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Review Article

LITERATURE REVIEW: DETERMINANT OF LATENT TUBERCULOSIS INFECTION (LTBI) IN DEVELOPING COUNTRY

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ABSTRACT

Background: The problem of TB in Indonesia is increasingly worrying considering that Indonesia is the second country with the most TB cases in the world. Serious efforts are needed to break the chain of TB transmission as early as possible by focusing on preventing risk factors for transmission. TB transmission often occurs within the family, the vulnerable group being infected with TB who live in the same house as TB sufferers. The study aims to review the determinants of latent TB infection in developing countries based from previous research findings.

Methods: This study used the literature review method by collecting journals from Google Scholar, PubMed, and ScienceDirect. Data collection using keywords Risk Factors AND ILTB AND Developing Country. The results of the livelihood obtained a total of 125 articles which were then carefully selected so that 8 of the most relevant articles were obtained for article review. The inclusion criteria are journals have titles and contents relevant to the purpose, in English and Indonesian and full text, research journals published between 2015–2024.

Results: The research results showed that the determinants of ILTB infection are individual factors in the form of history of BCG vaccination, gender, age, history of contact with TB patients, marital status, duration of work, and protozoan infection. The second factor is socioeconomic factors in the form of home ownership, poverty and employment. The third factor is behavior which includes the habit of sleeping in the same room, smoking, sharing needles, and keeping animals at home.

Conclusions: The determinants of ILTB infection are individual, behavioral and socioeconomic factors.

Keywords: *Latent TB, Risk Factor, Developing Country*

INTRODUCTION

The problem of TB in Indonesia is increasingly worrying considering that Indonesia is the second country with the most TB cases in the world(1). Serious efforts are needed to break the chain of TB transmission as early as possible by focusing on preventing risk factors for transmission(2). The number of tuberculosis sufferers globally reaches 10 million people with the death toll reaching 1.2 million people per year. The order of highest cases of global tuberculosis cases in India (26%), Indonesia (8.5%) in second place, and China (8%) of the total cases of tuberculosis throughout the world. Referring to Indonesian TB data for 2020, the number of cases of Tuberculosis increased by 845,000 cases compared to 843,000 cases in 2019 with a death toll of more than 98,000 people or the equivalent of 11 deaths per hour. This is a huge number of patients and deaths for a curable disease(3).

Many people are infected with TB bacteria but do not show symptoms of illness or are known as latent TB infection (ILTB)(4). Even though latent TB infection can develop into active TB which is very detrimental to the sufferer. Many ILTB sufferers who have a history of contact with TB patients(5). TB transmission often occurs within the family, the vulnerable group being infected with TB are children under 15 years of age who live in the same house as TB sufferers(6). Many risk factors can trigger the incidence of ILTB in developing countries, some of which are individual factors, socioeconomic, environmental, and behavioral factors(7)(8)(9). Socioeconomic factors include education, poverty, and knowledge of parent(10)(11). At the same time, behavioral

factors include the habit of sleeping together, clean and healthy living behavior, and the habit of expelling phlegm[12].

METHODS

This research uses the literature review method, which is to identify what researchers have written on a subject or topic that is done selectively, to produce a comprehensive report on the current position of science related to a particular topic.

1. Introductory question: What risk factors influence ILTB infection among children in developing countries? With keywords risk factor, ILTB, and Developing Country.
2. Inclusion criteria: journals have titles and contents relevant to the purpose, in English and Indonesian and full text, research journals published between 2015–2024. Exclusion criteria: journals that do not have a complete structure, review articles, and journals that do not discuss risk factors for anemia in farmers.
3. The journal collection process is carried out using several search engines to find journals related to ILTB risk factors in developing countries. The journals used in this literature review were obtained through the database of health journal providers in the form of PubMed, Google Scholar, ScienceDirect, and ResearchGate. Journal selection using the 2015-2024 Boundaries filter. From the keywords used, 128 articles were obtained, then the title and abstract with the topic to be discussed.
4. Each of the 8 research journals is read carefully from abstracts, objectives, and data analysis, to obtain information about risk factors for ILTB infection in developing countries. The method includes the design, population, sample, data sources, techniques/instruments of data collection, and data analysis procedures. Methods should make readers be able to reproduce the experiment. Provide sufficient detail to allow the work to be reproduced.

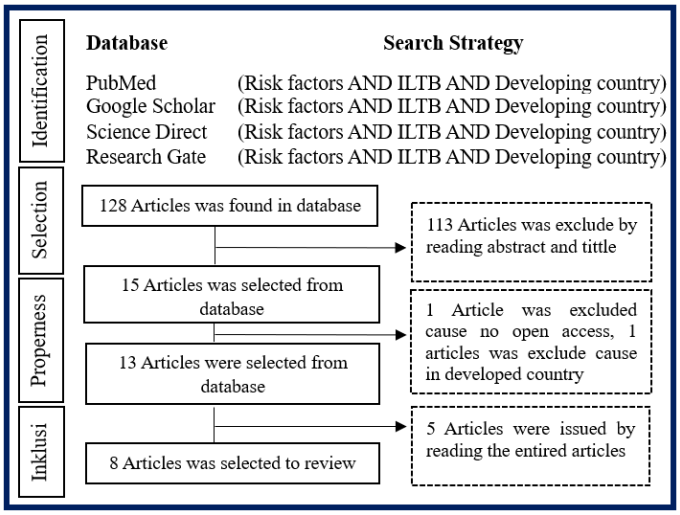

Figure 1. Prisma Method Determinants of ILTB in Developing Countries

RESULTS

Based on the search results from several sources, numerous articles were obtained, which were then selected based on inclusion and exclusion criteria. The articles that have been rigorously selected will then be reviewed to identify the factors influencing the occurrence of latent tuberculosis infection in developing countries. The articles that passed the review process are presented in Table 1 as follows.

Table 1. "Research Articles Selected for Review"

Author	Title	Country	Design	Sample	Result
Daniel Mumpe-Mwanja, Suzanne Verver, Adoke Yeka, Alfred Etwom, James Waako, Willy Ssengooba, Joseph KB Matovu, Rhoda K Wanyenze, Phillipa Musoke, Harriet Mayanja-Kizza	Prevalence and risk factors of latent Tuberculosis among adolescents in rural Eastern Uganda	Uganda	Crosectional	4981	The study was conducted on 4981 respondents in Uganda in 2015. In this study risk factor of ILTB was BCG scar, APR 1.29 (95% CI 1.12 – 1.48); male gender, APR 1.37 (95% CI 1.21 – 1.56); age 17 -18 years, APR 1.46 (95% CI 1.24 – 1.71) and 15-16 years, APR 1.25 (95% CI 1.07 – 1.46) compared to 12-14 years; being out of school, APR 1.31 (95% CI 1.05 – 1.62); and a known history of household TB contact in last 2 years, APR 1.91 (95% CI 1.55 – 2.35).
Jabulani R. Ncayiyana, Jean Bassett, Nora West, Daniel Westreich, Eustasius Musenge, Michael Emch, Audrey Pettifor, Colleen F. Hanrahan, Sheree R. Schwartz, Ian Sann and Annelies van Rie	Prevalence of latent tuberculosis infection and predictive factors in an urban informal settlement in Johannesburg, South Africa: a cross-sectional study	South Africa	Crosectional	446	This study had a sample of 446 respondents in Johanessburg South Africa 2016. In this study, the factors that influenced the ILTB infection are age (OR = 1.03 for every year increase in age, 95 % CI = 1.01–1.05), male gender (OR = 2.70, 95 % CI = 1.55–4.70), marital status (OR = 2.00, 95 % CI = 1.31–3.54), and socioeconomic status (OR = 2.11, 95 % CI = 1.04–4.31).
Ifedayo M. O. Adetifa, Abdul Khalie Muhammad, David Jeffries, Simon Donkor, Martien W. Borgdorff, Tumani Corrah, Umberto D'Alessandro	A Tuberculin Skin Test Survey and the Annual Risk of Mycobacterium tuberculosis Infection in Gambian School Children	Gambia	Crosectional	7052	The study was conducted on 7052 respondents with median age was 9 years old. The results showed that the risk factor ILTB are age (p-value 0.001 OR= 2.008 95%CI= 1.33-2.56) and gender (p-value 0.010 OR= 1.15 95%CI= 1.04-1.29).
Elzbieta Matulyte, Zavinta Kancauskiene, Aidas Kausas, Jurgita Urboniene, Vilnele Lipnickiene, Jelena Kopeykiniene, Tomas Gudaitis, Sarunas Raudonis, Edvardas Danila, Dominique Costagliola, and Raimonda Matulionyte	Latent Tuberculosis Infection and Associated Risk Factors among People Living with HIV and HIV-Uninfected Individuals in Lithuania	Lithuania	Crosectional	834	The study was conducted on 834 respondents with an average age of 43 years. In this study factor that influencing ILTB are injecting drug use (IDU) (p-value 0.01 OR 2.25, 95%CI=1.27–3.99), imprisonment (p-value= 0.02 OR 1.99, 95%CI= 1.13–3.52), history of contact with an active TB patient (p-value = 0.002 OR 3.33, 95%CI= 1.53–7.24).
Yuvaraj Krishnamoorthy, Komala Ezhumalai, Sharan Murali, Sathish Rajaa,	Prevalence and risk factors associated with latent tuberculosis infection among	India	Crosectional	1523	The study was conducted on 1523 respondents in India with the majority of respondents 54.8% female. The results from data analysis showed that factors that influence ILTB in India

Author	Title	Country	Design	Sample	Result
Maria Jose, Abilasha Sathishkumar, Govindarajan Soundappan, Charles Horsburgh, Natasha Hochberg, William Evan Johnson, Selby Knudsen, Padmini Salgame, Jerrold Ellner, Senbagavalli Prakash Babu, Sonali Sarkar	household contacts of smear-positive pulmonary tuberculosis patients in South India				are age (p-value 0.02 OR 1.4, 95%CI= 1.1-1.9) and shared bed with the case (p-value 0.04 OR=1.1 95%CI= 1.0-1.4). Respondents aged 18-19 have a 1.4 high risk of suffering ILTB, respondents with habbit shared bed with TB cases 1.1 higher risk of suffering ILTB than respondents that using bad alone.
Hamidah Retno Wardani, Ni Made Mertaniasih, Soedarsono Soedarsono	Risk Factors of Latent Tuberculosis Infection in Healthcare Workers At Hospitals in Jember City Indonesia	Indonesia	Crosectional	128	The study was conducted on 128 health workers in Jember City, East Java Indonesia. The results showed that the risk factor of ILTB is duration of work (p-value 0.039 OR= 2.984 95%CI= 1.067-8.342). Healthcare workers who have a duration of work >8 hours have a 3 times higher risk of suffering ILTB than respondents who have a duration of work <8 hours.
Diakourga Arthur Djibougoua, Gloria Ivy Mensahc, Tani Sagna, Leon Tinoaga Sawadogoe, Arsène Kiswensida Ouedraogo, Antoinette Kabore, Hervé Hienb, Clément Ziemlé Meda, Adjima Combarye , Adrien Marie-Gaston Belema, Kennedy Kwasi Addoc, Roch Konbobr Dabiré, Matthieu Perreaug , Jakob Zinsstag, Serge Potiandi Diagbouga	Magnitude and associated factors of latent tuberculosis infection due to Mycobacterium tuberculosis complex among high-risk groups in urban Bobo-Dioulasso, Burkina Faso	Burkina Faso	Crosectional	187	The study was conducted in Burkina Faso in 2020. The results showed that factors that influenced the incidence of ILTB are working in a slaughterhouse (p-value 0.001, OR=1.095, 95% CI=1.00–2.036), smoking (OR=4.214, 95%CI=1.051–16.899), ≥15 years of exposure (OR=5.617, 95%CI=1.202–32.198), having an animal at home (OR=2.735, 95%CI=1.102–6.789) and protozoal infection (OR=2.591, 95%CI=1.034–6.491).
Karbito, Siti Maisaroh	Prevalensi dan Faktor Risiko Infeksi TB Laten pada Anggota Keluarga Kontak Serumah dengan Pasien TB Aktif	Indonesia	Case-Control	241	The study was conducted on 241 respondents in Kedungmundu Healthcare Center, Semarang, Central Java. The research showed that a significant variable affecting ILTB is occupation (p=0,024)). laborers/farmers/fishermen (p=0.007; aOR=7.04; 95%CI=1.70–29.02), traders/entrepreneurs (p=0.021; aOR=4.29; 95%CI=1.25 – 14.76), employees/ASN/TNI/POLRI (p=0.009; aOR=4.55; 95%CI=1.46–14.15), students/students (p=0.014; aOR=5.27; 95%CI=1.40–19.83) compared to housewives (IRT)/not working, length of contact (p=0.016; aOR=4.70;

Author	Title	Country	Design	Sample	Result
					95%CI=1.33–16.66) and bedroom density (p<0.001; aOR=5.33; 95%CI=2.24–12.71).

DISCUSSION

Of the 8 journals that have been selected for this literature review, all use quantitative studies. The selection of study sites was carried out in various countries, namely Indonesia, Burkina Faso, Lithuania, Gambia, Uganda, and South Africa (Table. 1). Then all selected journals were read carefully starting from abstracts, objectives, methods, data analysis, and discussion to find out information related to determinants of ILTB in developing country. It is known that determinants for causing ILTB infection in developing countries are influenced by behavioral factors, sociodemographic factors, and environmental factors. The reason for the separation of risk factors into individual, behavioral, and socioeconomic factors.

1. Individual Factors

a. Age

Age is one of the individual factors that can increase the incidence of ILTB in developing countries. A review of research conducted by Mwanja et al in Uganda shows that the risk of suffering from ILTB is higher in certain age groups such as age 17 -18 years, APR 1.46 (95% CI 1.24 – 1.71) and 15-16 years, APR 1.25 (95% CI 1.07 – 1.46). This condition is caused in this age group interactions with many people become more intense, especially at school or when playing with friends[12]. A review of research conducted by Ncayiyana et al in South Africa shows the risk of suffering from ILTB. As you get older, the risk of being infected with ILTB increases (OR = 1.03 for every year increase in age)[11]. Other research in Gambia from Adetifa et.al 2015 shows that children aged 9-11 years are at higher risk of suffering from ILTB compared to those under 9 years of age. This condition is possible because children aged 9-11 years interact with more friends who may have been infected with TB[8]. The results of research in India conducted by Krisnamoorty et.al 2021 show that people aged >18 years are at higher risk of suffering from ILTB than younger people. This condition occurs because older people spend more time interacting with other people while younger people are busy at work. As a result, older people have a longer duration of contact with people suffering from TB[13].

b. Gender

Research in Uganda explains that gender is a factor that influences the incidence of ILTB infection. This study shows that men have a 1.37 times higher risk of experiencing ILTB (PR 1.37, 95% CI 1.21 – 1.56). This condition is caused because men tend to maintain a clean and healthy lifestyle that is worse than women[12]. This research is supported by research in South Africa which shows the same results, where men are more at risk of being infected with ILTB than women. The results of the analysis show that men are at 2.a7 times greater risk of being infected with ILTB (OR = 2.70, 95 % CI = 1.55–4.70) because men in South Africa like to gather with people around them, thereby increasing their vulnerability to contracting TB. Another study in the Gambia showed that gender is a risk factor for ILTB infection where men are more at risk than women[11]. In general, men have worse healthcare behavior than women, apart from that, men do more activities outside the home and interact with many people, so the possibility of contact with TB sufferers is greater[14].

c. BCG vaccination

BCG vaccination is given to children so that the body creates immunity against several diseases, one of which is tuberculosis. Children who receive BCG immunization are expected to have better immunity against TB bacteria. The results of research in Uganda show that people who do not receive BCG immunization are 1.29 times more likely to suffer from ILTB. BCG vaccination has the ability to increase the body's resistance so that the body has better antibodies to fight TB bacteria. If a child does not receive BCG immunization, it can increase the risk of the child contracting TB bacteria and becoming ill with ILTB[12].

d. History of Contact with TB Patients

Tuberculosis bacteria are transmitted through droplets that come out when sufferers sneeze or cough. Bacteria that come out of the lungs will be transmitted to other people who interact with the sufferer. People who have a history of close contact with TB sufferers are at greater risk of being infected with ILTB[15]. Research in Uganda shows that a history of close contact with TB sufferers for more than 2 years will increase the risk of suffering from ILTB 1.91 times[12]. This research is supported by research in Lithuania which shows that people with a history of close contact with TB sufferers have a 3.33 times greater risk of experiencing ILTB. The longer and more intense the interaction between healthy people and TB sufferers allows greater transmission of bacteria from sick people to healthy people, as a result, healthy people can be infected with ILTB and will become active TB when the body's immune system decreases and preventive measures are not taken[16].

2. Socioeconomic

a. Marital Status

Marital status is one of the factors that can increase a person's risk of suffering from ILTB. Research in South Africa shows that one of the risk factors for someone suffering from ILTB is marital status. In this study, it was discovered that

unmarried people have a 2 times greater risk of suffering from ILTB. In general, unmarried people spend more time playing and interacting with their peers, while married people spend more time at home taking care of the household. The higher the interaction with other people, the higher the risk of contracting various diseases such as tuberculosis compared to people who rarely interact[11].

b. Poverty

Poverty cannot be denied as a factor that plays a role in the spread of various diseases including ILTB. Several studies that have been conducted show that poverty in the form of not having a decent house, low income, and inadequate work increases a person's risk of being infected with ILTB. Research in southern Africa shows that people with low socio-economic conditions are 2.11 times more likely to experience ILTB due to poor access to health services[11]. Another study in Lithuania showed that people living in inadequate housing had a 1.99 times greater risk of suffering from ILTB. Poor living conditions can become a place for the growth of various disease-causing bacteria, including tuberculosis[16].

c. Occupation

A person's job can increase or decrease the risk of experiencing ILTB, someone who works in a good place and a healthy environment has a lower chance of suffering from ILTB. This is in line with research in Burkina Faso where people who work in slum areas have a 1,095 times greater risk of being infected with ILTB[7]. Other research in India showed that the duration of work becomes a risk factor for ILTB. Research in the city of Semarang also shows that a person's job, especially health workers who work >8 hours, has a higher risk of being infected with ILTB. This condition is caused by longer interactions, making it more likely for bacteria to enter the person's body[13].

3. Behavior

a. Smoking

Smoking has an adverse impact on health, one of which is the impact on the transmission of TB disease in the community. A study in Burkina Faso showed that people who smoke were 4.27 times more likely to suffer from ILTB[7]. This condition is caused by the chemical content in cigarettes in the form of tar, nicotine, and other chemicals which can reduce a person's immune system. This condition causes the immune system to be unable to kill TB bacteria that enter the body, as a result, the person suffers from ILTB[9].

b. Shared Bed

Research in India shows that a history of close contact is a risk factor for TB in children (p-value <0.001; OR= 1.1), In this study, it was discovered that many children suffer from TB because they interact with people who suffer from TB at school[13]. Research in Semarang shows that shared bedroom with TB index cases is a risk factor for positive tuberculin test in young children (OR= 5.33; 95%CI= 2.24-12.71), this condition is caused by sleeping habits with TB sufferers will increase the possibility of being infected with TB because it increases close contact and the duration of exposure to the index TB case[17].

c. Injection Drugs Use

Using illegal drugs or over-the-counter drugs is one of the risk factors for ILTB infection in adults. Research in Lithuania on prison inmates showed that people who shared syringes had a 2.25 times risk of suffering from ILTB (p-value 0.01 OR 2.25, 95%CI=1.27–3.99). People who share needles have increased interactions with other people who may have TB. The syringe used can contain TB bacteria and these bacteria will infect other people who also use the syringe[16].

d. Interaction with Animals

Research in Burkina Faso explains that interactions with animals can increase the risk of TB infection. People who keep animals at home are 2.73 times more likely to suffer from ILTB compared to people who do not keep animals at home. Apart from that, protozoan infection also increases a person's ILTB infection by 2.33 times. This condition is caused by unbalanced living environmental conditions which increase the resistance of bacteria including TB bacteria to survive. The dirtier and damper a person's house becomes, the more likely it is to become a nest for bacteria and other parasites that can infect the humans who live in it[7].

CONCLUSION

The determinants of ILTB infection are individual, behavioral and socioeconomic factors. It is hoped that further research will examine more physical environmental risk factors that can increase the incidence of ILTB infection. Future research focuses more on at-risk populations such as children with HIV/AIDS.

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