Factors Associated with Tuberculosis Treatment Success Among Human Immunodeficiency Virus - Tuberkulosis (HIV-TB) in H. Adam Malik General Hospital, Medan

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ABSTRACT

Introduction: Co-infection of TB/HIV is currently a serious health threat to the world population. Efforts to control tuberculosis and HIV programs still facing obstacles, especially if the two diseases allied, it will be more difficult and challenging for both prevention program. Both TB and HIV have higher burden disease and need to be cope urgently. Adequate treatment of TB in co-infected patients can reduce the high morbidity and mortality of patients, prevent treatment failure and improve the success rate.

Objectives: Determine the proportion of successful treatment of TB among HIV-TB patients in H. Adam Malik General Hospital between 2011-2013 and identified the factors that influenced the success of their TB treatment.

Methods: A case control study design using medical records of HIV-TB patients in VCT polyclinic of H. Adam Malik General Hospital from 2011-2013.

Results: The average success rate of TB treatment among HIV-TB patients in H. Adam Malik General Hospital was 68.56%. Male, age ≤40 years, pulmonary TB, CD4 count <200, anemia, HIV stage 3 and adherence to TB treatment dominated this research, (60,82%, 76,29%, 71,13%, 74,23%, 60,82%, 55,15% and 53,09% respectively). Gender (aOR 3.87 95% CI: 1.21 - 18.31), CD4 101-200 (aOR 5.06 95% CI: 1.06 - 24.04), CD4> 200 (aOR 15, 80 95% CI: 3.18 - 78.64), status of anemia (aOR 2.00 95% CI: 1.22 - 3.26) and adherence to TB treatment (aOR 6.16 95% CI: 2.07 - 18.31) were statistically significant in multivariate analysis. Other factors such as age, classification of TB disease and HIV stage were not significant (p values> 0.05).

Conclusion: Female, CD4 cell counts 101-200, CD4 count> 200, status of anemia and adherence to TB treatment determined the successful of TB treatment among HIV-TB patients. Implementation of TB/HIV collaborative program and DOTS strategy in TB treatment increases the success rate of TB treatment among HIV-TB patients at H. Adam Malik General Hospital.

Keyword: success, tuberculosis treatment, HIV-TB

INTISARI

Pendahuluan: Ko-infeksi TB/HIV saat ini menjadi ancaman kesehatan serius bagi penduduk dunia. Upaya penanggulangan program TB maupun HIV selama ini masih menghadapi kendala apalagi jika kedua penyakit

tersebut bersekutu akan lebih menyulitkan dan menjadi tantangan bagi penanggulangan kedua program. Baik TB maupun HIV, keduanya mempunyai *burden disease* yang cukup tinggi untuk segera ditangani. Pengobatan TB yang adekuat pada pasien koinfeksi dapat menekan tingginya angka morbiditas dan mortalitas pasien, mencegah kegagalan terapi serta meningkatkan angka keberhasilan.

Tujuan: Mengetahui proporsi keberhasilan pengobatan TB pada penderita HIV di RSUP H. Adam Malik Medan tahun 2011-2013 serta mengidentifikasi faktor-faktor yang mempengaruhi keberhasilan pengobatan TB-nya.

Metode: Desain penelitian yang digunakan adalah *case control*, menggunakan data sekunder Poliklinik VCT Pusyansus RSUP H. Adam Malik Medan 2011-2013.

Hasil: Rata-rata keberhasilan pengobatan TB pada penderita HIV di RSUP H. Adam Malik Medan tahun 2011-2013 sebesar 68,56%. Jenis kelamin laki-laki, umur ≤40 tahun, lesi TB di paru, jumlah CD4 <200, status anemia, stadium 3 HIV dan keteraturan pengobatan OAT mendominasi penelitian ini, masing-masing sebesar 60,82%, 76,29%, 71,13%, 74,23%, 60,82%, 55,15% dan 53,09%. Variabel jenis kelamin (aOR 3,87 95%CI: 1,21 - 18,31), jumlah CD4 101-200 (aOR 5,06 95%CI: 1,06 - 24,04), CD4 >200 (aOR 15,80 95%CI: 3,18 - 78,64), tidak anemia (aOR 2,00 95%CI: 1,22 - 3,26) dan keteraturan pengobatan TB (aOR 6,16 95%CI: 2,07 - 18,31) berhubungan signifikan dalam analisis multivariat. Faktor lain yaitu umur, klasifikasi penyakit TB dan stadium HIV tidak bermakna (nilai p>0,05).

Simpulan: Jenis kelamin perempuan, jumlah CD4 101-200, jumlah CD4 >200, tidak anemia dan teratur menjalani pengobatan OAT menentukan keberhasilan pengobatan TB pada penderita HIV-TB. Implementasi program kolaborasi TB/HIV dan penerapan strategi pengobatan TB dengan DOTS meningkatkan angka keberhasilan pengobatan TB di RSUP H. Adam Malik Medan.

Kata kunci: keberhasilan, pengobatan tuberkulosis, HIV-TB

INTRODUCTION

World Health Organization (WHO) in 2000 has launched a program known as the Millennium Development Goals (MDGs). The MDG program contained 8 main goals to be achieved within 15 years as an attempt to resolve issues related to human rights, poverty, education, health and environment. One of the targets to be achieved is the fight against HIV/AIDS, tuberculosis, malaria and other infectious diseases[1].

HIV/AIDS epidemic so far has infected almost 78 million people and caused 39 million deaths[2,3,4]. In 2014, about 36.9 million people were reported to be living with HIV/AIDS[4]. The HIV-infected individuals were vulnerable to other opportunistic infections, including TB. Tuberculosis was the second most common diseases found in people living with HIV (PLWH) after oral candidiasis. Along with HIV, both of them were the most leading deaths from all infectious diseases in the world[5,.6]. Approximately 13% or 1.1 million of the 9 million TB patients in the world were infected with TB/HIV and about 360,000 died in 2013 [6]. In people living with HIV, the risk of developing tuberculosis is increased 5-15% per year compared to immunocompetent individuals who only at risk of 5-10% throughout their lifetime[7].

The number of PLWH in North Sumatra province was increasing from year to year. Hence, it was not surprising that North Sumatra belonged to the top 10 provinces in Indonesia which has the highest cumulative cases of AIDS. Meanwhile the city of Medan was the main contributor of HIV/AIDS cases in North Sumatra

throughout 2013[5,8]. Similar trend has been seen in the number of HIV-TB cases in Medan. Since the TB program has integrated with HIV program at H. Adam Malik General Hospital, a total of 1026 coinfected patients have been getting treatment[9].

Both TB and HIV have a strong synergistic effect that mutually influence each other. HIV infection causes the depletion of CD4 cells such as lymphocytes, macrophages and monocytes. Besides that, the virus altered their function as well. These cells are very important in controlling the infection against pathogenic microorganisms that enter the body including Mycobacterium tuberculosis[10]. The presence of TB will increase HIV replication, accelerate the progression of the disease thus aggravate the condition of patients[11,12,13]. Meanwhile HIV infection will lead to increase proliferation of TB bacteria and activate latent TB [14,15,16]. Ultimately this will increase the risk of transmission and spread of the disease, affecting the clinical manifestations of TB in PLWH, treatment of patients and the outcomes of treatment[15,17].

The TB program in HIV patients also apply the same strategy with TB patients without HIV. Through the DOTS strategy, patients are directly supervised by health workers assisted by a medication supervisor. This is done to ensure the regularity and compliance of the patient during treatment[18,19]. According to WHO, the treatment of tuberculosis in HIV patient is given within a minimum of 6 months, generally among HIV it takes longer, approximately 8-9 months. Some cases have even reached 1 year of treatment and often the treatment outcome among HIV patients tend to be poor[9,18].

The enormous problem that arise due to both diseases give a challenge for tuberculosis and HIV disease control, and it will be more dangerous if the disease is allied. Some obstacles have been faced in handling coinfected patients starting from the detection of cases, diagnosis and management of treatment. These coinfected patients are more difficult to manage compare to individuals who have been infected with only one disease. Great effort, well coordination and strict supervision from various institution are needed in order to maximize the achievement of TB/HIV collaborative program. To achieve better treatment outcome, it is essential to know how well the implementation of TB program among HIV has been going which is indicated by the success rate of TB and identify the factors that influence the success of TB treatment. Hopefully, the burden disease of TB among HIV patients could be reduced so that the morbidity, mortality and treatment failure rate could be lowered thus preventing the emergence of MDR-TB cases[20,21].

MATERIALS AND METHODS

We conducted a case-control study using secondary data of HIV-TB patients in VCT polyclinic of H. Adam Malik General Hospital from 2011-2013. The inclusion criteria were PLWH who was also diagnosed with TB, aged > 17 years and followed the DOTS program. Meanwhile, the exclusion criteria were pregnant women, only one visit, patients referred in with incomplete baseline data and patient who moved out to other health centre.

We categorized the successful patients as a case group while the unsuccessful patients were assessed as a control group with a sample of 97 patients in each group. The successful outcome included patients who were declared as cured or have completed TB treatment while the patient who failed, default or died were classified as unsuccessful. We have collected data on patients gender, age, classification of

TB disease, CD4 cell count, hemoglobin level, stage of HIV, adherence to TB treatment and the outcome of TB treatment.

A Stata v.12. was used to process and analyze data. At first, the process of editing, cleaning, coding, entering and tabulating data were done. Then, the data was analyzed using univariate analysis, followed by bivariate using chi square test and multivariate analysis using logistic regression. The variable was statistically significant if the Odds Ratio (OR) > 1, the value 95% Confidence Interval (CI) does not exceed 1 and the p-value <0.05.

This study has received a permission from the ethics committee of Medical Faculty Gadjah Mada University and H. Adam Malik General Hospital.

RESULTS AND DISCUSSION

The average success rate of TB treatment among HIV patients in VCT polyclinic between 2011-2013 was 68.56% (Figure 1). Since the TB/HIV collaborative program was implemented at VCT polyclinic of H. Adam Malik, the success rate of TB treatment among HIV patients has increased significantly. Initially the success rate was only 56.92% in 2009, then accelerated 11.29% to 68.21% at the end of 2013. The success rate that has been found was lower than the success rate of TB treatment among HIV negative patients (85%). Nevertheless, it has reached an average rate of successful TB treatment among HIV patients globally[22].

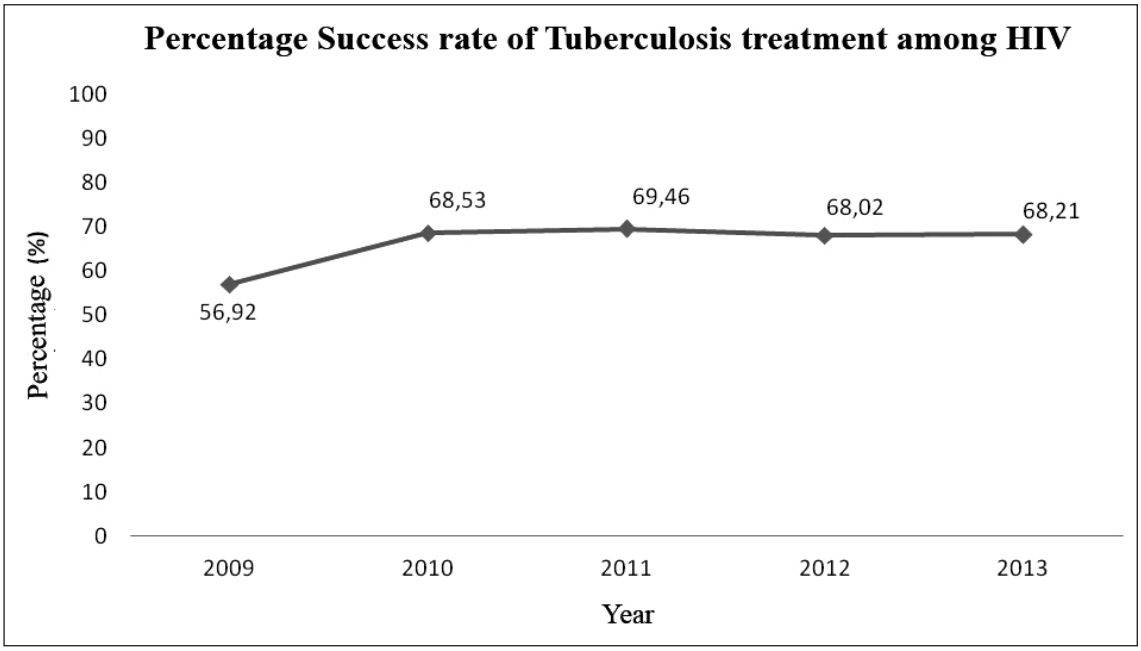

Figure 1. Success rate of tuberculosis treatment among HIV patients in VCT polyclinic of H. Adam Malik General Hospital between 2009-2013.

The proportion of male gender was 60.82%, aged ≤40 years (76.29%), TB lesions in the lung (71.13%), CD4 count <200 (74.23%), anemia (60, 82%), stage 3 of HIV (55.15%), and adherence to TB treatment (53.09%) (Table 1).

Table 1. Basic characteristics of HIV-TB patients in VCT polyclinic of H. Adam Malik General Hospital.

Basic characteristics	Successful n = 97 (%)	Unsuccessful n = 97 (%)	Total Patients n = 194 (%)
Age			
• > 40 years	21 (45,65)	25 (53,33)	46 (23,71)
• ≤ 40 years	76 (51,35)	72 (48,65)	148 (76,29)
Gender			
• Male	41 (34,75)	77 (65,25)	118 (60,82)
• Female	56 (73,68)	20 (26,32)	76 (39,18)
Classification of TB			
• Extrapulmonal	25 (44,64)	31 (55,36)	56 (28,87)
• Pulmonal	72 (52,17)	66 (47,83)	138 (71,13)
CD4 count			
• CD4 <50	11 (18,64)	48 (81,36)	59 (30,41)
• CD4 50-100	12 (31,58)	26 (68,42)	38 (19,59)
• CD4 101-200	32 (68,09)	15 (31,91)	47 (24,23)
• CD4 >200	42 (84,00)	8 (16,00)	50 (25,77)
Status of anemia			
• Anemia	52 (44,07)	66 (55,93)	118 (60,82)
• Not anemia	41 (59,42)	28 (40,58)	69 (35,57)
• Unknown	4 (57,14)	3 (42,86)	7 (3,61)
HIV Stage			
• Stage 4	41 (47,13)	46 (52,87)	87 (44,85)
• Stage 3	56 (52,34)	51 (47,66)	107 (55,15)
Adherence to TB treatment			
• No	18 (19,78)	73 (80,22)	91 (46,91)
• Yes	79 (76,70)	... (23,30)	103 (53,09)

From bivariate analysis (Table 2) variables on gender, CD4 count 101-200, CD4 count > 200, status of anemia and adherence to TB treatment were significantly associated with successful treatment of TB among coinfected patients . Then the variables with the value of p≤0,25 were included to be analyzed in multivariate analysis. A multivariate analysis was done to determine which factor contributed the most to the success of TB treatment among HIV-TB patients.

Table 2. Bivariate and multivariate analysis of factors associated to the success of tuberculosis treatment among HIV patients

	Bivariate analysis			Multivariate analysis		
Variables	**Unadj. OR**	**95% CI**	**p-value**	**aOR**	**95% CI**	**p-value**
Age						
• > 40 years	1.00	-				
• ≤ 40 years	1.26	0.65 - 2.44	0.500			
Gender						
• Male	1.00	-		1.00	-	
• Female	5.26	2.78 - 9.93	<0.001	3.87	1.21 - 12.43	0.023
Classification of TB						
• Extrapulmonal	1.00	-				
• Pulmonary	1.35	0.72 - 2.52	0.342			
CD4 count						
• CD4 <50	1.00	-		1.00	-	
• CD4 50-100	2.01	0.78 - 5.19	0.147	4.62	0.99 - 21.47	0.051
• CD4 101-200	9.31	3.79 - 22.84	<0.001	5.06	1.06 - 24.04	0.042
• CD4 >200	22.91	8.42 - 62.30	<0.001	5.80	3.18 - 78.64	0.001
Status of anemia						
• Anemia	1.00	-		1.00	-	
• Not anemia	1.36	1.01 - 1.84	0.044	2.00	1.22 - 3.26	0.006
HIV stage						
• Stage 4	1.00	-	0.471			
• Stage 3	1.23	0.70 - 2.17				
Adherence to TB treatment						
• Yes	1.00	-		1.00	-	
• No	13.35	6.70 - 26.59	<0.001	6.16	2.07 - 18.31	0.001

*Unadj. OR = *unadjusted* OR, aOR= *adjusted* OR

Male gender (aOR 3.87 95% CI: 1.21 - 18.31), CD4 count 101-200 (aOR 5.06 95% CI: 1.06 - 24.04), CD4> 200 (aOR 15, 80 95% CI: 3.18 - 78.64), unanemia (aOR 2.00 95% CI: 1.22 - 3.26) and adherence to TB treatment (aOR 6.16 95% CI: 2.07 - 18.31) were significantly related to the success of TB treatment after being analyzed in multivariate. Of the four variables which were significant in multivariate, CD4 count> 200 contributed the most to the success of TB treatment. Other factors such as age, classification of TB disease and HIV stage were not significant.

Female patients tend to be 3 times more succeed than men (aOR = 3.87 95% CI: 1.21 - 12.43). In this study, female patients were found to be more adhere to treatment. Probably because most of them were housewives, they could manage time very well between their activity and needs of treatment, unlike men who have lost a lot of time due to high mobility of work and outside activities. In addition, smoking habits, alcohol consumption and using drugs (IDUs) tend to be lower in women than men. All of these factors might influence the success of TB treatment in HIV patients [15,23,24].

Multivariate analysis showed that patients with CD4 counts> 200 had a chance of 15.80 (95% CI: 3.18 to 78.64) more succeed than patients with CD4 counts <50. Similar thing appeared on patients with CD4 counts between 101-200, they were 5 times more likely to be successful whereas patients with CD4 cell counts of 50-100 also has a tendency to succeed eventhough not statistically significant. Low CD4 count was identically associated with more advanced disease, heavier immunodeficient and more susceptibel against other infections, hence these patients were less likely to be successful in TB and ARV treatment[15,25,26].

The severity of anemia might indicate an increased in disease progression especially in chronic diseases such as TB and HIV. Moreover, the degree of anemia also determined patients prognosis and presented the progress of the given therapy, therefore, the anemic conditions need to be strictly supervised[27,28]. HIV-TB patients without anemia were more likely to succeed in treatment of TB than patients with anemia (aOR 2.00 95% CI: 1.22 - 3.26). Patients with severe anemia at the start of treatment could not survive longer. On the other hand, the less severe of anemia in patients, the lower the risk of death and failure of treatment[29].

Previous studies proved that there was a significant relationship between adherence and compliance during treatment with the cure and TB treatment success[30,31,32,33]. Similar result was found in this study. Adhered patients were nearly 14 times more likely to succeed than unadhered patients. Regularity in treatment will increase the chances of recovering, reducing the risk of failure and relapse, prevent TB transmission and reduce the risk of MDR-TB in co-infected patients[18,20,31,34].

CONCLUSION

Being female, CD4 count of 101-200, CD4 count> 200, unanemia and more adhere to TB treatment determined the successful of TB treatment among HIV-TB patients. Implementation of TB/HIV collaborative program and DOTS strategy have increased the success rate of TB treatment at H. Adam Malik General Hospital.

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