Microbes and Infectious Diseases 2025; 6(3): 3077-3085

Microbes and Infectious Diseases

Journal homepage: https://mid.journals.ekb.eg/

Original article

Prevalence and correlates of latent tuberculosis infection in adult population in Nigeria: Monitoring a silent epidemic

John O. Ogunkoya[1, 2], Olubunmi A. Ogunkoya[3], Akindele E. Ladele[1, 4], Bolanle O. Adefuye[5], Abiodun O. Osinaike[1], Oluwatofunmi Olarewaju[2], Opeyemi O. Osonuga[2], Chiyememma C. Worlu[2].

1- Benjamin Carson Senior College of Health and Medical Sciences, Babcock University, Ilishan-Remo, Ogun State, Nigeria
1. Division of Respiratory Medicine and Allergy, Department of Medicine, Babcock University Teaching Hospital, Ilishan-Remo, Ogun State, Nigeria.
2. Pharmacy Department, Local Government Service Commission, Oke Mosan, Abeokuta, Ogun State, Nigeria
3. Family Medicine Department, Babcock University Teaching Hospital, Ilishan-Remo, Ogun State, Nigeria
4. Department of Medicine, Olabisi Onabanjo University Teaching Hospital, Sagamu, Ogun State, Nigeria

ARTICLE INFO

Article history:
Received 17 April 2024
Received in revised form 10 May 2024
Accepted 26 May 2024

Keywords:
ELISA
Interferon Gamma Release Assay
Latent TB infection
QuantiFERON TB Gold
Tuberculosis

ABSTRACT

Background: Tuberculosis (TB) is a chronic disease caused by Mycobacterium tuberculosis. Latent TB infection (LTBI) is an asymptomatic state. This study aimed to measure the prevalence of latent tuberculosis infection using Interferon Gamma Release Assay (IGRA), among asymptomatic individuals in the general population in Ogun State, Nigeria from the 1st of January, 2022 to the 30th of June, 2023 and correlate the results of the IGRA with their socio-demographic characteristics. **Method:** Participants were recruited from the 3 senatorial districts with convenience sampling techniques. An interviewer-administered questionnaire was used to collect data on socio-demographic characteristics, clinical assessment for TB, history of past of chronic lung diseases and TB. Blood sample was taken from each participant for QuantiFERON TB Gold Plus testing. The data was analyzed with SPSS version 22.0. The level of significance was set at P <0.05. **Results:** A total of 390 individuals participated in this study: 162 (41.5%) males and 228 (58.5%) females. The mean age was 45.63±2.33. The prevalence of latent TBI was 19.7%. Gender (p=0.033), BMI (p=0.036), type of housing unit (p=0.027), and number of rooms persons per room (p=0.001) were the factors associated with a positive IGRA test. However, multiple regression analysis showed that BMI was the only factor that predicts latent TBI (OR = -12.12 + 0.26). **Conclusion:** Although our results showed a low prevalence of latent TBI in individuals asymptomatic for TB, with statistically significance associations between IGRA results and some socio-demographic characteristics, this depicts a low level of exposure to TB in Ogun State, Nigeria.

Introduction

Tuberculosis (TB) is a chronic inflammatory disease caused by the bacillus Mycobacterium tuberculosis. It commonly affects the lung, but it can also affect other tissues in the body (extra-pulmonary) [1,2]. The main route of transmission of the disease is through the inhalation of aerosolized droplets of Mycobacterium from an infected persons, who is coughing or sneezing or through the ingestion of contaminated cow milk [3].

DOI: 10.21608/MID.2024.283400.1905
* *Corresponding author:* John Omotola Ogunkoya
E-mail address: *ogunkoyaj@babcock.edu.ng*

According to the World Health Organization's 2018 Global TB Report, 23% of the World population, about 1.7 billion people, is latently infected [4]. This is made up of an asymptomatic state in which the individuals demonstrate an immunological response to mycobacteria [3]. Tuberculosis affects the active economic age group in society [5]. The burden of the disease is borne more by the poor, the neglected, and the homeless populations [5-7]. Over 80% of the TB burden in the world is in 22 countries, most of which are in Sub-Sahara Africa and Eastern Asia. According to the 2018 WHO TB report, Nigeria is ranked 6th, worse than poorer countries in Africa and Asia [4].

Individuals with latent tuberculosis infection represent a reservoir of infection, many of whom will progress to tuberculous disease, especially in the setting of HIV infection [8,9]. However, taking into consideration the more attendant difficulties encountered in active TB diagnosis in Human Immunodeficiency Virus (HIV) co-infection, because of non-specific symptoms, poor sputum yield, and atypical X-ray findings, it becomes a paramount task for healthcare to deplore more resources into TB infection diagnosis in this population before active disease develops [4]. WHO currently recommends isoniazid preventive therapy as part of the 3 I's of TB/HIV collaborative services after symptomatic exclusion of active tuberculosis [10].

Latent TB is diagnosed using the Tuberculin Skin Test (TST) method or the Interferon Gamma (IFN-g) Release Assay (IGRA) method. Most people who developed tuberculous disease are initially latently infected, but diagnosis is oftentimes not made at this time, when treatment is less cumbersome since there are no symptoms. Latent TB infection is characteristically found in individuals who appear healthy, with a normal chest x-ray and a negative sputum test. These individuals cannot spread the infection, but has positive TST and blood IGRA and needs treatment to prevent TB disease [11,12]. The treatment modalities for latent TB include the use of isoniazid (INH) 300 mg daily for 6-9 months if HIV-negative and 9-12 months in the first year of starting Highly Active Anti-Retroviral Therapy (HAART) if HIV positive after excluding active TB disease, otherwise known as Isoniazid Preventive Therapy (IPT) [13].

Many studies have been carried in Nigeria on the burden of latent TBI disease, but only very few were on the prevalence of latent TB infection using IGRA, which performs better and appears more specific than the Tuberculin Skin Test (TST) [12]. None of these previous studies was a population-based study in the southwestern region of Nigeria. This study aimed to measure the prevalence of latent tuberculosis infection using Interferon Gamma Release Assay (IGRA), among asymptomatic individuals in the general population in Ogun State, Nigeria and correlate the results of the IGRA with their socio-demographic characteristics of the study participants.

Materials and methods

Study population and setting

We conducted this study among the general population in Ogun State, Southwestern Nigeria, over a period of eighteen (18)-months, from the 1st of January 2022 to the 30th of June, 2023. Ogun State is one of the fastest developing states in Nigeria, with a landmass of 16.667 km^2. It is located in the southwestern part of the country between latitudes 6.2 0 N and 7.8 0 N and longitudes 3.0 0 and 5.0 0 E east of the Greenwich Meridian. The state is bounded on the west by the Republic of Benin and on the east by Ondo State. According to the 2006 population census, the population of Ogun State was approximately 3.75 million (42% were adults over 18 years old), with a projected annual population change of 3.4%.

Study Description

This was an analytical cross-sectional study carried out among the general population. The study recruited adult patients (aged ≥18 years) who gave informed consent and fulfilled the inclusion criteria.

Exclusion criteria

i. Individuals who were < 18 years of age.

ii. Individuals who were acutely ill.

iii. Individuals with symptoms suggestive of active pulmonary tuberculosis, chronic lung diseases (e.g. chronic obstructive pulmonary diseases (COPD), asthma, pulmonary fibrosis, sarcoidosis, etc.).

iv. Individuals who had been treated for TB in the past.

Study instruments and administration

A pre-validated interviewer-administered questionnaire was used to collect qualitative data on the study participants in two sections: A and B.

Section A: Data was collected on the socio-demographic characteristics (gender, age, occupation, marital status, residence, housing unit, and religion), and clinical assessment for pulmonary tuberculosis, previous history or ongoing treatment of chronic lung diseases or tuberculosis.

Section B: Whole blood samples were collected from participants from a peripheral vein for QuantiFERON TB Gold Plus testing using QFT-Plus test kits.

Procedure for Interferon Gamma Release Assay Quantification

Interferon Gamma Release Assay testing uses about a mill (1 mL) of whole blood in four different tubes. A gray cap tube contains no antigen, while the green cap tube is TB Antigen Tube 1 (TB1) and the yellow cap tube is TB Antigen Tube 2 (TB2). TB1 and TB2 contained peptide antigens from the Mycobacterium tuberculosis (MTB)–complex associated antigens, Early Secreted Antigenic Target of 6KDA (ESAT-6), and Culture Filtrate Protein-10 (CFP-10). Whereas the TB1 tube contained peptides from ESAT-6 and CFP-10 that were expected to elicit CMI responses from CD4+ T-helper lymphocytes, the TB2 tube contains an additional set of peptides targeted to the induction of cell-mediated immunity (CMI) responses from CD8+ cytotoxic T lymphocytes. The fourth tube is a purple cap bottle that contained mitogen used to assess the performance of circulating lymphocytes. Samples were then incubated at a temperature of 37°C for 16-24 hours. They were then centrifuged, and the plasma harvested to perform the enzyme-linked immunosorbent assay (ELISA). The interferon gamma values for TB-specific antigens were corrected by subtracting the values obtained for the respective negative controls. The test was considered positive only for Interferon gamma levels that were above the cut-off test value (0.35 IU/mL). The laboratory work was carried out at the chemical pathology lab of a private hospital, in Ogun State, Nigeria. The result interpretation was done using the manufacturer's software [14].

Sample size estimation and sampling method

The state has three (3) senatorial districts, and equal numbers of participants were recruited from each senatorial district using the convenience sampling technique, to ensure an adequate spread of study participants. Using a finite population of 1.575 million (42% of the state population), where the outcome variable is the proportion of patients with elevated levels of interferon-gamma release assay, the minimum sample required for this study was determined using the formula for finite population size. The prevalence of latent TB infection among black Africans is unknown; therefore, a prevalence of 50% was used for this study at a 95% confidence level and a 5% accuracy level. A sample size of 384 was calculated, with 390 participants recruited for this study (130 recruited from each senatorial district of the state). A simple random sampling technique was used to select respondents. The approach was a random assignment with two (2) adults chosen randomly from each street until the sample size was reached.

Data analysis

Data obtained was entered into IBM SPSS version 22.0 software [SPSS Inc., Chicago, USA] for analysis. Categorical variables were presented using frequency tables, while quantitative variables were presented as means and standard deviations. The associations between qualitative variables were tested using the chi-square test. All statistical analyses were carried out at a level of significance of $p < 0.05$.

Ethical consideration

Written and oral informed consent was obtained from all study participants. The study protocol was sought and approved by the Ogun State Research and Ethics Committee, Ministry of Health, Oke-Mosan, Abeokuta, Ogun State, Nigeria (HPRS/382/394).

Results

Socio-demographic characteristics of the participants

A total of 390 healthy individuals participated in this study; 162 (41.5%) were males and more than half (n =228, 58.5%) were females. The mean age was 45.63±2.33, with an age range of 18 to 84 years. The majority of study participants had a normal BMI (n =193, 49.5%), but a substantial number were also overweight (n =87, 22.3%). Most of the study participants were single (n = 154, 39.5%). with about a third being traders (n=129, 33.1%) and farmers (n =111, 28.5%).

More than half of the study participants lived in the urban centers (n =198, 50.8%) of the state and single rooms (n =222, 56.9%), with a mean

number of persons per room of 2.21±1.90. About two-thirds of the study participants were of Yoruba ethnicity and the Islamic faith. However, 103 (26.4%) had primary education, 156 (40%) had secondary education, 79 (20.3%) had tertiary-level education, with just 52 (13.3%) had no formal education **(Table 1)**.

Prevalence of latent tuberculous infection among participants

Figure 1 shows the prevalence of latent TB infection among study participants using IGRA. The figure shows that the majority of study participants had a negative LTB result (n =279, 71.5%), less than one-fifth (n=77, 19.7%) had a positive IGRA result and 34 (8.7%) results were indeterminate.

The relationship between socio-demographic parameters and IGRA

Table 2 shows the relationship between socio-demographic parameters and positive, negative, and indeterminate IGRA. Our study revealed that female participants (n =56, 14.4%) had more positive IGRA results compared to their male counterparts (n =21, 5.4%), while more male participants (n =20, 5.1%) had indeterminate IGRA results compared to the female participants (n=14, 3.6%). The difference was statistically significant. (p=0.033).

Also, participants who resided in rural communities (n =49, 12.6%) in the state had a higher number of positive IGRA results compared to those who lived in urban centers (n =28, 7.2%). However, the difference was not statistically significant (p=0.081). Furthermore, participants who lived in single-room apartments (n =61, 15.6%) had a higher number of positive IGRA results compared to those who were residents of flat apartments (n =16, 4.1%). The difference was, however, statistically significant (p=0.027).The study also showed that the mean number of people per room was highest among participants who had a positive IGRA result, and this was statistically significant (p =0.001) when compared to the mean number of persons per room among the negative and indeterminate groups.

The mean weight, and BMI were highest among participants with indeterminate IGRA results, with significant statistical difference in BMI when compared to the positive and negative groups ($p<0.05$). However, the mean height was highest among the positive IGRA group but was nor statistically significant ($p>0.05$).

Predictors of latent TB infection

Table 3 shows a multiple linear regression model to determine factors that predicted latent TB infection in the study population. The only factor that predicted latent TB infection, according to this study, was the body mass index (BMI). This factor that predicted latent TB was equal to -12.12 + 0.26 (BMI).

Table 1. Socio-demographic characteristics of the study population.

Socio-demographic parameters		**Frequency N= 390**	**Percentages (%)**
Age (years)	≤20	34	8.7
	21-30	47	12.1
	31-40	96	24.6
	41-50	138	35.4
	51-60	42	10.8
	61-70	23	5.8
	>70	10	2.6
Mean age± SD	45.63±2.33		
Gender	Male	162	41.5
	Female	228	58.5
Body Mass Index (BMI) in kg/m^2	Underweight (<18.5)	66	16.9
	Normal (18.5-24.9)	193	49.5
	Overweight (25-29.9)	87	22.3
	Obese (≥30)	44	11.3
Mean BMI± SD	27.96±11.32		
Occupation	Trader	129	33.1
	Unemployed	43	11.0
	Civil servant	40	10.2
	artisan	67	17.2
	Farmer	111	28.5
Marital status	Single	154	39.5
	Married	145	37.2
	Others (Divorced, separated, widowed)	91	23.3
Residence	Rural	192	49.2
	Urban	198	50.8
Housing unit	Single room	222	56.9
	Flats	168	43.1
Number of persons per room (mean± SD)	2.21±1.90		
Religion	Christianity	178	45.6
	Islam	181	46.4
	Traditional religions	31	8.0
Ethnicity	Yoruba	244	62.6
	Ibo	87	22.3
	Hausa	43	11.0
	Others	16	4.1
Educational status	Primary	103	26.4
	Secondary	156	40.0
	Tertiary	79	20.3
	No formal education	52	13.3

Table 2. The relationship between socio-demographic parameters and positive, negative, and indeterminate IGRA.

Anthropometric parameters		**Latent Tuberculosis N=390(%)**			**p-value**
	Positive IGRA Mean±SD	**Negative IGRA Mean±SD**	**Indeterminate IGRA Mean±SD**	**Total Mean±SD**	
Gender					
Male	21(5.4)	121(31.0)	20(5.1)	162(41.5)	0.033*
Female	56(14.4)	158(40.5)	14(3.6)	228(58.5)	
Residence					
Rural	49(12.6)	127(32.6)	16(4.1)	192(49.2)	0.081
Urban	28(7.2)	152(38.9)	18(4.6)	198(50.8)	
Housing Unit					
Single room	61(15.6)	159(40.8)	2(0.5)	222(56.9)	0.027*
Flat	16(4.1)	120(30.8)	32(8.2)	168(43.1)	
Number of persons per room	3.60±0.22	1.06±1.01	1.97±2.23	2.21±1.90	0.001*
Age	56.22±0.99	42.30±3,11	38.37±2.87	45.63±2.33	0.132
Weight (kg)	68.11 ± 10.94	76.96 ± 11.99	78.91±7.85	74.66±10.26	0.173
Height (m)	1.68 ± 0.28	1.64 ± 1.07	1.66±0.65	1.66±0.67	0.054
BMI (kg/m^2)	26.01 ± 2.04	29.97 ± 0.84	27.27±1.08	27.75±1.32	0.036*

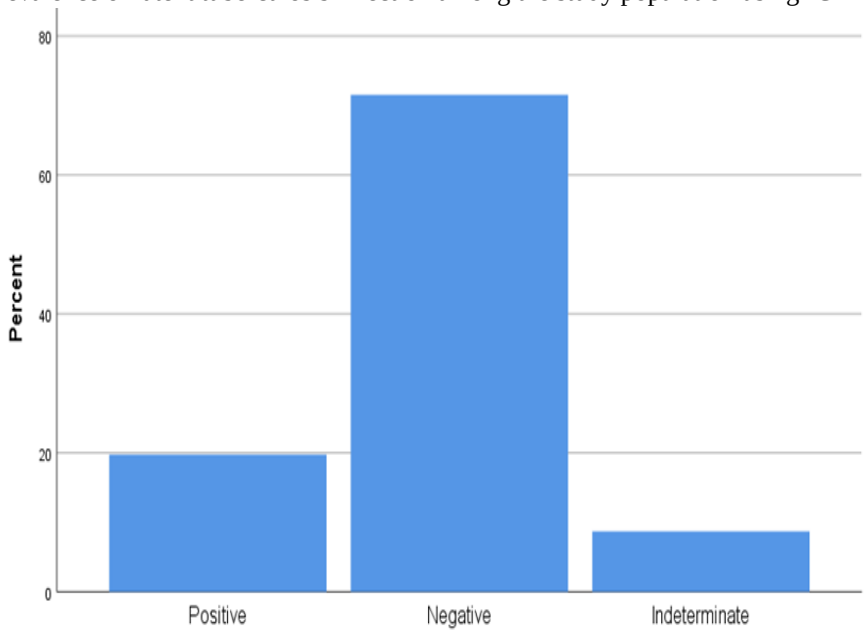
*-significant at p<0.05

Table 3. Linear Regression analysis of predictors of latent TB in the study population

Model	**Unstandardized coefficient**		**Standardized Coefficient**	**Significance**	
	B	**Stand error**	**Beta**	**t-value**	**p-value**
Constant	-12.02	6.31		-1.90	0.61
Age	-0.00	0,00	-1.31	-1.31	0.178
Weight	-0.09	0.04	-3.64	-2.01	0.082
Height	7.80	3.67	2.05	2.12	0.053
BMI	0.26	0.12	3.09	2.12	0.034*

*-significant at p<0.05

Figure 1. The prevalence of latent tuberculosis infection among the study population using IGRA



Discussion

The majority of participants in this study were females, between the ages of 41-50, which corresponds to the reproductive and productive age with the highest burden of tuberculosis worldwide. Over 60% of study participants were married, divorced, separated from their spouses, or widowed. This may be because married individuals are more concerned with the state of their health than unmarried ones, who have poor health-seeking behavior and are more sensitive to stigmatization.

The prevalence of latent TB infection among the general population living in diverse environments in Nigeria has been the subject of much speculation. This multi-community study of apparently healthy individuals in southwest Nigeria showed an overall prevalence of 19.7%, which is much lower than the prevalence of hospital-based studies done in Ilorin, north-central Nigeria, [15] and among HIV positive patients in Benin [16], Edo State, Nigeria, with prevalences of 66.7% and 22.5%, respectively. However, another review of the prevalence of latent TB infections by puts the worldwide prevalence of latent TB infection at 23.67% [17], which is comparable to the prevalence from this study. This variability, both geographically and by population, underscores the need for regular context-specific determination of the prevalence of latent TB infection.

One of these studies also discovered that in countries where the incidence of TB is well above the elimination threshold to which Nigeria belongs, preventing latent TB infection may be the final frontier of TB elimination [17], and it may be wise to allocate adequate resources to ensure prompt detection and treatment of latent TB infection.

We found that indeterminate results were reported in 8.7% of the cases, a rate similar to that found in the general population but lower than those reported among HIV-positive individuals [18,19]. Studies show that an immune response increases the likelihood of indeterminate results [20]. HIV positivity can lead to indeterminate IGRA results even with immune reconstitution as a result of altered T-cell function, and a low CD4 cell count [21]. Indeterminate IGRA results are usually due to either a decrease in IFN-γ production in the mitogen tube or an increase in the Nil-tube. In previous studies, interpreting indeterminate results was a clinical dilemma, as seen in our study [22].

Also, the majority of study participants who lived in single rooms and with a high number of people per room had a positive IGRA compared to those who lived in flat-apartments and those with a lower number of people per room. This shows that being a resident of a rural community, and living in a single-room apartment, particularly in a densely populated environment, are possible independent determinants of latent TB infection. This is corroborated by a study done in south India [23] in which living nearby, particularly in a highly dense population, was a possible risk factor for latent TB infection. Another study [24] also showed that living in a crowded environment was a major risk factor for latent TB infection among prison inmates, among other factors.

This study also revealed that BMI was found to be an independent factor that predicted latent TB infection among the general population in Ogun State. This is similar to the findings by Njagi LN et al. [18] among human immunodeficiency virus-positive patients in which BMI among other factors was a predictor of latent TB infection, especially among overweight-obese patients.

Conclusion

The prevalence of latent TB infection in this study population is lower than the global estimate. The positive IGRA results showed a low prevalence of latent TBI in individuals asymptomatic for TB in Ogun State, Nigeria, with statistically significance associations between IGRA results and some socio-demographic characteristics. The rates of indeterminate IGRA results were similar to those reported in other studies. A policy change should be considered so that vulnerable individuals, such as obese people, are targeted for screening and possible isoniazid preventive therapy (IPT). We recommend a more widespread analysis of the determinants of latent TB infection using a larger sample size.

Acknowledgement

We thank all 2022 final-year nursing students of the School of Nursing, Babcock University, Ilishan-Remo, Ogun State, Nigeria, for their participation and for working on this project.

Financial support

None

Conflicts of interest

The authors declare that they do not have any conflict of interest.

References

1- Saleem A, & Azher M. The next Pandemic-tuberculosis: the oldest disease of mankind rising one more time. British J of Medical Practitioners 2013 Jun 1; 6(2): 21. https://api.semanticscholar.org/CorpusID:74434780

2- World Health Organization. Global Tuberculosis Report 2013. WHO 2013. Available from: https://www.who.int/publications/i/item/9789241564656

3- Tiemersma EW, van der Werf MJ, Borgdorff MW, Williams BG, Nagelkerke NJ. Natural history of tuberculosis: duration and fatality of untreated pulmonary tuberculosis in HIV negative patients: a systematic review. PloS one 2011 Apr 4; 6(4): e17601. doi:10.1371/journal.pone0017601

4- World Health Organization; Global Tuberculosis Report 2018. WHO 2018. Available from: https://www.who.int/publications/i/item/9789241565646

5- Moss AR, Hahn JA, Tulsky JP, Daley CL, Small PM, Hopewell PC. Tuberculosis in the homeless. A prospective study. Am J Respir Crit Care Med 2000 Aug; 162(2 Pt 1): 460-4. doi: 10.1164/ajrccm.162.2.9910055.

6- Dodd PJ, Looker C, Plumb ID, Bond V, Schaap A, Shanaube K, et al. Age- and Sex-Specific Social Contact Patterns and Incidence of Mycobacterium tuberculosis Infection. Am J Epidemiol 2016 Jan 15; 183(2): 156-66. doi: 10.1093/aje/kwv160.

7- Pawlowski A, Jansson M, Sköld M, Rottenberg ME, Källenius G. Tuberculosis and HIV co-infection. PLoS Pathog 2012 Feb; 8(2): e1002464. doi: 10.1371/journal.ppat.1002464

8- Kizza FN, List J, Nkwata AK, Okwera A, Ezeamama AE, Whalen CC, et al. Prevalence of latent tuberculosis infection and associated risk factors in an urban African setting. BMC Infect Dis 2015 Mar 29; 15: 165. doi: 10.1186/s12879-015-0904-1

9- Fox GJ, Dobler CC, Marais BJ, Denholm JT. Preventive therapy for latent tuberculosis infection-the promise and the challenges. Int J Infect Dis 2017 Mar; 56: 68-76. doi: 10.1016/j.ijid.2016.11.006.

10- World Health Organization: WHO policy on collaborative TB/HIV activities; Guidelines for national programs and other stakeholders 2012.WHO 2012. Available from: https://www.who.int/iris/handle/10665/44789

11- Nayak S, & Acharya B. Mantoux test and its interpretation. Indian Dermatol Online J 2012 Jan; 3(1): 2-6. doi: 10.4103/2229-5178.93479.

12- Greco S, Girardi E, Masciangelo R, Capoccetta GB, Saltini C. Adenosine deaminase and interferon gamma measurements for the diagnosis of tuberculous pleurisy: a meta-analysis. Int J Tuberc Lung Dis 2003 Aug; 7(8): 777-86.

13- World Health Organization. BCG vaccine: WHO position paper, February 2018-recommendations. Vaccine 2018 Jun 7; 36(24): 3408-10. doi:10.1016/j.vaccine.2018.03.009

14- World Health Organization. Quantiferon-TB Gold Plus (QTF-Plus): WHO 2018 guideline on TB testing. WHO 2018. Accessed from: https://www.quantiferon.com/products/quantiferon-tb-gold-plus-qft-plus/who-guidelines/

15- Aladesanmi AO, Ojuawo OB, Aladesanmi OO, Fawibe AE, Desalu OO, Ojuawo AB, et al. Diagnosis of latent tuberculosis among HI-infected patients in Ilorin, Nigeria using tuberculin skin test and interferon-gamma release assay. Pan Afr Med J 2021 Jan 12; 38: 24. doi:10.11604/pamj.2021.38.24.24039.

16- Ajayi BD, Ogunkoya JO, Ajayi FO. Latent Tuberculosis Infection and Isoniazid Preventive Therapy among Human Immunodeficiency Virus positive adults in Southern Nigeria. Res. J. of Health Sci. 2022; 10(4): 305-318. doi:10.4314/rejhs.v10i4.1

17- Ding C, Hu M, Guo W, Hu W, Li X, Wang S,et al. Prevalence trends of latent tuberculosis infection at the global, regional, and country levels from 1990-2019. Int. J. Infect Dis. 2022 Sep; 122: 46-62. doi:10.1016/j.ijid.2022.05.029.

18- Njagi LN, Nduba V, Mereithi M, Mecha JO. Prevalence and predictors of latent tuberculosis infection among people living with HIV in a high tuberculosis burden context. BMJ Open Respiratory Research. medRxiv preprint doi: https://doi.org/10.1101/2022.12.04.22283086

19- Oni T, Gideon HP, Bangani N, Tsekela R, Seldon R, Wood K, et al. Risk factors associated with indeterminate gamma interferon responses in the assessment of latent tuberculosis infection in a high-incidence environment. Clin Vaccine Immunol 2012 Aug; 19(8): 1243-7. doi: 10.1128/CVI.00166-12.

20- Papay P, Eser A, Winkler S, Frantal S, Primas C, Miehsler W, et al. Predictors of indeterminate IFN-γ release assay in screening for latent TB in inflammatory bowel diseases. Eur J Clin Invest 2011 Oct; 41(10): 1071-6. doi: 10.1111/j.1365-2362.2011.02502.x.

21- Lawn SD, Bekker LG, Wood R. How effectively does HAART restore immune responses to Mycobacterium tuberculosis? Implications for tuberculosis control. AIDS 2005 Jul 22; 19(11): 1113-24. doi: 10.1097/01.aids.0000176211.08581.5a.

22- Akinshipe BO, Yusuf EO, Akinshipe FO, Moronkeji MA, Nwaobi AC. Prevalence and Determinants of Pre-diabetes and Latent Tuberculosis Infection Among Apparently Healthy Adults in Three Communities in Southern Nigeria. Int. J. of Immunol 2019; 7(2): 23-32. doi: 10.11648/j.iji.20190702.11

23- Krishnamoorthy Y, Ezhumalai K, Murali S, Rajaa S, Jose M, Sathishkumar A,et al. Prevalence and risk factors associated with latent tuberculosis infection among household contacts of smear-positive pulmonary tuberculosis patients in South India. Trop Med Int Health 2021 Dec; 26(12): 1645-1651. doi: 10.1111/tmi.13693.

24- Kawatsu L, Uchimura K, Izumi K, Ohkado A. [A SYSTEMATIC REVIEW ON THE PREVALENCE AND INCIDENCE OF LATENT TUBERCULOSIS INFECTION AMONG PRISON POPULATION]. Kekkaku. 2016 Apr; 91(4): 457-64.

Ogunkoya JO, Ogunkoya OA, Ladele AE, Adefuye BO, Osinaike AO, Olarewaju O, Osonuga OO, Worlu CC. Prevalence and correlates of latent tuberculosis infection in adult population in Nigeria: Monitoring a silent epidemic. Microbes Infect Dis 2025; 6(3): 3077-3085.