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Forward stepwise logistic regression approach for determinants of hepatitis B & C among Hiv/Aids patients

Faryal Shahzad[a], Fazeel Abid[a,*], Ahmed J. Obaid[b], Bipin Kumar Rai[c], Mohsin Ashraf[d], Azmi Shawkat Abdulbaqi[e]

[a]*Department of Information System, Dr. Hasan Murad School of Management, University of Management and Technology, Lahore, Pakistan*
[b]*Faculty of Computer Science and Mathematics, University of Kufa, Iraq*
[c]*Department of Information Technology, ABES Institute of Technology, Ghaziabad, UP, India*
[d]*Department of Computer Science, University of Central Punjab, Lahore, Pakistan*
[e]*Department of Computer Science, College of Computer Science and Information Technology, University of Anbar, Ramadi, Iraq*

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Abstract

Hepatitis-related liver diseases are a leading cause of mortality and morbidity among people with HIV/ AIDS taking highly active antiretroviral therapy due to shared transmission routes. An estimated 2–4 million HIV-infected persons have chronic HBV co-infection, and 4–5 million have HCV co-infection worldwide and 14,000 new infections each day. The purpose of this study was to determine the prevalence and associated factors of HBV and HCV co-infection in HIV-positive patients. A cross-sectional study was conducted among 235 HIV/ AIDS patients seeking medical care at special clinics of two public hospitals in Lahore, Pakistan, from February 2018 to May 2018. A structured questionnaire was used to collect information on socio-demographic and clinical characteristics of HIV/ AIDS patients after obtaining their written informed consent. Chi-square, Fisher's exact, and two independent sample t-tests as appropriate were used to find the association between risk factors and HBV, HCV co-infection with HIV. Further, a forward stepwise logistic regression model was used to evaluate the predictors of HBV and HCV co-infection with HIV. P-value ¡ 0.05 was regarded as

*Corresponding author
Email addresses: farishhzd001@gmail.com (Faryal Shahzad), Fazeel.abid@umt.edu.pk (Fazeel Abid), Ahmedj.aljanaby@uokufa.edu.iq (Ahmed J. Obaid), bipinkrai@gmail.com (Bipin Kumar Rai), Mohsin.ashraf@ucp.edu.pk (Mohsin Ashraf), azmi_msc@uoanbar.edu.iq (Azmi Shawkat Abdulbaqi)

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significant. Of 235 HIV-positive patients, 9% were co-infected with HBV, 41 were HCV co-infected, and 6% had HBV-HCV triple infection. The highest prevalence of HBV (55%), HCV co-infection (70%), and HBV-HCV triple infection (85%) were observed in intravenous drug users followed by heterosexual routes. Male, hypertensive, alcohol consumers, and smokers were statistically significantly associated with HBV co-infection ($P-value < 0.05$). The factors include being male, never married, having < 1 year of HIV diagnosis, having < 200 CD4 counts (cell/mm3), presence of physical disability, having been infected through sexual routes, injecting drug user, alcohol consumer, and smoker were statistically significantly associated with HCV co-infection ($P-value < 0.05$). Whereas the factors; heterosexual transmission, intravenous drug use, alcohol use, smoking, and presence of physical disability were statistically significantly associated with HBV, HCV triple infection ($P < 0.05$). The adjusted odds ratio obtained by fitted logistic regression model showed that HIV transmission routes (both hetero and homo) and never married had lesser odds of HCV co-infection whereas the person with HIV transmission through intravenous drug use, who smoke and aged more than 30 years, had greater odds of HCV co-infection. Co-infection with hepatitis B and C virus is common among this studied sample of HIV-infected patients. The study's finding reaffirms the need for routine baseline screening for this marker and as there is more chance of co-infection with these hepatitis viruses due to enhanced immunodeficiency by HIV and shared routes of transmission. It highlights the need for timely initiation of HAART. Furthermore, those found to be negative should be immunized with HBV and HCV vaccines to improve.

Keywords: HBV, HCV, HIV, logistic regression.

1. Introduction

Hepatitis has been identified as a major global public health concern, with high prevalence and burden of morbidity and mortality, with poor diagnostic and therapeutic techniques. Hepatitis affects individuals suffering from the human immunodeficiency virus significantly (HIV). HIV, hepatitis B (HBV), and hepatitis C (HCV) have different transmission efficiencies. These are typically more prevalent among persons infected by HIV common epidemiological characteristics as transmission routes; intravenous drug use (IDU), blood transfusion, sexual interaction, or transmission of mother to child, with a significant social-economic impact globally and can be associated with rapid liver damage [21, 25] This puts HIV-positive individuals at risk of co-infection for hepatitis B, C, or both. In addition, the World Health Organization's (WHO) latest report, 76 million individuals have been infected by HIV/AIDS pandemic, and around 33 million people die from HIV/AIDS. Hepatitis B or C virus infections account for around 325 million fatalities each year worldwide, accounting for 1.4% of the mortality, and the most common causes include hepatocellular carcinoma. Globally, the number of individuals living with HIV/AIDS is 38 million. It is estimated that 2-15% and 5-20% of whom 38 million individuals living with HIV are co-infected by HCV and HBV, respectively [9, 3, 24]. The co-infections of HIV-HBV and HIV-HIV negatively impact liver disease as hepatitis accelerates the development of liver disease [12] and faces a higher risk of liver-related deaths than those infected with only HIV and are less likely to be prone to acute infections spontaneously. Infections of both HBV and HCV cause acute and chronic liver infection with the potential for liver cirrhosis and hepatocellular carcinoma (HCC). The life expectancy of people with HIV infection who maintain long-term suppression from HIV replication and recover their CD4 counts has been improved by highly active antiretroviral therapy (HAART). But the presence of co-infection may further raise the risk for the administration of HAART-induced hepatotoxicity. Co-infected individuals are at higher risk of liver-related deaths, particularly those with low CD4 counts. Therefore, HIV co-infections

have important clinical consequences that pose several challenges for patients and health professionals [8, 20, 30].
However, many studies have been conducted on the co-infection of hepatitis B and C among HIV/ AIDS worldwide and have been a source of significant discussion on whether HBV or HCV impacts HIV development. But the evidence shows that HIV progresses more rapidly in co-infected individuals with either HBV or HCV. It has become a security concern in developing countries like Pakistan, situated among high risked countries. Millions are on the brink of extermination due to poverty, hunger, disease, medically insufficient facilities, illiteracy, and underdevelopment exacerbate the incidence rate. Based on these facts, we have conducted a novel cross-sectional study to recognize the prevalence rates of hepatitis B and C co-infection among HIV/ AIDS patients taking antiretroviral therapy (ART) and to assess socio-demographic and other factors associated with hepatitis B and C co-infection in HIV/ AIDS patients. This study supports the co-infection of HBV and HCV and includes factors that might improve clinical information for HIV-infected individuals to assess and effectively manage their illness. This study also helps the public health authorities to reduce the morbidity and mortality of these infections by empowering them with knowledge and awareness. To the best of our knowledge, there is no study on the relationship between HIV/ AIDS and hepatitis B and C co-infection. It, therefore, becomes necessary to conduct a baseline assessment of hepatitis B and C co-infection in HIV/ AIDS patients and their risk precautions. Following are the main contributions of this work

- After receiving informed consent, a standardized questionnaire was utilized to gather benchmark data on socio-demographic and clinical features of HIV/AIDS patients.
- To compare variables and assess the relationship of HIV-HCV and HIV-HBV co-infections with diverse independent factors, Chi-Square test or accurate Fisher test, and independent sample t-test, are conducted.
- Lastly, a forward stepwise logistic regression model was used to evaluate the predictors of HBV and HCV co-infection with HIV.

The rest of the paper is as follows. Section 2 contains related work, whereas the proposed methodology is presented in Section 3.

2. Related Work

Hepatitis affects individuals suffering from the human immunodeficiency virus significantly (HIV). HIV, hepatitis B (HBV), and hepatitis C (HCV) have different transmission efficiencies. Many studies have been conducted on the co-infection of hepatitis B and C among HIV/ AIDS worldwide and have been a source of significant discussion on whether HBV or HCV impacts HIV development. However, the evidence shows that HIV progresses more rapidly in co-infected individuals with either HBV or HCV [13, 18]. Anteneh conducted a multicenter case-control to investigate the determinants of co-infection among HIV patients. For this purpose, a binary logistics regression model was used to investigate the predictors of co-infections. This work statistically significantly addresses the relationship with HBV infection. The greatest HBV predictor in HIV patients was reported to have a high viral load. Also, they found that Targeted intervention should be implemented, such as behavioral modification intervention for unsafe intercourse and STI [26]. Another meta-analysis summarizes the prevalence of HBV-HIV co-infection among pregnant women in Africa from March 2020 to Jun 2020. For this purpose, a search was conducted using different search words, which yielded about 2560 articles with information about HIV infection is abundant in Sub-Saharan Africa among expectant

mothers receiving prenatal care. To analyze the heterogeneity of all relevant meta-analytical studies, Cochran Q testing and I2 statistics were carried out. The grouping studies showed substantial heterogeneity and usage of the Random Effect model to match the prevalence. The grouped prevalence estimate was produced for each study, and the prevalence was computed, whereas the confidence interval was 95%. HIV-positive pregnant mothers in Africa urgently need regular HBV screening to assess the degree of HBV/HIV co-infection in this group [2].

A cross-sectional study was conducted by [20] to investigate the prevalence rate of HCV and HBV co-infection among 4663 HIV/ AIDS patients at a teaching hospital in Nigeria. The prevalence was examined by several positive results over the total number of patients. A Chi-square test was performed for the determination of correlation. The results showed that the age and gender were significant with HBV and HCV co-infection, but CD4 count was found insignificant ($p > 0.05$). They concluded that co-infection with HBV was more common than HCV and a triple infection [22]. A study was conducted to determine whether the co-infection of hepatitis C with human immunodeficiency virus (HIV) promotes liver damage in end-stage patients more seriously than HCV infection alone. This aimed at assessing risked variables linked with HCV infection linked to HIV/AIDS patients visiting Northeastern Ethiopia. A total of 249 HIV-positive individuals were selected using systematic random sampling. The highest prevalence rate was found in males with p=0.078, followed by elders with > 50, which concluded that screening these high-risk populations should be essential to minimize the death rate and enhance treatment results [11].

To investigate the prevalence and the correlations between the risk of HBV infection and the relationship of ART results among the PLWH, a study was carried out in [6]. A random sample of 1000 PLWH was carefully selected for a fast hepatitis B surface antigen test (HBsAg) from the St. Mary's Hospital, Gulu, Uganda ambulatory clinic. Multivariate logistic regression and general linear model concluded that the HBV prevalence found inside the PLWH might be overestimated or the HBV signal in the area declined. The factors identified for horizontal HBV transmission suggest that HBV testing and prophylaxis of vaccines between PLWH are extended. The meta-analysis was conducted to bring data on HIV and HCV patients in Nepal about their prevalence and risk factors. For the systemic review of available literature, the researchers have followed MOOSE guidelines. The result was estimated by the odds ratio and the ratio at a confidence interval of 95% if applicable. The heterogeneity was examined by the I-squared (I2) test. The study concluded that the combined prevalence of HBV, HCV, and combination HBV and HCV co-infection among HIV-positive individuals was 4.6%, 19.7%, and 1.3%, respectively. HBV and HCV must thus be properly screened for those diagnosed with HIV and for high-risk groups. In co-infected people, IVDU continues to be the most prevalent risk factor.

In this work, 500 HIV-positive study subjects recruited from all areas of Kazakhstan examined hepatitis B (HBV), hepatitis C (HCV), tuberculosis (T.B.), and sexually transmission (STI) co-infections. To investigate how HIV prevalence in Kazakhstan and other Central Asian countries has risen in recent years [31]. The HIV co-occurrence among participants in this study highlights that HCV infections, HBV infections, and T.B. infection require regular HCV screening among HIV-infected patients and the protocols for HBV and T.B. alert vaccination. In addition, individuals injecting medicines should be specifically targeted towards reducing harm, including opioid replacement treatment, needle, and syringe swaps, frequent screening, and expanded access to ART and direct antivirals [32]. To assess the worldwide and regional prevalence of HCV, HBV, and HIV co-infection among HIV-positive inmates, Gharaei et al., 2021 carried out a systematic review and meta-analysis of available literature. The Meta-regression analysis indicated a gradual increase in the incidence of investigated co-infections among inmates over the last decades and a demand for improved screening and treatment programs. To prevent co-infections between inmates, health care, human rights, and

equity must be given seriously or exercised in prisons. The number of studies included was 50 for HCV co-infection and 23 for HBV co-infection to assess the prevalence of the HBV of HIV [14]. For this purpose, 176 HIV-infected individuals, 67 men and 109 females were recruited. These patients were screened with the presence of the enzyme-connected immunosorbent test for hepatitis B surface antigen. The study confirmed a high HIV/HBV co-infection rate, and all HIV-positive people need to be screened for HBV infection. The significant prevalence of HBV within individuals infected with HIV leads to pre-ART HBV testing.
To assess the HBV and HCV infection rates in HIV-populated persons in Santiago, Chile's public and private healthcare institutions were conducted. The results showed that the co-infection rate of HBV was lower than in non-industrialized regions in Asia and Africa but was within the range of other South American nations [29]. Also, the rate of HCV co-infection was quite low, most certainly because of the rarity of drug injection. Another cross-sectional survey was carried among 440 HIV-positive individuals seeking medical care at the HIV clinic of Aminu Kano Teaching Hospital. The study was carried out to determine hepatitis B and C infection prevalence among HIV patients [15]. The student sample t-test and chi-square test showed a greater co-infection with hepatitis B than hepatitis C in individuals infected with HIV/AIDS than the HIV/AIDS virus. This further emphasizes the necessity of this marker for common baselines since starting and choosing highly active antiretroviral treatment is important. A cross-sectional study in Nepal to assess the prevalence of Hepatitis B and C virus co-infection among 677 people living with HIV [19]. The research was conducted to evaluate the prevalence and characteristics of HBV and HCV co-infection among people living with HIV in Tuscany by [16]. The sample comprises 1402 new cases of HIV diagnosis recorded from 2009 to 2013 in the Regional Surveillance System.
In comparison to HIV infection in Italian patients, however, the frequency of HBV in foreigners was higher, especially in age ranges 35- 59. The HCV co-infection among drug users was higher. HBV was shown to be higher by the outcomes of this investigation. In addition, the perceived higher risk of HIV was suggested compared to HIV/HBV patients.

3. Methodology

The cross-sectional survey was performed among HIV/AIDS patients seeking medical care at the two special clinics of public hospitals in Pakistan from January 2021 to August 2021. The administrative authorization for data collection was sought and obtained from the Project Director of Punjab AIDS Control Program, Ministry of Health Punjab, Pakistan. The permission for data collection was obtained from the Incharge Medical Officers of HIV clinics of respective hospitals. Privacy, confidentiality, and anonymity were ensured at all stages of the study for both research participants and hospitals.

3.1. Sampling Technique, Size, and Inclusion and Exclusion Criteria

A multi-stage sampling technique was used for the selection of the sample. There are two voluntary counseling and testing (VCT) centers, three HIV monitoring centers, and five HIV treatment centers. Only two out of five HIV clinics were randomly selected for data collection since the research participants included the individuals receiving and being regularly monitored. There were no estimates of prevalence available for HBV/ HCV co-infection among HIV- AIDS patients in the study area in Pakistan. Therefore, 50% proportion for both HBV/ HCV co-infection with HIV-AIDS was assumed as an estimate of proportion to attain maximum sample size [23]. After considering a 5% error margin at a 95% confidence interval, the sampling size was determined using the single proportion formula:

$$n = \frac{z^2 pq}{d^2} \tag{3.1}$$

Where, $Z\alpha/_2$ =the value associated with 95% confidence level, p = Assumed proportion of HBV / HCV co-infection in HIV - AIDS patients, $q = 1-$Assumed proportion of HBV / HCV co-infection in HIV-AIDS patients and d = margin of error in estimating p

$$n = \frac{(1.96)^2 * 0.5 * 0.5}{(0.05)^2}$$

$$n = \frac{0.9604}{0.0025}$$

$$n = 384.16$$

Accordingly, the calculated sample size was 384. After adding 10% as a contingency modifier, the total sample size was 423. However, it was only possible to collect data from 235 patients due to the shortage of time. Both male and female HIV/ AIDS patients under treatment, aged more than 15 years, were included in the sample [27]. The patients with acute HIV/ AIDS infection, women with pregnancy or breastfeeding, or not giving consent were excluded from the study.

3.2. Data Collection

The data were collected by receiving patient's medical files included socio-demographic characteristics of the patients such as age (years), using gender, body mass index, HIV transmission route as well as comorbidities (hypertension, diabetes mellitus, renal diseases, presence of physical disability, alcohol consumption and smoking were considered. HIV care characteristics (duration since HIV diagnosis, delayed HIV testing, delayed HIV treatment, baseline CD4 count ($cells/mm^3$), CD4 count at initiation of ART ($cells/mm^3$), CD4 count at last follow-up visit ($cells/mm^3$), HIV clinical staging, history of opportunistic infections, HIV RNA viral load (copies/mL), ART regimen and duration, hemoglobin level were also taken into consideration. Further, Clinical characteristics anti-HCV serostatus, anti-HBV status, immunological response, the virological response including alkaline phosphate (ALP), alanine transaminase (ALT), aspartate amino transaminase (AST), direct bilirubin (D.B.), albumin (ALB), and total bilirubin (T.B.) were retrieved from medical records [14, 4].

3.3. Pre-Processing and Initial Analysis

Initial analyses included categorical variables distribution of the calculation frequency, mean ($\pm$*standard deviation*), and median (interquartile [IQR]) values to characterize the data with or without normal distribution, respectively [5]. To assess and analyze the combination of HIV/HCV and HIV-HBV co-infections with various independent parameters, the Chi-Square or Fisher's Exact test (categorical variables) and independent-sample t-test were used as appropriate to compare variables and to evaluate the association of HIV-HCV and HIV-HBV co-infections with various independent factors. To determine the adjusted odds ratios (OR) with 95% CI [24], stepwise logistic regression analyses also were performed for the evaluation of factors associated with HIV-HCV and HIV-HBV co-infection status [24]. A Hosmer and Lemeshow test was applied to know how effectively the model described the outcome variable using a stepwise forward method [13]. All the tests

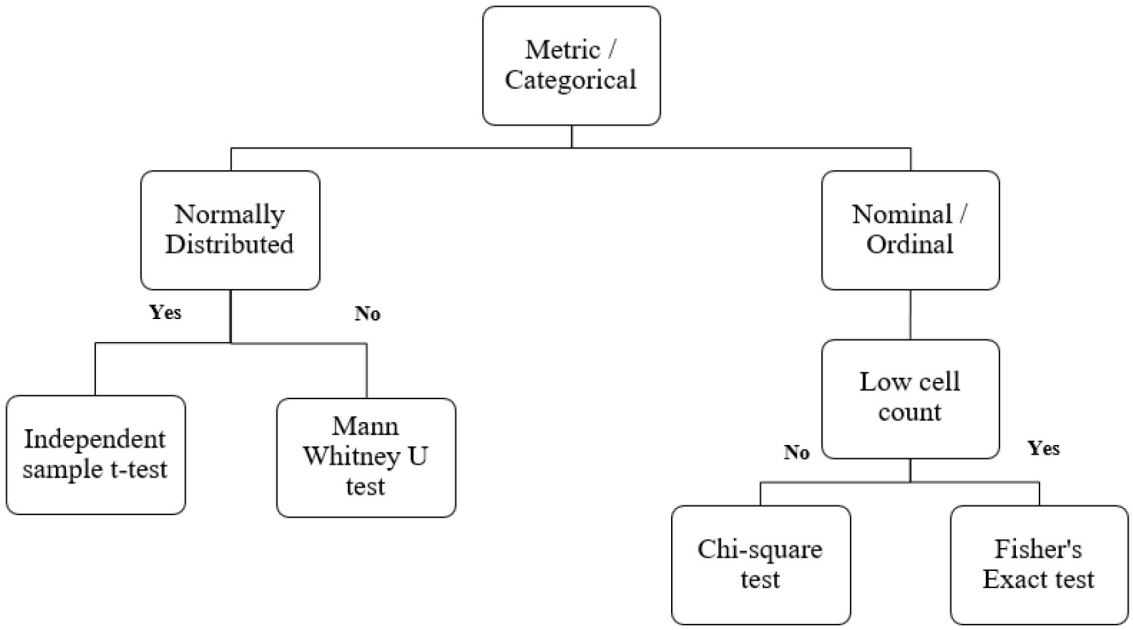

Figure 1: Statistical test Selection to Evaluate the Prevalence and Associated Factors of HBV/HCV Co-infection among HIV Positive Patients

performed were considered significant at the 5% significant level and were two-tailed [28, 1, 17], as shown in Figure 1.

Karl Pearson introduced the Chi-Square ($\chi 2$) **Test of Independence technique to test** whether two variables are independent or not or whether two variables are associated. Pearson's Chi-Square test is one of the varieties of Chi-Square tests. The observation may be tabulated in the chi-square test about the two variables of interest, and each observation may fall under one group only. Interest variables can be categorical or such quantitative variables, the value of which can be characterized as mutually exclusive. In each cell of cross-tabulation, the actual and anticipated frequency should be a minimum of 5.

Fisher Exact Test is a statistically significant test used in the testing of contingency tables. It was named after Ronald Fisher and is one of the classes for accurate testing since the meaning of the departure from a null hypothesis can be accurately determined rather than rely on a limited approximation as the sample size grows to infinity. For categorizing objects in two different ways, this test is helpful for categorical data. The association between the two types of categorizations is examined. Fisher has shown that the hypergeometric distribution gives the chance of receiving any such set of values:

$$p = \frac{(a+b)!(c+d)!(a+c)!(b+d)!}{a!b!c!d!n!} \tag{3.2}$$

Independent Sample t-test is an inferential statistical test to evaluate whether the means of two unrelated groups differ significantly or not. In an independent sample t-test, the dependent variable on a continuous scale should be measured. The independent variable must consist of two independent and categorical groups, and there must be no association between the observations. For every group of the independent variable, the dependent variable should be normally distributed. Levene must establish homogeneity of variances to test this assumption.

Logistic Regression Logistic regression is used to detect the risk factors of different infections. A logistics regression is a part of the generalized linear model. If the dependent variable (binary or categorical) has a discrete type, it can best suit the data. Whenever the data do not fulfill the assumptions of multivariate methods, a classification rule is applied for individuals to be allocated to their respective groups. The logistic regression function is defined and explained as mentioned below:

$$p_z = \frac{1}{1 + e^{(c-z)}} \tag{3.3}$$

Where C is the constant, and Z is the linear function of dependent variables. The above logistic function can be converted to an Odds ratio. The odds ratio can be defined as follows:

$$Odds = \frac{p_z}{1 - p_z} \tag{3.4}$$

In the logistic regression analysis, the essential assumption is that $\ln(odds)$ has a linear relation to the independent variables. However, there is no assumption that the independent variables are distributed. One of the major advantages is the discrete or continuous nature of independent variables. The model assumed is:

$$\ln(Odds) = \alpha + \beta_1 X_1 + \beta_2 X_2 + ... + \beta_P X_P \tag{3.5}$$

The probability of belonging to the population I can be written as,

$$p(popl) = \frac{1}{1 + exp[-(\alpha + \beta_1 X_1 + \beta_2 X_2 + ... + \beta_P X_P)]} \tag{3.6}$$

Logistic regression does not need many of the main assumptions of linear regression models based on the lesser-squares Method. Not only continuous but also discrete data can be handled by logistic regression as an independent variable. The error terms (residual), although multivariate normalcy results in a stabilized solution, do not need a multivariate distribution. The logistic regression requires a discrete, generally dichotomous dependent variable ($P(Y = 1)$, the expected result should be 1. The model does not need a linear relationship between the dependent and the independent variables, and independent variables must be related to the log odds of an event linearly. Large samples also need maximum probability estimates less strong than conventional lowest squares in a linear regression model.

Fitting the Logistic Regression Model The procedure for adopting the models and methods for the logistic regression to verify the meaning of Hosmer's and Lemeshow's variables is presented here; assume we have a sample of n independent pair observations (Xi, Yi), $(i = 1, 2, ..., n)$ where Yi denotes the value of a dichotomous dependent variable, and Xi indicates the value of the independent variable of the i^{th} subject. Suppose that the dependent variable, absence, and present, respectively, have been coded as null and one. The values of $\beta 0$ and $\beta 1$, unknown parameters, must also be estimated to match the logistic regression model.

$$\pi = \frac{e(\beta_0 + \beta_1 X)}{1 + e(\beta_0 + \beta_1 X)} \tag{3.7}$$

Forward Stepwise Method There are three methods available; enter, backward, and forward. The forward Method moves further when non-significant variables are dropped. The system develops several models in the forward step approach, which generates the first model without an independent model, and the following model includes an independent variable that has more effect on the dependent variable.

Hosmer-Lemeshow's Goodness of Fit Test evaluates the goodness of fit by dividing subjects into 10 ordered groups and comparing the observed and expected counts or frequencies. As a result, the test statistic is a chi-square statistic that indicates that "the model fits the data well." The Following Table 1 contains the interpretations:

Logistic Regression as a Classification Technique A classification is an interesting approach to summarize the results of the fitted logistic model. The outcome of cross classifying the dependent variable, y, with a dichotomous variable obtained from the calculated logistic probabilities. To acquire the derived dichotomous variable from the estimated logistic probabilities, we must establish a cut point, c, and compare each estimated probability to c; if the estimated probability exceeds c, we deduce the variable to be equal to 1; otherwise, it equals to 0.0.5 is the most often used number for c. When the distribution of the variables within the two outcome groups is multivariate normal, this sort of logistic regression is appealing to discriminant analysis. Classification is sensitive to the relative sizes of the two-component groups and will always prefer splitting up a table into a larger group, regardless of model fit.

4. Results

A total of 235 HIV/ AIDS patients visiting HIV clinics of the two largest public-sector hospitals, $X(n = 158)$ and $Y(n = 77)$, Lahore, participated in this study. Table 2 describes the socio-demographic characteristics of the study participants. Most of the patients were male (41%), ever married (69%), had no schooling (32%), and between the ages of 25-35 years (38.3%) with a mean age of 35 years. Mainly the sample comprised of Muslim participants (94%). Fifty-seven percent of patients belonged to East Punjab (42%) and residing in urban areas (69%). Before HIV diagnosis, 21.3% of respondents were unemployed, and after HIV diagnosis, there was a notable increase in unemployment (33.2%). About 39% of patients claimed their family's monthly income was less than 15,000 PKR. Based on the BMI, the frequency distribution of patients showed that about 29% of the patients were overweight/ obese, 12% were underweight.

Table 3 shows the clinical characteristics of HIV/ AIDS patients. A considerable proportion of patients (45%) were diagnosed with HIV/ AIDS at very young ages of 21-30 years, and 17% had advanced WHO clinical stage of the disease (stage III or IV). Thirty-four percent of the patients lived with HIV/ AIDS for an average of 2.32 ($\pm$2.86) years, and the mean duration of receiving HIV ART was 1.88 ($\pm$1.88) years. Most of the patients were ambulatory or bedridden (45%) at the last follow-up visit. Above half of the patients (52%) had CD4 counts at baseline, 54% at the time of initiation of treatment, and 36%, at last, follow-up visit $< 350 cells/mm^3$. Above 3/4th of patients (77%) had HIV RNA viral load $\leq 100,000 copies/mL$ with median HIV RNA viral load 1955715.796 ($\pm S.D = \pm 8990113.033$)$copies/mL$. Almost all the patients (98%) were on 1st regimen of ART. Most patients (93%) had disclosed their HIV/ AIDS status to their family or friends. The blood Hb levels of 77% of male and 41% of female patients were below normal ranges.

Figure 2 displays that among the sampled population, the major exposure to HIV was heterosexual transmission (42.1%) followed by intravenous drug use (39.1%), homosexual transmission (15.3%), blood products (7.2%), unsterilized needles/ syringes/ sharps (6.4%), and unknown/ unclear (3.4%). When inquired about the reason for HIV testing, the most frequent reason reported by patients was having HIV related symptoms (52%) followed by while performing the routine test (23%), having HIV positive partner (20%), just wanted to know whether they were HIV positive or not because they considered themselves at exposed to risk (5.1%) and other reasons (1%) shown in Figure 3.

Table 1: Interpretations of different Variables

Categorical Variables	The logistic model allows us to use categorical independent variables. Any number of independent variables can be used in the model. The slope coefficient b and its standard error can be used to compute approximate confidence intervals for the odds ratio of a binary variable. The odds ratio's 95 percent confidence interval is exp *[(b1.96* SE (b)]*. The odds ratio provides us a better understanding of the relationship between the outcome variable and a specified independent variable; however, because *p z=1 / (1+e ((c-z)))*, a nonlinear equation, the calculated coefficient is not linearly connected to the probability of occurrence.
Continuous and Mixed Variables	The number exp *(b)* is understood as the odds ratio for the person with value *(X+1)* compared to the odds for the individual with value *X* for a continuous independent variable *X* with the slope coefficient *b*. As a result, exp *(b)* is the incremental odds ratio corresponding to a one-unit increase in the variable *X*, assuming that all other *X* values are exp *(b)*, with 95 percent confidence intervals for the odds ratio derived as exp *[kbk (1.96) S.E. (kb)]*.
Log-Likelihood Ratio Test	The log-likelihood ratio test is used to determine the importance of a certain variable in the logistic regression model. The log-likelihood function is used in logistic regression to compare observed and predicted values. It has as many parameters as data points, and the order is the current model, which has fewer variables than the saturated model. $$D = -2\ln\left(\frac{likelihood\ of\ the\ current\ model}{likelihood\ of\ the\ saturated\ model}\right) \quad (3.8)$$ The quantity is called the likelihood ratio.
Wald Test	The Wald test is used to determine the significance of the independent variable. The null hypothesis is that 1=0 has a typical normal distribution. The logistic regression model's Wald test is as follows: $$z = \frac{\beta_1}{S.E(\beta_1)} \quad (3.9)$$ This squared z value corresponds to a Wald statistic with a chi-square distribution.
Odds Ratio	The odds ratio of the dependent variable is given by exponential beta. This odd ratio can be used to calculate the probability of the dependent variables. When the exponential beta value is larger than one, the likelihood of the higher category increases, and when the exponential beta value is less than one, the chance of the higher category falls. The reference category, where the dependent variable's likelihood increases or decreases, understands the exponential beta value. It is understood in continuous variables as a one-unit increase in the independent variable, equivalent to an increase or reduction in the units of the dependent variable.

Table 2: Demographic Characteristics of HIV/ AIDS Patients attending HIV Clinics of Public Hospitals ($N = 235$).

	Frequency	Percentage
Age (Years)		
17-25	36	15.3
25-35	97	41.3
35-45	67	28.5
>45	35	14.9
Mean ± S.D	35.03 ± 9.35	
Gender		
Male	174	74.0
Female	44	18.7
Change	17	7.2
Marital status		
Ever married*	162	68.9
Never married	73	31.1
Number of live children		
None	20	12.3
1-2	72	44.4
3-5	58	35.8
>5	12	7.4
Level of education		
No schooling	74	31.5
Up to primary school	56	23.8
Up to secondary school	66	28.1
Up to college/ up to university	39	16.6
Employment status before HIV diagnosis		
Employed	185	78.7
Unemployed	50	21.3
Family's monthly income (PKR)*		
< 15,000	91	38.7
15,000-30,000	72	30.6
30,001-45,000	23	9.8
> 45,000	40	17.7
Mean ±. S.D	28460.18± 25235.44	
Provincial distribution		
East Punjab	134	57.0
North Punjab	55	23.4
South Punjab	46	19.6
District		
Lahore	99	42.1
Others	136	57.9
Area of residence		
Urban	161	68.5
Rural	74	31.5
Religion		
Islam	221	94.0
Christian	14	6.0
Body Mass Index (BMI)		
Underweight	27	11.5
Normal	141	60.0
Overweight/ obese	67	28.5
Mean ±. S.D	23.49 ± 5.23	

*Ever married group also included separated, widowed, or divorced cases.

* N < 235 due to missing values.

Table 3: Clinical Characteristic of HIV/ AIDS Patients attending HIV Clinics ($N = 235$).

	Frequency	Percentage
Age at diagnosis (Years)		
17-20	18	7.7
21-30	105	44.7
31-40	69	29.4
>40	43	18.3
Duration of HIV diagnosis (Years)*		
<1	73	31.1
1-2	73	31.1
≥3	76	34.2
Mean ±. S.D	2.32 ± 2.862	
Baseline CD4 count (cells/ mm^3) *		
<200	61	31.3
200-350	42	21.0
>350	93	47.7
Mean ±. S.D	368.414 ± 257.331	
CD4 count at the time of initiation of HIV ART (cells/ mm^3) *		
<200	61	31.6
200-350	42	21.8
>350	90	46.6
Mean ±. S.D	360.46 ± 251.420	
CD4 count at last follow-up visit (cells/ mm^3) *		
<200	33	18.3
200-350	32	17.8
>350	115	63.9
Mean ±. S.D	478.77 ± 304.97	
Viral Load (copies/mL)		
≤100,000	140	76.9
>100,000	42	23.1
Mean ±S.D	1955715.81 ± 8990113.03	
WHO disease Stage (at last follow-up visit)*		
Stage I	78	34.5
Stage II	109	48.2
Stage III	30	13.3
Functional status		
Work	129	54.9
Ambulatory	62	26.4
Bedridden	44	18.7
Delayed HIV testing		
Yes	87	37.0
No	148	63.0
Delayed HIV treatment*		
Yes	35	14.9
No	178	75.7
Type of ART		
1st Regimen	230	97.9
2nd Regimen	5	2.1
Duration on ART (Years)*		
<1	94	40
1-2	71	30.2
≥3	65	27.7
Mean ±. S.D	1.88 ± 2.473	
Hb levels for males (g/dl)		
≤14	112	76.7
>14	34	23.3

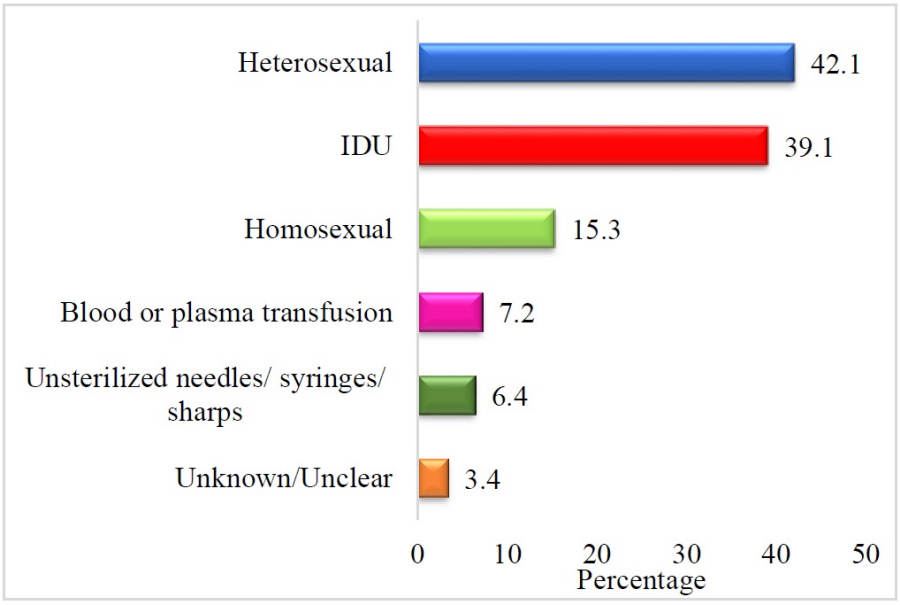

Figure 2: Transmission Routes of HIV Infection among HIV/ AIDS Patients attending HIV Clinics ($N = 235$)*.

Table 4 demonstrates the comorbidities that cohabit with HIV infection. Many patients (15%) had a history of tuberculosis, 3.4% had diabetes mellitus, 2% had hypertension, 1% had renal diseases, and 7.7% had other comorbidities. Slightly above a quarter of the respondents (26%) were physically disabled; among those, a vast majority (86.7%) were post-HIV disabled. Aside, a huge number of patients (49%) were alcohol consumers (past/ current) and smokers (past/ current) (59%) respectively. Among the studied population, an overwhelming number of patients (41%) had HCV-HIV co-infection, 9% had HBV-HIV co-infection, while 6% had HBV-HCV-HIV triple infection, as shown in Figure 4.

Table 5 shows the results of liver function tests of HIV/ AIDS. The mean value of alkaline phosphate (ALP) was 202.164 ± 211.414, and the mean aspartate amino transaminase (AST) was 44.49 ± 42.774. The mean value of alanine transaminase (ALT) was 50.115 ± 63.734, and the mean value of total bilirubin (T.B.) was 1.015 ± 3.036. The direct bilirubin (DB) was 0.374 ± 0.267 and albumin (ALB) was 0.374 ± 0.267.

The male gender was statistically significantly associated with positive HBV antigen status ($p - value < 0.05$). In comparison, the current age of the patient, age at diagnosis of HIV, marital status, employment status, and functional status of the patients was not found to be statistically associated with HBV co-infection ($p - value > 0.05$), as shown in Table 6. None of the transmission routes was statistically associated with HBV co-infection ($p - value > 0.05$), as shown in table 7. Being hypertensive, alcohol consumer (past or current), and smoker (past or current) was found to be statistically significantly associated with positive hepatitis B antigen status ($p - value < 0.05$). The hepatitis B antigen status was not significantly associated with tuberculosis and diabetes mellitus ($p - value > 0.05$) presented in Table 8.

Being male and never married was statistically significantly associated with HCV co-infection ($p - value < 0.05$). In comparison, the current age of the patient, age at diagnosis of HIV, and employment status were not found to be statistically associated with HCV co-infection ($p - value > 0.05$), as shown in Table 9.

The patients with < 1 year of HIV diagnosis, having < 200 CD4 counts ($cells/mm^3$) at the initiation of ART, having a physical disability were more likely to have HCV co-infection ($p -$

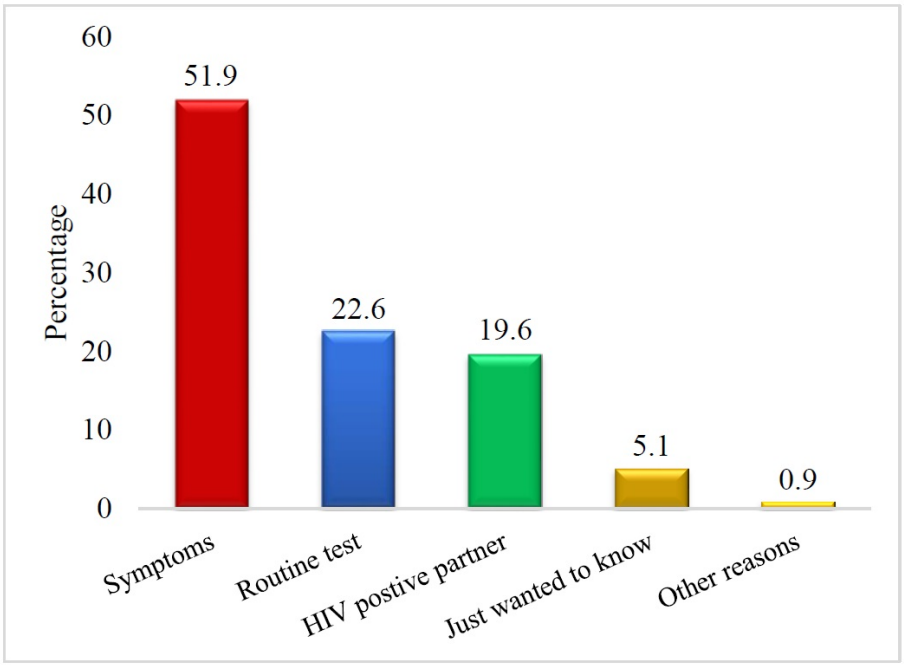

Figure 3: Reasons for HIV Testing among HIV/ AIDS Patients attending HIV Clinics ($N = 235$).

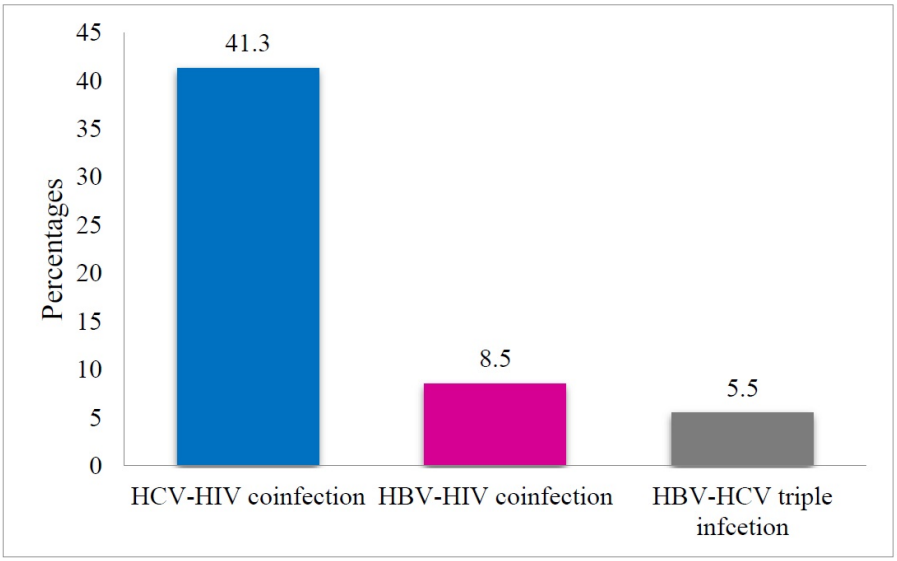

Figure 4: Hepatitis B and C Coinfection among HIV/ AIDS Patients attending HIV Clinics ($N = 235$).

Table 4: Presence of Comorbidities among HIV/ AIDS Patients attending HIV Clinics ($N = 235$).

	Frequency	Percentage
Alcohol use		
Past	111	47.2
Current	4	1.7
Never	120	51.1
Smoking		
Past	40	17.0
Current	100	42.6
Never	95	40.4
Physical disability		
Yes	60	25.5
No	175	74.5
If Yes, time of physical disability		
Pre-HIV	8	13.3
Post-HIV	52	86.7
Hypertension		
Yes	4	1.7
No	231	98.3
Diabetes mellitus		
Yes	8	3.4
No	227	96.6
Renal diseases		
Yes	2	.9
No	233	99.1
Tuberculosis		
Yes	35	14.9
No	200	85.1
Others		
Yes	18	7.7
No	213	92.3

Table 5: Liver Function Tests of HIV/ AIDS Patients attending HIV Clinics ($N = 235$).

	Mean	$\pm S.D$	Minimum	Maximum	N
Alkaline phosphate (ALP)	202.16	211.41	32.0	2450	149
Aspartate amino transaminase (AST)	44.49	42.77	14.0	433	145
Alanine transaminase (ALT)	50.12	63.73	0.50	672.0	158
Total bilirubin (TB)	1.02	3.04	0.22	36.0	158
Direct bilirubin (DB)	0.37	0.27	0.0	1.0	18
Albumin (ALB)	0.37	0.27	1.60	49.0	59

Table 6: Association of Hepatitis B with Socio-demographic Characteristics of HIV/ AIDS Patients attending HIV Clinics ($N = 235$).

	HBV antigen status		Total N (%)	χ^2 value	P-value
	Positive %	Negative %			
Age (Years)					
≤35	65.0	54.9	102 (56.0)	0.732	0.392
>35	35.0	45.1	80 (44.0)		
Age at diagnosis (Years)					
≤30	65.0	50.6	95 (52.2)	1.476	0.224
>30	35.0	49.4	87 (47.8)		
Gender					
Male	90.0	72.8	136 (74.7)	6.101	0.041
Female	0.0	20.4	33 (18.1)		
Change	10.0	6.8	13 (7.1)		
Marital status					
Ever married	60.0	72.8	130 (71.4)	1.438	0.230
Never married	40.0	27.2	52 (28.6)		
Employment status					
Employed	75.0	53.1	101 (55.5)	3.461	0.063
Unemployed	25.0	46.9	81 (44.5)		
Functional status					
Work	55.0	51.9	95 (52.2)	4.729	0.094
Ambulatory	40.0	24.1	47 (25.8)		
Bedridden	5.0	24.1	40 (22.0)		

Table 7: Association between HBV Coinfection Status and Transmission Routes HIV among HIV/ AIDS Patients attending HIV Clinics ($N = 235$).

	HBV antigen status		Total N (%)	χ^2 value	P-value
	Positive %	Negative %			
Blood transfusion or previous plasma donation					
Yes	5.0	7.4	13 (7.1)	0.156	0.693
No	95.0	92.6	169 (92.9)		
Heterosexual transmission					
Yes	30.0	43.2	76 (41.8)	1.277	0.258
No	70.0	56.8	106 (58.2)		
Homosexual transmission					
Yes	15.0	15.4	28 (15.4)	0.003	0.960
No	85.0	84.6	154 (84.6)		
Intravenous drug use					
Yes	55.0	37.7	72 (39.6)	2.240	0.134
No	45.0	62.3	110 (60.4)		
Others					
Yes	0.0	13.0	21 (11.5)	*	0.135
No	100.0	87.0	161 (88.5)		

*The value for Fisher's exact test cannot obtain from the tool.

Table 8: Association between HBV Confection Status and Comorbidities among HIV/ AIDS Patients attending HIV Clinics ($N = 235$).

	HBV antigen status		Total N (%)	χ^2 value	P-value
	Positive %	Negative %			
Tuberculosis					
Yes	20.0	14.8	28 (15.4)	0.368	0.518
No	80.0	85.2	154 (84.6)		
Hypertension					
Yes	10.0	0.6	3 (1.6)	9.667	0.032
No	90.0	99.4	179 (98.4)		
Alcohol use					
Past	70.0	46.3	89 (48.9)	12.566	0.002
Current	10.0	0.6	3 (1.6)		
Never	20.0	53.1	90 (49.5)		
Smoking					
Past	30.0	15.4	31 (17.0)	11.416	0.003
Current	65.0	40.7	79 (43.4)		
Never	5.0	43.8	72 (39.6)		
Others					
Yes	100.0	45.1	93 (51.1)	21.503	0.000
No	0.0	54.9	89 (48.9)		

$value < 0.05$). However, there was no statistically significant difference observed between HCV co-infected and HIV mono-infected patients regarding the duration of ART (years), baseline CD4 count ($cells/mm^3$), CD4 count, at last, follow up visit ($cells/mm^3$), HIV RNA viral load (copies/mL), functional status, delayed HIV testing, delayed HIV treatment initiation, and which disease staging ($p - value > 0.05$) shown in Table 10.

Patients with HCV co-infection were more likely to have been infected through sexual routes and intravenous drug use ($p - value < 0.05$). Whereas HCV co-infection status was not seen to differ significantly concerning the transmission of HIV through blood or plasma transfusion and other routes (piercing/tattooing, shaving, dental procedures, etc.) ($p - value > 0.05$) presented in Table 11.

Being an alcohol consumer (past or current) and smoker (past or current) was found to be statistically associated with HCV co-infection ($p - value < 0.05$). But HCV co-infection was not statistically significantly associated with tuberculosis, hypertension, and diabetes mellitus ($p - value > 0.05$) presented in Table 12.

Figure 5 displays that among the sampled population, the prevalence of HBV-HIV co-infection, HCV-HIV co-infection, and HBV-HCV triple infection was highest among IDUs (55%, 70.1%, and 84.6% respectively), followed by heterosexual transmission (30%, 22.7%, and 7.7% respectively), homosexual transmission (15%, 5.2%, and 7.7% respectively). Blood or plasma transfusion had the lowest prevalence of HBV-HIV co-infection, HCV-HIV co-infection, and HBV-HCV triple infection (5%, 6.2%, and 8.3%, respectively).

A statistically significant association was observed between HBV-HCV triple infection status regarding heterosexual transmission and intravenous drug use ($p - value < 0.05$). Whereas no statistically significant association was observed between HBV-HCV triple infection status regarding HIV transmission via blood or plasma transfusion and other routes (piercing/tattooing, shaving,

Table 9: Association of HCV Co-infection with Socio-demographic Characteristics of HIV/ AIDS Patients attending HIV Clinics ($N = 235$).

	HCV antibody status		Total N (%)	χ^2 value	P-value
	Positive %	Negative %			
Age (Years)					
≤35	58.8	53.4	119 (55.9)	0.605	0.437
>35	41.2	46.6	94 (44.1)		
Age at diagnosis (Years)					
≥30	53.6	50.9	111 (52.1)	0.160	0.689
<30	46.4	49.1	102 (47.9)		
Gender					
Male	87.6	64.7	160 (75.1)	15.053	0.001
Female	8.2	25.9	38 (17.8)		
Change	4.1	9.5	15 (7.0)		
Marital status					
Ever married	57.7	77.6	146 (68.5)	9.658	0.002
Never married	42.3	22.4	67 (31.5)		
Employment status					
Employed	59.8	54.3	121(26.8)	0.647	0.421
Unemployed	40.2	45.7	92 (43.2)		

dental procedures, etc.) ($p - value > 0.05$) as shown in table 13. Having past or current alcohol use, past or current smoking status, and presence of physical disability were found to be statistically associated with positive HBV-HCV triple infection ($p-value < 0.05$). Yet, HBV-HCV triple infection was not found to be statistically significantly associated with being hypertensive, tuberculosis, and diabetes mellitus ($p - value > 0.05$), as presented in Table 14.
A statistically significant difference was observed between aspartate amino transaminase, alanine transaminase, and HCV antibody status of HIV/ AIDS positive patients ($p-value < 0.05$). Whereas no statistically significant difference was observed between liver enzymes and HBV antigen status and HBV-HCV triple infection with HIV/ AIDS ($p - value > 0.05$), as shown in Table 15.

Binary Logistic Regression Model The binary logistic regression analysis is applied here to study the factors related to HCV co-infection in HIV/ AIDS patients seeking medical care at HIV clinics in public hospitals of Lahore. A logistic regression model is developed so that the dependence of HCV co-infection can be statistically determined.

The logistic regression provided the Hosmer- Lemeshow's goodness of fit statistic to know how effective the model was in describing the outcome variable. The null hypothesis to be tested here is as H_0: The model fits the data well. The value of Hosmer- Lemeshow's goodness of fit statistic computed from the frequencies which are $\chi^2 = 10.251$ and the corresponding p-value computed from a chi-square distribution with 8 degrees of freedom is $0.248 > 0.05$ model fits the data well shown in the above table 15.

The observed and expected frequencies for two groups, HCV negative and HCV positive status, were shown. It is observed by examining the expected frequencies that six expected frequencies were less than 5. The p-value estimate was accurate enough to support the hypothesis that the model fits well.

The Cox and Snell R-square statistics were used to compare the likelihood of the current model with the null model. The larger the value of this statistic, the more useful the model is to explain

Table 10: Association between HCV Coinfection Status and Clinical Characteristics of HIV/ AIDS Patients attending HIV Clinics ($N = 235$).

	HCV antibody status		Total N (%)	χ^2 value	P-value
	Positive %	Negative %			
Duration of HIV diagnosis (Years)					
<1	38.8	24.8	64 (31.7)	7.306	0.026
1-2	33.3	32.1	66 (32.7)		
≥3	26.9	43.1	72 (35.6)		
Duration on ART (Years)					
<1	45.3	35.7	84 (40.0)	5.437	0.066
1-2	33.7	28.7	65 (31.0)		
≥3	21.1	35.7	61 (29.0)		
Delayed HIV testing Association					
Yes	32.0	42.2	80 (37.6)	2.382	0.123
No	68.0	57.8	133 (62.4)		
Delayed HIV treatment					
Yes	12.0	22.1	31 (17.4)	3.115	0.112
No	88.0	77.9	147 (82.6)		
Baseline CD4 count (cells/ mm^3)					
<200	24.4	37.0	57 (31.1)	5.014	0.082
200-350	19.5	23.0	39 (21.4)		
>350	56.1	40.0	86 (47.3)		
CD4 count at the start of initial HIV treatment (cells/ mm^3)					
<200	24.7	38.8	58 (32.4)	6.063	0.048
200-350	19.8	23.5	39 (21.8)		
>350	55.6	37.8	82 (45.8)		
Most recent CD4 count (cells/ mm^3)					
<200	13.7	22.6	31 (18.7)	5.5.15	0.063
200-350	13.7	22.6	31 (18.7)		
>350	72.6	54.8	104 (62.7)		
Viral load					
≤100,000	70.7	81.9	130 (76.9)	2.973	0.085
>100,000	29.3	18.1	39 (23.1)		
Functional status (Current)					
Work	51.5	56.9	116 (54.5)	0.838	0.658
Ambulatory	25.8	25.0	54 (25.4)		
Bedridden	22.7	18.1	43 (20.2)		
Presence of physical disability					
Yes	32.0	18.1	52 (24.4)	5.496	0.019
No	68.0	81.9	161 (75.6)		

Table 11: Association between HCV Coinfection Status and Transmission Routes of HIV/ AIDS Patients attending HIV Clinics ($N = 235$).

	HCV antibody status		Total N (%)	χ^2 value	P-value
	Positive %	Negative %			
Blood transfusion or previous plasma donation					
Yes	6.2	8.6	16 (7.5)	0.451	0.502
No	93.8	91.4	197 (92.5)		
Heterosexual transmission					
Yes	22.7	59.5	91 (42.7)	29.239	0.000
No	77.3	40.5	122 (57.3)		
Homosexual transmission					
Yes	5.2	22.4	31 (14.6)	12.654	0.000
No	94.8	77.6	182 (85.4)		
Intravenous drug use					
Yes	70.1	15.5	86 (40.4)	65.383	0.000
No	29.9	84.5	127 (59.6)		
Others					
Yes	6.2	13.8	22 (10.3)	3.301	0.069
No	93.8	86.2	191 (89.7)		

*Multiple transmission routes were possible.

Table 12: Association between HCV Coinfection Status and Presence of Comorbidities among HIV/ AIDS Patients attending HIV Clinics ($N = 235$).

	HCV antibody status		Total N (%)	χ^2 value	P-value
	Positive %	Negative %			
Alcohol use					
Past	66.0	34.5	104 (48.8)	21.948	0.000
Current	2.1	1.7	4 (1.9)		
Never	32.0	63.8	105 (49.3)		
Smoking					
Past	23.7	12.9	38 (17.8)	33.884	0.000
Current	57.7	29.3	90 (42.3)		
Never	18.6	57.8	85 (39.9)		
Tuberculosis					
Yes	15.5	14.7	32 (15.0)	0.027	0.869
No	84.5	85.3	181 (85.0)		
Hypertension					
Yes	0.0	3.4	4 (1.9)	3.409	0.127
No	100.0	96.6	209 (98.1)		
Diabetes mellitus					
Yes	4.1	3.4	8 (3.8)	0.067	1.000
No	95.9	96.6	205 (96.2)		
Others					
Yes	99.0	13.8	112 (52.6)	153.711	0.000
No	1.0	86.2	101 (47.4)		

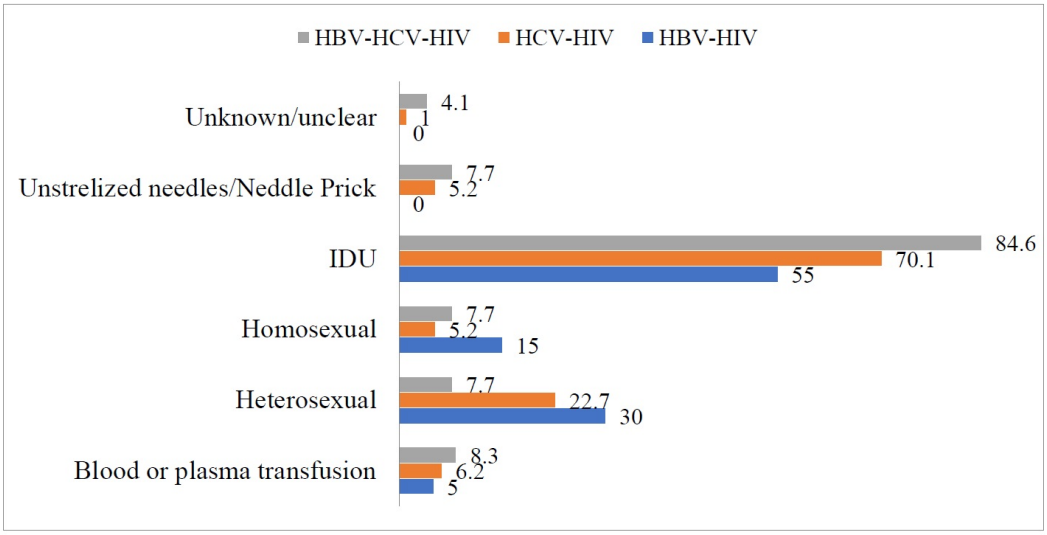

Figure 5: Transmission routes in HBV, HCV, and HCV/HBV Triple Infection with HIV among HIV/ AIDS Patients attending HIV Clinics ($N = 235$)

Table 13: Association between HBV-HCV Triple Infection Status and Transmission Routes of HIV/ AIDS Patients attending HIV Clinics ($N = 235$).

	HBV-HCV triple infection		Total N (%)	χ^2 value	P-value
	Positive %	Negative %			
Heterosexual transmission					
Yes	7.7	45.0	77 (42.3)	6.873	0.009
No	92.3	55.0	105 (57.7)		
Homosexual transmission					
Yes	7.7	16.0	28 (15.4)	*	0.695
No	84.0	92.3	154 (84.6)		
Intravenous drug use					
Yes	84.6	36.1	72 (39.6)	11.886	0.001
No	15.4	63.9	110 (60.4)		
Blood or plasma transfusion					
Yes	8.3	17.7	26 (17.0)	*	0.692
No	91.7	82.3	127 (83.0)		
Others					
Yes	0.0	11.8	20 (11.0)	*	0.366
No	100.0	88.2	162 (89.0)		

*The value for Fisher's exact test cannot obtain from the tool.

Table 14: Association between HBV-HCV Triple Infection Status and Presence of Comorbidities among HIV/ AIDS Patients attending HIV Clinics ($N = 235$).

	HBV-HCV-HIV triple infection		Total N (%)	χ^2 value	P-value
	Positive %	Negative %			
Tuberculosis					
Yes	30.8	14.8	29 (15.9)	*	0.132
No	69.2	85.2	153 (84.1)		
Diabetes mellitus					
Yes	7.7	3.6	7 (3.8)	*	0.410
No	92.3	96.4	175 (96.2)		
Alcohol use					
Past	76.9	47.3	90 (49.5)	8.697	0.015
Current	7.7	1.2	3 (1.6)		
Never	51.5	15.4	89 (48.9)		
Smoking					
Past	30.8	16.6	32 (17.6)	8.997	0.011
Current	41.4	69.2	79 (43.4)		
Never	42.0	0.00	71 (39.0)		
Presence of physical disability					
Yes	46.2	20.1	40 (22.0)	*	0.040
No	53.8	79.9	142 (78.0)		
Others					
Yes	100.0	47.3	93 (51.1)	13.398	0.000
No	0.0	52.7	89 (48.9)		

* The value for Fisher's exact test cannot obtain from SPSS.

Table 15: Difference between means of HBV Antigen Status, HCV Antibody Status, HBV/HCV/HIV Triple Infection Status, and Liver Enzymes of HIV/ AIDS Patients attending HIV clinics ($N = 235$)*.

Factors	HBV co-infection p-value	HCV co-infection p-value	HBV-HCV triple infection p-value
Alkaline phosphate (ALP)	0.778	0.106	0.706
Aspartate amino transaminase (AST)	0.208	0.004	0.197
Alanine transaminase (ALT)	0.183	0.013	0.174
Total Bilirubin (TB)	0.780	0.642	0.588
Direct Bilirubin (D.B.)**		0.227	
Albumin (ALB)	0.546	0.647	0.546

*N< 235 due to missing values.
**The value of the t-test cannot be computed because at least one of the groups is empty.

Table 16: Hosmer-Lemeshow's Goodness of Fit Test

Chi-Square	df	p-value
10.251	8	0.248

Table 17: Observed and the Expected Frequencies for the Two Groups

Step 1	HCV negative		HCV positive		Total
	Observed	Expected	Observed	Expected	
1	15	14.586	0	.414	15
2	14	13.715	1	1.285	15
3	13	13.037	2	1.963	15
4	11	11.832	4	3.168	15
5	12	9.741	3	5.259	15
6	7	7.585	8	7.415	15
7	4	5.045	10	8.955	14
8	1	3.769	14	11.231	15
9	2	1.757	13	13.243	15
10	3	.933	17	19.067	20

Table 18: Model Summary

-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
132.524	.406	.543

the variation in the outcome variable. The Nagelkerke R Square is the correlation of the Cox and Snell R-square statistics. The values of both statistics are 0.543 and 0.406, respectively.
Logistic Regression Model The logistic regression model (LR) model is: $g(x) = -1.974 - 1.041$ (Heterosexual transmission) -3.732 (Homosexual transmission) $+1.360$ (IDU) $+1.325$ (Smoking) $+0.087$ (Age at HIV/ AIDS diagnosis) -1.874 (Marital status)

The statistical significance of independent variables in the logistic regression model was tested by using the Wald statistic. By using Wald statistic, variables: heterosexual transmission, homosexual transmission, intravenous drug use, smoking, age at HIV diagnosis, and marital status was statistically significantly related with HCV positive patients ($p - value < 0.05$). Whereas the variables: gender, baseline CD4 count, functional status, duration of ART, duration of HIV/ AIDS diagnosis, employment status, delayed HIV testing, and alcohol consumption was not statistically significantly related to HCV positive patients and hence, excluded from the final model ($p - value > 0.05$).

The estimated logistic regression coefficient for heterosexual transmission is -1.041, which shows that heterosexual transmission is associated with a -1.041 decrease in the log odds of HCV co-infection. Since heterosexual transmission variable categorized into two categories as "0" and "1". The odds ratio for individuals exposed to heterosexual transmission is 0.353. This shows that in-

Table 19: Wald Test Results Obtained from Final Model after Applying Forward Step Wise Logistic Regression.

Variables	β	S.E.	Wald	df	p-value
Heterosexual transmission	-1.041	.509	4.191	1	.041
Homosexual transmission	-3.732	.941	15.723	1	.000
Intravenous drug use	1.360	.522	6.792	1	.009
Smoking	1.325	.462	8.230	1	.004
Age at HIV diagnosis	.087	.029	8.873	1	.003
Marital status	-1.874	.607	9.525	1	002
Constant	-1.974	.888	4.944	1	.026

Table 20: Odds Ratios and 95% Confidence Interval

Variables	β	OR	95% C. I for OR	
			Lower	Upper
Heterosexual transmission	-1.041	0.353	0.130	0.957
Homosexual transmission	-3.732	0.024	0.004	0.151
Intravenous drug user	1.360	3.898	1.401	10.843
Smoker	1.325	3.763	1.522	9.306
> 30 years age at HIV diagnosis	0.087	1.091	1.030	1.156
Never married	-1.874	0.153	0.047	0.505

dividuals exposed to heterosexual transmission decrease the risk of HCV co-infection 0.353 times compared to the individuals who are unexposed to heterosexual transmission. The estimated logistic regression coefficient for homosexual transmission is -3.732, which shows that homosexual transmission is associated with a -3.732 decrease in the log odds of HCV co-infection. Since homosexual transmission variable categorized into two categories as "0" and "1". The odds ratio for individuals exposed to homosexual transmission is 0.024. This shows that individuals exposed to homosexual transmission decrease the risk of HCV co-infection 0.024 times compared to the individuals who are unexposed to homosexual transmission.

The estimated logistic regression coefficient for intravenous drug use is 1.360, which shows that intravenous drug use is associated with a 3.898 increase in the log odds of HCV co-infection. Since intravenous drug use variable categorized into two categories as "0" and "1". The odds ratio for individuals exposed to intravenous drug use is 3.898. This shows that individuals exposed to intravenous drug use increase the risk of HCV co-infection by 3.898 times compared to those unexposed to intravenous drug use. The estimated logistic regression coefficient for smoking is 1.325, representing that smoking is associated with a 3.763 increase in the log odds of HCV co-infection. Since smoking variable categorized into two categories as "0" and "1". The odds ratio for individuals exposed to smoking is 3.763. This shows that individuals exposed to smoking increase the risk of HCV co-infection 3.763 times when compared to the individuals who are non-smokers.

The estimated logistic regression coefficient for age at diagnosis of HIV is 0.087, which shows that age at diagnosis of HIV is associated with a 1.091 increase in the log odds of HCV co-infection. Since age at diagnosis of HIV variable is categorized into "1" and "2". The odds ratio for individuals exposed to age " >30" years at diagnosis of HIV is 1.091. This shows that individuals exposed to age " >30" at diagnosis of HIV increase the risk of HCV co-infection 1.091 times compared to the individuals who are ≤ 30 years of age at diagnosis of HIV. The estimated logistic regression coefficient for marital status is -1.874, which shows that marital status is associated with a 0.153 decrease in the log odds of HCV co-infection. Since marital status variable categorized into two categories as "1" and "2". The odds ratio for individuals exposed to marital status is 0.153. This shows that individuals ever married groups decrease the risk of HCV co-infection 0.153 times than those who are never married.

The classification tables in logistic regression are used to match correct and incorrect estimates. The columns are two predicted values of the dependent variable, i.e., 0 and 1 (HCV negative and HCV positive), while the rows are the two observed (actual) dependent values. The cut point of 0.50 was used, and the estimated logistic probabilities were calculated for each individual and then compared with the cut point of C. If the estimated probabilities exceed the cut point of C, allocate

Table 21: Classification Table of HCV Negative and HCV Positive

Observed (Y)	Predicted (Y)		Percent Corrected
	HCV Negative	HCV Positive	
HCV Negative	70	12	85.4
HCV Positive	14	58	80.6
Overall Percent		83.1	

to the individual to 1, otherwise to 0. In the above table 21, 70 HCV negative patients out of 82 were correctly classified to their original group (0). i.e. (70/82 = 0.854), 85.4% of the HCV negative patients were accurately classified as HCV negative. Out of 72 HCV-positive patients, 58 were classified to their original group (1), and the percentage of the correctly classified HCV-positive patients was (58/72 = 0.805) 80.5%. So, the overall rate of correct classification was {(70+58)/(82+72) = 0.83} 83.1%.

5. Discussion

The present work examined the prevalence of HBV and HCV and their co-infection among 235 HIV/ AIDS infected patients seeking medical care in public hospitals of Lahore, Pakistan. Hepatitis B virus (HBV) and HCV infections and their co-infection with HIV/ AIDS are major health issues affecting billions of people globally. Further, HIV/ AIDS infection peaks at age 31-40 years (38%), lower than Sherman's findings, where 47% were between 30-39 years. The sex distribution of participants, 74% males, 19% for females, and 7% for trans-genders were similar to a study conducted in 2016, where 79% were male, and 18% were female [23]. Sixty-nine percent of respondents live in urban areas, where 71% were living in urban areas. The study reported that 32% of respondents were illiterate compared to Northeastern Ethiopia and Bangladesh, 29% and 36%, respectively [12].

- **HBV-HIV Coinfection** In the studied population, the prevalence of hepatitis B was 8.5% among HIV patients. In different studies, the prevalence of HBV-HIV co-infection was reported as; 5% in Nigeria and 2% in Libya [25]. The current population shows that the HBV-HIV prevalence rate was higher in intravenous drug users (55%), followed by heterosexual transmission (30%) and homosexual transmission (15%). However, in Chennai, India, the incidence of HBV co-infection among PLHIV injectors was recorded at 9% [21]. According to Brazilian research, over 50% HBV-HIV drug abuse, 20% heterosexual, 9% gay transmission, and 19% blood transfusion were recorded due to IV drug misuse [31]. IDUs were statistically associated in the present study, whereas heterosexual and homosexual transmission routes were not statistically associated with HBV-HIV co-infection. In comparison, in a study of England, IDUs, heterosexual transmission, and homosexual transmission routes were statistically associated with HBV-HIV co-infection [16]. This study estimated the highest prevalence of alcohol consumption (80%) followed by smoking status (95%) and hypertension (10%); these can infect patients for years before even symptoms are manifested. These comorbidities were found to be statistically significantly associated with HBV-HIV co-infection. In comparison, a study performed in South India where the HBV co-infection rate was higher in PWID (81%) followed by smoking status (93%), and these comorbidities were found to be statistically associated with HBV co-infection [28].

The study demonstrated that there was no difference found between means of HBV antigen status and liver enzymes. In contrast, the study showed that the mean level of liver enzymes was slightly higher in HBV antigen status [28]; a study in Belgium showed that the mean ALT levels were higher due to abnormalities in liver enzymes in people with PLWHIV are at more risk for liver diseases. The present study showed that HBV antigen status was not found to be statistically associated with tuberculosis. In comparison, a study by [3] showed that people with HIV were more likely to be at risk of tuberculosis and found it significantly associated with HIV in Nigerians.

- **HCV-HIV Coinfection** The prevalence of HCV among HIV/ AIDS infected patients in the present study was 41%. A study confirms that HCV is a major threat to HIV/ AIDS patients in China, as reported in other parts of the world [13]. Patients with HIV/AIDS with HCV prevalence were greater in Brazil studies (82%). In the ever-married group, the prevalence of HCV-HIV co-infection was greatest. Because married individuals are more likely to have high-risk sexual activity and, thus, are more vulnerable to sexual transmission of HCV. The research has shown the greatest frequency of HCV co-infection among divorced and widowed patients, whereas married people in China are now at the lowest prevalence [21].
  A highly significant association was observed between male and HCV co-infection was shown to be quite important among HIV-positive individuals. Men often have a higher risk behavior than women and are thus more prone to common HCV transmission routes; this is likely to contribute to their higher co-infection incidence. Since IV drugs users, heterosexual transmission, and homosexual transmission are very efficient routes for HCV transmission, the high prevalence rate in the present study accounted for a large number of injecting drug users (70%), followed by heterosexual transmission (23%) and homosexual transmission routes (5%) and these transmission routes found to be statistically associated with HCV co-infection. The interaction between HIV and HCV relates to HCV-HIV transmission; co-infection increases the vertical transmission of HCV, leading to increased incidence of HCV in adults, as reported in a study of China [13]. Moreover, the present population of PWIDs showed that HCV is more likely than other populations affected by PLHIV and was statistically associated with HCV co-infection, while heterosexual transmission and homosexually transmitted routes were not statistically identified as being associated with HCV co-infection [3]. In a study of Kathmandu, HCV-seropositive persons among blood donors were 3.6% also HIV-positive, and 0.71% was also HCV-positive.
  Alcohol consumption (68%) followed by smoking status (81%) was statistically associated with HCV co-infection. In contrast, a study estimated 70% alcohol consumption followed by a high rate of smoking status (90%) and found it to be statistically associated with HCV co-infection [5]. As found in the present study, there was an elevation of liver enzymes among all the patient groups, though there was no significant association. The mean level of liver enzymes was lower than those co-infected with hepatitis B. A study in Lagos corroborates this finding. In that study, liver enzymes were significantly higher in HIV patients than in controls and higher in HIV patients who were also positive for hepatitis C antibody status than those not co-infected [21]. The evaluation of liver enzymes in all patient groups was observed to increase in the present investigation; however, there was no significant association. The mean level of hepatitis B co-infected liver enzymes was lower; research in Lagos confirms this conclusion. In this study, liver enzymes were substantially higher than in controls in HIV patients, and HIV patients positively affected in hepatitis C antibodies compared with those not co-infected.

- **HBV-HCV-HIV Triple Infection** In the present study, the prevalence of triple infection

HBV-HCV-HIV was reported at 6%, highest among adults less than 35 years of age (69%) and significantly associated with the male gender. A study demonstrated that triple infection HBV-HCV-HIV was statistically associated with the male gender with a low prevalence of 2% [28]. The current population showed that the HBV-HCV-HIV prevalence rate was higher in intravenous drug users (85%), followed by heterosexual transmission (8%) and homosexual transmission (8%). In contrast, a study in Jos, Nigeria, found that the HBV-HCV-HIV co-infection prevalence among injection drugs was 80% [20]. In the present study, IDUs were statistically associated with HBV-HCV-HIV triple infection. In comparison, in a study conducted in Mississippi, IDUs were statistically associated with HBV-HCV-HIV infection [20]. The prevalence of triple infection HBV-HCV-HIV in sub-Saharan African was reported as 5%, where IDU's, heterosexuals, homosexuals were significantly associated with triple co-infection [28].

In the present study, the prevalence of HBV-HCV-HIV triple infection accounted for the highest alcohol use (85%), followed by smoking status (72%), and was found statistically associated. Similar results were concluded in a study in China where alcohol consumption and smoking were statistically associated with HBV-HCV-HIV triple infection [16]. The present study shows that physical disability was significantly associated among patients with triple co-infection HBV-HCV-HIV. In contrast, physical disability was not statistically associated with triple infection HBV-HCV-HIV [27, 7, 10].

This study is the first, to our knowledge, to characterize HBV and HCV co-infection in HIV-positive patients in Pakistan. The estimated results are supported by many HIV/ AIDS patients visiting special clinics of the two largest tertiary care hospitals located in a large metropolitan city Lahore. The patients from all over the Punjab province visit these selected hospitals; thus, the sample represents the whole province. The systematic random sampling method was used for the selection of study subjects. It is considered a fair way of selecting the sample. It was conducted in a population of HIV-infected persons with regular clinical follow-up and reliable information on antiretroviral use. Finally, the group studied is representative for two reasons: a large cohort of patients evaluated and a similar profile of patients who attended HIV clinics nowadays.

By providing the latest data that can help improve prevention and control of PLWH co-infection with viral hepatitis. Due to the apparent restrictions, the study results cannot be extrapolated to a broader scale. Since the study's design was cross-sectional, a causal connection could not be demonstrated between exposure and subsequent infection. The sample was limited, not all subjects took part in the survey, and only 20 subjects were identified with HBV, which confined statistical study to the identification of HBV risk factors. Due to the lack of necessary technology, the polymerase chain reaction to HBV DNA and HCV RNA has been delayed. A significant number of patients were eliminated for incomplete medical records. This can enhance HBV and HCV prevalence in our study as early diagnosis of HBV and HCV infections is possible before serum detection of the HBV surface antigen or HCV antibodies. The reporting of HIV-positive patients is another key limitation of this study; thus, the HBV-coinfection rate and HCV co-infection cannot be the real picture in the target population of these diseases.

Further, current findings in estimating and forecasting the overall burden of the disease to predict the future implications of the infection of hepatitis in Pakistan. Before initiating highly active antiretroviral treatment, HCV and HBV screening are highly suggested for HIV-infected patients since it would advise the right choice of the drug combination to treat these infections if necessary. Both HBV and HCV testing should be promoted for HIV-positive women as there is a need to explore the reasons for the unequal imputation of blame between men and women

regarding HIV infection. Patients co-infected with HBV and HCV should be informed about the transmission routes and methods to prevent the further spread of the viruses.

6. Conclusion

We concluded that hepatitis B and C co-infection is a major problem among HIV/ AIDS patients. The data confirms that HIV/HCV co-infection prevalence was mainly in drug addicts followed by sexual routes, especially in males younger than 40 years of age. The data demonstrated a higher prevalence of HCV/HIV co-infection than HBV/HIV co-infection and important medical consequences. A small proportion of patients had triple co-infection with HIV, HBV, and HCV. The number of CD4 pretreatment patients among HCV co-infection was substantially lower (less than 200 $Cell/mm^3$), whereas liver enzymes were slightly higher among those with HBV Co-infection. These findings underscore the importance of testing for HBV and HCV testing for all HIV-infected individuals in this research. Furthermore, to avoid future infections, HIV patients with HBV and HCV negatives who have not previously been vaccinated should be immunized against HBV or HCV. However, more studies on similar lines should be conducted to evaluate in-depth consequences on prevalence and risk factors in HIV-AIDS patients, so some strategies should be planned for better clinical care of patients with HIV infection.

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