

Factors of medication adherence among adult patients with tuberculosis: A literature review

Factores de adherencia a la medicación en pacientes adultos con tuberculosis: una revisión de la literatura

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SUMMARY

Introduction: Medication adherence is a critical factor in the success of tuberculosis (TB) therapy. Many factors are related to TB medication adherence among TB patients in clinical and community services. This study aimed to identify the factors of TB medication adherence based on the Social-Ecological Model. **Methods:** A literature review was carried out for this study. Articles published between 2016 and 2021 in three databases were included in this study. This study only targeted TB patients and assessed the determinants or factors related to tuberculosis medication adherence. Data were extracted using the Social-Ecological Model factors consisting of four levels: individual, relationship, community, and societal. A total of 17 articles were enrolled in this review.

Results: The results of the studies found that the determinants to improve medication adherence

include four-level factors, including individual, relationship, community, and societal factors, to design the medication adherence program for tuberculosis patients.

Conclusion: Multiple and holistic factors influence TB medication adherence. It is crucial to assist TB patients in overcoming the barriers that can prevent patients from adhering to treatment.

Keywords: Determinants factors, medication adherence, tuberculosis.

RESUMEN

Introducción: La adherencia a la medicación es un factor crítico en el éxito de la terapia de la tuberculosis (TB). Muchos factores están relacionados con la adherencia a la medicación antituberculosa entre los pacientes con tuberculosis en los servicios clínicos y comunitarios. Este estudio tuvo como objetivo identificar los factores de adherencia a la medicación para la TB a partir del Modelo Socio ecológico.

Métodos: Para este estudio se llevó a cabo una revisión de la literatura. En este estudio se incluyeron artículos publicados entre 2016 y 2021 en tres bases de datos. Este estudio se centró únicamente en pacientes con TB y evaluó los determinantes o factores relacionados con la adherencia a la medicación antituberculosa. Los datos se extrajeron utilizando los factores del modelo socio ecológico que consta de cuatro niveles: individual, relacional, comunitario y social. Un total de 17 artículos se inscribieron en esta revisión.

Resultados: Los resultados de los estudios encontraron que los determinantes para mejorar la adherencia a la medicación incluyen factores de cuatro niveles, que incluyen factores individuales, relacionales,

DOI: <https://doi.org/10.47307/GMC.2022.130.s5.45>

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Recibido: 11 de septiembre 2022

Aceptado: 7 de octubre 2022

comunitarios y sociales, para diseñar el programa de adherencia a la medicación para pacientes con tuberculosis.

Conclusión: *Múltiples y holísticos factores influyen en la adherencia a la medicación antituberculosa. Es crucial ayudar a los pacientes con TB a superar las barreras que pueden impedir que los pacientes se adhieran al tratamiento.*

Palabras clave: *Factores determinantes, adherencia a medicamentos, tuberculosis.*

INTRODUCTION

Tuberculosis (TB) is currently a health problem worldwide. World Health Organization (WHO) determined that pulmonary TB is a highly prevalent communicable disease, especially in developing countries (1,2). Pulmonary TB is the most common infectious disease and one of the leading global causes of mortality from infectious diseases (3-6). In addition, pulmonary TB is a threat because the cure rate is still low (2,7-9).

In 2020, an estimated 9.9 million patients will suffer from tuberculosis worldwide (127 per 100 000 population) (10). The major of tuberculosis cases geographically in 2020 reached 43 % occurred in Southeast Asia and Africa. The 30 nations with the highest incidence of TB accounted for 86 % of all estimated incident cases worldwide, with eight of these countries accounting for two-thirds of the global total (India, China, Indonesia, Philippines, Pakistan, Nigeria, Bangladesh, and South Africa) (4). TB was the 13th most prominent cause of death globally and the leading infectious agent-related cause. Globally, 1.3 million TB patients with HIV-negative persons died in 2020. And about 85 % of total tuberculosis deaths are from African and Southeast Asia regions, including Indonesia (4). In Indonesia, deaths caused by tuberculosis reached 93 000 per year, equivalent to 11 deaths per hour (11).

Adherence to TB treatment is vital to achieving a cure. Non-adherence to the treatments worsens TB conditions, increases infectiousness, initiates drug resistance, and can cause death (12-14). Non-adherence to TB treatment is the most significant obstacle to tuberculosis control globally. In addition, it contributes to treatment

failure (12,15). In 2019, the global success rate of patients treated for tuberculosis with first-line regimens was 86 %, which is lower than the standard (90 %) (4). And about 40 % of patients in developing countries worldwide had poor adherence to TB therapy (13).

Based on the Directly Observed Treatment Short-course (DOTS) program, patients with tuberculosis typically required at least six months of therapy (16-18). Numerous TB patients experience recurring symptoms because of inadequate treatment procedures. Patients with TB frequently re-enter the hospital because their condition worsens (19). Many factors can affect the success of tuberculosis treatment. To investigate successful therapies, it is crucial to determine the various causes of non-adherence and identify those that are adjustable. Hence, finding a suitable model or theory to summarize the factors that affect medication adherence behaviour is necessary. The social-ecological model is one of the models that has been suggested to comprehend chronic disease adherence (20).

The social-ecological Model of health takes a comprehensive view and focuses on various variables that may influence health. According to the social-ecological model, health is affected by the interplay of the individual, the group/community, and the physical, social, and political settings. The Centers for Disease Control and Prevention (CDC) developed a four-level model of health-related factors based on the social-ecological model, including individual, interpersonal, community, and societal (21). This literature review aims to summarize and identify the determinants related to TB medication using four-level of factors from the Societal-Ecological Model.

METHODS

A literature review was carried out for this study. This study extracted data from three databases (Scopus, EBSCO, PubMed) published between 2016 - 2021 and written in English publications. The articles used examined factors, determinants, and barriers related to compliance or adherence and loss to follow-up in the treatment of adult tuberculosis patients. The databases

search used the following terms (Determinants OR Factors) AND (Tuberculosis OR Tuberculosis Pulmonary) AND (Medication Adherence OR Patient Compliance) based on Medical Subject Headings (MeSH) terms. Both qualitative and quantitative research articles were included. However, only research articles were included that assess factors and determinants affecting tuberculosis medication adherence among tuberculosis (TB) and multi-drug resistance tuberculosis (MDR-TB) patients. Exclusion criteria consist of research published as a thesis or dissertation, studies that did not focus on the factors related to the successful treatment of TB, poor-quality study designs, and confusing arguments in the literature.

Researchers inferentially extracted data from each article. The literature review approach is

illustrated in Figure 1. Data were analysed and presented containing several aspects such as author, country, study design, sample, population, and findings that were utilized to extract the data. The first author of this work was responsible for article selection and data extraction, while the other authors screened and verified the consistency.

The data analysis in the literature review necessitates that the data from the main source be sorted, encoded, classified, and summarized to describe the research problem in this study (22). To reach the aim of this study, data were extracted using the social-ecological model, which consists of four levels: individual, interpersonal, community, and societal factors. The process of the review article is depicted in Figure 1.

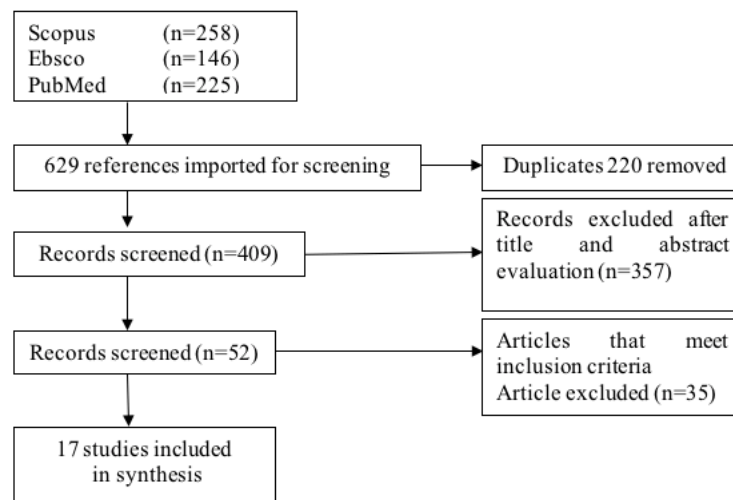


Figure 1. Flow chart of the identification process on review article.

RESULTS

Based on Table 1 Total below concerning on summary selection of studies that related tuberculosis medication adherence in adult patients of 17 studies was included in this literature review. Three articles were qualitative studies, 12 were quantitative studies (4 cross-sectional, 4 cohort, and 4 case-control studies), and 2 used a mixed-method design. These studies

were conducted in China (5), Ethiopia (3), Kenya (2), Indonesia (2), Washington D.C. (1), South Korea (1), Eritrea (1), Brazil (1), and Uganda (1).

Based on this review’s results, there are several factors or determinants of TB medication adherence that can be organized into four groups: individual, relationship, community, and societal. The categorization of each determinant is displayed in Table 2.

Table 1. Summarize Selected Studies of Factors that Related Tuberculosis Medication Adherence in Adult Patients.

N°	Study	Country	Design	Sample	Population	Factors Related to Medication Adherence
1	Bea et al. (2021)	South Korea	Cohort study	987	TB patients	Patients who initiate triple regimen (9 months), >60 years, patients with medical aid and comorbidities
2	Du et al. (2020)	China	Cross-sectional	564	TB patients	Age, unemployed, education, previous TB treatment, drug consumption, knowledge about TB, anxiety, stigma, alcohol consumption, medication supervision, adverse drug reaction
3	Asriwati et al. (2021)	Indonesia	Case-control study	136	TB patients	Role of health workers, the side effect, misperception of feeling healthy, knowledge
4	Zhang et al. (2020)	China	Qualitative study	17	TB patients	Patient-related factors (lack of knowledge of PTB treatment, poor self-management capability, poor self-regulation capability, and misperception of health condition), medication-related factors (medication side effects), health service-related (poor treatment skills of doctors in primary hospitals and a lack of directly observed treatment (DOT)), sociocultural factors (effect of traditional Tibetan medicine, lack of family member support and discrimination)
5	Yan et al. (2018)	China	Cross-sectional	1342	TB patients	Stigma, depressive symptoms
6	Eastment et al. (2017)	Washington D.C., U.S	Retrospective cohort study	393	Patients who initiated TB treatment	Behaviour (smoking and drinking alcohol), had more medical problems, type of treatment regimen, type of insurance
7	Boru et al. (2017)	Ethiopia	Qualitative study	22	TB patients	Inadequate eating, stigma and discrimination, the relationship between health workers and patients, beliefs in traditional medicine, lack of health facilities, drug side effects
8	Fang et al. (2019)	China	Cross-sectional	339	TB patients	Marital status (divorced or widowed), annual income, TB knowledge, and medical staff visit
9	Xing et al. (2021)	China	Mix method study	138	MDR-TB patients and health workers	The negative side effects busy work schedule, being female, self-perceived symptom improvement, financial difficulties, being from an urban area, being unmarried, having migrant status, being supervised by the health provider
10	Wanyonyi et al. (2017)	Kenya	Cross-sectional	252	Patients on DOTS	Age (over 60 years), income, daily alcohol consumption of > 3 days per week, and average waiting time of more than 1 hour in primary health care
11	Gebreweld et al. (2018)	Eritrea	Qualitative study	12	TB patients	knowledge, low income, drug side effects, treatment duration, distances to health care facility, stigma, lack of social support, health provider-patient relationship
12	De Oliveira et al. (2018)	Brazil	Case-control study	478	TB patients	Drugs consumption, non-adherence to a previous regimen, history of smoking, low income
13	Wekunda et al. (2021)	Kenya	Cohort study	291	TB patients	Alcohol consumption, female, lower education level, having treatment supporters, misperception of feeling healthy, stigma, distance from home to the health facility, lack of food, adverse event, perception of not having TB
14	Woimo et al. (2017)	Ethiopia	Mix method	261	TB patients	Knowledge, cost of medication other than TB, the distance of PHC from home, cost of transportation, having of health information at every visit, a lack of understanding concerning the importance of treatment completion
15	Ruru et al. (2018)	Indonesia	Case-control study	264	TB patients	Difficult access to healthcare, Lack of TB knowledge, treatment experience (TB education provided by the nurse)
16	Batte et al. (2021)	Uganda	Cohort study	227	MDR TB patients	Previous treatment
17	Mekonnen & Azagew (2018)	Ethiopia	Cross-sectional	314	TB patients	In the continuation phase, comorbidity, poor patient-provider relationship, alcoholic, being busy, being out of home/town, poor knowledge of TB, forgetting

TB: Tuberculosis; PTB: Pulmonary Tuberculosis; MDR-TB: Multi-Drug Resistant – Tuberculosis; DOTS: Directly Observed Treatment Short-Course

Table 2
Factors of Medication Adherence

Factors	Study
Individual	1,2,3,4,6-17
Relationship	2,4,7,8,9,13,17
Community	2,3,4,5,7,8,9,10,11,13,14,15,17
Societal	6,9

Individual

The individual is the first level of factors in the Social-Ecological Model. Sixteen studies mentioned individual factors related to tuberculosis medication adherence. The sociodemographic of individual factors found that low income, comorbidities, age, and education level impact TB medication compliance. We found 7 studies showed low income and experienced loss of job as a significant factor of adherence (12,16,23–27), 6 studies for comorbidities (16,28–31), and 2 studies for age/elderly (25,28), and 2 studies for the level of education (16,32). TB patients with low income have difficulty paying for transportation costs to health services and also face a lack of food during treatment (12,13,27,32). TB patients with comorbidities such as depression, diabetes mellitus, and HIV are more noncompliant with TB medication. Low treatment adherence in the elderly may be attributable to the increased probability of multimorbidity and resulting polypharmacy risk in this population (28). Moreover, less-educated patients may comprehend less about tuberculosis and the necessity of treatment adherence (32).

Sixteen studies confirmed that individual factors included side effects, lack of knowledge, misperception of TB treatment, behavioural factors, history of interrupted, and being away from home. It was found individual factors including 6 studies for side effects (12,13,16,24,33,34), five studies for lack of knowledge (12,16,33–35), four studies for the misperception of TB treatment (24,32–34), three studies for behavioural factors (16,25,30), three studies for the history of interrupted (16,32,36), and one studies for being away from home (29).

The side effect of the medication also a key factor related to TB medication compliance.

The side effect will lead to the misunderstanding that the condition worsens. If patients are not explained the side effects of anti-TB medications, the patient will discontinue the regimen (16,33). One of the critical factors of individual factors that affect successful TB medication is knowledge about TB and its medication. If patients had good knowledge about TB disease, management, and medication, they might adhere to the regimen. Appropriate knowledge will influence personal attitudes and behaviours toward treatment compliance, helping the patient's healing process (33). Patients also have a misconception and believe they have been cured even though they have not finished treatment yet (24,34). Behavioural factors such as alcohol, drug consumption, and smoking play an essential role in the success of TB treatment. Alcohol disrupts sleep patterns, affects judgment, and causes forgetfulness. Patients may forget to take their prescriptions or miss appointments, causing the therapy to be interrupted. TB patient who previously interrupted treatment has a chance to do the interruption again. Being away from home or town was cited as a factor for TB patients to stop taking anti-TB drugs because the patients tend to neglect pulmonary TB treatment (29).

Relationship

The relationship is the second level of factors in the Social-Ecological Model. The second level investigates intimate relations that may enhance the potential for health behaviour (37). Seven studies confirmed that relationship factors had supporters from social or family and patient-health provider relationships. There were six studies on the patient-health provider relationship (13,16,23,24,29,34) and two studies on support from social and family (32,34). Medication supporters from social and family lead to successful TB therapy. Support from social and family is critical for adherence to anti-TB therapy by supporting money for food and transportation, encouraging, motivating, and reminding patients of their medicine, helping with drug administration, and offering support to patients who have lost hope (13). A poor patient relationship with providers was also linked to lower TB drug adherence. Poor relationship between patients and healthcare professionals

has created a gap in providing patients with accurate information about the therapy. This may cause patients to withhold their concerns from caregivers (13).

Community

Community is the third level factor of the Social-Ecological Model. Community factors such as schools, offices, and society, where connections occur, aim to discover the aspects of these settings connected with health behaviour (37). In this study, thirteen studies related to the community factors, including health providers' attitudes, roles, and capability, stigma and discrimination, difficult access to health facilities, beliefs system, and health facility service. The most barrier to these factors was found in eight studies for health providers' attitudes, roles, and capability (13,23,24,27,29,33-35), six studies for stigma and discrimination (12,16,29,31,32,34), and five studies for difficult access to health facilities (12,13,27,32,35), two studies for beliefs system, and one study for health facility service (25).

Health providers' attitudes, roles, and capabilities in caring, giving information, and support are among the main factors in TB medication adherence. The role of health providers in assisting pulmonary tuberculosis patients can enhance awareness, motivation, and cooperation in treatment, so it can help them boost their spirit and willingness for successful treatment (33). Stigma is one of the critical determinants of the successful treatment of tuberculosis. Stigma and discrimination reduce patients' self-esteem, efficacy, and confidence, decreasing adherence to therapy (31). Difficult access to health facilities, particularly those from rural areas, has significantly impacted Adherence to TB treatment, especially in developing countries with restricted services and inadequate infrastructure (13). The belief system of traditional medicine can affect medication adherence among Tuberculosis patients because the patients believe that traditional medicine is more effective, affordable, and accessible, has less time for treatment, and keep away from bad spirits (13,34). A study in Nandi County revealed that the dropout of TB patients was associated with a long waiting time at the health

care facility because they are dissatisfied with the service and are reluctant to return for the next appointment (25).

Societal

The last factor in Social-Ecological Model is societal factors. Societal is the fourth level according to this model. Societal factors include national and international policies, cultural values, and norms (38). In this literature review, two studies related to societal factors include one for lack of insurance (20) and one for migrant status (24). Lack of insurance is connected with a lower rate of TB treatment completion (30). Lack of resources for basic insurance is likely a sign of poverty, implying that patients lack the finances to visit the clinic. However, TB treatment is free in the DOTS program (30). Patients with tuberculosis who were migrants had more non-compliance behaviours (24). Migrant status is connected with non-compliance with treatment, with migrants concealing or fleeing treatment centers out of fear of deportation (39).

DISCUSSION

The Social-Ecological Model is a framework designed to help people comprehend the many levels of society and how people and the environment interact in social systems. Factor interactions are examined at four levels, with components within a single level having equivalent effects. At all levels of health, different causes and determinants exist, making prevention, control, and intervention most successful when models are addressed from all levels. Therefore, working on multiple model levels simultaneously is required (37,40).

Adherence to TB medication is a complex issue influenced by multiple factors or determinants. The individual factor is the first level factor of the social-ecological model. All of the papers mentioned that individual factors affect medication adherence or successful treatment among TB patients. Individual factors are the most mentioned or frequent factor related to TB medication because patients undergo the treatment. Patient-based interventions are needed

to increase patients' awareness and attitude toward TB and its medication for the success or cure of tuberculosis patients. From the study, the most factors from the individual level are income, knowledge, and side effect. For income barriers, financial help or support for food, transportation, and medication adherence significantly increased when participants understood TB prevention and therapy. A study from Kenya showed that some participants were confused if the condition could be treated, while others were unaware of the length of treatment. As a result, comprehensive teaching and counselling at the start of TB therapy are critical to improving drug adherence (16). Side effects might lead the patients to stop taking their medication because they believe their symptoms are worsening. Explaining the symptoms of side effects while receiving therapy and monitoring may be done to prevent medication side effects (33).

The relationship factor is the second level factor of the Social-Ecological Model. The family plays a role in supervising and motivating the patient to regularly swallow the drug for up to 6 months to recover completely (41). Not only family, friends, neighbors, and partners, for example, impact a person's conduct and add to their experiences. At this level, prevention strategies may include family-focused prevention and social programs to build communication and encourage positive norms, problem-solving skills, and healthy behaviours to increase successful medication adherence (37).

The third level of factor from the Social-Ecological Model is community factors. Community factors play crucial parts in adhering to tuberculosis treatment. One of the community factors is the role of health providers and social workers, who are still needed to provide support, information, and motivation to make the treatment program for tuberculosis patients more successful. Their efforts in providing information related to TB and the treatment process, especially the side effects of DOTS, are needed for TB patients to take treatment without fear of side effects and learn how to manage DOTS side effects. Healthcare practitioners must pay greater attention to patients' opinions and concerns and devote additional time to listening to their experiences with sickness (42). Health workers need to increase trust in patients so that patients

can comply with tuberculosis treatment. One way to improve the role of health providers is that medical staff visits benefit treatment adherence because patients perceive that health workers pay them more attention and have greater trust in their ability to get treated (23).

Stigma, discrimination, and beliefs are community factors that can also affect the patient's success in recovering from tuberculosis. Unwanted social standards in society cause stigma and discrimination. As a result, the structure of a community's beliefs and norms regarding an illness and the associated stigma may significantly influence health (43). Social and psychological programs aimed at reducing stigma among tuberculosis patients should be implemented and refined to increase medication adherence (31). Community-scale program support is needed to reduce stigma and discrimination and change views on tuberculosis treatment with traditional medicine and by taking standardized tuberculosis drugs. Furthermore, paying attention to psychological support for the patients increases adherence to the therapy (16).

The fourth level factor of the Social-Ecological Model is the societal factor. The literature showed that lack of insurance can affect medication adherence among tuberculosis patients. Therefore, it is needed to find an intervention targeting the social or policy level. Changes in medical insurance coverage for prescription medications are one example of a societal-level factor (44). Even though the medication for tuberculosis is free, regulations are needed to improve the patient's economy and make it easier for patients to reach tuberculosis treatment.

Because these factors are classified using the Social Ecological Model into four levels of factors, further research is needed using other theories to organize factors related to adherence to tuberculosis medication. In addition, there are some limitations to this study. First, this study uses only three databases (Scopus, PubMed, and Ebsco), so there may still be unanalyzed journals from other databases. This study is limited to English, and factors originating from other languages cannot be analysed. Lastly, this study is only grouped into four factors, so there may be other factors or determinants affecting TB patients' adherence to treatment.

CONCLUSION

Many factors can affect patient compliance. The most mentioned from the literature review of determinants of tuberculosis medication adherence were individual factors. However, apart from individual factors, other factors, such as relationships, community, and societal factors, contribute to tuberculosis treatment success. Therefore, health workers must pay attention to multiple factors in developing or planning programs to increase patient success in undergoing tuberculosis treatment, focusing on individual and all factors. Family and health workers also play an essential role in tuberculosis treatment success.

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