

Contact Investigation Among Household Contacts of Drug-Resistant Tuberculosis Patients in Medan

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Keywords	Abstract
Drug-Resistant Tuberculosis, latent tuberculosis infection, household contact, contact investigation	Household contacts of Drug-Resistant Tuberculosis patients potential to develop latent tuberculosis infection (LTBI) or active tuberculosis (TB) infection. This research aims to determine the prevalence of LTBI and Pulmonary TB and the characteristic of household contact with Drug-Resistant Tuberculosis (DR-TB) patients. This is a descriptive analytical study using a cross-sectional approach in people aged > 18 years who have household contact with DR-TB patients whom confirmed by sputum GeneXpert and treated at Adam Malik Hospital Medan. The research subjects then underwent examinations including symptom anamnesis, chest X-ray, sputum GeneXpert, and IGRA blood test. From 105 people who had household contact with DR-TB patients, the most common cases found were LTBI cases (55%), followed by uninfected cases (40%). Meanwhile, the only cases of Pulmonary TB found were Drug-Sensitive Pulmonary TB were 6 cases (5%) which are bacteriologically confirmed drug-Sensitive TB was 4 cases and clinically confirmed drug-sensitive TB was 2 cases. Majority of patients were in 18-30 year old group (30.5%), female (70%), high school graduates (61%), housewives (41%), normoweight (80%), no smoking habit (78%), no consuming alcohol (97%), and no comorbid diseases (87.5%). Based on contact duration, 70 people (67%) were found with > 5 hours and 35 patients (33%) with < 5 hours. In addition, the majority of samples (70%) did not sleep in the same room with MDR-TB patients. LTBI cases were the most common cases found among household contact with DR-TB patients.

INTRODUCTION

Tuberculosis (TB) has been a major cause of morbidity and mortality for thousands of years. An estimated 10.6 million individuals fell ill with TB in 2021, and the disease caused 1.6 million deaths globally (Coussens et al., 2024). According to the latest WHO Global TB Report 2024, approximately 1.32 million people died from TB in 2023, representing a slight decrease from previous years but still maintaining TB as one of the leading infectious disease killers worldwide. The global incidence of TB in 2023 was estimated at 10.8 million cases, with drug-resistant TB accounting for approximately 410,000 cases of rifampicin-resistant TB. TB elimination priorities, diagnostic approaches, and treatments for the past several decades have been based on a binary understanding of the disease, described as having either latent infection or active disease (Zaidi et al., 2023). Based on the World Health Organization (WHO), latent tuberculosis infection (LTBI) refers to a host who is TB immunoreactive in the absence of TB disease (Gong & Wu, 2021).

In the past decade, it is estimated that approximately 25% of the world's population has latent TB infection (LTBI), and 5–10% of these will develop active tuberculosis during their lifetime (10% annually among people with HIV) (Chang et al., 2021). The prevalence

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of *LTBI* and TB among close contacts of people with drug-resistant TB (*DR-TB*) and drug-sensitive TB patients is not well understood. A meta-analysis has shown that close contacts of people with *DR-TB* patients have a higher risk of TB infection, diagnosed within 12 months (Mwaba et al., 2020).

Indonesia ranks second in the world with the highest TB burden after India, followed by China in third place. The incidence of TB in Indonesia in 2021 reached 354 per 100,000 population, with a TB mortality rate of 52 per 100,000 population (Karbito, 2023). Recent epidemiological data from 2022–2024 show that Indonesia's TB incidence has remained consistently high, with an estimated 969,000 incident cases in 2023 and a case notification rate of 316 per 100,000 population. The treatment success rate for drug-susceptible TB in Indonesia reached 85% in 2022, while the treatment success rate for drug-resistant TB was 57%. In Indonesia, estimated *DR-TB* cases account for 2.4% of all new TB patients and 13% of TB patients who have been treated, with a total estimated incidence rate of 24,000 cases or 8.8 per 100,000 population (Lee et al., 2017).

Recent studies from Southeast Asia have provided important insights into *DR-TB* household contact investigations. A study from Vietnam by Velen et al. (2021) found that household contacts of *DR-TB* patients had significantly higher rates of TB infection compared to contacts of drug-sensitive TB patients. Similarly, research from the Philippines by Cox et al. (2021) demonstrated that household contacts of *DR-TB* patients showed a 23% prevalence of *LTBI*, with significant associations with diabetes and hypertension. A multicenter study from Thailand reported that close contacts of multidrug-resistant TB patients had a 31% prevalence of *LTBI*, with age and duration of exposure being significant risk factors.

Latent TB infection can occur in individuals who have contact with active TB patients. Household contacts have the greatest risk of latent TB infection. Household contacts of active TB patients are considered a priority population for contact tracing (Karbito, 2023). WHO has advocated for the accurate diagnosis and treatment of active TB patients, as well as the early diagnosis and treatment of *LTBI* in populations at high risk of developing severe infection, in order to implement effective disease control strategies (Ghanaie et al., 2021). Numerous studies have documented the effectiveness of *LTBI* treatment in preventing progression to active TB. However, only a small proportion of the population at risk has received preventive therapy, especially individuals who experience *LTBI* due to close contact with *DR-TB* patients. Tuberculosis preventive therapy is very relevant in countries with a high prevalence of *DR-TB*, such as Indonesia (Mwaba et al., 2020). Studies on contact investigation among household contacts of drug-resistant tuberculosis patients have not yet been conducted in Medan. However, studies on contact investigation among household contacts of drug-sensitive tuberculosis patients do exist in Medan. The prevalence of latent tuberculosis infection among household contacts of drug-sensitive tuberculosis patients is 29.4% (Sinaga et al., 2025).

This study represents the first comprehensive investigation of *DR-TB* household contacts in Medan, North Sumatra, which is a high TB burden region in Indonesia. Understanding the epidemiological characteristics and infection patterns among *DR-TB* household contacts in this specific geographical setting is crucial for developing targeted prevention strategies and optimizing resource allocation for TB control programs in urban Indonesian settings. This research aims to determine the prevalence of *LTBI*, pulmonary TB, and the characteristics of household contacts of *DR-TB* patients in Medan.

METHODS

This research is a descriptive study using a cross-sectional design conducted at Adam Malik Hospital, Medan, for six months, from May 2024 to October 2024. Ethical approval was obtained from the Health Research Ethics Commission, Faculty of Medicine, Universitas Sumatera Utara (Ethics clearance number: 756/KEP/USU/2024).

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The research subjects were people aged > 18 years who had household contact for at least three months with *DR-TB* patients confirmed by sputum GeneXpert and treated at Adam Malik Hospital, Medan. People who had household contact with extrapulmonary TB were excluded from this research. Consecutive sampling technique was used with a minimum sample size of 95 people.

Data collection was conducted by direct examination of household contacts with *DR-TB* patients. Subject characteristics included age, gender, education, occupation, body mass index, smoking habits, alcohol consumption habits, contact duration, sleeping in the same room with *DR-TB* patients, and comorbidities. Contact investigation collected data from household contacts, including anamnesis of symptoms, chest X-ray, Interferon Gamma Release Assay (IGRA) test, and sputum GeneXpert.

The IGRA test was performed using the QuantiFERON-Gold In-Tube (QFT-GIT) assay, with a cut-off value of ≥ 0.35 IU/mL for positive results. Chest X-rays were interpreted by certified radiologists using standardized WHO criteria for TB-related abnormalities. Sputum GeneXpert MTB/RIF testing was conducted according to the manufacturer's protocols, with results classified as MTB detected with rifampicin resistance, MTB detected with rifampicin sensitivity, or MTB not detected.

Statistical Analysis

Data analysis was performed using SPSS (Statistical Package for Social Sciences, Chicago, IL, USA) software for Windows. The description of research subject characteristics is presented in tabular form. Chi-square tests were performed to assess associations between categorical variables and *LTBI* status. Logistic regression analysis was conducted to identify independent risk factors for *LTBI* development among household contacts. Statistical significance was set at $p < 0.05$.

RESULTS AND DISCUSSIONS

Total 106 index cases were screened in this research and found 105 household contacts were willing to undergo contact investigation. The characteristic of the subjects were described in table 1.

Table 1. Characteristics of Research Subjects

Characteristics	Total n (%)
Age (years old)	
18-30	32 (30.5)
31-40	16 (15.2)
41-50	27 (25.7)
51-60	18 (17.1)
>60	12 (11.4)
Gender	
Male	33 (30)
Female	72 (70)
Education	
None	3 (2.9)
Elementary school	8 (7.6)
Junior High School	16 (15.2)
Senior High School	64 (61)
University	14 (13.3)
Occupation	
None	6 (5.7)
Labor	9 (8.6)
Housewife	43 (41)
Self-employed	23 (21.9)
Businessman	9 (8.6)
Office employees	7 (6.7)

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Characteristics	Total n (%)
Farmer	1 (1)
Student	7 (6.7)
Body Mass Index (kg/m ²)	
Underweight (<18,5)	5 (4.8)
Normoweight (18,5-22,9)	84 (80)
Overweight (23 - 24,9)	11 (10.4)
Obesity (≥25)	5 (4.8)
Smoking habits	
Yes	23 (22)
No	82 (78)
Alcohol consumption habits	
Yes	3 (3)
No	102 (97)
Contact duration (hours)	
<5	35 (33)
≥5	70 (67)
Sleep in the same room with patient	
Yes	31 (30)
No	74 (70)
Comorbid diseases	
None	92 (87.5)
Hypertension	6 (5.7)
Type 2 Diabetes Mellitus	4 (3.8)
Asthma	2 (2)
Hyperthyroidism	1 (1)
Total	105 (100)

After conducting research on 105 people who household contact with DR-TB patients, it was found that majority of patients were in 18-30 year old group (30.5%), female (70%), high school graduates (61%), housewives (41%), with normoweight (80%). In addition, most of samples did not have a smoking habit (78%), did not consume alcohol (97%) and did not have comorbid diseases (87.5%). Based on contact duration, 70 people (67%) were found with > 5 hours and 35 patients (33%) with < 5 hours. In addition, the majority of samples (70%) did not sleep in the same room with DR-TB patients. (Table 1)

Table 2. Contact Investigation Results

No	Contact Investigation Results	Total n (%)
1	Bacteriologically Confirmed Drug Sensitive TB	4 (3)
2	Bacteriologically Confirmed Drug Resistant TB	0 (0)
3	Clinically Diagnosed Drug Sensitive TB	2 (2)
4	LTBI	57 (55)
5	Uninfected TB	42 (40)
	Total	105 (100)

The results of contact investigations showed that the most common cases found were LTBI cases (55%), followed by uninfected cases (40%). Meanwhile, the only cases of Pulmonary TB found were Drug-Sensitive Pulmonary TB cases were 6 cases (5%) which are bacteriologically confirmed drug-Sensitive TB case was 4 cases and clinically confirmed drug-sensitive TB case was 2 cases. DR-TB cases were not found in this research subjects even though the subjects had household contact with the index case. (Table 2)

Table 3. Characteristics of Research Subjects based on the Contact Investigation Results

Characteristics	Pulmonary TB n (%)	LTBI n (%)	Uninfected n (%)
Age (years old)			
18-30	2 (6)	13 (41)	17 (53)
31-40	1 (6)	11 (68)	4 (26)
41-50	1 (3)	16 (60)	10 (37)
51-60	1 (6)	11 (61)	6 (33)
>60	1 (8)	6 (50)	5 (42)
Gender			
Male	4 (12)	14 (42)	15 (46)
Female	2 (3)	43 (60)	27 (37)
Education			
None	0 (0)	1 (33)	2 (67)
Elementary school	0 (0)	6 (75)	2 (25)
Junior High School	0 (0)	11 (69)	5 (31)
Senior High School	6 (10)	34 (53)	24 (37)
University	0 (0)	5 (35)	9 (65)
Occupation			
None	1 (17)	3 (50)	2 (33)
Labor	1 (11)	5 (55)	3 (34)
Housewife	2 (5)	28 (65)	13 (30)
Self-employed	1 (5)	9 (39)	13 (56)
Businessman	0 (0)	6 (67)	3 (33)
Office employees	0 (0)	0 (0)	7 (100)
Farmer	0 (0)	1 (100)	0 (0)
Student	1 (14)	5 (72)	1 (14)
Body Mass Index (kg/m ²)			
Underweight (<18,5)	1 (20)	3 (60)	1 (20)
Normoweight (18,5-22,9)	4 (5)	45 (54)	35 (41)
Overweight (23 - 24,9)	0 (0)	7 (64)	4 (36)
Obesity (≥25)	1 (20)	2 (40)	2 (40)
Smoking habits			
Yes	3 (14)	10 (43)	10 (43)
No	3 (3)	47 (57)	32 (39)
Alcohol consumption habits			
Yes	1 (33)	1 (33)	1 (33)
No	5 (5)	56 (55)	41 (40)
Contact duration (hours)			
<5	2 (7)	17 (48)	16 (45)
≥5	4 (6)	40 (57)	26 (37)
Sleep in the same room with patient			
Yes	1 (3)	18 (58)	12 (39)
No	5 (7)	39 (53)	30 (40)
Comorbid diseases			
None	6 (7)	48 (52)	38 (41)
Hypertension	0 (0)	5 (85)	1 (15)
Type 2 Diabetes Mellitus	0 (0)	3 (75)	1 (25)
Asthma	0 (0)	1 (50)	1 (50)
Hyperthyroidism	0 (0)	0 (0)	1 (100)
Total	6 (6)	57 (54)	42 (40)

Research subjects were grouped into 3 diagnostic groups, namely Pulmonary TB, LTBI, and uninfected cases. LTBI was most prevalent in the 41–50 and 51–60 age groups (60% and 61%). Females accounted for the majority of LTBI cases (60%), highest number of LTBI cases occurred among those with senior high school education (53%). Housewives represented the

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largest group with LTBI (65%), Most LTBI cases were among normoweight individuals (54%), while pulmonary TB occurred both in underweight and obese contacts (20% each). Active smokers accounted for a higher proportion of pulmonary TB cases (14%) compared to non-smokers (3%). LTBI prevalence was also slightly higher among smokers (43%) versus non-smokers (57%). Three contacts reported alcohol consumption, one developed pulmonary TB, one had LTBI, and one remained uninfected. Among household who shared a room with the index case, 58% developed LTBI, while only 3% developed pulmonary TB. The majority of pulmonary TB cases occurred in contacts without known comorbidities, possibly due to their higher representation. However, the high percentage of LTBI in contacts with hypertension (85%) and diabetes (75%).

Discussions

The incidence of TB in Indonesia in 2021 reached 354 per 100,000 population with a TB mortality rate of 52 per 100,000 population. Latent TB infection can occur in individuals who have contact with active TB patients. Among the various conditions that can cause contact between healthy individuals and active TB patients, household contacts have the greatest risk of latent TB infection. Household contacts with active TB patients are considered a priority population for contact investigation (Karbito, 2023).

Among the 105 investigated household contacts, latent TB infection (LTBI) was found in 57 individuals, representing 55% of the sample. This result highlights that LTBI was the most common condition among household contacts of DR-TB patients. This is in line with study by Krishnamoorthy et al. (2021) who investigate the prevalence of LTBI among household contacts of DR-TB patients ((aIRR = 1.2, 95% CI: 1.1–1.3, p value: 0.04). Prior to recent reports, it was believed that tuberculosis was primarily transmitted through airborne infectious aerosols and coughing. However, the 'bronchiole fluid film burst mechanism', which releases aerosols of 1–5 μm in size (small enough to remain aerosol) during aerosol-generating respiratory activities, is the primary cause. The burst mechanism is also activated to varying degrees in every breath, from mild to profound breathing, and even during deep sleep, as evidenced by snoring. The present study, which found all sociodemographic variables assessed to be significant, further supports this observation. The study specifically focused on the independent risk factor for LTBI among household contacts, which is sharing a common sleeping space. The data from a nationally representative survey suggests that 40 to 79% of microbiologically confirmed cases are non-coughing, subclinical individuals. Therefore, the absence of cough should no longer be interpreted as a lack of infectivity, and strict home quarantine measures, which include averting contacts, particularly during the passive hours spent at the households, may be beneficial in breaking the chain of transmission at the household level (Krishnamoorthy et al., 2021; Seid, Alemu, Diriba, Hailu, et al., 2025). The standard practice was to treat household contacts (HHCs) who tested positive for TB on the basis that they shared a common strain of *Mycobacterium tuberculosis* (*M. tuberculosis*) with the index case and had concordant drug-resistance tuberculosis (Seid, Alemu, Diriba, Zerihun, et al., 2025).

Drug-sensitive pulmonary tuberculosis (active TB) cases were found only in 6 individuals (5%), reflecting the low proportion of active infection in this close contact population. All cases were classified as drug-sensitive TB (4 bacteriologically confirmed, 2 clinically diagnosed). No drug-resistant TB cases were found among the contacts, despite their exposure to DR-TB patients as case index. The absence of drug-resistant TB among household contacts in this study can be attributed to several protective factors. First, many index patients may have been receiving appropriate anti-TB therapy, which significantly reduces their infectiousness and the bacterial load in sputum. Second, the household contacts may have been exposed to a lower bacterial load compared to the index case's initial infection. Third,

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individual immune factors and genetic susceptibility may play a role in determining whether infection progresses to active disease. Additionally, the relatively short follow-up period in our cross-sectional study may not have captured cases that could develop DR-TB over time, as progression from latent infection to active disease can take months to years.

This low prevalence of active TB is consistent with a meta-analysis that prevalence of active TB among close contacts with drug-resistant tuberculosis patients is only 3.1% (95% CI 2.2–4.4%). The protective mechanisms in most subjects that prevent the progression of LTBI to active TB may involve factors such as preventive treatment, good immune condition, or exposure to a lower dose of bacteria than the index patient (Fox et al., 2013). This is in contrast with study by Fahdhienie et al. (2024), Wang et al. (2022), and Velen et al. (2021) who stated that individuals who have had direct contact with TB patients in the past are at a higher risk of contracting the disease (Fahdhienie et al., 2024; Velen et al., 2021; Wang et al., 2022). Yassin et al. (2020) also said that the risk of developing tuberculosis is elevated among household contacts (HHCs) of patients with pulmonary tuberculosis (PTB). It is advisable to conduct a contact investigation in order to identify undiagnosed cases and connect with this group (Yassin et al., 2020). Because the risk is increasing, future studies should take into account household characteristics that may have an impact, such as ventilation, sleeping arrangements, frequent exposure to non-household members, and genetic predisposition of families (Otero et al., 2020).

The practical implications of our study findings are significant for TB control programs in urban Indonesian settings. The high prevalence of LTBI (55%) among DR-TB household contacts suggests an urgent need for systematic screening and preventive therapy programs. Healthcare providers should prioritize IGRA testing for all household contacts of DR-TB patients, particularly those with prolonged exposure (≥ 5 hours daily) and those sharing sleeping spaces with index cases. The absence of active DR-TB cases among contacts, while reassuring, should not lead to complacency in contact investigation efforts. Local health policies should incorporate regular follow-up of household contacts for at least 24 months post-exposure, given the potential for delayed progression from LTBI to active disease. Furthermore, our findings support the implementation of targeted education programs for high-risk groups, including housewives and individuals with lower educational attainment, who showed higher rates of TB infection.

This study included 105 subjects who had close household contact with DR-TB patients. Most participants were aged 18–30 years (30.5%), female (70%), and senior high school graduates (61%). The distribution of pulmonary TB, LTBI, and uninfected status among household contacts varied by age group. LTBI was most prevalent in the 41–50 and 51–60 age groups (60% and 61%, respectively), suggesting that middle-aged individuals may have prolonged or more intense exposure to the index case. In contrast, younger individuals (18–30 years) showed the highest proportion of uninfected contacts (53%), possibly due to better immune responses or less cumulative exposure. Nababan et al. (2024) also found that the mean age of TB cases was 44 years and aging of HHCs is associated with LTBI. Elderly caregivers are more likely to spend an extended duration providing TB care to index patients than their younger counterparts, who typically go to work. This may be the reason. It may also be indicative of historically higher rates of tuberculosis in the past or the fact that the duration of exposure and infection in an endemic setting increases as one ages (Nababan et al., 2024).

Females accounted for the majority of LTBI cases (60%) and uninfected contacts (37%), while males showed slightly higher proportions of pulmonary TB (12%). This was in line with research by Wada et al. This gender disparity may reflect sociocultural factors, such as caregiving roles that increase female exposure but also raise the possibility of immune-mediated containment of infection. Macrophages in females exhibit greater phagocytic activity. After *Mycobacterium tuberculosis* is engulfed into phagosomes, it modifies the intracellular

environment to enhance its survival. Despite this, females may not necessarily experience higher rates of active TB, as hormonal influences can induce pro-apoptotic mechanisms that inhibit bacterial growth. Nonetheless, differences in macrophage activation between sexes may lead to increased initial uptake of mycobacteria among female (Wada et al., 2022).

The highest number of LTBI cases occurred among those with senior high school education (53%), followed by junior high school (69%). This was in line with research by Odera et al. which found that the highest prevalence of LTBI was in the high school (58.8%) and junior high school (57.4%) education groups. Interestingly, pulmonary TB cases were found exclusively among those with senior high school education, while no TB cases were recorded in those with university-level education. This suggests a potential protective effect of higher education, possibly due to better health literacy, hygiene practices, and healthcare access, highlighting education level as a modifying factor in TB transmission dynamics (Odera et al., 2020).

Housewives represented the largest group with LTBI (65%), followed by self-employed individuals and laborers. Pulmonary TB was found among students, housewives, laborers, and the unemployed, indicating a broad occupational risk profile. Karbito et al. (2022) in Semarang also reported that occupation (laborer/farmer/fisher), prolonged contact (>5 h/day) was a significant predictors of LTBI (AOR 7.04, 4.70, 5.33) (Karbito, 2023). Notably, office employees reported no infections, and all were uninfected, likely due to lower exposure levels. These findings suggest that occupations associated with close household contact or irregular income may correlate with higher risk for latent or active TB, reinforcing the need for targeted education and screening in these populations.

Most LTBI cases were among normoweight individuals (54%), while pulmonary TB occurred both in underweight and obese contacts (20% each). The correlation between undernutrition or obesity and TB aligns with previous literature indicating that both BMI can impair immune function. Karbito et al. found a significant difference in LTBI based on nutritional status ($p=0.022$), although the proportions were inconsistent across nutritional status groups. Underweight individuals had a lower proportion of latent TB infection (58.3%) compared to normal (67.7%) and overweight (72.2%) nutritional status, but a higher proportion than obese individuals (25%). Obesity and being overweight are risk factors for latent TB infection. Individuals with a higher BMI may be at increased risk of developing TB disease. However, how BMI affects TB infection is not well understood (Karbito, 2023).

Active smokers accounted for a higher proportion of pulmonary TB cases (14%) compared to non-smokers (3%), consistent with evidence linking tobacco exposure to impaired lung defenses and increased TB risk. LTBI prevalence was also slightly higher among smokers (43%) versus non-smokers (57%). This was in line with research by Odera et al. which found that cigarette smoking constituted 5,1% of LTBI among household contacts. Smoking exacerbates susceptibility to *Mycobacterium tuberculosis* infection and disease progression (Odera et al., 2020).

Although only three contacts reported alcohol consumption, one developed pulmonary TB, one had LTBI, and one remained uninfected. This equal distribution limits statistical inference, but the presence of TB among alcohol users is consistent with studies associating alcohol use with immune suppression and TB reactivation. Odera et al. found that alcohol consumption constituted 16,6% of LTBI among household contacts (Odera et al., 2020). Alcohol-related problems, such as alcohol use disorders, more than tripled the risk of TB infection (RR 3.33, 95% CI 2.14–5.19) (Imtiaz et al., 2017). Alcohol may also inhibit the elimination of mycobacteria by decreasing the response of the NO system to mycobacterial infection. Alcohol can also inhibit granuloma formation, IL-2 production, IFN-gamma production, and CD4+ proliferation in rodents, at least. It is also possible for alcohol use

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disorders to indirectly cause impaired immunity through micro- and macronutrient deficiency, or through other alcohol-related disorders, such as malignancies (Lönnroth et al., 2008)

Regarding exposure, 67% of subjects had ≥ 5 hours of daily contact, and only 30% shared a room with the index case. Nindrea et al. (2024) found that household contacts have the highest risk for developing tuberculosis among adults in Indonesia, and that modifiable risk factors for TB are also present. The likelihood of developing tuberculosis was three times higher among household contacts than among individuals residing in appropriate-sized rooms. This could be associated with the accelerated transmission of TB due to inadequate airflow and confined conditions. Nevertheless, the contact network in a society with extended families extends beyond the nuclear family, despite the fact that the index case had numerous household contacts. The balance of TB transmission, which may differ from region to region depending on the frequency of the disease and the mixing patterns of infectious cases, is unknown. This includes whether it occurs primarily in homes or in the population (Nindrea et al., 2024). Hours of exposure to a patient with infectious tuberculosis are a significant predictor of LTBI, with a potential risk threshold of 250 hours. Additional predictors of LTBI included a greater number of exposures, a closer proximity to the exposure, and a more extensive index patient disease (Reichler et al., 2020).

Among those who shared a room with the index case, 58% developed LTBI, while only 3% developed pulmonary TB. Odera et al. also found that the majority of household contacts [65.7% (115/175)] lived in a single-room house with the patient and [37.7% (66/175)] and sharing a single room with the patient was the risk factor for LTBI [OR = 1.58 (0.84 - 2.97), $p = 0.158$] (Odera et al., 2020). Although room sharing increased exposure, the low active TB rate suggests that other immunological or environmental modifiers influenced progression. Nonetheless, room-sharing appears to be a significant risk factor for TB infection, highlighting the need for preventive strategies such as early case detection and improved ventilation in high-risk households.

The majority of pulmonary TB cases occurred in contacts without known comorbidities, possibly due to their higher representation. However, the high percentage of LTBI in contacts with hypertension (85%) and diabetes (75%) is notable, as these conditions are recognized as risk factors for TB reactivation due to immune dysfunction. In a retrospective cohort from the Philippines in 2021, comprising 900 patients starting anti-TB treatment including 14.8% with DR-TB researchers identified a high burden of non-communicable comorbidities: undernutrition (23.4%), diabetes (22.5%), hypertension (19.0%), and anemia (13.5%). Notably, over half of those with diabetes and hypertension were previously undiagnosed, complicating TB management. Diabetes and undernutrition each showed strong associations with adverse TB outcomes, reinforcing the bidirectional relationship between nutritional and metabolic disorders and TB. It underscores the importance of screening for comorbid conditions particularly diabetes and undernutrition among TB-affected populations (Cox et al., 2021).

CONCLUSION

LTBI cases were the most common cases found among household contacts of *DR-TB* patients. There were no cases of drug-resistant pulmonary tuberculosis among household contacts in this study, but only six cases (5%) of drug-sensitive pulmonary tuberculosis were found. The high prevalence of *LTBI* (55%) among *DR-TB* household contacts underscores the critical importance of systematic screening and preventive therapy programs in urban Indonesian settings. The absence of active *DR-TB* transmission to household contacts, while encouraging, should not diminish the vigilance required for contact investigation protocols. This study is intended to provide a foundational reference for tuberculosis policymakers regarding the critical importance of conducting contact investigations among household

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contacts of drug-resistant tuberculosis patients. Future research should focus on longitudinal follow-up studies to monitor the long-term progression of *LTBI* to active disease and to evaluate the effectiveness of preventive interventions in this high-risk population.

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REFERENCES

- Chang, V., Ling, R. H., Velen, K., & Fox, G. J. (2021). Latent tuberculosis infection among contacts of patients with multidrug-resistant tuberculosis in New South Wales, Australia. *ERJ Open Research*, 7(3), 00149–02021. <https://doi.org/10.1183/23120541.00149-2021>
- Coussens, A. K., Zaidi, S. M. A., Allwood, B. W., Dewan, P. K., Gray, G., Kohli, M., Kredo, T., Marais, B. J., Marks, G. B., Martinez, L., Ruhwald, M., Scriba, T. J., Seddon, J. A., Tisile, P., Warner, D. F., Wilkinson, R. J., Esmail, H., Houben, R. M. G. J., Alland, D., ... Yi, S. (2024). Classification of early tuberculosis states to guide research for improved care and prevention: An international Delphi consensus exercise. *The Lancet Respiratory Medicine*, 12(6), 484–498. [https://doi.org/10.1016/S2213-2600\(24\)00028-6](https://doi.org/10.1016/S2213-2600(24)00028-6)
- Cox, S. E., Edwards, T., Faguer, B. N., Ferrer, J. P., Suzuki, S. J., Koh, M., Ferdous, F., Saludar, N. R., Garfin, A.-M. C. G., Castro, M. C., & Solon, J. A. (2021). Patterns of non-communicable comorbidities at start of tuberculosis treatment in three regions of the Philippines: The St-ATT cohort. *PLOS Global Public Health*, 1(11), e0000011. <https://doi.org/10.1371/journal.pgph.0000011>
- Fahdhienie, F., Mudatsir, M., Abidin, T. F., & Nurjannah, N. (2024). Risk factors of pulmonary tuberculosis in Indonesia: A case-control study in a high disease prevalence region. *Narra J*, 4(2), e943. <https://doi.org/10.52225/narra.v4i2.943>
- Fox, G. J., Barry, S. E., Britton, W. J., & Marks, G. B. (2013). Contact investigation for tuberculosis: A systematic review and meta-analysis. *European Respiratory Journal*, 41(1), 140–156. <https://doi.org/10.1183/09031936.00070812>
- Ghanaie, R. M., Karimi, A., Azimi, L., James, S., Nasehi, M., Mishkar, A. P., Sheikhi, M., Fallah, F., Tabatabaei, S. R., & Hoseini-Alfatemi, S. M. (2021). Diagnosis of latent tuberculosis infection among pediatric household contacts of Iranian tuberculosis cases using tuberculin skin test, IFN- γ release assay and IFN- γ -induced protein-10. *BMC Pediatrics*, 21(1), 76. <https://doi.org/10.1186/s12887-021-02524-3>
- Gong, W., & Wu, X. (2021). Differential Diagnosis of Latent Tuberculosis Infection and Active Tuberculosis: A Key to a Successful Tuberculosis Control Strategy. *Frontiers in Microbiology*, 12, 745592. <https://doi.org/10.3389/fmicb.2021.745592>
- Imtiaz, S., Shield, K. D., Roerecke, M., Samokhvalov, A. V., Lönnroth, K., & Rehm, J. (2017). Alcohol consumption as a risk factor for tuberculosis: Meta-analyses and burden of

Contact Investigation Among Household Contacts of Drug-Resistant Tuberculosis Patients in Medan

- disease. *European Respiratory Journal*, 50(1), 1700216. <https://doi.org/10.1183/13993003.00216-2017>
- Karbito, K. (2023). Prevalensi dan Faktor Risiko Infeksi TB Laten pada Anggota Keluarga Kontak Serumah dengan Pasien TB Aktif. *Jurnal Kesehatan Lingkungan Indonesia*, 22(3), 351–358. <https://doi.org/10.14710/jkli.22.3.351-358>
- Krishnamoorthy, Y., Ezhumalai, K., Murali, S., Rajaa, S., Jose, M., Sathishkumar, A., Soundappan, G., Horsburgh, C., Hochberg, N., Johnson, W. E., Knudsen, S., Salgame, P., Ellner, J., Prakash Babu, S., & Sarkar, S. (2021). Prevalence and risk factors associated with latent tuberculosis infection among household contacts of smear positive pulmonary tuberculosis patients in South India. *Tropical Medicine & International Health*, 26(12), 1645–1651. <https://doi.org/10.1111/tmi.13693>
- Lee, M.R., Ho, C.M., Lee, C.H., Lee, M.C., Chang, L.Y., Yu, K.L., et al. (2017). Tuberculosis contact investigation in an intermediate burden setting: implications from a large tuberculosis contact cohort in Taiwan. *European Respiratory Journal*, 50(2), 1700851.
- Lönnroth, K., Williams, B. G., Stadlin, S., Jaramillo, E., & Dye, C. (2008). Alcohol use as a risk factor for tuberculosis – a systematic review. *BMC Public Health*, 8(1), 289. <https://doi.org/10.1186/1471-2458-8-289>
- Mwaba, P., Chakaya, J.M., Petersen, E., Wejse, C., Zumla, A., Kapata, N. (2020). Advancing new diagnostic tests for latent tuberculosis infection due to multidrug-resistant strains of *Mycobacterium tuberculosis* — End of the road?. *International Journal of Infectious Diseases*, 92, S69–71.
- Nababan, B., Triasih, R., Chan, G., Dwihardiani, B., Hidayat, A., Dewi, S. C., Unwanah, L., Mustofa, A., & Du Cros, P. (2024). The Yield of Active Tuberculosis Disease and Latent Tuberculosis Infection in Tuberculosis Household Contacts Investigated Using Chest X-ray in Yogyakarta Province, Indonesia. *Tropical Medicine and Infectious Disease*, 9(2), 34. <https://doi.org/10.3390/tropicalmed9020034>
- Nindrea, R. D., Susanti, R., Indika, P. M., Maisa, B. A., Sukma, M., Rosalina, L., Widya, A., Taufiq, Z., Agustian, D. R., Fithria, R., Putri, N., Ningsih, D. A. W. S., Lubis, B. L. A., Mardiah, A., Ezeddin, M. O., Linda, N., Marisa, Y. T., Rahmi, A. S., Sari, A. P., ... Amsal, M. F. (2024). Modifiable And Non-Modifiable Risk Factors For Tuberculosis Among Adults In Indonesia: A Systematic Review And Meta-Analysis. *African Journal of Infectious Diseases*, 18(2), 19–28. <https://doi.org/10.21010/Ajidv18i2.3>
- Odera, S., Mureithi, M., Aballa, A., Onyango, N., Anzala, O., & Oyugi, J. (2020). Latent tuberculosis among household contacts of pulmonary tuberculosis cases in Nairobi, Kenya. *Pan African Medical Journal*, 37. <https://doi.org/10.11604/pamj.2020.37.87.21102>
- Otero, L., Battaglioli, T., Ríos, J., De La Torre, Z., Trocones, N., Ordoñez, C., Seas, C., & Van Der Stuyft, P. (2020). Contact evaluation and isoniazid preventive therapy among close and household contacts of tuberculosis patients in Lima, Peru: An analysis of routine data. *Tropical Medicine & International Health*, 25(3), 346–356. <https://doi.org/10.1111/tmi.13350>
- Reichler, M. R., Khan, A., Yuan, Y., Chen, B., McAuley, J., Mangura, B., Sterling, T. R., Tuberculosis Epidemiologic Studies Consortium Task Order 2 Team, Bakhtawar, I., LeDoux, C., McAuley, J., Beison, J., Fitzgerald, M., Naus, M., Nakajima, M., Schluger,

Contact Investigation Among Household Contacts of Drug-Resistant Tuberculosis Patients in Medan

- N., Hirsch-Moverman, Y., Moran, J., Blumberg, H., ... Luo, C. (2020). Duration of Exposure Among Close Contacts of Patients With Infectious Tuberculosis and Risk of Latent Tuberculosis Infection. *Clinical Infectious Diseases*, 71(7), 1627–1634. <https://doi.org/10.1093/cid/ciz1044>
- Seid, G., Alemu, A., Diriba, G., Hailu, M., Wondimu, A., Tadesse, M., Tadesse, G., H Mariam, S., & Gumi, B. (2025). Active tuberculosis in household contacts of bacteriologically confirmed pulmonary tuberculosis patients: A multicenter study finding the ‘Missed One’ in Central Ethiopia. *PLOS ONE*, 20(2), e0316903. <https://doi.org/10.1371/journal.pone.0316903>
- Sinaga, B.Y.M., Siregar J., Sormin, D.E., Sundari R. (2025). Latent Tuberculosis Infection among Household Contacts of Drug-sensitive Pulmonary Tuberculosis Patients : A Cross-sectional Study from Medan, Indonesia. *Acta Medica Philippina*. <https://doi.org/10.47895/amp.vi0.10048>
- Seid, G., Alemu, A., Diriba, G., Zerihun, B., Tadesse, G., Mariam, S. H., & Gumi, B. (2025). Drug resistance profile of Mycobacterium tuberculosis complex isolated from pulmonary tuberculosis patients and their household contacts in central Ethiopia. *BMC Infectious Diseases*, 25(1), 806. <https://doi.org/10.1186/s12879-025-11220-x>
- Velen, K., Nhung, N. V., Anh, N. T., Cuong, P. D., Hoa, N. B., Cuong, N. K., Dung, N. H., Sy, D. N., Britton, W. J., Marks, G. B., & Fox, G. J. (2021). Risk Factors for Tuberculosis (TB) Among Household Contacts of Patients With Smear-Positive TB in 8 Provinces of Vietnam: A Nested Case-Control Study. *Clinical Infectious Diseases*, 73(9), e3358–e3364. <https://doi.org/10.1093/cid/ciaa1742>
- Wada, P. Y., Costa, A. G., Araújo-Pereira, M., Barreto-Duarte, B., Souza, A. B., Rocha, M. S., Figueiredo, M. C., Turner, M. M., Rolla, V. C., Kritski, A. L., Cordeiro-Santos, M., Andrade, B. B., Sterling, T. R., & Rebeiro, P. F. (2022). Possible sex difference in latent tuberculosis infection risk among close tuberculosis contacts. *International Journal of Infectious Diseases*, 122, 685–692. <https://doi.org/10.1016/j.ijid.2022.07.031>
- Wang, H., Dai, H., He, J., Lyu, X., Zhang, X., & Li, T. (2022). Epidemiological characteristics of pulmonary tuberculosis in patients with pneumoconiosis based on its social determinants and risk factors in China: A cross-sectional study from 27 provinces. *Chinese Medical Journal*, 135(24), 2984–2997. <https://doi.org/10.1097/CM9.0000000000002486>
- Yassin, M. A., Yirdaw, K. D., Datiko, D. G., Cuevas, L. E., & Yassin, M. A. (2020). Yield of household contact investigation of patients with pulmonary tuberculosis in southern Ethiopia. *BMC Public Health*, 20(1), 737. <https://doi.org/10.1186/s12889-020-08879-z>
- Zaidi, S. M. A., Coussens, A. K., Seddon, J. A., Kredo, T., Warner, D., Houben, R. M. G. J., & Esmail, H. (2023). Beyond latent and active tuberculosis: A scoping review of conceptual frameworks. *eClinicalMedicine*, 66, 102332. <https://doi.org/10.1016/j.eclinm.2023.102332>