Factors Predicting Fatigue in Pulmonary Tuberculosis Patients Receiving Anti-Tuberculosis Drugs

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ABSTRACT

Objective: To explore the predictive factors on fatigue among pulmonary tuberculosis patients receiving anti-tuberculosis drugs.

Methods: This study is a predictive correlational research designed. The sample was comprised of 125 patients at the out-patient department, a tertiary hospital in Bangkok setting. The data were collected between January to February 2020. The questionnaires included mini-cognitive assessment instrument (Mini-Cog); the demographic characteristics questionnaire; Piper fatigue scale-12 (PFS-12); Nutrition alert form (NAF); the Pittsburgh sleep quality index (PSQI); and the Center for epidemiologic studies depression scale (CES-D). All data were analyzed by using descriptive statistics and multiple regression analysis.

Results: The sample had a mean age of 58.45 years (SD = 15.374) of which 60.8% were males. Overall, the mean score of fatigue was a moderate level (Mean = 4.90, SD = 2.455). From the multiple regression analysis, age, nutritional status, sleep quality, and depression could explain the variances on fatigue in the sample group as 52.5% (R^2 = .525, F = 33.119, $p < .001$). Nutritional status, sleep quality, and depression are the variables found to be capable in predicting fatigue of pulmonary tuberculosis patients with statistical significance ($\beta = .316$, $p < .001$, $\beta = .226$, $p < .05$ and $\beta = .340$, $p < .001$).

Conclusion: Nutritional status, sleep quality, and depression could affect fatigue. Healthcare teams should assess patients to prevent and manage the aforementioned symptoms to reduce suffering from fatigue and a better quality of life.

Keywords: Depression; fatigue; nutritional status; pulmonary tuberculosis patients; sleep quality (Siriraj Med J 2021; 73: 167-173)

INTRODUCTION

Due to consistently high incidence, Tuberculosis is a major public health problem of the past and present day. The primary causes of the spread of TB are the spread of HIV, poverty, migration and migrant labor movements. The World Health Organization expected the incidence of new patients and relapses for the world to be as high as 10.4 million baht, or 140 per hundred thousand people, or 1.7 million deaths per year.[1]

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Received 15 September 2020 Revised 31 December 2020 Accepted 14 January 2021
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http://dx.doi.org/10.33192/Smj.2021.22

Thailand is one of 14 countries with problems from high TB burdens. Incident reports found 108,000 new and relapsed patients, or 156 patients per hundred thousand people with 11,000 patients who had TB with HIV infections, 3,900 drug-resistant tuberculosis patients and 12,000 deaths per year. Tuberculosis is more predominant among males than females at a ratio of 1.91:1. In an ordinary tuberculosis patient case, the costs of drugs and pharmaceutical supplies amount to 2,600 baht, 200,000 baht in patients with drug-resistant tuberculosis and 1.2 million baht in patients with severe drug-resistant tuberculosis.[2] According to reports on tuberculosis patient statistics at a tertiary hospital in Bangkok setting for five years in retrospect, a tertiary hospital in Bangkok setting had 1,635 to 2,192 patients in 2014 to 2018.[3] Therefore, tuberculosis is a problem with international public health and economic significance.

Tuberculosis is a highly communicable respiratory disease. Medication adherence effectively treats and controls the transmission of tuberculosis in addition to relieving symptoms that cause patients discomfort until they recover. However, fatigue continues to be found.[4] In addition to being an effect of the pathology, fatigue can occur from side effects of many tuberculosis drugs.[5] Therefore, if patients have fatigue while receiving tuberculosis drugs, patients may become uncooperative in taking medications, causing multidrug-resistant tuberculosis, severe complications and higher treatment costs.[6] Therefore, the researcher's interest is in exploring the factors predicting fatigue in order to lead to assessment and planning of care to prevent factors affecting fatigue among patients with tuberculosis.

Research on the incidence of fatigue was found among many previous studies, (83%).[7] No studies on the predictors of fatigue among patients with pulmonary tuberculosis were found domestically or internationally. However, studies were found to have been conducted among patients with infections and other chronic illnesses. The conceptual framework of Piper et al.[8] was found to be an accepted theory on fatigue. In this study, however, the researcher selected four factors based on the aforementioned concept consisting of age, nutrition, sleep quality and depression.

MATERIALS AND METHODS

Ethical considerations

This study was considered and confirmed by the Institutional Review Board, Faculty of Medicine, a tertiary hospital in Bangkok setting (Si 783/2019). The researcher provided data by considering the participants' right protection in three areas consisting of potential risks, benefits, and maintaining data confidentiality. In addition, the researcher responded to inquiries until patients understood and consented to participate in the study along with signing the informed consent form.

Methodology

This cross-sectional study was based on a predictive correlational research design with a hypothesis stating age, nutrition, sleep quality and depression can co-predict fatigue among patients with pulmonary tuberculosis receiving anti-tuberculosis drugs. The sample was 125 patients diagnosed with pulmonary tuberculosis who came to follow-up on treatments at the Medical and Surgical examination unit, Out-patient building, a tertiary hospital in Bangkok setting, from January to February 2020. The sample was selected by purposive sampling of patients meeting the following inclusion criteria: ages more than or equal to 18 years, administration of anti-tuberculosis drugs for more than two weeks and ability to communicate in Thai. The following exclusion criteria was applied: cognitive deficiency, co-morbidities causing proneness to fatigue such as AIDS, heart failure, end-stage chronic renal failure, end-stage liver disease, cancer, stroke, chronic obstructive pulmonary disease, asthma, psychiatric disorders, obstructive sleep apnea, pregnant or breastfeeding women and patients with unstable physical symptoms and presenting symptoms.

Sample size was set by using the G*power program, Version 3.1.9.4. Predictive relationships were analyzed using multiple regression analysis. Power of test was 0.8. Reliability (α) was at 0.05 with an effect size of 0.1.[9] This study had four variables (k) and this study obtained 125 subjects for hypothesis testing.

Instruments

Data collection questionnaires in this study were divided into the following 6 parts:

1) The Mini-Cognitive Assessment Instrument (Mini-Cog) Thai version. The instrument contained three questions. In Question 1, the elderly were instructed to repeat and memorize three words. In Question 2, the elderly were instructed to draw a clock with the needle pointing at the time of 11:10 am. In Question 3, the elderly were instructed to speak the words in Question 1. Patients with a total score of three points and up met inclusion criteria for the sample.

2) The demographic data and illness background recording form for patients. Part 1 contained 17 questions on demographic data such as gender, age, marital status, level of education, religion, occupation, income, treatment entitlements, lodging characteristics,

environment, cohabitation with other family members, mask-wearing behavior, separation of items, smoking, alcohol consumption and tuberculosis symptoms. Part 2 contained 4 questions on illness background data such as duration of illness and time when patients began taking anti-tuberculosis drugs, type of patients with tuberculosis, chronic illnesses or co-morbidities, anti-tuberculosis drug formulas and other drugs.

3) The Piper Fatigue Scale-12 (PFS-12) Thai version. The scale was developed with 12 questions assessing fatigue with coverage of the following four aspects: 1) behavior and severity; 2) perception; 3) feelings of physical and psychological fatigue; and 4) intellect and emotions. The scale's interpretation of fatigue was divided into four levels. High fatigue was in a score range of 7.00 - 10.00. Moderate fatigue was in a score range of 4.00 - 6.99. Light fatigue was in a score range of 0.01 - 3.99. No fatigue was in a score range of 0.00.

4) The Nutrition Alert Form (NAF) Thai version. For monitoring malnutrition risks with 18 questions. Interpretation was divided into three levels. Scores of 0 - 5 points meant no risk of malnutrition, scores of 6 - 10 points meant risk of malnutrition and scores of more than or equal to 11 points meant malnutrition.

5) The Pittsburgh Sleep Quality Index (PSQI) Thai version. The form contains 9 questions with 7 components on subjective sleep quality, time before sleep, sleeping hours, sleep efficiency, sleep disruption, use of sleep medication and effects on daytime activities. Scores were interpreted in the range of 0 - 21 points. Scores of more than five points meant poor sleep quality.

6) The Center for Epidemiologic Studies Depression Scale (CES-D) Thai version. The scale contains 20 questions for assessing depression in the past week. The scale had a score range of 0 - 60 points. Scores of more than 15 points meant depression.

Instrument quality testing

Research instruments were standard instruments. Content validity was tested by qualified experts and instruments were translated into Thai by the back-translation method. In addition, instruments were used to assess many subjects. The researcher with 30 patients who had the same qualifications as the sample and data were used to calculate reliability. Cronbach's Alpha Coefficient of the PFS-12 form was 0.946, 0.803 for the PSQI form and 0.872 for the CES-D form. The NAF had an inter-rater reliability score of 1.000 when used with 10 subjects. In a sample group with 125 subjects, the PFS-12 form had a reliability score of 0.963, 0.822 for PSQI and 0.888 for CES-D.

Data collection methods

The researcher collected data in person by using a letter to request permission to meet with the Head of out-patient nursing and asking for cooperation from nurses at the Medical and Surgical examination unit to survey the names of patients with tuberculosis who met inclusion criteria and bring the researcher to meet with the sample group. The researcher introduced herself, explained research objectives, data collection procedures, protection of the rights of the sample group and asked for permission to use data from patient medical records. The researcher had the participants complete questionnaires by using 25 minutes per patient. After obtaining 125 subjects, the researcher ended data collection and analyzed data.

Statistical analysis

Data were analyzed and processed. The SPSS computer program was used to analyze demographic data and illness background. Descriptive statistics such as frequency distribution, percentage, mean and standard deviation were used to analyze predictive power of age, nutrition, sleep quality and depression. Fatigue among patients with pulmonary tuberculosis was analyzed using all enter multiple regression analysis.

RESULTS

Demographics, illness and treatment data

The sample was predominantly male (60.8%) with a male-to-female ratio of 1.55:1. The sample was aged 19-89 years at a mean of 58.45 years (SD = 15.374). Most of the sample was elderly (52.8%), married (60.8%), had highest level of education at the elementary level (40.8%) and Buddhist (96.8%). The sample was unemployed (42.4%), followed by the sample working as hired workers (17.6%) with income less than 5,000 baht (48.8%). The sample used universal health guarantee rights (40.8%) and lived in single homes (55.2%) with clean and clear environments (93.6%). During treatment, the sample was non-smoker (93.6%) and non-alcoholic (88.8%). Of the sample, 96.8% of the sample was new pulmonary tuberculosis patients with co-morbidities (48.8%). The top three co-morbidities encountered were hypertension (34.4%), diabetes mellitus (24%) and hyperlipidemia (23.2%). The sample (88%) had fatigue, received anti-tuberculosis drugs for one month (37.6%) and received the 2HRZE/4HR anti-tuberculosis drug formula (91.2%) with Vitamin B6 (96%).

Nutritional status

Mean nutrition scores were at the level of normal

nutrition (55.2%) (Mean = 5.38, SD = 4.065), followed by risk of malnutrition (36%) and malnutrition (8.8%).

Sleep quality

Mean sleep quality scores showed the participants to have poor sleep quality (65.6%) (Mean = 8.00, SD = 4.117) and some of the participants had good sleep quality (34.4%).

Depression

Mean depression scores showed the participants to have no depression (64.8%) (Mean = 13.70, SD = 9.813) and some of the participants had depression (35.2%).

Fatigue

Mean fatigue scores were at a medium level (52%) (Mean = 4.90, SD = 2.455), followed by high fatigue (18.4%). Concerning man fatigue scores in all four components, behavior and severity (Mean = 4.86, SD = 2.701), perception (Mean = 5.50, SD = 2.978) and physiological and psychological feelings (Mean = 5.69, SD = 2.997) were at a medium level while intelligence and emotions (Mean = 3.43, SD = 2.995) were at a low level (Table 1).

Correlation analysis

Correlation analysis using Pearson's Correlation Coefficient found age to not be correlated with fatigue among patients ($r = .034$, $p > .05$). Nutrition was positively correlated with fatigue with statistical significance ($r = .571$, $p < .01$), sleep quality was positively correlated with fatigue with statistical significance ($r = .580$, $p < .01$) and depression was positively correlated with fatigue with statistical significance ($r = .631$, $p < .01$) (Table 2).

Multiple regression analysis

All enter multiple regression equation analysis found all independent variables to be able to explain fatigue fluctuations in patients with pulmonary tuberculosis at 52.5% with statistical significance at .001 ($R^2 = .525$, $F = 33.119$, $p < .001$). Nutrition, sleep quality and depression were able to explain fatigue among patients with statistical significance ($\beta = .316$, $p < .001$, $\beta = .226$, $p < .05$ and $\beta = .340$, $p < .001$, respectively (Table 3).

TABLE 1. Piper Fatigue Scale-12 scores (n = 125).

Fatigue Level	Possible Range	Acquired Range	Amount	Percent
No Fatigue	0.00	0.00	15	12.0
Mild	0.01 - 3.99	1.50 - 3.92	22	17.6
Moderate	4.00 - 6.99	4.08 - 6.92	65	52.0
Severe	7.00 - 10.00	7.00 - 9.58	23	18.4

(Min = 0.00, Max = 9.58, Mean = 4.90, SD = 2.455)

TABLE 2. Results from analysis of correlation coefficients between age, nutritional status, sleep quality, depression and fatigue.

Variables	1	2	3	4	5
Age	1				
Nutrition	.141	1			
Sleep quality	.073	.445**	1		
Depression	.028	.469**	.635**	1	
Fatigue	.034	.571**	.580**	.631**	1

**Statistical significance at .01.

TABLE 3. Results from multiple regression analysis of age, nutritional status, sleep quality, depression and fatigue.

Variables	b	Std. Error	Beta	t	Sig
Constant	1.969	.661		2.977	.004
Age	-.006	.010	-.037	-.575	.566
Nutrition	.191	.044	.316	4.296	.000
Sleep quality	.135	.050	.226	2.707	.008
Depression	.085	.021	.340	4.007	.000

SE_{est} = ±1.72, R = .724, R^2 = .525, Adj. R^2 = .509, df = 4, 120, F = 33.119, Sig F = .000

DISCUSSION

This study found fatigue incidence at 88% with fatigue scores being at a medium level (52%). Fatigue can be explained as the most frequently encountered symptom among patients because the body needs energy from the oxygen metabolism process and reduced pulmonary functions from chronic inflammation due to the body's immune response to tuberculosis caused fatigue. In addition, loss of appetite was another nutritional problem resulting from cytokines related to inflammation, particularly TNF-alpha, causing patients to receive less energy and resulting in fatigue.[10] Furthermore, side-effects from anti-tuberculosis drugs also caused fatigue.[5]

Age was unable to predict fatigue among patients with pulmonary tuberculosis. This was inconsistent with the hypothesis and inconsistent with the conceptual framework on fatigue of Piper et al, which stated older persons can easily have fatigue due to reduced performance efficiency of various organs.[8] This study was consistent with previous studies conducted in similar population groups which found age to be unrelated to fatigue.[11] This was in conflict with this study, which found age to be related to fatigue.[12] Furthermore, age was not a factor with influence on fatigue.

Nutritional status was able to co-predict fatigue among patients with pulmonary tuberculosis with statistical significance ($\beta = .316$, $p < .001$). This was consistent with the hypothesis and conceptual framework on fatigue of Piper et al. who stated that, when the body receives insufficient nutrients, the body's internal mechanisms will use accumulated energy and muscles will release glycogen, protein and fat to use as energy, causing the body to be fatigued.[8] In the present study, the participants had poor nutrition, possibly due to weight loss (45.6%) from loss of appetite caused by cytokines related to inflammation, particularly TNF-alpha and Peptide YY.[5] Furthermore, the side-effects of anti-tuberculosis drugs were found to have effects on nutrition, thereby causing patients to lose appetite, feel nausea and vomit. Anti-tuberculosis drugs with side-effects consist of Isoniazid,[13] Rifampicin,[13] Pyrazinamide.[14] In particular, in the first two months during the intense stage, the participants were found to have significant energy use for metabolism, resulting in poor nutrition with more fatigue than the continuing stage. The findings from this study concurred with those of a previous study finding nutrition to be able to predict fatigue[15] and was in conflict with the findings from this study, which revealed nutrition to be uncorrelated with fatigue.[12]

Sleep quality was able to co-predict fatigue among patients with pulmonary tuberculosis with statistical significance ($\beta = .226$, $p < .05$). This was consistent with the hypothesis and the conceptual framework on fatigue of Piper et al., which stated that insufficient sleep, the body will be unable to produce high energy substances, accumulate protein or secrete hormones for growth, causing fatigue.[8] This can be explained physiologically that sufficient sleep was important for the body in storing and accumulating energy for use, causing individuals to feel fresh.[16] In this study, the participants were found to have poor sleep quality, possibly due to chronic coughing (31.2%).[17] In addition, the patients had night sweats (12.8%), which may be related to cortisol levels that suppress IL-1 functions. As a result, the patients had low fevers in the afternoon due to low cortisol and increases in TNF-alpha and IL-1, which were indicated to be cytokines secreted from cells in response to tuberculosis and to produce granuloma.[10] In addition, the side-effects

of anti-tuberculosis drugs such as Isoniazid, Rifampicin and Ethambutol were found to have effects on sleep quality.[18] This study was consistent with previous findings from studies revealing sleep quality to be correlated with and able to predict fatigue.[12,19] This conflicted with the findings revealing sleep quality to be unrelated to fatigue.[20]

Depression was able to predict fatigue among patients with pulmonary tuberculosis with statistical significance ($\beta = .340$, $p < .001$). This was consistent with the hypothesis and the conceptual framework on fatigue of Piper et al., which stated that psychological abnormalities are a cause of fatigue.[8] This can be explained in that the body triggers a response by synthesizing corticotrophin-releasing hormones when patients have depression, resulting in changes in the immune system with cytokines and TNF-alpha being detected. These substances cause effects cortisol and catecholamine secretion, resulting in tachycardia and increased metabolism. At the same time, insulin secretion will be suppressed. If the body accumulates stress over a long time, the body will use energy reserves, causing fatigue.[21] The participants were depressed, possibly due to thought they should isolate themselves in addition to feeling fear, hopelessness and stigmatization.[22] Furthermore, most of the participants were found to be income under 5,000 baht (48.8%), thereby causing patients to have insufficient income with effects on depression. This was consistent with the findings of a study which studied patients with low monthly income to be four times more likely to have depression,[23] ultimately resulting in fatigue. Anti-tuberculosis drugs with effects on depression consisted of Isoniazid.[13] This study was consistent with previous findings from studies revealing depression to be correlated and able to predict fatigue[19] which conflicted with the study which found depression to be uncorrelated with depression.[24]

Recommendations and implications

1. Healthcare team members should assess fatigue, nutrition, sleep quality and depression in every patients with pulmonary tuberculosis, particularly in the first two months of receiving anti-tuberculosis drugs in order to learn about problems while patients are being treated.

2. Nurse managers should be assigned to individual patients to provide knowledge and recommendations. In addition, programs for promoting nutrition and sleep quality should be prepared along with finding depression prevention guidelines for patients with pulmonary tuberculosis.

3. According to the findings, nutrition, sleep quality and depression were able to predict fatigue among patients with pulmonary tuberculosis at 52.5%, indicating other factors were related to fatigue. These factors may be used to study and explain fatigue phenomena more clearly.

4. An experimental research model for reducing fatigue should be developed such as nutrition programs and sleep quality promotion programs, etc., in order to provide guidelines to care for and support patients with pulmonary tuberculosis to be able to manage fatigue and have better quality of life.

CONCLUSION

Nutrition, sleep quality and depression had effects on fatigue in patients with pulmonary tuberculosis. Fatigue is a manageable factor. Healthcare teams should recognize the importance of consistent assessment, care and promotion of nutrition, sleep quality and depression to prevent and reduce suffering from fatigue, leading to recovery from pulmonary tuberculosis and better quality of life.

ACKNOWLEDGMENTS

This study was successful due to the kindness and excellent support from the team of advisory professors, qualified experts and researchers at the Faculty of Nursing, Mahidol University, including the participants and staff at the Out-patient Building, a tertiary hospital in Bangkok setting, who supported and facilitated data collection including all persons not named here.

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