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## Pyuria as a diagnostic test for urinary tract infection in children with sickle cell anaemia in Zaria, Nigeria

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**Abstract:** *Objective:* This study aimed at determining the significance of pyuria as a screening test for UTI in children with sickle cell anaemia (SCA).

*Methods:* Two hundred and seventy-two children with SCA, aged 6 months to 15 years, were studied out of which 185 (68.0%) were in stable state and 87 (32.0%) were in crises. Their urine was assessed for microscopy culture and sensitivity. Significant pyuria and bacteriuria was determined using standard methods.

*Results:* Significant bacteriuria was detected in 22 (8.1%) of the 272 subjects with SCA. The prevalence of significant bacteriuria was higher among those in crisis (18/87; 20.7%) than in those

in steady state (4/185; 2.2%) and the difference was statistically significant ( $\chi^2 = 27.323$ ,  $p = 0.001$ ). Of the 22 SCA subjects with confirmed UTI, 19 (86.4%) had significant pyuria with a sensitivity of 86.4%, specificity of 68.8%, and positive predictive value of 19.6%. The most common bacterial isolates were *Escherichia coli* 11 (50.0%) while the least isolated were *Salmonella typhi* 1 (4.6%).

*Conclusion:* This study indicates that pyuria as a screening test for UTI is not very specific but very sensitive necessitating a more test to be done for diagnosis of UTI.

**Keywords:** Sickle cell anaemia, bacteriuria, pyuria, children

### Introduction

Urinary tract infection (UTI) is an important contributing factor to morbidity and mortality in children with SCA and may be a precipitating event for the crises associated with the disease<sup>1</sup>. Bacteriuria, presence of bacteria in urine not due to contamination from sample collection,<sup>2</sup> can be symptomatic or asymptomatic. Bacteriuria can resolve spontaneously, especially when asymptomatic, or can progress to chronic nephropathies like chronic pyelonephritis, particularly in situations of altered immunity such as sickle cell anaemia<sup>3</sup>. Very often, the dramatic manifestations of vasoocclusive crisis and life-threatening anaemia cause the attending physician to overlook coexisting infection<sup>4</sup>. Urinary tract infections (UTI) in children with sickle cell anemia (SCA) may result in long term renal dysfunction<sup>5</sup>.

Various methods of screening for UTI have been employed globally but the most commonly used in this part of the world is urinalysis either by dipstick or direct microscopic examination of centrifuged urinary sediments<sup>6</sup>. Pyuria has been found to be a useful tool in the diagnosis of UTI. The prevalence of significant pyuria in children with SCA with bacteriuria and without bacteri-

uria was reported to be 55.4% and 22.2% respectively<sup>7</sup>. In comparison, Akor *et al*<sup>8</sup> in Jos, reported a much lower prevalence (1.5%) of significant pyuria in 650 apparently healthy primary school children aged 5 – 12 years. Therefore, this study was undertaken to determine the significance of pyuria as a screening test for UTI in children with SCA seen in ABUTH.

### Subjects and methods

The study was a prospective, descriptive and cross-sectional one. The study sample population consisted of consecutively selected children with SCA (in steady state and in crisis) aged 6 months to 15 years, seen in the Department of Paediatrics, Ahmadu Bello University Teaching Hospital (ABUTH), Zaria, over a period of six months. Children with SCA who had been on antibiotics one week preceding enrolment into the study, those with confirmed (or suspected) congenital urogenital anomalies and those who had recent (< 1 week) manipulative urogenital procedure (like catheterization and cystoscopy) were excluded from the study. Also those whose parents or guardians did not consent and those with

HbSC and other forms of sickle cell disease other than SCA were excluded.

Ethical approval was obtained from the ABUTH Research Committee and a written consent obtained from/guardians of subjects.

#### Sample collection, transportation and culture

For each patient that has achieved bladder control mid-stream urine specimen (5mls) was aseptically collected at the time of presentation into two sterile universal bottles. For adolescent girls a trained female resident doctor assisted in collection of the specimens. For infants, moribund patients and children who were not toilet trained, suprapubic bladder aspiration (SPA) was used for obtaining the urine specimens. All urine specimens were obtained under aseptic procedures as described by Anochie *et al.*,<sup>9</sup> as follows: each subject's external genitalia was cleaned, midstream urine was collected, stored in a refrigerator and then submitted to the laboratory within an hour of collection. This procedure was carried out in order to minimize bacterial contamination of the urine. Samples were analysed within an hour of collection, otherwise they were kept in a refrigerator and or preserved in boric acid and analysed within 3-5 hours. Five milliliters of the urine was centrifuged at the main microbiology laboratory of the teaching hospital at 2000 rpm for 5 minutes; a wet preparation was made from the sediment and examined under the microscope at x40 magnification. More than five pus cells per high power field (HPF) were regarded as significant pyuria. A portion of another aliquot was inoculated onto blood and MacConkey agar plates and incubated aerobically at 37°C for 48 to 72 hours. A pure colony count of  $\geq 10^5$  organisms/ml of urine were considered a significant growth. Other sets of culture plates were incubated in carbon dioxide extinction jar at the same temperature for isolation of anaerobes. In case of significant bacteriuria, systematic bacteriology and biochemical tests using standard techniques; catalase, oxidase, sugar fermentation, motility, urease, citrate, indole, hydrogen sulfide and gas production were carried out based on bacterial gram reactions. Antimicrobial sensitivity test were carried out using modified Kirby-Bauer's diffusion methods where zones of inhibition were measured.<sup>10</sup> Those with positive culture results were treated accordingly.

#### Data analysis

Data was analyzed using Epi Info version 3.5.3 statistical software. Values were expressed as frequency, mean and standard deviation. Chi-square test was used to determine the level of significance. P-values less than 0.05 were considered significant.

## Results

A total of 272 subjects with SCA were studied and their ages ranged from six months to 15 years with a mean age ( $\pm 1$  SD) of 6.4  $\pm$  3.8 years. The mean age of SCA

subjects in steady state was 6.8  $\pm$  3.9 years while that of those in crisis was 5.6  $\pm$  3.7 years and they were not significantly different from each other. There were 156 (57.4%) males and 116 (42.6%) females with male to female ratio of 1.3: 1 (Table I). There was no statistically significant difference in the distribution of age groups between the sexes ( $\chi^2=0.59$ ,  $df=2$ ,  $p=0.745$ ). One hundred and eighty five (68.0%) SCA subjects were in steady state and 87 (32.0%) were in crisis. (Table 1)

**Table 1:** Age and sex distribution of SCA subjects in crisis and in steady state

Ages (Years)	In steady state, n (%)		In crisis, n (%)		Total
	Males	Females	Males	Females	
< 5	35 (33.3)	27 (33.8)	26 (51.0)	18 (50.0)	106 (84.1)
5-9	40 (38.1)	35 (43.8)	16 (31.4)	11 (30.6)	102 (71.5)
10-15	30 (28.6)	18 (22.5)	9 (17.6)	7 (19.4)	64 (44.3)
Total	105(100)	80 (100)	51 (100)	36 (100)	272 (100)

Of the 185 SCA children in steady state, 62 (33.5%) were <5 years of age and 75 (40.5%) and 48 (25.9%) were 5-9 and 10-15 years of ages respectively. The corresponding proportions in children in crisis were 50.6%, 31.0% and 18.4% (Table I). There was a statistically significant difference in the proportions of children in the lowest age group; the proportion of those in steady state (33.5%) being less than the one for those with crisis (50.6%;  $\chi^2 = 7.28$ ,  $df=2$ ,  $p = 0.026$ ). Of the 87 subjects with SCA in crisis, 55 (63.2%) and 32 (36.8%) had vaso-occlusive and anaemic crises respectively. Their corresponding mean ages were 5.5 ( $\pm$ 3.6) and 5.0 ( $\pm$ 4.4) respectively and were not significantly different from each other.

Of the 272 children with SCA studied, 22 had significant bacteriuria giving an overall prevalence of 8.1%. Four (2.2%) of the 185 SCA subjects in steady state had significant bacteriuria while 18 (20.7%) of those in crises had significant bacteriuria, the difference in respective prevalence being statistically significant ( $\chi^2 = 27.3$ ,  $df = 1$ ,  $p < 0.001$ ). A total of 22 bacteria were isolated from the urine samples, mainly gram negative organisms. The most frequently isolated organisms were *Escherichia coli* (11; 50.0%) and *Klebsiella pneumoniae* (5; 22.7%). The least common isolates were *Staphylococcus aureus* (2; 9.1%) and *Salmonella typhi* (1; 4.6%; see Table 2). The organisms were mainly sensitive to ceftriazone and resistant to co-trimoxazole.

**Table 2:** Urinary bacterial isolates among patients

Organisms	Frequency (%)
<i>Escherichia coli</i>	11 (50.0)
<i>Klebsiella</i> species	5 (22.7)
<i>Proteus</i> species	3 (13.6)
<i>Staphylococcus aureus</i>	2 (9.1)
<i>Salmonella typhi</i>	1 (4.6)
Total	22 (100.0)

Of the 272 children with SCA, 97 (35.7%) had significant Pyuria. There were 56 (35.9%) males and 41 (35.3%) females and the difference was not statistically

significance ( $p = 0.97$ ). Pyuria was commonly found among the under-fives occurring in 45 (46.4%) children while 29 (29.8%) and 23 (23.7%) children with pyuria were among the 5-9 years and 9-15 years respectively. Of the 22 children with sickle cell anaemia and significant bacteriuria 19 (86.4%) had significant pyuria, while only 78 (31.2%) out of 250 with no bacteriuria had significant pyuria. The screening test had sensitivity, specificity and positive predictive values of 86.4%, 68.8% and 19.6% respectively. Pyuria was associated with increased risk of bacteriuria ( $p < 0.001$ ) (Table 3).

**Table 3:** Urine microscopy (pyuria) and culture

Pyuria	Urine culture Significant growth (%)	Insignificant growth (%)	Total
Significant pyuria	19 (86.4)	78 (31.2)	97 (35.7)
Insignificant pyuria	3 (13.6)	172 (68.8)	175 (64.3)
Total	22 (100)	250 (100)	272 (100)

$p < 0.001$  ( $\chi^2$ )

Sensitivity = 86.4%

Specificity = 68.8%

Positive predictive value = 19.6%

Negative predictive value = 98.3%

## Discussion

The overall prevalence of significant bacteriuria in children with SCA in this study was found to be 8.1%. This agrees with the study by Tarry *et al.*,<sup>11</sup> in USA, in which an overall prevalence of 9.0% bacteriuria was determined among children aged 1-18 years with SCA. Children in steady state had a significantly lower rates (2.2%) compared to those in crises. This was lower than that reported by Chukwu *et al.*<sup>12</sup> who documented a higher prevalence of 6% among steady state SCA children aged 2 – 12 years. The slightly lower prevalence observed in this study could be attributed to the variation in the age distribution in the two studies as well as differences in the environmental and genetic constitution of the study populations.

The 35.7% prevalence of significant pyuria in this study was lower than that obtained by Mava *et al.*<sup>7</sup> where they reported the prevalence of pyuria to be 55.4% among 65 SCA children with bacteriuria aged 6 months to 12 years. This may be due to the fact that most children with bacteriuria in steady state may have contributed to the lower prevalence as Mava *et al.*<sup>7</sup> studied febrile SCA children. The relationship between pyuria and bacteriuria was found to be statistically significant since pyuria was found to be associated with increased risk of bacteriuria ( $p < 0.001$ ). The lower prevalence, 31.2%, of significant pyuria among SCA children without bacteriuria obtained in this study was similar to that reported by Mava *et al.*,<sup>7</sup> 22.2%, among similar group of SCA children. However, the much lower prevalence obtained by Akor *et al.*<sup>8</sup> could be because children less than 5 years of age, who were more prone to developing UTI compared to older children, were not included in the study. The finding of significant pyuria to be commoner among children less than five years of age in this study might be explained by the immune-compromised nature of this

age group. This study also revealed that pyuria was commoner among boys than girls and this may be due to the fact that infection is generally commoner among boys than girls as a result of genetic variations between the two sexes.

This study revealed pyuria with a high sensitivity but low specificity of 86.4% and 68.8% respectively. These findings indicate that presence of pyuria is highly suggestive of UTI but absence of pyuria does not exclude UTI. The positive predictive value revealed that only 19.6% of patients with confirmed UTI have the disease. This suggests that pyuria is not a worthwhile screening test for UTI. However, the absence of pyuria in children with UTI is rare but can occur when a child is being evaluated so early in the course of the infection when the inflammatory response has not yet developed.<sup>13</sup> Many workers, on the contrary, reported low sensitivity of pyuria among children with UTI.<sup>7,14</sup> The higher sensitivity reported in this study as compared to the 55.4% reported by Mava *et al.*<sup>7</sup> may be due to the fact that most of the SCA children with bacteriuria in this study were in SCA crises which could have been precipitated by UTI. The negative and positive predictive values, for this study, were 98.3% and 19.6% respectively. This implies that to use significant pyuria to diagnose or predict bacteriuria in children with SCA will result in significantly large numbers of false-positive and false-negative results. The high sensitivity obtained in this study is comparable to that of Smith *et al.*<sup>10</sup> as well as Blum *et al.*<sup>15</sup> who reported sensitivities of significant pyuria to be 64% and 98% among subjects with significant bacteriuria. The specificity in our study was low in contrast with specificity of 68% reported by Blum *et al.*<sup>13</sup> The use of symptomatic women as their sample population for the study may contribute to the observed significant difference.

## Conclusion

This study has demonstrated that presence of pyuria is only suggestive of UTI but it is not a reliable screening test for UTI in children with SCA in crises as revealed by the very low positive predictive value. Routine screening of all such cases for pyuria is, therefore, not strongly advocated.

## Authors Contributors

MS conceived the study, participated in the design and coordination of the study, collected the samples, contributed in the laboratory work, analyzed the result and wrote the final manuscript. HA, GO and MA participated in the design, writing, analyzing and supervision of the study. A participated in the design and coordination of the study and collected the samples. A assisted in the aspect of laboratory coordination of the study. All authors read and approved the final manuscript.

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