

PROPORTION OF DEPRESSION IN NON-MULTIDRUG-RESISTANT PULMONARY TUBERCULOSIS PATIENTS AT CIPTO MANGUNKUSUMO GENERAL HOSPITAL AND ITS RELATED FACTORS

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ABSTRACT

Aim: To determine the proportion of depression in non-multidrug-resistant pulmonary TB patients at Cipto Mangunkusumo General Hospital and also its related factors. **Method:** A cross-sectional study of 122 non-multidrug-resistant pulmonary TB patients was done at outpatient department of Cipto Mangunkusumo General Hospital from August to October 2018. The diagnosis of depression was made by interview according to Diagnostic and Statistical Manual of Mental Disorder-V (DSM-V) criteria, and severity of depression is determined using Beck Depression Inventory-II (BDI-II). Bivariate and multivariate analysis using the logistic regression test was done using SPSS.

Results: From 122 patients with non-multidrug-resistant pulmonary TB, the proportion of depression is 48,4%. There are 2 factors related to depression in non-multi-drug resistant pulmonary TB patients, which are the occurrence of side effects from TB treatment ($p < 0,001$; OR 7,13; 95% CI 2,67 - 19,03), and the presence of other chronic disease ($p < 0,001$; OR 12,90; 95% CI 3,87 - 4,01 - 41,50).

Conclusion: The proportion of depression in non-multidrug-resistant pulmonary TB patients at Cipto Mangunkusumo General Hospital is 48,4%. The occurrence of TB treatment side effects, and the presence of chronic disease comorbidities are related to depression in non-multidrug-resistant pulmonary TB patients.

Keywords: depression, non-multi-drug resistant pulmonary Tuberculosis

ABSTRAK

Tujuan: Mengetahui proporsi depresi pada pasien TB paru tidak resisten obat di RS Cipto Mangunkusumo serta mengetahui faktor-faktor apa saja yang berhubungan dengan kejadian depresi pada pasien TB paru.

Metode: Studi dengan desain potong lintang terhadap 122 pasien TB paru tidak resisten obat yang berobat jalan di poliklinik paru RS Cipto Mangunkusumo dari bulan Agustus hingga Oktober 2018. Diagnosis depresi ditegakkan dengan wawancara menurut kriteria diagnosis dari Diagnostic and Statistical Manual of Mental Disorder-V (DSM-V) dan derajat depresi ditentukan menggunakan kuesioner Beck Depression Inventory-II (BDI-II). Analisa bivariat dan multivariat dengan uji regresi logistik dilakukan dengan menggunakan SPSS

Hasil: Dari 122 pasien dengan TB paru tidak resisten obat yang menjadi subyek penelitian,

didapatkan proporsi depresi sebesar 48,4%. Terdapat dua faktor yang berhubungan dengan kejadian depresi pada pasien TB paru tidak resisten obat yaitu adanya efek samping obat anti TB ($p < 0,001$; OR 7,13; IK 95% 2,67 - 19,03), dan adanya komorbiditas penyakit kronik ($p < 0,001$; OR 12,90; IK 95% 4,01 - 41,50)

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PROPORTION OF DEPRESSION IN NON-MULTIDRUG-RESISTANT PULMONARY TUBERCULOSIS PATIENTS AT CIPTO MANGUNKUSUMO GENERAL HOSPITAL AND ITS RELATED FACTORS

Simpulan: Proporsi depresi pada pasien TB paru tidak resisten obat di RS Cipto Mangunkusumo sebesar 48,4%. Adanya efek samping obat anti TB dan komorbiditas penyakit kronik berhubungan dengan kejadian depresi pada pasien TB paru tidak resisten obat.

Kata kunci: depresi, Tuberkulosis paru tidak resisten obat

INTRODUCTION

Depression comorbidity is common in pulmonary Tuberculosis (TB) patients. From a cohort study, the risk of having depression is 1.53 times higher in TB patients.¹ The prevalence of depression in TB patients varies between studies and ranging from 27.7% to 80%.²⁻⁶ A study conducted by Basuki, et al.⁷ found that there are strong linier relationship between depression and treatment compliance in pulmonary TB patients. Low treatment compliance will result in increased morbidity, mortality, re-hospitalization rate and risk of developing Multi Drug Resistant Tuberculosis (MDR-TB).^{2,8-10}

There are many factors contribute to depression. These factors include the socio-demographic profile of TB patients such as older age, female gender, low education level,³ marriage status,¹¹ and low income.² From the clinical aspects of TB infection, being underweight in which body mass index (BMI) < 18,5 kg/m²,³ persistent cough,⁵ still treated in the intensive phase,¹² being on retreatment for TB infection,⁶ having TB treatment side effects,¹³ having multiple chronic disease comorbidities,¹⁴ and more severe TB infection¹⁵ are factors associated with increased risk of having depression in pulmonary TB patients.

Either depression or pulmonary TB condition will activate the inflammation process in the body. Thus increasing the production of proinflammatory cytokines such as *Interleukin-6* (IL-6), *Tumor Necrosis Factor- α* (TNF- α), and *C-Reactive Protein* (CRP).¹⁶ The inflammation state in these conditions can be seen by examining the Neutrophil-Lymphocyte Ratio (NLR). From previous study, patients with depression have increased NLR value. This finding also correlates

to the degree of depression and increased risk of having cardiovascular event.¹⁷

METHOD

This is a cross-sectional study involving 122 non-MDR pulmonary TB patients at the outpatient department of Cipto Mangunkusumo Hospital. The study takes place from August to October 2018. The sample size is determined using the formula for comparing two proportions of independent variables and the formula to compare two means for the NLR variable. From calculation we determined the minimal sample size was 120. We used consecutive sampling technique in this study. The inclusion criteria was adult > 18 years old pulmonary TB patients, who are willing to participate in the study. Meanwhile, the exclusion criteria include having only extra pulmonary TB, MDR TB, HIV comorbidity, being hospitalized for at least 5 days in the last month, and having condition which involved the production of blood cells in the marrow.

The study participants were interviewed for depression symptoms according to the *Diagnostic and Statistical Manual of Mental Disorder-V* (DSM-V) criteria, and then asked to fill the Beck Depression Inventory II (BDI-II) questionnaire which has been validated before for the Indonesian population.¹⁸ We also obtained blood sample for the NLR evaluation for each participant. Statistical data processed using Statistical Product for Social Science (SPSS) program version 20,0. The bivariate analysis for categorical variables are done using the Chi square method, or using Fischer test if the requirements are not met. For the NLR variable, we used the Mann-Whitney test and the multivariate analysis are done using the logistic regression test.

RESULTS

From August to October 2018, we have 122 study participants who fulfill the inclusion criteria and not met the exclusion criteria. There are no drop out subject All participants are included in the analysis. Depression was found in 59 study participants (48.4%). Mild depression is found in 57,6% depressed subject participant, meanwhile moderate depression found in 27,1%, and severe depression in

15.3% subject with depression. From the BDI-II questionnaire, we found that fatigue is found in all subjects with depression. Other main depressive symptoms include feeling of guilt, sleeping problems, and change of appetite.

The ratio of male and female are 45,8%, and 54,2% respectively. Most of the study participants are more than 40 years old in age (57,4%). Most of them are married, have lower income compared to Jakarta regional minimal wage. The mean for BMI in all study participant are $20,13 \pm 3,506$ kg/m². Most of them (68%) have chronic disease comorbidities. These comorbidities include rheumatic and autoimmune disease in 23,8%, malignancy in 21.3%, hypertension in 19.7%, and diabetes mellitus in 16,4% subjects. Majority of the study participants are first time having pulmonary TB, were in the maintenance phase of TB treatment, have moderate TB symptoms, and no longer have cough symptom. There are 58.2% study participant who experience side effects from TB treatment. The most reported side effects

are nausea, followed by itching and allergic reaction. We found that the NLR value is higher in the depressed group with median value of 2,53 (1,14-9,22), and median of 2,15 (0,95-5,62) in the non-depressed group. The characteristic of study participants can be seen in table 1.

From bivariate analysis, we found that low education ($p = 0,029$; OR 4,082; 95%CI 1,06-15,65), having TB treatment side effects ($p < 0,001$; OR 6,36; 95%CI 2,84-14,34), and subjects with chronic disease comorbidities ($p < 0,001$; OR 12,66; 95%CI 4,47-35,88) are related to depression in non-MDR pulmonary TB patients. From multivariate analysis, we found that the occurrence of side effects from TB treatment ($p < 0,001$; OR 7,13; 95% CI 2,67 – 19,03), and the presence of other chronic disease ($p < 0,001$; OR 12,90; 95% CI 3,87 – 41,50) are related to depression in non-MDR pulmonary TB patients. The bivariate analysis can be seen in table 2, meanwhile the multivariate analysis can be seen in table 3.

Table 1. Study participant characteristics

Characteristics	N =122	Mean \pm SD / median (min-max)
Gender, n (%)		
Male	59 (48,4)	
Female	63 (51,6)	
Age (year), n (%)		46 (18-77)
18-29	28 (23)	
30-39	24 (19,7)	
40-49	18 (14,8)	
50-59	32 (26,2)	
≥ 60	20 (16,4)	
Ethnic, n (%)		
Betawi	34 (27,9)	
Sunda	16 (13,1)	
Jawa	31 (25,4)	
Tapanuli	9 (7,4)	
Padang	11 (9)	
Others	21 (17,2)	
Education level, n (%)		
Less than 9 years basic education program	13 (10,7)	
More than 9 years basic education program	109 (89,3)	
Marital status, n (%)		
Single	33 (27)	
Married/had married	89 (73)	
Income status, n (%)		
Low	81 (66,4)	
High	41 (33,6)	
Chronic disease comorbidities, n (%)		
Present	83 (68)	
Absent	39 (32)	

Table 1 (continued). Study participant characteristics

Characteristics	N =122	Mean ± SD / median (min-max)
Type of comorbidities n (%)		
Rheumatic and autoimmune disease	29 (23,8)	
Malignancy	26 (21,3)	
Hypertension	24 (19,7)	
Diabetes Melitus	20 (16,4)	
Others	19 (15,5)	
Cardiovascular	6 (4,9)	
Benign hematologic disorder	6 (4,9)	
Chronic liver disease	6 (4,9)	
Chronic kidney disease	5 (4,1)	
Asthma	3 (2,5)	
Thyroid disease	3 (2,5)	
Stroke	2 (1,6)	
TB treatment phase, n (%)		
Intensive	42 (34,4)	
Maintenance	80 (65,6)	
Retreatment for TB, n (%)		
Yes	40 (32,8)	
No	82 (67,2)	
Persistent cough, n (%)		
Yes	12 (9,8)	
No	110 (90,2)	
Sputum results, n (%)		
Positive	16 (13,1)	
Negative	63 (51,6)	
No data	43 (35,2)	
TB treatment side effects, n (%)		
Present	71 (58,2)	
Absent	51 (41,8)	
Side effects, n (%)		
Gastrointestinal	47 (38,5)	
Allergic reaction	37 (30,3)	
Neurological symptoms	19 (15,6)	
Liver dysfunction	5 (4,1)	
Eye problem	3 (2,5)	
Psychiatric symptoms	1 (0,8)	
TB severity, n (%)		
Mild	35 (28,7)	
Moderate	50 (41)	
Severe	37 (30,3)	
Presence of extra pulmonary TB, n (%)		
Present	12 (9,8)	
Absent	110 (90,2)	
Types of extra pulmonary TB, n (%)	n = 12	
Pleuritis	5 (41,7)	
Lymphadenitis	2 (16,7)	
Abdomen/Peritonitis	3 (25)	
Chorioretinitis	1 (8,3)	
Meningitis	1 (8,3)	
Osteomyelitis	1 (8,3)	
Neutrophil-Lymphocyte Ratio		2,35 (0,95-9,22)
Body mass index (kg/m ²), n (%)		20,13 ± 3,506
< 18.5	42 (34,4)	
≥ 18,5	80 (65,6)	

Table 1 (continued). Study participant characteristics

Characteristics	N =122	Mean ± SD / median (min-max)
Depression, n (%)		
Present	59 (48,4)	
Absent	63 (51,6)	
Depression severity n (%)	n = 59	
Mild	34 (57,6)	
Moderate	16 (27,1)	
Severe	9 (15,3)	

Table 2. Bivariate analysis

Variables	Depression		P	OR (IK 95%)
	Present	Absent		
Gender, n (%)				
Female	32 (54,2)	31 (49,2)	0,578	1,223 (0,601-2,492)
Male	27 (45,8)	32 (50,8)		
Age, n (%)				
≥ 60 years	13 (22)	7 (11,1)	0,103	2,261 (0,833-6,135)
< 60 years	46 (78)	56 (88,9)		
Educational level, n (%)				
Not Finished 9 years basic program	10 (16,9)	3 (4,8)	0,029	4,082 (1,064-15,655)
Finished 9 years basic program	49 (83,1)	60 (95,2)		
Marital status, n (%)				
Married/had married	45 (76,3)	44 (69,8)	0,424	1,388 (0,62-3,107)
Single	14 (23,7)	19 (30,2)		
Income level, n (%)				
Minimum wage	43 (72,9)	38 (60,3)	0,142	1,768 (0,823-3,797)
Above minimum wage	16 (27,1)	25 (39,7)		
BMI, n (%)				
< 18.5 kg/m ²	22 (37,3)	20 (32,3)	0,561	1,249 (0,590-2,642)
≥ 18.5 kg/m ²	37 (62,7)	42 (67,7)		
Chronic disease comorbidity, n (%)				
Present	54 (91,5)	29 (46)	<0,001	12,662 (4,468-35,880)
Absent	5 (8,5)	34 (54)		
TB treatment phase, n (%)				
Intensive	21 (35,6)	21 (33,3)	0,793	1,105 (0,524-2,333)
Maintenance	38 (64,4)	42 (66,7)		
Retreatment for TB, n (%)				
Yes	23 (39)	17 (27)	0,158	1,729 (0,806-3,710)
No	36 (61)	46 (73)		
Persistent cough, n (%)				
Yes	6 (10,2)	6 (9,5)	0,905	1,075 (0,327-3,541)
No	53 (89,8)	57 (90,5)		
TB treatment side effects, n (%)				
Present	47 (79,7)	24 (38,1)	< 0,001	6,365 (2,84-14,345)
Absent	12 (20,3)	39 (61,9)		
TB severity, n (%)				
Moderate - severe	46 (78)	41 (65,1)	0,116	1,899 (0,849-4,245)
Mild	13 (22)	22 (34,9)		
Neutrophil-Lymphocyte ratio, median (min-max)	2.53 (1,14-9,22)	2.15 (0,95-5,62)	0,101	

Table 3. Multivariate analysis

Variables	P	OR (IK 95%)
Age \geq 60 years old	0,694	1,30 (0,35 – 4,88)
Low educational status	0,057	4,78 (0,95 – 23,95)
Minimum wage	0,564	1,35 (0,49 – 3,76)
Presence of chronic disease comorbidity	< 0,001	12,90 (4,01 – 41,50)
On retreatment for TB	0,684	0,81 (0,29 – 2,25)
Presence of TB treatment side effects	< 0,001	7,13 (2,67 – 19,03)
More severe form of TB infection	0,09	2,44 (0,87 – 6,84)
Higher Neutrophil-Lymphocyte ratio	0,300	0,84 (0,60 – 1,17)

DISCUSSION

The proportion of depression in this study is 48.4%. This is similar with previous study done by Ige, et al⁴ who found the prevalence of depression is 45.5%, and study conducted by Buberwa¹² who found that the prevalence of depression is 46.9%. Our study result is not much different from previous study conducted in Indonesia by Nahda, et al¹⁴ who found the prevalence of depression is 67.4% among pulmonary TB patients.

Having chronic disease comorbidity is related to depression from our study. This finding agrees with other studies.^{6,14} Depression is known to be related to chronic disease and can influence treatment adherence, and also relationship with the health workers. Patients with depression will develop high risk behavior such as sedentary lifestyle and tendency toward smoking.¹⁹ Other study also showed that the risk of depression will increase with multiple comorbidities.²⁰

Side effects of TB treatment also a significant factor related to depression from our study. This finding also agrees with previous studies.^{11,13,21} The most side effects experienced by our study participants are gastrointestinal disturbance, particularly nausea. This finding maybe caused by the fact that many of our study participant consumes other drugs related to their comorbidities. Having treatment side effects will cause significant stress and also negative perception toward the TB treatment itself, causing increased risk of having depression.

Different from study conducted by Kehbila, et al,⁶ female gender is not related to depression from our study. In pulmonary TB population, gender influence to depression are still debatable. Other study conducted by Sulehri, et al² found that

male gender is more prone to depression. They tend to be depressed when having pulmonary TB infection because of the limitation in work, and also higher responsibilities in their family economic condition. They also face higher risk of stigmatization from the community.

Other factors evaluated in our study which include older age, low educational status, underweight, and being on retreatment for TB infection are not related to depression in our study. This difference from other studies may be caused of different sample size which can affect the power of this study.^{3,4,6,11}

From our study, having low income does not related to depression, eventhough most of our study participant have minimum wage. This finding also differ from previous study by Issa, et al⁵, and Sulehri, et al.² From literature, the psychological effect and burden of poverty will significantly increase stress in TB patients. Our finding can be caused by the national health insurance owned by > 95% of our study population. This may be the cause of the different result in our study, because having health insurance significantly reduce the cost of treatment needed by patients.

Tuberculosis treatment phase, and persistent cough symptoms are not related with depression in this study. This finding also differ from previous study by Buberwa, et al,¹² and Mandaknali, et al.¹¹ Their study found that being in the intensive phase of TB treatment, are related to depression. Our study have different results from the previous study because we exclude subjects who has history of hospital admission in the last month. Therefore, most of our study participant are already in the maintenance phase of TB treatment and

only few of them still having cough symptoms because of this exclusion criteria. Another cause of this difference is the characteristic of pulmonary TB patients in Cipto Mangunkusumo hospital. Many of our pulmonary TB patients diagnosed without classical symptoms such as chronic cough, but based on incidental finding or TB screening when doing the perioperative assessment or before giving chemotherapy or immunosuppressive agent.

We determined the degree of TB infection based on the initial symptoms and radiological features at first time diagnosis, meanwhile, our study participants are mostly in the maintenance phase. This may cause the difference between our findings compared to previous study regarding the degree of TB infection. The study conducted by Panchal¹⁵ found that the degree of TB infection are related to depression. More severe form of TB infection related to greater suffering, and consequent strain on psychological coping mechanism.

Neutrophil-Lymphocyte ratio are not related to depression in our study. Even though the median of NLR in the depressed group is higher than the non-depressive group, this result are not statistically significant. This finding did not agree with previous studies which showed that patient with depression will have increased NLR.^{22,23} From literature, we also know that NLR increased in chronic diseases such as diabetes,²⁴ systemic lupus erythematosus,²⁵ and malignancy.²⁶ The different result from our study may be caused by the number of samples, even though many of our study participant has chronic diseases comorbidities.

STUDY LIMITATION

This study used structured interview according to the DSM-V criteria of depression, and stratified depression using the validated BDI-II questionnaire for Indonesian population. This study also the first study who analyses NLR in TB patients with depression. Nevertheless, this study is a cross sectional study, so we can't explain the temporal relationship between the variables and depression. This study also takes place in only one centre which is Cipto Mangunkusumo hospital. The characteristic of pulmonary TB patients in this hospital is quite

different from the population because of the many comorbidities, and the non-classical symptoms of TB infection. Because of this reason, the result of this study can't be generalized to all the non-MDR pulmonary TB patients.

CONCLUSION

The proportion of depression in non-multidrug-resistant pulmonary TB patients in Cipto Mangunkusumo hospital is 48,4%. Having chronic disease comorbidities, and experiencing side effects of TB treatment are related with depression in non-multidrug-resistant pulmonary TB patients in Cipto Mangunkusumo hospital.

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