

Research article

## Prevalence and Risk Factors of Hepatitis E and Hepatitis C Virus Co-Infections Among People Living with HIV Attending a Tertiary Healthcare Facility in North-Central Nigeria

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**Abstract:** Hepatitis E virus (HEV) and hepatitis C virus (HCV) co-infections among people living with human immunodeficiency virus (HIV) remain an important public health concern because of their potential to accelerate liver disease progression and worsen clinical outcomes. This study aimed to determine the prevalence of HEV and HCV co-infections and identify associated risk factors among HIV-seropositive patients attending the Federal Medical Centre, Keffi, Nasarawa State, Nigeria. A facility-based cross-sectional study was conducted among 289 HIV-seropositive adults receiving healthcare services at the study centre. Blood samples were collected and analyzed for anti-HEV IgG and anti-HCV antibodies using rapid diagnostic tests and enzyme-linked immunosorbent assay (ELISA). Qualitative polymerase chain reaction (PCR) was employed for the detection of HEV and HCV co-infections. The prevalence of HEV-HIV co-infection was 12.8%, while HEV-HCV-HIV triple co-infection was observed in 9.3% of participants. Participants aged 31–40 years, males, individuals with multiple sexual partners, and those with CD4+ cell counts >250 cells/ $\mu$ L demonstrated higher odds of HEV co-infection compared with HCV and HEV-HCV co-infections among HIV-seropositive patients. The findings highlight the burden of viral hepatitis co-infections among people living with HIV in North-Central Nigeria and underscore the need for strengthened public health awareness, routine screening programs, voluntary counselling services, and preventive interventions targeting high-risk populations.

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## Introduction

The Human Immunodeficiency Virus (HIV), Hepatitis E Virus (HEV), and Hepatitis C Virus (HCV) are recognized as the three most widespread chronic viral infections across the globe [1]. It is estimated that 2.3 million

people worldwide are affected by HIV/HCV co-infection, while the rates of HIV/HEV co-infection fluctuate between 1% and over 40%, influenced by the specific region and the type of assay employed [2]. The diseases associated with Hepatitis E Virus and Hepatitis

C Virus are notably more prevalent in developing regions such as Africa and Asia. Nonetheless, these diseases have also been reported in other parts of the world, including developed nations [3]. Of the 49 countries in sub-Saharan Africa, HEV has been documented in 25, with varying levels of morbidity and mortality [3]. The inflammatory liver disease caused by the Hepatitis E virus is characterized by mild fever, loss of appetite, slight liver inflammation, jaundice, dark urine, and pale stools [4]. Conversely, the Hepatitis C virus is responsible for serious liver conditions, including liver cirrhosis and hepatocellular carcinoma [5].

These viral pathogens are spread through percutaneous and mucous membrane contact with infectious blood and bodily fluids that contain blood [6]. Instances of percutaneous exposure have led to the transmission of HCV and HIV among intravenous drug users (IDU), as well as through contaminated equipment utilized for therapeutic injections and various healthcare-related procedures. Additionally, perinatal transmission from mother to infant and sexual contact involving HEV, HCV, and HIV represent highly effective transmission routes, alongside the person-to-person dissemination of these viral diseases [7].

The prevalence of HEV and HCV in HIV-positive patients has raised significant public health issues, as either mono-infection (HEV or HCV alongside HIV) or dual co-infection (HEV and HCV with HIV) exacerbates the disease progression in affected individuals and can greatly influence treatment and management approaches [1, 8]. HEV and HCV are liver-targeting viruses associated with significant morbidity and mortality related to viral hepatitis. These conditions may present as either acute or chronic liver infections. Generally, infection with these viruses tends to have a greater likelihood of becoming chronic, which increases the risk of progression to end-stage liver disease, cirrhosis, hepatocellular carcinoma (HCC), and premature mortality among those infected [9].

Despite the fact that comparable research has been carried out previously in the study region [10], there is currently no established policy for the surveillance of hepatitis E and C viruses in this area, unlike in many other regions of Nigeria. Screening is performed solely when an individual is suspected of experiencing liver damage or exhibits symptoms of hepatitis. Consequently, there exists a significant gap in the early detection and management of HEV and HCV co-infection among patients with HIV.

This research aims to provide contemporary epidemiological data on the prevalence of Hepatitis E and C Virus infections, and to identify the associated

risk factors for HEV-HCV co-infection among seropositive HIV patients at the Federal Medical Centre, Keffi, Nasarawa State, Nigeria.

## Materials and Methods

The research conducted was a cross-sectional study that included both male and female participants from the adult population. Patients diagnosed with HIV who were seeking healthcare at the Federal Medical Centre Keffi were consecutively recruited into the study through random sampling. In accordance with the Helsinki code of conduct for biomedical research involving human subjects, ethical approval was secured from the Ethical Review Committee of FMC, Keffi. Before sample collection, consent was obtained from each participant, and socio-demographic as well as clinical information was gathered using a structured questionnaire.

The study included only HIV patients aged 18 years and older who accessed healthcare at FMC, Keffi, and provided informed consent. Conversely, HIV patients suffering from severe medical conditions, those who were mentally or emotionally incapacitated, and individuals who refused to give their consent were excluded from the study.

### Sample Size Determination

A minimum sample size was estimated using Cochran's formula for sample size determination, which was used as follows;

$(n = (Z)^2 \times P (1-P) / e^2$ , Where n= minimum sample size  
z=standard normal distribution [1.96] at 95% confidence interval

p = proportion in a similar population estimated to have variable characteristics = 38.2% or 0.382.

q = [1.0-p] = 0.618

d = degree of accuracy of 5% or 0.05

Therefore, n = 279

Attrition rate of 10% = 10

The total minimum sample to be collected was n=289)

### Data Collection

A structured questionnaire was completed by the participants themselves to gather their socio-demographic details (including age, gender, marital status, employment status, residence location, and educational attainment) as well as factors affecting HEV-HCV co-infection (such as CD4+ cell count, blood transfusion history, and the count of sexual partners). With the assistance of trained research aides, the questionnaire was explained to individuals who were not proficient in the English language. Before the

distribution of the questionnaire, the items underwent pre-testing to ensure clarity, reliability, and validity.

### Sample Collection and Processing

Approximately 3 mL of blood samples were aseptically obtained from each consenting HIV-seropositive patient through venipuncture and placed into appropriately labeled sterile Eppendorf tubes. The samples underwent centrifugation, after which the sera were collected and preserved in labeled cryovial tubes at -15°C until they were needed for testing. The samples were analyzed for anti-HEV IgG and total antibodies utilizing rapid test kits and ELISA.

### Laboratory Analysis

#### Antibodies Detection

All serum samples were analyzed for hepatitis E serological markers, including anti-HEV IgG and anti-HCV. The HEV rapid test kit (recomLine IgG, Mikrogen GmbH, Germany) was employed to detect anti-HEV antibodies, adhering to the manufacturer's protocols. Furthermore, the total anti-HEV antibodies were measured using the MP diagnostics HEV ELISA 4.0 (MP Biomedicals Asia Pacific, Singapore). Samples that were positive for total anti-HEV antibodies underwent further screening for acute infection with the MP diagnostics HEV IgM ELISA 3.0. The determination of the anti-HCV seromarker was conducted using the Wondfo One-Step Anti-HCV Rapid Test (Wondfo Biotech Co., Ltd, China), in line with the manufacturer's instructions.

#### Molecular Detection

A two-step nested reverse-transcriptase polymerase chain reaction (RT-PCR) was employed for the detection and genotyping of HEV and HCV, respectively. In this regard, RNA was extracted from serum samples utilizing the Bionner extraction machine, followed by cDNA synthesis through reverse transcriptase. The PCR products were validated on a 2% agarose gel and visualized under ultraviolet light. All procedures conformed to MIQE and WHO guidelines, thereby ensuring sensitivity, specificity, reproducibility, and compliance with biosafety standards.

### Data Presentation and Statistical Analysis

Data entry and statistical analysis were conducted using the Statistical Packages for the Social Sciences (SPSS) (SPSS, Inc., Chicago, IL). Descriptive data were displayed as straightforward summaries in tables, frequencies, and bar charts.

The relationships between independent predictors of infection in HIV-seropositive patients were examined through a Binary logistic regression model. Odds ratios with a 95% Confidence Interval were reported, and statistical significance was established at  $P < 0.05$ .

## Results

The socio-demographic characteristics of the participants are presented in **Table 1**. A total of 289 HIV seropositive individuals were enrolled in this study. The majority of the participants were aged between 18 and 30 years (48.4%), while more than half of the participants, totaling 180 (62.3%), were female, and their male counterparts numbered 109 (37.7%). A greater proportion of the participants were single (34.6%) and widowed/divorced (34.3%) compared to those who were married (31.1%).

**Table 1.** Socio-demographic characteristics of Participants.

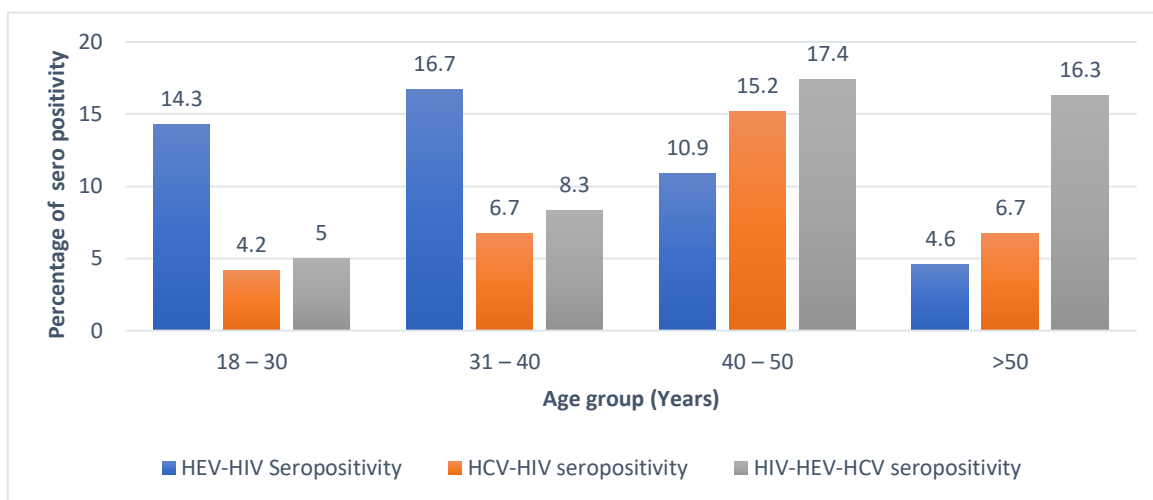
| Characteristics     | Frequency (%) |
|---------------------|---------------|
| Age (years)         |               |
| 18 – 30             | 140 (48.4)    |
| 31 – 40             | 60 (20.8)     |
| 40 – 50             | 46 (15.9)     |
| >50                 | 43 (14.9)     |
| Gender              |               |
| Male                | 109 (37.7)    |
| Female              | 180 (62.3)    |
| Marital Status      |               |
| Married             | 90 (31.1)     |
| Single              | 100 (34.6)    |
| Widow/Divorced      | 99 (34.3)     |
| Residency           |               |
| Urban               | 189 (65.4)    |
| Rural               | 100 (34.6)    |
| Employability       |               |
| Employed            | 192 (66.4)    |
| Unemployed          | 87 (30.1)     |
| Level of Education  |               |
| Primary             | 60 (20.8)     |
| Secondary           | 90 (31.1)     |
| Tertiary            | 49 (17.0)     |
| No formal Education | 90 (31.1)     |

In terms of residence, over half (65.4%) of the participants live in urban areas, while 34.6% reside in rural communities. Likewise, a significant majority of the participants (66.4%) are employed. The educational distribution among the participants indicated that the majority (31.1%) either lack formal education or possess only a secondary education, whereas only 17%

of the participants have attained tertiary education.

Six (6) socio-demographic characteristics and their correlations with HEV-HCV and HEV-HCV co-infections were analysed among 289 HIV-positive individuals (Table 2). Significant patterns emerged as follows: In terms of age, the highest HEV seropositivity (16.7%) was observed in patients aged 40 – 50 years, while the peak HCV seropositivity (15.2%) was noted in those aged 40 – 45 years. Co-infection with HEV and HCV was most common (17.4%) among patients in the 40 – 50

age bracket (Figure 1). The gender distribution of Hepatitis E virus infection indicated a greater prevalence among male patients, with 15 (13.8%), compared to a lower prevalence of 22 (12.2%) in females. Additionally, female patients exhibited a lower prevalence of Hepatitis C virus at 11 (6.1%), whereas the prevalence in males was higher at 9 (8.2%) (Table 2). The findings regarding the prevalence of HEV and HCV infections were statistically insignificant ( $P > 0.05$ ).



**Figure 1.** Distribution of HEV, HCV, and HEV-HCV Co-infection among HIV-Seropositive Patients accessing healthcare at Federal Medical Centre, Keffi, Nigeria.

**Table 2.** Distribution of Hepatitis E and C Con-infection with respect to Sociodemographic Characteristics of the HIV-seropositive Patient accessing healthcare at Federal Medical Center, Keffi, Nigeria.

| Characteristics           | Total number examines (n =289) | HEV-HIV Seropositivity | HCV-HIV Seropositivity | HIV-HEV-HCV Seropositivity |
|---------------------------|--------------------------------|------------------------|------------------------|----------------------------|
|                           |                                | n=37<br>Positive n (%) | n=20<br>Positive n (%) | n=27<br>+v (%)             |
| <b>Gender</b>             |                                |                        |                        |                            |
| Female                    | 180                            | 22 (12.2)              | 11(6.1)                | 15(8.3)                    |
| Male                      | 109                            | 15 (13.8)              | 9(8.2)                 | 12(11.0)                   |
| <b>Marital Status</b>     |                                |                        |                        |                            |
| Married                   | 90                             | 10 (11.1)              | 13(14.4)               | 15(16.7)                   |
| Single                    | 100                            | 15 (15)                | 4(4.0)                 | 5(5.0)                     |
| Widow/Divorced            | 99                             | 12 (12.1)              | 3(3.03)                | 7 (7.1) 12.1               |
| <b>Residency</b>          |                                |                        |                        |                            |
| Urban                     | 189                            | 30 (15.9)              | 18(9.5)                | 20(10.5)                   |
| Rural                     | 100                            | 7(7.0)                 | 2(2.0)                 | 7(7.0)                     |
| <b>Employability</b>      |                                |                        |                        |                            |
| Employed                  | 192                            | 12 (6.25)              | 4(2.1)                 | 10(5.2)                    |
| Unemployed                | 87                             | 25 (25.7)              | 16(16.5)               | 17(17.5)                   |
| <b>Level of Education</b> |                                |                        |                        |                            |
| Primary                   | 60                             | 12 (20)                | 4(6.7)                 | 5(8.3)                     |
| Secondary                 | 90                             | 5 (5.6)                | 5(5.6)                 | 6(6.7)                     |
| Tertiary                  | 49                             | 10 (20.4)              | 6(12.2)                | 7(14.3)                    |
| No formal Education       | 90                             | 10 (11.1)              | 5(5.6)                 | 9(10.0)                    |

Married patients exhibited a higher prevalence of HCV at 14.4% and a greater co-infection rate of 16.7%. In contrast, HEV was more prevalent among widowed/divorced patients at 12.1%, with a corresponding prevalence of 7.1% for HEV-HCV co-infection. Participants living in urban areas demonstrated a higher prevalence of HEV (15.9%), HCV (9.5%), and HEV-HCV co-infection (10.5%) when compared to those residing in rural areas.

Unemployed patients presented a higher prevalence of HEV (25.7%), HCV (16.5%), and HEV-HCV co-infection (17.5%) in comparison to their employed counterparts, who showed lower prevalence rates for HEV (6.25%), HCV (2.1%), and HEV-HCV co-infection (5.2%). The educational background of the patients revealed a diverse pattern in seropositivity. The highest

prevalence rates recorded across the infection categories were as follows: HEV (20.0%) among individuals with primary education, HCV (12.2%) among those with tertiary education, and HEV-HCV co-infection (10.0%) among individuals lacking formal education.

Based on age-specific evaluations, increased odds (OR = 2.1; 95%CI:1.6 – 2.1) of HEV-HCV co-infection were noted among participants aged 31-40 years, and (OR = 1.4; 95% CI: 0.8 -3.1) among those aged 40 – 50 years. Although these associations did not reach statistical significance, participants over 50 years exhibited reduced odds of co-infection (OR = 0.8; 95% CI:0.1 - 2.3), with the age group 18 – 30 years serving as the reference cohort (**Table 3**).

**Table 3.** Associated Risk Factor of HEV, HCV Co-infection among HIV infected adults accessing care at Federal Medical Center, Keffi, Nasarawa State.

| Risk Factors                 | Hepatitis E Surface antigen n (%) |                 | Hepatitis C antibodies, n (%) |                 | Hepatitis E/C Co-infection |               |
|------------------------------|-----------------------------------|-----------------|-------------------------------|-----------------|----------------------------|---------------|
|                              | HEV (+)                           | OR (95% CI)     | HCV ab (+)                    | OR (95% CI)     | HEV/HCV (+)                | OR (95% CI)   |
| Age (years)                  |                                   |                 |                               |                 |                            |               |
| 18 – 30                      | 20 (14.3)                         | 1               | 6 (4.2)                       | 1               | 7 (5.0)                    | 1             |
| 31 – 40                      | 10 (16.7)                         | 0.79 (0.36-2.0) | 4 (6.7)                       | 1.67 (0.3-9.2)  | 5 (8.3)                    | 2.1 (1.6-2.1) |
| 40 – 50                      | 5 (10.9)                          | 0.72 (0.33-2.9) | 7 (15.2)                      | 0.50 (0.2-4.0)  | 8 (17.4)                   | 1.4 (0.8-3.1) |
| <50                          | 2 (4.6)                           | 0.54 (0.20-2.9) | 3 (6.7)                       | 1.6 (0.18-10.2) | 7 (16.3)                   | 0.8 (1.0-2.3) |
| Gender                       |                                   |                 |                               |                 |                            |               |
| Male                         | 15 (13.8)                         | 1               | 9 (8.2)                       | 1               | 12 (11.0)                  | 1             |
| Female                       | 22 (12.2)                         | 3.41 (2.05-5.0) | 11 (6.1)                      | 0.30 (0.10-4.3) | 15 (8.3)                   | 0.9 (0.3-1.4) |
| CD4+ T Cell Count (cells/μl) |                                   |                 |                               |                 |                            |               |
| <250                         | 22 (22.2)                         | 1               | 11 (6.1)                      | 1               | 15 (8.3)                   | 1             |
| >=250                        | 15 (13.8)                         | 3.21 (2.0-5.0)  | 9 (8.2)                       | 0.48 (0.15-6.3) | 12 (11.0)                  | 0.4 (0.1-1.5) |
| History of Blood Transfusion |                                   |                 |                               |                 |                            |               |
| Yes                          | 30 (15.9)                         | 1               | 18 (9.5)                      | 1               | 20 (10.5)                  | 1             |
| No                           | 7                                 | 2.1 (1.8-4.0)   | 2 (2.0)                       | 2.17 (0.80-8.7) | 7 (7.0)                    | 0.8 (0.2-4.0) |
| Sexual Partners              |                                   |                 |                               |                 |                            |               |
| One                          | 25                                | 1               | 16 (16.5)                     | 1               | 10 (5.2)                   | 1             |
| Multiple                     | 12                                | 1.2 (1.1-3.0)   | 4 (2.1)                       | 0.30 (0.20-6.1) | 17 (17.2)                  | 0.7 (0.1-2.3) |
| Marital Status               |                                   |                 |                               |                 |                            |               |
| Single                       | 10 (11.1)                         | 1               | -                             | -               | -                          | -             |
| Married                      | 15 (15.0)                         | 2.1 (2.0-3.9)   | 13 (14.4)                     | 1               | 15 (16.7)                  | 1             |
| Divorce                      | 12 (12.1)                         | 1.7 (1.2-4.1)   | 4 (4.0)                       | 1.4 (1.3-4.0)   | 5 (5.0)                    | 0.4 (0.1-1.1) |
| Widowed                      | -                                 | -               | 3 (3.3)                       | 1.2 (1.0-4.5)   | 7 (7.1)                    | 0.6 (0.2-4.3) |

In terms of gender, females displayed marginally lower odds of HEV-HCV co-infection compared to males (OR = 0.9; 95% CI: 0.3 – 1.4), indicating no significant correlation between gender and co-infection. An examination of the immune status among

the participants indicated that individuals with CD4+ T-cell counts of 250 cells/μl or higher exhibited reduced odds of co-infection (OR = 0.4; 95% CI: 0.1 – 1.5) in comparison to those with counts below 250 cells/μl. It is important to note that this association lacks

statistical significance.

HIV-positive individuals with a history of blood transfusions demonstrated increased odds of HCV infections in isolation (OR = 2.17; 95% CI: 0.80 – 8.7). In contrast, those with a history of blood transfusions had diminished odds of HEV-HCV co-infection (OR = 0.8; 95% CI: 0.2 – 4.0) when compared to individuals without such a history. Nevertheless, these associations were not statistically significant.

Regarding sexual behaviour, participants with multiple sexual partners had lower odds of co-infection (OR = 0.7; 95% CI: 0.1 – 2.3) relative to those with a single sexual partner. Likewise, no statistically significant association was found between the number of sexual partners and co-infection.

Married participants exhibited higher odds of HEV-HCV co-infection (OR = 1.0 as reference; prevalence = 16.7%), whereas divorced (OR = 0.4; 95% CI: 0.1 - 1.1) and widowed participants (OR = 0.6; 95% CI: 0.2 – 4.3) showed lower odds in comparison to single participants. However, no statistically significant difference was observed.

## Discussion

This research highlights the occurrence of HEV and HCV infections in HIV patients receiving care at the Federal Medical Centre in Keffi. Among the 289 samples analyzed, 37 (12.8%) tested positive for HEV, while 20 (6.9%) were found to have Anti-HCV antibodies. Additionally, 27 (9.3%) of the samples were positive for both HEV and HCV, indicating instances of co-infection among the HIV-positive patients. This finding aligns with a prior investigation [11] at the same facility, which reported a seroprevalence of Hepatitis E and C viruses among 200 HIV-infected patients accessing healthcare at the Federal Medical Centre, Keffi, Nigeria, with HEV infection at 12.5% and HCV infection at 5.0%. In contrast, a study in Ethiopia within sub-Saharan Africa indicated a lower prevalence rate [12].

The persistent endemicity observed in this study, when compared to the findings of [11] after eight years, raises significant public health concerns. This is particularly relevant given the enhanced survival rates of HIV-infected individuals due to antiretroviral therapy (ART), as chronic infections with Hepatitis E and C have emerged as critical contributors to morbidity and mortality among co-infected patients in developed nations, including Nigeria [13].

In this research, the majority of participants were young individuals aged between 18 and 30 years, residing in urban areas, and primarily single, as illustrated in Figure 1. This finding aligns with the

research conducted in Kaduna state by [14], yet contrasts with the study, which reported the highest prevalence among patients older than 40 years. This discrepancy may be attributed to the heightened risky sexual behaviors and intravenous drug use prevalent in that age demographic [15].

The gender-based difference in prevalence may be explained by the specific anatomical and physiological traits of female reproductive organs, where lymph nodes are essential in facilitating the acquisition of these hepatitis viruses [16]. It also highlights the overall prevalence rates of HIV-HEV, HIV-HCV, and the HIV-HEV-HCV trio-infection at 12.8%, 6.9%, and 9.3%, respectively. The higher number of infections among urban inhabitants could be due to the growing trend of rural-urban migration.

As indicated in Table 3, the correlation between age and various risk factors for HEV, HCV, and HEV/HCV co-infections reveals that individuals aged 31-40, 40-50, and those over 50 years exhibit a reduced risk of contracting HEV infection (OR=0.79, 0.72, and 0.54, respectively). Conversely, individuals aged 31-40 and those over 50 years demonstrate an elevated risk of contracting HCV compared to other age groups (OR=1.7 and 1.6, respectively). This phenomenon may be attributed to fatalities resulting from HCV-related cirrhosis and hepatocellular carcinoma within this demographic. Respondents aged 31-40 years face a twofold increased likelihood of acquiring HEV/HCV co-infection relative to other age categories. This may stem from heightened sexual risk behaviors and intravenous drug use prevalent among the younger population [15]. Males exhibit a threefold higher risk of contracting HEV compared to females, while the male gender seems to confer a protective effect against HCV (OR 0.3) and HEV/HCV (OR 0.9) co-infection. This finding aligns with a report by [17].

As shown in Table 3, the association between age and the different risk factors for HEV, HCV, and HEV/HCV co-infections indicates that individuals aged 31-40, 40-50, and those older than 50 years have a diminished risk of acquiring HEV infection (OR=0.79, 0.72, and 0.54, respectively). In contrast, individuals aged 31-40 and those over 50 years are at a heightened risk of developing HCV compared to other age cohorts (OR=1.7 and 1.6, respectively). This may likely be due to mortality associated with HCV-related cirrhosis and hepatocellular carcinoma in this age group. Individuals aged 31-40 years are twice as likely to experience HEV/HCV co-infection compared to other age groups. This could be linked to increased sexual risk behaviors and intravenous drug use among younger individuals [15]. Males are three times more likely to contract HEV

than females, while being male appears to offer some protection against HCV (OR 0.3) and HEV/HCV (OR 0.9) co-infection. This observation is consistent with findings reported by [17].

Table 3 illustrates that the link between age and various risk factors for HEV, HCV, and HEV/HCV co-infections suggests that individuals in the age brackets of 31-40, 40-50, and those above 50 years have a lower likelihood of contracting HEV infection (OR=0.79, 0.72, and 0.54, respectively). On the other hand, individuals aged 31-40 and those over 50 years show a higher propensity for contracting HCV compared to other age segments (OR=1.7 and 1.6, respectively). This may be largely due to deaths resulting from HCV-related cirrhosis and hepatocellular carcinoma within this demographic. Respondents aged 31-40 years are twice as likely to develop HEV/HCV co-infection compared to their counterparts in other age groups. This could be attributed to increased sexual risk behaviors and intravenous drug use among the younger population [15]. Males have a threefold increased risk of contracting HEV compared to females, while the male gender appears to provide a protective effect against HCV (OR 0.3) and HEV/HCV (OR 0.9) co-infection. This finding is corroborated by a report from [17].

Individuals with CD4 cell counts of 250 or higher are three times more likely to contract HEV, while they are less prone to contracting HCV and HEV/HCV co-infection (OR=0.48 and 0.4, respectively). Concerning blood transfusion history, those without a history of transfusion have a twofold increased risk of contracting HEV and HCV (OR=2.1 for both), which contradicts the findings of [14], who recognized blood transfusion as a significant risk factor. This study also indicates that individuals with multiple sexual partners face a greater risk of contracting HEV (OR=1.2) but a lower risk for HCV and HEV/HCV co-infection (OR=0.3 and 0.7, respectively). These results are consistent with the [18], which reported a higher risk of HEV among those with multiple sexual partners, yet they contrast with the study by [19], which found an increased risk among single sexual partners. Married respondents exhibit a twofold higher risk of contracting HEV compared to singles and divorced individuals, while HCV infection presents an increased risk for both married and divorced individuals [11], which contradicts a study conducted in Kaduna State by [14].

Hepatocellular carcinoma resulting from HEV and HCV constitutes 60% and 80% of the worldwide cirrhosis burden, with 180 million individuals infected with HIV and 400 million with HEV globally [20]. Notably, HEV and HCV infections have been associated

with a broad spectrum of clinical manifestations in HIV-infected individuals who have experience with drugs, leading to an impaired immune response and liver toxicity related to ART [1, 21].

During the initiation of ART regimens in HIV patients, various clinical manifestations have been noted in individuals co-infected with HEV and HCV, resulting in heightened liver toxicity associated with ART [22]. Co-infection with HEV and HCV was included among the eligibility criteria for the enrollment and execution of the “treat all” policy mandated for all HIV-positive patients undergoing ART. Although the introduction of ART programs has led to a reduction in morbidity and mortality rates in the management of HIV infection, complications may arise due to other opportunistic infections co-infected with viral Hepatitis E and C in Sub-Saharan Africa, where resources are limited and access to viral load assessments is challenging. This viral co-infection in individuals infected with HIV has been linked to increased immune suppression, elevated liver enzymes, and liver toxicity related to ART [23].

## Conclusion

This study revealed that the Hepatitis E virus had the highest co-infection rate, while the hepatitis C virus had the lowest co-infection rate among patients who are HIV-seropositive. This finding implies a high level of endemicity of hepatitis E and C viruses among HIV patients in the region studied. Age, gender, and a history of blood transfusion were found to have higher odds for HCV and HEV-HCV co-infection rates.

Particularly, individuals aged between 31 and 40 years, male individuals, those with multiple sexual partners, and those with a CD4+ cell count greater than 250 cells/ $\mu$ l showed increased odds for HEV co-infection compared to HCV and HEV-HCV co-infection among HIV-seropositive patients in Keffi, North-Central Nigeria. As a result, we suggest a public health awareness campaign to educate residents about the risks associated with the transmission of these viral pathogens and to promote the establishment of regular voluntary counseling and screening for these viruses and their viral loads.

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