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Research Report

DETERMINANT FACTORS OF DROP OUT (DO) AMONG MULTI DRUGS RESISTANCE TUBERCULOSIS (MDR TB) PATIENTS AT JAKARTA PROVINCE IN 2011 TO 2015

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ABSTRACT

The prevalence of Drop out (DO) among Multi Drugs Resistant Tuberculosis (MDR TB) patients increases every year in Jakarta Province. The latest data of 2016 contains 367 drug resistant TB patients and 78 patients (21.2%) were DO. This study was aimed to analyze the determinant factors of Drop Out (DO) among MDR TB patients in Jakarta Province between 2011 to 2015 based on risk factors of age, sex, HIV status, sputum test, type of patient, number of previous treatments and number of drugs resistance. This study was used secondary data that source from cohort registration e-TB Manager from DKI Jakarta Health Office with total 516 samples. The design study was an observational cross sectional quantitative study. DO is a condition of patients who have been treated and drop out of treatment for 2 consecutive months or more. The crude prevalence of DO among MDR TB patients was 44.6%. Trend of DO among MDR TB was increased since 2011 to 2015. There was a further increase more than 10% in every year. The proportion of DO among MDR TB in Jakarta was more than 64 years old (63.6%), male (47.3%), patients with status HIV negative (44.9%), patients that never or ever consumed drugs less than 1 month (61.2%), and patients with >2 drugs resistance (45.7%). The results of this study indicated that proportion of DO among MDR TB patients at Jakarta Province in 2011-2015 was high. Therefore, it is necessary efforts that can decrease DO cases among MDR TB patients. This study was expected to be a reference for Jakarta Province Health Office in implement P2TB Program implementation and reach target precisely.

Keywords: *Drop Out, MDR, Tuberculosis, Jakarta, determinant factors*

ABSTRAK

Prevalensi Drop Out/ Putus Obat (DO) pada pasien Tuberkulosis Multi Drugs Resistant (TB MDR) terus meningkat setiap tahunnya di Provinsi DKI Jakarta. Data terakhir di tahun 2016 tercatat sebanyak 367 pasien TB MDR dan 78 pasien (21.2%) berstatus DO. Penelitian ini bertujuan untuk menganalisis faktor determinan kejadian Drop Out (DO) pada pasien TB MDR di Provinsi DKI Jakarta pada tahun 2011 sampai 2015 berdasarkan faktor risiko umur, jenis kelamin, status HIV, hasil test sputum, tipe pasien, riwayat pengobatan TB sebelumnya (jumlah), dan jumlah resistansi obat. Data yang digunakan adalah data sekunder yang bersumber dari data register kohort e-TB Manager dengan jumlah sampel sebanyak 516 sampel. Desain penelitian ini adalah studi kuantitatif observational cross sectional. DO ada studi ini adalah kondisi pasien yang telah diobati dan putus pengobatan selama 2 bulan berturut-turut atau lebih. Prevalensi DO pasien TB MDR pada penelitian ini yaitu 44.6% yang merupakan prevalensi kasar. Tren kejadian DO pada penelitian ini cenderung mengalami peningkatan dari tahun 2011 hingga 2015 dan prevalensi DO terus melebihi angka 10% setiap tahunnya. Proporsi DO pada pasien TB MDR di Provinsi DKI Jakarta tahun 2011-2015 banyak terjadi pada pasien dengan usia >64 (63.6%), jenis kelamin laki-laki (47.3%), status HIV negatif (44.9%), pasien yang belum pernah atau pernah menelan obat namun kurang <1 bulan (58.8%), dan paling banyak pada pasien dengan jumlah resistansi >2 obat (45.7%). Hasil penelitian ini menunjukkan bahwa proporsi kasus DO pada pasien TB MDR di Provinsi DKI Jakarta tahun 2011-2015 masih tinggi. Oleh karena itu, perlu adanya

upaya untuk dapat mengurangi jumlah kasus DO pada pasien TB MDR. Diharapkan penelitian ini dapat menjadi acuan bagi Dinas Kesehatan Provinsi DKI Jakarta dalam menjalankan program P2TB yang lebih baik dan tepat sasaran.

Kata kunci: *Drop Out, MDR, Tuberkulosis, Jakarta, Faktor Determinan*

INTRODUCTION

Multi Drug Resistant Tuberculosis (MDR TB) is a condition in which *Mycobacterium tuberculosis* resistant to the type of first-line drugs treatment such as rifampicin and isoniazid simultaneously, with or without being followed by other first-line drugs resistance treatment.[1] The number of incidences of MDR TB in the world by 2014 was estimated to be 300.000 new cases of MDR TB and by 2014 increased to 480.000 new cases of MDR TB.[2] In Indonesia, the number of confirmed cases of MDR TB discovery was likely to increase from 2009 to 2015.[3] The spread of MDR TB cases is mostly found in the provinces of Jakarta, West Java, and East Java.[3]

MDR TB takes 20-26 months of treatment, expensive requires, more complex treatment, and more side effects of drug sensitive TB, making it difficult to be controlled.[1] The bmain factor in TB treatment failure was treatment termination before the trial period was completed; it's called as Drop Out (DO) cases.[4] DO is a condition of patients who have been treated and drop out from treatment for 2 consecutive months or more.[1]

In Indonesia, the rate of DO among patients with drug resistant TB in 2009 was 10.7%. Unfortunately, this number increased in 2013 to 28.7%.[5] DO rates among TB patients exceeding 10% can result in a high proportion of future re-treatment cases.[4]

In Jakarta Province, the number of drug resistant TB patients based on e-TB Manager surveillance data in Jakarta Provincial Health Office 2011-2016 was tended to increase. While the rate of DO among drug resistant TB patients from 2011 to 2016 was very volatile, but the DO number of drug resistant TB patients was always more than 10% annually. The latest data of 2016 contained 367 drug resistant TB patients and 78 patients (21.2%) were DO. The purpose of this study was to analyze the determinant factors of Drop Out (DO) among MDR TB patients in Jakarta Province between 2011 to 2015.

MATERIAL AND METHOD

The design study was an observational cross sectional quantitative study. Independent variables include predisposing factors (age, sex, and HIV status), and enabling factors (duration of treatment, adherence, previous TB treatment history, and number of drugs resistances). Dependent variable was DO among MDR TB patients. The definition of DO in this study was MDR TB patients who didn't come for treatment and didn't take the medication for 2 consecutive months or more before the end of treatment. Inclusion criteria of this study include were patients with pulmonary MDR TB, age >15 years, domiciled in Jakarta Province, pulmonary MDR TB patients have been evaluated the final results of treatment, and pulmonary MDR TB patients that data were recorded fully in e-TB Manager of Jakarta Provincial Health Office. Exclusion criteria were pulmonary MDR TB patients who died and failed treatment related to discontinued treatment or requires a permanent change in MDR TB treatment; mixture of two or more MDR drugs. This study was using secondary data (e-TB Manager) from Jakarta Provincial Health Office with total 516 samples. The analysis data used Chi-Square through STATA 12 software. This study has obtained permission from the owner of the data Jakarta Provincial Health Office) with letter number 1713/SDK/XI/2017. In addition, this study also has passed ethical approval from Ethical Committee of Public Health Faculty, Universitas Indonesia Reg number: 08/UN2.F10/PPM.00.02/2018. Name of respondents/patients withheld by using ID for privacy of respondents.

RESULT AND DISCUSSION

Firstly, the total of eligible sample who include in this study was 602 samples. Then, there were 86 samples have been excluded which was consist of 71 of patients died and 15 of failed treatment. So, the percentage of participant rate was 85.7%. Table 1 was showed the percentage of multidrugs tuberculosis patients in this study.

Table 1 was showed the results of this study indicated the prevalence of DO among patients with MDR TB at DKI Jakarta Province in 2011-2015 was 44.6%.

Figure 1 was described about the prevalence of MDR TB patients at DKI Jakarta Province in 2011-2015 increased from 2011 to 2014, then it was decreased by 2015 to 24.6%. While the prevalence of MDR TB patients at DKI Jakarta Province in 2011-2015 tends to increased and >10% each year. The highest prevalence of DO occured in 2015 (53.50%) and the lowest in 2011 (16.7%).

Table 1. Description of prevalence of DO among MDR TB Patients

Patient Status	N	%
Not DO (Recover and Treatment Complete)	286	55.4
DO	230	44.6
Total	516	100

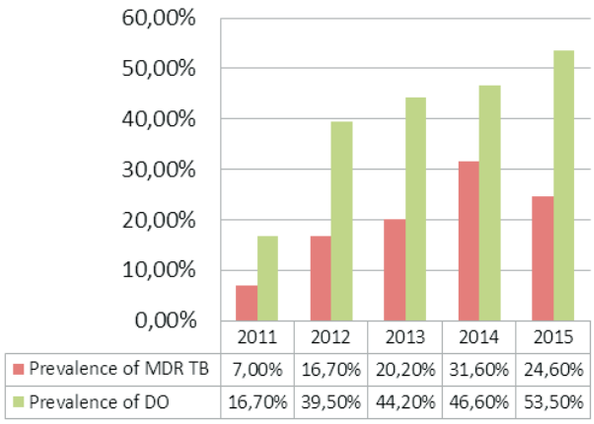

Figure 1. Trend of prevalence of DO among MDR TB Patients

In some previous studies, the prevalence of DO among MDR TB patients was lower than the prevalence of DO obtained in this study (44.6%) (Figure 1).[6] The prevalence of MDR TB patients with DO in previous studies in Russia was showed 12% prevalence of DO MDR TB patients.[6] Studies which conducted in Lima City, Peru showed as much as 10%.[7] Studies which conducted in KwaZulu-Natal, South Africa showed the prevalence of DO in patients with MDR by 21%.[8] A study in Uzbekistan which showed a large prevalence of DO in patients with MDR TB by 20%.[9] It was indicated that the prevalence of DO in MDR TB patients might be influenced by other factors such as geography, environmental, and behavioral variations.[9]

From previous similar studies in Indonesia, the findings of prevalence results in this study reached 41.1% higher than previous studies.[10] A study that has been done at Persahabatan Hospital in 2010 was showed the prevalence of DO in patients with MDR TB was 34.5%.[10] In Githrif's study (2016) was mentioned that the prevalence of DO in patients with MDR TB at Gresik in 2011-2015 was 33.7%.[11]

The high prevalence rate of DO which find in this study can be attributed to the limitations of this study. In this study, a considerable number of patients couldn't be included in the study because they did not met the inclusion criteria and the exclusion criteria, so the proportion of MDR TB patients at DKI Jakarta Province in 2011-2015 was high.

Table 2 was showed correlation between predisposing factors and DO among MDR TB patients. The results showed that the age group of 45-64 years had significant association with DO of MDR TB patients with p = 0.042 and DO risk in MDR TB patients increased with age of MDR TB patients. While gender and HIV status had no significant relationship with DO among MDR TB patients. This study is in line with Lalor's research, et al. in 2013 that indicating an association between age and incidence of DO in patients with MDR TB (P value 0.022), which patients aged >45 years had a risk of 1.71 (95% CI: 1.07-2.73) for experienced DO compared to patients aged ≤45 years of MDR.[9] Other previous study was showed that age had an effect on decreasing the success of MDR TB treatment and was statistically significant (OR = 0.955; 95% CI = 0.921-0.991; p = 0.014).[12] The older age of MDR TB sufferers were more likely to have a risk of drop out or have a tendency to experience irregularity in taking medication because the older age needs additional support to access TB treatment.[13]

The proportion of sex-based DOs is more prevalent in males than in females. However, they did not show much different proportions. The statistical test was showed no significant relationship between male and female. It was found that men had a risk of DO 1.151 times (95% CI: 0.715-1.852) than women. Previous studies was showed that sex were not statistically correlated with DO among MDR TB patients with OR values of 1.6 (95% CI: 0.8-3.0).[7,14] In addition, studies were also showed that there was no significant association between gender and DO

Table 2. The Correlation between predisposing factors and DO among MDR TB patients

Variable Predisposing Factors	Patient Status		PR (CI 95%)	P Value
	Not DO N (%)	Not DO N (%)		
Age (Years)				
15-24	23 (69.7%)	10 (30.3%)	Ref	Ref
25-44	105 (63.6%)	60 (36.4%)	1.314 (0.586 – 2.947)	0.507
45-64	**46 (48.9%)**	**48 (51.1%)**	**2.4 (1.031 – 5.589)**	**0.042***
> 64	4 (40%)	6 (60%)	3.45 (0.96 – 14.958)	0.098
Gender				
Female	69 (61.1%)	44 (38.9%)	1.151 (0.715 – 1.852)	0.646
Male	109 (57.7%)	80 (42.3%)		
HIV status				
Negative	134 (56.8%)	102 (43.2%)	Ref	Ref
Positive	4 (80%)	1 (20%)	0.328 (0.036 – 2.983)	0.323
Unknown	40 (65.6%)	21 (34.4%)	0.69 (0.383 – 1.241)	0.215

incidence in MDR TB patients, it was found that male MDR TB patients had a risk of 1.4 times (95% CI: 0.96-2.05) to have DO compared with female MDR TB patients (p value 0.083).[9] Regarding to the research from Indonesia, this study is in line with several previous which were research which were that showed there was no sex relationship with the incidence of MDR patient TB patients.[11,15,16] In contrast, previous study is showed Brust's research, et al. in 2010, a significant association between sex with DO in MDR TB patients, which men had 1.9 times greater risk (95% CI 1.2-3.1) to have DO than women.[8] Other study was suggested that women were more likely to seek health care and tend to be more adherent to treatment with DOTS compared with men (Wu et al., 2013). Different opinions were also obtained from studies in Africa, Bangladesh, and Syria which was stated that married women tend to have to ask their husbands for permission to come to health services for TB treatment (Ibrahim et al., 2014).

The proportion of DO patients with MDR TB in patients with HIV negative status was higher than the proportion of MDR patients with HIV positive status. The result of statistical test was showed that there was no significant relationship between HIV status and DO with MDR TB patients with p value = 1.00 (p > 0.05). The results of this study were consistent with the study in Nigeria in 2011-2012 which shows that HIV status has no statistically significant association with DO in MDR TB patients.[17] Similar research in Sagamu, Nigeria by Daniel, et al. and Hasker's research, et al. was showed similar results that HIV status had no significant relationship with the occurrence of DO in MDR TB patients.[18,19] In contrast, in KwaZulu-Natal, South Africa in 2000-2003 was showing that patients with HIV-positive status (TB-HIV co-infection) have risk factors that can increase DO of MDR TB by 2 times (95% CI: 1.3-3.1). This might be happened because of the research was done in South Africa which had a high prevalence of HIV cases. The absence of any association in this study can occur due to the large number of MDR TB patients whose HIV status is unknown. In addition, data on TB-HIV co-infection may also have unreported data on e-TB Manager so that the proportion of HIV-positive TB patients was low (under reporting).

The results of sputum examination is an early indication to be able to know the presence of BTA. The status of this BTA examination may reflect the extent of lesions in the lung. 3+ bacilli on initial pre-treatment can be used as a predictor for difficult conversion after two months of treatment. The longer the time required for conversion will be the longer the initial treatment. This may affect the patient in treatment and may cause the patient to drop out (Nwokeukwu & Awujo, 2013).

The proportion of DO in MDR TB patients between patients was exposed to smear positive with smear negative did not show much different numbers. The proportion of DO in MDR TB patients was more prevalent in patients exposed to smear negative than the proportion of DO in smear positive patients. The result of statistical test was showed that patients who had sputum smear + at the beginning of treatment had a risk of having positive smear-positive MDR TB patients at 0.836 (95% CI: 0.504–1.385) risk of drop out compared to negative smear-negative MDR TB patients. This study was showed similar results with the previous research which is showed no significant relationship between sputum examination result and DO incidence, the value of crude OR 1.15 (95% CI: 0.7-1.89) and adjusted OR 1.02 (95% CI: 0.43-1.30) (Table 3).[18] In contrast, the results of Alobu's research, et al. was showed a significant relationship between sputum examination results and the incidence of DO in MDR TB patients, which the value of crude OR 2.1 (95% CI: 1.4-3.1) and adjusted OR

Table 3. Distribution of DO among MDR TB Patients in 2011-2015 based on enabling factors

Variable Enabling Factors	Patient Status		PR (CI 95%)	P *Value*
	No DO N (%)	DO N(%)		
Sputum test				
Negatif	48 (55.8%)	38 (44.2%)		
Positif	130 (60.2%)	86 (39.8%)	0.836 (0.504 – 1.385)	0.571
Type of Patient				
New	3 (50%)	3 (50%)	Ref	Ref
Recurent	58 (58.6%)	41 (41.4%)	0.707 (0.136 – 3.679)	0.680
Defaulter	22 (55%)	18 (45%)	0.818 (0.147 – 4.557)	0.819
Failed in Category 1	41 (63.1%)	24 (36.9%)	0.585 (0.109 – 3.134)	0.532
Failed in Category 2	49 (61.2%)	31 (38.8%)	0.633 (0.12 – 3.335)	0.589
Others (Unclear)	5 (41.7%)	7 (58.3%)	1.4 (0.195 – 10.032)	0.738
Number of Previous Treatment				
≤2 times of treatment	150 (60%)	100 (40%)		
>2 times of treatment	28 (53.8%)	24 (46.2%)	1.286 (0.705 – 2.345)	0.506
Number of drugs				
2 drugs	48 (57.8%)	35 (42.2%)	Ref	Ref
3 drugs	55 (55.6%)	44 (44.4%)	1.097 (0.609 – 1.977)	0.758
≥4 drugs	75 (62.5%)	45 (37.5%)	0.823 (0.465 – 1.457)	0.504

2.3 (95% CI: 1.5–3.6).[17] The others study was showed a significant relationship between sputum and DO results, but the OR values which were obtained in this study resulted in protective PR, with OR values of 0.57 (95% CI: 0.33 - 0.97) and adjusted OR 0.42 (0.024 - 0.75).[19]

The statistical results were showed that there was no relationship between the types of patients with DO among MDR TB patients. It was found that the "other" type (unclear history) of patient group had a risk of 1.4 times (95% CI: 0.195-10.032) for drop out compared to the new patient type group. Patients who were failed in treatment of second category had 0.633 (95% CI: 0.12-3.335) times of risk to have DO compared with new patients. Patients who were failed at first category had 0.585 times (95% CI: 0.109-3.134) of risk having DO experience compared with new patients. Defaulter patients had a risk of 0.818 times (95% CI: 0.147-4.557) to have DO compared with new patients. Recurrent patients had a risk of 0.707 times (95% CI: 0.136-3.679) to have DO compared with new patients.

This research is in line with some previous research which indicate that the type of patient did not have statistical correlation with DO in MDR TB patients.[18,17,20] In contrast, previous study Santha study, et al. (2002) and Lalor, et al. (2013) were showed that the type of patient had a significant association with DO in MDR TB patients. In the Santha study, et al (2002) were showed re-treatment patients had OR 2.5 (95% CI: 1.5-4.3) of having DO compared with the new patient type and adjusted OR 2.8 times (95% CI : 1.6-4.9).[9,21] Research from Lalor, et al. (2013) was showed that the type of patient defaulter had a risk of 2.10 (95% CI: 1.02-4.37) for DO compared with the new patient type and adjusted OR 2.38 (95% CI: 1.09-5.24), patients failed in category 2 had a risk of 0.57 times (95% CI: 0.35 to 0.93) to have DO compared with the new patient type and adjusted OR 0.85 (95% CI: 0.49-1.49).

The proportion of DO patients with MDR TB in patients in the previous treatment group group was >2 times more than patients with previous treatment amount ≤2 times. The results of statistical tests showed that there was no statistically significant relationship between the amount of previous treatment with DO in MDR TB patients. It was found that patients with previous treatment >times had a risk of 1.286 (95% CI: 0.705-2.345) for drop out compared to patients with previous treatment ≤2 times.

In fact, most MDR TB patients in Indonesia are patients with a history of previous TB treatment. Treatment which performed previously treated petients with first-line OAT, requires treatment with second-line OAT, where second-line OAT is more complicated in its management, and second-line OATs have more and more severe side effects than first-line OAT, thus allowing MDR TB patients to drop out.[1]

This study was showed similar results with previous study which was showed there was no relationship between the number of previous treatments and the incidence of DO (p value = 1.0).[20] This study is also in line with the research of Franke, et al. (2008) indicating no significant association between the number of previous treatments and the incidence of DO in MDR TB patients. Patients with previous treatment amounts >2 treatments had a risk of 1.2 times (95% CI: 0.70-2.05) for dropouts compared to patients with previous treatment ≤2 times of treatment.

Researchers have not found previous research which results indicating that there was a significant relationship between the number of previous treatments and the incidence of DO in MDR TB patients, but based on the results of research Franke, et al. in 2008, the value of OR >1 means that the number of previous treatments is a risk factor for the incidence of DO in patients with MDR TB, so the researchers included this number of previous treatment factors to be investigated as independent variables of research and variables are substantially important.[7]

The amount of OAT resistance is divided into resistant to 2 drugs, 3 drugs and ≥4 drugs. The proportion of DO in patients with drug resistant MDR 3 was higher than the proportion of DO in the group of other OAT resistance levels. The result of statistical test was showed that there was no relationship between the amount of OAT resistance with DO patient of MDR TB. The results of this study was indicated that the patient group of the ≥4 drug resistance group had a risk of 0.823 times (95% CI: 0.465-1.457) for drop out compared to the 2-drug resistance group.

The researchers also have not found previous research which their results related to the variable amount of OAT resistance indicating a statistically significant relationship between the amount of OAT resistance and the incidence of DO in patients with MDR TB, but the researcher still incorporates this amount of OAT resistance factor to be studied as an important independent variable of research. From the results of this study it is known that the number of drug resistance has a risk of 1.097 times (95% CI: 0.609-1.977) for drop out compared to the 2-drug resistance group.

CONCLUSION

Determinant factors that associated with DO in MDR TB patients in DKI Jakarta Province 2011-2015 is aged 45-64 years old. While the others variables are not proved by statistically to have association with DO among MDR TB in this study. The age group that significantly associated with the incidence of DO in MDR TB patients was 45-64 years who had a risk of 2.4 times (95% CI: 1.031-5.589) for DO compared to the 15-24 age group.

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