Factors Affecting Treatment Adherence Among Patients with Tuberculosis in Indonesia: Literature Review

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**ABSTRACT**

**Introduction:** Tuberculosis (TB) is the leading cause of death from infectious diseases in the world and Indonesia is the second largest contributor to TB cases after India. Treatment adherence problems are a major obstacle to TB elimination. The purpose of this Literature Review is to determine the factors that affect treatment adherence among TB patients in Indonesia.

**Methods:** Literature obtained from Science Direct, PubMed, and Google Scholar; published from 2018 – 2023, research from reputable international journals and from national journals at least with SINTA 3, located in Indonesia. Indonesian and English with full text of all types of research designs. Article selection was carried out using the method “Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) and analyzed using descriptive analysis techniques.

**Results:** A total of 225 articles were deemed appropriate for the topic, but only 15 articles were included based on inclusion criteria. It was found that there are several factors that affect treatment adherence in tuberculosis patients in Indonesia, namely: predisposing factors as many as 11 articles (age, education, occupation, knowledge, self-efficacy, concordance, health behavior, motivation, marital status, income level, drug side effects, already feeling cured, and duration of treatment). Reinforcing factors as many as 2 articles (family support). Enabling factors as many as 5 articles (the role of officers, reminder SMS messages from officers, health counseling, and distance of residence to health services).

**Conclusion:** The most dominant factor affecting treatment adherence among tuberculosis patients in Indonesia is the Predesposising factors, namely education, knowledge and self-efficacy.

**KEYWORDS**

Adherence; Treatment; Tuberculosis

**INTRODUCTION**

Tuberculosis (TB) is the leading cause of death from infectious diseases in the world (1–3). In 2022, the Indonesian Ministry of Health detected more than 700,000 tuberculosis (TB) cases. This is the highest number since
TB became a National Priority Program (4). Indonesia is the second largest contributor to TB disease after India in terms of estimated incidence of cases per year, with 969,000 cases and 93,000 deaths per year, equivalent to 11 deaths per hour (5).

Based on the 2022 Global TB Report, the productive age group is the most suffering from TB in the world, especially at the age of 25-34 years, while in Indonesia, most cases at an older age are still classified as productive age, namely 45-54 years (6). One of the problematic factors of TB treatment is treatment adherence (7,8). Based on data from the Ministry of Health, the success rate of TB treatment has been decreasing since 2016. The treatment success of TB patients for ten years shows that the highest data in 2010 was 89.2%, while in 2020, the treatment success experienced the lowest decline of 82.7%, and in 2021, it was 83% (9).

The problem of treatment adherence is a significant obstacle to TB elimination (3,10–12). Patient compliance in taking medication is an essential factor in successful pulmonary TB treatment (13–17). Medication adherence significantly influences the success of tuberculosis treatment (18–21). Poor compliance or interrupted treatment results in a high risk of drug resistance (15,22–25). The incidence of drug resistance is a barrier to global TB eradication efforts, causing more comprehensive transmission and death (26–28). This causes patients with Tuberculosis to worry about their quality of life (29). There are many studies explain the factors that influence drug adherence of TB patients in Indonesia but have yet to be comprehensively summarized in a literature review. The writing of this literature review aims to determine what factors influence drug adherence in patients with tuberculosis in Indonesia.

**METHOD**

The method used was a literature review. The data used is secondary data from scientific article sources using English keywords: Compliance OR adherence AND treatment OR anti-tuberculosis drug OR anti-TB OR medication AND Tuberculosis AND Indonesia. And Indonesian keywords: “Kepatuhan” AND “Pengobatan” AND “Tuberkulosis”. Articles for this literature study were taken from reputable international journals and national journals with at least Sinta 3. Accessed using databases: Science Direct, Pubmed, and Google Scholar, published from 2018 - 2023, with research locations in Indonesia.

The selected articles with all research designs were available in full-text Indonesian and English. The selection of articles chosen was carried out adopting the "Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) method, which consists of identifying, filtering, and adjusting to criteria and eligibility, which are then extracted into tables and synthesizing data into tables and analyzing using descriptive analysis techniques.
**RESULTS**

Based on the search results, some articles matched the criteria set. A summary of included literature can be seen in Table 1.

<table>
<thead>
<tr>
<th>Factors Affecting Treatment Adherence Among Patients with Tuberculosis In Indonesia</th>
<th>Reference</th>
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<tbody>
<tr>
<td>Predisposing factors</td>
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<tr>
<td>Age</td>
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<td>Health behavior</td>
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<td>Motivation</td>
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<td>Income level</td>
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<td>Drug side effects</td>
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<td>Already feeling cured</td>
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<td>Duration of treatment</td>
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<td>Reinforcing factor</td>
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<td>Family support</td>
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<td>Enabling factors</td>
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<td>The role of officers</td>
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<td>Reminder Short messages from officers</td>
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<td>Health counseling</td>
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<td>Distance of residence to health services</td>
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**DISCUSSION**

Based on articles that have been reviewed in the last five years, it was found that several factors influence treatment adherence in tuberculosis patients in Indonesia. These factors are broadly divided into three categories: predisposing, reinforcing, and enabling.

**Predisposing Factors**

**Age**

Based on Lucya & Arief’s research (2022) shows that there is a relationship between drug compliance and age. People with age. Older people tend to follow doctors’ instructions because they are more responsible, orderly, conscientious, moral, and filial compared to younger people. Older patients tend to be more adherent to treatment because their activity is less dense compared to younger patients so they can seek treatment regularly(38).

Nasrullah’s research (2023) also obtained the results of bivariate analysis showing that age influences compliance with anti-tuberculosis drugs (OAT) in TB patients. Age is one of the influential factors in the adherence to treatment of patients with tuberculosis. This is because the experience of disease tends to be better at an older age. Older people have more experience than younger people, whether it comes from themselves or their environment, causing older people to be more compliant to seek treatment(39).
Marital Status

Nasrullah's research (2023) found that the results of the chi-square test found that marital status affected adherence to taking anti-tuberculosis drugs in patients with TB (p = 0.016). Unmarried marital status tends to be more compliant in treatment compared to married.

In general, the results of this study are different from previous studies that found that medication adherence was better in married respondents than those who were not married. Married people will receive support in the conversion of their spouse thus allowing patients to be more obedient to seek treatment.

Education

Based on research, Lucya & Arief (2022) found that the variable of education level p-value = 0.029 which means there is a significant relationship between education and medication adherence. Nasurullah's (2023) research also found that medication adherence is influenced by education level (p = 0.000). Treatment adherence is getting better in line with higher education levels.

The low level of education allows knowledge about handling health problems to also be low. Someone with a high level of education will increasingly need healthcare facilities if they are sick. Awareness about the importance of being healthy will be higher in people with a high level of education, so that if sick more motivated to do a treatment at better health care facilities. In addition, the individual will be more receptive to information and increase the knowledge possessed and vice versa.

Knowledge

Asriwati et al. (2021) research shows that the knowledge variable is related to compliance with taking anti-tuberculosis drugs. The knowledge possessed by respondents affected by pulmonary TB who want to seek information about adherence to taking medication, the ability of pulmonary TB respondents can be applied correctly so that they can behave well and obediently undergo the treatment process. High respondent knowledge about the length of TB treatment until it is declared cured, then the respondent is obedient in taking TB medication according to the schedule from the health worker's information. Based on field results, this is because every new pulmonary TB patient will be explained regarding pulmonary TB diseases, such as an explanation of how it is transmitted, treatment, and prevention.

This study aligns with research conducted by Sukartini et al. (2020), which found that knowledge with treatment compliance showed a significant relationship. Knowledge has a significant relationship with compliance with taking anti-tuberculosis drugs. Respondents who have high knowledge tend to be obedient in taking anti-tuberculosis drugs. The research of Perwitasari et al (2022) also found that patient knowledge and hepatotoxic effects were significantly associated with adherence. Patients may be more compliant with treatment at a high level of knowledge compared to patients with a low level of knowledge.

Employment Status

Based on research, Nasurullah (2023) found that the results of the chi-square test showed that the adherence to treatment of patients with TB was influenced by employment status (p = 0.000). The existence of this job will involve the utilization of existing health services. A person's career can reflect the amount of information received, with this information helping someone to decide or make a decision to utilize health services for themselves.

Income Level

Based on research by Nasrullah (2023), the bivariate analysis results show that income level affects compliance with OAT in TB patients. Adherence to patients seeking treatment is getting better in respondents who have a higher income level. This proves that someone with income can fulfil their needs, including medical expenses.
Self-efficacy

Based on research by Sutarto (2019) shows that self-efficacy is significantly related to adherence to taking medication in Pulmonary TB patients. High self-efficacy can create confidence in responding to certain things in obtaining reinforcement; conversely, if self-efficacy is low, someone will be anxious and unable to do it(35). Zainal's research (2020) also found that self-efficacy significantly affects treatment adherence(33).

Observation of the success of others doing the treatment will increase self-efficacy. Otherwise, self-efficacy will decrease if watching people (who are used as figures) whose abilities are approximately equal to their abilities. High self-efficacy in respondents have the confidence and motivation to change their behaviour by being obedient in taking drugs so that the TB disease suffered does not repeat the treatment. In contrast, respondents with low self-efficacy due to most respondents feeling pessimistic and resigned to the disease experience(35).

Motivation

Research conducted by Sukartini et al (2020) shows that adherence to taking anti-tuberculosis drugs is related to patient motivation. Respondents who have good reason tend to be obedient in taking anti-tuberculosis drugs. Patients who have good motivation always receive support from their family and those closest to them to achieve recovery. In addition, there are always health centre staff providing encouragement and support to all patients never to stop taking medicine and to conduct regular examinations and treatment to achieve recovery(40).

Health Behavior

Research conducted by Yani et al (2022) found that adherence to taking anti-TB drugs is significantly related to health behavior. Health behaviors are positive predictors of medication adherence. Health behaviors such as alcohol consumption, smoking, exercise, diet, and others contribute to the severity of TB disease. Some studies suggest that medication adherence is associated with healthy living habits(44).

Concordance

Concordance is an agreement between patients and doctors that includes aspects of cooperation or partnership, decisions taken based on the results of joint discussions, and mutual trust between the two. Concordance contributes to the improvement of compliance and the quality of life of tuberculosis sufferers. Pandia's research (2019) found that patients with good concordance had a probability of being more compliant by 2.6 times than patients with poor concordance(43).

Feeling Healed

Based on Asriwati's research (2021), shows that there is a relationship between drug adherence and patients who have felt cured OR = 4.643 (95% CI; 1.247–17.287). One of the risk factors related to non-adherence to taking medication in TB patients is that the patient has felt cured. The majority of TB treatments will show better results in the first 2 months of treatment, causing many patients to feel cured and stop treatment. This, of course, will have an impact on the success of treatment and allow drug resistance to occur(30).

Duration of Treatment

Based on research by Lucya & Arief (2022) shows that adherence to taking medication is significantly related to treatment ((p-value 0.027). The duration of TB treatment is quite long, which is about 6-9 months, causing TB patients to feel saturated and tired which results in decreased adherence to taking drugs. In addition, the symptoms experienced by patients began to decrease, especially at 2 months of treatment, and the side effects of drugs felt by patients caused patients to be lazy to seek treatment, even though at the beginning of treatment there was counseling about the treatment of Pulmonary Tuberculosis(38).

Drug Side Effects

Asriwati et al (2021) research found that adverse drug events are associated with pulmonary TB treatment adherence treatment. Common side effects of antituberculosis drugs include loss of appetite, nausea, abdominal
pain, joint pain, tingling to burning in the legs and reddish colour of urine. More severe side effects include itching and redness of the skin, deafness, impaired balance, visual disturbances, jaundice without other causes, confusion and vomiting to purpura and shock. The side effects of antituberculosis drugs are known to be one of the risk factors for default, so that they can increase the risk of non-adherence to treatment. However, not all OAT effects will cause adverse effects (30).

Lucya & Arief’s (2022) research found that drug side effects were significantly associated with medication adherence (p-value = 0.007) with a correlation at a moderate level (r = -0.460). This shows that the lower the side effects cause the higher the level of treatment adherence and vice versa. Patients who experience side effects decide to stop taking the given medication due to their ignorance about the side effects of the drug. As for patients who remain adherent to taking medication despite experiencing side effects influenced by other variables (38).

Reinforcing factor
Family Support
Research by Siregar (2019) shows that there is a significant relationship between family support and medication adherence (p = 0.002). Most patients have good medication adherence because they have good family support 31. This study also found that some patients remain adherent to treatment even though family support is not good. this is likely due to the motivation and strong desire of the patient to recover (37).

Lucya & Arief’s (2022) research also found that family living was significantly associated with medication adherence (p-value 0.018) (38). Family support in the form of financial assistance, affection, attention, enthusiasm, and motivation helps patients to comply with treatment (37). Family support becomes important for patients. With good family support, patients feel not alone in facing their problems. Family support makes patients feel comfortable, cared for, and feel their condition is acceptable (38).

Enabling factors
Role of Health Officers
Based on research, Asriawati et al (2021) found that adherence to taking anti-tuberculosis drugs is related to the role of officers. One of the officers’ roles is to provide information about pulmonary TB disease, motivate people with pulmonary TB to be patient in undergoing the treatment process for a long time, and also encourage people with pulmonary TB not to give up hope to carry out routine inspection actions (30).

Short Message Reminder from Health Officers
Research conducted by Dewi et al (2019) shows that the types of messages sent to TB patients differ from one another. Adjusted to the emotional state of each patient. Hopelessness, fear, and complaints at the beginning of treatment require motivational and informative messages regarding treatment mechanisms and side effects. Sufficient information related to the mechanism of taking medication and prevention of transmission is expected to provide high activation during treatment (42).

The study also found that positive messages were more effective in medication adherence than negative messages. Negative messages can cause fear and reinforce negative stigma against TB sufferers (42).

Health Counseling
Karuniawati’s research (2019) found a significant increase in compliance between before and after two weeks of counselling intervention, either with or without leaflets, compared to controls who did not receive counselling. This aligns with research conducted by Ernawati et al. (2020), which found that health counselling significantly affects TB patients’ treatment compliance (32).

One of the goals of counselling in chronic disease patients, including those with tuberculosis, is to improve medication adherence. With patient compliance, therapy outcomes are optimized. The addition of leaflets can help patients better understand information about their treatment (31).

Some of the benefits of health counseling include: patients obtaining additional information related to TB disease, can help patients overcome problems during treatment, ensuring the safety and effectiveness of
treatment, improve adherence in carrying out treatment so that it is expected to increase the effectiveness and efficiency of health costs (31).

Distance of Residence to Health Services
The results of Nasrullah's research (2023) showed that the location of residence influenced compliance with OAT in TB patients. The results of the bivariate analysis showed that residence factors affected TB patients' adherence to treatment ($p = 0.000$). It was found that people with good medication adherence lived in areas with clean environments and close access to health services. More immediate access to TB treatment and better infrastructure facilitates treatment delivery and enables TB patients to adhere more to the cure (39).

CONCLUSION
This review describes 15 factors that influence adherence to TB treatment in Indonesia. The findings of this study indicate that the most dominant factor influencing treatment adherence among tuberculosis patients in Indonesia is predisposing factors, namely education, knowledge, and self-efficacy. To address this issue, efforts to health promotion need to be intensified, and appointment of Directly Observed Therapy (DOT) for the Treatment of Tuberculosis originating from the nuclear family. Treatment adherence is a matter of concern in global efforts to reduce TB cases because irregularity or discontinuation of treatment can lead to resistance to antituberculosis drugs, ultimately increasing treatment costs and prolonging the required treatment duration.

AUTHOR'S CONTRIBUTION STATEMENT
Fahrul Islam, Haeranah Ahmad, Nurbaya, together with all authors, determine the topic, design, and research methods, and compile the literature review articles, as well as approving the articles prepared for publication.

Masnaeni Ahmad, Ansar, Kadar Ramadhan, Muhammad Syukri, Syafran Arrazy, Agung Aji Perdana, Deborah Siregar, together with all authors, determine the topic, design, and research methods, and are responsible for analyzing and synthesizing data, as well as approving the articles prepared for publication.

Nining Ade Ningsih, Ikes Dwi Astuti, St. Kadijah Hamid, and Asrul Hamonangan Pasaribu, together with all authors, determine the topic, design, and research methods, and are responsible for conducting article searches based on agreed-upon keywords, as well as filtering articles according to the inclusion criteria established collectively by all authors. They also approve the articles prepared for publication.

CONFLICTS OF INTEREST
The authors have no conflicts of interest to disclose.

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