

Human Immunodeficiency Virus And Hepatitis C Virus Co-Infection Among Children In An Antiretroviral Therapy Programme In Benue,

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Abstract

Background; Studies on HIV-Hepatitis C viral (HCV) co-infections in Nigeria have been done essentially among adult and pregnant women with a few in pediatric population. The study aims at documenting the burden and the characteristics of HIV-HCV co-infections in a cohort of Nigerian children.

Methods; A retrospective study among treatment-naïve HIV-infected children attending pediatric clinic of the AIDS PREVENTION INITIATIVE IN NIGERIA Plus/Harvard PEPFAR program of the Federal Medical Centre, Makurdi, between June 2008 and June 2012. Inclusion criteria included all subjects who were screened and got results for viral hepatitis B (HBV) and C. Results; The age range of the included 395 subjects was 16 months to 15 years with a mean age of 7.53 ± 4.23 years including 205 males and 190 females. Nine subjects (2.3%) tested positive for HCV. Thirty one subjects (7.8%) were positive for HBV. No subject was HIV-HBV-HCV triply infected. Significantly more male subjects were HIV-HCV co-infected compared to female subjects, p value of 0.04. Other baseline characteristics including age, route of HIV acquisition and WHO Clinical stage did not significantly affect HIV-HCV co-infection.

Conclusion; This study confirms a low seroprevalence of HCV among our HIV-infected children.

INTRODUCTION

Nigeria accounts for more than 10% of the global paediatric HIV burden, with an estimated 250,000 HIV-infected children (1). More than 95% of these infections were vertically acquired from mother to child. Nigerian coverage of prevention of mother to child transmission (PMTCT) strategies has meagerly increased from 5.3% in 2007 to 11% in 2010 (2). This implies that many new paediatric infections continue to occur, with Nigeria accounting for 30% of the global PMTCT gaps (1). Several other pathogens including Hepatitis C virus are also acquired vertically with the attendant risks of co-infections and the complex interactions (3). Studies on HIV-Hepatitis C viral (HCV) co-infections in Nigeria have been done essentially among adult and pregnant women, indicating a prevalence of HCV infection of between 2.9% to 11.1% (4-7). Rawizza et al (8) and Sadoh et al (9) had reported a prevalence of HIV/HCV co-infections of 2.7% and 5.2% respectively in two cohorts of Nigerian children. However, the burden of pediatric HIV-HCV co-infections may be high considering the fact that

perinatal acquisition of HCV has been shown to increase by 3–5-fold when mothers are HIV-HCV co-infected, particularly if the mother's HCV load exceeds 1million copies/mL (10, 11).

In adult population, HIV infection results in a higher viral load level of HCV in the blood, more rapid progression to HCV-related liver disease including increased risk for cirrhosis and liver cancer (12). Some evidence also indicates that HCV is associated with impaired CD4+ T cell recovery during antiretroviral therapy in an adult population (13). However, with an easier access to and success of HAART in reducing mortality from AIDS, longevity means that co-infected children are more exposed to the aforementioned complex interactions. The need to document the burden of HIV and viral hepatitis C co-infections in Nigerian children cannot therefore be overemphasized. This study therefore set out to determine the prevalence proportion, the clinical and demographic characteristics of HIV-HCV co-infections in a cohort of Nigerian children.

METHODS

Ethical approval for the study as well as written consent/assent procedure for the study was obtained from the Research and Ethics Committee of the Federal Medical Centre, Makurdi. Children were recruited into care and treatment if they were confirmed to be HIV infected and parents or caregivers had given their well documented written consent and the child also had given his/her documented written assent if older than age of 7 years. The study was carried out among HIV infected children receiving care and treatment at the Paediatric ART (Antiretroviral therapy) Clinic of the Riverside Specialist Clinics of the Federal Medical Centre (FMC), Makurdi. FMC, Makurdi is the only tertiary health hospital caring for children with HIV/AIDS in Benue State and is therefore a referral centre for primary and secondary health facilities in Benue State and the surrounding states of Taraba, Nasarawa and Kogi. It is one of the centres supported by the AIDS Prevention Initiative in Nigeria (APIN)/Harvard PEPFAR (The United States President's Emergency Plan for AIDS Relief) program. The program provides free ART to HIV-infected children according to the Nigerian Guidelines on Paediatric HIV/AIDS Treatment and Care. Inclusion criteria included subjects who were screened and got results for hepatitis B surface antigen and HCV antibody at the time of the HIV diagnosis and before the commencement of ART. A proforma was designed to extract the following information from the subjects' data bank at recruitment; age, gender, immunization history, mode of transmission of HIV and WHO clinical stage. All subjects had an initial double rapid HIV antibody tests using Determine™ HIV 1/2 (by ABBOTT JAPAN CO., LTD. Minto-Ku, Tokyo, Japan) first and then HIV 1/2STAT-PAK™ (by CHEMBIO DIAGNOSTICS SYSTEMS, INC. Medford, New York 11763 USA) in serial algorithm. HIV infection was confirmed in those with a reactive rapid test by Western Blot test if aged ≥18 months. Two HIV DNA PCR positivity tests for those <18 months confirmed HIV infection in this age group. Detection of HBsAg was done using ELISA technique (EIAgen HBsAg Kit). IgG antibodies to HCV were detected using an ELISA technique (EIAgen HCV Ab Kit). The tests were done according to instructions of the manufacturer (Diaspot, U.S.A).

Data analysis

Data were entered and analyzed using SPSS version 19. The proportion of subjects with HIV- HCV co-infection was expressed in percentages and by age and gender. Fisher's exact test was used to determine the association between HCV antibody status and age groups, gender, route of HIV

acquisition and WHO staging at recruitment. In order to eliminate the confounding of hepatitis B virus, the data of 31 subjects who were infected with HBV were excluded before Fisher's exact test was used to test the association of HIV-HCV co-infections with WHO stage. The mean ages between the HIV-HCV status groups were compared using the t- test. $P < 0.05$ was taken as significant.

RESULTS

Table 1. Clinical and demographic characteristics of all subjects

A total of 936 children were seen within the study period (June 2008 to June 2012), but only 395 subjects were screened and got results for Hepatitis B and C. The remaining 541 were not screened for reasons bordering on failure to request for screening for the viral hepatitis and occasional instances when the testing kits went out of stock. Among the 395 subjects screened, 31 subjects (7.8%) were positive for HBV. Nine subjects (2.3%) were positive for Hepatitis C antibody. No subject was dually infected with HBV and HCV. The age range of the included 395 subjects was 8 months to 15 years with a mean age of 7.53 ± 4.23 years. There were 205 males and 190 females with a M: F ratio of 1:0.9. Majority (159) were less than 5 years, while others were fairly distributed within the age range of 6-10 years (122) and 11-15 years (114).

Table 1

Clinical and demographic characteristics of all subjects

Characteristics	Number	Percentage
Mean age \pm Standard Deviation	7.53 \pm 4.23	
Gender		
Male	205	51.9
Female	190	48.1
Total	395	100.0
Age groups in Years		
<5	159	40.3
6-10	122	30.8
11-15	114	28.9
Total	395	100.0
Hepatitis B sAg Status		
Positive(HIV-HBV-dually infected)	31	7.8
Negative	364	92.2
Total	395	100.0
Hepatitis C antibody status		
Positive(HIV-HCV-dually infected)	9	2.3
Negative	386	97.7
Total	395	100

Table 2. Clinical and demographic characteristics of HIV-HCV Co-infection Status

HIV-HCV co-infections by age and gender

For HIV-HCV co-infection, younger subjects were dually infected with a mean age of 6.67 ± 3.78 compared to HIV-monoinfected subjects with a mean age of 7.55 ± 4.24 years; this was not significant, p value 0.53. A majority, (5, 3.1%), of HIV-HCV co-infections occurred among the subjects that are less than 5 years, two subjects (1.6%) were HIV-HCV co-infected in age group 6-10 years and two others (1.8%) were in age group 11-15 years, but this was not significant, p value of 0.76. More male subjects (8, 2.6%) were dually infected with HIV and HCV than female subject (1, 0.5%) and this was significant, p value 0.04.

HIV-HCV co-infections and route of HIV acquisitions

Eight subjects (2.2%) that were co-infected with Hepatitis C viral infection also acquired the HIV infection via Mother to Child Transmission but this was not statistically significant, p value of 0.50. The route of acquisition of HIV for one subject (1, 5.0%) with HIV-HCV viral co-infection could not be ascertained.

HIV-HCV co-infections and WHO clinical staging

Although more HIV-HCV co-infected subjects (5, 1.9%) presented in WHO Stage 1 & 2 than Stages 3 & 4 (4, 3.7%), this was not a significant finding, p value 0.46.

Table 2

Clinical, demographic and laboratory characteristics of HIV-HCV Co-infection status

Characteristics	HCV positive(HIV-HCV dually infected)	antibody HCV negative	antibody	P value
Mean age in years \pm SD	6.67 \pm 3.78	7.55 \pm 4.24		0.53
Age group in years				
≤ 5	5	154		0.76
6-10	2	120		
11-15	2	112		
Total	9	386		
Gender				
Male	8	197		0.04
Female	1	189		
Total	9	386		
Route of HIV acquisitions				
MTCT	8	358		0.50
Blood transfusion	0	7		
Others(Sexual)	0	2		
Unknown	1	19		
Total	9	386		
WHO Staging*				
1&2	5	250		0.46
3&4	4	105		
Total	9	355		

*Subjects with HBV are excluded from the analysis.

DISCUSSION

The proportion of 2.3% of HIV-HCV co-infections in this study was similar to 2.7% reported by Rawizza et al (9), but lower than 5.2% reported by Sadoh et al (8) among other

cohorts of HIV-infected Nigerian children. Furthermore, the prevalence of 2.3% is higher than 1.5% reported by Schuval et al (14) in USA but lower than the respective 3.1%, 9.6% and 13.8% published by Toussi et al (15) in USA, Zhou et al (16) in China and by Telatela et al (17) in Tanzania- also among cohorts of HIV-infected children. Rouet et al (18) did not find HCV among a cohort of HIV-infected children in Cote d'Ivoire. Information on the epidemiology of HCV infection in Nigerian children is however limited and had been majorly among those with sickle cell anaemia. Ejiofor et al (19) in Enugu found a higher sero-prevalence of 6.6% and 5.3% among transfused and non-transfused sickle cell anaemia children respectively. Also, Leshi and Kehinde (20) reported a higher sero-prevalence of 5% among children and adults with sickle cell anaemia in Lagos. Above all, Mutimer et al (21) in Benin reported a prevalence of 20% among adolescent and adult sickle cell anaemia patients. The difference in the seroprevalence of HCV in this study and those of other studies may reflect the differences in its geographical distribution, the methodologies and clinical setting of subjects as well as the different sensitivities of tests employed.

Although, a majority, (5, 3.1%), of HIV-HCV co-infections occurred among our under-fives subjects and the majority, (8, 2.2%) that were co-infected with Hepatitis C viral infection also acquired the HIV infection via Mother to Child Transmission, these findings were not significant. Thus vertical transmission of HCV in our under-fives cannot be substantiated. Telatela et al (17) reported that most HIV-HCV co-infected children in their study were under-fives, although, most of the HIV-HCV co-infected children in the study of Sadoh et al (8) were not under-fives, the two studies also did not set out to study mode of HCV acquisition in the first place. It is however, well known that both intrauterine and intrapartum transmission of HCV is possible. For example, HCV has been detected in amniotic fluid (22) and HCV RNA positivity found on the first day of life in some children (23). Intrapartum transmission of HCV is also supported by obstetric factors such as mode of delivery, premature rupture of membranes, and exposure to maternal blood through perineal or vaginal laceration (24, 25). However, the primary risk factor for mother to-child HCV transmission, which is the level of maternal HCV viremia as well as the HCV status of the mothers of our subjects were unknown.

Our study also showed that significantly more male subjects were dually infected with HIV-HCV than female subjects, although, little more males than females were also screened

for HCV. While the import of this finding cannot be ascertained, it however contrasts that of Telatela et al (17) in Tanzania whereby HCV infection was found significantly higher among girls than boys with HIV. However, Zhou et al (16) in China found gender distribution to be similar for HIV-HCV co-infected children.

Although, more HIV-HCV co-infected subjects presented in WHO stages 1 & 2, this was not a significant finding. Zhou et al (16) in China also did not find significant difference in WHO stage at baseline between anti-HCV antibody positive and negative sub-groups. Toussi et al (15), however, found that HCV-co-infected children were more symptomatic presenting in CDC category C disease. Although, HCV genotype 1 has been suggested to be associated with rapid progression to AIDS (26), genotyping for HCV was outside the scope of present study.

Bearing in mind that the burden of HIV-HCV co-infection is low in our study, we could not be sure, whether the HAART, which majority of the mothers of our subjects were exposed to, was responsible for the low prevalence of the HCV infection in the study population. Also, a survival bias may also explain the low prevalence of HIV-HCV co-infection in our study as co-infected children may not be surviving long enough to be recruited into our care and treatment program. It is however, desirable to know the HCV status of HIV-infected pediatric population for the following reasons accruing from adult studies. Firstly, HAART may slow liver disease progression and might therefore be initiated earlier in co-infected than HIV monoinfected patients (27). Secondly, interruption of ART has been found to be unsafe in HIV-HCV co-infected individuals because of elevated non-opportunistic disease deaths (28). Thirdly, ART drugs containing, zidovudine, didanosine, stavudine, and abacavir should be avoided and others closely monitored for hepatotoxicity in HIV-HCV co-infected patients (29). On the other hand, treatment of chronic HCV in co-infected individuals is a priority because of their more rapid progression to ESLD, poor tolerance of ART, and greater risk of hepatotoxicity (30).

Our study is limited by the fact that enzyme immunoassay was used for HCV screening. It cannot therefore be exempted from the pitfalls of the antibody test including; failure to detect early HCV infection and false negativity in immune-suppressed individuals (although less with the more sensitive third generation immunoassay employed in the present study). More also, the antibody test may also have reported a false positive test as young children, even with HIV co-infection can resolve HCV early in life and still have

persistent antibody. However, diagnosing HCV viremia by molecular testing is not a routine test at our centre.

Furthermore, the sample size of the study has limited testing to Fisher's exact test.

In summary, the findings of this study would sum up to indicate that there is a low prevalence of HCV-infection in our children with HIV and that HIV-HCV co-infection occurred significantly more in boys than girls.

It is therefore recommended that more studies (involving primary and secondary health care facilities) be carried out to determine the sero-prevalence of HIV-HCV among Nigerian children. Furthermore, longitudinal studies of HIV-HCV infected children are desirable in order to evaluate the impacts of the HCV on HIV disease and vice versa, especially after commencement on HAART.

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