Asian Science Bulletin

OPEN ACCESS

Latent Tuberculosis Infection in Dutsin-Ma, Nigeria: A Cross-Sectional Study among Healthy and High-Risk Groups

Ignatius Mzungu, Vivian Vieren Tyough and Emmanuel Dayo Alabi
Department of Microbiology, Federal University Dutsin-Ma, Dutsin-Ma, Katsina State, Nigeria

ABSTRACT

Background and Objective: Latent tuberculosis infection (LTBI) is a common condition affecting a substantial number of people globally. Individuals with LTBI have a 5-10% chance of progressing to active tuberculosis (TB) disease if left untreated. This cross-sectional study aimed to determine the prevalence of LTBI in healthy and immunocompromised patients in Dutsin-Ma, Katsina State, Nigeria. **Materials and Methods:** Blood samples were randomly collected from 170 participants across three healthcare facilities and screened for anti-TB antibodies using the Rapid Tuberculosis Test Card™. The sociodemographic data of the participants were analyzed for risk factors using descriptive statistics and Chi-square tests to investigate associations between variables. **Results:** Findings showed that 12.94% (22/170) of the participants tested were serologically positive for anti-TB antibodies. While several risk factors for LTBI were identified, statistical analysis did not establish significant associations between these factors and LTBI at a 95% confidence level ($p \leq 0.05$). **Conclusion:** This study is the first to investigate the prevalence of LTBI in Dutsin-Ma. This is crucial for reducing the global burden of LTBI and active TB, especially in resource-constrained settings.

KEYWORDS

Latent tuberculosis, immunocompromised, diabetes mellitus, human immunodeficiency virus, rapid tuberculosis test card, Dutsin-Ma

INTRODUCTION

Latent tuberculosis infection (LTBI) is a condition in which the body's immune system responds to *Mycobacterium tuberculosis* (MTB) antigens without any symptoms of active tuberculosis (TB) infection. It is noteworthy that, not everyone who is infected with LTBI progresses to active TB disease, some individuals only harbor MTB in a dormant state. However, people with LTBI have a 5-10% chance of developing active TB during their lifetime[1-4]. Latent tuberculosis infection is a widespread condition affecting a significant portion of the global population. Vynnycky and Fine[5] estimated that approximately one-third of the world's population is infected with MTB infection. However, according to the World Health Organization's fact sheet, an estimated one-quarter of the global population is infected with MTB bacteria[4].

ISSN: 1813-0070 (Print)
https://doi.org/10.3923/asb.2024.290.296

Received: 08 Jul. 2024
Accepted: 03 Sep. 2024
Published: 30 Sep. 2024

The risk for TB infection is particularly high for immunocompromised individuals with weakened immune systems, such as those living with the human immunodeficiency virus (HIV), malnutrition, pregnancy or other underlying health conditions. In the World Health Organization's Global Report 2022, an estimated 10.6 million people including 5.8 million men, 3.5 million women and 1.3 million children fell ill with TB worldwide. This report emphasized that TB exists in all countries and age groups[2]. Tuberculosis infections have continued to be a significant global health problem, with Nigeria accounting for 8% of global incidence cases in 2016. However, these numbers are likely underestimated, as only a small portion of TB cases were officially reported in 2015[6]. Tuberculosis has been the leading infectious cause of death since 2020, ranking second only to COVID-19 (above HIV/AIDS) as the leading cause of death from a single infectious agent[7].

In addition, approximately 28% of global maternal mortality occurs for reasons other than problems related to childbirth, such as TB infections, which still play a significant role in maternal mortality[8]. Furthermore, the co-infection of TB with diabetes and HIV has been described as one of the most expensive and challenging health issues of our era due to its negative impact on the immune system[9,10]. Several reports have suggested that the majority of TB patients reside in low and middle-income countries (LMICs). The incidence of extensively drug-resistant tuberculosis has further raised worries about the spread of drug-resistant TB in regions where tuberculosis and HIV co-infection are common[11-13]. Although, individuals with LTBI do not transmit MTB to others because they are not contagious. However, asymptomatic TB may progress into active TB infection if the immune system becomes compromised[14]. This necessitates routine LTBI testing to reduce the global burden of LTBI and active TB infections.

Over the years, several methods have been used to diagnose active TB and LTBI, including tuberculin skin test (TST), sputum smears, cultures and chest X-rays. The TST uses purified protein derivative (PPD) and has been used for almost a century to detect LTBI. However, TST has limitations such as reader variability and false-positive outcomes due to cross-reactivity with environmental non-tuberculous *Mycobacterium* and Bacillus Calmette-Guérin (BCG) vaccines. Furthermore, the test procedure is inconvenient for patients who need to return after 48-72 hrs to obtain the test read[15,16]. On the other hand, newer tests such as polymerase chain reaction-DNA amplification (PCR-DNA Amplification) and interferon-gamma release assays (IGRAs) were recently developed. However, these newly developed methods (PCR-DNA amplification and IGRA) are not cost-effective, require laboratory equipment, skilled personnel or expertise and may not be practical or affordable in rural settings, particularly LMICs[17,18]. To prevent the spread of MTB infections, it is crucial to identify both individuals with LTBI and those with active TB infections, which is vital for effective TB control globally. Several strategies, including contact monitoring and targeted testing and treatment, have been developed to detect and manage LTBI[19].

The Rapid Tuberculosis Test Card is a rapid immunochromatographic test for the qualitative detection of anti-TB (*Mycibacterium tuberculosis, Mycibacterium bovis* and *Mycibacterium africanum*) antibodies (all isotypes: IgG, IgM and IgA) in human serum or plasma that are present during MTB infections[20]. However, studies have shown that antibody tests have low reliability for diagnosing active tuberculosis because people with LTBI, a history of MTB infection, BCG vaccination, or infection with other *Mycobacterium* infections in addition to *M. tuberculosis* may have antibodies against *Mycobacterium tuberculosis*. This issue with antibody tests is often considered a drawback and can lead to false positive results[20]. Several studies have been conducted on the coinfection of MTB with HIV in the Northwestern region of Nigeria. However, there is a lack of data on the prevalence of LTBI in healthy and immunocompromised individuals in the Dutsin-Ma metropolis. Therefore, this cross-sectional study aimed to determine the prevalence of LTBI in healthy and immunocompromised (high-risk) patients in the Dutsin-Ma metropolis, Katsina State, Nigeria.

MATERIALS AND METHODS

Study area: The study was conducted in September 2023 at the Federal University's Campus in Dutsin-Ma, Katsina State, Nigeria. The Dutsin-Ma town serves as the administrative center for the Dutsin-Ma Local Government Area. It is positioned at the coordinates 12°27'17''N, 7°29'29''E, Latitude 12°27'16.13" N and Longitude 7°29'51.55"E. The Local Government Area covers an expanse of 527 square kilometers and has a population of 169,829 dwellers based on the data from the 2006 census[21]. The Dutsin-Ma town is home predominantly to farmers, shepherds and traders.

Ethical statement: The Ethical Clearance Committee of the Katsina State Ministry of Health reviewed and authorized the study protocol with the approval number MOH/ADM/SUB/1152/1/768. All participants provided informed consent and anonymity was preserved throughout the data analysis and reporting.

Questionnaire aurvey and data collection: The participants were administered structured questionnaires that included demographic information, medical history, health status and lifestyle/habits, knowledge about tuberculosis and willingness to undergo LTBI screening.

Sample collection: One hundred and seventy (170) blood samples were randomly collected from healthy individuals (n = 50), pregnant women (n = 65) attending antenatal clinics, diabetic patients (n = 25) and HIV-positive patients (n = 30) attending routine follow-ups in September 2023 at the Federal University Dutsin-Ma Clinic, Comprehensive Health Care Centre, Dutsin-Ma and the General Hospital Dutsin-Ma. The samples were immediately transported to the Microbiology Laboratory at the Federal University Dutsin-Ma under a standard laboratory protocol and were tested for anti-TB antibodies using the Rapid Tuberculosis Test Card (Xiamen, China).

Statistical analysis: Descriptive statistics and Chi-square tests with 95% CIs were used to measure the strength of associations between variables. Values were considered statistically significant at 95% ($p \leq 0.05$).

RESULTS

A total of 170 participants were included in this survey. The healthy individuals had the highest prevalence (24%; 12/50) of anti-TB antibodies, followed by the diabetic patients (20.0%; 5/25) and the pregnant women had the lowest prevalence (11.1%; 5/65) of anti-TB antibodies in this study (Table 1).

A greater percentage of females (18%) tested positive for anti-TB antibodies than males (4.17%). This suggests that females may be more susceptible to LTBI than males (Table 2).

According to the demographic data analyzed in this survey, the 25-34 years old group had the highest prevalence of LTBI, which was 35.9%. On the other hand, the lowest prevalence of LTBI, which was 6.0%, was found in the 18-24 years age group. These findings suggest that LTBI may be more prevalent in individuals aged 25-34 years than in other age groups (Fig. 1).

Several risk factors associated with LTBI were deduced from the administered questionnaire in this survey. The risk factors included having a family history of MTB infection, urban exposure, immune suppression, lifestyle factors (such as smoking and malnutrition) and occupation. The percentage prevalence of LTBI among participants who worked as cleaners in healthcare facilities and smokers was 25 and 13.3%,

Table 1: Prevalence of latent tuberculosis infection among the studied groups

Variables	Number tested	Number positive	Percentage prevalence
Pregnant women	65	5	11.1
Diabetic patients	25	5	20.0
HIV patients	30	0	0.00
Healthy individuals	50	12	24.0
Total	170	22	12.94

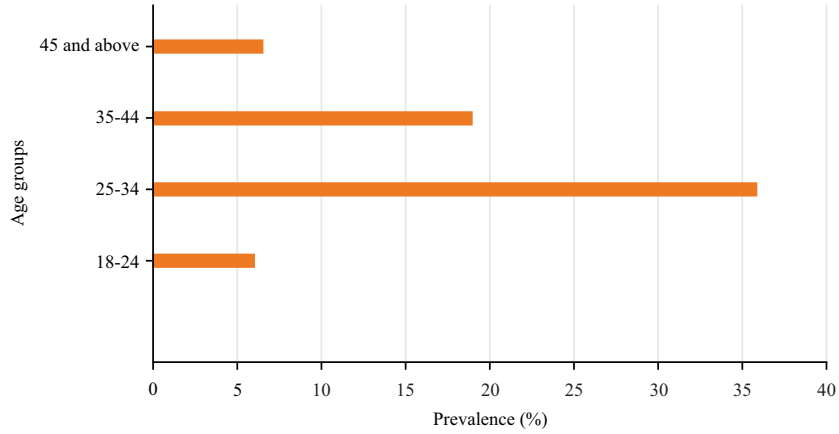

Fig. 1: Prevalence of latent tuberculosis among age groups

Table 2: Prevalence of latent tuberculosis by patient gender

Gender distribution	Number tested	Number positive	Percentage prevalence
Female	122	20	18.0
Male	48	2	4.17
Total	170	22	12.94

respectively. Those who had a family history of MTB infection or who suffered from malnutrition had prevalence rates of 11.1 and 18.2%, respectively. At the same time, 12% of the participants who lived in urban areas had LTBI. In addition, the study revealed a greater prevalence of anti-TB antibodies in nondiabetic patients (12.0%) than in diabetic patients (8.0%).

DISCUSSION

In this study, an overall prevalence of 12.94% of LTBI among the participants was detected. Previously, a high risk of LTBI activation has been reported in individuals with significant immunosuppression, including pregnant women, people living with HIV and those with diabetes[22,23]. The concurrent presence of HIV and TB in pregnant women can result in severe outcomes, as it is a major contributor to maternal morbidity and mortality, as reported by Orazulike *et al.*[24]. The high frequency of anti-TB antibodies observed in this study may be attributed to several factors. Firstly, individuals with limited or no knowledge about the risks for LTBI and lower socioeconomic status may be at higher risk for LTBI due to various risk factors or lifestyles that predispose them to these conditions. Secondly, poor living conditions, such as overcrowding, inadequate ventilation, poor personal hygiene and poor nutrition, may also contribute to the high prevalence of LTBI. These factors can potentially lead to increased exposure to *Mycobacterium tuberculosis*, resulting in higher rates of LTBI and MTB infections, as previously reported by Mack *et al.*[19].

In comparison, females had a higher percentage (18%) who tested positive for LTBI than males (4.17%) in this survey. The higher proportion of LTBI observed in females may be attributed to the majority of participants in this study (122/170) being women of reproductive age between 18 and 44 years old. This group is more susceptible to immunosuppression during pregnancy, which can exacerbate LTBI and potentially lead to reactivation or active disease. As reported by Alene *et al.*[25], the coexistence of HIV infection in this age group contributes significantly to the burden of tuberculosis infection. Furthermore, the comorbidity of diabetes mellitus and TB infections poses a substantial global health challenge, particularly in LMICs where both diseases are prevalent and increasingly common[26,27].

The study found that participants aged 25-34 years had the highest prevalence rate of LTBI at 35.9%, while those aged 18-24 years had the lowest prevalence rate at 6.0%. The high occurrence of LTBI in this age group may be linked to various risk factors, including lack of childhood BCG vaccination, certain

occupations, diabetes, poor nutrition and lifestyle. Notably, no anti-TB antibodies were detected among vaccinated participants in this study. Hino *et al.*[28] reported a significant increase in LTBI among Japanese children following a change in the recommended age for routine infant BCG vaccination from 3-6 months to under 1 year in 2013. The transmission of MTB from an infectious source to others through shared air may be another factor influenced by proximity and duration of exposure. Studies consistently show a correlation between transmission level and contact degree with the infectious source. Household contacts are particularly susceptible to LTBI and active MTB infections due to their proximity to the infected individual. Therefore, assessing individuals likely to have recently acquired MTB infection is crucial, as they have a higher risk of developing active tuberculosis within 1-2 years after exposure[29].

Risk factors associated with LTBI in this survey include: Working as a cleaner in healthcare facilities (25%), malnutrition (25%), having a family history of MTB infection (18.2%), smoking (13.3%; 2/15) and living in urban (overcrowded) areas (12.0%). The high prevalence of LTBI among healthcare cleaners and those with a family history of MTB infection may be attributed to their proximity to infectious sources. This was consistent with Akinshipe *et al.*[30] reports, where they found that certain factors increase the likelihood of having LTBI and pre-diabetes, including not receiving the BCG vaccine, having a family history of diabetes and MTB infection, smoking, living in specific locations and aging. This information can help identify individuals at higher risk of LTBI and inform preventive measures[29,30].

These findings will inform public health policies and resource allocation for LTBI control and targeted interventions for high-risk groups, which is vital for mitigating the global burden of LTBI and active TB infections, especially in low-and middle-income countries. Further research is needed to elucidate the relationships between risk factors and LTBI. Limitations of this study include its cross-sectional design, small sample size, single screening test and lack of follow-up data.

CONCLUSION

To our knowledge, this is the first study to report the prevalence of LTBI in Dutsin-Ma, Nigeria, with a 12.94% prevalence among the participants, highlighting the need for routine screening and treatment of LTBI, particularly in high-risk groups and healthy individuals in resource-constrained settings to mitigate the burden of LTBI and active TB. Future research should prioritize studies with larger sample sizes and varied screening methods to better understand LTBI risk factors and progression.

SIGNIFICANCE STATEMENT

This study assessed the prevalence of latent tuberculosis infection (LTBI) among healthy and immunocompromised individuals in Dutsin-Ma, Nigeria, revealing a 12.94% overall seroprevalence for anti-TB antibodies. The survey highlights a notably higher prevalence among healthy individuals (24%) compared to other groups and a greater occurrence among females (18%) and those aged 25-34 years. Although several potential risk factors were identified, such as poor nutrition, family history of TB and living in an overcrowded area, there were no significant associations at the 95% confidence interval. These findings underscore the need for routine LTBI screening and targeted interventions among vulnerable populations. Future research should aim to expand the sample size and explore more comprehensive risk factors to inform public health and intervention strategies.

ACKNOWLEDGMENTS

The authors would like to thank the management and staff members of the Katsina State Ministry of Health for granting us the approval to conduct this study and all the staff members of the hospital and clinics where samples were collected. The authors would like to express their gratitude to the individuals who willingly consented to participate in this study, their cooperation is greatly appreciated.

REFERENCES

1. Bloom, B.R. and C.J.L. Murray, 1992. Tuberculosis: Commentary on a reemergent killer. Science, 257: 1055-1064.
2. Bagcchi, S., 2023. WHO's global tuberculosis report 2022. Lancet Microb., Vol. 4. 10.1016/S2666-5247(22)00359-7.
3. Simmons, J.D., C.M. Stein, C. Seshadri, M. Campo and G. Alter *et al*., 2018. Immunological mechanisms of human resistance to persistent *Mycobacterium tuberculosis* infection. Nat. Rev. Immunol., 18: 575-589.
4. Kiazyk, S. and T.B. Ball, 2017. Latent tuberculosis infection: An overview. Can. Communicable Dis. Rep., 43: 62-66.
5. Vynnycky, E. and P.E.M. Fine, 2000. Lifetime risks, incubation period, and serial interval of tuberculosis. Am. J. Epidemiol., 152: 247-263.
6. Kyu, H.H., E.R. Maddison, N.J. Henry, J.E. Mumford and R. Barber *et al*., 2018. The global burden of tuberculosis: Results from the Global Burden of Disease Study 2015. Lancet Infect. Dis., 18: 261-284.
7. Falzon, D., M. Zignol, M. Bastard, K. Floyd and T. Kasaeva, 2023. The impact of the COVID-19 pandemic on the global tuberculosis epidemic. Front. Immunol., Vol. 14. 10.3389/fimmu.2023.1234785.
8. Say, L., D. Chou, A. Gemmill, Ö. Tunçalp and A.B. Moller *et al*., 2014. Global causes of maternal death: A who systematic analysis. Lancet Global Health, 2: E323-E333.
9. Dixon, B., 2007. Diabetes and tuberculosis: An unhealthy partnership. Lancet Infect. Dis., Vol. 7. 10.1016/S1473-3099(07)70144-5.
10. Harries, A.D., S. Satyanarayana, A.M.V. Kumar, S.B. Nagaraja and P. Isaakidis *et al*., 2013. Epidemiology and interaction of diabetes mellitus and tuberculosis and challenges for care: A review. Public Health Action, 3: 3-9.
11. Alexander, P.E. and P. De, 2007. The emergence of extensively drug-resistant tuberculosis (TB): TB/HIV coinfection, multidrug-resistant TB and the resulting public health threat from extensively drug-resistant TB, globally and in Canada. Can. J. Infect. Dis. Med. Microbiol., 18: 283-317.
12. van Rie, A. and D. Enarson, 2006. XDR tuberculosis: An indicator of public-health negligence. Lancet, 368: 1554-1556.
13. Viswanathan, V., S. Kumpatla, V. Aravindalochanan, R. Rajan and C. Chinnasamy *et al*., 2012. Prevalence of diabetes and pre-diabetes and associated risk factors among tuberculosis patients in India. PLoS ONE, Vol. 7. 10.1371/journal.pone.0041367.
14. Migliori, G.B., C.W.M. Ong, L. Petrone, L. D'Ambrosio, R. Centis and D. Goletti, 2021. The definition of tuberculosis infection based on the spectrum of tuberculosis disease. Breathe, Vol. 17. 10.1183/20734735.0079-2021.
15. Pesanti, E.L., 1994. The negative tuberculin test. Tuberculin, HIV, and anergy panels. Am. J. Respir. Crit. Care Med., 149: 1699-1709.
16. Lyashchenko K.P., M. Singh, R. Colangeli and M.L. Gennaro, 2000. A multi-antigen print immunoassay for the development of serological diagnosis of infectious diseases. J. Immunol. Methods, 242: 91-100.
17. Denkinger, C.M., S.G. Schumacher, C.C. Boehme, N. Dendukuri, M. Pai and K.R. Steingart, 2014. Xpert MTB/RIF assay for the diagnosis of extrapulmonary tuberculosis: A systematic review and meta-analysis. Eur. Respir. J., 44: 435-446.
18. Heidebrecht, C.L., L.J. Podewils, A.S. Pym, T. Cohen, T. Mthiyane and D. Wilson, 2016. Assessing the utility of Xpert® MTB/RIF as a screening tool for patients admitted to medical wards in South Africa. Sci. Rep., Vol. 6. 10.1038/srep19391.
19. Mack, U., G.B. Migliori, M. Sester, H.L. Rieder and S. Ehlers *et al*., 2009. LTBI: Latent tuberculosis infection or lasting immune responses to *M. tuberculosis*? A TBNET consensus statement. Eur. Respir. J., 33: 956-973.
20. Gounder, C., F.C. de Queiroz Mello, M.B. Conde, W.R. Bishai, A.L. Kritski, R.E. Chaisson and S.E. Dorman, 2002. Field evaluation of a rapid immunochromatographic test for tuberculosis. J. Clin. Microbiol., 40:1989-1993.

21. Abdulmumini, L., E.L. Irmiya and I. Musab, 2023. Factors influencing youth participation in maize production in Dutsin-MA Local Government Area, Katsina State. J. Agric. Ext., 28: 59-67.
22. Corbett, E.L., B. Marston, G.J. Churchyard and K.M. de Cock, 2006. Tuberculosis in sub-Saharan Africa: Opportunities, challenges, and change in the era of antiretroviral treatment. Lancet, 367: 926-937.
23. Churchyard, G.J., F. Scano, A.D. Grant and R.E. Chaisson, 2007. Tuberculosis preventive therapy in the era of HIV infection: Overview and research priorities. J. Infect. Dis, 196: S52-S62.
24. Orazulike, N.C., J.O. Alegbeleye, C.C. Obiorah, T.K. Nyengidiki and S.A. Uzoigwe, 2017. A 3-year retrospective review of mortality in women of reproductive age in a tertiary health facility in Port Harcourt, Nigeria. Int. J. Women's Health, 9: 769-775.
25. Alene, K.A., K. Viney, H.C. Moore, M. Wagaw and A.C.A. Clements, 2019. Spatial patterns of tuberculosis and HIV co-infection in Ethiopia. PLoS ONE, Vol. 14. 10.1371/journal.pone.0226127.
26. Al-Rifai, R.H., F. Pearson, J.A. Critchley and L.J. Abu-Raddad, 2017. Association between diabetes mellitus and active tuberculosis: A systematic review and meta-analysis. PLoS ONE, Vol. 12. 10.1371/journal.pone.0187967.
27. Firănescu, A.G., A. Popa, M.M. Sandu, D.C. Protasiewicz, S.G. Popa and M. Moţa, 2016. The global prevalence and incidence of diabetes mellitus and pulmonary tuberculosis. Rom. J. Diabetes Nutr. Metab. Dis., 23: 319-326.
28. Hino, Y., N. Eshima, O. Tokumaru, K. Bacal, Y. Tanaka, S. Karukaya and Y. Yamashita, 2022. A change in the timing of the Bacillus Calmette-Guérin vaccination in 2013 was associated with an increase in the incidence rate of infants with latent tuberculosis infection. J. Infect. Chemother., 28: 929-933.
29. Morrison, J., M. Pai and P.C. Hopewell, 2008. Tuberculosis and latent tuberculosis infection in close contacts of people with pulmonary tuberculosis in low-income and middle-income countries: A systematic review and meta-analysis. Lancet Infect. Dis., 8: 359-368.
30. Akinshipe, B.O., E.O. Yusuf, F.O. Akinshipe, M.A. Moronkeji and A.C. Nwaobi, 2019. Prevalence and determinants of pre-diabetes and latent tuberculosis infection among apparently healthy adults in three communities in Southern Nigeria. Int. J. Immunol., 7: 23-32.