

Urinary Profile of Sickle Cell Disease Patients in Acute Crisis in Brazzaville

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ABSTRACT

Introduction: The renal complications of sickle cell disease have a spontaneous evolution towards chronic renal failure, with the need for dialysis or renal transplantation. Renal damage is frequent, early and disabling; it is a major cause of mortality. It appears as early as the first decade, it is most often asymptomatic, evolves insidiously and is sometimes discovered by chance. The aim of our study is to describe the urinary profile of patients living with sickle cell disease and in acute crisis.

Patients and method: This is a descriptive cross-sectional study, conducted over a period of four months (from 01 August to 29 November 2019) at the National Reference Centre for Sickle Cell Disease. It focused on homozygous sickle cell patients admitted for an acute crisis. Urine dipstick was performed in each patient, and we assessed parameters such as pH, leukocyturia, hematuria, proteinuria, ketonuria and nitrites.

Results: 219 patients were included in the study (58 % female and 42 % male). The mean age was 20 ± 11 years with extremes of 3 and 59 years. Acute hemolysis crisis was the most frequently encountered emergency (49.3 %). 27.9 % of patients had positive proteinuria; 21.9 % had hematuria; 11.9 % had leukocyturia; 3.2 % had positive nitrites on urine dipstick.

Conclusion: The urine dipstick is a simple means of screening for renal damage in sickle cell disease. It should be performed routinely in all patients seen in acute crisis or during routine visits.

Keywords: Urinary profile, Sickle cell disease, Acute crisis, Brazzaville

INTRODUCTION

Sickle cell disease is a single mutation genetic disease with an autosomal recessive transmission related to a qualitative abnormality in the structure of hemoglobin, which results in the formation of hemoglobin (Hb) S [1].

Under favorable conditions such as hypoxia, dehydration, acidosis or infection, this abnormal hemoglobin polymerizes in the red blood cell [2], causing rheological changes, rigidification and falciformation; origin of acute and chronic complications [3], with repercussions on the organs, including the kidneys. The renal manifestations have a spontaneous evolution towards the installation of a chronic renal insufficiency, with the necessity of dialysis or even renal transplantation [4,5].

Renal damage in patients with sickle cell disease is frequent, early and disabling; it is a major cause of mortality. It appears as early as the first decade [6-10]; its global prevalence is estimated at 25% in children aged 2 to 8 years [7-10].

In young adults with sickle cell disease, the prevalence of

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renal damage reaches 40% with in half of the cases a rapid progression to end-stage renal failure [7,11-13].

Renal damage is most often asymptomatic, evolving insidiously and sometimes being discovered sometimes discovered by chance.

The aim of our study is to describe the urinary profile of patients with homozygous sickle cell disease admitted in acute crisis.

PATIENTS AND METHOD

This is a descriptive cross-sectional study conducted over a period of four months (from August 1 to November 29, 2019) at the National Reference Center for Sickle Cell Disease (NRCSCD) “Antoinette SASSOU NGUESSO” in Brazzaville. It focused on sickle cell patients admitted to the emergency room for an acute crisis (vaso-occlusive crisis, anemic crisis, fever, etc.). All homozygous sickle cell patients were included in the study. Any patient who came for a routine check-up (who was in apparent good health) was excluded. We systematically performed a urine dipstick (UD) on freshly passed urine collected in a clean jar, and assessed pH, leukocyturia, hematuria, proteinuria, ketonuria, and nitrites in each patient. Data collection was done using a

survey form, the patient follow-up form, and the NRCSCD emergency room consultation log. Data entry was done using Excel 2013 software. R software version 4.1.0 was used for data analysis.

RESULTS

We included 219 patients in our study. There were 127 female patients (58%) and 92 male patients (42%). The sex ratio was 0.42. The mean age of the patients was 20 ± 11 years with extremes of 3 and 59 years. The most represented age group was 15-59 years (67.6%). Of these 219 patients, 136 were being followed up (62.9%); and 83 were not (37.1%). 108 patients (49.3%) had an acute hemolysis crisis; 106 patients (48.4%) had a Vaso occlusive crisis (bone or abdominal). Fever was found in 32.4% of cases. Malaria was the most common etiology. The hematological parameters are shown in **Table 1**. 61 patients (27.9%) had positive proteinuria; 48 patients (21.9%) had positive hematuria; 26 (11.9%) had positive leukocyturia; 7 (3.2%) had positive UD nitrites (**Table 1**). Only 47 patients had achieved creatinine levels and the mean was 93 ± 89 $\mu\text{mol/l}$ with extremes of 17 and 532 $\mu\text{mol/l}$. Acute attacks of hemolysis were the most frequent emergency encountered, in 49.3% of cases (108 patients) (**Table 2**).

Table 1. Patients' parameters.

Parameters	Mean	Standard deviation	Median	Q1	Q3	Minimum	Maximum
Age (years)	20	11	19	12	24	3	59
SpO2 (%)	93	6,9	95	90	98	55	99
pH	6	0,63	6	6	6	5	9
Hb (g/dl)	6,5	1,8	6,4	5,3	7,7	2,1	11
Hct (%)	19	5	19	16	22	6,2	34
MCV	81	11	80	74	87	56	123
CCMH	34	2,4	34	33	36	27	49
WBC (G/l)	19	13	16	11	22	3,5	98
Platelets (G/l)	329	159	315	211	416	14	940
Creat ($\mu\text{mol/l}$)	93	89	66	56	88	17	532

Q1: quartile 25; Q3: quartile 75

Table 2. Frequency of abnormalities at UD.

UD Findings	n=219	Percentage (%)
Positive proteinuria	61	27,9
Positive hematuria	48	21,9
Positive leukocyturia	26	11,9
Positive Nitrites	7	3,2

DISCUSSION

Renal manifestations in sickle cell disease are secondary to sickle cell disease, which is promoted and maintained by acidosis and hypoxia in the renal medullary [8,14]. Intracapillary sickle cell disease increases the blood viscosity of the renal medullary. This results in the formation of micro-thrombosis of the vasa recta, reactive secretion of vasodilating substances and deposition of interstitial hemosiderin. These phenomena are responsible for functional disorders, glomerular hyperfiltration, hematuria, renal infarction, papillary necrosis and interstitial fibrosis that can progress to chronic renal failure [14,15]. The lack of perfusion may lead to increased sensitivity of the renal parenchyma to infectious agents [8].

Study population

Our study population was predominantly female. The sex ratio was 0.42 in favor of women. This result is similar to those of other studies [16-19] which reported ratios ranging from 0.33 to 1.1 in favor of females. The study by Kaze [20] found a ratio in favor of men. This difference could be explained by the small sample size of their study which was 72 (one third of our sample size). The mean age of our patients, 20 ± 11 years, was identical to those found in the literature by many authors and ranged from 19.4 to 23.5 years [16,19-21]. This average age is slightly lower than that of the Malian series by Fongoro [9], which was 30.1 years. This result reflects an increase in the life expectancy of our sickle cell patients over the last few years, an increase that would be linked to the improvement of their management.

Proteinuria (UP)

This is the first urinary anomaly found in our study in terms of frequency. It was found in 27.9% of cases. This result of a positive UP at the UD is similar to those of other studies which reported values of between 20% and 54% in homozygous sickle cell patients [9,20,21]. This result is significantly higher than those reported by Nke Ateba [16] in Yaoundé, Ogwu [22] in Port Harcourt, Nigeria, Olorukooba [23] in Zaria, Nigeria, Uchenna [24] in Nigeria and Osei-Yeboah [25] in Accra, Ghana, which were respectively 10.8%, 7, 6.5%, 3.4% and 2.8%. This difference could be explained in the case of the Nke Ateba study by the inclusion criteria which eliminated any subject who was ill or had been transfused in the last three months before the study period. As for Ogwu, Olorukooba, Uchenna and Osei-Yeboah, their work focused only on pediatric populations (children aged 16 months to 16 years, 2 to 17 years, 2 to 18 years and 1 to 12 years respectively). It is therefore appropriate to recall that proteinuria and microalbuminuria do not appear before the age of 7 years and their prevalence increases with age [14,18,25-27]. This increase with age would explain the prevalence observed in samples consisting mainly of adults. This is in agreement with Ebah who emphasizes that proteinuria is related to the duration of

sickle cell disease [11,28]. It is therefore important to test at least twice a year for dipstick UP or microalbuminuria, starting at the age of 5 years [7,22,25].

Hematuria (UH)

This is one of the most common manifestations in sickle cell disease (sickle cell nephropathy), regardless of age. It is almost always macroscopic and painless, but can also be microscopic and painful or not. Hematuria may originate in one or both kidneys. It results from papillary necrosis or micro thrombotic infarcts in the vasa-recta and peritubular capillaries of the renal medulla, with extravasation of blood into the collecting tubes [14,15,29]. It is also associated with infections or delayed transfusion reactions. Hematuria should be investigated systematically for urinary tract infection or papillary necrosis.

UH is the second most common renal event in our series. It was positive in 21.9% of our patients. This result is in line with those of many African series south of the Sahara which report frequencies ranging from 10.3% to 26% [17,20,23,30,31]. The frequencies of 11% [22], 6.7% [24], 5.6% [19] and 3.3% [25] reported respectively by Ogwu, Uchenna, Fall and Osei-Yeboah were lower than the 21.9% frequency found in our study. The small number of patients (36 in Fall's study; 60 in Uchenna's study and 72 in Ogwu's study) could justify this difference. The disparity in frequencies could also be explained by the fact that these studies are pediatric series, and that they were carried out in the inter-critical phase only. Also, possible errors in the reading of urine strips cannot be excluded.

Leukocyturia and nitrites

The increased susceptibility of sickle cell patients to urinary tract infections compared to the general population has been widely demonstrated in the literature.

Asymptomatic bacteriuria is common in sickle cell patients compared to the general population [25,32-36], and even more so in female sickle cell patients [35,36]. It can lead to overt urinary tract infection. In our series, leukocytes and nitrites, known to be indicators of a potential urinary tract infection, were found at frequencies of 11.9% and 3.2% respectively. These values are identical to those found by Osei-Yeboah in Accra, Ghana, who reported leukocyturia at 12.6% and 2.2% for nitrite in a pediatric series [25]. In this series, the controls with AA children were 5.7% and 1.4% respectively. Kaze [20] in Yaoundé, Cameroon, reported a frequency of leukocyturia of 77.8%. This difference could be explained by the small sample size of their study (72) compared to ours. Any asymptomatic urinary tract infection should therefore be identified and treated to prevent renal complications. The urine dipstick is a key means of early detection of these infections specially in a resource limited setting, in order to initiate treatment to minimize these complications.

Our study had limitations: creatinine levels in admitted patients and cyto-bacteriological examination of urine requested in patients with leukocyturia and/or nitrites at BU were only performed by a minority of patients. 24-hour proteinuria was not performed in any of the patients with positive UD proteinuria. Renal ultrasound was not routinely requested in patients with elevated creatinine levels. The main reason for these shortcomings is a financial problem.

CONCLUSION

Urinary anomalies are common in sickle cell disease. The urine dipstick is a simple and effective means of screening for sickle cell nephropathy. It should be performed systematically in all sickle cell patients, whether they are seen in an acute crisis or as part of a routine visit. This would allow early detection of nephropathy and the initiation of measures to avoid spontaneous progression to chronic renal failure, which is not easy to manage in our context.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

AUTHORS' CONTRIBUTIONS

Data collection and entry, interpretation of results and writing of the article were carried out by Talomg Tamekué. Data analysis was carried out by Simo Louokdom. Tchidjo Ngamo, Malanda and Ngolet Ocini contributed to the writing of the article and its critique. Elira Dokékias supervised the work. The final version of the manuscript was read and approved by all authors.

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