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Influence of Epidemiological Risk Factors for Occurrence of Hepatitis B Virus (HBV) Co-Infection in HIV/AIDS Patients: (Study in dr. Kariadi Hospital, Semarang, Indonesia)

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ABSTRACT

Background: Chronic hepatitis, liver cirrhosis, and hepatocellular carcinoma are all have a major cause which is Hepatitis B virus (HBV). Given the fact that HIV and HBV are all transmitted through the same routes, co-infection is common. The objective of this research is to identify several risk factors which influence the occurrence of Hepatitis B virus infection in HIV/AIDS patients at Kariadi, Semarang, Indonesia**.**
Method: This research is analytical observational with a case control study design, a sample of 68 (34 cases and 34 controls) For all HIV patients involved in the study, samples were determined by a positive HBsAg test, The dependent variable is HBV occurrence in HIV/AIDS individuals and dependent variable were CD4≤100, Age>30, gender, marital status, level of education, male who have sex with other male(MSM), Analysis of data was done through univariate, bivariate and multivariate analysis with logistic regression.
Result: Variables that were proven to influence the occurrence HBV infection in HIV/AIDS individuals, after analysis were CD4≤100(p= 0.003 OR=7.535, 95% CI=(2.029-27.990), being male who do sex with male(MSM) (P=0.027, OR=3.544, 95% CI=(1.158-10.848). The probability for HIV/AIDS patients to be infected by HBVirus when they have both these risk factors is equal to 88.18%.
Conclusion: The factors that were proven to affect the influence of occurrence Hepatitis B virus in HIV/AIDS patients were, CD4≤100 and being male who do sex with other male (MSM).

Keywords: Hepatitis B virus; risk factors; HIV/AIDS patients; RSUP Dr. Kariadi-Semarang.

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Introduction

HIV is the virus that causes AIDS and impairs the body's capacity to fight diseases, HIV destroys CD4 cells causing the human immune system to decline and being susceptible to various infections like other viruses[1]. Virus that infect HIV patients include Hepatitis B Virus (HBV), because the transmission routes are almost the same, namely through sexual intercourse, blood Transfusion, mother to child, infected body fluids, and the use of contaminated needles. HBV is easily replicated in patients with low immunity such as in HIV/AIDS patients[2].

HIV infection is a severe public health concern around the world, the world health organization have estimated 37.7 million individuals that were infected by HIV /AIDS.In Indonesia it was estimated that 640,000 persons were infected with HIV, accounting for about 0.4 percent of the adult population in the age range of 15 to 49 years. AIDS-related deaths have increased in Indonesia 60% from 2010 from 24,000 to 38,000 in 2016[3].

The report of world health organization at the end of the year 2019 indicated that 296 million individuals had chronic hepatitis B virus including 1.5 million new cases annually, 2.7 million people infected with HBV are also infected with HIV, and world health organization estimated the global prevalence of this co-infection of HIV/HBV to be 7.4% in 2015.

In Indonesia, Hepatitis B virus is considered a serious public health concern as the country is ranked the second in the South East Asia Region with high endemicity after Myanmar[4]. Based on the 2013 Basic Health Research (Riskesdas),have found that HBV Is prevalent by 7.1 percent or around 18 million individual[5].

Patients living with HIV/AIDS who also have HBV infection are more likely to develop severe liver damage and increase death rate compared to those who are mono-infected with only HBV[6]. No previous research that had been done in the region concerning influence of epidemiological risk factors for HBV occurrence in HIV/AIDS individuals. The refore this research aimed to explain the various epidemiological risk factors that influence the occurrence of HBV in HIV/AIDS patients at Kariadi Hospital, Semarang, Indonesia.

Methods

Study population

The study population in this research were HIV/AIDS individuals with 18 years old and up whom attended RSUP Dr Kariadi hospital throughout 2016 till 2021, who were positively and negatively co-infected with HBV. This hospital was selected because it is one of Indonesia's major providers of HIV/AIDS services and care.

Study design and data collection

This is a case control study design. Cases were the HIV/AIDS patients diagnosed with Hepatitis B virus evident from the clinical record) and received care from 2016-2021 at RSUP Dr. Kariadi, Semarang. While Controls were HIV/AIDS patients who were negative to Hepatitis B virus and received care from 2016-2021 at RSUP Dr. Kariadi, Semarang.

The research was carried out in November, 2021 through February 2022. The total Sample size is 68 where 34 cases and 34 controls and sampling method which is used is by proportional random sampling that is sampling in such a way to the population contained in sub-populations in this study are those who seek treatment at the Kariadi Hospital with the stipulation that every members of the population have the same opportunity to be taken as a sample.

The dependent variable in this study is the occurrence of Hepatitis B virus infection in HIV/AIDS patients while the independent variables in this study consist of CD4 count ≤100 cells/mm3, marital status ,level of education, age, gender, and being (MSM).

Statistical Analysis

The correctness, completeness, and consistency of the data obtained and used in this study were all double-checked.the data was analyzed with the SPSS version 22.0 for windows.Analysis of data was done through univariate, bivariate and multivariate analysis

with logistic regression. In this study we used a p value less than 0.05, or 5 percent, significance level.

Results

General description of the characteristics of respondents in both case and control groups including: age of respondent, their gender, and their marital status were presented in Table 1.

Tables 1. Distribution of Respondents by Age, Gender, Marital status, and Level of Education

	HBV in HIV/AIDS patient				
Characteristic of Respondent	Cases			control	
(n:34)	f	%	f	%
1.Age					
Mean	45.26		36.12	
Median	48.00		34.00	
Standard Deviation	11.46		7.189	
Minimum-Maximum	27-64		22-55	
2. Gender					
Men	26	76.5%	24	70.6%
women	8	23.8%	10	29.4%
3. Marital status					
Married	27	79.4%	21	52.9%
Single	7	20.6%	13	47 .1%

Table 1 shows that age distribution in the case group has a median of 48.00, the standard deviation is 11.461, and the minimum age is 27years whereas the maximum age is 64years. In this study the control group, have a median value of 31.50, it has standard deviation which is equal to8.1115, the minimum age is equal to 22years with maximum age which is equal to 55years. The gender characteristics of the respondent showed that there were 50 men or (83.3%) and 18 (30%) women in total. Percentage of men that is recorded among the set of cases is 76.5% while in the set of controls is 70.6%. This therefore shows that the proportion of male respondents in the case group is more than the proportion of male respondents in the set of controls.

The marital status of the respondents revealed that there were 48 respondents who were married (including the widows and divorced), where 79.4% of respondents in the case group were married and 52.9% of respondents in the control group were married. This therefore indicated that the proportion of married respondents in the set of cases was more than the proportion of those in the set of controls.

From the bivariate analysis, it was found that 2 variables were proven as risk factors for occurrence of HBV infection in Individuals who have HIV/AIDS that attended Kariadi Hospital, namely CD4 ≤100, and being MSM. Results of bivariate analysis were presented in Table 2

Table 2. Analysis of Bivariate Results Summary of Independent Variables for the Occurrence of Hepatitis B in HIV/AIDS Patients

No	Variable	OR	95% C1	P-value
1	Age (>30)	1.782	0.390-8.132	0.707
2	Gender (Men)	1.354	0.459-3.998	0.783
3	Marital Status (Married)	2.388	0.810-7.041	0.183
4	Level of Education (< 9years)	1.294	0.477-3.509	0.800
5	CD4 Count (≤100)	7.500	2.168-25.946	0.001*
6	MSM	3.429	1.255-9.370	0.028*

* P < 0.25 entered as a variable for multivariate test

From the above analysis, logistic regressions were carried out in determining variables that were predictors of the occurrence of HBV in HIV/AIDS individuals. The 2 variables namely CD4 cells count≤100, and being MSM were both selected for being run in multivariate analysis with logistic regression. Table 3 summarizes the results of the multivariate analysis**.**

Table 3. Multivariate Analysis with Logistics Regression Results

Variables	Coefficient	P-value	OR	95% CI	
				Lower	Upper
CD4 Count (≤100)	2.020	0.003	7.535	2.029	27.990
MSM	1.265	0.027	3.544	1.158	10.848
Constant	-1.277				

The research results of a multivariate analysis by logistic regression revealed that factors that were proven to have an effect on the occurrence of Hepatitis B virus in HIV/AIDS patients attending Kariadi Hospital are CD4≤100 (p=0.003) OR=7.535, 95% CI(2.029-27.9900) and being MSM p=0.027 OR=3.544, 95%CI(1.158-10.848) while the variables that was proven not to have an effect on the occurrence of Hepatitis B virus infection in HIV/AIDS patients attending Kariadi include marital status, Age of respondents, their Gender, and their level of education.

According to the probability calculations, two risk factors, CD4≤100 which has a 67.76% and being male that have sex with other Male (MSM) which has a 50.3% chance of causing Hepatitis B virus infection in HIV/AIDS individuals.

The probability for HIV/AIDS patients to be infected by Hepatitis B virus when have these 2 risk factors is equal to 88.18%.

Discussion

Independent Research Variables proven to affect the HBV infection occurrence in HIV/AIDS individuals in RSUP Kariadi. The effect of having CD4≤100 cells/µL. The effect of having CD4≤100 was proven in this research as the risk factor that influences the occurrence of HBV infection in HIV/AIDS patients. Having CD4 that is less than or equal to 100 in HIV/AIDS individuals can lead to being infected by HBV in this group of immunocompromised individuals and being infected with two viruses (HIV and HBV) can lead to subsequent death to these patients.

The multivariate test analysis results indicated that there is influence of CD4 cell count less than or equal to 100(CD4≤100) and the occurrence of HBV infection in HIV/AIDS individuals, P-value of 0.003, OR = 7.535, and 95% C1 = 2.029-27.990.

Greater attention is needed for patients with lower CD4<100, since their immunity is reduced and they become vulnerable to other infection. The results of statistical analysis shows that HIV/AIDS patients who have CD4≤100 are 7.535 times more at risk of being infected with Hepatitis B compared to the control group.

This result is in accordance with the findings obtained by Chandra and colleague in South India which indicated that CD4≤100 was a risk factor for Occurrence of hepatitis B infection in HIV/AIDS patient, Their results gave a p value which is equal to 0.002,OR=3.4 at 95% CI(0.93-14.06)[7].

The effect of being MSM

The effect of being a man who has intercourse with other men (MSM) was proven in this research as the risk factor that influence the occurrence of HB virus in HIV/AIDS patients at Kariadi Hospital with a P-value of 0.027, OR = 3.544 and 95 % C1 = 1.158-10.848). HIV/AIDS patients who are MSM tend to be the one infected with Hepatitis B virus. The results also shows that HIV/AIDS men who do sex with other male are 3.54 times more at risk of being infected with Hepatitis B virus when compared to the control group.

The findings of this investigation contradict the findings of Olusegun's research which revealed that there were no significant association between being MSM(male who have sex with other male) with Hepatitis B virus occurrence in HIV/AIDS patients[8].

This research is in accordance with the research done in china by Zhang and colleagues that also have indicated that MSM as one of the risk factor for occurrence of Hepatitis B virus in HIV/AIDS patients their results were , P-value which is equal to 0.001, (P=0.001, and OR=4.57)[9]. Vaccination is needed to prevent HBV in HIV/AIDS individuals[10].

Research Variables that were not proven as risk factors for the occurrence of Hepatitis B virus in HIV/AIDS patients in RSUP Dr. Kariadi.

Age

The Results obtained from this study showed that the proportion of HIV/AIDS with age which more than 30 years who have Hepatitis B virus the case group were high, which may be explained that they were infected with Hepatitis B virus before the measure of vaccinating children were put in place.

Bivariate analysis showed no effect of age on the Incidence of Hepatitis B virus in HIV/AIDS patients. The statistical calculation results gave a p value = 0.707.

The age was not risk factor in this research may be because the proportion of patients in case who are aged more than 30 years old were almost the same as the proportion of patients in control who are aged more than 30 years old, (85.3% and 91.2% respectively).

This study is not in accordance with the research that was done in central Brazil where the age was indicated as risk factor for occurrence of Hepatitis B infection in HIV/AIDS patients, where Multivariate analysis gave a p value which were less than 1 among the different age group , for patients age more than 26 years and above 55 years of age where p=(<0.01) [11].

This study is accordance with study done In Nepal, which revealed that there were no relationship between Age and the occurrence of Hepatitis B virus in HIV/AIDS patients (p=0.86)[12].

This study is also in line with the study done at Razi hospital Rasht city in Iran, after univariate analysis, the results showed no relationship between the Age and the infection of Hepatitis B virus infection in HIV/AIDS patients ,their result has a p-value which was greater than 0.05 (p>0.05)[13].

Gender

The result obtained from this study showed that the proportion of male sex in the case group was 76.9% while the proportion of female sex in the case group was 8%, this could be explained by the fact that men tend to engage in activities that could put them at risk of contacting the diseases (HIV/AIDS and Hepatitis B). It could also be as a result of the fact that women tend to take proper care of their health than men by reporting to the clinic early enough to get tested as well as following up with treatment unlike the men.

The bivariate analysis results gave a p value = 0.783 meaning that gender has no influence on the occurrence of Hepatitis B virus in HIV/AIDS patients.

The gender was not risk factor in this research may be because the proportion of male patients in case group were almost the same as the proportion of male patients in the control who are (76.5% and 70.6%% respectively).

This research is not in accordance with the research done in central Brazil, where gender was revealed as risk factor for occurrence of Hepatitis B infection in HIV/AIDS patients where Multivariate analysis gave a p value which were less than 0.001 (p<0.001) with OR=1.97 in male gender[11].

The greater proportion of male sex that is in the case group which is 76.9% while the proportion of female sex in the case group is 8%, this could be explained by the fact that men tend to engage in activities that could put them at risk of contacting the diseases (HIV/AIDS and Hepatitis B. multivariate analysis results indicated that male gender were not the risk factor for the occurrence of HB virus infection in HIV/AIDS patients.

This research is in accordance with the research conducted in Nepal, which revealed that there were no relationship between Gender(male sex) and the occurrence of Hepatitis B virus in HIV/AIDS patients (p= 0.707)[12].

Marital status

The result of bivariate analysis on marital status obtained from the statistical analysis have given the p-value which is equal to 0.183, meaning that there is no relationship between marital status and the occurrence of Hepatitis B infection in HIV/AIDS patients.

The marital status (being married) was not a risk factor in this research may be because the proportion of married patients in the case group were almost the same as the proportion of married patients in the control group who are (27 cases and 21 controls).

This study is in accordance with the research done in China, where Multivariate analysis of this research have also proven that there was no association between marital status and the occurrence of HBV in HIV/AIDS individuals,

the p-value o was equal to 0.454, OR=1.153, 95%CI (0.785-1.718)[14].

This study is also in accordance with the research done in Turkey which revealed that there was no association between marital and the occurrence of hepatitis B virus infection in HIV/AIDS patient where p value=0.06, OR=1.05, 95% (1.03-1.07)[15]. There were no previous research that proved that being married was a risk factor for occurrence of Hepatitis B virus infection in HIV/AIDS patients.

Level of education

Result obtained from this study shows that the proportion of respondents with education level lower than 9years in the case group was 13 (38.2%) and they were more than those in the control group which were only 11 people (32.4%). Whereas, the proportion of respondents with education level higher than 9years in the control group was 23 (67.6%) and they were more than those in the case group which were about 21people (61.8%). From these results it's evident that more HIV/AIDS patients without Hepatitis B virus infection have an educational level higher than 9 years as compared to HIV/AIDS patients with Hepatitis B infection. Bivariate analysis results have given the p value which is equal to 0.800, this results indicate that there is no influence of the levels of education and the occurrence of Hepatitis B infection in HIV/AIDS patients.

The level of education (< 9 years) was not a risk factor in this research may be because the proportion of patients whose level of education is below 9 years in case group were almost the same as the proportion of patients in the control group whose level of education is below 9 years of education in the control group (13 (38.2%) cases and 11 (32.4%) controls).

This research is in accordance with the research done by Anteneh and colleagiues where after univariate analysis, the results revealed no relationship between level of education and the Hepatitis B virus infection in HIV/AIDS patients pregnant women with p-value of 0.39 (p-value=0.39) and OR=4.2, this results implies no relationship among Hepatitis B virus infected individuals who are also

Infected with HIV/AIDS in pregnant women in Ethiopia[16].

This research is accordance with the research done at Razi hospital Rasht city in Iran, the results revealed no significant relation between the level of education and the infection of Hepatitis B virus infection in HIV/AIDS patien, p-value of 0.5611, OR=2.0714 (0.177-24.1495), this means that there is no relationship between the levels of education and Hepatitis B virus infection in HIV/AIDS patients[13].

The small sample size used in this study was a limitation and this is due to the fact that screening of Hepatitis B virus infection is not done in most of HIV/AIDS patients attending RSUP Dr.Kariadi hospital.

Conclusions

The proven factors as risk factors for HBV infection in HIV/AIDS patients are CD4≤100, and being MSM.While the factors that have not proven to be a risk factor for the occurrence of HBV infection in HIV/AIDS patients are, Age of the respondents , their gender, marital status(being married), and level of education(,9 years of education. Vaccination, promotion of safe sex and screening for Hepatitis B virus infection in HIV/AIDS patients is highly suggested in order to prevent Hepatitis B virus in HIV/AIDS patients.

Acknowledgement

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