

## Hepatitis C virus coinfection in human immunodeficiency virus-infected pregnant women in Anyigba, Kogi State, Nigeria

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**Abstract:** Co-infection of human immunodeficiency virus (HIV) positive pregnant women with hepatitis C virus (HCV) is associated with increased morbidity and mortality globally. Due to the dearth of documented HCV studies among HIV patients in this study area, there was a need for determining the seroprevalence and risk factors of HCV infection among HIV seropositive mothers in the study population. Blood samples obtained from 200 HIV seropositive pregnant women in a cross-sectional study design were screened for anti-HCV antibody using the commercial ARIA® HCV-Ab test kit. Patient's demographic data, behavioural and obstetric characteristics were collected using a structured questionnaire. Five (2.5%) of the patients were co-infected with HIV/HCV and pregnant women aged  $\geq 41$  years have the highest prevalence of dual infection by both viruses. Women in their first trimesters of pregnancy had higher rate of coinfection although, gestation was not statistically related to acquisition of HCV infection ( $P > 0.05$ ). Factors such as blood transfusion ( $P = 0.002$ ; OR = 24.89; 95% CI: 2.68-231.15) and history of abortion ( $P = 0.001$ ; OR = 47.25; 95% CI: 6.62-337.17) were significantly associated with HCV seropositivity. In conclusion, HCV is a public health concern in HIV positive pregnant women in Lokoja and epidemiological study on larger scale is needed to unravel the true burden of the disease in the study area.

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### 1. Background

Hepatitis C virus (HCV) is a small, enveloped, single-stranded, positive sense RNA virus in the family flaviviridae [Kesson, 2002]. HCV, a blood borne virus, remains one major etiologic agent of chronic hepatitis and frequent causes of morbidity and mortality Worldwide. Hepatitis C is often asymptomatic, but once established, chronic infection can progress to fibrosis and cirrhosis which is generally apparent after many years [Afolabi et al., 2002; Ryan and Ray, 2004]. In some cases, those with cirrhosis will go on to develop hepatocellular carcinoma, the commonest reason for liver transplantation in many countries [Charlton, 2001; Wasley and Alter, 2000].

The prevalence of HCV in the general population is high and has a wide local variation [Collenberg et al., 2006]. Global health report revealed that more than 170 million people making up 3% of the world population are carriers of HCV with developing countries having majority of cases.

Co-infection of HIV patients with HCV is a serious public health concern globally due to its potential risk of mother to child transmission [Okeke et al., 2012], negative effects HIV exerts on the life

cycle of HCV and afterwards on the hepatic system. HIV – specific CD8 T-cells for instance, accumulate in the liver in co-infection and produce TNF -  $\infty$ , which is associated with liver fibrosis [Hernandez and Sherman, 2011; Vali et al., 2008]. HCV and HIV are similar in their transmission routes, leading to possible co-infection with both viruses [Jamieson et al., 2008; Plamondon et al., 2007]. Previous studies have shown that HCV co-infection increases the risk of vertical transmission of HIV from infected mothers to the child by about 4 to 5 fold. Likewise, the perinatal transmission of HCV is estimated at 4–8% and transmission rate increases to 17–25% if the mother is concomitantly infected with HIV [Arshad et al., 2011]. The increased risk of HCV mother-to-child transmission (MTCT) in maternal HIV coinfection is attributed to factors such as high levels of HCV in maternal plasma [Polis et al., 2007; Zanetti et al., 1995], altered immunity at the placental barrier and physical disruption of the placenta due to HIV infection of trophoblasts [Le Campion et al., 2012].

Approximately 36.9 million people are living with HIV/AIDS worldwide and burden of co infection with HCV is estimated to be 4-5 million [Mbotto et al., 2006]. Evidence of HCV infection has been found in

an average of 5% of infants born to HCV mothers and ranges between 5 – 36% of children born to women co-infected with human immunodeficiency virus (HIV) and HCV [Safir et al., 2010]. Maternal HCV carrier status has been reported as an independent risk factor for an adverse perinatal outcome [Operskalski and Kovacs, 2011].

Coinfection with HCV increases risk of liver toxicity in people on HAART and the burden of metabolic disease thus, contributing to a faster progression of liver fibrosis. Activation of immune cells by HIV causes release of cytokines that increase liver inflammation and fibrosis [Thein et al., 2008]. Co-infection also increases apoptosis of hepatocytes through a Fas/Fas L pathway. Thus, HIV patients co-infected with HCV tend to have faster progression to cirrhosis and liver cancer [Labarga et al., 2007].

In sub-Saharan Africa, the increasing access to life-prolonging antiretroviral therapy in HIV-infected populations is a major concern especially among HIV seropositive patients that are co-infected with hepatitis. The anti-HCV treatment is less effective in co infected patients [AASLD,2015] and no standard antiviral drug therapy is currently available for HCV-infected women during pregnancy [Lavanchy,1999]. Consequently, prevention of the infection remains a key. To prevent HCV and reduce the burden of liver diseases and hepatocellular carcinoma, it is imperative to evaluate the contribution of risky parenteral and non-parenteral exposures [Lavanchy, 2011]. This study was therefore designed to determine the prevalence of HCV and predisposing risk factors among pregnant women living with HIV/AIDS in Lokoja, Kogi State.

## 2. Methods

### 2.1 Study Area

Study was carried out in Lokoja metropolis the capital of Kogi State located in the north central region of Nigeria. Lokoja town situated on geographical coordinates 7° 48' North of the equator and 6° 44' East of the greenish meridian, has an estimated population of 60,579 people from the 2006 population census.

### 2.2 Study Design and Population

This was a hospital based prospective cross-sectional study in which HIV positive pregnant women accessing the antiretroviral treatment centres at the Kogi State Specialist Hospital (KSSH) and Federal Medical Centre (FMC) Lokoja were consecutively recruited for the study by method of random sampling. These hospitals are reference centres for the programme of prevention against mother-to-child HIV transmission (PMTCT) in Kogi State. Informed consent was sought and obtained from each participant after thorough explanation of the study aim. Blood samples were collected from 200

HIV positive pregnant women within the ages of 18-45years. Demographic variables as well as information considered as risk factor were also obtained by means of structured questionnaires.

### 2.3 Ethics approval and consent to participate

The survey was reviewed and approved by the Kogi State Specialist and Federal Medical Centre hospital management boards on ethical issues in line with the code of conducts for biomedical research involving human subjects. All participants signed informed consent form before been enrolled in the study and agreed with publication of the findings related to the study.

### 2.4 Specimen collection and processing

For each enrollee, 2 milliliters of whole blood was aseptically collected by venepuncture method from the cubital vein into sterile non-anticoagulated bottles. The blood samples were allowed to clot and afterwards spun at 2000rpm for 10 minutes to separate sera from clotted blood.

### 2.5 HCV testing

The test was done using ARIA® HCV-Ab kit (manufactured by CTK Biotech, Inc. San Diego USA). Test is a double antigen sandwich immunoassay for the qualitative detection of anti-hepatitis C antibodies in human serum. ARIA® HCV-Ab kit utilizes purified recombinant antigens produced by *Escherichia coli* from clones selected in the nonstructural area of the hepatitis virus genome (NS3 and NS4), two peptides coded by capsid area of the hepatitis C virus genome. The test is more than 99.55% sensitivity and 98.5% specificity.

### 2.6 Statistical analysis

Statistical analysis was performed with SPSS version 16.0 for windows (SPSS Inc., Chicago,IL) and different proportions were compared using chi square. Logistic regression was used as the test of association to describe the relationship between the predictor variables (risk factors for maternal infection found to be statistically significant) and the outcome variable (anti-HCV antibody). P values  $\leq 0.05$  was set as level of statistical significance.

## 3. Results

Five (2.5%) patients out of 200 women screened were positive to anti- HCV antibody. Patients >40 years had the highest prevalence (11.1%) of HCV infection although, patients age in relation to HCV seropositivity was not statistically significant ( $P>0.05$ ) (Table-1).

Table 1. Age distribution of HCV infection among HIV positive pregnant women in Lokoja, 2018

Age range	No tested	No positive	P-value
≥20	2	0(0.0)	0.62
21-25	37	1(2.7)	
26-30	76	2(2.6)	
31-35	50	1(2.0)	
36-40	26	0(0.0)	
>40	9	1(11.1)	
<b>TOTAL</b>	<b>200</b>	<b>5(2.5)</b>	

Higher prevalence (4.4%) was found in women who were in their first trimesters while women in their second trimester had the least prevalence (1.6%). However, gestational age was not statistically related to anti-HCV antibody positivity ( $P>0.05$ ) (Table-2).

Table 2. HCV infection distribution in relation to gestation age of HIV positive pregnant women in Lokoja, 2018

Trimester	No. tested	No. (%) positive	P-value
First trimester	45	2(4.4)	0.57
Second trimester	123	2(1.6)	
Third trimester	32	1(3.1)	
<b>Total</b>	<b>200</b>	<b>5(2.5)</b>	

Divorced patients in the study population had higher HCV prevalence (20.0%) in comparison with the 4.8%, 1.7% and 0.0% of those who were single, married and widowed respectively. HCV prevalence was higher (3.3%) in women with more than 4 pregnancies while those with 2-4 parity and the primiparous patients respectively had 2.5% and 2% prevalence. Analysis in relation to patient's educational qualification revealed higher HCV prevalence (5.6%) in patients with primary level of education and lowest prevalence (1.0%) among those with tertiary education. The observed difference between HCV infection status and participants'

marital status, parity and level of education was not statistically significant ( $P>0.05$ ) (Table 3).

Table 3. HCV infection distribution in relation to socio-demographic characteristics of HIV positive pregnant women in Lokoja, 2018

Variable	No tested	No (%) positive	P-value
<b>Marital Status</b>			
Single	21	1(4.8)	0.07
Married	173	3(1.7)	
Divorced	5	1(20.0)	
Widowed	1	0(0.0)	
<b>Parity</b>			
1	50	1(2.0)	0.97
2-4	120	3(2.5)	
More	30	1(3.3)	
<b>Type of Family</b>			
Monogamy	147	3(2.0)	0.49
Polygamy	53	2(3.8)	
<b>Highest qualification</b>			
None	8	0(0.0)	0.49
Primary	18	1(5.6)	
Secondary	76	3(3.9)	
Tertiary	98	1(1.0)	

History of blood transfusion and abortion were statistically associated with anti-HCV antibody seropositivity ( $P<0.05$ ). Factors such as history of intravenous drug use, multiple sexual partnerships, mouth-to-mouth kissing, knowledge of HCV infection, history of surgery, alcoholism and history of circumcision were not significantly associated with acquisition of hepatitis C virus infection ( $P>0.05$ )

#### 4. Discussion

Our study describes the prevalence and risk factors of HCV infection among HIV seropositive pregnant women attending KSSH and FMC, reference centres for the program of prevention against mother-to-child HIV transmission in Lokoja, Kogi State. Overall prevalence of 2.5% of HCV infection was observed among the HIV positive pregnant women in this study. This is comparable to the estimated prevalence rates of 2.1% previously reported by Lavanchy, (2011) for Nigeria in the Hepatitis C global prevalence data and 2.4% reported by Madhava *et al.* (2002) for West Africa. In conformity with this finding, two cross-sectional surveys from Burkina Faso (Zeba *et al.*, 2011) and Ivory Coast (Rouet *et al.*, 2004) reported similar prevalence rates among

HIV seropositive pregnant women. However, lower prevalence rates of 1.39% and 0.5% were reported by Esan *et al.* (2014) and Buseri *et al.* (2010) among HIV infected pregnant women in Federal Medical Centre

Ido-Ekiti and pregnant women in Yenagoa, Bayelsa State, Nigeria respectively. These differences might be attributable to cultural and behavioral differences for the risk factors of HCV infection.

Table 4. Distribution of Hepatitis C virus serological marker and principal risk factors among pregnant women attending ante-natal clinics in Lokoja, 2018

Variable	Responses Sought	No. Tested	No. Positive (%)	Odds Ratio (OR)	Confidence Interval (CI)	P-Value
<b>Knowledge of HCV</b>						
	Yes	110	3(2.7)	1.23	0.20-7.55	0.82
	No	90	2(2.2)			
<b>Mouth-to-mouth kissing</b>						
	Yes	127	4(3.1)	2.34	0.26-21.36	0.44
	No	73	1(1.4)			
<b>History of Shared sharp object(s)</b>						
	Yes	58	2(3.4)	1.65	0.27-10.17	0.58
	No	142	3(2.1)			
<b>Circumcision</b>						
	Yes	45	0(0.0)	-	-	0.22
	No	155	5(3.2)			
<b>No of sexual partners</b>						
	1-2	176	4(2.3)	0.53	0.06-5.0	0.58
	>2	24	1(4.2)			
<b>History of STDs</b>						
	Yes	67	3(4.5)	3.07	0.50-18.84	0.20
	No	133	2(1.5)			
<b>Use of condom</b>						
	Yes	15	1(6.7)	3.23	0.34-30.90	0.28
	No	185	4(2.2)			
<b>History of blood transfusion</b>						
	Yes	31	4(12.9)	24.89	2.68-231.15	0.002
	No	169	1(0.6)			
<b>History of surgery</b>						
	Yes	92	4(4.3)	4.86	0.53-44.31	0.12
	No	108	1(0.9)			
<b>History of IDU</b>						
	Yes	7	0(0.00)	-	-	0.67
	No	193	5(2.59)			
<b>Abortion</b>						
	Yes	9	3(33.3)	47.25	6.62-337.17	0.001
	No	191	2(1.0)			
<b>Tribal marks</b>						
	Yes	63	2(3.2)	1.46	0.24-8.99	0.68
	No	137	3(2.2)			
<b>Alcohol consumption rate</b>						
	Low	176	4(2.3)			
	Moderate	22	1(4.5)	-	-	0.79
	High	2	0(0.0)			
<b>Occupation</b>						
	Business woman	56	1(1.8)			
	Student	17	0(0.0)			
	Housewives	47	2(4.3)	-	-	0.69
	Civil servant	52	2(3.8)			
	Unemployed	28	0(0.0)			

Note: OR and CI were computed for only data that satisfy 2 by 2 contingency table

Age has been argued as a major factor in HCV studies, with infection more predominant in older persons (Cozzolongo et al., 2009; Qureshi et al., 2009). Finding from present study is in consonance with this assertion as the majority of HCV positive women in this study were in the age group 41–50 years old. 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 (Choo et al., 1989). Also, the fact that older people are less likely to clear the virus from circulation may be a possible reason for the higher infection.

Our study found history of blood transfusion to be significantly associated with anti-HCV antibody positivity among the HIV positive women ( $P=0.002$ ). Several other studies (Laurent et al., 2007; Omatola et al., 2016) earlier observed significant association of blood transfusion with HCV infection. Laurent *et al.* (2007), in a similar study conducted among pregnant women in Democratic Republic of Congo, observed that parenteral transmission mainly by means of blood transfusion plays a significant role in acquisition of HCV infection. Finding from present study is corroborated by the assertions of Sohail and Azhar (2017) that unsafe blood transfusion remains the predominant routes of HCV transmission in pregnant women. Pregnant women with history of blood transfusion were 25 times more likely than those without such history at risks of contracting HCV infection in this study. Because blood transfusion is a common practice in this region of the World, comorbidity with HCV and HIV infection is not uncommon as both viruses are predominantly blood borne. History of abortion is the most outstanding risk factors in the present study as women who aborted one or more pregnancies were about 47 times more likely to contract HCV infection in the present study than those without such history ( $P=0.001$ , 95% CI:6.62–337.17).

Women with primary education as the highest level of qualification had higher HCV prevalence rate of (5.6%) compared to women with secondary and tertiary levels of education. Reason could be attributed to the fact that those with higher education are more likely to be knowledgeable of HCV infection and consequently could implement control strategies. This finding although not statistically significant is similar to the findings of Zeba *et al.*, (2011) who reported a higher rate of concomitant HCV/HIV infection among pregnant women with low level of educational qualification in Burkina Faso.

One limitations of this study is that plasma HCV-RNA was not determined in patients that were seropositive to HCV and this makes it difficult to distinguish active HCV infection from spontaneously cleared infection. Also, findings from present study

cannot be generalizable to the whole population in Kogi State since survey only covered pregnant women in sentinel sites.

## 5. Conclusion

Compared with previous reports from similar studies in Nigeria, the prevalence of HCV/HIV co-infection among pregnant women in the present study is worrisome and efforts encompassing public health education to highlight the dangers of co-infection of HIV and HCV especially in pregnancy, proper screening of blood and blood products should be heightened towards reducing the rate of co-infection among the clinically tested HIV positive pregnant women and also its associated maternal and pre-natal mortality and morbidity. Routine screening of pregnant women for co-infection should be enforced as it would enable early management and reduction of vertical transmission of both infections.

## Competing interests

No competing interests declared

## Authors' contributions

CAO designed the study; RB collected samples; CAO supervised data collection; CAO and RB ran assay; CAO performed statistical analysis; CAO drafted manuscript; CAO, RB, MOO, JOA, NSA, DMA, POA, OJTC, KEB contributed to fund mobilization, administrative and technical support. All authors read and approved the final manuscript.

## Abbreviations

HCV: Hepatitis C virus; *HIV*: Human immunodeficiency virus; Anti-HCV: Anti-HCV antibody; KSSH: Kogi State Specialist Hospital; FMC: Federal Medical Centre; Ab: Antibody; AIDS: Acquired Immunodeficiency Syndrome; CI: Confidence interval; ELISA: Enzyme-Linked Immuno-Sorbent Assay; OR: Odds ratio; PMTCT: Prevention of mother to child transmission; WHO: World Health Organization; HAART: Highly Active Anti-Retroviral Therapy.

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