Socio-demographic Factors associated with Asymptomatic Bacteriuria in Children with Sickle Cell Anemia in a Tertiary Health Facility in South Eastern, Nigeria.

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SUMMARY

Background: Urinary tract infection (UTI) is a common cause of chronic kidney disease in children. It is second only to respiratory tract infection in developed countries as a cause of morbidity and mortality arising from microbial infections. It is also common in a developing country like Nigeria and is the commonest cause of renal disorders in Port Harcourt, South South, Nigeria.

UTI can be symptomatic or asymptomatic (asymptomatic bacteriuria). Asymptomatic bacteriuria is said to be more common in school aged girls and children of low socio-economic class. It has also been documented to be more common in children with sickle cell anaemia.

Objectives: To determine the relationship between asymptomatic bacteriuria and age, sex and socio-economic status of children with sickle cell anaemia.

Methods: One hundred children with sickle cell anaemia in stable state were screened for asymptomatic bacteriuria using midstream urine samples. The age, sex and social class of the children were obtained through a structured questionnaire administered to the parents/care-givers. The relationship between age, sex and social class with asymptomatic bacteriuria in these children was analyzed using SPSS software.

Results: The age of the children ranged from 2-12 years. Six of the 100 children were noted to have asymptomatic bacteriuria and five of the six children were females (p=0.04).Five (83.3%) of the six children were five years and above. There was a predominance of positive cases (66.7%) in the higher socioeconomic class (p=0.03).

Conclusion: Asymptomatic bacteriuria is commoner in school aged female sickle cell anaemia children of higher socioeconomic class. However, we suggest that further studies be done to confirm this finding especially with regards to the socioeconomic status of these children.

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INTRODUCTION

Urinary tract infection (UTI) is a common cause of childhood morbidity and mortality.[1, 2] It is described by Eke et al[3] as the commonest cause of renal disorders in Port-Harcourt, South South, Nigeria. Urinary tract infection is noted by some authors[4] to be more common in the lower socioeconomic class while others[5] did not show any social class difference in the incidence of UTI.

Asymptomatic bacteriuria, described as significant bacteriuria (100,000 or more bacterial colony forming units per milliliter of uncentrifuged clean voided mid stream urine specimen plated within one hour of collection)[6] in repeated urine samples from a child without symptoms occurs commonly in school aged girls[7] and may predispose to UTI.

Children with sickle cell anemia by virtue of their altered immunological state are prone to developing recurrent infections including UTI.[8, 9] Ajasin and Agbola[10] in Lagos, Nigeria, documented the prevalence of asymptomatic bacteriuria of 5.8% and 1.9% among children with sickle cell anemia and their counterparts with normal hemoglobin respectively. In view of the fact that children with sickle cell anemia are susceptible to developing UTI, this study intends to determine the influence of age, sex and social status on the incidence of asymptomatic bacteriuria in children with SCA at UNTH, Enugu, Nigeria in comparison with their counterparts with normal hemoglobin.

SUBJECTS AND METHODS

This was a prospective study carried out at The University of Nigeria Teaching Hospital (UNTH), Enugu, South East Nigeria. The subjects were sickle cell anaemia children in stable state, recruited consecutively as they presented to the weekly sickle cell anaemia clinic of UNTH (convenience sampling method) while the controls were selected from day-care centers, nursery and primary schools in Enugu urban using the multi-stage sampling method. A list of all the public primary schools in five major populated areas in Enugu urban was made from which schools were selected by simple random sampling. There were 17 schools from the 5 major populated areas in the city (Achara Layout/Uwani, New Haven/Independence Layout, Coal Camp, Asata/Obiagu, Abakpa). One school was selected by simple random method from each of these areas. Each school has classes 1-6 in the primary section as well as a nursery school while two of the schools have day care centres as well. Each class has an average of 120 pupils. In the selected schools, the pupils were stratified according to their classes and in each class, they were stratified according to sex. The controls were

then finally selected using the systematic sampling method. Here the first pupil was selected by simple random sampling and every other 5th child was then selected. Three pupils were selected from each class giving a total of 111 pupils. One of the selected pupils was found to have HbSS and was excluded. The last two selected pupils from each school were then dropped so that twenty pupils were selected from each school. Subjects and controls were matched for age and sex.

Ethical approval for the study was obtained from the ethical and research committee of UNTH, Enugu while consent was obtained from parents and care-givers before commencing the study. A questionnaire was prepared and administered to the parents/caregivers/teachers of the subjects and controls. Information obtained or recorded in the questionnaire included age as at last birthday, sex, history of fever, bedwetting, and use of antibiotics in the preceding two weeks. Social class of the children was determined using the method proposed by Oyedeji.[11] Children with fever, dysuria, urine frequency and/or have been on antibiotics in the previous two weeks were excluded from the study.

The weight, height, pulse rate, blood pressure, and axillary temperature of the children were measured by one of the researchers and recorded in a case record form. Spot mid-stream urine specimens were collected into sterile boric acid bottles without prior cleansing of the genitalia [12] and transported in an ice containing box for analyses. Venous blood samples were collected from the controls for determination of their genotype.

Laboratory procedure

The urine samples were cultured in cystine lactose electrolyte deficient(CLED) and blood agar media within one hour of urine collection by employing the semi-quantitative method as described by Guttmann and Stokes.[13] A well calibrated standard wire loop of internal diameter 3mm and delivering 0.003ml of urine per loopful was sterilized over a Bunsen burner flame before immersing in well mixed uncentrifuged urine and then streaked into well dried plates of CLED and blood agar media (which were earlier incubated) as described by Uquarhart and Gould.[14] Cultures were incubated aerobically at 37^0C for 24 hours and the colonies counted by using a colony counter. Only samples that yielded pure bacterial growth of 10^5 or more colony forming units (cfu) per milliliter were regarded as yielding significant bacteriuria. Counts between 10^4 and 10^5 were repeated while countsd" 10^4 CFU were regarded as negative. Mixed growths were regarded as contaminants and therefore disregarded. Second urine samples were collected from children with significant bacteriuria and those whose second urine samples yielded significant bacteriuria were regarded as having asymptomatic bacteriuria.

Data analysis

Data was analyzed using the Statistical Package for the Social Sciences (SPSS) version 15.0. Proportions were tested using chi-square test while means were compared with t-tests. The level of significance was taken as $p<0.05$.

RESULTS

The children (subjects and controls), aged 2-12 years were recruited over an 8 month period (Dec. 2007- July 2008). There were 100 subjects and 100 controls. The subjects comprised 43(43%) females and 57(57%) males while the controls comprised 48(48%) females and 52(52%) males). There was no difference in the sex distribution of the population ($\div^2$ =0.8, df=1, p=0.37). The age of the subjects and controls ranged from two to 12 years. The mean age of subjects was 7.51±3.31 years while that of the controls was 7.10±3.35 years. The subjects and controls were also well matched with respect to their age (t=0.89, df=198, p=0.39). The age and sex distribution of the subjects and controls are as in Tables I and II.

The social class of the subjects and controls ranged from 1 - 5. There was no significant statistical difference in the mean social class of the subjects and the controls ($\div^2$ =13.18, df=16, p=0.6). The social class of subjects and controls is shown in figure 1. Out of the 100 urine specimens from the subjects, 94 (94%) had no bacterial growth while six (6%) had significant bacterial growth on 2 consecutive cultures showing a prevalence of asymptomatic bacteriuria of 6% among children with sickle cell anaemia. Five (83.3%) of these were from the females giving a female prevalence of 11.6% while one (16.7%) was from a male with a male prevalence of 1.7%. This gave a male: female ratio of 1:5 which is statistically significant ($\div^2$=4.2, df=1, p=0.04). One (16.7%) of the positive cultures was from a subject below five years while five (83.3%) were from subjects five years and above with prevalence values of 3.8% and 6.7% respectively.

On the other hand, out of 100 urine specimen from the controls, two had significant bacterial growth on two consecutive cultures showing a prevalence of asymptomatic bacteriuria of 2%. However, there was no significant difference in the prevalence of asymptomatic bacteriuria between the subjects and the controls (p=0.6). The two controls with asymptomatic bacteriuria were females, giving a female prevalence of 4.1% and a male prevalence of 0%. The sex distribution of subjects and controls with asymptomatic

Table 1: Age distribution of subjects and controls

Age in years	Subjects	Controls
≤2	7	9
3-4	19	22
5-6	15	16
7-8	14	13
9-10	19	18
11-12	26	22
Total	**100**	**100**

t=0.89, df=198, p=0.39

Table 2: Sex distribution of subjects and controls

Sex	Subjects	Controls
Male	57	52
Female	43	48
Total	100	100

$\div^2$ = 0.8, df= 1, p=0.37

bacteriuria is shown in Table III while Table IV shows the age distribution of subjects and controls with asymptomatic bacteriuria. The social class of the subjects with positive culture varied from 1 to 3. There was a predominance of positive cases (66.7%) in the higher social class (social classes 1&2) which is statistically significant ($\div^2$=4.73, df=1, p=0.03). The social classes of the two controls with asymptomatic bacteriuria were 2 and 4 respectively. There was no relationship between social class and bacteriuria among the controls ($\div^2$=0.72, df=1, Fisher's exact test, p=1.0). Table V depicts the social class distribution of subjects and controls with asymptomatic bacteriuria.

Table 3: Sex distribution of subjects and controls with asymptomatic bacteriuria

Sex	Subjects n=100	Controls n=100
Male	1(1%)	0
Female	5(5%)	2(2%)
Total	6(6.0 %)	2(2.0 %)

χ^2 =4.2,df=1,p=0.04 χ^2=2.3,df=1,p=0.13

Table 4: Age distribution of subjects and controls with asymptomatic bacteriuria

Age in years	Subjects n=100	Controls n=100
≤2	0	0
3-4	1	0
5-6	2	0
7-8	0	1
9-10	0	1
11-12	3	0
Total	6	2

Table 5: Social class distribution of subjects and controls with aymptomatic

Social class	Subjects n=100	Controls n=100l
1	1	0
2	3	1
3	2	0
4	0	1
5	0	0
Total	6	2

$\div^2$=4.37,df=1,p=0.03 $\div^2$=0.72,df=1,p=1.

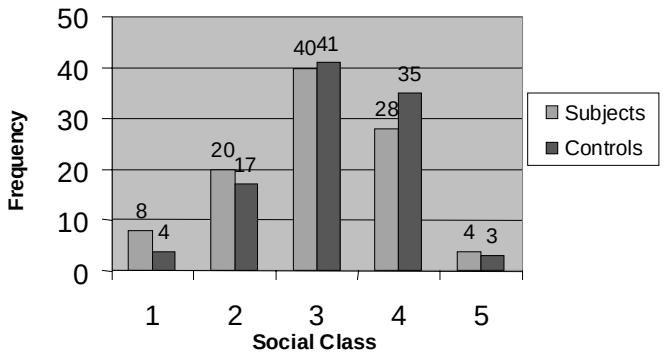

Figure 1: Compound bar chart showing the social class of subjects and controls

DISCUSSION

Studies on asymptomatic bacteriuria in sickle cell anaemia children are very few. However, in this current study, the prevalence of asymptomatic bacteriuria in children with sickle cell anaemia is 6% and this is comparable with the result obtained from Lagos by Ajasin et al[10] who documented 5.8%

The proportion of children with sickle cell anaemia who had significant bacteriuria in the current study is quite high when compared with the prevalence (2%) among children with normal haemoglobin genotype. At same time it is higher than the figures obtained by Abdulrahman[15] (1%) and Okafor[16] (2.1%) among children with normal haemoglobin in Kaduna and Enugu respectively. The current study shows that children with sickle cell anaemia are more susceptible to urinary tract infection (UTI) and that the risk of having asymptomatic bacteriuria is three times more in them than their counterparts with normal haemoglobin genotype. The reason for this higher risk may be partly due to the functional aspenia, impairment in the humoral immunity, and defective phagocytic function of neutrophils and alternate pathway of the complement system in these patients. It may also be due to the defect in urine concentrating and acidifying ability of the kidneys of children with sickle cell anaemia making them to have abnormally dilute urine which favours bacterial proliferation.[17] The renal medulla is particularly susceptible to damage in sickle cell anaemia because of its unique environment that is characterized by anoxia, hyperosmolarity and low pH which predispose to sickling with consequent repeated vaso-occlusion, ischaemia, infarction and loss of concentrating and acidifying function.

In the current study, amongst children with sickle cell anaemia who had significant bacteriuria, females out-numbered the males in a ratio of 5:1. The ratio is in agreement with that obtained by Tarry et al[18] (10:1) and Ajasin et al[10] (3:2). Of the 43 female subjects, 5 had asymptomatic bacteriuria giving a prevalence of 11.6% while the prevalence among the males is 1.7% suggesting that female sex is a high risk factor for developing asymptomatic bacteriuria. These prevalence values are in agreement with findings from other studies [10], [19], [20]. However, they are much higher than values from controls in this study (4.1% for females and 0% for males) and other studies [21], [22]. The higher prevalence in females is attributed to the short course of the female urethra and its proximity to the anal region making it easier for entero organisms to colonize, ascend and subsequently attach to the uroepithelium.

More cases of asymptomatic bacteriuria were noted in children above five years with prevalence of 6.7% than those less than five years with prevalence of 3.8% among the subjects. The age prevalence of asymptomatic bacteriuria among the controls shows 0% for those less than five years and 2.9% for those five years and above. The reason for this may be because children above five years have achieved urinary continence and can consciously delay voiding especially when not at a convenient place with consequent prolonged retention of urine which favours growth of bacteria and UTI. The flushing mechanism of the bladder is a known host defense factor against developing urinary tract infection. These children are also more

prone to sexual abuse which has been noted to increase the risk of UTI.

In the current study, children with significant bacteriuria were noted to be more from the higher social class (social classes 1 and 2)[11] with prevalence of 14.2%. The prevalence of asymptomatic bacteriuria in the lower social class (social classes 3-5) is 2.8%. The reason why children with sickle cell anaemia from the higher social class had more cases of asymptomatic bacteriuria is still not clear. Further studies, probably involving larger sample size may need to be done to give a clearer picture on the influence of social class on asymptomatic bacteriuria in these children. Though the influence of social class difference on asymptomatic bacteriuria has not been documented in children with sickle cell anaemia, the observation in this study is in contrast to what was obtained in some studies in Nigeria among children with normal haemoglobin genotype. In Ile-Ife, Western Nigeria, Elegbe et a[23] noted that a higher proportion of the children with significant bacteriuria who have normal haemoglobin were from the lower social class (8.5%) compared to 1.8% in those belonging to the higher social class. Savage et al[4] also documented a higher proportion in the lower social class. However, other studies[5, 24] including this study did not find an association between asymptomatic bacteriuria and social class among children with normal genotype.

CONCLUSION

In view of the high prevalence of asymptomatic bacteriuria in children with sickle cell anaemia especially among the females, we advocate for a routine urine screening in the clinics, at least using the economical and fast chemical tests for detecting bacteriuria. Those detected at this point should be treated appropriately so as to reduce the morbidity and mortality associated with these infections.

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