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Full Length Research Paper

Urinary tract infection and malaria co-morbidity in febrile children with sickle-cell anaemia in Sokoto, Nigeria

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BACKGROUND: Urinary tract infection (UTI) accounts for 10% to 30% of end-stage renal failure in children. Sickle –cell anaemia (SCA) is one of the predisposing conditions for UTI in Nigerian children. OBJECTIVES: The objectives of this study were to determine the prevalence of UTI and malaria co-morbidity in febrile children with SCA and to determine renal ultrasound findings in them. METHODS: This was a prospective cross-sectional and descriptive study conducted amongst febrile children with SCA (Haemoglobin SS) that presented at the sickle-cell clinic, Department of Paediatrics, Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria over a one-year period (1st July 2008 to 30th June 2009). The results of urine microscopy, culture and sensitivity, blood smears for malaria parasite and abdominal ultrasounds were analyzed, and p-value < 0.05 was considered statistically significant. RESULTS: Of the 259 febrile children with SCA that were studied, 72(27.8%) of them had UTI giving a prevalence rate of 27.8%. Uncomplicated malaria was present in 112(43.2%) of the 259 febrile children with SCA. Forty-five (40.2%) out of 112 that had malaria also had UTI. That is, 4 out of 10 febrile children with SCA with malaria may have UTI. Escherichia coli were the commonest cause of UTI in febrile children with SCA, in 37(51.4%). Normal renal ultrasound scans were in 228/259(88%) patients. Abnormal renal scans were more in those with UTI, 22/72(30.6%) compared to 4/112(3.6%) in those with malaria (p < 0.001). CONCLUSION: The prevalence of UTI and malaria were very high in febrile children with SCA. It is therefore, recommended that every febrile child with SCA and malaria should be investigated for UTI.

KEYWORDS: UTI, Malaria, Co-morbidity, Febrile Children, Sickle cell anaemia

INTRODUCTION

Urinary tract infection (UTI) is a syndrome defined by demonstration in urine of pathogenic organisms, bacteria, tubercle bacilli or fungi or colony of 10^5 /µl of urine (Water, 2005). UTI is commonly acquired by ascending route through which the organisms of the bowel flora enter the urinary tract especially in older children (Water, 2005; Eke and Eke, 1999). UTI has been known to be a significant cause of morbidity and mortality in childhood (Houston and Hendrickse, 1991; Gonzalez, 1996; Eke and Eke, 1999). It accounts for 10% to 30% of end-stage renal failure in children (Airede, 1992; Gonzalez, 1996; Eke and Eke, 1999). Sickle–cell anaemia has been reported to be a predisposing condition for UTI in children (Ajasin and Adegbola, 1998). This may be as a result of depressed immunity, both cellular and humoral, and from repeated vaso – occlusive crises resulting in papillary necrosis and loss of urinary concentrating and acidifying ability of the kidneys (Molineaux et al,1979; Ajasin and Adegbola, 1998;). Asinobi et al, (2003) has shown that UTI is common in febrile children with sickle-cell anaemia in Ibadan, south western Nigeria with prevalence rate of 21.6% compared with 15.8% in the controls. While Mora et al, (2011) reported significant bacteriuria of 26% among children with sickle-cell anaemia in Maiduguri, north eastern Nigeria.

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TABLE I: Age and Gender distribution of febrile sickle cell anaemia children with urinary tract infection (UTI)

AGE(YEARS)	GENDER		TOTAL (%)
	MALE	FEMALE	
0.5-1.0	11	4	15(20.8)
1.1-5.0	20	16	38(50.0)
5.1-10.0	9	10	19(26.4)
10.1-15.0	1	1	2(2.8)
TOTAL	41	31	72(100)

$X^2 = 2.617$; DF = 3; $p < 0.50$

Common presenting feature of UTI and malaria is fever. Malaria occurs often in combination with other diseases like UTI and it (Malaria) is responsible for 45.4% to 63% of outpatient consultation (FMOH, 2005; Jiya et al, 2010). Sickle-cell anaemia subjects have partial protection against Plasmodium falciparum (like HbAS) (Molineaux et al, 1979). Malaria is a common cause of death in children with sickle-cell anaemia (Molineaux et al, 1979). However, there is paucity of data in Nigeria to the best of the investigators' knowledge that compares the UTI and malaria co-morbidity in addition to the renal ultrasonographic findings in febrile children with sickle-cell anaemia. UTI is both under diagnosed and under investigated in both the hospital and the community (White, 1989; SBPG, 1990a, b). Hence this study set out with the following objectives: to determine the prevalence of UTI and malaria in febrile children with sickle-cell anaemia; and to report renal Ultrasound findings in febrile children with sickle-cell anaemia.

SUBJECTS AND METHODS

This was a prospective cross-sectional and descriptive study conducted at the Sickle-cell clinic, Department of Paediatrics, Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria over one-year period, 1st July 2008 to 30th June 2009. The subjects were febrile children with sickle-cell anaemia that presented at the Sickle-cell clinic and have not been on antimalarial or antibiotics for at least one week before presentation at the clinic. The sickle-cell anaemic children were those whose haemoglobin electrophoresis (genotype) patterns were Haemoglobin SS. A febrile patient was that with history of fever and or feels hot or has axillary temperature of ≥37.5^{o}C at presentation at the clinic (WHO, 2005). History and thorough clinical examinations were conducted. Those with obvious clinical causes of fever like acute respiratory infections (bronchopneumonia, lobar pneumonia, otitis media, purulent sinusitis, and pharyngotonsilitis), severe vaso-occlussive crisis, osteomyelitis, septicaemia, and those with WHO criteria for the diagnosis of severe malaria were excluded from the study. Their early morning clean catch urine samples collected in sterile bottles were taken to the main microbiology laboratory for microscopy, culture and sensitivity testing by standard methods. In those with positive isolates, the same tests were repeated one week after full course of antibiotics while abdominal ultrasounds were done for them four weeks thereafter inclusive of those with negative culture results. Finger pricks blood smear were taken for thin and thick films using Giemsa stain for the parasitological diagnosis of malaria according to World health Organisation (WHO, 2003) monograph. Ethical approval for the study was given by UDUTH Ethical committee. Informed/written consent was obtained from each parent or guardian of each subject.

Statistical analysis: The age, gender, and other relevant information were entered into data sheet. Data generated were analyzed by simple proportions, percentages and where applicable with Chi-square using Epi Info version 3.3.2; and p-value of < 0.05 was considered statistically significant.

RESULTS

Of the 259 febrile children with sickle cell anaemia that were recruited for the study, 72(27.8%) of them had urinary tract infection (UTI). Hence prevalence of UTI in this group of children was 27.8%. Of the 72 patients with UTI, males were 41(56.9%) and females were 31(43.1%) giving a male to female ratio of 1.3:1, while 51(70.8%) of them were aged 5years and below. There was no statistical significant difference in the age and gender (X2 = 2.617; DF = 3; p< 0.5). (See Table I). Similar pattern was obtained for those with uncomplicated malaria as depicted in table II. That is, the age and gender distribution of children with UTI were similar to those of sickle cell anaemia children with uncomplicated malaria. The age range of all our patients in this study was 0.5 to 15years.

Table III below depicts the age-specific prevalence rates of the febrile sickle-cell anaemia children with urinary tract infection (UTI). There was significant statistical difference between those with UTI and without UTI (X2 =11.55; DF =3; p< 0.01). This is in

Table II: Age and Gender distribution of febrile Sickle cell anaemia children with Uncomplicated Malaria

AGE (YEARS)	GENDER		TOTAL (%)
	MALE	FEMALE	
O.S - 1.0	18	10	28(25.0)
1.1 – 5.0	32	25	57(50.9)
5.1 – 10.0	12	10	22(19.6)
10.1 – 15.0	3	2	5(4.5)
TOTAL	**65**	**47**	**112(100)**

$X^2 = 0.648$; DF = 3; $p > 0.50$

Table III: Age – Specific Prevalence Rates of 72 febrile Sickle cell anaemia children with Urinary tract infection (UTI)

Age (Years)	Number of Febrile SCA Children		Total (% with UTI)
	With UTI	Without UTI	
O.S - 1.0	15	38	53 (28.3)
1.1 – 5.0	36	59	95(37.9)
5.1 – 10.0	19	65	84(22.6)
10.1 – 15.0	2	25	27(8.0)
TOTAL	**72**	**187**	**259(27.8)**

$X^2 = 11.55$; DF = 3; $p < 0.01$

Table IV: Age – Specific Prevalence Rates of 112 febrile Sickle cell anaemia children with Uncomplicated Malaria

Age (Years)	Number of Febrile SCA Children		TOTAL (% with Malaria)
	With Malaria	Without Malaria	
O.S - 1.0	28	35	63(44.4)
1.1 – 5.0	57	65	122(46.7)
5.1 – 10.0	22	35	57(38.6)
10.1 – 15.0	5	12	17(29.4)
TOTAL	**112**	**147**	**259(43.2)**

$X^2 = 3.048$; DF = 3; $p < 0.50$

Table V: Comparism between the Prevalence of UTI with that of Uncomplicated Malaria in Febrile Children with Sickle Cell Anaemia

Type of Infection	Urinary Tract Infection		Total (%)
	Number Positive	Number Negative	
Malaria Number Positive	45	67	112(43.2)
Number Negative	27	120	147(56.8)
TOTAL	**72**	**187**	**259(100)**

$X^2 = 15.067$; DF = 1; $p < 0.001$

contrast to those with uncomplicated malaria where statistical difference was not significant (X2=3.048; DF=3; p < 0.50; Table IV).

UTI was present in 72(27.8%) of the 259 febrile children with sickle cell anaemia in this series, compared to 112(43.2%) that had malaria. Of the 72 patients that had UTI, 45 (62.5%) of them also had malaria. Hence 45 (40.2%) out of 112 that had malaria also had UTI. This was very statistically significant (X2=15.067; DF = 1; p < 0.001). (See Table V below) That is, 4 out of 10 febrile children with sickle-cell anaemia with malaria may have UTI.

Escherichia coli was the commonest cause of UTI in febrile children with sickle cell anaemia, in 37/72(51.4%), followed by Staphylococcus aureus in 14/72(19.4%), Proteus mirabilis in 7/72(9.7%), and

Table VI: Renal Ultrasound findings in Febrile Sickle cell anaemia children with Urinary tract infection (UTI) and Uncomplicated Malaria

Type of Infection	Renal Ultrasound Findings		TOTAL (% Abnormal)
	Number Abnormal	Number Normal	
Urinary Tract Infection	22	50	72(30.6)
Uncomplicated malaria	4	108	112(3.6)
No Urinary Tract Infection Or Uncomplicated Malaria	5	70	75(6.7)
TOTAL	**31**	**228**	**259(12.0)**

X2 = 21.516; DF = 2; $p < 0.001$

Pseudomonas species in 5/72(6.9%) patients respectively. E. coli UTI was slightly preponderant in females than the males while Staph. aureus UTI was found in 71.4%(10/14) male subjects.

Renal ultrasound scan findings showed normal renal parenchymal echogenicity in 228/259 (88%) of the patients. Abnormal renal scan findings were in 31/259 (12%) of the studied subjects. Of this 31, 22/72 (30.6%), 4/112 (3.6%) and 5/75(6.7%) had UTI, malaria, and neither UTI or malaria (only sickle cell anaemia) respectively. Most of the abnormal results were grade I or II renal parenchymal diseases in 24/31(77.4%) while 7/31(22.6%) had features suggestive of structural obstructive uropathy like vesico - ureteric reflux or posterior urethral valve. The differences in prevalence of abnormal renal ultrasound scan findings in all groups were statistically significant (X2= 21.516; DF=2; $p < 0.001$) as depicted in Table VI.

DISCUSSION

The prevalence of UTI in febrile children with Sickle cell anaemia of 27.8% is similar to 26% that was reported by Mora and colleagues (2011) from Maiduguri, north east Nigeria but higher than 21.6% reported by Asinobi et al (2003) from Ibadan, southwest Nigeria, 6% by Chukwu et al (2011) from Enugu, south east Nigeria and 2.4% in 144 Jamaican patients that were studied by Wierenga K et al (2001). The difference between the prevalence rates of UTI that was reported in this series from those that were reported from southern parts of Nigeria which are temperate rain forest may be due to weather climatic condition which is hotter in Sokoto, a city located in the extreme end of Guinea savannah region of Sub Saharan Africa just like Maiduguri. Our patients might have decreased urinary frequency as a result of increased insensible loss from hot weather, thereby retaining more urine and giving the bacteria pathogens more time to multiply compared to those children from temperate region of Nigeria.

The prevalence rate 43.2% of uncomplicated malaria in this series is similar to that of 45.4% that was previously reported in children attending the outpatient clinic of the same hospital (Jiya et al, 2010). This implies that children with sickle cell anaemia are slightly less prone to malaria compared to normal children. Malaria, even if less intense than in normal persons, has grave consequences; as it is a frequent trigger to haemolytic and infarctive (vaso-occlussive) crises as earlier reported in Nigeria by Molineaux et al (1979).

There was male preponderance with UTI especially in age group 1.1 – 5.0 years which is in contrast to what has been reported in literature as females of this age group are usually more affected (Gonzalez, 1996; Chukwu et al, 2011). UTI occurred more significantly in those aged 5years and below. This is similar to what has been documented in previous studies (Abdurrahman et al, 1990; Eke and Eke, 1994). It should be noted that persons with sickle cell anaemia are often abnormally susceptible to bacterial infection, especially those under the age of 7years (Barret-Connor, 1971; Powars, 1975; Hand and King, 1978). Similar pattern was obtained for malaria in this series as was earlier reported (Jiya et al, 2010).

Furthermore, 43.2% of the 112 that had malaria also had UTI. The difference is statistically significant. The implication of this finding in this series is that 4 out of every 10 febrile children with sickle-cell anaemia may have UTI. Even though it has been stated that malaria do co –exist with UTI (Molineaux et al, 1979; Ajasin and Adegbola, 1998; Asinobi et al, 2003), it appears co-existence may be more in febrile children with sickle cell anaemia.

Escherichia coli were the commonest isolates from the urine of the febrile children with sickle-cell anaemia in this study which is similar to what was obtained in Ibadan (Asinobi et al, 2003), Maiduguri (Mora et al, 2011) and Enugu (Chukwu et al, 2011) series. Staphylococcus aureus was the second commonest isolate in this series compared to the Klebsiella species that was in Ibadan (Asinobi et al, 2003) and Maiduguri (Mora et al, 2011) series.

Escherichia coli UTI was slightly preponderant in females than the males subjects studied; similar pattern has been reported for UTI in children generally

(Gonzalez, 1996) and in particular in children with sickle cell anaemia in Enugu series (Chukwu et al, 2011). However, the organisms isolated from sickle cell anaemia patients with bacteriuria commonly include E. coli, Coliforms and Klebsiella (Barret- Connor, 1971; Powars, 1975; Hand and King, 1978).

Staphylococcus aureus UTIs were predominantly found in males. Males being less endured compared to female children with double XX sex chromosomes may be more prone to infections with virulent organisms like Staph. Aureus (Gonzalez, 1996).

Other isolates in this series were mainly gram negative organisms including Proteus mirabilis, Pseudomonas species, Salmonella Typhii and Klebsiella pneumoniae which is similar to what has been reported in the literature (Hand and King, 1978; Eke and Eke, 1994; Gonzalez, 1996; Gonzalez, 1996; Water, 1998).

In this series, ultrasound scans showed normal renal parenchymal echogenicity in 88% of patients compared to 100% and 95.6% that were reported in Ghanaian (Osei- Yeboah and Rodrigues, 2011) and Sudanese (Attalla, 2010) children with Sickle cell anaemia, respectively. The reason for the difference in our figure compared to those quoted above may be that some of our subjects had UTI that is, 22/259 (8.5%). Both Ghanaian and Sudanese study did not screen for UTI in their studied subjects. A report of abnormal renal ultrasound scan findings in 6.7% of our subjects that had neither UTI or malaria but only sickle cell anaemia and 12% of all studied subjects is higher than zero percent and 4.4% that was reported from Ghana and Sudan respectively Osei- Yeboah and Rodrigues, 2011; Attalla, 2010). It has been reported that in children with sickle cell anaemia, relative hypoxia, hypertonic and acidotic environment of vasa rectae in the medulla leads to sickling, vaso-occlusion, papillary necrosis, reduced glomerular filtration rate (GFR) – Sickle cell nephropathy (Pearson, 1984). UTI may accelerate the above processes in the kidneys of the children with sickle-cell anaemia than malaria.

In conclusion therefore, the prevalence rates of UTI and malaria were very high, Escherichia coli is the commonest causative organism of UTI, and 4 out 10 febrile children with sickle cell anaemia may have UTI in this series. It is therefore, recommended that every febrile child with sickle cell anaemia and malaria should be investigated for UTI, and those with UTI should be investigated further for possible underlying functional and structural renal abnormality.

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