Symptom experience of adverse drug reaction among male and female patients with newly diagnosed pulmonary tuberculosis in Thailand

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Abstract

Background: Patients with newly diagnosed pulmonary tuberculosis often suffer from adverse drug reaction symptoms, which leads to the automatic discontinuation of anti-tuberculosis drugs. Thus, understanding symptom experience of adverse drug reactions is necessary.

Objective: This study aimed to examine differences in symptoms experienced in four dimensions: presence, frequency, severity, and distress of adverse drug reactions, between male and female patients.

Methods: This was a quantitative survey with a cross-sectional design, with data collected between January and April 2020. A total of 394 patients with newly diagnosed pulmonary tuberculosis was selected through a purposive sampling technique. The symptom experiences of adverse drug reactions were measured using a validated instrument. Data were analyzed using mean, standard deviation, and independent t-test.

Results: The most commonly reported symptom was itchiness (24.1% in males and 34.9% in females). Vomiting occurred as the most frequent symptom among males ($\bar{x}$ ± *SD* = 2.73 ± .88), and fatigue was found to be the most severe and distressing symptom across male patients ($\bar{x}$ ± *SD* = 2.50 ± 1.61 and 2.06 ± 1.30, respectively). In contrast, yellowing of the eyes and skin was most frequent and severe among females ($\bar{x}$ ± *SD* = 3.17 ± .75 and 3.83 ± 1.47, respectively). In addition, flu-like symptoms were evaluated as the most distressing symptom for female patients ($\bar{x}$ ± *SD* = 2.80 ± 1.09). The symptom burdens of the females ranged significantly and reached higher than those of the male patients at a *p*-value of .05 (*t* = 3.33).

Conclusion: Females taking anti-tuberculosis drugs should be carefully monitored to deal with adverse drug reaction symptoms. This finding would help to decrease the severity of disease and improve their quality of life.

Keywords

adverse drug reaction; pulmonary tuberculosis; symptom experiences; quality of life; drug-related side effects; nursing; Thailand

Tuberculosis (TB) is a transmissible disease and one of the ten leading causes of death worldwide (World Health Organization, 2020). TB is caused by bacillus Mycobacterium TB, which spreads through the air by, for example, coughing. In 2019, the World Health Organization (WHO) reported 87,789 new TB cases, and 85.0% of these relapses were pulmonary TB (WHO, 2019). In addition, the WHO indicated that Thailand is one of the top 20 countries affected by TB and that only 85.0% of new cases and relapses in 2019 had successful outcomes

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(WHO, 2019). Moreover, the Ministry of Public Health of Thailand reported that, among new TB cases, 68.9% were males over the age of 15, and 31.1% were female (Health Data Center, 2020).

TB is treatable and preventable, and about 85.0% of people who develop TB can be successfully treated with regimental 6-month drugs, or first-line anti-TB drugs, which are Isoniazid (H), Rifampicin (R), Pyrazinamide (Z), and Ethambutol (E) (WHO, 2019). Although most TB patients are under self-medication, a failure to take medication or premature discontinuation of medication caused by an adverse drug reaction (ADRs) from first-line anti-TB drugs occurs in approximately 60.0-83.5% of cases (Qureshi & Kausar, 2013; Abhijeet Singh, Prasad, Balasubramanian, Gupta, & Gupta, 2015). Previous studies have shown that the most common adverse symptoms of first-line anti-TB drugs are rashes, peripheral neuropathy, flu-like symptoms, arthralgia, hyperuricemia, nausea, vomiting, and optical neuritis (Mathew & Joseph, 2017; Naser et al., 2016; Saputra, Rakhmawati, Hendrawati, & Adistie, 2020; Anita Singh, Bhat, & Sharma, 2011). Moreover, drug interaction of first-line anti-TB drugs is the cause of drug-induced liver damage (Ramappa & Aithal, 2013).

In addition, the literature shows that significant ADRs most commonly occur between one and five weeks after beginning the medication and that ADRs associated with anti-TB drugs persist, on average, for two months after patients start taking anti-TB drugs (Mathew & Joseph, 2017; Naser et al., 2016; Anita Singh et al., 2011). ADRs can also cause severe harm to patients, resulting in hospitalization. Many patients suffer from ADRs, leading to the automatic discontinuation of anti-TB drugs. However, patients who adhere to anti-TB drugs through the management or control of ADR symptoms increase their chance of recovery, reduce transmission, and improve their quality of life (QOL) (Pal, Duncombe, Falzon, & Olsson, 2013).

Furthermore, the literature review found that gender differences are linked to ADRs in terms of physiological, hormonal, and genetic conditions, which has an impact on the pharmacokinetics and pharmacodynamics of a drug and may be the cause of the difference in ADRs between females and males. Some studies have focused on gender differences in the reporting of ADRs and found that females report ADRs more often than males. Several other studies have looked at a particular drug or class of drugs to look more closely at gender differences in the reporting of ADRs. They found that the reported prevalence was higher among females compared to males; however, differences in the rate of reporting by gender varied by category of event or sub-class of the drug (Rademaker, 2001; Watson, Caster, Rochon, & den Ruijter, 2019; Zucker & Prendergast, 2020). Nurses are caring for patients with newly diagnosed pulmonary TB and playing a role in assessing the ADRs between males and females in order to suggest appropriate strategies for the management of ADRs. Thus, a study of gender differences and symptom experience of ADRs among patients with newly diagnosed TB is needed. This study was undertaken to investigate related differences between genders in symptoms experienced in four dimensions: presence, frequency, severity, and distress of ADRs.

Methods

Study Design

The study employed a cross-sectional survey designed to compare differences in ADRs according to gender.

Sample and Setting

Purposive sampling was used to approach participants from among Thai pulmonary TB patients. The study was undertaken in TB clinics, with permission from the institutional review board of seven hospitals in Bangkok, Thailand. The sample size was calculated by using Taro Yamane (Yamane, 1973); the level of statistics was set at a *p*-value of .05, and 10% was added to protect against a loss of data that could lower than the minimum simple size below the level that is acceptable to obtain the statistical power of analysis (Grove & Gray, 2018). Thus, a total of 394 newly diagnosed pulmonary TB patients were recruited into the study. The inclusion criteria for the participants were: (1) first-line anti-TB drugs received, (2) 25-59 years of age, (3) not receiving anti-HIV drugs, (4) being able to communicate in Thai, (5)having no cognitive impairment, nor complications from the disease; and (6) being willing to participate. However, participants with any physical disability (e.g., increased shortness of breath or increased cough) were excluded from this study. The purpose of this study, its potential benefits, risks, and the length of the interview were communicated to all patients. All participants signed a consent form, and the information on the topic was encoded for anonymity.

Instruments

In this study, symptom experiences have been defined as the perception of an individual symptom or a change in how a patient feels (Armstrong, 2003). The instrument to measure symptom experiences was developed based on symptom management by Dodd et al. (2001), along with a related literature review by the authors. The questionnaire is composed of two parts: a demographic questionnaire and a symptom experience questionnaire. The details of each questionnaire are as follows.

1) Demographic data questionnaire. The demographic data of participants, including age, gender, marital status, education, income, and type of health care coverage, were assessed.

2) Symptom experiences questionnaire. The questionnaire consists of 35 items of symptoms in four dimensions: presence, frequency, severity, and distress. For presence dimension, participants were asked to rate as 0 = absent or 1 = present; frequency dimension was rated as 1 = rarely, 2 = sometimes, 3 = often, or 4 = always; severity, and distress dimensions were rated as 1= very low, 2 = low, 3 = moderate, 4 = high, or 5 = very high. A higher score

indicates higher levels of symptom perception. The internal consistency reliability of the symptom experiences questionnaire was in four dimensions: presence, frequency, severity, and distress, with Cronbach's alpha of .86, .81, .84, and .86, respectively.

To calculate the score of symptom experience, we used a method for calculating symptom burden from the Chronic Kidney Disease Symptom Burden Index (CKD-SBI) questionnaire by Almutary, Bonner, and Douglas (2015). There was no difference between symptom experience and symptom burden in this study. The dimensions and scales are completely the same. The presence dimension ranges between 0 – 35, the frequency dimension ranges between 0 – 140, and severity and distress dimensions range between 0 - 175. Higher scores indicate greater symptom presence, frequency, severity, and distress.

A total symptom burden score of the symptom experiences questionnaire is calculated by summing subscale score (presence, frequency, severity, and distress) then divided by 4 (a minimum score of four dimensions that could be achieved from only one symptom from a participant report), and then multiplied by a fixed number of .191 (a constant number - mathematical maneuver to convert the total of symptom experiences questionnaire to 100). The total score for the symptom experiences questionnaire ranged between 0 and 100 for each participant, which was calculated for all symptoms. In the interpretation of the symptom burden score, a score of 100 indicates that the participant had the highest symptom burden.

Data Collection

Simple random sampling was used to generate a probabilistic sample of newly diagnosed TB. Participants were selected from among the 50 districts in Bangkok, Thailand. The researcher divided the 50 districts into three areas by location in Bangkok: inner-city, urban fringe, or suburb. There were 23 hospitals in total: 16 inner-city hospitals, four urban fringe hospitals, and three suburban hospitals. The following numbers of the hospital in each zone were required for statistical analysis: inner-city = 3, urban fringe = 2, and suburb = 2. The number of hospitals needed in each zone is based on the proportion of affiliation with hospitals in Bangkok. Then, the proportion of patients available per hospital in each zone was calculated by quota sampling. Purposive sampling was used to select the study participants who met the inclusion criteria.

The study was conducted at the TB clinics in seven hospitals in Bangkok, Thailand, after approval from each hospital's Institutional Board (IRB). The researcher described the benefits and risks of protecting human rights in non-technical terms prior to obtaining patient approval to participate in the study. If patients met the inclusion criteria and accepted participation, they were asked to sign a consent form. Participants were then asked to complete the symptom experiences of the adverse drug reaction questionnaire. During the process of data collection, participants were able to decline or leave without consequence. It took approximately half an hour to complete each interview. The data were collected from January to April 2020.

Data Analysis

Statistical analysis was carried out with the software package SPSS Statistics version 22. The level of statistical significance was set at a *p*-value of .05. Normality testing used Q-Q Plots. As data were normally distributed, descriptive statistics and independent t-test were used for data analysis.

Ethical Consideration

The study was approved by: 1) Human Research Protection Unit, Faculty of Medicine Siriraj Hospital (REF: Si 864/2019), 2) The Research Ethics Review Committee for Research Involving Human Research Participants, Health Sciences Group, Chulalongkorn University (REF: 287/2562), 3) Nopparat Rajathanee Hospital Ethics Committee (REF: 4/2563), 4) Lerdsin Hospital Ethics Committee (REF: LH621088) and 5) Bangkok Metropolitan Administration Human Research Ethics Committee (REF: 24).

Results

Characteristics of Participants

The baseline study consisted of 394 pulmonary TB patients, 62.2% of whom were males and 37.8% were females. Almost half of all males were between 30 and 49 years old. Over half of males were married (58.4%), and nearly half of males had completed primary education (40.4%). Almost half of the males had universal health care coverage (45.7%), and almost a third of males had a monthly income of between 1,001 and 15,000 Thai baht per month (28.6%), while more than half of females were aged 30 to 49 years and married (58.4%). Over a third of participants were attending secondary school (38.3%). Roughly half of the females were covered by universal health care coverage (49.7%) and just under one-third of females had no income (30.9%) (Table 1).

Symptom Experiences in the Presence Dimension

The three symptoms reported by the male patients that occurred most frequently in the presence dimension were itchiness (24.1%), decreased appetite (20.0,%) and numbness of the hands and feet (20.0%). In females, the three symptoms most frequently reported in the presence dimension were itchiness (34.9%), nausea (34.9%), and decreased appetite (24.2%) (see Table 2).

Table 1 Demographic and clinical characteristics of the pulmonary tuberculosis patients (*N* = 394)

Characteristics	Male (*N* = 245)				Female (*N* = 149)			
	n	*(%)*	$\bar{x}$	*SD*	*n*	*(%)*	$\bar{x}$	*SD*
Age (Years)			42.7	11.4			41.8	11.0
25-29	49	20.0			25	16.8		
30-49	105	42.9			74	49.7		
50-59	91	37.1			50	33.6		
Marital Status								
Single	89	36.3			45	30.2		
Widowed	5	2.0			6	4.0		
Divorced	5	2.0			9	6.0		
Separate	3	1.2			2	1.3		
Married	143	58.4			87	58.4		
Education								
Uneducated	5	2.0			4	2.7		
Primary School	99	40.4			53	35.6		
Secondary School	85	34.7			57	38.3		
Diploma	33	13.5			15	10.1		
College or More	23	9.4			20	13.5		
Occupation								
Unemployed	60	24.5			46	30.9		
Employee	111	45.3			54	36.2		
Merchant	21	8.6			18	12.1		
Company Employee	45	18.4			28	18.8		
Government Service	8	3.3			3	2.0		
Type of Healthcare Coverage								
Universal Coverage	112	45.7			74	49.7		
Civil Servant Medical Benefit Scheme	14	5.7			5	3.4		
Social Security Scheme	110	44.9			62	41.6		
Pay by Yourself	9	3.7			8	5.4		
Monthly Income (Thai Bath)			11,791.4	9,747.7			9,776.5	8,757.4
No income	60	24.5			46	30.9		
2,000 – 5,000	1	0.4			2	1.3		
5,001 – 10,000	56	22.9			45	30.2		
10,001 – 15,000	70	28.6			32	21.5		
15,001 – 20,000	33	13.5			13	8.7		
≥ 20,000	25	10.2			11	7.4		

Symptom Experiences in the Frequency Dimension

The three symptoms that occurred most frequently in males were vomiting ($\bar{x}$ ± *SD* = 2.73 ± .88), fatigue ($\bar{x}$ ± *SD* = 2.65 ± .95), and insomnia ($\bar{x}$ ± *SD* = 2.62 ± .8. In comparison, the three most common symptoms among females were yellowing of the eyes and skin, insomnia, and fatigue ($\bar{x}$ ± *SD* = 3.17 ± .75, 2.88 ± .85, and 2.78 ± .90, respectively) (see Table 3).

Symptom Experiences in the Severity Dimension

The three symptom experiences in the severity dimension that were found to be the most severe among males were fatigue, vomiting, and yellowing of eyes and skin ($\bar{x}$ ± *SD* = 2.50 ± 1.61, 2.30±1.04, and 2.10 ± 1.55, respectively). Yellowing of eyes and skin, flu-like symptoms, and abdominal pain were the three symptom experiences found to be most severe in the symptom severity dimension among females ($\bar{x}$ ± *SD* = 3.83 ± 1.47, 2.80±1.10, and 2.67 ± 1.21, respectively) (see Table 4).

Table 2 The top 20 highest symptom experiences that participants reported in present dimension(*N* = 394)

	Present Dimension	Gender					
	Symptom	(*N* = 394)		Male (*N* = 245)		Female (*N* = 149)	
		n	*%*	*n*	*%*	*n*	*%*
1.	Itchiness	111	28.2	59	24.1	52	34.9
2.	Nausea	94	23.9	42	17.1	52	34.9
3.	Decreased Appetite	85	21.6	49	20.0	36	24.2
4.	Numbness of the Hands and Feet	79	20.1	49	20.0	30	20.1
5.	Rash	70	17.8	39	15.9	31	20.8

Table 2 (*Cont.*)

6.	Fatigue	57	14.5	34	13.8	23	15.4
7.	Vomiting	53	13.5	22	9.0	31	20.8
8.	Joint Pain	53	13.5	27	11.0	26	17.4
9.	Insomnia	50	12.7	26	10.6	24	16.1
10.	Muscle Pain	48	12.2	37	15.1	11	7.4
11.	Dry Mouth	41	10.4	20	8.2	21	14.1
12.	Blurred Vision	17	4.3	10	4.1	7	4.7
13.	Headache	16	4.1	11	4.5	5	3.4
14.	Abdominal Pain	15	3.8	9	3.6	6	4.0
15.	Yellowing of Eyes and Skin	14	3.6	8	3.3	6	4.0
16.	Dysuria	11	2.8	8	3.3	3	2.0
17.	Mood Change	10	2.5	1	0.4	9	6.0
18.	Flu-like Symptoms	8	2	3	1.2	5	3.4
19.	Tinnitus	6	1.5	3	1.2	3	2.0
20.	Swollen Face, Hands, and Feet	6	1.5	3	1.2	3	2.0

Table 3 The top five highest symptom experiences that participants reported in frequency dimension (*N* = 394)

Symptom	Male					Symptom	Female				
	Frequency Dimension						Frequency Dimension				
	1	2	3	4	$\bar{x}$ ± *SD*		1	2	3	4	$\bar{x}$ ± *SD*
1) Vomiting	2	6	10	4	2.73±.88	1) Yellowing of eyes and skin	0	1	3	2	3.17±.75
2) Fatigue	4	11	12	7	2.65±.95	2) Insomnia	1	7	10	6	2.88±.85
3) Insomnia	2	10	10	4	2.62±.85	3) Fatigue	1	9	7	6	2.78±.90
4) Rash	6	12	16	5	2.51±.91	4) Rash	3	12	8	5	2.68±.98
5) Yellowing of eyes and skin	3	1	1	3	2.50±1.41	5) Vomiting	3	13	11	4	2.52±.85

Note: Possible range for symptom score was 1 to 4 (1 = rarely 2 = sometimes 3 = often 4 = always)

Table 4 The top five highest symptom experiences that participants reported in severity dimension (*N* = 394)

Symptom	Male						Symptom	Female					
	Symptom Severity Dimension							Symptom Severity Dimension					
	1	2	3	4	5	$\bar{x}$ ± *SD*		1	2	3	4	5	$\bar{x}$ ± *SD*
1) Fatigue	1	13	5	8	1	2.50 ± 1.61	1) Yellowing of Eyes and Skin	0	2	0	1	3	3.83 ± 1.47
2) Vomiting	5	9	4	4	0	2.30 ± 1.04	2) Flu-like Symptoms	1	0	3	1	0	2.80 ± 1.10
3) Yellowing of Eyes and Skin	5	0	0	3	0	2.10 ± 1.55	3) Abdominal Pain	1	2	1	2	0	2.67 ± 1.21
4) Flu-like Symptoms	1	1	1	0	0	2.00 ± 1.00	4) Vomiting	8	12	5	3	3	2.39 ± 1.26
5) Abdominal Pain	2	5	2	0	0	2.00 ± .71	5) Fatigue	6	8	4	4	1	2.39 ± 1.20

Note: Possible range for symptom score was 1 to 5 (1 = very low 2 = low 3 = moderate 4 = high 5 = very high)

Table 5 The top five highest symptom experiences that participants reported in distress dimension (*N* = 394)

Symptom	Male						Symptom	Female					
	Symptom Severity Dimension							Symptom Severity Dimension					
	1	2	3	4	5	$\bar{x}$ ± *SD*		1	2	3	4	5	$\bar{x}$ ± *SD*
1) Fatigue	17	7	2	7	1	2.06 ± 1.30	1) Flu-like Symptoms	1	0	3	1	0	2.80 ± 1.10
2) Flu-like Symptoms	1	1	1	0	0	2.00 ± 1.00	2) Insomnia	10	7	5	2	0	1.96 ± 1.00
3) Muscle Pain	20	8	3	6	0	1.86 ± 1.13	3) Joint Pain	15	5	2	1	3	1.92 ± 1.38
4) Insomnia	13	7	3	3	0	1.85 ± 1.05	4) Fatigue	11	6	4	1	1	1.91 ± 1.13
5) Joint Pain	13	8	3	3	0	1.85 ± 1.03	5) Muscle Pain	4	3	3	1	0	0.91 ± 1.04

Note: Possible range for symptom score was 1 to 5 (1 = very low 2 = low 3 = moderate 4 = high 5 = very high)

Symptom Experiences in the Distress Dimension

The three symptoms that were found to be the most distressing among males were fatigue, flu-like symptoms, and muscle pain ($\bar{x}$ ± *SD* = 2.06 ± 1.30, 2.00 ± 1.00, and 1.86 ± 1.13, respectively). The top three symptom experiences among females in the symptom distress dimension were flu-like symptoms, insomnia, and joint pain ($\bar{x}$ ± *SD* = 2.80 ± 1.10, 1.96 ± 1.00, and 1.92 ± 1.38, respectively) (see Table 5).

Symptom Burden Perceived Among the Participants

The range of symptom burden reported by female patients (Mean= 2.97, *SD*= 3.48) reached significantly higher than that of the males (*Mean* = 1.88, *SD* = 2.46; t = 3.33; *p* = .05) (see Table 6).

Table 6 The burden of symptoms in 4 dimensions (*N* =394)

Gender	The Symptom Burden in Four Dimensions			
	Mean	***SD***	***t***	***p*-value**
Male (*n* = 245)	1.88	2.46	3.33	.001
Female (*n* = 149)	2.97	3.48		

Discussion

This study was undertaken to investigate related differences between genders in symptom experiences of ADRs among newly diagnosed pulmonary TB patients. In this study, it was found that more male patients experienced ADRs than did female patients. A possible explanation for this is that males usually participate in more social and work activities than do females, which promotes the transmission of the disease. Males are more likely to smoke and also have addictions to alcohol or drugs in comparison to females. This increases their risk for TB (Imam et al., 2020).

Additionally, itching was the most common symptom among males (24.1%) and females (34.9%). This may be caused by Rifampicin as all study participants receive the same anti-TB drug regimen, which is widely used for intrahepatic cholestasis-related itching. Rifampicin is not only found in medications that cause liver damage, but it also inhibits the absorption of biliary acid by hepatocytes, increasing the concentration of biliary acid in plasma. However, it breaks down the entero-hepatic circulation of biliary acids on liver metabolic processes (Pongcharoen & Fleischer Jr, 2016). Previous studies have also commonly reported this side effect (Fei, Zainal, & Ali, 2018; Nazir, Farhat, Adil, & Asrafv, 2019; Sinha, Marak, & Singh, 2013).

Vomiting was found to be more severe in males ($\bar{x}$ ± *SD* = 2.73 ± .88). Vomiting may be caused by anti-TB drugs such as Isoniazid, Ethambutol, and Pyrazinamide and is common in the early weeks of treatment (Raftery, Tudor, True, & Navarro, 2018). A possible explanation for this is that males may be more likely to consume alcohol, which can induce liver injury, and which also inhibits absorption irritation that can cause vomiting. So males are more likely to experience greater severity of vomiting than females (Iranpour & Nakhaee, 2019; Marçôa, Ribeiro, Zão, & Duarte, 2018).

Yellowing of the eyes and skin was the most frequent and severe symptom among females ($\bar{x}$ ± *SD* = 3.17 ± .75, and 3.83 ± 1.47, respectively). These symptoms can be caused by anti-TB drugs like Isoniazid and Rifampicin, which induce liver injury. Thus, if the liver is damaged, it may cause leakage of bilirubin from the liver into the bloodstream, and it may also leak into the surrounding tissues. This is known as hyperbilirubinemia and causes a yellow color in the skin and eyes (Anita Singh et al., 2011). One possible explanation for this difference between genders is that females usually have lower lean mass, reduced liver clearance, and differences in cytochrome P450 (CYP) enzyme activity than males. Additionally, the females may be reporting yellowing of eyes and skin as the most severe symptom due to the sclera changing from white to yellow and skin changing from their own skin color to yellow, which is a clinical symptom of hepatitis. In this case, these females need to stop anti-TB drugs, change regimens, or begin a new treatment regimen (Raftery et al., 2018).

In our study, fatigue was found to be the most severe and distressing symptom reported by males ($\bar{x}$ ± *SD* = 2.50 ± 1.61, and 2.06 ± 1.30, respectively). Fatigue can be caused by any anti-TB drugs (Raftery et al., 2018). This difference between genders could be explained by the fact that males usually have more social and labor-based activities than females and that associated issues like unhealthy diets, work duration, and sleep problems with fatigue are often linked to long-term health problems (Lin et al., 2015). Flu-like symptoms were the most distressing symptoms among female patients ($\bar{x}$ ± *SD* = 2.80 ± 1.10). These symptoms can be caused by anti-TB drugs, which induce hypersensitivity, modified thermoregulation, the pharmacological action of the drug, idiosyncratic sensitivity of inherited biochemistry defects, and related administration. In the narrowest sense, as a sort of hypersensitivity, drug fever is a febrile reaction specific to the individual in the treatment process depending on the drug and the idiosyncrasy of the patient. Clinically, it occurs when anti-TB drugs become antigens after the formation of the complex. Therefore, most of the females suffered from a high fever. In most cases, the temperature reached a peak on the initial day, whereas body temperature increases caused by Rifampicin increase day by day and reach a peak of above 40 degree Celsius within 3 – 6 days (Fang et al., 2016; Yee et al., 2003).

Based on the symptom burden data, gender was a significant variable in symptom burden at the *p*-value of .05 (*t* = 3.33) because of identifiable differences between females and males in terms of pharmacokinetic and hormonal factors when taking anti-TB drugs. Females have a slower gastric emptying time, leaner body mass indices, and differences in total body water compared to males, resulting in females absorbing more anti-TB drugs. As a result, females experienced a higher symptom burden level than males (Zucker & Prendergast, 2020).

This study has several limitations. The results may lack international generalization due to the setting and cultural influences in Bangkok, Thailand. Other limitations were data-based and related to self-reported data, which could have caused an overestimated or underestimation of values. The instrument for measuring these variables has been used only once in a Thai context. Testing of validity and reliability within a Thai context is needed. Future

studies should be conducted across an entire country's population to assess the change of symptom experience for ADRs among newly diagnosed pulmonary TB patients. Developing intervention programs for females to decrease ADR symptoms such as itchiness and nausea is needed to encourage the continuous taking of anti-TB drugs.

This study can contribute to knowledge development and strengthen nursing science to care for patients with newly diagnosed pulmonary TB. The findings provide knowledge that offers direction for the development of interventions to decrease ADR symptoms regarding the differences between male and female patients. Such intervention should incorporate the promotion of strategies to manage ADR symptoms to enhance adherence to anti-TB drug regimens in order to reduce transmission and improve quality of life.

Conclusion

This study found that ADRs were more reported among male patients, but female patients reported a significantly higher symptom burden than males. The results of this study suggest that females receiving anti-TB drugs should be carefully appropriately monitored for symptoms of ADRs to deal with ADR symptoms. This would help patients continue taking anti-TB drugs, which should decrease the severity of the disease and improve their quality of life.

Declaration of Conflicting Interest
There are no potential conflicts of interest to declare.

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Authors' Contribution
All the authors participated in the final manuscript. A.T. and R.P. designed the study, collected data, analyzed the data, wrote, and revised the manuscript.

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Data Availability Statement
Data sets generated and/or analyzed during the current review are available from the corresponding author upon reasonable demand.

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