorded, representing a frequency of 3.8%. There is a male predominance with a sex ratio of 1:3. The 0-15 age group was the most represented with 34.5% with an average age of 9.25 years. 34.1% of the patients came from a consanguineous marriage. Of the 249 deaths, 94% (n=234) were SS, 5.6% (n=14) were SC and 0.4% (n=1) was S/β. The majority of patients died at the time of registration, i.e. 58.25% (n=145 (SS=137. SC=8.)). 90.4% had died in a health-care facility. The main cause of death was anemia in 73.1% of cases.

Conclusion: The management of sickle cell disease requires adequate preventive action to reduce the rate of early mortality.

Keywords: Death- Major sickle cell syndrome; CNRD; Niamey; Niger

Abbreviations

SDM: Major Sickel Cell Disease Syndrome; CNRD: National Reference Centre for Sickle Cell Disease; PRN: President of the Republique of Niger; ALDN: Association for the Fight Against Sickle Cell Disease in Niger; CVO: Vasooclusive Crisis; STA: Acute Thoracic Syndrome; AVP: Public Road Accident

Introduction

Sickle cell disease is the most common genetic disease in the world, characterized by the substitution of glutamic acid by valine in position 6 on the beta chain of globin, which generates multiple clinical manifestations [1]. It is recognized as a public health problem and affects around 50 million people worldwide [2]. Its evolution is interspersed with acute and chronic complications. In recent years there has been an improvement in the care of sickle cell anemia, which considerably reduces the mortality and morbidity rate of this disease. Thus, the precise analysis of the causes and co-morbidities associated with death in sickle cell patients is important for each center in order to recognize risk situations and improve hospital care, hence the goal to carry out this study at the National Reference Center for Sickle Cell Disease (CNRD) in Niamey.

Purpose: Improve the management of sickle cell anemia by studying the circumstances surrounding the death by this disease in patients who'd been followed up at the National Reference Center for Sickle Cell Anemia (CNRD) in Niamey.

Methods

Study framework

The study took place at the National Reference Center for Sickle Cell Disease (CNRD) in Niamey. The CNRD was created by decision N°011/PRN of August 12, 2009, thanks to a partnership and a financing agreement 2007-2008 between the Republic of Niger through the Ministry of Public Health (MPH), the Principality of Monaco, AMADE Mondiale and the Association for the Fight against Sickle Cell Disease in Niger (ALDN). It is a Public Scientific and Technical establishment.

Type of study and sample

It was a retrospective descriptive and analytical study conducted at the National Reference Center for Sickle Cell Disease (CNRD) in Niamey, running from January 1, 2010 to December 31, 2018, i.e. a period of 9 years. The records of patients who died during the study period served as a source of data collection. The information collected was: age, sex, socio-demographic data, acute and chronic complications, the reasons and the conditions of death. After collecting the data on a pre-established survey form, they were analyzed by SPSS 20.0 software. A value was considered statistically significant if the P-value is less than 0.05.

Results

Sociodemographic characteristics

Frequency: During the 9-year study period, two hundred and forty-nine (249) patients died out of six thousand four hundred sixty-

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Table 1: Reason for admission before death.

Reason for admission	Effective	Percentage (%)
File opening	145	58,2
Vaso-Occlusive Crisis (CVO)	82	32,9
Fever	6	2,4
Anemia	3	1,2
No determine	13	5,3
Total	249	100

Table 2: Distribution of patients by reason of death.

Reason of death	Number	Percentage
-Bind of Sickle cell anemia		
Anemia	67	26,9
Infectious	65	26,10
CVO	42	16,86
STA	40	16,02
Renal complications	10	4,3
AVC	9	3,6
Sous total	233	93,82
-Not Bind of Sickle cell anemia		
AVP	2	0,8
drowning	1	0,4
Sous total	3	1,02
-Bind not determine	13	5,2
Total	249	100

five (6,465) patients followed, representing a frequency of 3.8%. The majority of deaths occurred in 2015, i.e. 17% (n=43).

Age and gender: The CNRD are a center for the care of both children and adults with sickle cell anemia, so the majority of patients were under 15 years of age, or 38.5% (n=96). The average age was 9.25 years with the extremes of age ranging between 3 months and 49 years. Our patients were divided into 106 women or 42.6% and 143 men or 57.4%. A sex ratio of 1:3.

Level of education and consanguinity: Most of our patients were out of school, 33.3% of cases. 34.1% of the patients were the result of a consanguineous marriage.

Clinical characteristics (Table 1): The causes of admission before death were as follows, 58.2% (n=145) died when the file was opened, i.e. at the inclusion stage, followed by vaso-occlusive crisis in 32, 9% (n=82). Fever was identified in 2.4% (n=6) of the cases. Hepatic complications dominated chronic complications in 4.8% of cases, followed by cardiac complications and necrosis of the femoral heads in 3.2% of cases respectively.

Biological characteristics: Of the 249 patients, the majority were of the SS phenotype (n=234), followed by the SC (n=14) and S/β (n=1) in 94%, 5.6% and 0.4% of the cases, respectively. The last Blood Formula Count (BHC) before death was considered, all our patients had anemia, those with a hemoglobin level between 6 and 10 g/dl were predominant in 76.7% (n=191) of the cases, with a microcytosis in 42% (n=105) of the cases.

Cause of death (Table 2): We had collected the causes of death, noted in the files in association with the death certificates. Of the two hundred and forty-nine (249) patients who died, thirteen (13) were registered at home or 5.2% and 236 in a health-care center or 94.8% of cases. Among the causes of death related to sickle cell anemia, decompensated anemia was the most common at 26.90% (n=67), followed by infectious complications, vaso-occlusive crises, acute thoracic syndrome and Cerebrovascular Accidents (Stroke) in respectively 26.10% (n=65), 16.86% (n=42), 16.02% (n=40) and 3.61% (n=9). The causes of death not related to sickle cell anemia were mostly due to Road Traffic Accidents (RTA) in 0.80% (n=2). The deaths at home did not have a known cause.

Treatment: None of our patients were on specific treatment (Hydroxyurea (hydreaR), transfusion exchange), they received folic acid, painkillers and anti-inflammatory drugs as needed.

Correlation

Causes of death and age: We correlated the causes of death from sickle cell anemia, which was dominated by decompensated anemia and an age younger than15 years old. No statistically significant correlation was found with p=0.174.

The number of follow-ups and the causes of death linked to sickle cell anemia: During our study period, 6% (n=15) of patients had regular follow-ups. In correlation with the causes of death linked to sickle cell anemia, we found a statistically significant value with a p=0.003.

Discussion

In Niger, Sickle cell anemia is currently the most screened genetic disease at birth. Several authors have studied mortality linked to sickle cell anemia. It varies depending on the location and the quality of care and other factors that may decrease the life-expectancy of these patients. However, the comparison of the different published series remains difficult, since the conditions of the different studies weren't identical. So, there's an agreement that the mortality varies depending on the environment, socio-economic conditions, location and quality of care [3-5]. In our study, sickle cell disease was responsible for 3.9% of deaths recorded during 9 years. This rate varied according to the authors, since 1970, several series of studies have been published, for Seeler, it was 8.4% in Chicago, 11% of cases for Rogers [4,6]. Leikin and al, in a study carried out in the United States reported 11% of cases [7]. Kampatibe and al, in Lome reported 4.1% of cases [8]. In Libreville these rates seem low compared to ours, with in particular 3.6% of cases, 2.3% for Gendrel and al, 2.6% for Gueye B and al, in Senegal and Powars and al, in a series published in 1990, noted a mortality of 0.5% in a population of children and adults [9-11].

The peak frequency of death was observed in 2015 at 18.09% (n=43) and in children under 15 years of age (n=96) whose average age was 9.25 years. Koko J and al, in a study carried out in Gabon on the mortality of sickle cell children in a pediatric unit in Central Africa reported that the majority of deaths concerned children under 15 years old in 60.9% of cases [12]. This tendency is found in many studies, it was 68.4% in the series of Seeler, 33.3% in that of Kampatibe and Doucoure D in Mali reported 55.5% in children under 4 years of

age [4,8,13]. This could be explained by the fact that at around 12 and 48 months, HbS almost completely replaces HbF, hence the high frequency of life-threatening complications of sickle cell disease [1]. Mortality was higher in boys in our study with a sex-ratio of 1:3. Our findings are similar to those of Seeler, and Doucoure D, who reported a male predominance, but different from kampatibe and al in Togo who reported a female predominance [4,8,13].

The majority of our patients weren't schooled in 33.3% of cases and had a low socioeconomic level. 34.1% of the patients came from a consanguineous marriage. According to the literature review, the low level of education, economic difficulties, giving-up and negligence by the parents, added to the lack of information, largely explain this high mortality [14-16]. At the time of admission, the vast majority of our patients 58.2% (n=145) were seen at the inclusion stage (when the file was opened), followed by vaso-occlusive crisis in 32.9% (n=82). They were SS homozygotes (234/294). Acute anemia and infectious causes were identified as the major causes of death in 26.90% (n=67) and 26.10% (n=65) of the cases, respectively. According to the literature review, anemia and/or infection are the most common causes of mortality and morbidity, mostly in children, especially in those under 5 years of age. Asplenia and decreased opsonizing activity of the serum are the two factors that favor the onset of infection in these patients. The progression of the infection is strikingly fast, giving a clinical picture associating hyperthermia, shock, diffuse hemorrhagic syndrome with disseminated intravascular coagulation (CIVD). The deficiency in factor C3, C4, and D of the alternate pathway of complement would lead to immediate non-response to bacterial polysaccharides, hence the brutal and rapid deterioration of the patient's state [17-19]. Thus, our findings are similar to those of Thomas C and al, Seeler RA, Thomas AN and al, and Camara E, who reported a high frequency of infectious causes and anemias. None of our patients were on specific treatment [4,5,20,21]. According to the literature, early diagnosis, but above all good preventive care (vaccination, transfusion program, transfusion exchange and Hydroxyurea), will allow the majority of children to reach adulthood. However, morbidity remains important, after the age of 15-20 years appears the functional sequelae. Thus, a large clinical and biological variability has been reported, diversifying the topography of complications according to the sickle cell phenotype which are factors of poor prognosis (hemoglobin F level below 15%), especially the haplotype of the disease. The Central African haplotype has a poor prognosis; the Senegalese haplotype decreases the incidence of acute complications [7,11,22,23]. Using the combination of genetic, clinical and paraclinical criteria, it seems possible to screen a population at risk for developing irreversible complications of the disease. It is to patients of this population that the new therapies will be aimed at first: bone marrow allograft [20,24].

Conclusion

Sickle cell anemia, an inherited genetic disorder that was once known to be fatal in the first years of life, but the improved management has allowed a lower incidence of complications. However, it still remains significant. Quality of life and chronic degenerative complications, more than mortality, remain determining factors for the use of new "invasive" therapies by hydroxycarbamide or bone marrow transplant.

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