

Factors Related to Medication Adherence among Pulmonary Tuberculosis Patients: A Literature Review

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Abstract

Tuberculosis (TB) is a communicable disease that is a major cause of ill health, one of the top 10 causes of death worldwide. Actually, TB is curable disease if the patients adhere and treatment be effective. This study aims to identify factors related to medication adherence among pulmonary TB patients. This study was a systematic literature review by identifying cross-sectional study, published in 2016-2021, in English and Indonesian, and full-text. The electronic database that used was Google Scholar and Science Direct with the keywords “Factors” “Medication” AND “Adherence” “TB Pulmonary”. The results obtained 10 articles that related to medication adherence among pulmonary TB patients. There were five dimensions of factors: therapeutic factors, health system factors, environmental factors, socioeconomic factors, and family support factors. Health workers need to consider these factors so that medication adherence among pulmonary TB patients will increase.

Keywords: Factors, Medication, Adherence, TB Pulmonary.

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INTRODUCTION

Tuberculosis (TB) is a communicable disease that is a major cause of ill health, one of the top 10 causes of death worldwide and the leading cause of death from a single infectious agent (ranking above HIV/AIDS) [20]. TB is caused by *Mycobacterium tuberculosis* which can be transmitted through the air, for example when cough. Usually, TB will attack the lungs (pulmonary TB), but can also spread or attack organs other than the lungs in the body (extra pulmonary TB). TB can be experienced by men and women at various ages, especially adults.

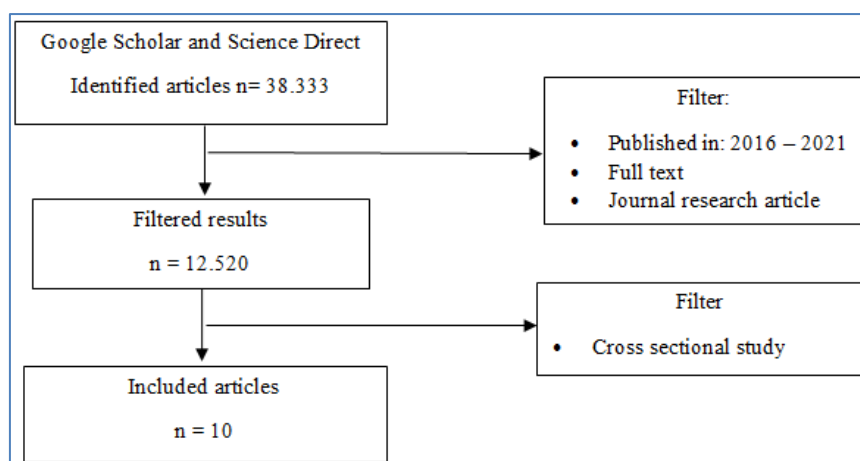
TB disease is still a challenge in public health in many countries. Based on Global Tuberculosis Report by WHO, 7.1 million people with TB were reported to have been newly diagnosed and notified in 2019, up from 7.0 million in 2018 and a large increase from 6.4 million in 2017 and 5.7–5.8 million annually in the period 2009–2012. The biggest contributors to the global increase were India and Indonesia, the two countries that rank first and second worldwide in terms of estimated incident cases per year [20].

Low adherence increases the risk of poor outcomes, including treatment failure, relapse, and

development or amplification of drug resistance. TB patients' medication adherence should not only be considered as a clinical issue but also a public health problem [7]. Based on the issues above, researcher was interested to identify factors related to medication adherence among pulmonary tuberculosis patients by conducting a literature review from Indonesia and other countries.

RESEARCH METHODS

This study was a systematic literature review. In this method, the researcher identifies, collects, summarizes, and analyzes relevant articles to answer research question or hypothesis [15]. In this study, researcher did a literature review about factors related to medication adherence among pulmonary tuberculosis patients. The electronic database that used in this study was Google Scholar and Science Direct. The researcher searched literatures with a cross-sectional study type and used keywords “Factors” “Medication” AND “Adherence” “TB Pulmonary”. Literature search was limited from 2016 to 2021. 3.833 articles were obtained and 10 articles were selected based on criteria and related to medication adherence of pulmonary TB patients (Picture 1).



Picture-1: Algorithm of Article Searched

Table-1: Articles Synthesis

Writer/ Country	Research Objectives	Research Design	Samples	Variables and Instruments	Results
(Yadav <i>et al.</i> , 2021) Nepal	To determine the factors associated with medication adherence and its effect on health related quality of life among tuberculosis patients in selected districts of Gandaki province	A cross-sectional	180 respondents by <i>multistage sampling</i> Inclusion criteria: <ul style="list-style-type: none"> Registered under DOTS and receiving treatment more than or equal to 60 days in the selected districts of Gandaki province TB medication patients who were above 15 years of age Exclusion criteria: <ul style="list-style-type: none"> TB patients from selected DOTS center who were disagree to participate in study Mentally severely ill Deafness 	<ul style="list-style-type: none"> Medication adherence, using Morisky medication adherence scale (MMAS-8) Quality of life, using WHOQOL-BREF tool 	<ul style="list-style-type: none"> More than three-fourth (79,4%) respondents were adhered to medication Tuberculosis patients who were adhered to medication had good quality of life Medication adherence was found associated with co-infection, health worker, and favorable time for taking medicine.
(Fitri, L., Marlindawani, J., & Purba, A., 2018) Indonesia	To determine medication adherence in pulmonary tuberculosis patients at the Sadabuan Public Health Center Kota Padang	A cross-sectional	51 respondents by simple random sampling Inclusion criteria: <ul style="list-style-type: none"> Pulmonary tuberculosis registered at the Sadabuan Public Health Center Kota Padang 	<ul style="list-style-type: none"> Characteristics and medication adherence by interviewed and used the questionnaire compiled by the researcher 	<ul style="list-style-type: none"> As many as 78.4% respondents were medication non-adherence in pulmonary tuberculosis patients Knowledge, family support, education level, occupation, and attitude had influence on medication adherence in pulmonary tuberculosis patients ($p < 0,05$) Knowledge variable were the strongest influence variable on medication adherence in pulmonary tuberculosis patients

Writer/ Country	Research Objectives	Research Design	Samples	Variables and Instruments	Results
(Woimo, T., Yimer, W., Bati, T., & Gesesew, H., 2017) Ethiopia	To assess the prevalence of and associated factors for anti-Tb treatment non adherence in public health care facilities of South Ethiopia	A cross-sectional	271 respondents by simple random sampling Inclusion criteria: <ul style="list-style-type: none"> Tb patients who registered 6 months before data collection Exclusion criteria: <ul style="list-style-type: none"> Patients on MDR treatment regimen Patients too ill to be interviewed 	<ul style="list-style-type: none"> Anti-Tb treatment adherence status by depth interview and questionnaire compiled by the researcher 	<ul style="list-style-type: none"> The prevalence of anti-Tb non-adherence was 24.5%. Factors that statistically associated with non-adherence: having poor level of knowledge, absence of health information at every visit, pill burden, distance to Tb clinic beyond 10 km, not decentralizing of DOT service, and cost of medication other than anti-Tb.
(Gunawan, A., Simbolon, R., & Fauzia, D., 2017) Indonesia	To determine the factors associated with medication adherence of pulmonary tuberculosis patients in 5 Pekanbaru Public Health Centers	A cross-sectional	75 respondents by proportional random sampling Inclusion criteria: <ul style="list-style-type: none"> Registered pulmonary tuberculosis patients Undergoing treatment of pulmonary tuberculosis at least 1 month Agreed to participate the research and signed the informed consent Pulmonary tuberculosis patients who were still living in Pekanbaru Pulmonary tuberculosis patients who diagnosed by doctor with: positive BTA, BTA negative with positive x-ray, and pulmonary tuberculosis patients with complete treatment Exclusion criteria: <ul style="list-style-type: none"> Died Patients who did not possible to be interviewed Patients who had mental disorder Patients were extra pulmonary type Relapsed Negligent MDR pulmonary tuberculosis 	<ul style="list-style-type: none"> Factors associated with medication adherence used interview method 	<ul style="list-style-type: none"> Patient's adherence to pulmonary TB treatment was grouped into three: the most influential factors, moderately influential factors, and less influential factors. The most influential factors to pulmonary TB treatment were the motivation to recover (97.3%), the role of family (80%), and the role of medication supervisor (33.3%). The moderately influential factors were the benefits from universal health coverage/insurance (25.3%), the number of drugs that must be taken (17.3%), and duration of treatment for pulmonary TB (16%) The less influential factors were the side effect of drugs after taking pulmonary TB drugs and the distance from the pulmonary TB patients' home to public health center (13.3%), transportation cost (2.7%), and other types of drugs taken (1.3%)

Writer/ Country	Research Objectives	Research Design	Samples	Variables and Instruments	Results
(Dogah <i>et al.</i> , 2021) Ghana	To determine the rate of treatment adherence, knowledge of TB infection, and the possible factors influencing adherence to TB treatment in the Ketu North District in the Volta Region of Ghana	A cross-sectional	125 respondents by convenient and purposive sampling Inclusion criteria: <ul style="list-style-type: none"> Registered patients with pulmonary and or extra pulmonary TB Traceable Consented to be part of the study Exclusion criteria: <ul style="list-style-type: none"> Drug abusers Terminally ill Did not give informed consent Patients were not traceable 	<ul style="list-style-type: none"> Knowledge about TB, TB treatment, and factors that influence adherence used a structured questionnaire by researcher 	<ul style="list-style-type: none"> The adherence rate (81.6%) in this study The gender was a significant factor associated with treatment adherence. Educational level, having treatment supporter, staff attitude, self-perceived wellness, food availability, being on other medication, and household size were not significantly associated with treatment adherence
(Pameswari, P., Halim, A., & Yustika, L., 2016) Indonesia	To determine medication adherence level of pulmonary tuberculosis patients at Mayjen H.A Hospital in Kerinci district	A cross-sectional	27 respondents by total sampling Inclusion criteria: <ul style="list-style-type: none"> Pulmonary TB patients who were undergoing treatment at Mayjen H.A Hospital in Kerinci Agreed to participate in research 	<ul style="list-style-type: none"> Medication adherence used Morisky Medication Adherence Scale (MMAS) 	<ul style="list-style-type: none"> 74.07% of the respondents were in the productive age (15-54 years) Most of the respondents were in low economy 55.56% of respondents were adherent, 33.33% of respondents were quite adherent, and 11.11% of respondents were not adherent. Factors that related to: from the patients themselves, therapeutic factors, health system factors, environmental factors, socioeconomic factors, and family support factors. Motivation or a strong desire from within is a major factor in the high level of patient compliance in undergoing pulmonary TB drugs therapy
(Fang <i>et al.</i> , 2019) China	To assess the adherence rate among pulmonary TB patients in Anhui Province, eastern China and to explore the factors affecting adherence to anti-TB treatment	A cross-sectional	339 respondents by stratified sampling method Inclusion criteria: <ul style="list-style-type: none"> patients were diagnosed and registered between January 1, 2015 and December 30, 2015 TB patients were over 15 years old 	<ul style="list-style-type: none"> General information, status of treatment, knowledge on TB prevention and treatment, and access to information on TB, questionnaire was developed and administered by trained doctors and health workers. 	<ul style="list-style-type: none"> Only 66.4% of the patients were considered adherent. Most patients had a low annual income (less than 10 000 yuan). Most demographic factors, including gender, occupation, and educational level, were not related with TB patient's adherence to treatment (P>0.05) Marital status and annual income were independent influencing factors. With regard to annual income, patients whose annual income was less than 5000 yuan had the highest

Writer/ Country	Research Objectives	Research Design	Samples	Variables and Instruments	Results
					<p>frequency of missing doses of medication (54.65%), while patients whose annual income was greater than or equal to 20 000 yuan had the lowest rate of non-compliance (22.97%)</p> <ul style="list-style-type: none"> • Patients knowledge about TB were related to patients' adherence • Having medical staff visits and the level of the visiting personnel were confirmed to be associated factors
(Ulfah., Windiyarningsih, C., Abidin, Z., & Murtiani, F., 2017) Indonesia	To determine the factors that related to medication adherence of pulmonary TB patients at Cipunagara Subang Public Health	A cross-sectional	<p>168 respondents by consecutive sampling</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • TB patients being treated at Cipunagara Community Health Center in the duration of 2015 to June 2017. 	<ul style="list-style-type: none"> • Drug side effects, family support, the role of medication supervisor, knowledge and attitude of health worker, used structured questionnaire by researcher 	<ul style="list-style-type: none"> • Age (Pvalue=0,535) and income (Pvalue=0,164) were not related to medication adherence of pulmonary TB patients • Variables that significant and related to medication adherence of pulmonary TB patients were family supports, the role of medication supervisor, and distance to health facilities.
(Du <i>et al.</i> , 2020) China	to explore the level of medication adherence among pulmonary tuberculosis outpatients and the predictive factors based on the bio-psycho-social medical model	A cross-sectional	<p>564 respondents by stratified sampling method</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • Outpatients with pulmonary TB who had been taking anti-TB medicine for >2 months <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • patients aged < 15 years • Patients who were unable to complete the questionnaire due to unconsciousness 	<ul style="list-style-type: none"> • Medication adherence was assessed using the eight-item Morisky Medication Adherence Scale (MMAS-8) 	<ul style="list-style-type: none"> • As many as 41.84% and 32.45% of respondents were exhibited high and medium medication adherence, respectively, but 25.71% of respondents exhibited low medication adherence. • Multivariate ordinal logistic regression showed that patients who were older (OR: 1.02, p=0.013) were employed (OR: 1.61, p=0.011), had better tuberculosis knowledge (OR: 1.34, and did not consume alcohol (OR: 1.84, p=0.032) exhibited higher medication adherence. • Patients who did not follow their doctors' advice to take adjuvant drugs (OR: 0.44, p=0.001), had a history of TB treatment (OR: 1.76, p=0.009), experienced adverse drug reactions (OR: 0.65, p=0.017), experienced stigma (OR: 0.67, p=0.032), and needed supervised treatment (OR: 0.66, p=0.012) exhibited lower medication adherence

Writer/ Country	Research Objectives	Research Design	Samples	Variables and Instruments	Results
(Tukayo, I., Hardyanti, S., & Madeso, M., 2020) Indonesia	To analyze the factors that influence adherence to taking anti-tuberculosis drugs in patients' pulmonary tuberculosis at Waena Public Health Center	A cross-sectional	66 respondents by simple random sampling Inclusion criteria: <ul style="list-style-type: none"> Adults Currently on treatment Agreed to participate in research Respondents were at the place of data collection Exclusion criteria: <ul style="list-style-type: none"> Did not agree to participate in research Extra pulmonary TB Respondents could not read and write 	<ul style="list-style-type: none"> Knowledge and attitude of patients, side effect of drugs, access to health services, attitude of health worker, and family support assessed using questionnaire developed by researcher 	<ul style="list-style-type: none"> There was significant relationship between knowledge ($p = 0,043$), attitude ($p=0,001$), side effect of drugs ($p=0,012$), access to health services ($p = 0,002$), attitude of health worker ($p = 0,04$), family support ($p = 0,014$) on medication adherence.

RESULT

From the literature review, it was found that research conducted by Pameswari *et al.* [14] 74.07% of the TB pulmonary patients were in the productive age (15-54 years) and most of them were in low economy. Medication adherence level in some studies showed the level non-adherent. Research conduct by Fitri *et al.* [7] showed that 78.4% respondents were medication non-adherence in pulmonary tuberculosis patients. Du *et al.* [5] divided medication adherence level into: high medication adherence (41.84%), medium medication adherence (32.45%), and low medication adherence (25.71%). Meanwhile, research conduct by Pameswari *et al.* [14] identified as many as 55.56% of respondents were adherent, 33.33% of respondents were quite adherent, and 11.11% of respondents were not adherent.

Several studies revealed the factors that related to medication adherence among TB pulmonary patients. In short, Pameswari *et al.* [14] grouped to five dimensions of factors that related to medication adherence: therapeutic factors, health system factors, environmental factors, socioeconomic factors, and family support factors. On health system factors, Woimo *et al.* [21] showed that factors statistically associated with non-adherence: having poor level of knowledge, absence of health information at every visit, pill burden, distance to Tb clinic beyond 10 km, not decentralizing of DOT service, and cost of medication other than anti-Tb. According to research by Fang *et al.* [6], marital status and annual income were independent influencing factors. It could be the socioeconomic factors.

Research conducted by Yadav *et al.* [22], medication adherence was found associated with co-infection, health worker, and favorable time for taking medicine. Meanwhile, research by Fitri *et al.* [7] showed that knowledge, family support, education level, occupation, and attitude had influence on medication adherence in pulmonary tuberculosis patients ($p<0,05$). Ulfah *et al.* [17] also stated that family supports related to medication adherence of pulmonary TB patients.

It was almost the same as the research conducted by Tukayo *et al.* [18] that there was significant relationship between knowledge ($p = 0,043$), attitude ($p=0,001$), side effect of drugs ($p=0,012$), access to health services ($p = 0,002$), attitude of health worker ($p = 0, 04$), family support ($p = 0,014$) on medication adherence. However, these results were not in accordance with the research conducted by Dogah *et al.* [4], showed that educational level, having treatment supporter, staff attitude, self-perceived wellness, food availability, being on other medication, and household size were not significantly associated with treatment adherence.

DISCUSSION

Medication adherence can be defined as the extent to which a patient's behavior corresponds with the prescribed medication dosing regime, including time, dosing and interval of medication intake [8]. Non-adherence among pulmonary TB patients is a problem that influenced by several factors. In this literature review, several factors could be identified in five dimensions: therapeutic factors, health system factors, environmental factors, socioeconomic factors, and family support factors. These factors must be concern to

health workers in order to determine interventions that can be carried out to increase the level medication adherence level among pulmonary TB patients.

Therapeutic factors

Therapeutic factors are factors related to treatment, such as types of drugs be taken, their side effects, and the duration of treatment. Tuberculosis (TB) is curable disease if the patients receive effective and uninterrupted anti-TB medication within the recommended time. Based on WHO in the guideline for treatment of drug-susceptible tuberculosis [19], the 6-month rifampicin-based regimen 2HRZE/4HR is recommended in patients with drug-susceptible pulmonary TB. It means, patients will receive 4 types of drugs (isoniazid, rifampicin, pyrazinamide, ethambutol) during intensive phase and be followed to 2 types of drugs (isoniazid, rifampicin) for the next 4 months. After an intensive phase treatment for 2 months with a four-drug regimen the TB patients have to accept the continuation phase lasting more than 4 months according to the WHO recommendation [5]. TB patients could be more likely to show nonadherence in continuation phase because they have improved signs and symptoms of the disease and even might think they are cured; thus, they might be careless in taking medications [11].

Health system factors

Health system factors affect to medication adherence among pulmonary TB patients. These factors include: health education, home visit, availability of anti-TB drugs, and quality of drugs, transportation availability and distance to public health center [14]. The role of health workers in providing health service to pulmonary TB patients is very important, especially in providing information about the importance of taking medication regularly and uninterrupted, the rules of taking medication, the symptoms of side effect that may be experienced by patients, listen to patients complain, and provide the solution.

Promoting knowledge through health education can increase adherence to tuberculosis treatment. With adequate knowledge, many patients with tuberculosis will become more compliant and complete treatment [10] Vice versa, the lack of knowledge will increase the rate of non-adherence among pulmonary TB patients. This is in line with research conducted by Woimo *et al.* [21], showed that factors statistically associated with non-adherence were having poor level of knowledge that was caused by none or lack of information provided by health workers at every visit.

Environmental factors

One of the environmental factors that affects medication adherence among pulmonary TB patients is negative stigma about pulmonary TB that spreads in public. The term 'stigma' refers to "exclusion, rejection, blame, or devaluation resulting from experience or

reasonable anticipation of an adverse social judgment" because of a particular condition [13]. Because of the negative stigma about TB, patients feel ashamed and afraid of being ostracized if the neighbors find out that they have been diagnosed TB. This causes delay in diagnosis, TB patients do not want to receive the treatment, and medication adherence increases. Stigma leads to feelings of shame, tainted identity, increases the stress associated with illness, and contribute to psychological and social morbidity.

Socioeconomic factors

From the literature review, it was found that the TB pulmonary non-adherence patients were in the productive age and most of them were in low economy. Although diagnostic examinations and anti-TB drugs are obtained for free, patients need additional costs for food during healing process, transportation cost to the public health center, and other drugs that are not covered by health insurance. About 75% of TB cases arise during people's most productive years between the ages of 15 and 54, while people who are infected by TB are often unproductive and unable to work which affected their family members [3]. This causes medication non-adherence increases.

Family support factors

Family support means the existence of comfort, attention, appreciation or to help people with an attitude of accepting the conditions, obtained from individuals and group [12]. The role of family as taking drugs supervisor is very necessary to ensure medication adherence among pulmonary TB patients in the intensive and advanced phase. In the intensive phase, medication adherence is needed to prevent resistance to anti-TB drugs. Meanwhile in advanced phase supervision is needed because this phase lasts longer so that non-adherence is very likely to occur. Patients with frequent medication supervision by family members and patients whose family members often encouraged them mentally were more likely to have a high level of adherence [2].

Theoretically, according to Friedman (1998) family support is divided into four dimensions: emotional support, appraisal, material, and information support [12]. Emotional support is a form of affection given by the family to one family member who suffers from an illness. Emotional support provided by the family to patients will encourage patients to be able to undergo treatment regularly; this is because the support provided is used as a driving force for patients in carrying out a therapy program [1]. Emotional support to patients is needed to increase the self-esteem of pulmonary TB patients because they usually feel ashamed of their disease). Information support can be in the form of giving advice, suggestions, instruction, and providing information to the patients about treatment. Material support provided by family to the patients can be in the form of funds, assistance, and strict

supervision. Appraisal support is given to the pulmonary TB patients focuses on positive aspect in the form of praise for health progress, always loves, and pays attention to the patient's condition during illness and accepts patients as they are [16].

SUMMARY

From the literature review, factors related to medication adherence among pulmonary TB patients divided into five dimensions: therapeutic factors, health system factors, environmental factors, socioeconomic factors, and family support factors. Health workers need to consider these factors so that medication adherence among pulmonary TB patients will increase.

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