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Research

The Effect of Non-Compliance with Medication on Multidrug Resistant of Tuberculosis

Widya Kurnianingsih[1)], Didik Gunawan Tamtomo[2)], Bhisma Murti[1)]

[1)]Masters Program in Public Health, Universitas Sebelas Maret
[2)]Faculty of Medicine, Universitas Sebelas Maret

ABSTRACT

Background: Multidrug Resistant Tuberculosis (MDR-TB) is the biggest problem in the prevention and eradication of TB in the world. MDR TB exists in 27 countries where there are at least 6,800 MDR TB cases every year and 12% of new TB cases registered are MDR TB. MDR-TB is a disease caused by resistant Mycobacterium tuberculosis. This study aims to examine the effect of non-compliance with taking medication on the incidence of multidrug resistant tuberculosis (MDR TB).

Subjects and Method: The problems of this study with PICO are as follows: Population= TB patients, Intervention = Non-compliance with taking medication. Comparison= Adherence to taking medication, and Outcome= Incidence of Multidrug Resistant Tuberculosis. Meta- analysis was carried out by systematically reviewing articles from Google Scholar, Pubmed and Springer Link. The articles used in this research are articles that have been published from 2010-2019. The keywords to look for articles are as follows: "Risk Factor MDR TB" OR "Previous Treatment" AND "Multidrug resistant tuberculosis". The inclusion criteria used were full paper, used English, case control study design and the results reported were adjusted odds ratio. Articles were collected using the PRISMA diagram and analyzed using the Review Manager 5.3 application with a fixed effect model.

Results: A total of nine articles reviewed in this study came from Bangladesh, Malaysia, Pakistan and Ethiopia. This resulted in a study showing that the effect of incomplete treatment increased the risk of multidrug resistant tuberculosis (aOR= 10.04; 95% CI= 8.90 to 11.32; p <0.001).

Conclusion: The effect of incomplete treatment increases the risk of multidrug resistant tuberculosis in Taiwan, Bangladesh, Malaysia and Ethiopia.

Keywords: Effect of incomplete treatment, Multidrug resistant tuberculosis (MDR TB)

Correspondence:
Widya Kurnianingsih. Masters Program in Public Health, Universitas Sebelas Maret. Jl. Ir. Sutami 36A, Surakarta 57125, Central Java. Email: widyakurnianingsih08@gmail.com. Mobile: 081556837033.

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BACKGROUND

Pulmonary tuberculosis (pulmonary TB) is still a public health problem in the world, although control efforts with the Direct Observed Treatment Shortcourse (DOTS) strategy have been implemented in many countries since 1995. Multidrug Resistant Tuberculosis (MDR-TB) is a the biggest problem in the prevention and eradication of TB in the world, given the difficult and costly treatment (Utomo, 2017).

Tuberculosis (TB) is one of the top ten causes of death worldwide. WHO reported that between 2013 and 2017 there was an increase in pulmonary TB cases from 9 million cases to 10 million cases (WHO, 2018). TB cases have caused 1.6 million deaths. WHO in 2018 reported 7

countries with the most TB cases, namely India, Indonesia, China, the Philippines, Pakistan, Nigeria and South Africa (WHO, 2018).

Globally, MDR TB cases were detected as many as 161,000 cases, 29% of the estimated 558,000 cases in 2017, an increase compared to 2016, which were 153,119 cases detected (WHO, 2018). MDR TB causes patients to have to repeat the anti-tuberculosis (OAT) drug treatment from the beginning with more expensive costs (100 times), more toxic drugs, and a longer time using second-line drugs, besides that the results are not necessarily satisfactory 2010). Many factors contribute to drug resistance in developing countries (Sarwani et al., 2012). Inadequate MDR TB treatment is known to be the main cause both in terms of regimen, dose and duration of therapy so that it affects the cure rate for MDR TB patients (Pratama, 2011).

The low prevalence of MDR-TB was estimated at 0.2% among new TB cases and 6.1% among previously treated and since then TB sufferers have shown a progressive increase from year to year. The most recent national survey conducted in 2008 indicated that MDR-TB was 2.5% among new cases and 5.5% among previously treated TB cases (Gamino et al., 2014). The prevalence of MDR pulmonary TB is influenced by. Factors that contribute to drug resistance in developing countries include the patient's ignorance of the disease, poor patient adherence, administration of monotherapy or drug regimens that are ineffective, inadequate doses, poor instruction, low medication regularity, poor patient motivation, insufficient drug supply. regularly, drug availability and drug quality contribute to secondary drug resistance, it is very important to reduce the burden, to decide health priorities and to allocate resources (Mekonnen et al., 2015).

Malnutrition and tuberculosis are serious problems and are the most left behind in the world (1). Malnutrition increases the risk of multidrug resistant tuberculosis (MDR TB) and nutritional status is a major determinant of morbidity and mortality due to multidrug resistant tuberculosis. Multidrug resistant tuberculosis affects the metabolism of essential nutrients such as protein and some micronutrients. Malnutrition on the other hand limits cell-mediated immunity and increases susceptibility to infection. This causes nutritional stress and weight loss, thereby reducing the body's ability to fight infection (weakens immune function) and nutritional status (Bhargava et.al 2014). A systematic review showed a strong association between malnutrition (defined as a low body mass index [BMI]) and the incidence of MDR TB, and concluded that low BMI is a risk factor for developing MDR TB (Bragava et.al 2014). Several studies reported that patients with active TB were more likely to be thin or have a lower body mass index (BMI= kg/m^2) than healthy controls and was associated with increased mortality in MDR TB patients. Nutritional deficiencies can delay recovery by impaired immune function. So that good nutrition will be able to improve recovery in people being treated.

WHO (2014) states that if TB sufferers do not comply with taking anti-tuberculosis drugs, the final result of concern is the failure of TB cure coupled with the emergence of TB germs that are resistant to tuberculosis drugs. The results of the analysis in this study indicate that there is a direct relationship between patients taking tuberculosis drugs and the incidence of MDR TB. That states that the most dominant factor that can affect the incidence of MDR TB is non-compliance with

tuberculosis patient treatment (Hirpa et.al 2013).

SUBJECTS AND METHOD

1. Study Design

This research is a systematic review and meta-analysis. The articles used in this study were obtained from several databases including PubMed, Google Scholar, and Science Direct. Keywords for searching articles are as follows: risk incomplete medicine treatment "OR" nutritional status ") AND" Multidrug resistant tuberculosis ". "Risk factor multidrug resistant", "incomplete medicine treatment factor multidrug resistant tuberculosis", "Nutrition status of multidrug resistant tuberculosis risk factor".

2. Inclusion Criteria

Articles included in this study must be full paper, case control study design and in English. The article must be appropriate wherein it is tested the independent variable of medication non-adherence to the incidence of multidrug resistant tuberculosis, based on a multivariate analysis of the adjusted odds ratio.

3. Exclusion Criteria

The articles published in this study are not in English. The articles are articles whose result is not the adjusted Odss Ratio. As well as the number of research samples (n <100).

4. Operational Definition

The article search was carried out by considering the eligibility criteria defined using the PICO model. The population in the study was tuberculosis patients with intervention in the form of non-adherence to taking medication, comparison of adherence to taking medication and outcomes in the form of multidrug resistant tuberculosis.

5. Data Analysis

Data processing was carried out by the Review Manager (RevMan 5.3) by calculating the effect size and heterogeneity to determine which research models were combined and formed the final meta-analysis result.

RESULTS

The article review process can be seen in the PRISMA flow diagram in Figure 1. Figure 2 shows the areas where articles were taken according to the inclusion criteria. This meta-analysis analyzes 9 primary studies conducted on 2 continents, namely the African Continent (Ethiopia), the Asian Continent (Bangladesh, China, and Pakistan).

Assessment of the quality of the primary studies was carried out quantitatively and qualitatively. This research uses Critical

Appraisal Checklist for Case-Control Study sourced from the Center for Evidence Based Management (CEBMa, 2014).

Based on the assessment of the quality of the primary articles above, the score for the quality of the articles is 11 to 12. This indicates that the articles are of good quality for meta-analysis (CEBMa, 2014).

A summary of the primary articles used for the meta-analysis of the effect of incompleteness taking medication on the incidence of multidrug resistant tuberculosis can be seen in Table 3.

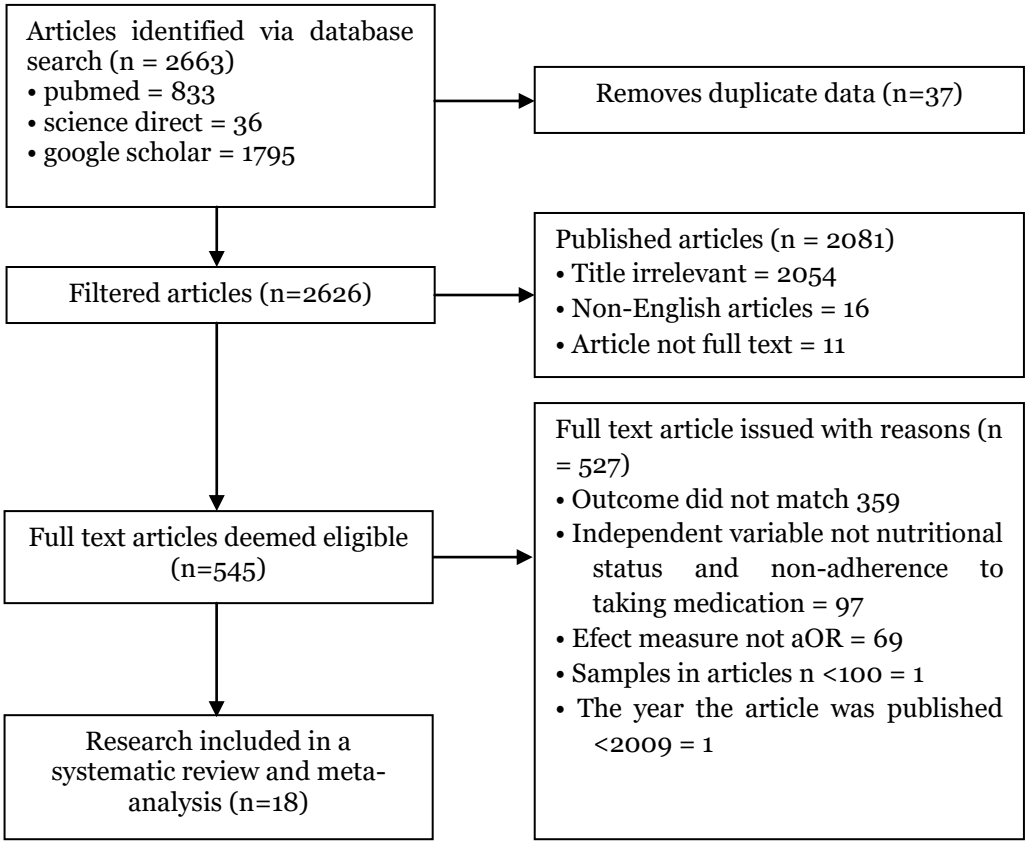

Figure 1. PRISMA Flow Diagram

Figure 2. Map of the research area

Table 3. Descriptions of primary studies included in the meta-analysis

Author (year)	County	Desain Studi	Sampel	P (Population)	I (Intervension)	C (Comparison)	O (Outcome)
Tong lv et al., 2018	China	Case Control	3552	Tuberculosis patient	Obediently take medicine	Not obedient to taking medicine	Incidence of MDR TB
Tombo et al 2019	Botswana	Case Control	2568	Tuberculosis patient	Complete taking medication	Incomplete medication	Incidence of MDR TB
Elmi et al 2016	Malaysia	Case Control	314	Tuberculosis patient	Obey taking medicine	Not obedient to taking medicine	Incidence of MDR TB
Wang et al 2013	China	Case Control	111	Tuberculosis patient	Obey taking medicine	Not obedient to taking medicine	Incidence of MDR TB
Workicho et al 2017	Ethiopia	Case Control	180	Tuberculosis patient	Complete taking medication	Incomplete taking medication	Incidence of MDR TB
Rifat et al 2015	Bangladesh	Case Control	250	Tuberculosis patient	Complete taking medication	Incomplete taking medication	Incidence of MDR TB
Dessica et al 2017	Ethiopia	Case Control	255	Tuberculosis patient	Obey taking medicine	Not obedient to taking medicine	Incidence of MDR TB
Mulisa et al 2015	Ethiopia	Case Control	349	Tuberculosis patient	Obey taking medicine	Not obedient to taking medicine	Incidence of MDR TB
Ahmad et al 2019	Pakistan	Case Control	125	Tuberculosis patient	Obey taking medicine	Not obedient to taking medicine	Incidence of MDR TB

a. Forest Plot

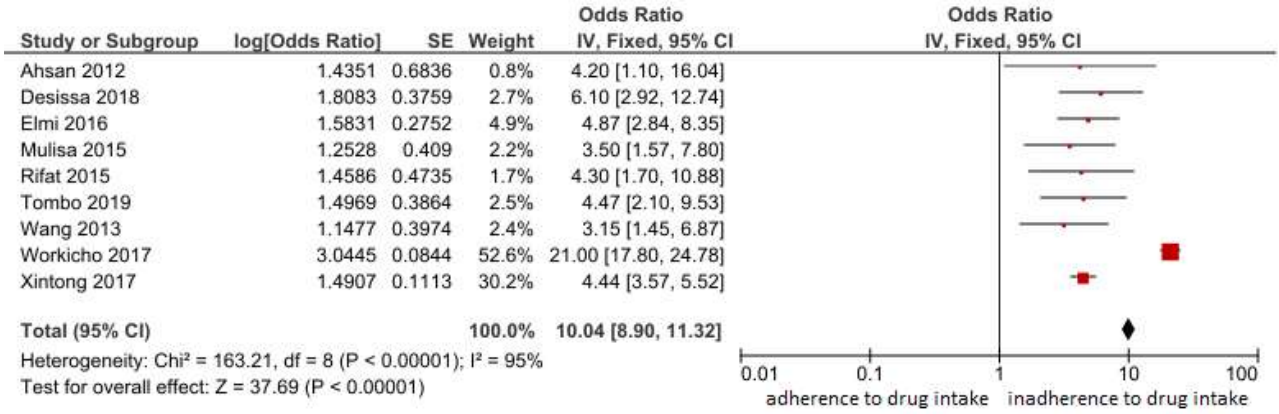

Figure 3. Forest plot the effect of non-compliance with taking medication on the incidence of multidrug resistant tuberculosis

Based on the results of the forest plot (Figure 3), non-adherence to taking medication would have an effect on the incidence of multidrug resistant tuberculosis by 1.04 times compared to patients who were adherent taking medication against the incidence of multidrug resistant tuberculosis and statistically significant (p <0.001). The heterogeneity of the research data showed I^2= 95%. So that the distribution of data is declared heterogeneous (random effect model).

b. Funnel Plot

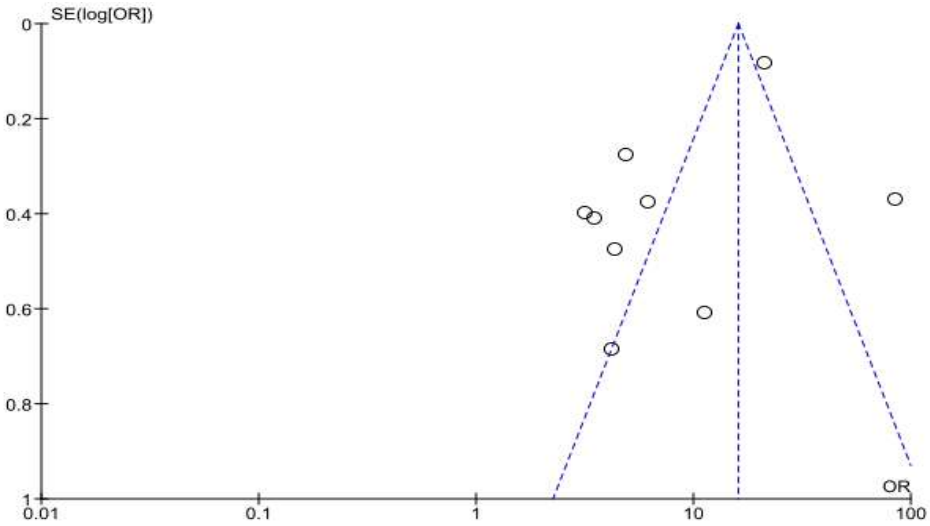

Figure 4. Funnel plot the effect of non-compliance with taking medication on the incidence of multidrug resistant tuberculosis

Figure 4 shows that some of the primary studies used have an asymmetrical distribution of plots, where 2 plots are on the right side and 7 plots are on the left. The plot on the right side of the graph appears to have a standard error between 0.0 and 0.4, while the plot on the left has a standard error between 0.2 and 0.7. This

indicates that there is a publication bias in the study.

DISCUSSION

This systematic study study and meta-analysis raised the theme of the effect of non-adherence to medication on the incidence of multidrug resistant tuberculosis. This meta-analysis study used research sources that controlled for confounding factors or confounding factors which could be seen from the study inclusion requirements, namely multivariate analysis and the statistical results reported were adjusted odds ratio (aOR). The combined results of the effect of non-compliance with taking medication on the incidence of multidrug resistant tuberculosis were processed using the RevMan 5.3 application, while the results of the systematic study and meta-analysis were presented in the form of a forest plot and a funnel plot.

Treatment adherence is important to avoid MDR TB and treatment failure. Patient adherence is highly demanded in undergoing this long-term treatment. Adherence to taking this medication is needed in all diseases, especially tuberculosis, which requires extra supervision in its treatment (Nurismi, 2014).

The results of this study are in accordance with Fauziah (2013), which shows that MDR TB sufferers are more frequent in respondents who are not adherent to treatment than those who are adherent. Patients who were not adherent had a 10.8 times chance of developing MDR TB compared to patients who were adherent to their treatment.

AUTHOR CONTRIBUTION

Widya is the main researcher who chooses topics, explores and collects research data. Didik Tamtomo and Bhisma Murti played a role in analyzing data and reviewing research documents.

CONFLICT OF INTEREST

There is no conflict of interest in this study.

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