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Inappropriate use of Tuberculosis medications among TB patients in Vientiane capital, Lao People's Democratic Republic

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ABSTRACT

Background: Tuberculosis (TB) is an important communicable disease caused by *Mycobacterium* tuberculosis, which has been declared a global public health emergency by World Health Organization.

Objectives: To study the inappropriate use of anti-tuberculosis medications among tuberculosis patients in Vientiane Capital, Lao PDR.

Methods: This study was a cross-sectional survey, conducted in three central hospitals in Vientiane Capital. The study focused on tuberculosis patients aged 18 and older who were receiving anti-tuberculosis drug treatment. The sample was selected using a random sampling method. Data collected from face-to-face interviews were analysed with descriptive statistics and chi-squared tests using statistical analysis software (IBM SPSS, version 17).

Results: The study involved 221 participants of whom 60.6% were men, and 31.2% of all patients were between 29 and 39 years old. 36.3% of participants were found to have low knowledge regarding appropriate medication use and practices. Nearly 81.4% of participants answered incorrectly or did not know that tuberculosis can be resistant to medication. In total, 38.9% of the participants used inappropriate drugs, 29.0% did not take their medication on time every day, and 20.4% forgot to take medication. The study found inappropriate medication administration or behaviours were associated with increased risk of treatment failure or disease recurrence ($\chi^2 = 4.73$, P-value < 0.05).

Conclusion: Inappropriate medication use among those treated for TB is common in Lao PDR. This raises concerns about possible treatment failure and increased risk of drug-resistant tuberculosis in the sample group.

Keywords: Behaviour, Tuberculosis, Anti-Tuberculosis drugs

1. Introduction

Tuberculosis (TB) is a significant communicable disease caused by *Mycobacterium* tuberculosis (MTB). It primarily affects the lungs but can also spread to other parts of the body [1]. While it can be successfully treated with medication, the treatment can last up to 24 months [2]. The World Health Organization (WHO) has declared TB a global public health emergency [3]. Epidemiological data have identified three central issues with TB: the high prevalence, the increasing incidence, and finally, the rise of multi-drug-resistant TB (MDR-TB) [4].

The control of TB in developing countries is hindered by the spread of drug-resistant TB (DR-TB), especially multi-drug resistant strains, which are resistant to at least the first-line drugs isoniazid (INH) and rifampicin (RMP), significantly reducing the effectiveness of treatment. Among new cases, the estimated global rates of resistance are 17% for drug-resistant TB, 2.9% for MDR, and 35% for any drug resistance, and 15.3% for MDR in previously treated cases [5].

The burden of TB remains high in Lao PDR, ranking as the seventh leading cause of death in adults. In 2009, the prevalence of all forms of TB was estimated at 289/100,000, the incidence at 151/100,000 and mortality at 24/100,000 [6]. Inappropriate treatment and the emergence of drug-resistant TB leading to treatment failure are significant contributors to deaths caused by TB [7]. Multidrug-resistant tuberculosis (MDR-TB) is a major global concern. According to the WHO's global MDR-TB surveillance report, 3.5% of new TB cases worldwide are MDR-TB, and more severe MDR-TB has emerged [8].

Drug-resistant TB is often the result of improper use of tuberculosis drugs due to irregular or inadequate medication intake, discontinuous treatment, intolerance to side effects, co-morbidities affecting drug absorption, or inappropriate storage of tuberculosis drugs [9]. Treating DR-TB is challenging and costly due to its heightened risk of relapse, treatment failure, prolonged bacilli transmission, and increased risk of mortality [10]. Therefore, this present study aimed to identify the inappropriate use of anti-tuberculosis medications among tuberculosis patients in Vientiane Capital, Lao PDR.

2. Methods

2.1 Study Area

Data was collected from August to October 2023 at three central hospitals in Vientiane

Capital that routinely provide care for tuberculosis patients.

2.2 Study Design

This study comprised a cross-sectional survey of patients undergoing TB therapy.

2.3 Sample size and sampling

The sample population included tuberculosis patients over the age of 18 who had received anti-TB medication treatment (Cat I: 2 RHZE /4 RH). The sample size was determined using Yamane's formula (1967) [11]. During the initial eight months of 2023, 496 tuberculosis patients were registered for treatment at three central hospitals, according to the Lao National TB Control Centre [12]. The sample was computed using the subsequent formula:

$n = N/1+N(e)^2$

n = the sample size

N = the population of TB patient

e = The margin of error in the computation is 5%.

$n = 496/1+494(0.05)^2$

n = 221

Inclusion criteria

Individuals were enrolled for treatment at one of the three central hospitals.

They received anti-TB drug treatment Category I: 2 Rifampicin, Isoniazid, Pyrazinamide & Ethambutol (RHZE) / 4 Rifampicin & Isoniazid (RH) or followed a single-medication regimen.

They adhered to the prescribed medication for a minimum duration of one month.

Participants provided consent to take part in the study and were able to comprehend written communications.

Exclusion criteria

Patients under 18 years of age and patients with drug-resistant tuberculosis. Eligible participants were selected using a random selection technique. The patients were chosen from the list of registered individuals undergoing TB treatment at the central hospitals. Patients receiving their medication were invited to participate in the study. Researchers identified prospective participants, described the study and its objectives, and requested their consent to participate.

2.4 Data Collection

Interviews were conducted in a setting where only the researcher and the participant were present, ensuring that the influence of medical staff was minimized. The researchers

posed the questions and documented the participants' responses.

In-person interviews were conducted using structured and semi-structured questions. Both closed-ended and open-ended questionnaires were employed to evaluate content validity and reliability. Content validity was assessed by three experts with expertise in tuberculosis treatment and control. Following the expert's review and scoring of the questionnaires, the researcher computed the content validity index (CVI) for scores ranging from 1 to 4 (1 indicating no relevance, 2 indicating low relevance, 3 indicating moderate relevance, and 4 indicating high relevance). The CVI for the 'knowledge' questions was 0.86, while the 'medication use' section received a score of 0.8. Subsequently, the questionnaires were administered to a sample group of 30 individuals. Reliability was determined by calculating the Kuder Richardson Coefficient (KR-20) for both sections. The KR-20 for the knowledge section was 0.7, and for the medication use section, it was 0.8.

2.5 Data Analysis

The data were examined through descriptive statistics which encompassed frequencies, percentages, means, medians, and standard deviations, as well as minimum and maximum values, to encapsulate the features of the study population. The analysis was conducted using SPSS (IBM, version 17). The outcome measures focused on patient knowledge and instances of inappropriate medication use, detailed in the following sections. Comparisons were drawn between patients reporting appropriate versus inappropriate medication use, alongside their demographic characteristics and knowledge scores, using chi-square tests for the analysis.

2.5.1 Patient knowledge

A survey consisting of 13 questions was employed to evaluate patients' understanding of tuberculosis and its treatment. Each correct response earned one point, while incorrect answers received zero points. Participants' knowledge levels were categorized into three tiers based on Bloom's taxonomy [13].

- High level of knowledge = score greater than80% (≥ 10 points)
- Medium level of knowledge = score between 60 and 79% (7-9 points)
- Low level of knowledge = score less than 60% (< 7 points)

2.5.2 Medication use

A 12-point questionnaire was used to investigate patient behaviours related to medication use. Questions 1, 2, 3, and 8 served as indicators of inappropriate

medication use. If a patient engaged in any of these behaviours, it was considered inappropriate medication use. Scoring criteria were as follows: a patient received one point for each question if they engaged in the behaviour, and zero points if they did not. Therefore, a score of four indicated appropriate medication use, while a score of less than four suggested inappropriate medication use.

2.6 Ethical Clearance

This research received approval from the Research Ethics Committee at the University of Health Sciences (Approval No. 527/REC).

3. Results

General characteristics of participants

Two hundred twenty-one participants were included in the study. A majority (60.6%) were men and 31.2% of respondents were between 29 and 39 years of age. Half (50.7%) were married, a minority (21.7%) were employed, and about one-third (31.9%) had completed high school. Most (85.5%) of the patients had new diagnoses. Seventy-one percent had pulmonary tuberculosis, 67.5% were being treated with drugs in the 4RH regimen (Rifampicin and Isoniazid), and 50.2% were taking their medications without assistance from family members (Table 1).

Table 1: General characteristics of participants. (n=221)

Characteristics	Number (n)	Percentages (%)
Sex		
Male	134	60.6
Female	87	39.4
Age (Years)		
18-28	56	25.3
29-39	69	31.2
40-48	31	14.0
49-59	34	15.4
Over 60	31	14.0
Mean (±SD)	40.7(±15.7)	
Min: Max	18:82	
Marital status		
Single	94	42.5
Married	112	50.7
Divorced	6	2.7
Widowed	9	4.1
Occupation		
Farmers, cultivate and raise animals	25	11.3
Trading/doing private business	28	12.7
Employed	48	21.7
Government employees/employees of state enterprises	37	16.7
Unemployed	44	19.9
Student	18	8.1
Other	6	2.7
Retire	11	5.0
Monk	4	1.8

Characteristics	Number (n)	Percentages (%)
Education level		
Primary School	67	30.3
Secondary School	86	38.9
Undergraduate degree	28	12.7
Bachelor's degree	38	17.2
Higher than bachelor's degree	2	0.9
Type of patient		
New case	189	85.5
Re-infection	29	13.1
Re-treatment after fail	3	1.4
Type of disease		
Pulmonary tuberculosis	158	71.5
Extra-pulmonary tuberculosis	63	28.5
Chronic Disease		
Heart diseases	6	5.4
Hypertension	14	12.6
Diabetes	26	23.4
Stomach	6	5.4
Gout	2	1.8
Joint disease	4	3.6
Hyperlipidaemia	3	2.7
COPD	1	0.9
Other disease	49	41.1
Current medications used		
2RHZE (Rifampicin, Isoniazid, Pyrazinamide and Ethambutol)	45	20.4
4RH (Rifampicin and Isoniazid)	169	76.5
Single drug	7	3.2
Duration of drug use		
1 month	20	9.0
2 months	25	11.3
3 months	44	19.9
4 months	36	16.3
5 months	42	19.0
6 months	54	24.4
Assistants monitor patient medication		
Farther or Mother	28	12.7
Husband or Wife	41	18.6
Children	26	11.8
Family's member or Cousin	1	0.5
Self	111	50.2
Sister or Brother	12	5.4
Friend or Lover	2	0.9

The knowledge of using medication to treat tuberculosis

According to the study's findings, 37.6% of participants had moderate knowledge, and 36.3% had low knowledge. Around three-quarters of participants (77.8%) believed that taking drugs to treat tuberculosis can cure the disease. Most participants (90%) knew the duration of tuberculosis therapy, 88.2% were aware of adverse effects from the medication,

and 81.9% knew when to take the medicine. However, almost 91% of participants either answered incorrectly or did not know whether to take their medication before or after a meal. Similarly, 81.4% answered incorrectly or did not know whether tuberculosis can be resistant to anti-TB drugs, and 64.7% did not know the duration of their current treatment.

Tuberculosis medication use and behaviour

In terms of medication use, the study found that 29% of the participants did not take their medication on time every day, 20.4% forgot to take their medication, 14.9% never came to pick up their medication from the doctor on time, and 9% had temporarily stopped taking their medication without consulting a doctor. Only 2.3% had taken the wrong medication dose. When participants did not pick up their medication on the scheduled day, half (51.6%) picked it up the next day, and about one-third (35.0%) temporarily stopped taking the medication. Overall, more than one-third of participants (38.9%) used medication inappropriately.

Associations between demographic, knowledge, information, and inappropriate drug use

Among demographic characteristics, knowledge level, and patient reports of receiving information, only the type of infection was related to inappropriate use of tuberculosis drugs ($\chi^2 = 4.73$, $P < 0.05$), with patients with a new infection being more likely to use medications appropriately compared to those with reinfection or treatment failure (Table 2).

Table 2: Associations between demographic, knowledge, information, and inappropriate drug use. (n=221)

Variable	Behaviours		χ^2	P-value
	appropriate	inappropriate		
Sex				
Male	85(63.4)	49(36.6)	0.79	0.37
Female	50(57.5)	37(42.5)		
Age				
40 years old or lower	74(57.4)	55(42.6)	1.81	0.18
Upper 40 years old	61(66.3)	31(33.7)		
Marital status				
Married	73(65.2)	39(34.8)	1.60	0.21
Single, divorced and widowed	62(56.9)	47(43.1)		
Occupation				
Government strafe/private strafe	23(62.2)	14(37.8)	0.02	0.89
Farmers, cultivate and raise animals, employed, Unemployed and Other	112(60.9)	72(39.1)		
Education level				
Bachelor's degree or higher	24(60.0)	16(40.0)	0.02	0.88

Variable	Behaviours		χ^2	P-value
	appropriate	inappropriate		
Lower bachelor's degree	111(61.3)	70(38.7)		
Type of patient				
New case	121(64.0)	68(36.0)	4.73	0.03
Re-infection and re-treatment after failure	14(43.8)	18(56.2)		
Type of disease				
Pulmonary tuberculosis	94(59.5)	64(40.5)	0.59	0.44
Extra-pulmonary tuberculosis	41(65.1)	22(34.9)		
Other personal diseases				
Don't have other diseases	76(60.8)	49(39.2)	0.01	0.92
Have other diseases	59(61.5)	37(38.5)		
Current medications used				
2RHZE (Rifampicin, Isoniazid, Pyrazinamide and Ethambutol)	31(68.9)	14(31.1)	1.44	0.23
4RH (Rifampicin and Isoniazid) and single drug	104(59.1)	72(40.9)		
Duration of drug use				
2 months or lower	34(69.4)	15(30.6)	1.82	0.18
More than 2 months	101(58.7)	71(41.3)		
Assistants monitor or guide and monitor patient medication use				
Have an assistant	67(60.9)	43(39.1)	0.01	0.96
Don't have	68(61.3)	43(38.7)		
Level of knowledge				
Medium and high level of knowledge	89(63.1)	52(36.9)	0.68	0.41
Low level of knowledge	46(57.5)	34(42.5)		
Ever received health education about tuberculosis and tuberculosis treatment				
Yes	27(67.5)	13(32.5)	0.85	0.36
No or not sure	108(59.7)	73(40.3)		
Ever received brochures or documents on the use of TB drugs				
Yes	22(68.8)	10(31.2)	0.92	0.34
No or not sure	113(59.8)	76(40.2)		

Sources of information on drug use.

Almost all the advice participants reported receiving from a doctor or pharmacist was related to the administration of medicine (99.1%), including recommendations to take medicine every day (80.1%). Most participants (72.9%) reported never receiving any health education about tuberculosis or tuberculosis treatment; 83.7% of the participants had not received any brochures or documents on the use of anti-TB medications; however, a majority (68.4%) expressed a need for such materials. Two-thirds (66.5%) of the participants had never received information about drug-resistant tuberculosis.

4. Discussion

A cross-sectional survey was conducted in three central hospitals in Vientiane Capital to assess the knowledge and medication

practices of patients with tuberculosis regarding the disease and its treatment. Inappropriate anti-tuberculosis medication use was found to be higher among patients with treatment failure or reinfection. Knowledge levels of participants regarding TB treatment were split relatively evenly across three levels – low, medium, and high. These findings likely reflect the demographic characteristics of the participants, with a minority being employed and a majority not having completed high school. In addition, regardless of their education baseline, few reported receiving education on how to correctly take tuberculosis medications or the importance of adherence.

While similar studies have not been found in the literature review, related studies have explored patient understanding of the effectiveness of tuberculosis treatment. For example, around three-quarters of patients understood that TB medication courses cure the disease, which is less than that found in a study by *Hulisani Matakanye et al*. (2021) [14], in which 97.58% of participants believed that TB can be cured if treated correctly.

A lack of belief in the value of medication may translate to inappropriate use. A substantial proportion (38.9%) of participants in this study used anti-TB medication incorrectly. The most common inappropriate behaviour was not taking medication at the correct time every day or forgetting, but a worrying proportion also stopped temporarily when they did not collect the next supply on time. Notably, the rates of taking the wrong medication dose were significantly lower than in other studies. For example, the study conducted by Pamorn Lertworawit in 2019 [15] found that 30.4% of the participants had taken an incorrect dose of medication. The difference between the two studies lay in the fact that the sample group in this study mostly received a combination of 2 RHZE/4 RH, while the sample group in Pamorn Lertworawit's study used single drug doses, providing easy opportunities to adjust the daily dose of medicine.

These findings highlight the importance of ensuring proper prescription, education, and use of anti-TB medications to ensure the disease is effectively treated and to prevent the development of drug resistance. Further efforts are needed to educate and monitor patients to ensure the correct use of TB drugs, and particular attention should be paid when treatment is failing, or the disease is recurrent. In addition, most of the participants in this study reported self-administering

drugs without family members helping to monitor and engaging families may be another source of support that is not sought often enough in this setting.

The high levels of inappropriate medication use found in this study are concerning for inadequate tuberculosis treatment, which has potential implications for future treatment. This may lead to drug resistance and consequently increase the cost of tuberculosis treatment, particularly for drug-resistant cases that require longer hospital stays and more extensive drug regimens.

5. Conclusion

This study found a range of knowledge levels among patients being treated for TB about their treatment. These findings highlight multiple opportunities for improving patient education about their treatment, engaging families to support treatment adherence, and should be acted upon to avoid the risk of an increasing prevalence of drug-resistant tuberculosis in Lao PDR.

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