

## Research Article

### Prevalence and Correlates of HBV and HCV among HIV Positive Patients: A Facility based Cross-Sectional Retrospective Study from Malaysia

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#### Abstract

**Background:** HBV and HCV become severe cause of chronic liver diseases and immunological impairment among the HIV positive individuals. The aim of this study is to evaluate the prevalence of HBV and HCV among the HIV infected patients receiving HAART treatment and their correlation with CD4 cell count and liver enzymes.

**Methods:** A retrospective, cross-sectional study was conducted from September 2013 to April 2014 at Hospital Palau Pinang, Pinang, Malaysia. Socio-demographic data as well as clinical data was collected with the help of data collection form from the patient's records. Then the data was entered and analyzed by using statistical software SPSS version 20.0 and  $p < 0.05$  was considered as significant.

**Results:** The overall prevalence of viral hepatitis among 808 HIV infected study population was 230 (28.4%). The prevalence of HIV-HBV, HIV-HCV and HIV-HBV-HCV co-infected patients was 86 (13%), 130 (18.4%) and 14 (2.4%) respectively. Individuals with HIV-HBV, HIV-HCV and HIV-HBV-HCV showed raised levels of liver enzymes than the HIV mono-infected patients. Study participants who had HIV-HBV, HIV-HCV and HIV-HBV-HCV co-infections also had a

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slight increase in the level of CD4 count than the HIV mono-infected study population. The mean CD4 value observed in this study was higher in females than males.

**Conclusion:** The prevalence of HBV and HCV was slightly higher in this study than some other reports from the world. Raised levels of CD4 count and liver enzymes were also observed in HIV-HBV, HIV-HCV and HIV-HBV-HCV co-infected patients than HIV mono-infected patients. These findings suggest the importance of screening for all HIV positive individuals before the initiation of the HAART treatment.

**Keywords:** Co-infection; HAART; HBV; HCV; HIV

#### Introduction

Globally, Hepatitis B Virus (HBV) and Hepatitis C virus (HCV) are the common causes of chronic liver diseases. Usually the infection is asymptomatic and has a severe and invasive impact on the health of millions of people throughout the world [1,2]. Co-infection of HIV with HBV and HCV is common due to similar routes of transmission [3]. It is estimated that 10% of all HIV infected population has HBV co-infection and around a third estimated to have HCV co-infection throughout the world [2,3]. Many studies reported that the rates of HBV and HCV co-infection in HIV infected population may vary region to region, study population and risk factors involved [4-7]. The prevalence of HBV and HCV co-infection among HIV individuals ranged from 3.9-7.3% and 6.9 respectively reported in a systemic review of 18 Sub Saharan African countries [8].

After the initiation of Highly Active Antiretroviral Therapy (HAART) there is a decline in the mortality and morbidity of HIV individuals however, liver diseases due to HBV and HCV become a main cause of death. In many reports the impact of HCV on HIV disease progression remains controversial [6,9-13]. HIV causes increased rate of persistent HBV infection, increased risk of hepatocellular carcinoma at lower CD4T cell counts and liver related mortality in HIV-HBV co-infected patients [14]. Similarly, there is a more rapid progress to hepatocellular carcinoma, Cirrhosis and end-stage liver disease in HIV-HCV co-infected population [15].

There is a risk of liver hepatotoxicity results in failure to improve the immunological recovery in HIV positive patients co-infected either with HBV or HCV. This shows in a study conducted in Tanzania which reported that after the initiation of HAART treatment there is a slow rate of immunological recovery and greater risk of hepatotoxicity among co-infected patients of HIV and HBV/HCV [16]. In some countries before initiation of anti-viral treatment it is highly recommended to screen the HIV patients for HBV and HCV [17]. The management of HBV and HCV in HIV infection becomes complicated as a result HIV, HBV and HCV become the major public health concerns worldwide [18,19].

In Malaysia, the prevalence of HBV and HCV among HIV individuals is not reported. In addition, there is no report present which shows the liver enzymes and CD4 count determination in HIV-HBV and HIV-HCV co-infected patients. Therefore, the main objective of this study was to assess the prevalence of HIV-HBV, HIV-HCV co-infected patients and CD4 cells as well as liver enzyme levels among these co-infected individuals at Hospital Palau Pinang, Pinang, Malaysia.

## Materials and Methods

### Ethics statement

This study was conducted after the approval from National Institute of Health and Medical Research and Ethics Committee, Malaysia. This study was conducted according to the principles expressed in the approval.

### Study design, area and period

A retrospective, cross-sectional study was conducted from Aug 2013 to March 2014 at Hospital Palau Pinang, Pinang, Malaysia.

### Inclusion and exclusion criteria

All HIV patients receiving HAART under treatment from 2007 to 2012 and with confirmed diagnosis of HBV and HCV which were older than 18 years of age were included. Diagnosed with other co-morbidities and which were not in the specified time period was excluded from the study.

### Source population and study participants

The source population was all HIV positive individuals who were under treatment in the infectious unit at Hospital Palau Pinang. The study participants were all treated with HAART HIV positive individuals. A convenient, non-probability sampling technique was employed and no scientific methods were used to calculate the sample size, instead, we enrolled all the patients which were eligible according to inclusion criteria.

### Data abstraction and collection

Socio-demographic, clinical information and other relevant possible risk factors of the study participants were collected with the help of comprehensive data collection form from the medical records of the patients.

### Data analysis

The data was entered and analyzed using SPSS Version 20.0 statistical software and the differences in proportions was evaluated by Pearson's Chi-square test and p value less than 0.05 was considered as statistically significant. Mean plus standard deviation with 95% Confidence Interval (CI) was also used for continuous variables and the difference in means was compared with independent-sample t-test.

## Results

### Socio-demographic characteristics

Among 808 study participants, 627 (77.6%) were males (mean age: 41±9 years) and 181 (22.4%) were females (mean age: 39±10 years). The lowest and highest age of the study population was 21 and 73 years respectively. The median age of 39 years was observed

in the study participants. The majority of the participants was Chinese 500 (61.9%), married 380 (47.0%) and had primary education 328 (40.6%). The main route of transmission of HIV in the study population was observed in heterosexual contact 572 (70.8%). Most of them were smokers 457 (56.6%) and non-alcoholic 499 (61.8%) (Table 1).

Variables	Frequency (%) N= 808
<b>Gender</b>	
Male	627(77.6)
Female	181 (22.4)
<b>Race</b>	
Malay	161(19.9)
Chinese	500 (61.9)
Indian	104 (12.9)
Others	43 (5.3)
<b>Age groups (year)</b>	
≤40	407 (50.4)
>40	401 (49.6)
<b>Marital status</b>	
Single	342 (42.3)
Married	380 (47.0)
Divorced	48 (5.9)
Widow	38 (4.7)
<b>Education status</b>	
No formal	223 (27.6)
Primary	328 (40.6)
Secondary	196 (24.3)
Graduation	61 (7.5)
<b>Smoking</b>	
Smoker	457 (56.6)
Non-smoker	351 (43.4)
<b>Alcohol use</b>	
Alcoholic	309 (38.2)
Non-alcoholic	499 (61.8)
<b>IVDU</b>	
Yes	128 (15.8)
No	680 (84.2)
<b>Risk factors</b>	
Heterosexual	572 (70.8)
Homosexual	53 (6.6)
Unknown	183 (22.6)

Table 1: Socio-demographic characteristics of HIV positive study population at Hospital Palau Pinang, Malaysia.

### Prevalence of HBV and HCV among HIV study population

The overall prevalence of Viral Hepatitis (HBV and HCV) was 230 (28.4%). The prevalence of HBV and HCV were 86 (13%) and 130 (18.4%) respectively. Only 14 (2.4%) of HIV positive study participants showed triple (HIV-HBV-HCV) infections.

### Association between HIV-HBV and HIV-HCV co-infection and their demographic characteristics

Higher prevalence of HIV-HBV co-infection was observed significantly in males 76 (11.4%) as compared to females 10 (1.5%) (p=0.001). Although non-significant higher prevalence of HIV-HBV

co-infection was seen in Chinese race 64 (9.6) ( $p = 0.091$ ) and in the age group of  $>40$  years 48 (7.2%) ( $p=0.165$ ). Those who were single 42 (6.3%) ( $p=0.254$ ) and had primary level of education 32 (4.8) ( $p=0.581$ ) showed non-significant higher prevalence in HIV-HBV positive individuals. A significant higher prevalence of smokers 56 (8.4%) ( $p=0.004$ ) and non-alcoholic 46 (6.9) ( $p=0.055$ ) were also observed in the HIV-HBV positive individuals.

Significant higher prevalence of HIV-HCV co-infection was observed in males 122 (17.2%) ( $p<0.001$ ), those who were categorized in Malay race group 76 (10.7%) ( $p<0.001$ ), single 70 (9.9%) ( $p=0.001$ ) and had primary educational status 60 (8.5%) ( $p=0.050$ ). Those who were smokers 112 (15.8%) ( $p<0.001$ ) and intravenous drug users 76 (10.7%) ( $p<0.001$ ) also showed high prevalence of HIV-HCV co-infection which was statistical significant. The co-existence of both HBV and HCV in males and females were 10 (1.7) and

4 (0.7) ( $p=0.930$ ). The significantly higher prevalence of this triple infection was observed in the non-intravenous drug users group 10 (1.7%) ( $p=0.002$ ) (Table 2).

### Mean CD4 count and liver enzyme levels in HIV-HBV, HIV-HCV and HIV-HBV-HCV co-infections

In HIV mono infected participants the mean CD4 count was 243 cells/mm<sup>3</sup>. While the mean CD4 counts were 283 cells/mm<sup>3</sup>, 243 cells/mm<sup>3</sup> and 313 cells/mm<sup>3</sup> observed in HIV-HBV, HIV-HCV and HIV-HBV-HCV respectively. The statistical significant difference was seen in HIV-HBV and HIV-HBV-HCV co-infections (Table 3). The CD4 count is higher in females as compared to males (268±79 vs 243±113). Females infected with triple infection (HIV-HBV-HCV) shows the lowest CD4 mean count. The highest and lowest mean CD4 count was observed in  $\leq 40$  year's age group (Table 4).

Variables	HIV-HBV		p value	HIV-HCV		p value	HIV-HBV-HCV		p value
	Negative N (%)	Positive N (%)		Negative N (%)	Positive N (%)		Negative N (%)	Positive N (%)	
<b>Gender</b>									
Male	419 (63.1)	76 (11.4)	0.001	419 (59.2)	122 (17.2)	<0.001	419 (70.8)	10 (1.7)	0.930
Female	159 (23.9)	10 (1.5)		159 (22.5)	8 (1.1)		159 (26.9)	4 (0.7)	
<b>Race</b>									
Malay	75 (11.3)	8 (1.2)		75 (10.6)	76 (10.7)		75 (12.7)	2 (0.3)	
Chinese	391 (58.9)	64 (9.6)	0.091	391 (55.2)	36 (5.1)	<0.001	391 (66.0)	9 (1.5)	0.987
Indian	82 (12.3)	6 (0.9)		82 (11.6)	14 (2.0)		82 (13.9)	2 (0.3)	
Others	30 (4.5)	8 (1.2)		30 (4.2)	4 (0.6)		30 (5.1)	1 (0.2)	
<b>Age groups (year)</b>									
$\leq 40$	304 (45.8)	38 (5.7)	0.165	304 (42.9)	60 (8.5)	0.109	304 (51.4)	5 (0.8)	0.212
$>40$	274 (41.3)	48 (7.2)		274 (38.7)	70 (9.9)		274 (46.3)	9 (1.5)	
<b>Marital Status</b>									
Single	223 (33.6)	42 (6.3)		223 (31.5)	70 (9.9)		223 (37.7)	7 (1.2)	
Married	294 (44.3)	38 (5.7)	0.254	294 (41.5)	44 (6.2)	0.001	294 (49.7)	4 (0.7)	0.3
Divorced	30 (4.5)	4 (0.6)		30 (4.2)	12 (1.7)		30 (5.1)	2 (0.3)	
Widow	31 (4.7)	2 (0.3)		31 (4.4)	4 (0.6)		31 (5.2)	1 (0.2)	
<b>Education Status</b>									
No formal	157 (23.6)	26 (3.9)		157 (22.2)	36 (5.1)		157 (26.5)	4 (0.7)	
Primary	229 (34.5)	32 (4.8)	0.581	229 (32.3)	60 (8.5)	0.05	229 (38.7)	7 (1.2)	0.425
Secondary	145 (21.8)	18 (2.7)		145 (20.5)	32 (4.5)		145 (24.5)	1 (0.2)	
Graduation	47 (7.1)	10 (1.5)		47 (6.6)	2 (0.3)		47 (7.9)	2 (0.3)	
<b>Smoking</b>									
Smoker	279 (42.0)	56 (8.4)	0.004	279 (39.4)	112 (15.8)	<0.001	279 (47.1)	10 (1.7)	0.087
Non-smoker	299 (45.0)	30 (4.5)		299 (42.2)	18 (2.5)		299 (50.5)	4 (0.7)	
<b>Alcohol Use</b>									
Alcoholic	207 (31.2)	40 (6.0)	0.055	207 (29.2)	56 (7.9)	0.074	207 (35.0)	6 (1.0)	0.587
Non- alcoholic	371 (55.9)	46 (6.9)		371 (52.4)	74 (10.5)		371 (62.7)	8 (1.4)	
<b>IVDU</b>									
Yes	38 (5.7)	10 (1.5)	0.091	38 (5.4)	76 (10.7)	<0.001	38 (6.4)	4 (0.7)	0.002
No	540 (81.3)	76 (11.4)		540 (76.3)	54 (7.6)		540 (91.2)	10 (1.7)	
<b>Risk Factors</b>									
Heterosexual	408 (61.4)	56 (8.4)		408 (57.6)	98 (13.8)		408 (68.9)	10 (1.7)	
Homosexual	43 (6.5)	4 (0.6)	0.186	43 (6.1)	4 (0.4)	0.183	43 (7.3)	2 (0.3)	0.545
Unknown	127 (19.1)	26 (3.9)		127 (17.9)	28 (4.0)		127 (21.5)	2 (0.3)	

Table 2: HIV-HBV and HIV-HCV co-infection and their association with demographic characteristics.

Immunological and liver biomarkers	HIV alone	HIV-HBV	p value	HIV alone	HIV-HCV	p value	HIV alone	HIV-HBV-HCV	p value
CD4 mean ± SD	243±88	283±136		243±88	230±141		243±88	313±170	
Normal value	410-1590 cells/uL	410-1590 cells/uL	<0.001	410-1590 cells/uL	410-1590 cells/uL	0.957	410-1590 cells/uL	410-1590 cells/uL	0.004
ALT mean ± SD	32±40	56±54		32±40	59±45		32±40	65±33	
Normal Value	0-55 u/L	0-55 u/L	<0.001	0-55 u/L	0-55 u/L	<0.001	0-55 u/L	0-55 u/L	0.002
ALP mean ± SD	100±40	105±37		100±40	126±51		100±40	98±27	
Normal value	40-150 u/L	40-150 u/L	<0.001	40-150 u/L	40-150 u/L	<0.001	40-150 u/L	40-150 u/L	0.887

**Table 3:** Liver enzymes level and mean CD4 count and their association with HBV and HCV co-infection.

Variables	Mean CD4 Count				
	HIV alone	HIV-HBV	HIV-HCV	HIV-HBV-HCV	Over all
<b>Gender</b>					
Male	235±92	271±137	245±144	328±192	243±113
Female	264±73	373±82	213±79	109±52	268±79
<b>Age groups (year)</b>					
≤40	252±83	294±122	215±125	388±186	252±98
>40	232±92	274±147	268±150	273±155	244±114

**Table 4:** Mean CD4 count associated with gender and different age groups.

In HIV mono-infected patients the mean ALT and ALP levels are 32µ/L and 100µ/L respectively. However, in the group of HIV-HBV co-infected patients there is a significant increase in the levels of ALT and ALP was observed (56µ/L and 105µ/L respectively). Similarly, in HIV-HCV co-infected patients the mean ALT and ALP levels are significantly increased (59µ/L and 126µ/L respectively) (Table 3).

## Discussion

The main objective of this study is to investigate the prevalence of HBV and HCV among the HIV positive individuals which were under the treatment of highly active antiretroviral therapy and tried to assess the levels of CD4 count and liver enzymes among HIV-HBV and HIV-HCV co-infected, HIV-HBV-HCV triple infected and HIV mono infected study population. The prevalence of hepatitis (both HBV and HCV) was 28.4% among the study participants. In the current study the prevalence of HIV-HBV was 10.6% which is comparable with a prevalence of 10.9% and 9.2 % reported in Ethiopia and Nigeria respectively [20,21]. A study reported in Malawi reported 20.4% prevalence of HIV-HBV co-infected individuals which was higher than the present study [22]. The prevalence of HIV-HBV co-infected individuals in present study was higher in males as compared with females (11.4% vs 1.5%) which are in line with some other reports [23-25]. The difference in the prevalence of such co-infections may be due to differences in exposures, geographic regions and types of risk groups involved [21,26-30].

The prevalence of HIV-HCV co-infection in the current study was 16.1% which is higher than the studies which were done in Nigeria (5.8%), Malawi (5.0%), Burkina Faso (4.8%) and Senegal (8.0%) [21,22,31,32]. But HIV-HCV co-infection ranges from 3.6-13.3% in some recent studies [33-38]. The reasons behind the variation of HCV prevalence among HIV individuals could share the same factors in variation in HBV prevalence discussed above. HIV-HBV-HCV triple infection observed in this study was 1.7% which is less or more comparable to some studies from Senegal (0.5%), Kenya (0.26%),

Nigeria (1.5%) and Egypt (0.44%) [32,39,40]. However, in Argentina and Iran the prevalence of HIV-HBV-HCV triple infection was higher to (9.5%) and (9.2%) respectively [41,42]. Risk factors associated in the variation of HIV-HBV prevalence might work for the triple infection.

The statistical significant difference was observed in the means levels of liver enzymes between the HIV mono-infected and HIV-viral hepatitis co-infected individuals in the present study. There was a raised level of ALT and ALP was found in the HIV-HBV, HIV-HCV and HIV-HBV-HCV co-infected patients comparable with a study conducted in South Africa that reported the raised level of ALT and ALP in HIV-HBV and HIV-HCV co-infected individuals [30]. Similarly, significantly elevated ALT levels also reported in HIV-HBV and HIV-HCV co-infected patients in India [43]. The differences in the liver enzyme levels in many other reports might be due to the difference in the study design, duration of viral hepatitis as well as the patient's condition like drug induced hepatotoxicity or having chronic alcoholism.

In the present study, there is statistical significant CD4 count mean was observed in HIV-HBV and HIV-HBV-HCV co-infected patients and non-significant CD4 mean was found in HIV-HCV co-infected individuals. The mean CD4 count in HIV-HBV individuals was 283 cells/mm<sup>3</sup> which was not comparable with the mean CD4 of 141.6 cells/mm<sup>3</sup> and 121 cells/mm<sup>3</sup> reported in studies conducted in South Africa and Nigeria respectively [30,39]. The differences in the results may be due to high HIV and HBV viral replication that may contribute in the impairment of the immune system of the patients in HIV-HBV co-infected individuals. In addition, may be due to the differences in the immune system of the study participants or due to viral hepatitis.

In this study the mean CD4 count in HIV-HCV co-infected individuals was 243 cells/mm<sup>3</sup> which is comparable with the mean CD4 counts of 260 cells/mm<sup>3</sup> and 288.6 cells/mm<sup>3</sup> reported in the studies

conducted in Nigeria and India respectively [39,43]. Such low levels of CD4 mean count in HIV-HCV individuals than HIV-HBV co-infected patients was still unclear. The CD4 count in HIV mono-infected patients was relatively higher than the HIV-HCV co-infected individuals. This lower CD4 count in HIV-HCV co-infected reflecting the immunosuppressed state of patients due to increased replication of HIV and HCV.

In the current study, the difference was observed on the mean CD4 values in relation to the gender. The mean CD4 value in the males was lower than the females (235 cells/mm<sup>3</sup> vs 264 cells/mm<sup>3</sup>). Some studies conducted in Nigeria and Uganda also showed same findings [44,45]. Males who had Triple Infection (HIV-HBV-HCV) had highest CD4 count. This increase of CD4 count in males may be linked with their daily life activities. Moreover, mostly males have muscular body and they do not take the mental stress to accept the HIV-HBV-HCV disease status that contribute in the recovery of the immune system or improves CD4 count. We also analyzed the CD4 mean values in different age groups and the lowest CD4 mean value was observed in the ≤40 year's group co-infected with HIV-HCV (215 cells/mm<sup>3</sup>). As this disease is almost asymptomatic so that younger people cannot be tested regularly so that their CD4 count was lowered than the older one because they were more conscious about their health due to many diseases in older age than in young age.

In conclusion, the prevalence of HBV and HCV among HIV positive individuals was very high so, screening of HBV and HCV in HIV population before the initiation of antiretroviral treatment is mandatory and strict monitoring of liver enzymes and CD4 count status to minimize the complication of the liver and effective HIV treatment.

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