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Sickle Cell Disease in Burundi-An Un-explored Terrain?

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ABSTRACT

Introduction: Sickle Cell Disease (SCD) is one of the most common causes of mortality and morbidity in Africa. There is paucity of data on SCD from Burundi.

Methods: A cross-sectional study was conducted using a predetermined questionnaire that included socio-demographic characteristics, basis of diagnosis, common clinical scenarios, transfusion requirements, usage of hydroxyurea, usage of folic acid, and knowledge about bone marrow transplantation.

Results: Participants were 174 patients with SCD with male: Female ratio of 1:1. The median age was 10 years (1.3-42 years). The diagnosis of SCD was made by Emmel test in 139/168 (82.74%) and electrophoresis in 29/168 (17.26%) patients. Nearly 150/164 (91.4%) patients ≥ 1 episode of veno-occlusive crisis in the preceding year. Out of 165 patients, 77(45.8%) required ≤ 3 admissions, 55 (39.4%) > 3 times and 24 (14.5 %) patients reported no admission in past 1 year. Out of 166 patients, 131 (79%) reported no usage of hydroxyurea, while 35 patients (21%) reported taking hydroxyurea. Among 35, only 17 were taking hydroxyurea on regular basis and 18 were taking irregularly. Majority of patients (96.5%) were unaware of bone marrow transplantation as a curative treatment option.

Conclusion: Our data from Burundi points towards an urgent need to make hydroxyurea available and affordable. Health systems strengthening with focus on education and training of the healthcare professionals is a priority.

Keywords: Sickle cell disease; Burundi; Emmel test; Hydroxyurea

Abbreviations: SCD: Sickle Cell Disease; VOC: Veno-Occlusive Crisis

INTRODUCTION

Sickle Cell Disease (SCD) is one of the most common monogenic inherited disorders of hemoglobin worldwide and is most prevalent in Africa, with more than 80% of the disease burden in the sub-Saharan region [1,2].

An estimate 300000 babies are born each year with SCD, and this figure is expected to increase to 400 000 by 2050 and is a major contributor to childhood mortality [3]. Approximately 50% of them succumb to disease under age of 5 year.

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There's a drastic difference in the survival of patients with SCD in high income countries and low middle income countries and low income countries. Burundi is a small, landlocked, low-income nation, with practically no information reported in the medical literature on SCD. In sub-Saharan Africa, multiple datasets are available from Uganda, Rwanda, Congo, and Tanzania, bordering Burundi. One of the highest incidences of sickle cells is reported in western Uganda, which is as high as 40%, and it borders Burundi [4]. In the literature search, we could not find any substantial information related to SCD in this African country [5,6].

Most SCD manifestations are readily amenable to treatment using available interventions; however, the interventions are not accessed by most of the patients. Hydroxyl-urea increases fetal hemoglobin, reduces episodes of veno-occlusive crisis, reduces episodes of acute chest syndrome, reduced organ damage and decreased need for blood transfusions and hospital admissions [7,8]. In addition, laboratory facilities for accurate diagnoses are limited in sub-Saharan Africa. The study aimed at assessing the clinico-demographic characteristics of SCD patients in Burundi and their adherence to the recommended treatment.

MATERIALS AND METHODS

Here, we did across sectional prospective study in the patients diagnosed with SCD in Burundi.

A preformed validated questionnaire was administered to the participants after obtaining informed consent. This questionnaire included family status, basis of diagnosis, common clinical scenarios, transfusion requirements, usage of hydroxyurea, usage of folic acid, and knowledge about bone marrow transplantation.

RESULTS

A total of 174 patients of SCD participated. The study included 87 men (49.4%) and 88 women (50.7%) with a median age of 10 years (1.3-42 years). Thirty-two (23.9%) participants had ≥ 6 siblings (**Table 1**). The basis of diagnosis of SCD was Emmel test in 139/168 (82.74 %) and electrophoresis in 29/168 (17.26%) patients.

Table 1: Baseline characteristics of patients with sickle cell disease.

Baseline characteristics		Number	
Gender (Total no 175)	Male	87	49.70%
	FeMale	88	50.30%
Median age (range)		10	1.3-42
Age group (years)	<10	86	49.10%
	10-19	54	30.90%
	20-29	32	18.30%
	30-39	2	1.10%
	40-49	1	0.60%
Number of siblings in the family (evaluated 134)	1	5	3.70%
	2	12	9.00%
	3	30	22.40%
	4	28	20.90%
	5	27	20.10%
	6 or more	32	23.90%

Veno Occlusive Crisis (VOC) remains the most common clinical symptom reported. Questions about pain crisis were answered by 164 participants. Nearly 150 (91.4%) reported ≥ 1 episodes of VOC in the preceding year. Fourteen patients (9%) reported no episode of VOC in the last year. Admissions attributed to pain were not uncommon. One hundred thirty four (81.7%) patients attributed their admission for pain crisis in the past 1 year. The most common site of pain was joint pain, followed by generalized body ache. Nine patients reported experiencing Acute Chest Syndrome (ACS) in the preceding year. Avascular necrosis of hip was reported by five patients, and two patients reported frank arthrosis of the joints.

Blood transfusions are an important hallmark of this disease. Only 29/160 (18.2%) reported that they had not received any

blood transfusion in the preceding two years, whereas 76/160 (47.5%) had received ≤ 3 transfusions, and 55/160 (34.3%) had received >3 blood transfusions. Patients require regular admission to healthcare facilities for various reasons. Only 24/165 (14.5%) patients reported that they had no requirement for admission, in recent past, whereas 77/165 (45.8%) required up ≤ 3 admissions in last two years, and 64/165 (39.4%) needed to be admitted >3 times.

Four patients reported to have a history of stroke. Skin ulceration was rare and was observed in only two patients. One case of cardiomyopathy has been documented.

Globally, hydroxyurea remains the cornerstone for treatment. Only 35/166 (21%) patients were reported to have used hydroxyurea, while 131/166 (79%) had never used hydroxyurea for disease management (**Table 2**).

Table 2: Treatment details of patients with sickle cell disease.

Hydroxyurea	Number (percentage)
Is patients taking hydroxyurea	
Yes	35 (21)
No	131 (79)
If patient taking hydroxyurea	
Are they taking hydroxyurea	
Regularly	18 (52)
Irregularly	17 (48)
If patient taking hydroxyurea	
Age group	
<10	20 (57)
45218	11 (31.5)
20-29	4 (11.5)

Of these patients, only 18/166 patients were regularly taking hydroxyurea and 17/166 were irregularly taking hydroxyurea. Among the 131 participants, who had never used hydroxyurea, 102 (78%) patients attributed it to non-prescription by a physician, 22 (16.8%) attributed it to non-availability of drug and 7 (5.2%) to the high cost of drug. More than 70% of the patients were regularly taking folic acid. Only 6/175 patients reported their knowledge of bone marrow transplantation as a treatment alternative; all others (96.5%) were unaware of such a procedure.

DISCUSSION

Africa has always been a focus of SCD research. This is the first report on Burundi that attempts to understand the clinico-demographic parameters and treatment details of patients with SCD. Interestingly most of the families were large in size, 87% of the families had more than three siblings in the family and about 24% more than six siblings. A greater number of siblings increase the likelihood of finding a donor with HLA match for a transplant.

The median survival of SCD patients in Africa is less than five years; about 50%–80% of the estimated 400,000 infants born yearly with SCD in Africa die before the age of five years [1,9-11]. The age distribution in our series showed that patients who attended the camp were in the younger age group. This could be the result of early death. Confirmatory testing for a diagnosis remains a significant challenge. Most patients are diagnosed and live with a report of the Emmel test [12]. The Emmel test, is a screening test based on the observation of red blood cell sickling when exposed to low oxygen tension, is often the only available option. However, it cannot distinguish between sickle cell traits (*i.e.,* heterozygote carriers) and sickle cell disease; electrophoretic confirmation and quantification of hemoglobin were observed in only 17% of patients. Studies published from Mali and Congo has showed low sensitivity and high specificity of Emmel test [13,14]. There is an urgent need to establish proper diagnostic facilities that can help with the confirmation and follow-up of these patients.

Pain crises in the preceding year were reported by more than 90% of patients. This high incidence could be explained by the lack of disease-modifying treatments. The number of admissions to healthcare facilities is a major indication for transplant for sickle cell disease. In our series, 85.5% of the patients required hospital admission. Providing transfusion support is a large burden on the public health system.

The proportion of transfused SCD patients varies from different studies, between 30% and 90% [15]. In our cohort 82% of patients had received transfusion in the recent past. Transfusion requirements may not be true measure of the blood requirement as there are no transfusions guidelines followed. The decision to transfuse is based on hemoglobin level and many a times “as judged by the patient.” Inadequate

blood supply is one of the biggest challenges when dealing with transfusion in SCD in Africa. There is an urgent need to establish and popularize transfusion guidelines for both patients and healthcare workers to reduce the burden on health systems and raise safety bars for patients.

Hydroxyurea is the most important pharmacological intervention to reduce pain and improve survival. Subsequently, reports described the short term safety and efficacy for pediatric patients receiving open label hydroxyurea treatment [16-18]. Baby hug trial confirmed the safety and efficacy of hydroxyurea therapy for very young children (9 months-18 months) with sickle cell anemia [19]. REACH trial assessed the feasibility, safety, and benefits of hydroxyurea treatment in young children with sickle cell anemia living in sub-Saharan Africa and have showed reduced rates of vaso-occlusive pain, non-malaria infection malaria, transfusion and death [8]. In our cohort, 79% patients were not taking hydroxyurea. Access to hydroxyurea is the most important contributor to this disparity. Making Hydroxyurea Affordable for Sickle cell disease in Tanzania is Essential (HASTE) study from Tanzania showed that the cost of a monthly supply of hydroxyurea ($35.16 USD) was equivalent to approximately 25 days' pay for the average unskilled Tanzanian government employee [20]. Our data further reiterate this point in Burundi. Therefore, there is an urgent need to make hydroxyurea available and affordable. A very small number of patients (17/163) regularly took hydroxyurea, whereas more than 90% experienced pain crises. Similar to our findings, sectional study from Nigeria, on barriers to therapeutic use of hydroxyurea for sickle cell disease concluded that 27.1% of the physicians reported no formal training on prescribing hydroxyurea, 7.1% physicians were not confident about prescribing hydroxyurea to their patients, 25.7% physicians stated that hydroxyurea is expensive and could not be afforded by their patients and majority (67.1%) of physicians believed that hydroxyurea is expensive [21]. Education of healthcare workers and creation of a chain of workers with complete prescription skills is the immediate mandate.

Care for SCD in Burundi appears to be an unmet urgent need. Therefore, it is necessary to establish appropriate, accessible, and cost-effective diagnostic facilities. Hydroxyurea availability and accessibility must be established without delay. Large international efforts, such as Global Alliance for Vaccine and Immunization (GAVI) and The U.S. President's Emergency Plan for AIDS Relief (PEPFAR), are required to change the situation, allowing easy access to disease modifying treatments [22]. To achieve this, a structured approach is needed to strengthen the health system.

CONCLUSION

Our data from Burundi points towards an urgent need to make hydroxyurea available and affordable. Health systems strengthening with focus on education and training of the healthcare professionals is a priority.

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AUTHOR'S CONTRIBUTION

The study planning, designing, analysis and review of drafts was equally done by both the authors.

CONFLICTS OF INTEREST

Both authors DP and GN have no conflict of interest to disclose.

FINANCIAL INTEREST

Both authors DP and GN have no financial interest to declare.

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