CHAPTER I

INTRODUCTION

A. Background of study

Human Immunodeficiency Virus (HIV) is a retrovirus that destroys CD4+ cells, causing the human immune system to decline and being susceptible to various infections such as fungi, bacteria, parasites and 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 products, mother to child, infected body fluids, and the use of contaminated needles. HBV will also easily replicate in patients with low immunity such as in HIV/AIDS patients[2].

Research have indicated that HIV has the significant impact on HBV, where the patient co-infected with both virus resulted in increased HBV-DNA, there is also faster liver disease advancement and elevated liver-related death compared with patient who are only mono-infected with HBV. the research have revealed that the evolutionary history of HIV-HBV co-infection has improved dramatically as a result of widespread absorption and early beginning of antiretroviral therapy (ART) for HBV; however the incidence of liver disease in this group stays high[3].

In HIV patients receiving Anti-Retroviral Treatment (ART), it is necessary to check the status of HBV co-infection in order to lessen the chance of hepatotoxic complications, liver fibrosis, and cirrhosis[4]**.**Theprevious studies have revealed that treatment of HIV/AIDS is a problem when

patients are having the two virus which are Hepatitis B Virus together with HIV ,Virus that infect HIV patients include Hepatitis B Virus (HBV), because the research have revealed that their routes of transmission 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[5]. HIV infection is a severe public health concern around the globe, as it was indicated by the world health organization , it is estimated that 37.7 million individuals that were infected by HIV /AIDS and it was reported that Since the beginning of the epidemic, 36.3 million individuals have died from AIDS-related diseases. 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[6].

Hepatitis B virus is indeed among the leading reasons of death in HIV/AIDS Patients. Co-infection with HBV and HIV has been linked to a worse chance of survival, an elevated risk of liver disease progression, and a higher risk of hepatotoxicity from antiretroviral therapy[7].HIV infection progresses more quickly in Hepatitis B virus (HBV) infected individuals and ,becoming an AIDS-defining condition, the patient's prognosis is worsened, and their life expectancy is reduced. Hepatitis B virus attacks liver cells, and causes malignant hepatoma and , cirrhosis[8].

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.

Liver-related death is s two times higher as in people who have HIV infection together with Hepatitis B only have HIV. Patients with such a CD4 cell count of lower than 200 cells per mL have a 16.2 times higher chance of dying from liver disease than those with a CD4 cell count of more than 350 cells per mL[10,11]**.**this could be due to the fact that HIV and HBV, all have same transmission pathways, allowing for co-infection. Parenteral (blood and blood products, hazardous injection practices between people who inject drugs, tattoos) and sexual transmission are common modes of transmission (MSM, people who do sexual intercourse with multiple partners), According to available studies, HBV co-infection with HIV varies greatly between geographic areas, risk categories, and types of exposure involved[12]**.**

Antiretroviral should indeed be begun irrespective of CD4 T cell level in HIV-infected individuals with Hepatitis. However, the choice of regimen is dependent on which viral infection is present or whether the patient is at higher risk of hepatotoxicity. Knowing your HBV status has ramifications for how you treat these viruses, The World Health Organization's global hepatitis plan, which aims to eradicate hepatitis in 20230 , relies on 80 per cent of people being eligible for treatment for Hepatitis B Virus HBV infection, therefore a diagnosis is required before therapy[13].

The incidence of HBV and is crucial for gathering data for targeted action. A few studies on the prevalence of HBV co-infection in HIV patients have been conducted in various geopolitical zones in Indonesia[6].Various studies have been done to find the prevalence of hepatitis B virus

co-infection with HIV/AIDS, but no studies that have been conducted to determine the risk factors for HBV co-infection in HIV/AIDS patients in the region. There is no recent epidemiological data on the risk factors of HBV co-infection in HIV/AIDS patients that is available and has not been reported in at Kariadi hospital; therefore the researchers aimed to conduct a research on the influence of epidemiological risk factors that influence the occurrence of Hepatitis B Virus co-infection in HIV/AIDS patients, in Kariadi hospital, Semarang.

B. Problem statement

1. People who are HIV-positive and co-infected with HBV have a greater rate of chronic hepatitis infection and a faster development to fibrosis, cirrhosis, Hcc, and final liver disease than those who are only infected with HBV[14].

2. There's a continuous increase in the number of people living with HIV/AIDS (PLWHIV), hence becoming a global pandemic. An increase to 37.7 million of PLWHIV in as well as 1.5 million newly infected individuals was reported by United Nations Program on HIV / AIDS (UNAIDS) in 2021.

3. Forty six thousand (46 000) new cases of HIV infected individuals as well as 38 000 AIDS-related deaths was reported in Indonesia in the year 2018 by UNAIDS. Even though HIV prevalence in the overall population of Indonesia is estimated to be (0·4%), an estimate of 640 000 PLWHIV was reported in 2018 and the country is among the countries in the world with steady increase in new HIV infections.

4. HIV and HBV co-infection is still poorly documented in Indonesia and more information is needed to better understand the risk factors associated with this co-infection in HIV/AIDS patients[6].

5. The presence of one virus alters the natural history of the other virus in co-infection. HIV speeds up the natural course of HBV infection, allowing liver disease to proceed more quickly to cirrhosis and hepatocellular cancer; according to prior studies, the progression of the disease to cirrhosis in HIV positive patients was nearly three times faster than in HIV negative people[15].

6. Indonesia has considerable deficiencies in the HIV testing and treatment pathway, and it is falling behind the 90–90-90 targets the same as the majority of Southeast Asian countries[6].

7. The ability of High Activity Antiretroviral Therapy (HAART) to improve the quality of life and extend the lifespan in HIV patients has fundamentally altered the field of HIV treatment. Co-infections with virus like HBV appear to jeopardize the effects of effective antiretroviral medications by increasing morbidity and death in HIV-positive people[16].

8. Different research has been carried out on the prevalence of HIV co-infection with either hepatitis B or hepatitis C, but there were limited research that was done to find the risk factors for HVB co-infection in HIV/AIDS patients in this region. The continuous high rate of HIV/AIDS cases in the region provides an inherent risk of co-infection with HBV as they share the same mode of transmission. As such, further research is needed to understand the risk factors of HBV co-infection in HIV/AIDS patients.

C. Problem formulation

Based on the problems identified above, the research questions formulated include:

1. General problem formulation

What are epidemiological risk factors that influence the occurrence of HBV co-infection in HIV/AIDS patients?

2. Specific problem statement

What are the epidemiological risk factors that influences for occurrence of HBV co-infection in HIV/AIDS patients,

a) Value of CD_4 cell count $\leq$100 cells/mm^3

b) Age >30 years old

c) Male having Sex with Men(MSM)

d) Level of education

e) Male gender

f) Marital status

D. Originality of research

Previous studies that have been carried out on the risk factors of the occurrence of Hepatitis B virus in HIV/AIDS patients are as follows:

Table1 1: List of Several studies that were previously conducted concerning the risk factors of HBV co-infection in HIV/AIDS patients include:

NO	Researcher, year and place of research	Title of research	Research variable	Research design	Results
1.	Kye-Duodu1 &,Priscillia Nortey, Keziah Malm,Kofi Mensah Nyarko, Samuel,Oko Sackey, Sampson Ofori, Edwin Andrews Afari1 published in (2016). done at east region of Ghana[17]	Prevalence of hepatitis B virus co-infection among HIV-seropositive persons attending antiretroviral clinics in the Eastern Region of Ghana	Age,sex, serum-ALT levels, and HBsAg	Case-control	HBsAg positivity was found in 28 /320 PLHIV enrolled for the study, with a median age of 40 years (IQR: 33-50 years) and an overall prevalence of 8.8%. HBV infection and being an adult (p=0.004), increased serum **Alanine Transaminase** levels (p which was equal to0.002), and having a spouse who has a history of Hepatitis B Virus infection (p=0.010) all had significant relationships. In the "general knowledge" and "management practice" indices, Healthcare workers scored 84.2 per cent (SD 20.53; 95 per cent CI: 89-98.1) and 53.1 per cent (SD 35.06; 95 per cent CI: 13.0-88.9), respectively.
2.	Cynthia,Semá,Baltazar,Makini Boothe, Timothy Kellogg, Paulino Ricardo, Isabel Sathane, Erika Fazito ,	Prevalence and risk factors associated with HIV/hepatitis B and HIV/hepatitis C co-infections	Gender, injection drug Older age, history of needle/syringe sharing and history of injection with used	Cross-sectional	Males made up 93.3 percent of the 492 eligible PWID, and the average age was 32 years [IQR: 27–36]. HIV, HBV, and HCV prevalence were 44.9 percent (95 percent confidence interval: 37.6–52.3), 32.8 percent (95 percent confidence interval: 26.3–39.5), and 38.3 percent (95 percent confidence

	Henry F. Raymond, Marleen Temmerman and Stanley Luchters publishe in (2020) . in Maputo and Nampula/Nacala, Mozambique[18]	among people who inject drugs in Mozambique			interval: 30.6–45.9), correspondingly. HIV/HBV, HIV/HCV,and HIV/HBV/HCV co-infections were found in 13.1 percent (95 percent confidence interval: 7.2–18.9), 29.5 percent (95 percent confidence interval: 22.2–36.8), and 9.2 percent (95 percent confidence interval: 3.7–14.7) of PWID, correspondingly.
3.	Naval Chandra, Nayana Joshi , Y.S.N. Raju, Ajit Kumar & Vijay D. TejaPublished in (2013). south India[19]	Hepatitis B and/or C coinfection in HIV infected patients: A study in a tertiary care centre from south India.	Marital status Sexual promiscuity,blood transfusion,CD4 count	Case-control	Sexual promiscuity (79%) was the most prevalent mechanism of transmission, and the following were spouse which were positive (15%) and w thos who have history of blood transfusions had (6 per cent). In HIV-infected patients, HBsAg and anti-HCV were found to be positive in 18 (15%) and 10 (8.3%) of the participants, correspondingly; in control subjects, the findings were 2 (1.6%) and 0 (0%). (P0.0001). HBeAg and anti-HBe antibodies were identified in 33.3 and 55.5 percent of Disease patients, correspondingly; 11.1 percent of Disease individuals had both HBeAg and anti-HBe antibodies negative. HBV DNA and HCV RNA was confirmed in 10 of the 18 samples, as were all anti-HCV positive samples. Three patients were infected with HBV, HCV, and HIV all at the same time. The CD4+ T-lymphocyte count was less than 200/l in 22 of the 28 co-infected cases.

4.	Azzania Fibriani , Rudi Wisaksana , Bachti Alisjahbana , Agnes Indrati , Martin Schutten, Reinout van Crevel, Andre van der Ven , Charles A B Boucher published in (2014) done at west java, Indonesia[20]	Hepatitis B virus prevalence, risk factors and genotype distribution in HIV infected patients from West Java, Indonesia	Gender ,Injecting druguse, tattoing, HBV-DNA levels, AST level	cross-sectional	HBV coinfection was 7% in 636 HIV-positive patients. Males were more prevalent in HBV/HIV coinfected patients (93 per cent vs. 72 per cent, P=0.001) than in HIV mono-infected individuals. HBV coinfection was linked to a history of injecting drug use (IDU) but not tattooing [P=0.035 OR 2.41 (95 per cent CI 1.06-5.47)]. CD4 cells count 50 cells/mm in HIV and HBV therapy-naive patients. Patients with high HBV-DNA levels (20,000IU/ml) were more likely to have HIV-RNA plasma of 10,000 copies/ml and an AST level above normal (P0.05) than those with low HBV DNA (20,000IU/ml)
5.	Jayeeta Sarkar,Bhaswati Bandyopadhyay, Runu Chakrabarty, Nemai Bhattacharya, Srima Adhikari,Saiantani Mondal,Anurita Mukherjee,and Subhasish Kamal Guha. Published in 2013 in west , bangal India[21]	HIV-HBV Coinfection among Individuals Attending the ICTC of a Tertiary Care Hospital in West Bengal, India	Age,Gender, HBsAg,MSM ,Blood transfusion	Cross-sectional	This study has results that show that Anti-HIV antibody prevalence rate was 17.3 percent. 8.3 percent of the samples tested positive for HBsAg. they Concluded that The significant prevalence of HIV/HBV co-infection among the many attending the ICTC in this center was concerning and necessitates immediate care.
6.	S C Hadler, F N Judson, P M O'Malley, N L Altman,	Outcome of hepatitis B virus infection in	Age , gender,vaccination status,ALT	**Case-control**	Among 134 unvaccinated HI\'-I-negative men, 7% became HBV carriers, 64% had viremia, and 42% had

	K Penley, S Buchbinder, C A Schable, P J Coleman, D N Ostrow, D P Francis[22]	homosexual men and its relation to prior human immunodefi ciency virus infection			clinicalillness.Among vaccinated HIV-l-negative men, HBY infection severity decreased with number of vaccine doses administered. When the chances of developing HBV carrier, viral load, continuous ALT elevation, and clinical disease was adjusted for preceding hepatitis B vaccination condition, people who had HIV-l infection prior to HBV infection had a significantly higher risk of developing HBV carriage, viremia, prolonged ALT elevation, and clinical illness. Unimmunized men (21%) and those who refused to respond to vaccination (31%), and those who did receive vaccine dosage just at time they started developing Hepatitis b (56 percent-80 percent), had a higher risk of HBV carriage, suggesting that inactive hepatitis B vaccine may momentarily impede the innate immunity to Hepatitis b in HIV-infected men. In the first 36 months of follow-up of men who've become HBV carriers, HIV-l infection was likewise linked to lower alanine ALT levels.
7.	Patricia Gita Naully Published in 2018 at CIMAHI, , Indonesia[23]	Coinfection of human immunodefi ciency virus and hepatitis b virus in people tattooed in cimahi	**Age,Gender, having tatoo**	**Cross-sectional**	From 50 respondents consisting of 25 women and 25 men with an age range between 17-48 years, two people (4%) were positive infected with HIV and one person (2%) was positive for HBV. This research demonstrated that there was one case of HIV-HBV

					coinfection that occurred in a person tattooed in Cimahi.
8.	Andri Hendratno ;Diana Natalia; WiwiE Susanti Published in 2016, in Pontianak,Indonesia[24]	Prevalensi koinfeksi HBV (Hepatitis B Virus) pada pasien HIV/AIDS di klinik Melati RSUD Dr. Soedarso Pontianak	Age,gender,CD4 lympcyte count,marital status	**Cross-sectional**	Hepatitis B was found in 9 out of 98 patients (9.18%). The majority of the study individuals with Hepatitis B coinfection are between the ages of 23 and 41, are married, work in the private sector, have transmission lines from heterosexual relationships, and have a CD4 lymphocyte count of less than 100 cells/l. Conclusion. In 2016, the Melati Clinic RSUD dr. Soedarso Pontianak saw 9.18 percent of HIV/AIDS patients who had hepatitis B coinfection.

Things that distinguish this research from previous studies that has been done include:

1. Research variables

a) Independent variable:

Many previous studies that were done , their Independent variables were having tattoo, use of condom, and Intravenous drug user, In this research independent variables like Level of education, Religion, These variables haven't been researched and according to literature, these variables also contribute to the risk of occurrence of hepatitis B virus infection in HIV/AIDS patients.

b) Dependent variable:

Many previous researches, dependent variable are HBV in homosexual infection and others are hepatitis B and C, in this study the dependent variable is the occurrence of Hepatitis B virus co-infection in HIV/AIDS patients and there was no other previous research done in the region that studied this variable.

2. Research subjects

Subjects that were used in this research were HIV/AIDS patients who were positive for Hepatitis B virus infection and attended RSUP Dr. Kariadi hospital Semarang, from 2016-2021, the were no previous research that was carried at this Hospital .

3. Research design

This is a retrospective study with a case-control research design, whereas most previous studies were cross-sectional and prospective case control.

E. Research objectives

1. **General objective**

This document proposes:

To explain the various epidemiological risk factors for Hepatitis B Virus co-infection in HIV/AIDS patients in RSUP Kariadi hospital.

2. **Specific objective**

Analysis of many risk factors for occurrence of Hepatitis B virus infection in HIV/AIDS patients namely:

a) Value of CD4 cell count ≤100 cells/mm3

b) Age >30 years old

c) Male having Sex with Men (MSM)

d) Level of education

e) Male gender

f) Marital status

F. Benefits of research

The findings of this study are intended to benefit several stakeholders, including:

1. Health Service Institutions

This study will provide information related to the risk factors for occurrence of HBV co-infection in HIV/AIDS patients, so that it can be used as a consideration for the Central Java Provincial Health Service and the Office of Health of the City of Semarang in the management and control programs.

This study is intended to be used as input for the implementation of the control program and eradication of HIV/AIDS with co-infection of HBV and management of these cases to reduce hepatic complications.

This research is hoped to be used as an input material to determine the extent to which the viruses affects patients and to ascertain better outcome.

For the local health agencies, this is study is expected to be able to ensure the promotion of awareness of the disease, its risk factors and prevention to the citizens in closest health care centers , in other to reduce the mortality rate in future occurrences.

2. Science Development

This study will be used as source of reference for knowledge relating to the prevention, control and management of HBV co-infection in HIV/AIDS patients.

As a source of information related to various risk factors that influence of the occurrence of HBV co-infection in HIV/AIDS patients so that it can be used as library material in the development of internal health science.

3. For the community

This research hopes to promote the rate of awareness of risk factors for occurrence of Hepatitis B Virus in the community especially in HIV/AIDS patients so that they can prevent themselves from contacting the diseases.