# Pulmonary Tuberculosis and Sleep Quality: A Review

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**Abstract**

Tuberculosis is an infectious disease that is caused by Mycobacterium tuberculosis that is still being a global health problem. Long term anti-TB regimens comprising several drugs are a major components of current TB treatment. Combinations of a several drugs in this TB regimens may cause adverse drugs reaction on TB patients. Tuberculosis patients that are experiencing chronic symptoms, medications, and adverse drug reaction leads to decreasing of sleep quality. Sleep itself is very important to help body maintain its equilibrium and help recovery faster. This review aimed to discuss tuberculosis in general and sleep quality aspects of tuberculosis patients.

Keywords: Tuberculosis, infectious disease, sleep quality

## 1. Introduction to Tuberculosis

Tuberculosis can be defined as a chronic infectious disease caused by the *Mycobacterium* group of bacteria, *Mycobacterium tuberculosis* (Zaman, 2010). In general, tuberculosis infection can be manifest in the lungs, but tuberculosis can affect other organs (Deutsch-Feldman et al., 2021). *Mycobacterium tuberculosis* is a rod-shaped or bacillus-shaped bacterium and has acid-resistant properties using the Ziehl Neelsen (ZN) staining method because it contains a lot of complex lipids (Turner *et al.*, 2018).

## 2. Classification of Tuberculosis

Referring to the Indonesian Ministry of Health's tuberculosis management guidelines (2021), patients can be categorized into suspected TB patients, bacteriologically confirmed patients, and clinically diagnosed patients.

Suspected TB patients are patients who have complaints or clinical symptoms that support TB. Bacteriologically confirmed patients are patients who are proven positive for bacteriology by examining samples of sputum, blood or tissue through direct microscopic examination, TCM TB or culture. Clinically diagnosed patients are patients who do not meet the criteria for bacteriological confirmation, but are diagnosed with active TB by a clinician, including clinical diagnosis by radiography (chest x-ray) without bacteriological confirmation.

Once the patient has been diagnosed bacteriologically or clinically, the patient can be further classified based on the anatomical location of Mycobacterium tuberculosis infection, treatment history, and drug sensitivity test results.

**a. Classification based on anatomical location**

Based on anatomical location, tuberculosis can be classified into intrapulmonary and extrapulmonary tuberculosis. Intrapulmonary tuberculosis (TB) or often called pulmonary TB is a common manifestation of tuberculosis infection in the lung organs. Extrapulmonary tuberculosis (TB) is a tuberculosis infection in organs other than the lungs, for example the pleura, lymph nodes, abdomen, genitourinary tract, skin, bones, joints and meninges. Extrapulmonary tuberculosis occupied 16% of the 7.5 million incident cases worldwide in 2019 (WHO, 2020).

**b. Classification based on medication history**

Based on their medication history, tuberculosis patients can be classified into newly diagnosed TB patients, patients who have been treated for TB, and patients with unknown medication history. Newly diagnosed TB patients are patients who have never received TB treatment before or have received therapy and taken OAT for less than 1 month (< 28 doses). Patients who have been treated for TB are patients who have received therapy and taken OAT for at least 1 month or more (>28 doses). These patients can be further classified based on the results of the last TB treatment, such as patients who relapsed, patients who were treated again after failure, and patients who were treated again after.

**c. Classification based on drug sensitivity test**

Based on drug sensitivity test tuberculosis patients can be divided into five groups. First, monoresistant (TB-MR) is a patients whom resistant to one type of first-line anti-tuberculosis (OAT) drug only. Second, polyresistant (TB-PR). TB-PR patients is resistant to more than one type of first-line anti-tuberculosis (OAT) drug other than Isoniazid (H) and Rifampicin (R). Third, multidrug resistant (MDR-TB) is a patient who simultaneous resistance to Isoniazid (H) and Rifampicin (R). Fourth, extensive drug resistance (TB-XDR). This type of tuberculosis patient is resistant to fluoroquinolones and at least one of three second-line injection drugs (capreomycin, kanamycin, or amikacin). Last, rifampicin Resistance (TB-RR). Rifampicin resistant patient is patient who resitant to rifampicin detected using phenotypic or genotypic methods either with or without resistance to other anti-tuberculosis drugs (OAT).

## 3. Tuberculosis pathogenesis

Patients experiencing infection with tuberculosis are able to transmit the disease to other people by aerosol droplets or droplets (typically 1 to 5 μm in diameter) that contain M. tuberculosis. According to Turner and Bothamley (2015), coughing, sneezing, talking, and singing can all generate these droplets, which can linger in the air for several hours. Following the inhalation phase, M. tuberculosis enters the respiratory system through the mouth or nose, travels through the bronchial tubes and upper respiratory tract, and finally reaches the alveoli. Goblet cells, whose function it is to release mucus to either remove or prevent foreign things from entering the respiratory system, trap the majority of M. tuberculosis in the respiratory tract. This first-line mucociliary defense system can be circumvented by droplets carrying M. tuberculosis, allowing the disease to enter the lung organs.

It is attainable to recruit second line immune mechanisms during an infection. Tumor necrosis factor alpha (TNF-α) and interferon gamma (IFN-γ) are two examples of the proteolytic enzymes and cytokines that alveolar macrophages use to try and kill infected bacilli. Dendritic cells and alveolar macrophages play a role in the innate immune response. This response initiates a cell-mediated immune response that can either kill the infecting organism or cause granuloma development by signaling the translocation of T cells to the infection site (Luies and Preez, 2020).

Through the action of many macrophage receptors, such as complement receptors that detect various components of the mycobacterium cell wall and macrophage mannose receptors, Mycobacterium tuberculosis enters macrophage endosomes. To enable the mycobacterium to survive and multiply, mycobacteria in

macrophages obstruct the typical microbicidal response by blocking the fusion of lysosomes with phagocytic vacuoles. The first stage is typified by the growth of bacilli in the lung alveolar and air space macrophages, which causes bacteremia. Most people with this condition have a mild flu-like illness or no symptoms at all..

Amorphous aggregates of immune cells (macrophages, monocytes, neutrophils, Natural Killer (NK) cells, etc.) that form to stop the spread of germs are known as tuberculomas or pathological granulomas that occur in pulmonary tuberculosis (Luies and Preez, 2020). Granulomas travel through blood arteries and vascular endothelial growth factors in the early stages of development. The development of granulomas is accompanied by the differentiation of macrophages into several morphotypes, including epithelioid cells, multinucleated giant cells, and foamy macrophages. This process produces stratified structures, wherein layers of lymphocytes are deposited outside a fibrous cuff that encircles a layer rich in macrophages.

## 4. Tuberculosis risk factor

Factors that influence the incidence of pulmonary tuberculosis include age, gender, smoking history, history of diabetes mellitus, and contact with sufferers.

Analysis carried out using Indonesian Tuberculosis Prevalence Survey (SPTB) data shows that those aged 35-54 years have a 1.22 times greater risk of contracting TB (95% CI; 0.96-1.54) and those aged over 55 years have a risk of 1.22 years. .73 times the incidence of TB compared to those aged 15-34 years (CI 95%; 1.32–2.27) (Pangaribuan et al., 2020).

People who have medical conditions such as HIV, diabetes mellitus, low body weight (CDC, 2016). Participants who had been diagnosed with DM by a doctor were 1.44 times more likely to develop TB than those who had never been diagnosed with DM (Pangaribuan et al., 2020). This is supported by research which shows that people with diabetes are 2.2 (CI 95%, p, 0.001) more likely to develop tuberculosis than people who do not suffer from diabetes (Faurholt-Jepsen *et al.*, 2011). Respondents with poor nutritional status are 9.4 times more likely to suffer from pulmonary TB compared to respondents with normal or excessive nutritional status (Izzati, Basyar and Nazar, 2015). Participants who smoke have a 1.25 times risk of developing TB compared to those who do not smoke (Pangaribuan *et al.*, 2020).

Contact with other tuberculosis patients can also increase the risk of developing TB. Participants who have lived with TB sufferers have a 1.84 times risk of developing TB compared to those who have never lived with TB patients (Pangaribuan *et al.*, 2020).

## 5. Introduction to Quality of Sleep

Sleep is a period of rest for the body which is characterized by decreased awareness of the surrounding environment (Turner et al., 2018). Sleep is very important for several vital body functions including development, energy conservation, modulation of immune responses, cognitive function, disease development, and psychological state (Zielinski, McKenna and McCarley, 2016). Apart from that, sleep also plays a role in the body's immune function. Sleep supports the initiation of adaptive immune responses. The invading antigen is taken up and processed by antigen presenting cells (APCs) which present antigen fragments to T helper cells (Th), with the two types of cells forming an 'immunological synapse'. Concomitant release of interleukin (IL)-12 by APCs induces a Th1 response that supports the function of antigen-specific cytotoxic T cells and initiates antibody production by B cells. This response ultimately results in a long-lasting immunological memory for the antigen. Sleep, particularly slow wave sleep (SWS), and the circadian system act together to produce a pro-inflammatory hormonal environment with increased growth hormone and prolactin release as well as decreased levels of the anti-inflammatory stress hormone cortisol (Besedovsky, Lange and Born, 2012).

Sleep quality has four main aspects, among some are sleep efficiency, sleep disturbance, sleep latency, and sleep duration (Nelson, Davis and Corbett, 2022). Sleep efficiency can be defined as the ratio of the total amount of time sleeping compared to the total time in bed. Sleep disorders can be a combination of events that occur before and during sleep that cause interruption of sleep. Sleep latency is the time it takes a person from waking up to falling asleep completely.

Sleep duration is the total sleep time minus interruptions over a period of one day or 24 hours. The two main processes that influence the regulation of sleep timing and duration are the circadian rhythm (C) and the homeostasis process (S) which is determined by wakefulness and sleep (Borbély, 1982). The American Heart Association and CDC recommend that adults receive at least 7 hours of sleep every night to promote optimal health and reduce the risk of several diseases such as obesity, diabetes, hypertension, coronary heart disease, stroke, mental distress (Liu et al., 2017).

## 6. Measurement of Sleep Quality

Sleep quality is an important component that may provide an overview of a person's sleep disorders. Sleep quality can be measured subjectively using the Consensus Sleep Diary and questionnaires and objectively using polysomnography and actigraphy (Landry, Best and Liu-Ambrose, 2015). Questionnaires that can be used to measure subjective sleep quality include PSQI, AIS, JSS, ISI, MSQ, LSEQ, and ESS. As the most frequently used subjective measure of sleep quality, the PSQI has good reliability and internal validity (Buysse *et al.*, 1998). Sleep disturbance scales (AIS, ISI, MSQ, JSS, LSEQ) have good psychometric properties, but the AIS and ISI have been found to have different factorial models. Meanwhile, LSEQ, MSQ, and JSS still require further validation studies (Fabbri *et al.*, 2021).

## 7. Factors Affecting Sleep Quality

Sleep quality can be influenced by physiological factors, psychological factors, and environmental factors. These factors include age, gender, BMI, stress level, anxiety level, depression level, room temperature, sleeping during the day, and use of devices (Nelson, Davis and Corbett, 2022). Age had a significant association with low sleep quality (OR: 1.05; 95% CI: 1.03 to 1.06). Women were almost twice as likely as men (OR: 1.88; [95% CI]: 1.54 to 2.28) to have poor sleep quality.

## 8. Sleep Quality of Tuberculosis Patients

Based on previous research, measuring sleep quality in pulmonary TB patients usually uses the Pittsburgh Sleep Quality Index (PSQI) questionnaire instrument. The prevalence of tuberculosis patients (CI 95%) who had poor sleep quality was 17% (12, 23%), lack of knowledge about sleep hygiene was 33% (27, 40%), and excessive daytime sleepiness was 12% (8, 17). %) (Raj and Ramesh, 2021). In tuberculosis patients at the Sitopeng Community Health Center, Cirebon City, the results showed that 6 respondents (18.8%) had poor sleep quality and 26 respondents (81.3%) had good sleep quality (Erna Marisa and Syaripudin, 2020). There were 24 pulmonary tuberculosis patients (80%) who had good sleep quality and 6 people (20%) had poor sleep quality (Muftiani, 2012).

## 9. Conclusion

Sleep is one of important aspect to help patient recovered well. It has been acknowledged that some of tuberculosis patients has poor sleep quality and this cannot be overlooked. Following that, tuberculosis patients that has poor sleep quality might need more attention from medical personnel.

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