JMBR: A Peer-review Journal of Biomedical Sciences
June 2012, Vol. 11 No.1 pp 88-94

ASYMPTOMATIC BACTERIURIA IN HIV POSITIVE NIGERIAN CHILDREN

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ABSTRACT

This study was carried out to determine the prevalence of asymptomatic bacteriuria in HIV positive children and to identify the causative organisms. We studied 155 Human Immunodeficiency Virus (HIV) infected children aged 10 months to 17 years attending the Paediatric HIV clinics of the University of Benin Teaching Hospital. Children who were febrile, those with complaints suggestive of urinary tract infection, those with known anatomic abnormalities of the urinary tract and those with a history of antibiotic use in the 2weeks proceeding recruitment were excluded. Analysis was carried out on clean catch mid-stream urine sample obtained from each subject. Asymptomatic bacteriuria was found in 10.3% of the children. It was higher in the school age group of 6-12years and significantly more prevalent in females (P = 0.004). Escherichia coli, Klebsiella species and Staphylococcus aureus were the isolates cultured from urine, accounting for 62%, 25% and 12.5% respectively. We conclude that the prevalence of asymptomatic bacteriuria is high in HIV infected children especially those in the school age group.

INTRODUCTION

The presence of significant growth of bacteria in the urine without manifestation of clinical symptoms and signs of urinary infection in an individual is referred to as asymptomatic bacteriuria (ABU). The prevalence of ABU varies in different groups of individuals. In the healthy pediatric age group, studies in developed countries have reported prevalence of 0.7% in full term newborn and 2.9% in preterm newborn.[1]

KEY WORDS: *Asymptomatic Bacteriuria, Human Immunodeficiency Virus, Children*

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Large scale surveys documented prevalence of 0.8% in preschool girls and 0% in boys,[2] while at school age it was 1.7% in girls.[3]

In Nigerian children however, higher prevalence rates have been reported. In a study of preschool children aged 2-5years in Enugu, South Eastern Nigeria, prevalence was 1.9% in girls and 0.1% boys.[4] For children aged 10-17years the prevalence was reported to be 6.5% in girls and 4.5% in boys in a study in Port-Harcourt.[5]

In healthy children, extensive long-term follow-up studies on untreated ABU in developed countries have demonstrated that ABU is a mere colonization of the

bladder with non-virulent organisms,[6] which usually resolves without sequelae.[7, 8] The colonization is believed to be beneficial as it prevents infection from more virulent organisms, through competition for nutrients or receptor sites and by eliciting cross-protective host immune response.[9] Conversely, in studies where children with asymptomatic bacteriuria were treated, there was an increased risk of developing symptomatic urinary tract infection (UTI) in the immediate post-treatment period.[8, 10] Hence, screening for, and treatment of ABU in healthy children is not recommended.[7-9]

However, in chronic illnesses where there is complex interaction between immunity, nutrition and infection such as chronic malnutrition and sickle cell anemia, studies in children have shown higher prevalence of asymptomatic bacteriuria compared to healthy children. In a study of ABU in malnourished Indian children aged 6months to 5years, the prevalence was 15.2% compared to 1.8% of the healthy controls.[11] While in a study of Nigerian children with sickle cell anemia in steady state, overall prevalence of asymptomatic bacteriuria in children aged 2 – 12 years was 6% compared to healthy age and sex matched controls, which was 2%.[12] Though the clinical significance of ABU in these group of children, with regard to development of symptomatic UTI is controversial, correspondingly high prevalence of symptomatic UTI in children with sickle cell anemia[13] and chronic malnutrition [11, 14] have consistently been documented in the literature. Altered immunity has been speculated as the reason for the high prevalence of UTI in these groups of patients.

The hallmark of Human Immunodeficiency Virus (HIV) disease is the profound immunosuppression that results from continued depletion of CD4 cells.[15] This immune deficient state predisposes to a wide variety of infections, such that even avirulent organisms become pathogenic. In addition, some HIV infected children are malnourished. It is possible therefore that the prevalence as well as the clinical significance of ABU in children infected with HIV may be different from that of healthy children. This is especially so, as studies in adult population have also documented a higher prevalence of symptomatic urinary tract infection in HIV infected adolescent/young adults compared to healthy general population.[16] There is however paucity of information on ABU in HIV infected children.

This study was therefore conducted to determine the prevalence of asymptomatic bacteriuria in HIV positive children and to identify the causative organisms.

SUBJECTS AND METHODS

The study was carried out in the paediatric HIV/AIDS clinics of University of Benin Teaching Hospital (UBTH), Benin City, from October to December 2009. The paediatric HIV/AIDS clinics is one of the President's Emergency Plan For AIDs Relief (PEPFAR) sites where general and pediatric care of HIV/AIDS patients including antiretroviral therapy are provided free. In PEPFAR clinics, the CD_4 count and Packed Cell Volume are monitored every three

months. Serum electrolytes, urea and creatinine level and liver function tests are performed once yearly to assess the state of the kidneys and liver. Urine microscopy, culture and sensitivity are performed only when patients have symptoms relating to the urinary system.

The Study subjects were consecutive children aged 10 months to 17 years, attending the paediatric HIV/AIDS clinics that were confirmed to be HIV positive by DNA PCR in the children younger than 18months and by serology for children older than 18 months. A total of 155 HIV positive children were recruited for the study.

Children who were febrile with or without complaints of urinary symptoms, those with complaints suggestive of symptomatic UTI (such as dysuria, loin pain, suprapubic pain, frequency, urgency.), those with known anatomic abnormalities of the urinary tract and those with a history of antibiotic use (except cotrimoxazole prophylaxis) in the 2weeks preceding recruitment were excluded.

Ethical clearance was obtained from UBTH Ethics Committee. Verbal parental consent as well as assent from children older than 10 years was obtained for all subjects. Information on age, sex, the presence of dysuria, frequency, lower abdominal pain, flank pain and fever, antibiotic use and duration of the HIV infection were obtained. Socioeconomic class of the family was determined by the method described by Olusanya et al.[17] Physical examination of each child was carried out aimed at eliciting features suggestive of UTI. The most recent CD_4 count and the World Health Organization (WHO) clinical stage of the subjects at enrolment into the treatment programme were obtained from the medical records.

A clean catch mid-stream sample of urine was obtained from each enrolled child. In females, samples were collected after due preparation of the urethral orifice. Each sample was transported immediately to the research laboratory of the Department of Child Health, UBTH, where it was worked on within 2 hours of collection. Urine for culture including handling, staining and microscopy were carried out using standard procedure.[18] The presence of bacterial growth of $>10^5$ colony-forming units/ml was considered as significant bacteriuria.[18]

Urinalysis was carried out using Combi 10 test strips which examined for protein, blood, pH among others.

RESULTS

Of the 155 patients, there were 91males and 64 females with a male: female ratio of 1.4:1. The mean age of the children was 6.8 years ± 3.8. Children of the age group <6years constituted 48.4% of study population, while children 6-12years and 12-17years constituted 38.7% and 12.7% respectively. Socio-economic class was derived for only 105 children who had complete data. Of the children with available data for socio-economic class, 24.8% were from the upper social class, 17.1% from middle social class and 58.1% lower social class (Table I).

Out of the 155 children, 16(10.3%) had significant bacteriuria. Age group specific

TableI. Demographic distribution of study population.

Demographic features	n (%)
Age group	
>6years	75 (48.4%)
6-12years	60 (38.7%)
>12 years	20 (12.7%)
Gender	
Male	91 (58.7%)
Female	64 (41.3%)
Socio-economic class	
High social class	26 (24.8%)
Middle social class	18 (17.1%)
Low social class	61 (58.1%)

TableII . Characteristics of those with and without asymptomatic bacteriuria.

Characteristics	ABU Present (n=16)	ABU Absent (n=139)	P Value
Age group			
<6 years	4	71	
6 -12 years	8	52	0.099
>12 years	4	16	
Gender			
Male	4	52	0.004
Female	12	87	
Socio-economic class			
High	3	23	0.177
Middle	0	18	
Low	10	51	
WHO Staging			
P1	3	35	0.413
P2	2	36	
P3	8	52	
P4	0	8	
A1	0	1	0.308
A2	0	3	
A3	3	4	

prevalence of ABU was 2.6% in children aged less than 6 years, 5.2% in those aged 6 – 12years and 2.6% in those older than 12years. It was highest at the 6- 12years age group, but it was not statistically significant (p = 0.099). Gender specific prevalence was significantly higher in female 7.7% than in male 2.6% (p = 0.004). (Table II)

Only three types of Uro-pathogens were isolated from the sixteen subjects with ABU. Escherichia coli was isolated from 62% (10) Klebsiella species 25% (4) and Staphylococcus aureus 12.5% (2).

There was no significant association between asymptomatic bacteriuria and socio-economic class (P=0.177), presence of proteinuria (P=0.830), hematuria (P= 0.715), microalbuminuria (P= 0.788), mean CD_4 count (P= 0.251), and clinical stage of the HIV disease Adolescent (P=0.308)
Child (P= 0.413).

DISCUSSION

The overall prevalence of 10.3% of asymptomatic bacteriuria in HIV infected children in this study is high in comparison with figures of 1.1% and 1.9% from healthy paediatric population in America[19] and Britain[8] respectively. Such high prevalence of significant bacteriuria is also documented in the adult population infected with HIV. In the study of De Pinho and co-workers a prevalence of 3.2% was reported in HIV infected men and much higher prevalence of 6.6% was also documented in the men who had AIDS but had no risk factor for or symptom of UTI.[20] These findings of higher prevalence of ABU in HIV infected individuals compared to healthy population suggests that immunosuppression may be responsible for the increased susceptibility of HIV infected individuals to bacteriuria. However in this study there was no significant association between prevalence of ABU and CD_4 count. The reason for this may be because all the children were in a treatment programme.

There is no comparable overall prevalence of asymptomatic bacteriuria in the healthy Paediatric population in Nigeria, since healthy controls could not be recruited as their parents declined HIV testing. This is a limitation of this study.

The age specific prevalence of 2.6% of asymptomatic bacteriuria in HIV infected children below 6years in this study is high compared to that of healthy American children of the same age.[2] However, it is similar to the study of Okafor et al in healthy preschool children in Enugu.[4] Also observed in this study is a high prevalence of 5.6% in children aged 6-12years compared to 1.7% of healthy British[3] children of similar ages. The finding in this study that ABU was more prevalent at the school age group is similar to that of healthy paediatric population of similar ages. The reason for this high prevalence at this age group may be because of the relative independence children have at this age, such that they are no more routinely supervised when they use the toilet, and so adherence to stringent hygienic practices that keep the perineum clean may be poor.

Various studies on asymptomatic

bacteriuria also report a higher prevalence of ABU in females.[2, 4,] The finding in this study was consistent with the literature. The reason for this has been ascribed to the short length of the female urethra and the close proximity of its orifice to the anus which encourages easy contamination by organisms from rectum.[21] Conversely, the lower prevalence in males compared to females in this study may be due to circumcision which is widely practiced in our culture. Removal of the foreskin of the penis in male has been reported to reduce colonization of the urethral opening. Studies have also demonstrated increased risk of symptomatic UTI in uncircumcised males.[22]

The organisms isolated in this study are similar to those isolated in healthy children with ABU.[4, 6,] They are also similar to those reported by De Pinho and co-workers in asymptomatic HIV infected men.[20] These organisms have also been reported as causative organisms in symptomatic UTI in adolescents and young adults in the study locale.[16] From the literature, Escherichia coli is the most predominant organism isolated in urine of healthy children with asymptomatic bacteriuria. [4, 6-8] This was also the finding in this study.

The prevalence of asymptomatic bacteriuria is high in the studied HIV infected children especially those in the early school age group. However, further long term studies are needed to determine its clinical significance with regards to development of UTI. This is especially so as pyelonephritis is known to result in renal scarring which in the long term can result in hypertension and chronic kidney failure. Findings from such studies would be useful in the development of practice guidelines with regard to the need for screening of and treatment of HIV infected children with asymptomatic bacteriuria.

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