Predictors of Tuberculosis in HIV Patients in the Clinic Voluntary Counseling and Testing in Medan City

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Abstract

Background: The incidence of tuberculosis in HIV patients (TB-HIV) was estimated at 126 per 100,000 in the world. The number of HIV infected patients in Indonesia around 190,000 to 400,000 and the prevalence of TB-HIV is 5%. Data TB-HIV still increases and they are unaware of that until a late stage. Understanding the risk factors of people with TB-HIV co-infection is important to know. This study aims to know the predictors of TB-HIV patients in the clinic voluntary counseling and testing (VCT) in Medan city.

Methods: This is a case-control study. The case is TB-HIV patients (aged > 20 years) seen at clinic VCT Medan in 2016. Control is HIV patients without TB (aged > 20 years) seen in the same clinic VCT. The number of cases was 120 and the number of control 120. Data were collected from the medical record. Data were analyzed using the chi-square test in SPSS software.

Results: The total was 240 patients. The majority were in the age group 31-40 years old (52.9%), male (75.8%), married (71.7%), had tertiary education (85.4%), had employment (89.2%). Significant factors were CD4 < 500 cells/ml (OR 3.92; 95% CI 2.13-7.22), BMI < 18.5 kg/m² (OR 5.79; 95% CI 3.25-10.21), had history of TB family (OR 7.9; 95% CI 3.67-18.18), adherence ARV (OR 1.35; 95% CI 1.02-1.79).

Conclusions: The predictors of incidence TB-HIV co-infection was low CD4, low BMI, and had a family history of TB. Pay the attention for the nutritional status of TB-HIV patients and provide appropriate nutritional intake needs and adherence ARV.

Background

The World Health Organization (WHO) reported that 37.9 million (32.7–44.0 million) people are HIV infected worldwide in 2018 and Africa having the greatest absolute number of HIV-infected patients in the world¹. Globally, the World Health Organization estimates that 10.4 million TB cases were reported in 2016 and 1.2 million (11.5%) of these being co-infected with HIV². Human immunodeficiency virus (HIV) and tuberculosis co-infection is a major public health problem in the world. Tuberculosis is the leading cause of mortality and morbidity in HIV infected patients. These two infections interact with each other, worsening the prognosis and increased mortality but estimated about 49% of them are unaware of their co-infection and they did not under treatment².

In developing countries incidence of TB occurrence has been associated with factors like socio-economic³, lifestyle habits⁴, clinical and laboratory⁵, also other co-morbidities for example diabetes⁶. Many patients either have a history of TB in family, or they develop TB while receiving HIV treatment in the developing world⁷. It has not been well delineated what factors influence the development of TB in HIV infected patients on antiretroviral therapy (ART)⁸. In Indonesia, the number of TB cases in 2017 reaches the second rank in the world, and it is endemic in the general population and has a high incidence of TB-HIV⁹. Incidence of Tuberculosis per 100,000 population per year is 254 in 2017, tuberculosis in adults

receiving ART is higher than in HIV negative adults ¹⁰. Studies on risk factors of TB were done in the general population but determinants of active TB among HIV patients are not well described in resource limited settings. Few studies have reported on factors associated with the development of TB among HIV infected patients. There are not enough studies about associated factors co-infection TB-HIV in Sumatera Utara province, especially in Medan city. This study assessed the determinant factors for the tuberculosis co-infection in HIV infected patients receiving treatment in Clinic voluntary counseling and testing (VCT) in Medan city.

Tuberculosis is a major cause of death in people with HIV, which is most likely due to delays in diagnosis and TB therapy. People with HIV will be at risk 26 times more likely to get Tuberculosis compared to people without HIV or HIV negative ¹¹. Uyainah (2009) states that TB co-infection is a problem because one of the factors is the high incidence of TB itself in Indonesia, which increases the risk of contact with HIV patients. The higher the prevalence of HIV in an area, the higher the prevalence of HIV-TB co-infection in the area. Consequences of HIV and TB co-infection is HIV infection will facilitate the occurrence of TB infection. HIV infection increases the risk of reactivating latent TB and increases the risk of TB disease after infection or reinfection by *Mycobacterium tuberculosis* ¹².

Methods

This is a case-control study was conducted in three Clinic VCT in Medan city consist of Clinic VCT in Dr. Pirngadi Hospital, in Haji hospital and Adam Malik hospital. Data collection from June to September 2018. The inclusion criteria of cases were defined as adult HIV infected patients aged 20 years old and above who develop TB after ART initiation. Controls were adult HIV infected patients aged 20 years old and above who did not develop TB after ART initiation. The number of cases was 120 and the number of control was 120. TB Diagnosis in HIV infected patients was made by a clinician based on signs and symptoms of clinical. Acid Fast Bacilli (AFB) direct microscopy laboratory test done three times that is sputum at random, sputum in the morning after wake up and sputum at random. At least one AFB positive can be diagnosed with TB. The exclusion criteria are patients who are severely ill and who not on antiretroviral therapy (ART).

Data collection from medical records of three clinic VCT in Medan city. Cases and controls were identified by the principal investigator through the help of the ART and TB registries. The ratio of case and control was 1:1. The sample size was calculated using the following parameters: 5% significance level, power of 80%, and by using the two proportion formula. The calculated sample size was 120 for cases and 120 for controls; the resulting minimum sample size was 240. The sample size was calculated for exposure status in different variables of the most significant predictors of TB-HIV. The data were collected from medical record and the variables were age, gender, ethnicity, marital status, education level, occupational type, CD4 count, Hb, BMI, had a family history of TB.

Data were entered, cleaned and using SPSS software for analysis. Frequencies and proportions were used to describe the study population in relation to relevant variables. Bivariate analysis was performed

to examine the effect of each variable of interest on the risk of TB-HIV. Odds ratios (OR) and their 95% confidence intervals (CIs) were estimated using the Chi-square test, with TB-HIV as an outcome.

Results

A total of 240 patients included in this study. More proportions of case and control patients were in the age group of 30–39 (53.3% and 52.5%) respectively. High proportions of men, Batakese and married status were reported in both groups, 73.3%, 57.5% and 65% in cases and 78.3%, 56.7% and 78.3% in controls respectively. More than half the patients have completed secondary school, 59.2% in cases and 45% in controls. The majority of subjects, 65% in cases and 60% in controls were non-manual workers of occupational type (Table 1). Majority of cases 84.2% had CD4+ cell count less than 500 cells/dl. But 57.5% of patients in controls had CD4+ cell count less than 500 cells/ml. Among cases, 75.8% of them had Hg level less than 11 mg/dl and 66.6% of controls had Hg level less than 11 mg/dl (Table 2). Of the total 120 patients in cases, 59.22% of patients had BMI less than 18.5. On the contrary, 80.0% of controls had BMI of more than 18.5. Regarding TB family history, the majority of cases and control did not have a history of TB, in cases, only 39.1% had TB family history (Table 1)

The bivariate analysis showed that a higher proportion of male patients (OR = 1.73; 95% CI: 1.23, 2.46) develop TB compared to female patients. The divorced/widowed (OR = 0.560; 95% CI: 0.36, 0.87) patients were less likely to develop TB compared with unmarried (single) individuals. But educational status and occupation were not associated with the occurrence of TB (Table 2).

In multivariate analysis, the risk for TB-HIV was higher among persons with low education, low CD4 counts (< 500 cells/dl), BMI < 18.5, had a family history of TB. We did not find any interactions among the significant predictor variables in the model, multivariate analysis showed in Table 3:

Discussion

It was found that from nine variables, four variables were the strongest predictors of TB-HIV patients in this study. The majority of patients were in the age group of fewer than 40 years (77.9%) and it was found that age variables did not significantly contribute to TB-HIV ($p = 0.876$). These results are consistent with research conducted by Melkamu and Mama in Ethiopia which states that age is not a predictor of cases of TB-HIV patients^{13,14}. From these results, it can be interpreted that any age group still has the same risk of developing TB. This finding similar to a study from Addis Ababa which showed a high frequency of infection in patients with age less than 50 years¹⁵.

Regarding the gender, the majority of patients were men (75.8%) both in the case and control groups. After the results of the multivariate test showed that gender was not a predictive factor for TB-HIV patients ($p = 0.366$). Similar to the research conducted in India which states that male is more than female of TB-HIV patients caused by their different lifestyles¹⁶. The behavior of males who are vulnerable to unhealthy behaviors such as cigarettes and alcohol are the strongest boosters and drivers

for TB¹⁷. Whereas in general, it can be seen that TB attacks any class of male or female. This is consistent with this study. When viewed from the poverty factor, it is the strongest predictor of TB-HIV in any gender, both male and female. Research conducted in US (2013) states that HIV and AIDS is not only hitting adults in their most economically productive years¹⁸.

A person's marital status is not a predictor of TB-HIV patients. In this study, it can be seen that the majority of patients are married (71.7%). The results of the bivariate test showed that $p = 0.022$. This study is different from the research conducted in Africa (2016) which states that marital status is a predictor of TB-HIV that attacks more unmarried people¹⁹. This study states that unmarried patients will increase the risk of contact with many people because it is associated with socioeconomic activities. Whereas in Indonesia it can be seen that whether married or unmarried, there is no difference in the risk of contact with other people who can contribute to TB-HIV. A study in Iran (2014) showed that seroprevalence of TB-HIV co-infection was higher among unmarried males and those living singly than male tuberculosis patients living with their spouses²⁰.

Based on the results of the bivariate test, it was found that education level was a predictor of TB-HIV patients ($p = 0.006$). The majority of patients have a low level of education at the primary and secondary level (66.7%). Even based on the results of the multivariate test showed that patients with low education will be at risk 2,319 times for TB-HIV than patients with higher education. It appears that as low as education, the higher the risk. Research conducted in Tehran stated that the level of education can influence behavior. A person with low education is closely related to low knowledge about maintaining health and the risk of exposure to diseases including TB co-infection²⁰. A person with higher education tends to pay attention to his health with his knowledge of health for not being exposed and in contact with many people. The educational level can affect the behavior of HIV patients and understanding of education can help target interventions in order to prevent infection²¹. There was a significant association between educational level and drinking or smoking. Most of the TB-HIV patients had less than nine years of schooling and also had low incomes. This apparent association might be a consequence of other health hazards, including a lack of health education and having access to health care²².

The results of the analysis state that employment is not a predictor of TB-HIV patients ($p = 0.196$). In this study, the majority of patients were working (89.1%). The results of this study are different from the statement of The National AIDS Fund which states that HIV sufferers are at risk of being exposed to TB co-infection at their workplace. In this study, work is related to one's socioeconomic status. Patients with low socioeconomic conditions are closely related to unhealthy living behavior due to lack of access to adequate health facilities. Patients with high socioeconomic will pay more attention to lifestyle with their work. Work is also closely related to low education and knowledge. The majority of patients in this study work as labor with low education in the factory and close rooms so that the spread of TB was more widespread. A similar explanation was delivered by UNAIDS (2012) which stated that patients working in the transport and construction as well as business sectors were a high-risk group for TB-HIV²³.

Based on the results of the bivariate test in this study a group of patients with TB-HIV and had CD4 levels less than 500 cells / mm³ were at risk of 3.929 times compared with patients non-TB-HIV patients had CD4 levels more than or same as 500 cells / mm³. The results of the analysis showed that CD4 levels were predictors and contributed to TB-HIV patients ($p < 0.001$), wherein this study the majority of patients had CD4 levels less than 500 cells / mm³ (70.0%). This study is in line with a systematic review by Ellis (2017) which states that the decreasing level of CD4 levels increases the risk of TB. High viral load increased disease progression. The results of multivariate analysis showed that patients with CD4 levels less than 500 cells / mm³ were at risk of being infected with 3,141 times compared to patients with CD4 levels more than 500²⁴.

The majority of patients were classified as anemia (71.3%). The results of the bivariate analysis showed that Hb levels were not predictors of TB-HIV ($p = 0.117$). This result is different from the research conducted by Karima, et al (2017) which states that there is an increased risk of TB in groups with anemia. In this case, anemia is associated with malnutrition and conditions of immune deficiency which increases risk. But in this study different results were obtained which stated that the anemia condition of patients did not contribute to TB-HIV¹¹.

The majority of patients with a BMI of more than 18.5. It was found that BMI was a predictor of TB-HIV ($p < 0.001$). The results of the multivariate test also stated that patients with low BMI levels would be at risk of 8,632 times than patients with normal BMI. This study is in line with research conducted in Africa (2013) which states that the risk of TB is greater in patients with low BMI¹³. The same thing was stated by Choun, et al (2013) in Cambodia which states that risk factors for early TB included low BMI. Nutritional factors of patients who are not good can reduce a person's immunity so that the range is more susceptible to disease, one of them is TB. So it is better for patients with HIV positive to pay more attention to nutritious food intake to avoid disease²⁵

The results of the multivariate analysis also state that a family history of TB is the most predictive contributing factor to TB-HIV. Patients with a family history of TB will be at risk of 10,584 times than negative ones. Similar to study in Uganda (2015) showed that the prevalence of a family history of TB of 17.5 is high and needs further investigations²⁶.

Conclusion

This study concludes that there are predictors of TB-HIV patients, namely education level, CD4 level, BMI, and family history of TB. The dominant factor is a family history of TB. All people living with HIV should be screened for TB especially those who have close contact in the TB family. Also, pay more attention to increasing the nutritional status and adherence antiretroviral therapy the impact to increase the immunity of TB-HIV patients

Declarations

Ethics approval and consent to participate

Ethical approval was obtained from The Institutional Review Board (IRB) of the Nursing faculty

Consent for publication

All authors declare that they have given approval for publication

Availability of data and material

The data and material are available

Competing interests

All authors declare that they have no competing interests" in this study.

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Authors' contributions

RL contributor in writing the manuscript. SU contributor of data collection. JM contributor to analyzed the data, RAS contributor to interpreted the data All authors read and approved the final manuscript

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Tables

Table 1 Socio-demographic characteristics and clinical condition of the respondents

Characteristics	Cases n (%)	Controls n (%)	Total n (%)
<i>Age (years)</i>			
20-29	29 (24.2)	31 (25.8)	60 (25.0)
30-39	64 (53.3)	63 (52.5)	127 (52.9)
≥ 40	27 (22.5)	26 (21.7)	53 (22.1)
<i>Gender</i>			
Male	88 (73.3)	94 (78.3)	182 (75.8)
Female	32 (26.7)	26 (21.7)	58 (24.2)
<i>Ethnicity (race)</i>			
Bataknese	69 (57.5)	68 (56.7)	137 (57.1)
Javanese	30 (25.0)	30 (25.0)	60 (25.0)
Chinese	8 (6.7)	10 (8.3)	18 (7.5)
Others	13 (10.8)	12 (10.0)	25 (10.4)
<i>Marital status</i>			
Unmarried	42 (35.0)	26 (21.7)	68 (28.3)
Married	78 (65.0)	94 (78.3)	172 (71.7)
<i>Education level</i>			
Primary	19 (15.8)	16 (13.4)	35 (14.6)
Secondary	71 (59.2)	54 (45.0)	125 (52.1)
Tertiary	30 (25.0)	50 (41.7)	80 (33.3)
<i>Occupational type</i>			
Non-manual worker	78 (65.0)	72 (60.0)	150 (62.5)
Manual worker	26 (21.7)	38 (31.7)	64 (26.7)
Unemployment	16 (13.3)	10 (8.3)	26 (10.8)
<i>CD4count (cell/dl)</i>			
< 500	101 (84.2)	69 (57.5)	170 (70.0)
≥ 500	19 (15.8)	51 (42.5)	70 (30.0)
<i>Hb (gr %)</i>			
< 11 (Anemia)	91 (75.8)	80 (66.6)	171 (71.3)
≥ 11 (not anemia)	29 (24.2)	40 (33.3)	69 (28.7)
<i>BMI(kg/m²)</i>			
< 18.5	71 (59.2)	24 (20.0)	95 (39.6)
≥ 18.5	49 (40.8)	96 (80.0)	145 (60.4)
<i>Had family history of TB</i>			
Yes	47 (39.1)	9 (7.5)	56 (23.3)
No	73 (60.8)	111 (92.5)	184 (76.7)

Table 2 Bivariate analysis of variables

Characteristics	Cases n (%)	Controls n (%)	Total n (%)	OR (95% CI)	<i>p-value</i>
<i>Age (years)</i>					
< 40	93 (77.5)	94 (78.3)	187 (77.9)	0.953	0.876
≥ 40	27 (22.5)	26 (21.7)	53 (22.1)	(0.5-1.7)	
<i>Gender</i>					
Male	88 (73,3)	94 (78,3)	182 (75,8)	0.761	0.366
Female	32 (26,7)	26 (21,7)	58 (24,2)	(0.4-1.4)	
<i>Marital status</i>					
Unmarried	42 (35,0)	26 (21,7)	68 (28,3)	1.947	0.022
Married	78 (65,0)	94 (78,3)	172 (71,7)	(1.1-3.5)	
<i>Education level</i>					
Primary+Secondary	90 (75,0)	70 (58,3)	160 (66,7)	2.143	0.006
Tertiary	30 (25,0)	50 (41,7)	80 (33,3)	(1.2-3.7)	
<i>Occupational</i>					
Unemployment	16 (13,6)	10 (8,3)	26 (10,9)	1.725	0.196
Employment	102(86,4)	110 (91,7)	212(89,1)	(0.7-3.9)	
<i>CD4count (cell/dl)</i>					
< 500	101(84,2)	69 (57,5)	170 (70,0)	3.929	< 0.001
≥ 500	19 (15,8)	51 (42,5)	70 (30,0)	(2.2-7.2)	
<i>Hb (gr %)</i>					
< 11 (Anemia)	91 (75,8)	80 (66,6)	171 (71,3)	1.569	0.117
≥ 11 (Not anemia)	29 (24,2)	40 (33,3)	69 (28,7)	(0.8-2.7)	
<i>BMI(kg/m²)</i>					
< 18.5	71 (59,2)	24 (20,0)	95 (39,6)	5.796	< 0.001
≥ 18.5	49 (40,8)	96 (80,0)	145 (60,4)	(3.3-10.3)	
<i>TB family history</i>					
Positive	47 (39,1)	9 (7,5)	56 (23,3)	7.941	< 0.001
Negative	73 (60,8)	111 (92,5)	184 (76,7)	(3.7-17.2)	

Table 3 Multivariate analysis of variables

Variable	B	SE	Wald	<i>p-value</i>	Exp B	95% CI
<i>Education level</i>	0.841	0.380	4.896	0.027	2.319	1.101-4.884
<i>CD4 level</i>	1.145	0.387	8.727	0.003	3.141	1.470-6.713
<i>BMI</i>	2.155	0.365	34.810	< 0.001	8.632	4.218-17.664
<i>Had family history of TB</i>	2.359	0.448	27.678	< 0.001	10.584	4.395-25.491
<i>Constant</i>	-4.266	0.603	50.063	< 0.001	0.014	