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Prevalence of HIV co-infection with Hepatitis B and C viruses among children at a tertiary hospital in Ilorin, Nigeria

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Abstract

Background: The understanding of the shared routes of infection by Human immunodeficiency virus and blood borne hepatotropic viruses such as Hepatitis B and C viruses has raised concern about the possibility and impact of coinfection with the viruses. Studies especially among adults and few paediatric studies have shown that coinfection is indeed common and that coinfection adversely affects the outcome of the diseases. The burden of HIV coinfection in African children and particularly Nigeria is not well known. This study assessed the prevalence of hepatitis B and C in newly diagnosed HIV infected children managed at a tertiary Hospital. **Methodology:** The study was a descriptive cross-sectional determination of hepatitis B surface antigenaemia and antibody to hepatitis C of newly diagnosed HIV infected children aged 2months to 13 years who were managed at the Paediatric Antiretroviral Clinic or admitted to the hospital after obtaining informed consent. **Result:** A total of 60 subjects, of whom 31 were males were recruited into the study with a mean age of 5.6±3.0 years. The prevalence of HBsAg and anti-HCV were 10% and 1.7% respectively, making the prevalence of coinfection to be 11.7%. No patient had coinfection with the three viruses. HIV coinfecting children were significantly older than their monoinfected counterparts. There was no significant gender difference among the coinfecting children ($p=0.011$). **Conclusions:** HIV coinfection with viral hepatitis is a significant emerging problem whose impact in childhood is yet to be fully characterized. Routine screening of all HIV infected children for HBV and HCV and appropriate adjustment of Highly Active Anti-Retroviral Therapy (HAART) of patients with coinfection according to the National guideline is recommended.

1. Introduction

The Joint United Nations Programme on HIV/AIDS (UNAIDS) reported significant reduction in new paediatric HIV infections between 2009 and 2012, while access to highly active antiretroviral therapy is improving among children.¹⁻⁴ Despite this significant progress on the global front, some sub-Saharan African countries including Nigeria which accounted for one third of all new HIV infection in childhood in 2012 are facing enormous challenges in

meeting the global target of halving new paediatric HIV infection by 2015.³ The improvement in access to antiretroviral therapy (ART) has resulted in better survival of people living with HIV/AIDS and made obvious the burden of chronic complications of HIV infection whose manifestation may have been masked by high AIDS-related mortality in the pre-ART era.⁵ The understanding of the shared routes of HIV infection and blood-borne hepatotropic viruses such as hepatitis B virus (HBV) and hepatitis C virus (HCV) has raised concern of the possibility co-infection of HIV with these viruses, and adverse effects of such co-infection on the manifestations and outcome of these infections.⁶⁻⁸ Studies have indeed shown that HIV co-infection with hepatitis B virus or hepatitis C virus is indeed common.⁹⁻¹⁰

Some studies have reported that HIV/HBV and HIV/HCV co-infection have a negative impact on liver disease caused by these viruses. Hepatitis C virus infection has been found to accelerate the evolution and progression of liver disease in HIV-infected individuals.^{8-9, 11}

Vertical transmission also known as mother to child transmission accounts for almost all HIV infections in children younger than 13 years (greater than 90% of paediatric HIV infections in general).¹²⁻¹³ Similar to HIV transmission in children, vertical transmission has been reported as the most important route of transmission of both hepatitis B and C viruses in childhood.^{9, 14} Other significant mode of transmission of HIV in children as shared with hepatitis B and C viruses include parenteral exposure to HIV infected blood and blood products, sexual contact with HIV infected persons (especially among adolescents and victims of sexual assaults), and intravenous drug use especially among adolescent boys,¹⁴ believed to be less important in West African children than those in developed countries.^{13, 15}

Few published studies worldwide have reported the prevalence of HIV co-infection with HBV, HCV, or both viruses in children.^{7, 16-18}

The prevalence of HBV infection among HIV-infected adults varies markedly, from 5-10% in United States¹⁹⁻²⁰ to 20-30% in Asia and parts of sub-Saharan Africa.^{9, 12, 21, 22} In Nigeria, studies show that up to 9.7-30% of HIV infected adult patients are co-infected with HBV.²²⁻²⁴

Olatunji and Iseniyi²⁴ evaluated the prevalence of HBV and HCV co-infections among HIV-infected adults at the Haematology Clinic of a tertiary hospital in Ilorin using seroprevalence of HBsAg and antibody to HCV as markers of HBV and HCV infections respectively. They compared the prevalence of HIV co-infection with HBV or HCV in this cohort with those of HIV-negative blood donors who were used as controls. The number of controls was determined by the availability of reagents for HBV and HCV screening, thus, 2006 and 347 controls were screened for seroprevalence of HBsAg and anti-HCV antibodies respectively. The prevalence of HIV/HBV co-infection was 31.4% in the cohort, while none of the patients had

HIV/HCV co-infection. The seroprevalence of HBsAg was significantly higher in HIV-infected adults (31%) compared to that of HIV-negative controls (16.6%, 332 of 2006) [$p=0.0001$]. Although two (0.6%) of 345 HIV negative controls were seropositive for anti-HCV antibodies, there was no significant difference in the prevalence of anti-HCV antibodies between the HIV-infected group and the control ($p>0.61$).²⁴

In Nigeria, Rawizza *et al*¹⁶ published the first paediatric study carried out to determine the prevalence of hepatitis co-infection among HIV-infected children. The study was a multicenter retrospective evaluation of HIV-infected children enrolled in the Harvard PEPFAR/APIN Plus programme.¹⁶ The prevalence of hepatitis B surface antigenaemia and anti-HCV antibody in the cohort was 8.3% (54 of 648) and 2.7% (17 of 637) respectively.

The prevalences of HIV/HBV from the two paediatric studies in Nigeria are similar, however, the prevalence of HIV/HCV co-infection reported by Sadoh *et al*¹⁸ (5.2%) is almost twice the reported 2.7% by Rawizza *et al*,¹⁶ but lower than 13.8% reported in Tanzania.²⁵ No case of HIV/HCV was found in children studies in Cote d'Ivoire.¹⁷ This possibly reflects the earlier reported wide regional differences in the prevalence of HBV and HCV in Africa.^{18, 26}

The marked variation in prevalence of HIV co-infection with HBV and HCV across the difference geopolitical regions especially among adults requires that more studies are required to determine the magnitude of this problem, risk factors, and the impact of co-infection among children.¹⁶

This study was carried out to highlight the burden of the problem, and also to serve as data base for further studies especially on the impact of HIV co-infection with HBV and HCV.

2. Methodology

This was a prospective descriptive cross-sectional study of children age 2 months to 13 years who were HIV infected.

This study was conducted in University of Ilorin Teaching Hospital (UITH), a tertiary institution located in Ilorin, in the North Central geopolitical zone of Nigeria. Recruitment of patients was carried out at the Paediatric Antiretroviral Therapy (ART) Clinic, Emergency Paediatric Unit (EPU), and Paediatric medical ward of the hospital. A total of 60 HIV-infected children were recruited into the study using the Andrew Fisher's formula to calculate the minimum sample size. The National seroprevalence of HIV used was 4.1%, and the tolerable margin of error was set at 0.05. Ethical clearance was obtained from the Ethical Review Committee of the hospital while individual informed consent was also obtained from the respective parent or care-giver of the

child and written assent was also obtained from children aged 7 years and above before subject recruitment.

Subject recruitment

This study was carried out over eleven month period, from January to October 2011. Consecutive patients who met the recruitment criteria were recruited into the study after informed consent. Recruitment of subjects was done by the investigator.

Data collection

Semi structured questionnaire was used to obtain information on: socio-demographic characteristics, Educational qualifications and occupations of parents, risk factors for transmission of HIV, HBV, and HCV, presenting symptoms of patients, anthropometric measurements, and laboratory parameters.

Socio-economic index scores were awarded to the occupations and educational attainments of parents or caregivers of subjects using the Oyediji socio-economic classification scheme.²⁷ The anthropometry of each subject was taken and a detailed medical examination was conducted on each patient.

Two millilitres of blood was taken in plane specimen bottles for HBV and HCV screening. The clotted blood in plane specimen bottle was then taken to the ART Laboratory of UITH where the serum was separated by the investigator at 3000rpm for five minutes in a bench-top centrifuge. HBV infection was confirmed using Diaspot HBsAg (AZOG Inc. Phillipsburg, USA), a one step hepatitis B surface antigen test strip,²⁸ while Hepatitis C infection was screened for using DiaSpot HCV, a one step hepatitis C virus test strip (AZOG Inc. Phillipsburg, USA).²⁹⁻³⁰ The investigator, using appropriate strip and following the procedure described by the manufacturer, screened the serum for HBsAg and HCV antibody. Sera of patients were screened for HBsAg and anti-HCV antibody by the investigator under the supervision of the Chief Laboratory Scientist in charge of the desk of the ART laboratory UITH, Ilorin. As a quality assurance mechanism, ten randomly selected samples were tested for HBsAg and anti-HCV antibody by the investigator and the Chief laboratory Scientist independently and the results compared to ensure reliability.

Data analysis

Data was analyzed using Epi-info version 6 software. The results of investigation and other data collected on the proforma were entered into a master sheet using numerical codes. Frequency distribution tables and cross tabulation of variables were generated. Measures of central tendency and dispersion of quantitative variables were also determined. A thematic approach was used to analyze some quantitative variables. Mean, standard deviation, range and variance values (SD^2) were provided as appropriate. Chi-square test (with Yates correction or Fishers exact was used where applicable) and student t-test were used to test for significance of the difference between categorical variables and continuous variables respectively. Level of significance was put at less than 0.05.

3. Results

A total of 60 HAART naïve HIV-infected children aged two months to 13 years were recruited into the study, 51.7% of whom were males with a male female ratio of 1.1:1. Approximately 7% of the subjects were younger than 18 months, while 35% and 45% were within the age ranges of 18 to less than 60 months, and 5 to less than 10 years respectively, and 13.3% were within age range of 10 years to 13years. Children younger than 18 months were predominantly females (75%), while 57.1% and 54.8% of the subjects within the age groups 18 to less than 60 months and 5 years to less than 10 years respectively were males. Subjects aged 10 to 13 years had equal gender proportion.

Of the sixty HIV infected children, six (10%) tested positive for HBsAg, while only one (1.7%) of the subjects tested positive for anti-HCV antibody. The prevalence of HIV co-infection with HBV and HCV among this cohort was thus 11.7%.

Regarding gender distribution of subjects with HIV co-infection with HBV and HCV, four (57.1%) were males while three (42.9%) of the co-infected patients were females, thus, HIV co-infection with HBV and HCV had no relationship with gender ($p=0.925$).

The mean age of HIV-monoinfected children was 5.25 ± 3.96 years, while children with HIV co-infection had a mean age of 8.43 ± 2.37 years. Children with HIV co-infection were significantly older than HIV-monoinfected children ($t=-3.034, p=0.011$).

Over eighty percent of children with HIV/HBV and HIV/HCV co-infections were older than five years. Only one child whose age was less than 60 months had HIV/HBV co-infection, while the only child with HIV/HCV co-infection was 9 years old.

Seventy seven percent of the subjects were from the Yoruba tribe, while subjects from the Hausa and the Ibo tribe constituted 5.7% and 9.4% respectively. The remaining 7.5% of the subjects were from Nupe, Baruba, Ogoja, and Bokobani tribes. There was no significant difference in terms of ethnicity between children with HIV-monoinfection and HIV co-infections ($p=0.707$).

About sixty percent of the study population were from Muslim homes, while the rest came from Christian homes. Among children with co-infection, 57.1% were from Christian homes, while 42.9% were from Muslim homes. There was no significant difference between study groups in terms of the religion of the family ($p=0.377$).

The predominant family type among subjects was monogamy (69.8%), while 24.5% were from polygamous homes, and 5.7% of the subjects were from single parents home or divorced parents. There was no significant difference between HIV-monoinfection and HIV co-infection with either HBV or HCV with regards to family type ($p=0.184$).

With respect to socioeconomic background, 16.7% of the study population were from socio-economic class I,

10% from socio-economic class II, 41.7% from socio-economic class III, while 30% and 1.6% were from socio-economic classes IV and V respectively. It thus implies that 26.7% of the study population were from the upper socio-economic class (classes I and II), 41.7% from middle class (class III), while 31.6% were from the lower socio-economic class (class IV and V). There was no significant difference with respect to social class between HIV-monoinfected, HIV/HBV and HIV/HCV co-infected children ($p=0.535$).

4. Discussion

The prevalence of HIV co-infection in this study was 11.7%, with the prevalence of hepatitis B surface antigenaemia coexisting with HIV infection being 10%, while the prevalence of antibody to HCV was 1.7%. No child had HIV co-infection with both HBV and HCV. The prevalence of HIV/HBV co-infection from this study is slightly higher than 7.7% and 8.8% previously reported in Nigerian children, and slightly lower than 12% found among children in Cote de Ivoire.¹⁶⁻¹⁸ The high prevalence of HIV/HBV co-infection in this study possibly reflects regional differences in risk factors for co-infection and the incidences of both hepatitis B and C infections among the population.⁸ Two studies had reported high prevalence of HBV in HIV infected adults in North Central Zone of Nigeria.^{22, 23} Olatunji *et al*²³ found HBsAg seropositivity rate of 31% in a cohort of HIV infected adults in Ilorin, a report that is similar to the reported prevalence of 25% in Jos by Uneke *et al*,²² and in sharp contrast to a much lower prevalence of 11.5% in South West geopolitical Zone of Nigeria.²³

The prevalence of HIV/HCV co-infection of 1.7% in this study was similar to the relatively low prevalence of HIV/HCV co-infection previously reported in Nigerian children.¹⁶ This low prevalence of HIV/HCV co-infection was consistent with the relatively lower prevalence of HCV among Nigerian,¹⁶ and in fact, African¹⁷ children population. Previous studies corroborated that efficient routes of HCV transmission like intravenous drug use are very rare in Africa.^{9, 24} The prevalence of HIV co-infection with HBV or HCV reported in this study is similar to the prevalence of HBV reported in the general childhood population which ranges between 9.7 to 44%.^{18, 31, 32} Thus, the prevalence of HBV or HCV in HIV infected children is probably a reflection of the prevalence of HBV or HCV in the general population, suggesting that HIV infected children are not more predisposed to viral hepatitis than the general population; this had earlier been suggested by Sadoh *et al*.¹⁸

Comparison of the mean ages of HIV/HBV and HIV/HCV co-infected children and HIV-monoinfected children showed that children with co-infection were significantly older than their HIV-monoinfected counterparts. This finding is similar to the report from Benin where a tendency towards older age group was

reported among HIV/HCV co-infection,¹⁸ and in contrast to the findings of earlier studies among children that did not find significant association of HIV co-infection with either HBV or HCV with age.^{16-18, 25} The finding of HIV co-infection with HBV and HCV in older children does not support vertical transmission of HBV and HCV because it takes time to interact with the environment to get infected with either HBV or HCV.

The finding rather supports the possibility of high horizontal transmission of HBV infection under the background of inadequate HBV vaccine coverage as main factors for co-infection in this cohort. The younger HIV monoinfected ones probably benefited from improved access to effective universal HB vaccination in infancy, resulting in low prevalence of co-infection among the under-fives.

There was no significant gender difference in the prevalence of HIV co-infection with HBV or HCV in this study similar to findings of previous studies in Nigeria, West Africa, and Tanzania.^{16-17, 25} This finding is however contrary to the belief that HIV/HBV co-infection is more common among males because of the more explorative and risk taking behaviours of boys predisposing them to injuries which are potential portals of transmission.³³ The similar gender prevalence of co-infection found in this study shows that the observed differences in activities between boys and girls is probably not a significant risk factor for co-infection. Other sociodemographic factors such as ethnicity, family type, and religion of father did not pose as significant risk factors for co-infection in this study.

5. Conclusions

Co-infection of HIV with HBV and HCV is a common health problem, occurring predominantly in older children, without gender disparity. Since the impact of co-infection is yet to be fully characterized, routine screening of HIV infected children for HBV and HCV should be carried out, while necessary adjustment of HAART should be done so as to prevent possible adverse outcome later in life. There must be continuous follow up of children with co-infection so that the clinical course can be determined.

The Ministry of Health should strengthen routine HBV vaccination of newborn and older children who missed HB vaccine in infancy to ensure high HB vaccine coverage and reduction of both vertical and horizontal transmission of HBV.

6. Limitations

Screening for HBV co-infection in this study was by the use of HBsAg alone, which does not necessarily indicate current infection. Secondly, HCV infection was not confirmed by plasma PCR for HCV-RNA, making it impossible to distinguish active HCV infection from spontaneously cleared infection.

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