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Original Article

Relationship between Side Effects of Anti-tuberculosis Drugs (ATDs) and Adherence to Medication in Elderly Patients with Tuberculosis

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ABSTRACT

One of the obstacles to the treatment of tuberculosis (TB) patients is the side effects of anti-tuberculosis drugs (ATDs) which cause patients to be reluctant to continue the medication. The elderly experience various physical and physiological changes in the body system, including susceptibility to drug side effects, decreased knowledge and memory, resulting in non-compliance with taking the medication. This study aims to determine the relationship between ATDs side effects and compliance with taking medication for elderly patients at the Tanjung Selor Health Center, Bulungan Regency, North Kalimantan Province. This study used a quantitative *cross-sectional* approach. The sample was taken by total population, namely elderly tuberculosis patients undergoing tuberculosis treatment as many as 30 respondents. The research instrument was a questionnaire of drug side effects and ATDs compliance. Statistical test used *Fisher's Exact*. The results showed that most patients (76.7%) complained of OAT side effects and the rest without OAT side effects (23.3%). Treatment compliance was 20% compliant, and 80% were non-compliant. *Fisher's Exact* statistical test obtained *p-value* = 0.016 (< α = 0.05). It was concluded that there was a significant relationship between OAT side effects and treatment compliance in elderly patients with tuberculosis. Recommendations for health workers to give special attention to elderly patients with medication monitoring and compliance motivation. Future researchers should identify the involvement of family and health workers to monitor the side effects of anti-tuberculosis drugs.

Keywords : Drug Side Effects, Anti-Tuberculosis Drugs (ATDS), Medications Adherence, Elderly People.

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INTRODUCTION

Tuberculosis is a major serious public health problem, and be included in one of the top 10 causes of death worldwide [1], and is one of the top 10 causes of death worldwide [2]. Even WHO estimates that the death rate from tuberculosis is twice as high as HIV/AIDS, estimated in 2021 due to to HIV / AIDS as much as 0.47 million [3].

In 2021, the number of people with TB worldwide is estimated to be 10.6 million, an increase of about 600,000 cases compared to 2020. Of these, 6.4 million (60.3%) people have been reported and are receiving treatment and another 4.2 million (39.7%) are undetected/undiagnosed, at least 6 million adult men and 3.4 million productive women, and the remaining children, 1.2 million cases[2].

The number of tuberculosis patients in Indonesia in 2021 increased by 12.9% from 2020. Most TB cases were found in the age group of 45 - 54 years (17.5%), followed by the age group of 25 - 34 years (17.1%) and 15 - 24 years (16.9%).4. The *Case Detection Rate (CDR)* of tuberculosis in North Kalimantan Province in 2020 was 64% of the 1,607 cases found, while in 2021 it decreased to 33% of people with a cure rate or *Succes Rate (SR) of* 75% and *Drop Out (DO)* in treatment as many

as 226 people (14%), in 2022 there was a decrease in case finding with 338 people with a *Succes Rate (*SR) of 63% there were 67 people who *dropped out* [4,5].

The elderly are vulnerable to various infectious diseases such as tuberculosis due to the degeneration process which has an impact on the decline in body system function and immunity[6]. In addition, comorbid factors such as diabetes miletus, which commonly occurs in the elderly, become a risk factor for contracting tuberculosis infection[7,8]. The number of elderly people with tuberculosis in Bulungan Regency in 2021 was 64 people with an average of 4 people / month. In 2022 at Puskesmas Tanjung Selor from January to June 2022 there were 24 people, the most new positive *pap smear* cases were recorded at Puskesmas Tanjung Selor. Of the total number of patients at Puskesmas Tanjung Selor, no less than 45 people were diagnosed and treated, 24 of them were elderly, the rest were productive age and children[5].

Anti-Tuberculosis Drugs (OAT) are a combination of drugs consisting of Isonoazid (H) Rifampicin (R) Pyrazinamide (Z) and Ethambutol (E) each of which has side effects such as nausea, decreased appetite, abdominal pain, tingling, joint pain, and redness of urine[9]. Some patients complain of itchinh, redness of the skin, hearing loss, visual disturbances, balance disorder dan yellowing of the skin[10].

The patients undergoing ATD treatment are susceptible to experiencing side effects, particularly during the initial intensive phase due to daily medication intake[11], these side effects may include nausea and red urine, which are associated with rifampicin[9]. Additionally, fatigue, fever, runny nose, and bone pain or ostealgia may arise as side effects of isoniazid[12,13]. The side effects of the medication are experienced by the patient, even causing the patient to feel apathetic towards the symptom experienced during therapy[13]. In order to ensure compliance with medication ingestion and achieve the optimal treatment outcomes, it is essential to provide monitoring and education regarding the potential adverse effects of ATDs (anti-tuberculosis drugs). [14] .

Non-compliance should not exceed 10% as it leads to a higher proportion of relapse in the future due to ineffective tuberculosis control. Therefore, it is crucial to monitor patients' symptom conditions during tuberculosis treatment, especially to prevent patients from non-compliance, which can result in serious side effects[14].

The preliminary study results from healthcare providers in Tanjung Selor Primary Health Center, Bulungan Regency, indicate the presence of complaints regarding medication side effects, leading to non-compliance among elderly individuals in taking their medication daily. In fact, some elderly individuals have discontinued medication intake due to a lack of understanding regarding the importance of regular medication adherence and managing medication side effects.

The author assumes that elderly individuals, who have specific characteristics such as age, physical changes, physiological changes in the body systems, memory capacity, social and psychological status, are vulnerable to non-adherence in tuberculosis treatment. The presence of side effects from various types of tuberculosis medication increases the risk of medication discontinuation or reluctance to visit the community health center (Puskesmas), requires special attention.

This study aims to analyze the relationship between the side effects of anti-tuberculosis drugs (ATDs) and treatment adherence among elderly patients at the Tanjung Selor Community Health Center in Bulungan Regency.

METHOD

This study used a quantitative correlational design with a cross-sectional approach. The data was collected and conducted at the Tanjung Selor Community Health Center, Bulungan Regency, from September 1st to September 30th 2022. The population of this study consisted of all elderly individuals with tuberculosis who were undergoing tuberculosis medication at the Tanjung Selor Community Health Center, Bulungan Regency. The total sample size was 30 people, selected through a total sampling method.

The research instrument consisted of a questionnaire on medication adherence using the Medication Adherence Rating Scale (MARS), which was adopted from Rob Horne. The MARS-5 comprises 5 items to assess non-adherence (forgetting, changing doses, stopping, deciding to take a lower dose, and taking less medication than prescribed)[15]. Meanwhile, the questionnaire on medication side effects utilized the Naranjo algorithm form for Monitoring Adverse Drug Reactions

(MESO), consisting of 10 items.[16].

Univariate analysis was conducted to determine the frequency and percentage distribution of each variable, while bivariate analysis utilized Fisher's Exact test to examine the relationship between the variables of medication side effects and treatment adherence. This research has undergone ethical clearance from the Research Ethics Commission of Health (KEPK) at the Health Polytechnic of the Ministry of Health in East Kalimantan and has obtained the Ethical Clearance Certificate No. LB.02.01/77.1/16170/2022.

RESULTS

Table 1. Characteristics of Respondents (n=30).

Characteristic of Respondents	f	%
Age		
l-60 years old	21	70
l-70 years old	9	30
Gender		
Male	19	63.3
Female	11	36.7
Marital Status		
Married	16	53.3
Widow	4	13.3
Widower	10	33.3
Educational Background		
No Formal Education	11	36.7
Elementary School	6	20
Junior High School	5	16.7
Senior High School	7	23.3
Higher Education	1	3.3
Occupaation		
Housewives	9	30
Farmers	8	26.7
Civil Servants (PNS)	6	20
Labourer	4	13.3
Retiree	1	3.3
Self-employed	2	6.7
Time of TB Affliction		
1-12 Months	29	96.7
>12 Months	1	3.3

Table 1 shows the characteristics of the respondents, consisting of 30 respondents aged 51-60 years, with 21 individuals (70%) falling within this age range, while the remaining respondents were above 61 years old. Among the respondents, 19 individuals (63.3%) were male, 11 individuals (36.7%) had no formal education, 9 individuals (30%) worked as housewives, and almost all of them had experienced tuberculosis for a duration of 1-12 months (96.7%). Only one respondent had been suffering from tuberculosis for more than 12 months.

Table 2. Side Effects of Medication and Adherence to Anti-Tuberculosis Medication (n=30)

Side Effects	f	%
Present	23	76.7
Absent	7	23.3
Adherence to Medication	f	%
Non-adherent	24	80
Adherent	6	20

Table 2 demonstrates the side effects of anti-tuberculosis medication, where 23

respondents (76.7%) reported experiencing side effects, while 7 respondents (23.3%) did not complain of any side effects. The majority of respondents (80%) were identified as non-adherent in taking the medication, while the remaining 20% were adherent in taking the anti-tuberculosis medication.

Table 3. Relationship between the Side Effects of the Medication and Medication Adherence

ATDs Side Effects	Medication Adherence				Total		*p-value*
	Non-adherent		Adherent				
	f	%	f	%	f	%	
Present	21	70	2	6,7	23	76,7	0,016*
Absent	3	10	4	13,3	7	23,3	
Total	24	80	6	20	30	100	

Table 3 presents the results of the Fisher's Exact test, yielding a p-value of 0.016, which is lower than the significance level $\alpha = 0.05$. This indicates a statistically significant relationship between the side effects of anti-tuberculosis medication (ATDs) and treatment compliance among elderly patients with pulmonary tuberculosis at the Tanjung Selor Health Center, Bulungan Regency.

DISCUSSION

The study findings indicate that tuberculosis mostly affects individuals in the pre-elderly age group, with a higher prevalence among males compared to females. Only a small proportion of individuals have attained high school and higher education, while the majority of elderly patients did not complete their education. On average, elderly individuals suffer from tuberculosis for an extended period, requiring prolonged treatment processes.

Previous studies largely depict the characteristics of tuberculosis patients as predominantly found in the productive age group, predominantly affecting males, those with lower educational attainment, commonly engaged in labor-intensive or unemployed occupations, and having low socioeconomic status.[17–19].

The increase in age may influence the dose-response relationship and the occurrence of mild and severe side effects[20]. The risk of medication side effects is affected by age, as the liver's drug metabolism function declines with advancing age, leading to a higher risk of side effects[21]. In contrast, when individuals are younger, their body systems are more efficient in drug metabolism and controlling various medication side effects[22].

Elderly individuals who still live with their partners will mutually remind each other about their treatment. However, in this study, it was found that among the elderly age group, there were more married individuals who suffered from tuberculosis compared to widowed individuals. The risk factors for tuberculosis transmission include household contact, [23,24], due to physical proximity, duration of contact, and inadequate preventive behavior[25].

Low education is generally associated with a higher prevalence of tuberculosis, as indicated by the findings of this study. The majority of respondents had a basic education, specifically elementary and junior high school, with some even lacking formal education. The lack of formal education serves as a contributing factor to the insufficient understanding and ability of individuals to absorb the importance of tuberculosis treatment[10].

On the other hand, occupational, social, and economic conditions are also parts of the respondents' characteristics. In order to meet their daily needs, patients are also engaged in work and other social activities, which often leads to neglecting their treatment adherence, especially when patients start feeling better. The findings of this study align with the fact that younger individuals are more compliant with medication intake compared to older respondents[26], However, this differs from the results of the study conducted by Liang Du et al., which stated that treatment adherence increases with age, possibly because older patients exhibit more socially conscious behavior and have more life experiences and ideologies[27], it can be said that there are multiple response characteristics that influence patient adherence to medications.

1. *ATDs Side Effects*

The results of this study illustrate that the side effects of medication are mostly experienced by elderly tuberculosis patients, which generally occur in other tuberculosis patients as stated in previous research. Complaints of medication side effects such as nausea, vomiting, tingling sensation, reddish urine color, decreased appetite, weakness, and bone pain are the expected consequences of drug interactions in tuberculosis patients. However, these effects can be prevented and modified to avoid health problems and treatment program issues[11,13,28,29].

The side effects of anti-tuberculosis drugs need to be monitored, and if necessary, multiple alternatives and recommended management of side effects should be employed to ensure the continuity of tuberculosis treatment[30]. Inappropriate tuberculosis treatment, such as low or high dosage and improper treatment duration, can lead to ineffective treatment outcomes, relapse, and drug resistance in tuberculosis patients[31]. The use of rational drug therapy is defined as meeting the specific needs of patients, including appropriate indications, drug types, dosages, diagnoses, administration methods, timing, and providing patients with accurate information regarding the efficacy of the medication[12].

2. Medication Adherence

The medication adherence variable among the elderly is predominantly non-compliant, indicating that the elderly population differs from other adult groups. Previous research on treatment adherence in tuberculosis patients has shown mixed results, with the majority of studies conducted in the past five years reporting a relatively high level of treatment adherence to tuberculosis [32–34].

Patient adherence to medical appointments is a manifestation of the patient's compliance with regular check-up schedules or healthy behaviors, highlighting the significant role of health behavior in treatment adherence [35].

The author assumes that age plays a crucial role in medication adherence behavior among tuberculosis patients. This is proven by the fact that the majority of elderly respondents were non-compliant in taking anti-tuberculosis medication, which differs from previous studies that focused on the general population. Education serves as a means for individuals to acquire knowledge and broaden their insights, thereby influencing patients' level of understanding. Employment supports the family's economy and can encourage patients' awareness of seeking treatment and preventing tuberculosis. In this study, the majority of respondents had a basic education level (elementary and junior high school), and some had no formal education, implying a lack of understanding of treatment and consequently leading to non-adherence. The higher the level of education, the greater the individual's communication skills, facilitating the management of the treatment process.

The level of education and knowledge determine health behaviors, the higher levels of education associated with better health behaviors. The education level of the community influences the overall health status[36]. Despite the advanced improvement, access to healthcare services does not seem to be aligned with the progress. Meanwhile, elderly patients encounter obstacles in local conditions, a significant proportion of whom face difficulties in accessing healthcare facilities in contrast to adults[37].

The statistical analysis results indicate a significant relationship between the side effects of anti-tuberculosis drugs (ATDs) and medication adherence in elderly patients with pulmonary tuberculosis. The relationship between the type of drug, dosage, and frequency of medications and the body's response to the occurrence of mild to severe side effects may vary with age. The probability of drug side effects depends on age, because liver function in drug metabolism decreases with age, leading to an increased risk of various drug-related adverse effects[21].

On the other hand, in younger individuals, their body systems are still functioning well to metabolize various substances and minimize the occurrence of drug side effects[22].

The findings of this study are supported by previous research which states that the more severe the side effects of anti-tuberculosis drugs, the more patients tend to experience fear of swallowing or non-adherence to medication. Conversely, if the side effects of anti-tuberculosis drugs are mild, patients are more likely to be compliant in completing their treatment[10].

The research conducted by Nyorong et al. (2021) reveals that the pharmacological side

effects variable has the most significant value (p=0.000)[38]. Patients and their families should be supported by the Primary Health Center or healthcare professionals who are responsible for implementing the tuberculosis treatment program. This support enables them to oversee the medication adherence of their loved ones and prevent drug withdrawal and resistance. As part of the health education provided by healthcare professionals, they explain the side effects of tuberculosis drugs and encourage patients to continue taking them until they are sufficiently healthy to do so.

Medication adherence is a condition that influences a patient's behavior in making decisions regarding their treatment. The severity of side effects from anti-tuberculosis drugs (ATDs) commonly experienced by tuberculosis patients affects their adherence to treatment, leading to patient reluctance to continue tuberculosis treatment[39].

The author assumes that the presence of drug effects is undoubtedly concerning and unpleasant for tuberculosis patients, thus influencing the adherence of individuals with tuberculosis. There may be different levels of severe, moderate, or mild side effects experienced by each elderly patient, which consequently reduces treatment adherence among elderly patients with pulmonary tuberculosis.

The limitations of this study include the possibility of other factors contributing to patient non-compliance, such as family support and the role of healthcare providers. The author did not conduct direct observation, and the data was collected based on questionnaires filled out by the respondents. The number of respondents was only 30 individuals, and it is possible that a larger sample size would yield more varied analysis results.

CONCLUSION

From the results of this study, it can be concluded that there is a significant relationship between the side effects of anti-tuberculosis drugs (ATDs) and medication adherence among the elderly at the Tanjung Selor Community Health Center in Bulungan Regency. This is supported by the Fisher's Exact statistical test, which yielded a p-value of 0.016, lower than $\alpha = 0.005$. It is recommended that healthcare professionals give a special attention to elderly patients undergoing tuberculosis treatment by monitoring and providing motivation to both the patients and their families. Future researchers are advised to identify the involvement of family members and healthcare providers in monitoring the side effects of anti-tuberculosis drugs.

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