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Full Length Research Paper

Renal disease in HIV infected Nigerian Children coinfected with hepatitis B and C

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HIV, HBV and HCV are known to individually cause chronic glomerulopathies. This cross sectional study was carried out to identify renal disease and the risk of developing renal disease in HIV/Hepatitis B and C co-infected Nigerian children aged 10 months to 17 years. Each child was tested for hepatitis B surface antigen, antibody to hepatitis B core antigen and antibody to hepatitis C virus. Serum creatinine levels were determined and used in calculating the glomerular filtration rate. Urine was tested for proteinuria and microalbuminuria. Renal disease was defined as presence of proteinuria of ≥1+ on dipstick with or without GFR <60 ml/ min/1.73 $m^{2.}$ Renal disease risk was defined as presence of microalbuminuria of ≥20mg/l. Of the 114 HIV infected children HIV/HBV coinfection was observed in 10(8.8%) and HIV/HCV coinfection in 7(7%). All HIV/HBV coinfected children had risk of renal disease 6(60%) or established renal disease 4(40%). Two HIV/HCV coinfected children had risk of renal disease while 1 had established renal disease. The mean CD4 count 497±333.5 in HIV/HBV coinfected children with renal disease was significantly lower than the 1222.6±400.6 in HIV monoinfected children with renal disease p<0.01. HIV/HBV coinfected children with renal disease were more likely to be unimmunized compared to HIV monoinfected children with renal disease. P= 0.02. We conclude that renal disease was common in HIV/HBV coinfected children and this was associated with being unimmunized against hepatitis B.

Keywords: Renal disease, Human immunodeficiency virus, Hepatitis B and C, Coinfection, Children.

INTRODUCTION

Improved survival of Human Immunodeficiency virus (HIV) infected individuals has been made possible with the availability of effective antiretroviral therapy (ART), antibiotics and antifungal agents against AIDs related illnesses and opportunistic infections (Selik et al 2002, Palella et al 1998). However, with the longer survival of HIV infected individuals, chronic diseases especially of the liver and kidneys have emerged as important causal factors of mortality and morbidity (Selik et al 2002, Chung et al 2001). The risk of developing hepatitis associated liver disease (fibrosis, cirrhosis, end stage liver disease) is high (Graham et al. 2001). The rate of progression of such liver disease has been reported to be accelerated in those coinfected by HIV and the hepatitis viruses, especially in those with hepatitis C virus (HCV) (Operskalski and Kovacs, 2011). These morbidities negatively affect survival of HIV infected individuals. In a study by Monga et al, 11% of the HIVHCV coinfected patients died (compared to 7% of the patient who had HIV alone) and 47% of these deaths were due to liver related causes (Monga et al. 2001). In another study of HIVHBV coinfected patients, the liver-related mortality rate was 14.2/1000 person years it was 8.4 times higher than in those with only HIV infection (1·7/1000) (Thio et al. 2002).

The major extra hepatic contributor to these morbidities in HIV individuals who are coinfected with hepatitis B (HBV) and C infection is chronic kidney disease (CKD). All three viruses are known to cause chronic glomerulopathies wh-

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ich can result in end stage renal disease (Appel 2007). In the EuroSIDA large population study, HIV/HCV coinfected patients had increased risk of developing chronic kidney disease compared with HIV monoinfected patients (Peters et al. 2012). This has also been confirmed by Wyatt et al in a meta-analysis (Wyatt et al 2008) while in a biopsy based study by Izzedine et al (Izzedine et al 2009) HIV/HCV coinfection induced nephropathies were also reported to be associated with reduced survival. Proteinuria a marker of the presence of established glomerular disease has been reported to be more significantly associated with HIV positive patients co-infected with HCV than those coinfected with HBV (Szczech et al 2002). In a study on CKD in HIV infection (Wyatt et al 2007), (using proteinuria and /or GFR less than 60ml/min/m^2 as defining criteria), HIV/HCV coinfection rather than HIV/HBV coinfection was also identified as an independent predictor of renal disease. These studies were carried out in adult populations limiting their applicability in children.

Studies have reported high rates of coinfection in Nigerian adults, 12-28% for HIV/HBV and 5-15% for HIV/HCV coinfection (Otegbayo et al 2008, Forbi et al 2007, Balogun et al 2012). There is a dearth of studies on renal disease in these adult coinfected patients in Nigeria.

With 13% of the total number of persons living with HIV/AIDS in sub- Saharan Africa and 55,000 new infections in children in 2013 Nigeria has the second largest burden of paediatric HIV in Africa (UNICEF 2014). A significant proportion of these children are also coinfected with either hepatitis B or C or both. Studies have reported rates of HIV/HBV coinfection of 5.8-12.8% in children and HIV/HCV coinfection of 2.3-5.2% in children from various parts of Nigeria (Rawizza et al 2010, Sadoh et al 2011, Nwolisa et al 2013, Anigilaje and Olutola et al 2013). Although renal disease and its risks have been reported in HIV monoinfected patients few, if any, studies have been carried out in children. It is not known if coinfected children are at higher risk of renal disease or if indeed they already have established renal disease. In a resource limited setting like Nigeria where only 13% of HIV infected children assess ART and where routine screening for renal disease is not done, there may exist a hidden burden of renal disease.

This study was set out to identify renal disease and those at risk for developing renal disease among the HIV infected children co-infected with hepatitis B and C viruses.

Patients and Methods

Study setting and subjects

This descriptive cross-sectional 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 paediatric care of HIV/AIDS patients including antiretroviral therapy (ART) are provided free. The clinics attendees receive general paediatric and specialist care as required. Their CD4 counts and packed cell volumes are monitored on a 3-monthly basis, while liver function tests and electrolytes, urea and creatinine are monitored biannually. Screening for proteinuria, hepatitis B and C viruses is not routinely done at enrolment into the treatment programme.

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. Children who were febrile, those with complaints suggestive of symptomatic UTI (such as dysuria, loin pain, suprapubic pain, frequency, and urgency), those with preexisting renal or liver conditions not related to HIV infection and those diagnosed with tuberculosis were excluded

Data collection

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.

Data obtained included age, sex, socioeconomic class of the family derived using the method described by Olusanya et al. (Olusanya et al 1985), the HIV status of their mothers, possible route of acquisition of the HIV infection, duration of the HIV illness, the presence of tuberculosis co-infection, duration of HAART and type of HAART. The hepatitis B vaccination status of each child was also ascertained.

Physical examination of each child was carried out to eliciting features suggestive of chronic kidney disease. Parameter evaluated included anthropometric measurements, blood pressure, presence/ absence of edema and anaemia. World Health Organization (WHO) clinical stages (WHO 2006) of the subjects at enrolment into the treatment programme were obtained from their medical records. Stages 1-3 were classified as the non-advance HIV stage while stages 4 and 5 were classified as advanced HIV stage. In addition, the most recent CD4 counts obtained from the medical records were utilized in the immunological staging of each child (WHO 2006). Severe immunodeficiency was defined as CD4 count less than 200cells/ml

Laboratory workup

Five milliliters of blood was obtained from each child and

Table 1. Demographic and clinical characteristics of the children with Hepatitis B and C coinfected children and the HIV monoinfected children.

Characteristics	Monoinfection n=89(%)	HIVHBV Coinfection n=10(%)	HIVHBV Exposure n =7(%)	HIVHCV Coinfection n=8(%)	P value
Mean Age ± SD (years)	6.8 ± 3.6	7.9 ± 4.8	8.1 ± 4.6	7.6 ± 3.9	P= 0.66
Age Group in years					
<6	40(44.9)	4(40)	3(42.9)	3(37.5)	P=0.86
6 – 12	38(42.7)	3(30)	3(42.9)	4(50.0)	
>12	11(12.4)	3(30)	1(14.3)	1(12.5)	
Gender					
Male	54(60.7)	5(50)	3(42.9)	4(50)	P= 0.7I
Female	35(39.3)	5(50)	4(57.1)	4(50)	
Mean duration of illness In years	3.0 ± 1.6	2.5 ± 2.3	3.4 ± 3.3	2.6 ± 0.7	P= 0.68
Route of Acquisition					
Vertical	76(85.4)	7(70)	5(71.4)	7(87.5)	P= 0.62
Blood	4(4.5)	2(20)	0(0)	0(0)	
Sexual	0(0)	0(0)	1(14.3)	0(0)	
Scarification	1(1.1)	0(0)	0(0)	0(0)	
Unknown	8(9.0)	1(10)	1(14.3)	1(12.5)	
HAART					
On HAART	80(89.9)	9(90)	6(85.7)	8(100)	P= 0.79
HAART naïve	9(10.1)	1(10)	1(14.3)	0(0)	
Mean duration of HAART therapy in months	34.6 ± 20.2	31.9 ± 26.5	42.8 ± 18.2	34.8 ± 12.2	P= 0.73
Mean SBPmmHg	89.4 ± 13.8	95.3 ± 11.5	88.6 ± 10.7	92.5 ± 11.7	P= 0.55
Mean DBPmmHg	57.7 ± 12.6	60.9 ± 13.2	54.3 ± 12.7	61.3 ± 10.9	P= 0.63
Mean BMI	15.2 ± 1.7	15.5 ± 2.3	16.3 ± 1.9	15.1 ± 1.8	P= 0.44
HIV CLINICAL STAGING					
Non advance	54(60.7)	5(50)	1(14.3)	3(37.5)	P= 0.07
Advanced	35(39.3)	5(50)	6(85.7)	5(62.7)	

used for testing for hepatitis B surface antigen (HBsAg), antibody to hepatitis B core antigen (anti- HBc), antibody to hepatitis C virus (anti-HCV) and for the estimation of packed cell volume and serum creatinine levels. All the screening tests were by ELISA using the respective AUTOBIO diagnostic kits (a sensitivity of 100% and specificity of 99.5%). ALL the ELISA assays were third generation and the protocols, cut-offs and interpretations were according to the manufacturer's instructions.

Each child was instructed to pass urine into a sterile universal bottle and urinalysis was carried out for each specimen using Combi 10 multi test strips. The same urine sample was also tested for the presence of microalbuminuria using Mitral test strips.

The obtained serum creatinine was used to determine the glomerular filtration rate (GFR) by the Schwartz formula (Schwartz et al 1976).
Renal disease was defined as presence of significant proteinuria of 1+ and above on dipstick with or without GFR <60 ml/ min/1.73 m^2 based on the National kidney foundation practice guideline (Levey et al, 2003).
Renal disease risk was as defined as presence of microalbuminuria of ≥20mg/L (Glassock 2010, Ruggenenti and Remuzzi, 2006).

Data handling /Statistical analysis

Based on the result of the antibody testing the children were categorized into HIV/HBV group, HIV/HCV group and the HIV monoinfected group.
Data was entered into an Excel spread sheet and analyzed using SPSS package version 16. Chi-square test was used to assess the association between variables and Student t- test to was used to compare means. Level of significance was set at P values less than 0.05.

Results

General characteristics of study population

We recruited 155 HIV-infected children for the study. Of the 155 HIV-infected children recruited 41 were excluded from this study, 12 because they had tuberculosis co-infection while the remaining 29 were excluded due to absence of serum creatinine to calculate GFR. Thus only 114 children were analyzed and reported. Of the 114 HIV infected children analyzed 66 (57.9%) were male, their mean age was 7.0 ± 3.9 years and majority were in the age group less than 6years. Only 76 children had complete data to determine socioeconomic class and of these,majority were from the lower socio economic class.

Characteristics of HIV hepatitIs B and C coinfected and the HIV monoinfected children

Co-infection with hepatitis B and C was observed in 18(15.8%) of the 114 HIV infected children studied. Of these 10(8.8%) were HIV/HBV co-infected while the remaining 8 (7%) were HIV/HCV co-infected. In addition, 7(6.1%) of the studied children had evidence of prior exposure to HBV (they were antiHBc positive). Of the 96 HIV monoinfected children 12(12.5%) had risk of renal disease /established renal disease whereas all (100%) of evidence of HBV exposure only 1(14.3%) had renal disease. Amongst the 89 HIV monoinfected children studied 7(7.9%) had renal disease.
The HIV/HBV coinfected children with renal disease were statistically significantly older than the HIV monoinfected disease (100% vs. 14.3% P=0.02). They were also more likely to have lower mean CD4 counts (497.3 ± 333.5 vs. 1222.6 ± 400.7 P=0.01). There were however no significant differences between the proportions of HIV/HBV coinfected children had risk of renal disease/ established renal disease. Among HIV/HCV coinfected children 3(37.5%) had risk of renal disease/ renal disease. The association between the presence of risk of renal disease/established renal disease and HIV coinfection with HBV was significant p<0.0001.
The HIV hepatitis B and C co-infected children were older than those with HIV monoinfection. The mean ages ± SD of HIV/HBV coinfected, HIV/ HBV exposed, HIV/HCV coinfected and HIV monoinfected children were 7.9 ± 4.8years, 8.1 ± 4.6year, 7.6 ± 3.9 years and 6.8 ± 3.6years respectively. These differences in age were however not statistically significant P= 0.66. The male to female ratio was equal in the HIV/HBV co-infected children and the HIV/HCV co-infected children. The HIV infected children previously exposed to HBV were predominantly females while HIV monoinfected children were predominantly male, male to female ratio 1.5:1 (Table 1).
Vertical transmission was the predominant route of acquisition of the HIV virus in all the groups of children studied. The mean duration of exposure to the HIV illness was slightly shorter for the HIV/HBV coinfected and the HIV/HCV coinfected children compared to HIV monoinfected children. The differences were however not statistically significant P= 0.68 (Table 1). Coinfected children were more likely to be in advanced stages of HIV disease than those who were monoinfected although the difference did not reach statistical significance p=0.07
The mean duration on HAART therapy, mean systolic and diastolic blood pressures, mean body mass indexes were similar for all the groups studied. (Table 2)
Proteinuria and microalbuminuria were statistically significantly more likely to be present in coinfected and HBV exposed children than in HIV monoinfected children p =0.001and p<0.0001 respectively. The mean GFR was similar in all groups studied. Presence of renal dysfunction determined by reduction of GFR below 60ml/min/1.73m^2 was observed in only one child with HIV/HBV coinfection and in 4(4.5%) HIV monoinfected children. None of the HIV infected /HBV exposed or HIV/HCV coinfected children had renal dysfunction.

Renal disease in HIV Hepatitis B coinfected children

Of the 10 children with HIV/HBV coinfection 4 (40%) had renal disease, 3 of these children had proteinuria alone, while 1 child had a combination of proteinuria and reduced GFR <60mls/min/1.73m^2). Of the 7 children with children with renal disease (13.0 ± 1.4years versus 5.6 ± 1.9years P=< 0.0001).
The HIV/HBV coinfected children with renal disease were more likely not to have been immunized against hepatitis B compared to the HIV monoinfected children with renal

Table 2. Laboratory features of the children with Hepatitis B and C coinfected children and the HIV monoinfected children.

Characteristics	Monoinfection n=89(%)	HIVHBV Coinfection n=10 (%)	HIVHBV Exposure n =7(%)	HIVHCV Coinfection n=8(%)	P value
Mean CD4 Count	959.38 ± 575.57	1087.0 ± 710.6	588.6 ± 387.9	918.75 ± 765.05	P= 0.37
Severity of immunodeficiency					
<200 cells/ml	6(6.7)	1(10)	2(28.6)	0(0)	P= 0.17
>200 cells/ml	83(93.3)	9(90)	5(71.4)	8(100)	
Mean PCV%	33.7 ± 3.2	32.3 ± 3.2	32.3 ± 4.5	30.75 ± 3.9	P= 0.06
Proteinuria					
Positive	2(2.2)	4(40)	1(14.3)	1(12.5)	P= 0.001
Negative	87(97.7)	6(60)	6(85.7)	7(87.5)	
Microalbuminuria					
Positive	7(7.9)	10(100)	6(85.7) 1(14.3)	3(37.5)	P<0.0001
Negative	82(92.1)	0(0)		5(62.5)	
Mean GFR. ml/min/1.73m^2	123.4 ± 31.9	107.4 ± 32.0	124.0 ± 17.7	105.0 ± 37.4	P= 0.22
GFR					
<60 ml/min/1.73m^2	4(4.5)	1(10)	0(0)	0(0)	P= 0.70
>60 ml/min/1.73m^2	85(95.5)	9(90)	7(100)	8(100)	

HIV/HBV coinfected children with renal disease and those with HIV monoinfection with renal disease in terms of duration of their HIV illness, duration on HARRT therapy, HIV clinical staging and their immunological status. Table 3 shows clinical characteristics of the HIV/HBV coinfected children with renal disease and those with HIV monoinfection with renal disease.

Amongst the 7 HIV infected children with evidence of HBV exposure, the only child with renal disease was a 5year old female who was completely immunized against HBV. She had mild anaemia but was neither at an advanced clinical stage of HIV infection nor severely immunodeficient.

Renal disease risk in HIV Hepatitis B coinfected children

Table 3 shows clinical characteristics of the HIV/HBV coinfected children at risk of renal disease and those who were HIV monoinfection at risk of renal disease. Six (60%) of the 10 HIVHBV coinfected children had evidence of the risk of developing renal disease. while the HIV monoinfected children with risk of renal disease were 5(5.6%).The HIV/HBV coinfected children at risk of renal disease were younger compared to the HIV monoinfected children at risk of renal disease (4.5 ± 2.5years vs. 10.2 ± 5.1years P=< 0.04). The HIV/HBV coinfected children at risk of renal disease had a statistically significantly higher mean CD4 counts than the HIV monoinfected children at risk of renal disease (1480.2 ± 615.1 vs. 769.0 ± 284.0 P=0.04).

Of the 7 HIV infected/ HBV exposed children 5 (71.4%) had evidence of the risk of developing renal disease. These HIV/HBV exposed children with risk of renal disease were younger although; their mean age was not significantly lower than those of the HIV monoinfected children at risk of renal disease (7.2 ± 3.6years vs. 10.2 ± 5.1years P=< 0.31).

Table 3. Clinical characteristics of the HIVHBV coinfected children with renal disease and those at risk and the monoinfected HIV with renal disease with those at risk of renal disease.

Characteristics	HIVHBV with renal dx n =4	Monoinfection with renal dx n =7	P Value	HIVHBV at risk of renal disease n =6	Monoinfection at risk of renal dx n =5	P Value
Mean Age years	**13 ± 1.4**	**5.6 ± 1.9**	**P< 0.001**	**4.5 ± 2.5**	**10.2 ± 5.1**	**P= 0.04**
Age group						
<6	**0(0)**	**2(28.6)**	**P= 0.49**	**4(66.7)**	**1(20)**	**P= 0.24**
6-12years	**1(25)**	**5(71.4)**		**2(33.3)**	**2(40)**	
>12	**3(75)**	**0(0)**		**0(0)**	**2(40)**	
Gender						
Male	**3(75)**	**5(71.4)**	**P= 1.00**	**2(33.3)**	**2(40)**	**P= 1.00**
Female	**1(25)**	**2(28.6)**		**4(66.7)**	**3(60)**	
Mean duration of illness years	**2.0 ± 1.8**	**3.1 ± 1.3**	**P= 0.27**	**2.8 ± 2.6**	**3.4 ± 1.1**	**P= 0.64**
Route of Acquisition						
Vertical	**1(25)**	**6(85.7)**	**P= 0.08**	**6(100)**	**3(60)**	**P= 0.18**
Blood	**2(50)**	**0(0)**		**0(0)**	**0(0)**	
Unknown	**1(25)**	**1(14.3)**		**0(0)**	**2(40)**	
Mean duration on therapy	**34.7 ± 24.1**	**38.9 ± 16.8**	**P= 0.74**	**30.5 ± 29.7**	**35.4 ± 10.6**	**P= 0.74**
Hepatitis B immunization status						
Complete	**0(0)**	**2(28.6)**	**P= 0.02**	**3(50.0)**	**2(40)**	**P= 0.24**
Incomplete	**0(0)**	**4(57.1)**		**2(33.3)**	**0(0)**	
No Immunization	**4(100)**	**1(14.3)**		**1(16.7)**	**3(60)**	
HIV Clinical Stage						
Non advanced	**2(50)**	**2(28.6)**	**P= 0.58**	**3(50)**	**2(40)**	**P= 1.00**
Advanced	**2(50)**	**5(71.4)**		**3(50)**	**3(60)**	
Mean CD4 Count cells/ml.	**497 ± 333.5**	**1222.57 ± 400.7**	**P= 0.01**	**1480.2 ± 615.1**	**769.0 ± 284.0**	**P= 0.04**
CD4 count cells/ml.						
<200	**1(25)**	**0(0)**	**P= 0.36**	**0(0)**	**0(0)**	**P= 1.00**
>200	**3(75)**	**7(100)**		**6(100)**	**5(100)**	
Mean PCV%	**31.0 ± 4.0**	**34.1 ± 3.6**	**P= 0.22**	**33.2 ± 2.6**	**33.4 ± 4.1**	**P= 0.92**
PCV%						
<30	**2(50)**	**1(14.3)**	**P=0.49**	**0(0)**	**1(20)**	**P=0.45**
>30	**2(50)**	**6(85.7)**		**6(100)**	**4(80)**	

The HIV/HBV exposed children at risk of renal disease had significantly lower mean CD4 counts compared to the HIV monoinfected children at risk of renal disease (473.8 ± 269.0 vs. 769.0 ± 284.0 P=0.04) . There were however also no significant differences between the proportions of HIV/HBV exposed children at risk of renal disease and those with HIV monoinfection at risk of renal disease in terms of duration of their HIV illness, duration on therapy, route of acquisition of the HIV infection, hepatitis B immunization status, presence of anaemia, severe immunodeficiency and clinical staging of the HIV infection.

Renal disease and renal disease risk in HIV Hepatitis C coinfected children

Of the 8 children with HIV/HCV coinfection in this study only 1(12.5%) had renal disease; proteinuria was the only defining criteria in this child. The HIV/HCV coinfected child with renal disease was a 6½ years old male. He had mild anaemia , non-advanced clinical stage of HIV infection and was not severely immunodeficient. Of the remaining HIV/HCV coinfected children, 2(25%) had evidence of the risk of developing renal disease. The two HIV/HCV coinfected children at risk of renal disease were both 5years old females. They had no anaemia and were not severely immunodeficient. (Table 3).

DISCUSSION

Human immunodeficiency virus (HIV) and the hepatotropic DNA viruses- Hepatitis B and C have complex interactions (McNair et al 1992). These interactions result in chronic liver disease as well as extra hepatic manifestations of which renal disease is significant.

From our study, a high proportion of children with HIV/HBV coinfection had renal disease. Although the dearth of data on renal disease in HIV/HBV coinfected children precludes comparison, these finding are in keeping with scientific evidence. It has been proven that the HIV infection results in considerable modification of the natural history of HBV infection in the setting of HIV/HBV coinfection (Horvath and Raffanti ,1994, Colin et al 1999), causing persistence of the HBV infection with failure of spontaneous clearance. This results in a high prevalence of chronic HBV infection (Bodsworth et al, 1991, Alter, 2006) especially in HBV endemic regions (Africa and Asia) (Hoffmann and Thio, 2007). Chronic HBV infection is an etiologic factor in secondary glomerulopathy (Chan, 2010). Hepatitis related glomerular damage manifests as proteinuria which in most cases is rarely associated with impaired renal function especially in children (Chan, 2010, Lai, 2011).This was observed in our studied cohort.

The typical age of presentation of HBV related nephropathy in individuals without HIV is 2-12years with a mean age of 6years (Johnson and Couser, 1990, Wiggelinkhuizen et al, 1983). This early age of onset may be due to exposure to the HBV at an early age (vertical transmission) and the development of a chronic carrier state which is more likely to follow vertically acquired HBV infections or those acquired infancy (Chan, 2010, Johnson and Couser, 1990). In our study however, the HIV/HBV coinfected children who had renal disease were older with a mean age of 13years (range 11-14years). The older age of renal presentation may connote late acquisition of the HIV and hepatitis viruses. Two of the children acquired their HIV infection from blood transfusion and the duration of their HIV illness was less than 1 year. It is thus possible that there may have been accelerated development of hepatitis related glomerulonephritis.

In contrast, to the HIVHBV coinfected children with renal disease, only one child with HIVHCV coinfection had evidence of renal disease. The fact that HCV related nephropathy occurs many years (usually at second to third decade) after initial acquisition of the virus (Perico et al, 2009) may explain the low prevalence of HIV/HCV coinfected children with renal disease in this study. This study is however, also limited by the very small numbers of HIV/HCV coinfected children studied. Amongst the HIV/HCV coinfected children, proteinuria (12.5%) was the only evidence of renal disease and it was not observed to be significantly more common in them compared to the HIV monoinfected children. These findings are in contrast to those in HIV/HCV coinfected adults in which proteinuria was observed in 35% of studied patients (Monga et al, 2001). It was also noted that proteinuria was significantly more common in HIV/HCV coinfected patients compared to their HIV monoinfected adult patients. The observed differences between our study and Monga et al's may be due to our small sample size and it may also be due to the inherent difference between adults and children. In another study in adults by Izzedine H. et al (Izzedine et al, 2009), proteinuria was observed in up to 80% of HIV/HCV coinfected patients. The much higher proportion of individuals with proteinuria in that study maybe due to their study design which involved retrospective recruitment of individuals already known to have renal disease and the fact that the study population were adults who also had other co morbidities that cause proteinuria, such as hypertension and diabetes mellitus. All the HIV/HCV coinfected children in our study had normal blood pressure and were in normal clinical state.

In this study a high proportion of the HIV/HBV and HIV/HCV coinfected children had albuminuria. Measurable albuminuria of any degree, even as low as 2.5mg is considered a significant risk of renal and cardiovascular event (Gerstein et al, 2001,Hillege et al, 2002, Klausen et al, 2004) This implies that these coinfected children with albumiuria are at risk of developing renal disease. This finding is important as early institution renal preservation measures such as Renin Angiostensin Aldosterone System (RAAS) inhibition therapy, control of blood pressure and blood glucose levels etc can ameliorate albuminuria which is a marker of glomerular hyperfiltration (Ruggenenti and Remuzzi, 2006).

Among the HIV infected children who had only antiHBc there was also an increased risk of renal disease. It is known that some individuals who are only antiHBc positive may in fact have high viral HBV DNA (Lok and

McMahon, 2009) which was not tested in this study. Perhaps the presence of antiHBc in these children may not just be indicative of past exposure to HBV but may indicate occult hepatitis thus explaining the presence of possible renal effects of the hepatitis B virus. On the other hand, it could also be that exposure to hepatitis B virus infected children may be a risk for development of renal disease.

This study is limited by the small number of coinfected children. However we note that the risk of renal disease was significant in HIV infected children coinfected with hepattis B and C viruses while renal disease was common in HIV/HBV coinfected children. The absence of immunization against hepatitis B virus was associated with the development of renal disease in the HIV/HBV coinfected children.

Resource limited settings which are already overburdened with taking care of HIV infected persons may be ill-equipped to take on the additional burden of managing renal disease. Thus early identification of those at risk with the institution of renal preservation measures is the best strategy. We therefore recommend screening for hepatitis B, C and renal disease at the time of diagnosis of HIV as well as six monthly screening for renal disease thereafter. For children found to have anti HBc, viral DNA should be assessed to exclude occult hepatitis B. It may however be expedient to regularly screen these categories of children for renal disease. Efforts should be made to immunize all HIV infected children who are found to be unimmunized against hepatitis B while universal infant immunization against hepatitis B should be strengthened.

Limitation of the study

The small number of coinfected patients limits the interpretation of the findings in this study.

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Authors' contribution

Iduoriyekemwen Nosakhare Joyce conceptualized the work, collected the data, analyzed and interpreted the data, wrote the manuscript and approved the final manuscript. Sadoh Ayebo Evawere contributed to the concept, was involved in data collection, analysis and interpretation of data reviewed and approved the final manuscript.

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