

# Incidence Density and Risk Factors of Hepatitis B and Hepatitis C Co-infection Among Newly Enrolled HIV Patients at the Treatment Hub in a Tertiary Government Hospital

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## Abstract

**Introduction:** Individuals who are at high risk of acquiring human immunodeficiency virus (HIV) are also considered high risk of other sexually transmitted infections including hepatitis B and hepatitis C infection. Worldwide, there have been 10.6 million cases recorded for hepatitis B alone and 615,000 for hepatitis C, with total chronic cases of more than 11 million people for the year 2022. This study aimed to determine the incidence density and risk factors of Hepatitis B and/or Hepatitis C coinfection among HIV patients enrolled at the treatment hub of Eastern Visayas Medical Center (EVMC).

**Methods:** A retrospective cross sectional study was conducted among newly enrolled HIV patients at EVMC for the last 3 years. Data collection form was used to extract pertinent information. Chi-Square test of independence was used to analyze the association of variables in the socio-demographic and clinical profile to the occurrence of hepatitis B and/or C co-infection.

**Results:** Included were 65 patients. The incidence density of Hepatitis B Co-infection was generally low at 7.69%, Hepatitis C Co-infection at 1.54%, and both Hepatitis B and C coinfection at 1.54%. Educational attainment and the history of intravenous illicit drug use had statistically significant correlation with the occurrence of hepatitis co-infection ( $p$  value=0.001).

**Conclusion:** Based on the results of this study, it can be concluded that the incidence density of Hepatitis B, Hepatitis C, and Hepatitis B and C co-infection are low. The results however only depended on the available laboratory results upon enrollment hence some cases with incomplete Hepatitis profile were excluded. It can also be concluded that educational attainment remains to be significant risk factor that can affect the occurrence of Hepatitis B, Hepatitis C co-infection or both while history of Illicit drug use is a significant risk factor for Hepatitis C co-infection alone.

**Keywords:** Human Immunodeficiency Virus, Hepatitis B Coinfection, Hepatitis C Coinfection, Incidence Density.

## Introduction

Individuals who are at high risk of acquiring human immunodeficiency virus (HIV) are also considered high risk of other sexually transmitted infections including hepatitis B and hepatitis C

infection. HIV, hepatitis B and C all share a common epidemiological nature such as the mode of transmission through sexual contact, sharing of needles during recreational intravenous drug use and even through transplacental transmission during preg

nancy. Hepatitis B and C infection are not uncommon among people living with HIV (PLHIV).<sup>1</sup>

In the Philippines, there have been 10.6 million cases recorded for hepatitis B alone and 615,000 for hepatitis C, with total chronic cases of more than 11 million people. Cirrhosis and hepatocellular carcinoma remain to be the most common complications of these infections and may occur in 30% of the infected individuals. <sup>2</sup> According to World Health Organization (WHO), 37.5 million people were estimated to be living with HIV at the end of 2020. Because of shared routes of transmission, hepatitis B coinfection among PLHIV is common. In some regions, over two-thirds of HIV-infected persons have been reported with a history of Hepatitis B virus (HBV) infection, which means 2–4 million people have HBV-HIV coinfection. <sup>3</sup> According to various reports, approximately 21% of adults with HIV turned out positive with Hepatitis C virus (HCV) infection. Besides percutaneous drug exposure, coinfection can also be seen in hemophiliacs who received contaminated blood without routine serological screening.<sup>4</sup>

Currently, with respect to our region and institution, there is still no published data regarding the risk factors and prevalence of Hepatitis B and C coinfection in patients with HIV. This study emphasizes the importance of awareness on the risk factors of acquiring hepatitis B and C among HIV patients to facilitate early intervention and prevent complications [1].

## Methods

### Study Design

A Retrospective cross-sectional analytic research design was used in this study.

### Study Setting

The study was conducted at the HIV and AIDS Core Team (HACT) clinic of Eastern Visayas Medical Center (EVMC).

### Study Population and Sample

The study included all newly enrolled HIV patients enrolled at the EVMC HIV treatment hub from January 1, 2020, to Dec 31, 2022.

#### Inclusion Criteria:

- Patients > 18 years old
- With HBsAg and anti-HCV results documented in the patient's file

#### Exclusion Criteria:

Patients with incomplete baseline laboratory results was excluded from the study

## Data Collection

A review of the census of the EVMC HACT clinic was done to identify population sample based on the inclusion criteria. Charts of patients included in the study were reviewed [2].

A data collection form was utilized for each patient that contains data necessary in the conduct of the study.

Data that were collected include socio-demographic profile: age, sex, marital status, sexual orientation, educational attainment and occupation; clinical profile: history of intravenous illicit drug use and history of blood transfusion; baseline laboratory profile: CD4 count, alanine aminotransferase (ALT), aspartate aminotransferase (AST); hepatitis profile: Hepatitis B surface antigen (HBsAg), Hepatitis C antibody (anti-HCV); and the antiretroviral regimen among patients with hepatitis B coinfection.

## Statistical Analysis

The socio-demographic, clinical and laboratory profile were summarized accordingly using frequencies, percentages, mean, and standard deviation.

Chi-Square test of independence was used to analyze the association of variables in the socio-demographic and clinical profile to the occurrence of hepatitis B and/or C infection [3].

Results are considered statistically significant if the p value is <0.05.

## Ethical Considerations

An assessment of risks and benefits was undertaken for this study. There was a risk for potential invasion of patient's privacy as medical records are to be viewed for collection of relevant data. This risk was however rated low and minimal. Only the data stated in the data collection plan and data collection form were collected. All the data gathered remained confidential and protected for record keeping by the principal investigator and co-investigator.

## Results and Discussion

A total of 65 newly enrolled HIV patients from the year 2020 to 2022 was included in the study.

Table 1 shows the newly enrolled HIV patients from the year 2020 to 2022 per annum. The year 2022 has the greatest number of enrollees with 32 patients or 49% of the total study population. The data depicts that there is an increasing trend on the number of enrollees per year. This is congruent with the current data by the UNAIDS revealing a steady increase in the number of HIV cases in the Philippines.<sup>1</sup>

**Table 1:** Newly Enrolled HIV Patients from 2020 to 2021 per Annum n=65, January 2020 – December 2022

Year	Frequency (N)	Percentage (%)
2020	10	15.40
2021	23	35.40
2022	32	49.20
Total	65	100.00

## **Patient Characteristics**

### **Socio-Demographic Profile**

#### **Age**

More than half of the respondents belong to the age group of 19-29 years old or 52.30% of the study population, closely followed by 30-49 at 47.7%. The mean age was at 29-30 years old.

The data revealed that majority of the newly enrolled HIV patients are adolescents and middle aged. This data is congruent with the latest Findings of the HIV/AIDS and ART Registry of the Philippines (HARP) which revealed that majority of the newly enrolled HIV patients were at 24-34 age group. This trend has been persistent since the year 1984 up to 2021.<sup>2</sup>

#### **Sex**

Majority (92.3%) or 60 patients were male and only 5 were female. This implies that there were more males who were diagnosed with HIV. The predominance of the male sex among the newly enrolled HIV patients were also similar with that of the national registry. According to the HIV/AIDS and ART Registry of the Philippines, the proportion of yearly diagnosed cases among males were more than 93% for the past 10 years majority of the HIV cases were males for the past 10 years (2011-2021).<sup>2</sup>

#### **Sexual Orientation**

The data revealed that majority of the new HIV enrollees identify themselves as homosexuals with 30 patients or 45% of the total population, 23 were bisexual at 35.4% and 12 were heterosexual at 18.5%.

The results were similar in a study conducted by the Center for Disease Control, USA, where majority of the newly diagnosed cases in the US identified themselves as homosexuals estimated at almost 70% for the year 2017 to 2021. According to HARP, with data from 1984 to 2021 rates as high as 59% identified themselves as homosexuals and 27% for bisexuals.<sup>3</sup> A research by Zuckerman et al., revealed that anal intercourse both insertive and receptive confers a high risk of transmission due to high levels of HIV in the rectal mucosa and as well as semen. This explains the high number of HIV infection among homosexuals or those men who have sex with men.<sup>4</sup>

#### **Marital Status**

Majority (89.25%) of the respondents were single, 9.25% were married, and 1.5% was common law.

#### **Educational Attainment**

More than half of the respondents or 56.9% were college graduate, 21.5% were college level, 16.9% were high school graduate, 3.10% were high school level, and only 1.5% was elementary level [4].

This depicts that most of the newly enrolled HIV patients were literate. Similar results were noted in a study conducted by Hargreaves et al in Africa, it revealed that higher educational attainment was associated with a greater risk of HIV infection. Large studies in four areas in Africa showed an increased risk of HIV-1 infection among the more educated respondents.<sup>5</sup> Furthermore, a study at Ethiopia by Bradley et al., revealed that more than 50% of their HIV patients had educational attainment at least secondary education. This depicts that majority of HIV

patients belong to the literate group.<sup>6</sup>

#### **Occupation**

Majority of the respondents were employed. Among these, majority (29.20%) works as a private employee and 16.9 were government employees, 12.3% had elementary occupation, 3.10% were self-employed and 1 or 1.5% was an overseas worker. On the other hand, 18.6% were students, 18% were unemployed. The data shows that majority of the respondents had a source of income [5].

#### **History of Illicit Drug Use**

Most (95%) of the respondents denied illicit drug use, and 3 or 4.6% had history of drug use. Among the drug users, one had reactive result to both HBsAg and Anti-HCV and the others were non-reactive to either of the two.

#### **Number of Sexual Partners**

The data shows that almost all of the respondents (96.905%) have more than 1 or have multiple sexual partners.

#### **History of Blood Transfusion**

Only 5 patients have had previous history of blood transfusion accounting to 7.70% of the total population.

#### **Baseline Laboratory Profile**

##### **CD4 Cell Count**

Majority (63%) of the newly enrolled HIV patients at the treatment hub had a CD4 cell count of less than 200 cells/uL. The mean CD4 count was 183 cells/uL.

##### **Alanine Aminotransferase (ALT)**

Majority (58.50%) of the study population had elevated levels of ALT (>31), with a mean ALT value of 53.34.

This shows that majority of newly enrolled HIV patients had associated liver injury at the time of consult or enrollment at the HACT clinic. Among those who had Hepatitis B coinfection, liver, all had elevated liver enzymes. Furthermore, among the two cases of Hepatitis C coinfection, one had liver injury [6].

##### **Aspartate Aminotransferase (AST)**

Majority (52.3%) or 38 of the respondents also had elevated levels of aspartate aminotransferases with values greater than 31, with a mean AST value was of 43.90.

##### **Hepatitis B, Hepatitis C Coinfection**

HIV causes liver damage through direct interactions with both parenchymal and non-parenchymal liver cells. These HIV-infected liver cells then cross-talk with uninfected cells, causing liver damage to spread. HIV's impact in causing liver inflammation and fibrosis can be attributed to a variety of processes. The most significant are HIV's pro-apoptotic effects on hepatocytes, as well as HIV-associated microbial translocation and microbiota alterations. ART causes liver injury due to drug toxicity and/or drug metabolism, mitochondrial damage, immunosuppression, and drug hypersensitivity reactions, in addition to the cytotoxic effects of HIV on hepatocytes and stimulation of non-parenchymal liver cells [7].

While HIV alone raises liver transaminase levels, the worsen

ing of liver injury is exacerbated when HIV patients are also infected with hepatotropic viruses, hepatitis C virus (HCV) and hepatitis B virus (HBV).<sup>7</sup>

#### Hepatitis B, Hepatitis C coinfection or Both per Year

Table 2 shows the proportion of HIV patients with Hepatitis B and Hepatitis C co-infection per year. About 7.69% had reactive HBsAg and 78.46% had non-reactive results from the year 2020 to 2022. There were 2 patients who had reactive HBsAg for the years 2021 and 2022 and 1 patient for the year 2020. Due to the unavailability of HBsAg reagents in the institution as well as failure to request for hepatitis profile, some of the newly enrolled patients had no results for the Hepatitis B screening which accounted for 13.85% of the total respondents [8].

There were only 3.08% patients had reactive Anti-HCV results. One was from the year 2020 and the other from 2021. There were no recorded Hepatitis C coinfections during the year 2022. Furthermore, there were 44.62% who were non-reactive to Anti-HCV. There was a high number of respondents having no results of the Hepatitis C screening which accounted for 25.15% of the total population. This is still due to unavailability of the tests as well as the omission of the Hepatitis profile during the indicated time period.

There were 31 respondents who had screening tests for both Hepatitis B and C coinfection. Among these, only 1 (1.5%) had a reactive result to both Hepatitis B and Hepatitis C which was recorded during the year 2020.

**Table 2:** HIV Patients with Hepatitis B and Hepatitis C Infection per Year n=65, EVMC, January 2020 – December 2022

Year	Hepatitis B						Hepatitis C						HBV and HCV							
	Reactive		Non-Reactive		Not Stated		Reactive		Non-Reactive		Not Stated		Reactive to Both		Non-reactive to Both		Reactive to One		Not Specified	
	(n)	(%)	(n)	(%)	(n)	(%)	(n)	(%)	(n)	(%)	(n)	(%)	(n)	(%)	(n)	(%)	(n)	(%)	(n)	(%)
2020	2	3.08	5	7.69	3	4.62	1	1.54	0	0.00	9	13.85	1	1.54	0	0.00	0	0.00	9	13.85
2021	1	1.54	19	29.23	3	4.62	1	1.54	12	18.46	10	15.38	0	0.00	11	16.92	2	3.08	10	15.38
2022	2	3.08	27	41.54	3	4.62	0	0.00	17	26.15	15	23.08	0	0.00	16	24.62	1	1.54	15	23.08
Total	5	7.69	51	78.46	9	13.85	2	3.08	29	44.62	34	52.31	1	1.54	27	41.54	3	4.62	34	52.31

These data were not congruent with the other studies previously mentioned. In a study conducted by Yu et al., pooled HBsAg prevalence in HIV-patients was 13.7% while the HCV coinfection was higher at 24.7% with notable variations over age and study period. The prevalence of both Hepatitis B and Hepatitis co-infection was even lower at 3.5%. In a study conducted by Yu et al., pooled HBsAg prevalence in HIV-patients was 13.7% while the HCV coinfection was higher at 24.7% with notable variations over age and study period. The prevalence of both Hepatitis B and Hepatitis co-infection was even lower at 3.5%.<sup>8</sup>

#### Antiretroviral Therapy

The antiretroviral therapy was almost equally distributed be-

tween Lamivudine/Tenofovir/Efavirenz and Lamivudine/Tenofovir/Dolutegravir at 49.2% and 50.80% respectively.

#### Socio-Demographic Profile and Occurrence of Hepatitis B, Hepatitis C Co-Infection or Both

Table 3 shows the association between the sociodemographic and clinical profile to the occurrence of Hepatitis co-infection. Among the sociodemographic and clinical profile of the respondents, only the educational attainment and the history of intravenous illicit drug use had statistically significant correlation with the occurrence of hepatitis co-infection with p-values less than 0.05.

**Table 3:** Association Between Socio-Demographic and Clinical Profile to the Occurrence of Hepatitis Co-Infection n=65, January 2020 – December 2022

Variables	Hepatitis B			Hepatitis C			HBV and HCV		
	X <sup>2</sup>	p-value	interpretation	X <sup>2</sup>	p-value	interpretation	X <sup>2</sup>	p-value	interpretation
Socio-demographic Profile									
Age (years)	2.844	0.241	Not Significant	1.900	0.387	Not Significant	3.907	0.272	Not Significant



Sex	0.566	0.753	Not Significant	1.696	0.428	Not Significant	1.732	0.630	Not Significant
Sexual orientation	9.399	0.052	Not Significant	5.665	0.226	Not Significant	8.426	0.209	Not Significant
Marital status	1.097	0.895	Not Significant	1.172	0.883	Not Significant	1.447	0.963	Not Significant
Educational attainment	17.382	0.026	Significant	35.300	0.0001	Significant	70.325	0.0001	Significant
Occupation	7.735	0.805	Not Significant	6.537	0.887	Not Significant	11.734	0.861	Not Significant
History of Intravenous illicit drug use	4.367	0.113	Not Significant	9.664	0.008	Significant	21.079	0.0001	Significant
Number of sexual partners	0.566	0.753	Not Significant	1.881	0.390	Not Significant	1.881	0.597	Not Significant

This table shows the association between the sociodemographic and clinical profile to the occurrence of Hepatitis co-infection. Among the sociodemographic and clinical profile of the respondents, only the educational attainment and the history of intravenous illicit drug use had statistically significant correlation with the occurrence of hepatitis co-infection with p-values less than 0.05.

Furthermore, educational attainment had shown statistically significant relationship to the occurrence of Hepatitis B (p-value 0.026), Hepatitis C (p-value 0.0001), and Hepatitis B and C coinfection (p-value 0.0001). The history of illicit drug use revealed significant correlation to Hepatitis C (p-value 0.008) and Hepatitis B and C coinfection (p-value 0.0001) but failed to show significance to Hepatitis B infection alone (p-value 0.113).

### Summary

From 2020-2022, the year 2022 had the most (49.2%) number of newly enrolled cases. Among the 65 respondents, most belong to age group 19-29 years. Majority (92.3%) of the respondents were males. Many (46.2%) respondents identify themselves as homosexuals. Majority (89.2%) of them were single. More than half of the respondents were College graduate and majority (63%) were employed. Majority (63%) of the newly enrolled HIV patients at the treatment hub had a CD4 cells less than 200 cells/uL, and more than half (58.50%) of the study population had elevated levels of alanine aminotransferases (>31). Only 7% had history of blood transfusion while only 4.6% had history of illicit drug use. The antiretroviral therapy utilized was almost equally distributed between Lamivudine/Tenofovir/Efavirenz and Lamivudine/Tenofovir/Dolutegravir at 49.2% and 50.80% respectively. All patients who were reactive to Hepatitis B, Hepatitis C, and both received a regimen containing Tenofovir disoproxil fumarate plus Lamivudine plus Dolutegravir or Efavirenz.

There was a total of 8 (12%) patients who had Hepatitis B, Hepatitis C co-infection or both. 7.69% had reactive HbsAg from the year 2020 to 2022. There only 3.08% patients had reactive Anti-HCV results. There were 31 respondents who had screening tests for both Hepatitis B and C coinfection. Among these, only

1 (1.5%) had a reactive result to both Hepatitis B and Hepatitis C which was recorded during the year 2020.

Among the sociodemographic and clinical profile of the respondents, only the educational attainment and the history of intravenous illicit drug use had statistically significant correlation with the occurrence of hepatitis co-infection with p-values less than 0.05. The history of illicit drug use revealed significant correlation to Hepatitis C (p-value 0.008) and Hepatitis B and C coinfection (p-value 0.0001) but failed to show significance to Hepatitis B infection alone (p-value 0.113).

### Conclusion

Based on the results of this study, it can be concluded that the incidence density of Hepatitis B, Hepatitis C, and Hepatitis B and C co-infection are low. The results however only depended on the available laboratory results upon enrollment hence some cases with incomplete Hepatitis profile were excluded. It can also be concluded that educational attainment remains to be significant risk factor that can affect the occurrence of Hepatitis B, Hepatitis C coinfection or both while history of Illicit drug use is a significant risk factor for Hepatitis C coinfection alone.

### Recommendations

Recommendations for a larger scale study involving the whole region to be able to come up with the incidence of Hepatitis B and or Hepatitis C co-infection among HIV patients that could serve as a baseline data for future studies. A prospective study is recommended to be able to explore the risk factors of Hepatitis B and or C coinfection in the local setting. Furthermore, it also recommended that screening for Hepatitis B and or Hepatitis C coinfection among newly enrolled HIV patients should be strictly adhered since management for these special population may vary.

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