

# Human immunodeficiency virus and Hepatitis C virus co-infection in children in Jos, Nigeria

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## Abstract

Background: Human Immunodeficiency Virus (HIV) and Hepatitis C virus (HCV) share similar modes of transmission and hence co-exist in the same host at significantly high rates. The effect of HIV infection on progression of HCV infection in adults is well established. HCV infection also increases the toxicity to antiretroviral medications. Co-infection with HCV may lead to rapid progression of HIV disease. This study aimed to determine the rate of co-infection with hepatitis C in HIV-infected children in Jos, Nigeria and compare the baseline laboratory parameters of mono and co-infected patients. Methods: We reviewed the clinical records of three hundred and sixty-two treatment-naïve children aged 18 months to 15 years confirmed HIV positive with Western blot enrolled at AIDS Prevention Initiative in Nigeria (APIN)-supported HIV clinic at Jos University Teaching Hospital (JUTH), Jos, Nigeria between January 2008 and December 2012. Their HCV antibody test, CD4<sup>+</sup>T count for children  $\geq 5$  years, CD4<sup>+</sup>T % generated by automated method for children  $< 5$  years, viral load and alanine transaminase (ALT) results were analysed. Results: Three hundred and forty-four (95.0) were mono-infected with HIV while 18 (5.0) were co-infected with HIV and HCV. The median viral load was 4.6 log copies/ml for mono-infected compared to 4.8 log copies/ml for HIV/HCV ( $P = .09$ ). The median CD4<sup>+</sup>T count was 366 cells/ $\mu$ l for mono-infected compared to 359 cells/ $\mu$ l for HIV/HCV ( $P = .82$ ). The median CD4<sup>+</sup>T % was 19% for mono-infected compared to 20% for HIV/HCV ( $P = .43$ ). The median ALT level was 23 IU/L for mono-infected compared to 28 IU/L for HIV/HCV ( $P = .12$ ). Sixty-seven (18.5%) children had elevated ALT ( $> 41$  IU/L) but there was no difference between the 2 groups: HIV mono-infection 18.3%, HIV and HCV co-infection 22.2% ( $P = .51$ ). Conclusion: Five percent of HIV-infected children in this cohort were co-infected with hepatitis C; however more severe HIV disease and increased liver enzymes were not observed. Early detection is however necessary in order to develop an appropriate treatment plan for children co-infected with HIV and HCV.

## Keywords

HIV, Hepatitis C, Co-Infection, CD4<sup>+</sup>T, Viral Load, Alanine Transaminase, Nigeria

## 1. Introduction

Human immunodeficiency virus (HIV) and hepatitis C virus (HCV) are common chronic viral infections seen in

the world. [1] Co-infection with HCV varies widely among HIV infected children in sub-Saharan African countries. [2], [3], [4], [5] The two viruses share similar modes of transmission and hence co-exist in the same host at

significantly high rates. [6] Hepatitis C is likely to lead to chronic infection in up to 60 - 80% of patients after an acute infection. [7], [8]

The effect of HIV infection on progression of HCV infections in adults is well established. [9] HIV-induced immunosuppression has deleterious effects on the natural history, pathophysiology, diagnosis, and therapeutic responses to hepatitis viruses. [6] Co-infection with HIV enhances the risk of severe liver disease caused by HCV infection. [10], [11] HCV infection also increases the toxicity to antiretroviral medications. [6] Co-infection with HCV may lead to rapid progression of HIV disease. [4], [11] A previous study in adults in Nigeria showed that patients with HIV and HCV co-infection had higher HIV RNA loads and more severe immune suppression prior to initiation of HAART compared to HIV mono-infected patients. [12]

As more HIV-infected children co-infected with HCV are put on highly active anti-retroviral therapy (HAART), they will live longer and complications of chronic HCV infection will likely become a major health care catastrophe in the coming years especially in resource-limited countries. This study therefore aimed to determine the rate of co-infection with HIV and HCV in children in Jos, Nigeria and compare the baseline laboratory parameters of mono and co-infected patients.

## 2. Materials and Methods

The study was carried out at AIDS Prevention Initiative in Nigeria (APIN)-supported HIV clinic of Jos University Teaching Hospital, Jos, Plateau State, Nigeria. The programme cares for patients in and outside Plateau state. HIV care, treatment and support services are free for all patients enrolled in the program.

A written informed consent was obtained from parents/guardians for use of data for research. Ethical clearance was obtained from the Ethical committee of Jos University Teaching Hospital.

The medical records of all treatment-naïve HIV-infected children aged 18 months to 15 years enrolled in the Pediatric ART program between January 2008 and December 2012 were reviewed for the study. Those aged <18 months were excluded because HCV antibody test is not diagnostic of HCV infection at that age. HIV infection was confirmed with Western blot results. The baseline laboratory parameters assessed include HCV antibody, CD4<sup>+</sup>T count and CD4<sup>+</sup>T percent, viral load, and Alanine transaminase (ALT). Serological assay for HCV antibody was used to categorize hepatitis status of the patients. HCV antibody was tested using third generation enzyme Immunosorbent assay (DIA.PRO Diagnostic, Bioprobes srl, Milan, Italy). HIV RNA levels were measured using Roche COBAS Amplicor HIV-1 monitor test version 1.5 (Roche Diagnostics, GmbH, Mannheim, Germany) with a detection limit of 400 copies/mL. Flow cytometry was used to determine CD4<sup>+</sup>T cell count (Partec, GmbH Munster,

Germany) and the CD4<sup>+</sup>T percent determined by automated method.

HCV and HIV characteristics at baseline were compared using nonparametric univariate methods; the Kruskal-Wallis test was used for continuous variables. Linear regression analyses were used to determine whether HCV status was associated with baseline CD4<sup>+</sup>T cell counts/percent, HIV load, or ALT values. *P* value <0.05 was considered significant. Analysis was done with EpiInfo version 3.5.1.

## 3. Results

Three hundred and sixty-two treatment-naïve children between the ages of 18 months and 15 years were enrolled between January 2008 and December 2012. There were 203 (56.1%) males 159 (43.9%) females. The mean age was 4.72±3.18 years. The mean age for the males was 4.24±2.78 years and that of the females was 5.34±3.55 years (*P* = .06). Three hundred and forty-four (95.0) were mono-infected with HIV while 18 (5.0) were co-infected with HIV and HCV (HIV/HCV). The characteristics of the patients are shown in Table 1.

*Table 1. Characteristics of the patients.*

<b>Sex</b>	
Males	203 (56.1%)
Females	159 (43.9%)
<b>Age</b>	
1-5years	231 (63.8%)
6-10years	111 (30.7%)
11-15years	20 (5.5%)
<b>Hepatitis status</b>	
Negative	344 (95.0%)
HCV positive	18 (5.0%)

Based on age group, 5.2% of those aged 1-5 years were co-infected with HCV compared to 4.5% of 6-10 year age group and 5.0% of 11-15 year age group (*P* = .92). Although more males than females were co-infected with HCV, the differences were not significant: males 5.4%, females 4.4% (*P* = .66).

The median viral load was 4.6 log copies/ml (IQR, 3.8-6.8 log copies/ml) for mono-infected compared to 4.8 log copies/ml (IQR, 3.6-6.1 log copies/ml) for HIV/HCV (*P* = .09).

The median CD4<sup>+</sup>T count was 366 cells/μl (IQR, 4-2322 cells/ μl) for mono-infected compared to 359 cells/μl (IQR, 34-2108 cells/μl) for HIV/HCV (*P* = .82). The median CD4<sup>+</sup>T % was 19% (IQR, 1-68%) for mono-infected compared 20% (IQR, 9-37%) for HIV/HCV (*P* = .43).

The median ALT level was 23 IU/L (IQR, 2-155 IU/L) for mono-infected compared to 28 IU/L (IQR, 3-193 IU/L) for HIV/HCV (*P* = .12). Sixty-seven (18.5%) children had elevated ALT (>41IU/L) but there was no difference between the 2 groups: HIV mono-infection 18.3%, HIV and HCV co-infection 22.2% (*P* = .51).

Hepatitis C status was not associated with a reduced CD4<sup>+</sup>T count or CD4<sup>+</sup>T %, or an elevated viral load or ALT (Table 2).

**Table 2.** Co-infection status and median of different parameters.

Parameter	HIV alone n= 376	HIV/HCV n= 12	P value
Median viral load (IQR)*	4.6 (3.8-6.8)	4.8 (3.6-6.1)	.09
Median CD4 <sup>+</sup> T (IQR) <sup>#</sup>	366 (4-2322)	359 (34-2108)	.82
Median CD4 <sup>+</sup> % (IQR)	19 (1-68)	20 (9-37)	.43
Median ALT (IQR) <sup>^</sup>	23 (2-155)	28 (3-193)	.12

IQR= interquartile range \* log copies/ml # cells/ $\mu$ l ^ IU/L

## 4. Discussion

The prevalence rate of hepatitis C co-infection in this cohort was 5.0%. The HIV/HCV co-infection rate was higher than 2.3% reported in Makurdi, Nigeria [13]; 1.5-3.1% reported in USA, [14], [15] and 0% reported by Rouet in Cote d'Ivoire [16] and Chakraborty in Kenya. [4] The rate was however lower than 9.6% reported in China [17] and 13.8% in Tanzania. [5] The difference in the prevalence of co-infection in this study and that of other studies may reflect the differences in the geographical distribution, population studies and the methodologies as well as the different sensitivities of tests employed.

No significant difference was observed in the rate of co-infection with HCV between the different age groups, and between males and females. This is similar to what was reported in China by Zhou. [17] Anigilaje [13] observed that more males than females were co-infected with HCV in Makurdi, Nigeria while Telatela [5] reported that more girls than boys were co-infected with HCV in Tanzania.

We did not observe any significant difference in the median viral load, CD4<sup>+</sup>T count and CD4<sup>+</sup>T % of mono and co-infected patients. This is similar with what was reported elsewhere in developing countries. [4], [13], [18] Toussi [15] however observed that HIV-HCV co-infected children had a lower CD4% and a higher HIV RNA levels compared to their mono-infected counterparts in USA.

In this study, 18.5% of the patients had elevated ALT levels. This is comprised of 18.3% of mono-infected patients and 22.2% of HCV co-infected patients. Although HCV co-infected patients had a slightly higher median ALT level compared to mono-infected patients, the difference was not significant. This is similar to earlier reports in developing countries and China. [13], [17], [18] In a study in Tanzania [5], elevated ALT value was associated with HIV-HCV co-infections in the univariate analysis but not in multivariate analysis. A report from USA [15] showed that HCV co-infected children were more likely to have mildly elevated transaminase levels (57%), compared with the mono-infected group (19%). In contrast to adults, studies have shown that most children

with chronic HCV infection are asymptomatic with normal or mildly elevated liver enzymes and mild histological findings. [19], [20], [21], [22]

Currently there is no recommendation on the treatment of children co-infected with HIV and HCV. In adults, studies have shown that treatment of chronic HCV co-infected individuals is a priority because of more rapid progression to end stage liver disease (ESLD), poor tolerance of ART, and greater risk of hepatotoxicity. [23], [24] A recent report showed that HIV/HCV co-infected children in Europe had poor hepatitis C treatment outcome mainly because treatment of HCV was started late. [25] A recommendation on the treatment of children co-infected with HIV and HCV is most desirable in order to improve their overall treatment outcome.

## 5. Conclusion

Hepatitis C co-infection rate of 5% was observed in HIV-infected children in this study; but more severe HIV disease and increased liver enzyme were not observed. Early detection is however necessary in order to develop an appropriate treatment plan for them. Appropriate recommendations also need to be developed for the treatment of children co-infected with HIV and HCV.

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