

# Seroprevalence and factors associated with hepatitis C coinfection among HIV-positive pregnant women at the University College Hospital, Ibadan, Nigeria

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## ABSTRACT

**Aim:** This study estimated the hepatitis C virus (HCV) prevalence in a population of human immunodeficiency virus (HIV) infected pregnant women, compared women who were positive or negative for HCV and described risk factors associated with HCV infection.

**Materials and Methods:** A retrospective, case control study was conducted at the University College Hospital, Ibadan among 1821 women. Twenty-six (1.65%) women were HCV positive, 139 (8.83%) were HBsAg positive and 1407 (89.33%) were negative for both viruses. Three patients (0.19%) were positive for both viruses. These patients, i.e., the HBsAg positive women and 246 women with no result, for either virus were excluded from analysis. Data from 1433 pregnant women is presented. Chi square test and student's *t*-test examined associations, with level of significance set at  $P < 0.05$ .

**Results:** Overall, the mean age of the HCV positive women was lower ( $26.77 \pm 6.53$  vs.  $28.95 \text{ years} \pm 5.33$ ;  $P = 0.04$ ), most women had attained primary (28.49%) or secondary (42.44%) education, over 90% were married and heterosexual sex (88.67%) was the most likely risk for HIV. HCV prevalence was higher in the lower age groups (5% in the  $\leq 19$  years group,  $P = 0.021$ ). The coinfecting had more unmarried women (3.6% vs. 1.7%;  $P = 0.164$ ) and more likely to indicate blood transfusion as a risk factor for HIV (6.2%;  $P = 0.34$ ).

**Conclusion:** Only age showed any significant association with HCV infection. Lack of identifiable risk factors sum up challenges for developing screening strategies in sub-Saharan Africa. Further studies will identify factors facilitating HCV transmission in the region.

**Key words:** Human immunodeficiency virus; hepatitis C virus; pregnancy; risk factors.

## Introduction

Hepatitis C (HCV), a blood borne virus, was identified in 1989. It is a small, enveloped, single-stranded, positive sense RNA virus in the flaviviridae family.<sup>[1]</sup> It is a major global public health problem affecting 3% of the world population, i.e., 170 million people globally.<sup>[2]</sup> In Nigeria, the estimated prevalence of HCV infection varies widely

(0.4–14.7%) depending on the sub-population being considered.<sup>[3-11]</sup> HCV is important because it predisposes to eventual development of liver fibrosis, as well as hepatocellular carcinoma.<sup>[12]</sup>

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The main modes of transmission of Hepatitis C include intravenous drug use,<sup>[13,14]</sup> unsafe blood and blood products, risky sexual behaviour<sup>[15]</sup> and vertical transmission.<sup>[16]</sup> Many of these modes of transmission are similar to those of HIV, leading to coinfection.<sup>[17,18]</sup> The result is that of the 40 million people living with the human immunodeficiency virus type-1 (HIV); 4.5 million of these are estimated to be infected with hepatitis C as well.<sup>[19]</sup> Some studies have established that HIV coinfection accelerates the progression of HCV infection and vice-versa.<sup>[20]</sup> In addition, although the mechanism is unclear, several studies have reported a higher risk of vertical transmission of HCV in HCV/HIV coinfecting women.<sup>[16,21,22]</sup> Previous studies have shown that coinfection with HIV and HCV increases the transmission risk of HIV from the mother to her baby.

The average rate of Mother-to-child transmission (MTCT) of HCV is 5% to 6%.<sup>[23]</sup> The timing and route by which HCV passes from the mother to child, and the host defense mechanisms that govern this transmission, remain poorly understood. Clinical risk factors for MTCT are similar to those seen in HIV.<sup>[21]</sup> Although several risk factors for vertical transmission have been identified, none are modifiable and there are currently no interventions available to prevent such transmission.<sup>[23]</sup> Finally, treatment of HCV during pregnancy has safety issues.<sup>[16]</sup> Ribavirin has been labeled as a Food and Drug Association (FDA) pregnancy category X drug, whereas pegylated IFN- $\alpha$  is an FDA pregnancy category C drug.<sup>[24]</sup>

In sub-Saharan Africa, coinfection with HCV and HIV is of particular concern. This is because the high prevalence of HIV infection and increasing access to life-prolonging antiretroviral therapy in sub-Saharan Africa, liver disease is expected to emerge as a major cause of morbidity and mortality among HIV-infected persons, especially those co-infected with hepatitis.<sup>[25]</sup>

The objective of this study was to estimate the prevalence of HCV infection in a large population of HIV-infected pregnant women. We also compared the characteristics of the HCV positive and HCV negative women with a view to describing possible risk factors associated with HCV infection in this group of pregnant women.

## Materials and Methods

The University College Hospital Ibadan offers prevention of mother-to-child transmission (PMTCT) services supported by the Government of Nigeria and the acquired immunodeficiency syndrome (AIDS) Prevention Initiative in Nigeria (APIN) program. HIV-positive pregnant women access these services having being referred from the UCH antenatal clinic, and other clinics in the region. PMTCT services provided include

antiretroviral therapy for PMTCT, infant feeding counseling and family planning counseling. In addition, women are monitored by periodic assay of CD4 count and viral load. The program maintains an electronic database of the records, including laboratory results, of all patients enrolled between January 1<sup>st</sup> 2006 and 31<sup>st</sup> December 2013; during this period, 1821 women registered for care at the PMTCT unit of the hospital. Variables recorded at the first clinic visit include sociodemographic characteristics, possible risk factors for HIV acquisition, CD4 counts, viral load and hepatitis B and C status. These baseline laboratory testing are conducted using third-generation enzyme-linked immune absorbent assay (ELISA) for detection of hepatitis B surface antigen (HBsAg) and testing for HCV antibodies (anti-HCV) using third-generation assays. Only those with HIV monoinfection or HIV/HCV coinfection were included in the review. A retrospective case-control study was conducted among those with HIV/HCV coinfection as cases and those with HIV monoinfection as controls.

The baseline characteristics of HCV-infected and uninfected pregnant women were analyzed. Data was entered and analysed using the Statistical Package for Social Sciences (SPSS Inc, Chicago, IL, USA, version 15). Continuous variables were presented as mean and standard deviation whereas categorical variables were presented as frequencies or percentages. Associations between categorical variables were investigated using Chi-square test whereas student's *t*-test was used to test for significant difference in continuous variables, with level of significance set at  $P < 0.05$ .

## Results

During the study period, 1821 women presented for care. Two hundred and forty six (246) of the women had no available result for screening tests for either HBV or HCV, and hence were excluded from the analysis. Table 1 shows the distribution of the patients according to hepatitis status over the years under consideration. The number of new HIV-positive pregnant women seen at the clinic is noted to have declined gradually over the years. The prevalence of HCV is noted to reduce in a similar pattern.

Overall 26 (1.65%) women were positive for HCV, 139 (8.83%) were positive for HBsAg and 1407 (89.33%) were negative for both HBV and HCV. Three patients (0.19%) were positive for both HBV and HCV. These patients and the HBsAg positive pregnant women were also excluded from further analysis because the presence of HBV could confound the results.

In the final analysis, a total of 1433 pregnant women were eligible for inclusion in the study [Figure 1].

Table 2 shows the distribution of the sociodemographic characteristics. Overall, the mean age of the patients was  $29.16 \pm 7.14$ . The mean age of the HCV-positive and HCV-negative women was 26.77 years  $\pm$  6.53 and 28.95 years  $\pm$  5.33, respectively ( $P = 0.04$ ). Most of the women were of low socioeconomic status and had attained

**Table 1: Distribution of hepatitis status over the years**

Year	Total No (%)	Hepatitis	Hepatitis	Hepatitis	Hepatitis
		B/C negative No (%)	C positive No (%)	B positive No (%)	B&C positive No (%)
2006	315 (20.0)	285 (90.5)	7 (2.2)	23 (7.3)	0 (0.0)
2007	379 (24.1)	330 (87.1)	7 (1.8)	41 (10.8)	1 (0.26)
2008	204 (12.94)	181 (88.7)	6 (2.9)	17 (8.3)	0 (0.0)
2009	185 (11.74)	172 (93.0)	2 (1.1)	11 (5.9)	0 (0.0)
2010	166 (10.53)	144 (86.7)	3 (1.8)	18 (10.8)	1 (0.6)
2011	142 (9.02)	129 (90.8)	1 (0.7)	12 (8.5)	0 (0.0)
2012	127 (8.05)	115 (90.6)	0 (0.0)	11 (8.7)	1 (0.79)
2013	57 (3.62)	51 (89.5)	0 (0.0)	6 (10.5)	0 (0.0)
Total	1575 (100.0)	1407 (89.33)	26 (1.65%)	139 (8.83)	3 (0.19)

**Table 2: Sociodemographic characteristics of participants**

Year	Total No (%)	Hepatitis	Hepatitis	<i>P</i>
		C positive No (%)	B/C negative No (%)	
<b>Age group</b>				
≤19 years	40 (2.82)	2 (5.0)	38 (95.0)	0.021
20-24 years	247 (17.39)	10 (4.0)	237 (96.0)	
25-29	492 (34.65)	6 (1.2)	486 (98.8)	
30-34	426 (30.0)	3 (0.7)	423 (99.3)	
35-39	172 (12.11)	4 (2.3)	168 (97.7)	
≥40 years	43 (3.03)	1 (2.3)	42 (97.7)	
<b>Occupation</b>				
Unemployed/trainee				0.642
/student	79 (8.54)	3 (3.8)	76 (96.2)	
Low skilled/farming	278 (30.05)	6 (2.16)	272 (97.84)	
Trading	405 (43.78)	10 (2.47)	395 (97.53)	
Civil servant (junior)	29 (3.14)	0 (0)	29 (100.0)	
Civil servant (senior)	61 (6.6)	2 (3.28)	59 (96.72)	
Housewife	68 (7.35)	0 (0.0)	68 (100.0)	
Uniformed	5 (0.54)	0 (0.0)	5 (100.0)	
<b>Level of education</b>				
None	108 (7.81)	0 (0.0)	108 (100.0)	0.756
Primary school	394 (28.49)	8 (2.0)	386 (98.0)	
Secondary school	587 (42.44)	12 (2.0)	575 (98.0)	
Tertiary level	294 (21.26)	5 (1.7)	289 (98.3)	
<b>Marital status</b>				
Married	1299 (92.06)	22 (1.7)	1277 (98.3)	0.164
Not married	112 (7.94)	4 (3.6)	108 (96.4)	
<b>Risk factor for HIV</b>				
Heterosexual sex	892 (88.67)	22 (1.8)	870 (97.97)	0.336
Transfusion	11 (1.09)	1 (6.2)	10 (90.91)	
Heterosexual/transfusion	41 (4.08)	2 (3.7)	39 (95.12)	
Unknown	60 (5.96)	1 (1.7)	59 (98.3)	
IVDU	2 (0.2)	0 (0.0)	2 (100.0)	

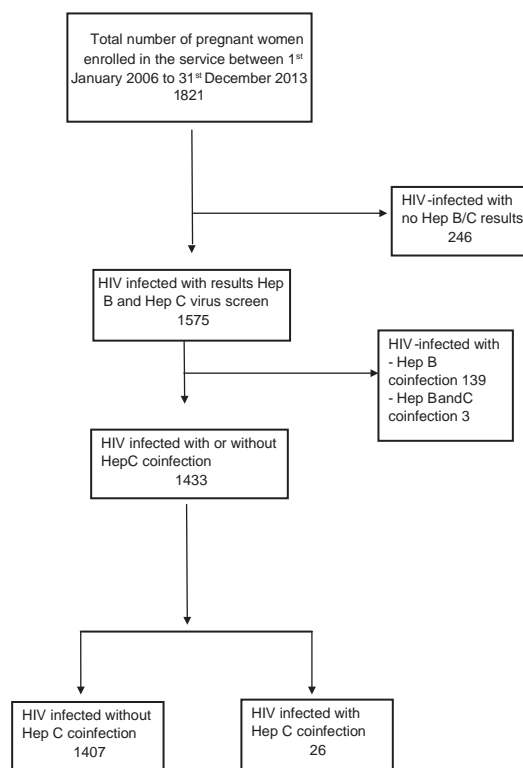
only primary or secondary level of education. Over 90% were married and had heterosexual sex as the most likely route of HIV transmission.

The prevalence of HCV was higher in the lower age groups with 5% and 4% prevalence reported in the 19 years and below age group and the 20–24 years age group, respectively. The difference in HCV prevalence in the different age groups was statistically significant.

The pattern of occupation and level of education was similar among HIV/HCV coinfecting and HIV mono-infected women. A large proportion of the patients were involved with low-skilled employment or trading. Most of the HCV positive women were in the low skilled groups. Finally, the coinfecting group had more unmarried women and were more likely to have indicated blood transfusion as a risk factor for HIV. However, these differences were not statistically significant. Two patients admitted to a history of intravenous drug use, however, neither was reported as being HCV positive.

## Discussion

The prevalence of HIV/HCV coinfection in our population of HIV-infected pregnant women is low. Age was the only identifiable risk factor for HCV in this cohort. Intravenous



**Figure 1: Flow diagram of pregnant women enrolled in the study**

drug use, which features prominently in most series, was not a risk factor in this group of pregnant women.

Worldwide, HCV prevalence in pregnant women has been estimated to be approximately 1%.<sup>[26]</sup> The HCV coinfection rate of 1.65% in this cohort of HIV positive women is in the range of 1.5% and 2.4%, respectively, reported among HIV positive pregnant women in Lagos by Ezechi *et al.*<sup>[3]</sup> and Zeba *et al.* in Ouagadougou.<sup>[27]</sup> It is, however, lower than the rate of 5.3% reported by Chasela *et al.* from Malawi,<sup>[28]</sup> and much lower than 29.69% reported by Seisededos *et al.* from Spain<sup>[29]</sup> among HIV-positive pregnant women. In the general obstetric population (from various parts of Nigeria), rates of hepatitis C prevalence of 2.7%, 2.6%, 3.6% and 0.4% have been reported from Osogbo,<sup>[9]</sup> Enugu,<sup>[30]</sup> Benin<sup>[11]</sup> and Calabar,<sup>[6]</sup> respectively. In the adult HIV-positive population (also in Nigeria), rates of 11.3%, 2.3%, 3.1% and 4.8% have been reported from Jos,<sup>[4]</sup> Lagos<sup>[31]</sup> and Ibadan,<sup>[10]</sup> respectively.

Some of the reasons given for these wide variations in prevalence include the screening algorithms adopted. It has been suggested that most HCV prevalence estimates from sub-Saharan Africa based on screening systems without supplemental testing are overestimates.<sup>[28]</sup> These supplemental testing include confirmatory tests such as nucleic acid and test for HCV RNA or Recombinant immunoblot assay (RIBA).<sup>[2]</sup> Studies using supplemental testing have reported lower prevalence estimates.<sup>[32,33]</sup> These authors have noted that continued HCV screening without supplemental confirmatory testing of blood donations could result in discarding uninfected blood. In addition, the disclosure of test results may cause unnecessary despair to those misdiagnosed and the permanent withdrawal of uninfected donors from the small donor pool. There is, thus, a need for increased focus on improving the HCV testing algorithms in sub-Saharan African.

Apart from a higher prevalence of HCV in the young age groups, there were no remarkable differences in the sociodemographic characteristics between the HIV monoinfected and HIV/HCV coinfecting pregnant women. Age has been argued to be a major factor in HCV studies. However, in contrast to our cohort, a higher prevalence of infection in older individuals has been reported.<sup>[34,35]</sup> It has been suggested that the reported higher prevalence of HCV in older individuals may be due to the prolonged period of incubation of the virus.<sup>[1]</sup> In a study conducted in 2000 in Egypt, Abdel-Aziz found anti-HCV antibody prevalence to increase sharply with increasing age, with persons currently or previously married more likely to be seropositive than those who never married.<sup>[36]</sup> In our study, while the possible reason for the higher prevalence in the younger age groups

is not clear, the unmarried group actually had a higher prevalence of HCV positive women. The difference observed in marital status was, however, not statistically significant.

In most series the main route of acquiring HCV in pregnant mothers was intravenous drug use, whereas previous blood transfusion was a risk factor in up to 11% of cases.<sup>[22,37,38]</sup> Only 2 patients admitted to a history of intravenous drug use in the group of pregnant women we studied. Intravenous drug use is uncommon in this part of the world.<sup>[6]</sup> However, the group of HIV-positive women who reported previous blood transfusion as a risk factor for HIV infection had a higher prevalence of HCV infection in our cohort. Globally, transfusion-associated infection was a predominant risk factor before HCV testing became available.<sup>[7]</sup> Indeed, in communities that have implemented routine testing of donors, it has been virtually eliminated. However, in other communities, receipt of unsafe blood and blood products remain an important source of infection.<sup>[7]</sup> A contributory factor is the continued use of commercial donors to supplement blood supplies by some countries.<sup>[32]</sup>

With the exception of age, other putative risk factors evaluated in this study showed no significant association with anti-HCV seropositivity. The risk factors for HCV infection may be unidentified in a significant proportion of patients in many parts of the world. In some studies, risk factors accounting for infection remain unknown in 10–40% of patients, with acute or chronic Hepatitis C.<sup>[39,40]</sup> Indeed in 60 of the patients we studied, the risk factors were unknown. These findings pose major implications for developing strategies for HCV screening.<sup>[7]</sup> Individuals infected with the virus with no identifiable risk factors sum up the problems associated with HCV studies in the sub-saharan Africa region.<sup>[6]</sup> This finding, therefore, suggests the need for further studies that would evaluate factors that may facilitate HCV transmission in the region.

This study has several limitations. First, the risk factors for viral hepatitis acquisition were not directly evaluated. Instead, the risk factors for HIV infection were used as proxy on account of the similarity in modes of transmission of both viruses. Second, plasma HCV-RNA was not quantified in patients who had anti-HCV, making it impossible to distinguish active HCV infection from spontaneously cleared infection. Third, this was a retrospective study. However, data collection and retrieval via an electronic platform afforded a robust information collection.

## Conclusion

In conclusion, the seroprevalence of anti-HCV in the population of HIV positive Nigerian pregnant women

evaluated in this report is 1.65%. The risk factors associated with anti-HCV seropositivity are largely obscure, and this calls for more studies into the epidemiology of HCV infection to develop effective strategies for screening.

### Ethical considerations

The antiretroviral treatment program was approved by the University of Ibadan/University College Hospital Ibadan, Joint Institutional Review Board. Informed consent forms were signed by all patients during enrollment procedures. The electronic medical record systems for the patient data are implemented on a password-protected computer systems for the purpose of privacy and confidentiality of data. Patients' folders containing case report forms were kept in safe cabinets with locks in the medical records section, and access was restricted to authorised persons only.

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### Conflicts of interest

There are no conflicts of interest.

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