ORIGINAL ARTICLE

Microalbuminuria in Children with Human Immunodeficiency Virus (HIV) Infection in Port Harcourt, Nigeria

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Abstract

Background: *Microalbuminuria is an early manifestation of HIV associated nephropathy (HIVAN). This study was to determine the prevalence and risk factors for microalbuminuria in children with HIV infection in Port Harcourt, Nigeria*

Methods*: Urine specimen of 50 children with HIV infection seen over a 4months period (October 2007-February 2008) was assayed for albumin and creatinine to determine urinary albumin to creatinine ratio (ACR). Microalbuminuria was defined as urinary albumin to creatinine ratio (ACR) of greater than 2.5 -25mg/mmol. The glomerular filtration rate (GFR) was calculated using the Schwartz formula.*

Results*: There were 28 (56%) males and 22 (44%) females with a male to female ratio of 1.3:1. They aged 1 month to 18 years with a mean age of 4.07 ± 3.61years. Microalbuminuria occurred in 6 (12%) patients; 3 males and 3 females, mean age of 5.5 ± 4.6 years. Five (83.3%) of the patients with microalbuminuria had clinical AIDS and CD4^{+} cell count less than 200cells/µL. All the patients with microalbuminuria were not receiving highly active antiretroviral therapy (HAART) at the time of study. One (16.7%) patient had overt HIV-associated nephropathy (HIVAN) with ACR greater than 2.5 mg/mmol, elevated serum creatinine 400µmmo/L, urea of 20mmol/L and a GFR of 69ml/min/1.73m^2.*

Conclusion*: The prevalence of microalbuminuria in Nigerian children with HIV infection is high, and it occurs mainly in older children with clinical AIDS who are not on HARRT.*

Key words*: Microalbuminuria, HIV infection, children. Port Harcourt, Nigeria.*

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Introduction

Since the early years of HIV epidemic, renal disease has been increasingly recognized as a significant cause of morbidity and mortality in patient with human immunodeficiency virus (HIV) infection[1-10]. Renal involvement in HIV infection results from either the direct effect of the virus on the renal epithelium, opportunistic infections, immune complex deposition or from the side effect of medications used to treat HIV infection or opportunistic infections[11-15]. The broad spectrum of clinical presentation includes acute renal failure, HIV associated nephropathy (HIVAN), nephrotic syndrome, tubular functional abnormalities and electrolyte disorders[1-15]. HIVAN is the most common renal disease in HIV seropositive patients[14,16,17]. It has been widely reported in children with HIV infection[3,5,6,9,1821]. The characteristic features of HIVAN are proteinuria and rapidly deteriorating renal function[22-25]. Most published reports described heavy proteinuria in children with HIV infection[3,9,19,21,26]. Studies carried out in the United States of America (USA) reported that proteinuria is present in approximately 30% of patients with HIV infection[25,27] . Although, microalbuminuria has been reported to be an early manifestation of HIVAN[27,28,29]. Microalbuminuria is a subclinical condition that is associated with high morbidity and mortality and a well recognized risk indicator for renal disease[30,31,32].

The present study was carried out to determine the prevalence and risk factors for microalbuminuria in children with HIV infection in our hospital. This is to enable intervention measures to enhance early detection of HIVAN and effect prompt treatment to prevent rapid progression to end stage renal disease (ESRD).

Patients and Methods

This was a single center prospective pilot study conducted in the Infectious Disease Clinic (IDC) of the department of Paediatrics, University of Port Harcourt Teaching Hospital (UPTH). The Hospital is the only tertiary and referral centre in Port Harcourt, capital of Rivers State of Nigeria. Most patients are self -referred, with only few being referrals from local clinics. The

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hospital cares for children with HIV infection in the Infectious Disease Unit (IDU). During the period of study, there were 180 registered HIV infected children attending the IDC.

We prospectively studied children with HIV infection aged 1 month to 18 years over a period of 4 month from October 2007 to February 2008. The HIV status of the children was confirmed with the Western blot Proviral DNA method. Information on the biodata, clinical data, mode of transmission of HIV infection, $CD4^+$ cell count and drug medication were entered into a questionnaire that was used for each patient. Early morning urine specimens were collected from the subjects into a universal bottle and submitted to the laboratory within two hours of collection. Specimens were stored at 4°C and batch analyzed within one week of collection. Cloudy specimens were centrifuged and the supernatants were used for the assay. Urine albumin was assayed by immunoturbidimetry (Randox Laboratories UK Antrim). Urinary and serum creatinine were determined by the Jaffe Kinetic method (Biolabo SA Maizy, France). Absorbances were read in a Jenway 6320D spectrophotometer. Routine laboratory precision and accuracy controls were utilized. The urinary albumin to creatinine ratio (ACR) was determined by dividing the albumin concentration by the creatinine concentration. Results were expressed in milligram per millimole (mg/mmol). Microalbuminuria was defined as ACR of 2.5-25 mg/mmol. The glomerular filteration rate (GFR) was calculated using the Schwartz formula [height (cm) × 0.55/serum creatinine (mg/dl)][33].

Results

Fifty patients with HIV infection aged 1 month to 18 years (mean 4.07 ± 3.61 years) were studied. There were 28 (56%) males and 22 (44%) females with a male to female ratio of 1.3:1. The modes of transmission of HIV infection were vertical in 47 (94%) patients; blood transfusion in 2 (4%) patients and from unsterilized objects used for scarification mark in 1 (2%) patient. Only 7 (14%) were on highly active antiretroviral therapy (stavudine 1mg/kg twice daily; nevirapine 2mg/kg once daily for 2 weeks, then increased to 4mg/kg twice daily and lamivudine 4mg/kg twice daily). The mean serum creatinine and urea were 67.5µmmol/L (range 40-400µmmol/L) and 4.1m mol /L (range 1.2-20mmol/L) respectively. The mean glomerular filtration rate (GFR) was 100ml/min/1.73m^2 (range 69-125ml/min/1.73m^2

Microalbuminuria occurred in 6 (12%) patients; 3 males and 3 females with mean age of 5.5± 4.6years. Although, microalbuminuria was present in the older children, this was not statistically significant (P>0.2). One (16.7%) patient had overt HIVAN with ACR of 15 mg/mmol, elevated serum urea and creatinine of 20mmol/L and 400µmmo/L respectively and a GFR of 69ml/min/1.73m^2. The remaining 5 (83.3%) patients had normal serum urea, creatinine and GFR. Clinical AIDS ((persistent diarrhea, weight loss greater than 10%, chronic cough, oral candidiasis and skin rash) and low $CD4^+$ cell count of less than 200cells/µL was seen in 5 (83.3%) patients. The mode of transmission of HIV infection in all the patients with microalbuminuria was vertical. None had received highly active antiretroviral therapy (HAART) at the time of study.

Discussion

The prevalence of overt proteinuria in patients with HIV infection has been widely published both in adults[4,10,14,21,23] and in children[3,19,26,34]. However, there are yet few published reports on the prevalence of microalbuminuria in HIV seropositive patients[26,35]. In our present study, the 12% prevalence of microalbuminuria in HIV infected children is comparable to 11.1% prevalence reported by Leroy et al[35] in children in USA and the 11% prevalence reported by Szczech et al[36] in adults also in USA. However, it was lower than the 64% prevalence reported by Han et al[29] in HIV seropositive adults in South Africa, a similar African country. Although HIVAN have been reported to occur in younger children from 30 months of age[34], we found microalbuminuria more in older children. This is similar to the findings of Chaparro et al[34] where proteinuria was found only in older children with mean age of 8.7years. Most published studies agree that HIVAN is a late manifestation of HIV infection[1,16,22,37]. The finding of microalbuminuria in older patients in our study although not statistical significant may suggest that the risk for HIVAN is greatest in those with longer duration of HIV infection since all the patients acquired the infection perinatally. Although HIVAN has been reported to be more prevalent in males[1-4,22] there was no significant sex difference in those children with microalbuminuria in this present study.

Microalbuminuria is a sign of early damage to the kidneys and cardiovascular system[32,38]. Individuals with microalbuminuria may have a rapid progression to overt proteinuria, progressive deterioration in renal function and may eventually develop end stage renal disease (ESRD)[39]. Some studies have noted that HIVAN progress to ESRD at a very rapid rate, varying form weeks to months[1,2,23]. However, Strauss et al[5] and Ray et

al[19] noted a less fulminant course in children. In our present study, all except one of the patients with microalbuminuria had normal renal function. This will suggest that Nigerian children with HIVAN may have a slower progression to ESRD.

The majority (83.3%) of the patients with microalbuminuria including the one with overt HIVAN had AIDS in clinical stage 3 as defined by the World Health Organization (WHO)[40] with severe immunosuppression. This is similar to the findings of Chaparro et al[34] where 32.2% of the patients with proteinuria were in advanced stages of AIDS.

Highly active antiretroviral therapy (HAART) and angiotensin-converting enzyme inhibitors (ACEI) are standard therapeutic regimen for the treatment of HIVAN [1,5,41.42]. Retrospective studies in adults have shown the efficacy of zidovudine alone and HAART in slowing progression to ESRD in patients with HIVAN[43,44]. However, Michel et al[44] suggested that the efficacy of zidovudine in preventing renal failure in HIVAN patients is greatest when started before the onset of renal failure. In our present study, all 6 patients with microalbuminuria were yet to commence HAART at the time of study. Early commencement of zidovudine and ACEI may be beneficial in slowing the progression to ESRD in those patients with normal renal function.

In conclusion, the prevalence of microalbuminuria is high in Nigerian children with HIV infection. It occurred mainly in older children with clinical AIDS who are not receiving HAART. We recommend routine screening for microalbuminuria in HIV infected patients and early treatment with HAART and ACEI to slow the rapid progression to ESRD.

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