WEST AFRICAN JOURNAL OF MEDICINE

ORIGINAL ARTICLE

Urinary Tract Infection in Febrile Children with Sickle Cell Anaemia

L'infection des voies urinaires chez les enfants fébriles avec l'anémie falciforme

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ABSTRACT

BACKGROUND: **Sickle cell anaemia (SCA) is very common in Maiduguri, North-Eastern Nigeria. Children with this disease have increased tendency to develop frequent and severe infections especially of the urinary tract, bones and lungs. The prevalence of urinary tract infection (UTI) has however not been reported in this part of the Nigeria.**

OBJECTIVE: **To determine the prevalence of bacteriuria and bacterial isolates in the urine of febrile children with sickle cell anaemia.**

METHODS: **This was a prospective study carried out on 250 children with SCA and 250 controls with HbAA aged 6 months to 15 years. Following clinical assessment, midstream urine or urine obtained by suprapubic bladder aspiration was collected and subjected to microscopy and culture.**

RESULTS: **Bacteriuria was found in 65 (26%) of children with SCA and controls 514 (20.4%) of controls, p>0.05. *Escherichia coli* [16 (27.7%)] and *Klebsiella species* [16*(24.6%)*] were the predominant isolates in SCA group, while *Escherichia coli* [13(37.3%)] and *Coliforms* (25.4%) were predominant in the control group. Significant bacteruria occurred in patients with other clinical conditions such as pneumonia and septicaemia.**

CONCLUTION: **Urinary tract infection is common in children with SCA. Routine screening is therefore recommended during febrile illnesses. WAJM 2011; 30(4): 268–272.**

Keywords: **Sickle cell anaemia; children; fever; urinary tract infection; bacteriuria; North-Eastern Nigeria.**

RÉSUMÉ

CONTEXTE: La drépanocytose (SCA) est très commun à Maiduguri, Nord-Est du Nigeria. Les enfants atteints de cette maladie ont une tendance accrue à développer des infections fréquentes et graves en particulier de l'appareil urinaire, les os et les poumons. La prévalence de l'infection des voies urinaires (IVU) n'a toutefois pas été signalés dans cette partie du Nigeria.

OBJECTIF: Déterminer la prévalence de la bactériurie et isolats bactériens dans l'urine des enfants fébriles atteints de drépanocytose.

MÉTHODES: Il s'agissait d'une étude prospective réalisée sur 250 enfants atteints de SCA et 250 contrôles avec HbAA âgés de 6 mois à 15 ans. Suite à l'évaluation clinique, l'urine ou urine midstream obtenu par aspiration vésicale sus-pubienne a été recueilli et soumis à la microscopie et la culture.

RÉSULTATS: bactériurie a été trouvé dans 65 (26%) des enfants atteints de SCA et de contrôle 514 (20,4%) des contrôles, p> 0,05. Escherichia coli [16 (27,7%)] et des espèces Klebsiella [16 (24,6%)] ont été les isolats prédominants dans SCA groupe, alors que Escherichia coli [13 (37,3%)] et des coliformes (25,4%) étaient prédominantes dans le groupe contrôle. Bactériurie significative survenus chez des patients avec d'autres conditions cliniques telles que la pneumonie et la septicémie.

CONCLUTION: L'infection urinaire est fréquente chez les enfants avec SCA. Le dépistage systématique est donc recommandé lors de maladies fébriles. **WAJM 2011; 30(4): 268–272.**

Mots-clés: drépanocytose, les enfants, la fièvre, infection des voies urinaires; bactériurie; Nord-Est du Nigeria.

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Abbreviations: HbAA, Normal Haemoglobin; **HbSS**, Haemoglobin AA; **SCA,** Sickle Cell Anaemia; **SPA**, Suprapubic Bladder Aspiration; **SSH**, State Specialist Hospital Maiduguri; **UMTH**, University of Maiduguri Teaching Hospital; **UTI**, Urinary tract infection.

INTRODUCTION

Sickle cell anaemia (SCA) is one of the most extensively studied hereditary blood disorders,[1] since it was first described in 1910.[2] Urinary tract infection represents the commonest genitourinary disease of children.[3] Children with SCA have increased tendency to develop frequent and severe infections.[4] They are often susceptible to infections of bones, lungs and urinary tract. These are thought to bedue to abnormalities of the body defence mechanisms.[4]

Various workers in deferent parts of the world have reported increased incidence of UTI in individuals with SCA.[5–8] However most of these studies did not have appropriate controls for direct comparison with SCD patients. Some of the studies included adults; others involved a heterogeneous group of haemoglobinopathies such as HbSS, HbSC and HbS – thalassaemia .[5,8] There are few studies done on UTI in Nigerian children with SCA[9-10]. Such studies found high prevalence in SCA children.

There has been no study of the prevalence of symptomatic UTI in SCA children in North-Eastern Nigeria. This study was designed to determine the prevalence of significant bacteriuria and the nature of bacterial isolates from the urine of febrile Children. The study also determined the relationship between clinical features and laboratory diagnosis of UTI. Prompt diagnosis and early treatment will reduce the morbidity associated with urinary tract infection.

SUBJECTS, MATERIALS, AND METHODS

Study Site

This prospective study was carried out at the Department of Paediatrics; University of Maiduguri Teaching Hospital and State Specialist Hospital Maiduguri, from Oct. 2005 to Jan. 2008. Maiduguri is a cosmopolitan city situated in the North-Eastern part of Nigeria. The two hospitals are tertiary health institutions situated within the city.

Subjects

The study populations were selected using systematic random sampling technique and participant information recorded in a structured questionnaire. Two hundred and fifty children aged 6 months to 15 years with haemoglobin electrophoresn pattern of SS (HbSS) and 250 age – and sex – matched controls with HbAA who both presented with fever (temperature ≥ 37.5°C)[11] were selected.

Inclusion and Exclusion Criteria

The criteria for inclusion consisted of: age 6 months to 15 years, fever (temperature ≥ 37.5°C),[11] non usage of antibiotics seven days before presentation and duly signed consent form. Patients with the following conditions were excluded from the study; children with history of antibiotic usage seven days before presentation, those with conditions associated with increased risk of UTI such as glomerulopathy, obstructive uropathy, diabetes mellitus and malnutrition,[12,13] and children with non infective causes of fever such as dehydration and tetanus.
ETHICS: Ethical clearance was obtained from the Ethics Committee of University Teaching Hospital Maiduguri. Informed consent was obtained from parents or guardian of each child studied.

Procedure

The subjects were recruited from the out-patient consultant clinic of UMTH, Sickle Cell Anaemia clinic of the State Specialist Hospital or on admission in Emergency Peadiatric Unit and Paediatric Medical Ward of both UMTH and SSH. The authors took histories from the parents or guardians and sometimes the child, and carried out complete physical examination on each of the patient.

Physical examination was directed first at confirming the occurence of fever, by measuring the axillary's temperature[11] 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 armpit and the thermometer was left in place for until its alarm rang. Readings were taken to the nearest 0.1°C.

Definition of Terms: A *clinical diagnosis of UTI* was made in the patients that had any of the following; dysuria, increased urinary frequency, crying on micturation, loin pain, renal angle tenderness, suprapubic tenderness, and secondary enuresis associated with febrile episode. *Clinical diagnosis of otitis media* was made in any child presenting with ear *Pharyngotonsilitis*; was taken as enlarged tonsils or tonsil/pharyngeal erythema or exudates. *Pneumonia*; when there were signs of respiratory distress with crepitations or signs of consolidations or chest X-ray evidence. *Meningitis*; diagnosis was based on signs of meningeal irritation with positive cerebrospinal fluid findings.[14] *Clinical diagnosis of malaria* was confirmed with peripheral blood film for malaria parasites.

Investigations: Mid-stream urine sample was carefully collected into a sterile universal container by the researchers. Children who were toilet-trained provided clean voided samples. In infants and children who were not toilet-trained, supra-public bladder aspiration was used to obtain urine specimen under aseptic procedures.[15,16] The specimens collected at the State Specialist Hospital were kept in a refrigerator at 4°C, for period of the clinic (2–3 hours) before being taken to the Teaching Hospital, about 10–20 minutes drive, where they were processed immediately by microscopy and culture. Each urine specimen was well mixed, inoculated onto blood and MacConkey agar plates and innoculated aerobically at 37°C.[17] A pure colony count of 10^5 organisms/ml of urine was considered a significant growth.[18] In case of significant bacteriuria, systematic bacteriology and biochemical tests using standard techniques, were carried out to identify the organisms.[17]

Haemoglobin electrophoresis was done in all the patients using cellulose acetate electrophoresis at pH 8.9 in the Haematology laboratory of the Teaching Hospital.

Statistical Analysis: The data were entered into a computer. Statistical analysis was done using SPSS version 13 software. The occurrence of the variables were compared among SCA and the control group, using Chi-square test. continuity The level of statistical significance was taken as $p < 0.05$.

RESULTS

A total of 500 febrile children were studied, 250 were SCA patients and 250 controls with HbAA, matched for age and sex. The mean age of the children with SCA was 5.6 ± 4.4 years, while the mean age of the controls was 5.4 ± 4.3 years. There were 145 boys and 105 girls in the SCA group and the control group, giving a male female ratio of 1.4:1. All subjects had fever, with those in the SCA group ranging from 37.8 to 42.0^{0}C and in the control group 37.6^{0}C to 41.5^{0}C. The mean, median and mode of axillary temperatures of the studied population were 38.6^{0}C, 38^{0}C and 38^{0}C respectively.

Clinical Diagnoses of Fever

Table 1 show the clinical diagnoses in SCA and control patients. The commonest clinical diagnosis in both groups was malaria which accounted for 161(64.4%) consultation in the SCA group and 145(58%) in the controls. The second commonest clinical diagnosis in SCA patients was bone pain crises (45.2%). Suspected UTI was the third commonest clinical diagnosis in the SCA group and the second commonest clinical diagnosis in the control group.

Prevalence of Bacteriuria

Table 2 show the prevalence of bacteriuria in SCA group and controls: 65(26.0%) and 51(20.4%) respectively. Although bacteriuria was more common in children with SCA, the difference was not statistically significant (P = 0.950).

The most frequently isolated organism in both the SCA and the control groups was *Escherichia coli*. *Klebsiella spp* was the second commonest in the SCA group [16 (24. 6%)] while *coliforms* were the second commonest in the control group [13 (25.4%)]. Salmonella was isolated from two patients with SCA and none among the controls.

Table 3 shows the distribution of children with bacteriuria by age and sex. Twenty eight (19.3%) boys with SCA had bacteriuria, whereas 37 (35.2%) girls with SCA had bacteriuria. Similarly in the controls, bacteriuria was more common in girls than boys, being found in 28(26.7%) of the 105 girls and 23(15.9%) of the 145 boys. Bacteriuria was more common among females with SCA than females in the control group, (35.2% compared to 26.7%), the difference being statistically significant p=0.035.

Table 4 shows that of the 61 SCA with symptoms referable to the urinary tract, 32 (52.5%) had confirmed UTI compared to 37.5% (30 of the 80) controls, (p = 0.350).

In both SCA and the controls confirmed UTI occurred in association with other clinical conditions. Malaria occurred with UTI in 24.4% of the children with SCA and 17.9% of the controls. Septicaemia and UTI were confirmed in 58.3% of the children with SCA and 29.2% of the controls. Other conditions associated with bacteriuria in the SCA children were pneumonia 14.7%, bone pain crises 26.5%, pharyngotonsilitis 25.5% osteomyelitis 30.8%.

Table 1: Cause of Fever in Participating Children

Clinical Diagnosis of Fever*	Number (%)			
	SCA	Control	χ^2	P
Malaria	161 (64.4)	145 (58.0)	2.120	0.150
Pain crisis	113 (45.2)	–	–	–
Suspected UTI (no lab. diagnosis)	61 (24.4)	80 (32.0)	1.966	0.200
Pharyngotonsilitis	47 (18.8)	40(16.0)	1.352	0.275
Pneumonia	34(13.6)	58(23.2)	5.470	0.025
Osteomyelitis	13(5.2)	6(2.4)	0.312	0.600
Septicaemia	12(4.8)	24(9.6)	4.137	0.035
Gastroenteritis	6(2.4)	16(6.4)	3.126	0.065
Otitis media	6(2.4)	10(4.0)	0.445	0.500
Meningitis	4(1.6)	9(3.6)	2.948	0.075

** Some patients had more than one clinical diagnosis*

Table 2: Bacterial Isolates from the Urine of Children with SCA and Controls

Organism	Number (%)		
	SCA	Control	Both Groups
E. coli	18(27.7)	19(37.3)	37(31.9)
Klebiella	16(24.6)	6(11.8)	22(19.0)
Proteus	11(17.0)	2(3.9)	13(11.2)
Staphylococcus aureus	9(13.8)	11(21.6)	20(17.2)
Coliforms	9(13.8)	13(25.4)	22(19.0)
Salmonella	2(3.1)	0	2(1.7)
Total	**65(100)**	**51(100)**	**116(100)**

DISCUSSION

Urinary tract infection in SCA has been a subject of interest to many researchers in different parts of the world.[6,7,8,10] The UTI prevalence of 26% in this study is similar to 21.1% reported by Asinobi *et al*[9] in a prospective study of febrile children with SCA in Ibadan, and 20% reported from Ghana.[19] It is however much higher than the 10% observed by Tarry *et al,*[20] Barret-Connor[5] in California, USA (6%) and Elbashier and Badu in Saudi Arabia (11.5%).[8] The comparison should however be interpreted with caution because some of the workers studied adults and children. Some of the studies were retrospective with the risk of under-detection of cases.[5,20] Furthermore, some of the study like that of Tarry *et al,*[20] included patients with haemoglobin genotype other than HbSS, unlike the current study and the Ibadan study[9] in which, only HbSS patients were studied.

In the current prospective work, although bacteriuria was more common in SCA patients than controls, the differences were not statistically significant. This finding is similar to that of a study done in Ibadan by Asinobi *et al.*[9] This suggests that there are some

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Table 3: Distribution of SCA and Control Children with Bacteriuria by Age and Sex

Age (yr)	Number (%)*			
	Male	Female	χ^2	P-value
Sickle Cell Patients				
0.5 – 5	16(24.6)	19(29.2)	3.040	0.075
6 – 10	6(9.3)	9(13.8)	2.927	0.135
11 – 15	6(9.3)	9(13.8)	2.226	0.150
All	28(43.1)	37(56.9)	8.036	0.005
Control Subjects				
0.5 – 5	16(31)	17(33.3)	0.614	0.801
6 – 10	4(7.8)	6(11.8)	2.190	0.150†
11 – 15	3(5.9)	5(9.8)	3.472	0.652†
All	23(45.1)	28(54.9)	4.380	0.035

**The denominators for these percentages (%) are total number of SCA and controls with bacteriuria, 65 and 51 respectively. †Fisher exact 2-tailed test.*

Table 4: Occurrence of Bacterium in Febrile Co-existing with other Clinical Conditions in SCA and Controls

Clinical Diagnosis†	Number (%) with Bacteriuria*		P-value
	SCA Patients	Controls	
Malaria	40(24.8)	26(17.9)	0.250
Suspected UTI without Lab Diagnosis	32(52.5)	30 (37.5)	0.350
Otitis media	1(16.7)	2 (20.0)	0.850
Pneumonia	5(14.7)	14 (24.1)	0.300
Osteomylitis	4(30.8)	2 (33.3)	0.925
Bone pain crisis	30(26.5)	–	–
Pharyngotonsilitis	12(25.5)	5 (12.5)	0.150
Septicaemia	7(58.3)	7 (29.2)	0.075
Meningitis	1(25)	2 (22.2)	0.920
Gastroenterit	1(16.7)	4 (25.0)	0.500

**Percentages calculated on the number of subjects with clinical diagnosis. †Some patients had more than one clinical diagnosis*

other factors in operation than differences in the immune status among SCA and control. Poor hygiene, socio/ religious practices of cleanliness and other factors may be contributions. Robinson and Halpern[21] reported a statistically significant increase in susceptibility to UTI in SCA children. However, the study population of eight SCA patients was very small.

Our results shows that Bacteriuria is commoner in girls in both SCA and control groups. This is similar to findings reported from within and outside Nigeria,[5,8,9,22–24] where there is female preponderance. This has been attributed to the short female urethra with its close proximity to the anal canal, allowing easier contamination and ascending infection. Clinical diagnosis of UTI (suspected UTI without Lab. diagnosis) had low sensitivity in this study and its ability to predict bacteriuria was also low. This agrees with the fact that signs and symptoms referable to UTI are not specific in children[8]. In contrast Asinobi et al[9] found 78% positive predictive value of clinical features in detecting UTI. This disparity may be explained by the differences in mean age of SCA children which is higher in the later than the present study. The older a child especially above age five years the more likely he will have symptoms of UTI referable to urinary tract.

There was a predominance of *E coli* and *Klebsiella spp* in the current study. The predominance of these two pathogens among the SCA and control group is in agreement with other studies which showed the organisms to be the predominant bacterial pathogen in childhood UTI.[5,8,10,25] *Staphylococcus aureus* was also common in the present study. This is similar to the finding reported by Akuse,[26] where it accounted for 29% of the bacterial isolates from urine of ill children. This contrasts with finding by Asinobi *et al*[9] where they isolated only one case of *Staphylococcus aureus*. This difference may be that there is epidemiological difference in the prevalence of *Staphylococcus aureus* UTI across the country. Urinary tract infection is an important cause of morbidity amongst patients with SCA; it can precipitate crises, lead to septicaemia, and may worsen severity of anaemia.[27,28] Prompt diagnosis and appropriate treatment are important to reduce morbidity.

This study has shown UTI to be common during febrile illness in children with SCA. Routine screening for UTI is therefore recommended. This study also shows that UTI can exist alongside other clinical conditions. Children with SCA whose fever can be attributed to some other overt causes should also be screened for UTI so as not to miss concurrent infection.

AKNOWLEDGMENT

We wish to acknowledge the immense contribution of Dr Omeza of Federal Neuropsychiatric Hospital Maiduguri for his assistance in statistical analysis.

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