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SIGNIFICANCE OF PYURIA IN THE DIAGNOSIS OF URINARY TRACT INFECTION IN CHILDREN WITH SICKLE CELL ANAEMIA IN MAIDUGURI, NIGERIA

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ABSTRACT

Urinary tract infection (UTI) is a significant cause of morbidity and mortality in children, especially in those with sickle cell disease, who are at higher risk of infections. It will be useful to have a simple test which can be used in resource limited health facilities as a means of screening such children for UTI with the view to instituting prompt treatment. This study is carried out to determine the usefulness of significant pyuria in detecting UTI in febrile children with sickle cell anaemia (SCA).

Two hundred and fifty febrile children with sickle cell anaemia that attended State Specialist Hospital and University of Maiduguri Teaching Hospital (UMTH) were prospectively studied with their consent. Urine sample was collected using standard procedure, examined for pus cells and was cultured at the Microbiology laboratory of UMTH.

The study showed UTI prevalence of 26%. Significant pyuria was found to have sensitivity of 55.4%, specificity of 77.8%, the efficacy of the test was 72.0% and the test has low positive predictive value of 46.8% in detecting bacteriuria in SCA patients.

The significant pyuria observed in this study support its usefulness in the diagnosis of UTI among children with SCA especially in communities having limited facilities or personnel for carrying out urine culture.

Keywords: *Sickle Cell Anaemia, Bacteriuria, Pyuria*

INTRODUCTION

Urinary tract infection is a significant cause of morbidity in children and those with sickle cell anaemia (SCA) have been reported to be at high risk (1, 2). Diagnosis is often missed in children because symptoms and signs are not overt and usually not necessarily referable to the urinary tract (3). This may be compounded in SCA children who may be having vaso-occlusive crisis involving the abdomen, making it more difficult to differentiate from urinary tract infection (UTI). The prevalence of UTI varies from 0.4% to 7.5% in different childhood populations and there is no age limit for this disease; even newborn are susceptible (4, 5). High prevalence of 6% to 26% has been reported in SCA children (6, 7, 8, 9, 10, 11). Prompt diagnosis of all cases of UTI in children with SCA is highly desirable. Simple test that is sensitive to allow initiation of treatment to relieve symptoms and prevent long term complications of UTI such as renal scarring and other complications is vital (12). There are various methods of diagnosing UTI in children. The gold standard of diagnosis is by culture of clean voided midstream urine or by suprapubic bladder aspiration: A pure growth of $>10^5$ colony-forming units (CFU) per milliliter of freshly passed urine (13) or any growth from urine that has been obtained by correctly performed suprapubic bladder puncture (14, 15). Transurethral bladder catheterization (TUBC) can also be done to obtain urine for culture (16). The

diagnoses of pyuria (leucocyturia) are done on fresh, uncentrifuged / centrifuged urine (17, 18). Quantification of pyuria and its relationship to

bacteriuria and presence of symptoms is important in differentiation between colonization and infection (18, 19). A urinary white cell count of ≥ 10 cells/ μ l in uncentrifuged urine is taken as significant, while value of ≥ 5 cells/ μ l of centrifuged urine is taken as significant (13, 18, 19). There has been a report of pyuria being absent in 50% of patients with significant bacteriuria (18). On the other hand there are numerous other causes of pyuria such as urinary calculi, appendicitis, non infective glomerulonephritis, severe dehydration and chemical injury to the urinary tract (13, 18). Other findings that can be seen in a child with suspected UTI include; haematuria which occurs in one third of children with UTI, proteinuria can also occur in UTI but its absence does not exclude it (14, 15, 18). Urine samples obtained must be processed immediately or preserve in a boric acid solution which preserve pus cells and the bacteria (17). However, this culture could cause delay and the facilities may not be there in most impoverished economies. This will lead to delay in treatment of acutely ill child. Urine microscopy looking for pus cells can provide immediate diagnostic information to enable initiation of treatment. Looking at the techniques and the

resources needed to diagnosed UTI using the gold standard may not be possible in a developing economy like Nigeria that are often confronted with varying degree of challenges ranging from absent or inadequate quality equipment and reagents to unqualified personnel, as well as operational logistics (20, 21, 22). Any method that could be used to solve these problems should be encouraged. It would be useful to have a simple test which can be used in resource limited health facilities as a means of screening such children for UTI with view to instituting prompt treatment. There has been a doubt as to whether assessment of pyuria can be an indicator for infection of urinary tract (19, 23, 24). The use of significant pyuria as a screening test for UTI has not been evaluated recently in our region. Therefore, this study was designed to evaluate the usefulness of significant pyuria in detecting UTI in febrile children with SCA.

MATERIALS AND METHODS

Settings and ethics

This was a prospective and analytical study conducted in the Department of Paediatrics University of Maiduguri Teaching Hospital (UMTH) and State Specialist Hospital Maiduguri between October 2005 and January 2008. Ethical clearance was obtained from the UMTH Ethical Committee. The study site serves as both primary and tertiary level health institution to Borno State and other State in the North Eastern part of Nigeria. It also provides medical services to neighboring countries of Chad, Niger and Cameroon Republics. The study group consisted of two hundred and fifty children aged 6 months to 15yrs that presented with fever and were confirmed to have SCA were enrolled into the study. Consent from parents or guardians and in addition assent from older children were obtained.

Inclusion and exclusion criteria

Patients with SCA aged 6 months to 15 years having axillary temperature of $\geq 37.5^{\circ}\text{C}$ and underwent haemoglobin electrophoresis diagnostic test (HbSS) were enrolled into the study. Patients presented with positive history of antibiotic use within one week, children with non infective cause of fever such as tetanus and dehydration and those patients with clinical condition associated with increased risk of UTI (glomerulopathies, obstructive uropathies, diabetes mellitus, severe malnourishment, catheterized patients, autoimmune diseases and malignancies), as well as those patients that decline to give their consent were excluded from this study.

Sampling procedures and measurement of biophysical parameters

Two hundred and fifty consecutive SCA patients based on Singer (24) aged 6 months to 15 years were recruited from the Sickle Cell Clinics of UMTH and State Specialist Hospital (SSH) or while on admission in Emergency Paediatric Units of both Hospitals. Physical examination was directed first at confirming the history of fever, by measuring the temperature (axillary) with a high accuracy LCD (liquid crystal display) Digital Thermometer with a measuring range of 32°C to 44°C . Measurement sensor head was put into the center of the armpit and left in place until there is an alarm from the thermometer. Reading was taken to the nearest 0.01°C . All the patients were weighed appropriately and recorded to the nearest 0.5kg.

Sample collection, transportation and culture

Midstream urine specimen (5 ml) was carefully collected at the time of presentation into 2 sterile universal bottles for each patient that has achieved bladder control. The following steps were performed to minimize the degree of bacterial contamination of the urine; social cleanliness and local disinfection of the meatus and adjacent mucosa with a swab containing eusol solution and dried with sterile gauze, the hand was gloved with autoclaved latex glove and the foreskin in uncircumcised boys was pulled back while in girls spreading of the labia was done to minimize contact of urinary stream with mucosa. For the adolescent girls a trained female resident doctor assisted in collecting some of the specimens. For infants and children who were not toilet trained, suprapubic bladder aspiration (SPA) was used for obtaining the urine specimen under aseptic procedures. The samples were sent immediately to Microbiology Department of the UMTH. The specimen taken at the SSH were kept in a refrigerator at 4°C for period of the clinic (2 - 3 hrs) before being taken to UMTH (10 - 20 minutes drive), where it was processed immediately for microscopy and culture. Pyuria: five milliliters (5 mls) 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 $\times 40$ magnification. More than five pus cells per high power field (HPF) were regarded as significant pyuria. Each urine specimen was mixed with the remaining supernatant and inoculated onto blood and MacConkey agar plates and incubated aerobically at 37°C for 48 to 72 hours. A pure colony count of 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 (25, 26). Those with positive culture results were treated accordingly.

Data management and data analysis

All the values were expressed as frequency, mean and standard error of the mean. Chi-square test where appropriate was used to determine the level of significance of the categorical variables using computer software SPSS version 16. P-value less than 0.05 were considered significant. Indices to determine the diagnostic usefulness of pus cells in detecting significant bacteriuria was calculated separately using the methods of Galen and Gambino (27).

RESULTS

TABLE 1: AGE AND SEX DISTRIBUTION OF PATIENTS

Age (years)	Number (percentage)		Total
	Male	Female	
0.5 - 5.0	78 (31.2)	56 (22.4)	134 (53.6)
5.5 - 10.0	39 (15.6)	27 (10.8)	66 (26.4)
10.5 - 15.0	28 (11.2)	22 (8.8)	50 (20.0)
Total	145 (58.0)	105 (42.0)	250 (100)

Two hundred and fifty febrile children with SCA were studied out of which 145 (58%) were boys while 105 (42%) were girls. The mean age of children was 5.6 ± 4.4 years. The ages of the patients studied ranged from 0.5 to 15 years with largest number of patients falling within the group 0.5 to 5 years (Table 1). The result of this study showed that 161 (64.4%), 113 (45.2%) and 61 (24.4%) had malaria, bone pain crises and suspected UTI as clinical diagnoses at presentation respectively. Other less common clinical diagnoses presented by the patients include; pharyngotonsillitis (18.8%), pneumonia (13.6%), osteomyelitis (5.2%), septicaemia (4.8%), gastroenteritis (2.4%) and otitis media (2.4%) as well as meningitis (1.6%) (Table 2). The frequently isolated organism was *Escherichia coli* 18 (27.7%) and *Klebsiella pneumoniae* 16 (24.6%). The least were *Coliforms* (13.8%) and *Salmonella spp* (3.1%) (Table 3).

TABLE 2: CLINICAL DIAGNOSIS AMONG PATIENTS*

Clinical diagnoses	Number (percentage)
Malaria	161 (64.4)
Bone pain crises	113 (45.2)
Suspected UTI	61 (24.4)
Pharyngotonsillitis	47 (18.8)
Pneumonia	34 (13.6)
Osteomyelitis	13 (5.2)
Septicaemia	12 (4.8)
Gastroenteritis	6 (2.4)
Otitis media	6 (2.4)
Meningitis	4 (1.6)

*Some patients had more than one clinical diagnosis

TABLE 3: URINARY BACTERIAL ISOLATES AMONG PATIENTS

<i>Type of organism</i>	<i>Number of isolate (percentage)</i>
<i>Escherichia coli</i>	18 (27.7)
<i>Klebsiella pneumonia</i>	16 (24.6)
<i>Proteus mirabilis</i>	11 (17.0)
<i>Staphylococcus aureus</i>	9 (13.8)
Coliforms	9 (13.8)
<i>Salmonella specie</i>	2 (3.1)
Total	65 (100)

Out of 65 (100%) sickle cell anaemic children with bacteriuria 36 (55.4%) had significant pyuria, while only 41(22.2%) out of 185 (100%) with no bacteriuria had significant pyuria. The test had sensitivity,

specificity and positive predictive values of 55.4%, 77.8% and 46.8% respectively. The efficiency of the test was found to be 72.0%. Pyuria was associated with increased risk of bacteriuria ($p < 0.001$) (Table 4).

TABLE 4: URINE MICROSCOPY (PYURIA) AND CULTURE

<i>Pyuria</i>	<i>Urine culture</i>		<i>Total</i>
	<i>Significant growth (%)</i>	<i>Insignificant growth (%)</i>	
Significant pyuria	36 (55.4)	41 (22.2)	77 (30.8)
Insignificant pyuria	29 (44.6)	144 (77.8)	173 (69.2)
Total	65 (100)	185 (100)	250 (100)

$p < 0.001$ (χ^2)
 Sensitivity = 55.4%
 Specificity = 77.8%
 Positive predictive value = 46.8%
 Negative predictive value = 83.3%

DISCUSSION

Urinary tract infection is common in children as demonstrated in this study. The prevalence of 26% found in this study only confirms how high is UTI in children with SCA, which also agrees with previous studies done within and outside Nigeria (6, 7, 9, 10, 11). This increased risk has been attributed to slugging of sickled cells in the renal vasculature which causes papillary necrosis and loss of urinary concentrating and acidifying ability of the nephrons,

resulting in abnormally diluted and alkaline urine which favours bacterial proliferation (28, 29, 30).

In this study significant pyuria or leucocyturia was found to have sensitivity of 55.4% and specificity of 77.8%. The negative and positive predictive values were 83.3% and 46.8% 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. Our study with slightly high sensitivity is comparable to that of Smith and colleagues (31) who reported significant pyuria being present in 64% of patient with significant bacteriuria. The specificity in our study was high which also agrees with specificity of 68% reported by Blum *et al* (32). However, the relatively higher sensitivity of 98% reported by Blum *et al* (32) compared with 55.4% of the present study is still not clear, but the use of symptomatic women as their sample population for the study may contribute to the observed significant difference. Again, this may show the variability of significant pyuria in detecting bacteriuria in other related studies (33, 34, 35, 36, 37).

Furthermore, the low positive predictive value with relatively higher negative predictive value observed in this study means that relying on this test (pyuria) alone may not be a good predictor of UTI. Therefore, there is a need to look for a more reliable test, otherwise some patients with pyuria and possible UTI would be overlooked and these could be potentially dangerous. It has previously been reported that the risk of renal damage is greater in sickle cell disease (SCD) children (9, 38). Thus early diagnosis and prompt treatment are important and recommended (14).

Interestingly to mention is the findings of other workers among adults and paediatric population irrespective of their haemoglobin genotype status, where they found significance of pyuria as a possible screening method for UTI (31, 32, 39). Although significant pyuria as a method to diagnose UTI or suggest the presence of bacteria appears to be limited in the foregoing study, we still support the view that the test still proves a veritable fall back tool for laboratory diagnosis in rural and some urban communities in our localities and across Africa where

laboratory personnel, reagents and equipments for appropriate diagnosis by culture are still lacking (40). In remote areas, it is not practicable to do culture and probably the newer test by strips like nitrite dipstick test (11, 41) or leucocyte esterase dipstick test (33, 42) may not be available. Therefore practitioners can fall back on microscopy of urine for pus cells to tentatively diagnose UTI in SCA children and even non SCA children. Finally, the limitation of pyuria should be factored into final outcome of the test, considering the present study and other referenced studies. Method of urine collection, transportation, storage, degree of precision in the interpretation of either spun or unspun urine specimen (13, 19, 43, 44, 45) are some key factors that needs to be appropriately considered before pyuria become more useful in the diagnoses of UTI.

CONCLUSION

The study has shown that significant pyuria has slightly high sensitivity with apparently high specificity, but low positive predictive value. The efficiency of the test is high as such we recommend for screening purposes in areas where laboratory facilities are inadequate. However, it could still be better that the test be interpreted along with culture results where it is practicable.

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