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Prevalence of tuberculosis among symptomatic individuals and the risk areas in Ondo State, Nigeria

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ABSTRACT: Tuberculosis (TB) has been one of the diseases that are of public health problem globally. Of the global gap in TB case detection and notification, Ondo State reportedly had a notification gap of almost 11,100 TB cases in the year 2019 out of which only 1,891 cases were detected. The research was carried out in Ondo State. Participants were recruited through outreaches from the selected communities. The participants were screened for HIV seropositivity by standard protocols while screening for TB was conducted by a combination of Acid Fast Bacilli (AFB) microscopy and Nucleic Acid Amplification Test (Gene Xpert MTB/RIF®). Over 10,000 participants were screened, of which 3200 subjects were found to have symptoms related to TB. 513 were tested positive for HIV. Overall, TB prevalence was found to be 623(19.5%). Akure South LGA recorded the highest overall prevalence of 39.0%. In the North district, Owo LGA recorded the highest prevalence (18.0%) while the lowest prevalence of (3.5%) was obtained in Ose LGA. The males were more infected (26.5%) than the females (15.3%). According to age groups, the group above 55 years recorded the highest prevalence of 26.8% while the lowest prevalence of 15.3% was obtained in the group 16-25. Compared to the wet season, the dry season had a higher prevalence of TB. Ondo State, Nigeria, has a high prevalence of TB disease. Therefore there is a need to increase public awareness and monitoring of individuals resident in the State.

Keywords: *Mycobacterium tuberculosis*; Prevalence; Ondo; Nigeria; HIV; Xpert® MTB/Rif.

1. INTRODUCTION

Mycobacterium tuberculosis, the causative agent of tuberculosis (TB), is one of the world's most devastating human pathogens because of its ability to persist within humans for long periods in a clinically latent state [1]. It was reported that about 95% of the people who become infected develop a latent infection. It is spread through the air- when an infected person coughs, sneezes, laughs, etc. TB is usually spread between family members, close friends and people who work or live together. TB is spread most easily in closed spaces over a long period of exposure [2].

Tuberculosis (TB) remains a global public health problem and one of the top ten leading causes of death worldwide, with developing countries bearing the highest burden [3]. Over 95% of TB deaths occur in low- and middle-income countries, especially Africa. Eighteen deaths are recorded every hour, while 47 also develop active TB per hour, of which seven are estimated to be children [3]. A person with active TB disease

may have any or all of the following symptoms: persistent cough, constant fatigue, weight loss, loss of appetite, fever, coughing up blood and night sweats [2, 4].

Each day, about 4,500 people lose their lives to tuberculosis (TB) and close to thirty thousand people fall ill with TB, which is preventable and curable. Despite substantial progress over the last decades, TB remains the world's dreadful infectious disease, which requires build-up effort to end its epidemic in Nigeria. Over 95% of TB deaths occur in low and middle-income countries, especially in Africa [5].

In 2018, Nigeria was listed as first in Africa and sixth among the 30 countries in the world with the highest TB burden [3]. Unfortunately, the problem of TB in Nigeria has been complicated by the emergence and spread of drug-resistant TB and a high burden of HIV/AIDS [6]. The problem of TB is worsened when there is also a high burden of HIV infections, as people with HIV are more likely to develop active TB. According to WHO reports, an estimated 63,000 Nigerians living with HIV/AIDS develop TB, while about 39,000 die from the disease each year [6]. WHO in 2019 reported that Nigeria ranked 4th in the world and 1st in Africa in terms of the number of people with Tuberculosis (TB) disease with over 600,000 new cases in 2018. The prevalence, incidence and death rate of the disease have been high consistently with values above 20/100,000, 140/100,000 and 200/100,000 in populations over the past decade [7].

About 2,537 people were having TB disease in Ondo State in year 2021 out of a total presumptive figure of 20,470 cases in the year. In the year 2020, Nigeria was one out of eight countries that accounted for two-thirds of people who developed TB. She also contributed two-thirds of the estimated cases of TB undetected with a TB mortality rate of 62 per 100,000 population and treatment coverage [8]. Ondo State was expected to notify a total of 11,100 TB cases in 2019. However, only 1,897 were detected and placed on treatment by the state TB, Leprosy and Buruli Ulcer Control Programme with a gap of 83% undetected. In 2020, a total of 1,900 TB cases were notified out of a total presumptive TB of 14,688 and 12,803 GeneXpert diagnostic tests done. Also, in the year 2021, a total of 2,537 (33.5%) TB cases were notified compared to the year 2020 [3]. The major challenges of TB response in Nigeria and Ondo State are attributed to inadequate records on the prevalence, poor knowledge about TB, low treatment, the risk factor (s) and the emergence of drug-resistant TB. There is a need to have regular updates from States or regions on the burden of TB in order to assist the local and global bodies in their goals to curtail the spread of TB [9]. This study is aimed at Tuberculosis prevalence and the risk Areas in Ondo State.

2. MATERIALS AND METHODS

2.1. Study Area

The research was carried out in the three geopolitical zones of Ondo State: North, South and Central. Ondo State has 18 LGAs and an area of 14,788.7 km² with a population of 3,460,877 [10]. It lies between 4˚30" and 6˚ East of the Greenwich Meridian, 5˚45" and 8˚15" North of the Equator. Ondo State has two seasons: the rainy (wet) season, from March to October and the dry season, from November to February with an average annual rainfall of 1500mm, a temperature ranging from 21.4˚C to 31.1˚C and relative humidity of 80%.

2.2. Recruitment of Participants

Participants were recruited through outreaches for the selected communities in each of the zones. The only inclusion criterion for participation in the study was those who had been coughing consistently for more than two weeks. All procedures and objectives for the study were explained to each participant in English and the native languages and informed consent was obtained. This study was carried out in accordance with the international ethical guidelines for experiments involving human subjects for research [11].

2.3. Sample Size Determination and Sampling Technique

The study population involved presumptive TB patients (with clinical signs and symptoms suggestive of TB) who were in the study area during the sampling period. The sample size was generated using the Raosoft sample size calculator at 5% margin of error and 95% confidence level. Nevertheless, over 10,000 participants were screened for presumptive TB.

2.4. Sputum Collection and Analysis

2.4.1. Acid Fast Bacilli (AFB) Microscopy

Sputum samples were collected using dry, clean, leakproof and translucent screw-capped plastic containers and put in ice ice-packed box, and transported to the laboratory. Smears were prepared, air dried and stained with Ziehl-Neelsen (ZN) stain. Smears were heated briefly and flooded with Carbol fuchsin solution. For slide preparation, heat was applied and allowed to stand for 5 min. Slides were washed with distilled water, decolorized with acid alcohol for 1 min and stained with Methylene blue for 30s. Slides were washed, air dried and observed under 100x oil immersion objective with bright field illumination. Microscopy results were recorded following the reporting methods [4] (plate 1).

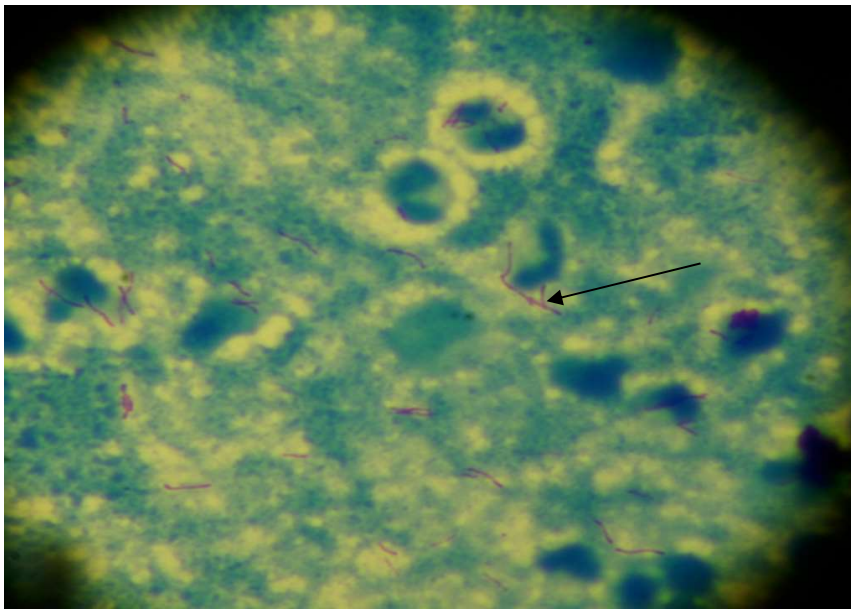

Plate 1. Positive Ziehl-Neelsen (ZN) staining.

2.4.2. Gene Xpert Analysis

One spot sputum specimen was collected into the sputum cup from each of the participants. The sputum specimens collected were analyzed using the Gene Xpert MTB/RIF® to detect M. tuberculosis infection. Gene Xpert MTB/RIF® (Ceheid Inc., USA) system is a platform for rapid and simple-to-use nucleic acid amplification tests. The test is based on a real-time semi-nested PCR test principle, which detects the presence of M. tuberculosis complex bacilli by using five molecular beacons probes that span the rpoB gene (gene that encodes the β-subunit of RNA polymerase) 81-bp RR-determining region, the test simultaneously determines susceptibility to RIF, which can be used as a surrogate marker for multidrug resistance. The probes can differentiate between the conserved wild-type sequence and mutations in the core region that are associated with RR. The results are interpreted by the Gene Xpert® from measured fluorescent signals and embedded calculation algorithms, which will be displayed in the "View Results" window of the computer.

A volume of 1.0 ml of sputum sample was mixed with 2.0 ml of buffer to liquefy the sputum and was incubated at room temperature for 15 min. inside a closed tube. The closed tube was manually agitated twice during the 15 min. incubation. Thereafter, 2.0 ml of the diluted sample was transferred into the cartridge for ultrasonic lysis of the Mycobacteria to release target DNA. The cartridge was loaded into the Gene Xpert machine (Cepheid) in batches of 4 at once within 30 minutes of preparing the cartridge for running. After 1 hour 26 minutes or less, depending on the outcome, the comprehensive test result was read on a computer screen and was ready for printing.

2.5. Data Analysis

All data will be entered in an Excel spreadsheet to ensure accuracy and exported into a statistical package for Social Sciences (SPSS) software (version 21, SPSS Inc. Chicago, Illinois, USA) for analysis. Bivariate analysis will be carried out to test the association between the various demographic and clinical factors. All factors that will be significant in the Bivariate analysis will be entered into the multivariate logistic regression analysis and results will be expressed as odd ratios (OR) with a 95% confidence interval (CI). For all statistical analyses, a P value of < 0.05 will be considered significant.

2.6. Ethical clearance

Prior to the commencement of the research, approval was sought from Ministry of Health of Ondo State (with the issuance of an ethical clearance protocol number OSHREC/11/12/2018/079, the Chief Medical Director (CMD) of various Health Centres and Community leaders where sample were collected. Also, consent was obtained from the volunteers whose samples were collected.

3. RESULTS

Out of 3200 TB presumptive sampled subjects, 623(19.5%) tested positive with a significant difference ($p<0.005$). Figure 1 shows the geographical distribution of TB disease in the study area. Akure South recorded 36-45% distribution, Ondo West, Odigbo and Okitipupa (South Senatorial district) recorded 31-35% distribution and the least distribution of 0-5% was recorded in the North Senatorial district. Table 1 shows the prevalence of tuberculosis disease in relation to the senatorial districts and each of the Local Government Areas (LGAs). Of all the LGAs, Akure South LGA recorded the highest overall prevalence of 39.0%. In the North district, Owo LGA recorded the highest prevalence (18.0%), while the lowest prevalence of (3.5%) was obtained in Ose LGA. For the Central senatorial district, Akure South LGA, recorded (39.0%) prevalence while Ondo East LGA recorded the least prevalence (12.4%). Odigbo LGA recorded the highest (30.0%) prevalence, while Ese Odo LGA recorded the least prevalence in the South senatorial district. There is a significant difference in the rate of the disease among the LGAs ($p<0.005$).

Table 2 shows the prevalence of TB according to the gender of the patients. The males recorded a higher prevalence of 26.5% than the females 13.2%. There is a statistically significant difference between the sexes. The prevalence according to the age group of the patients is revealed in Table 3. The age group 55 years and above recorded the highest prevalence of 26.8% followed by the age group 46-55 (26.6%), and 36-45 (22.8%) while the least prevalence of 15.3% was recorded in the age group 16-25. However, there is a significant difference among the age groups ($p<0.05$).

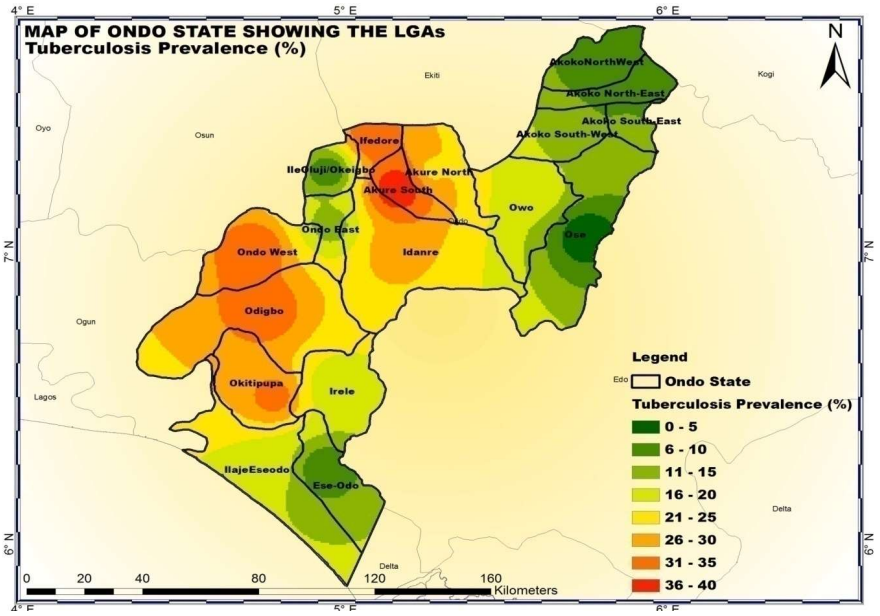

Figure 1. Prevalence of tuberculosis by LGAS.

Table 1. Prevalence of tuberculosis among presumptive TB in the LGAs of the study area.

Senatorial Districts	Lga	Number Examined	Positive	Prevalence (%)
North	Akoko North East	158	13	8.2
	Akoko North West	149	12	8.1
	Akoko South East	137	17	12.4
	Akoko South West	166	25	15.1
	Ose	142	5	3.5
	Owo	206	37	18.0
	Total	958	109	11.4
χ^2 =15.269, Df = 5, P = 0.003, Phi= 0.003, Cramer's V= 0.003				
Central	Akure North	198	44	22.2
	Akure South	200	78	39.0
	Idanre	198	50	25.2
	Ifedore	188	56	29.8
	Ondo East	185	23	12.4
	Ondo West	205	61	29.8
	Total	1174	312	26.6
χ^2 =58.418, Df = 5, P = 0.001, Phi= 0.001, Cramer's V= 0.001				
South	Ese Odo	126	10	7.9
	Ilaje	142	24	17.0
	Ile Oluji/Okeigbo	189	15	7.9
	Irele	168	27	16.1
	Odigbo	220	66	30.0
	Okitipupa	214	60	28.0
	Total	1059	202	19.1
χ^2 =0.086, Df = 4, P = 0.762, Phi= 0.762, Cramer's V= 0.762				
	Grand Total	3200	623	19.5

Table 2. Prevalence of tuberculosis disease in relation to sex of patients in the study area.

Sex	Number Examined	Positive	Prevalence (%)
Male	1501	398	26.5
Female	1699	225	13.2
Total	3200	623	19.5

χ^2 =0.286, df = 1, P = 0.020, Phi= 0.020, Cramer's V= 0.020.

Table 3. Prevalence of Tuberculosis disease in Relation to Age of Patients in the Study Area.

Age	Number Examined	Positive	Prevalence (%)
1-15	401	74	18.5
16-25	810	124	15.3
26-35	781	128	16.4
36-45	657	150	22.8
46-55	305	81	26.6
Above 55	246	66	26.8
Total	3200	623	19.5

χ^2 =28.326, df = 5, P = 0.001, Phi = 0.001, Cramer's V = 0.001.

According to the prevalence in relation to the educational status of the patients, those who did not attend school (illiterates) recorded the highest prevalence of 33.1% while the lowest prevalence of 6.7% was obtained in patients who attended primary school only. However, there is no significant difference in the prevalence of TB infection. For the patients' occupation, the traders recorded the highest prevalence of 22.5%, followed by the artisans at 21.5% while the lowest prevalence (15.2%) was obtained among the Civil servants. There is a significant difference in the prevalence of TB in relation to Occupation. According to the income of the patients, those who earned between #19,000 and #49,000 recorded the highest prevalence of 20.2% while those who earned less or equal to #18,000 recorded the lowest prevalence of 19.1%. However, there is no significant difference in the prevalence of TB in relation to their income (Table 4).

Table 5 shows the prevalence of TB in HIV-infected patients. Out of 513 positive patients, 41% were positive for TB while of 2687 negative for HIV, 15.3% were positive for TB infection. However, there was no significant difference ($p>0.05$).

Table 4. Prevalence of tuberculosis in relation to educational, occupation and income status of patients in the study area.

Variables	Number Examined	Positive	Prevalence (%)
Educational Status			
Illiterate	1202	398	33.1
Primary	193	13	6.7
Secondary	408	62	15.2
Tertiary	1397	150	10.7
Total	3200	623	19.5
χ^2 =9.113, df = 3, P = 0.013, phi= 0.013, Cramer's V= 0.013			
Occupation			
Civil Servant	776	118	15.2

Variables	Number Examined	Positive	Prevalence (%)
Trader	796	179	22.5
Artisan	905	195	21.5
Unemployed/Student	723	131	18.1
Total	3200	623	19.5
χ^2 =21.326, df = 3, P = 0.001, Phi = 0.001, Cramer's V = 0.001			
Income			
≤ ₦18,000	1101	210	19.1
₦19,000 to ₦49,000	913	184	20.2
≥ ₦50,000	1186	229	19.3
Total	3200	623	19.5
χ^2 = 0.912, df = 3, P = 0.634, Phi= 0.634, Cramer's V= 0.634			

Table 5. Co-infection and Prevalence of TB and HIV in patients in the study area.

		TB Status	
HIV Status	**Number Examined**	**Positive (%)**	**Negative (%)**
Positive	513	211 (41.1)	302 (58.9)
Negative	2687	412 (15.3)	2275 (84.7)
Total	3200	623	2577

χ^2 =10.476, df = 1, P = 0.030, Phi= 0.030, Cramer's V= 0.030.

Figure 2 shows the seasonal prevalence of TB according to the LGAs. For Ondo North Senatorial District (ONSD), all the LGAs recorded high prevalence during the dry season with Ose LGAs recording the highest prevalence of TB infection. Akure North and Idanre LGAs recorded a high prevalence of TB infection during the dry season compared to the rainy season in Ondo Central Senatorial District (OCSD). In Ondo South Senatorial District (OSSD), Ilaje, Ese-Odo and Odigbo LGAs also recorded a higher prevalence of TB infection during the dry season.

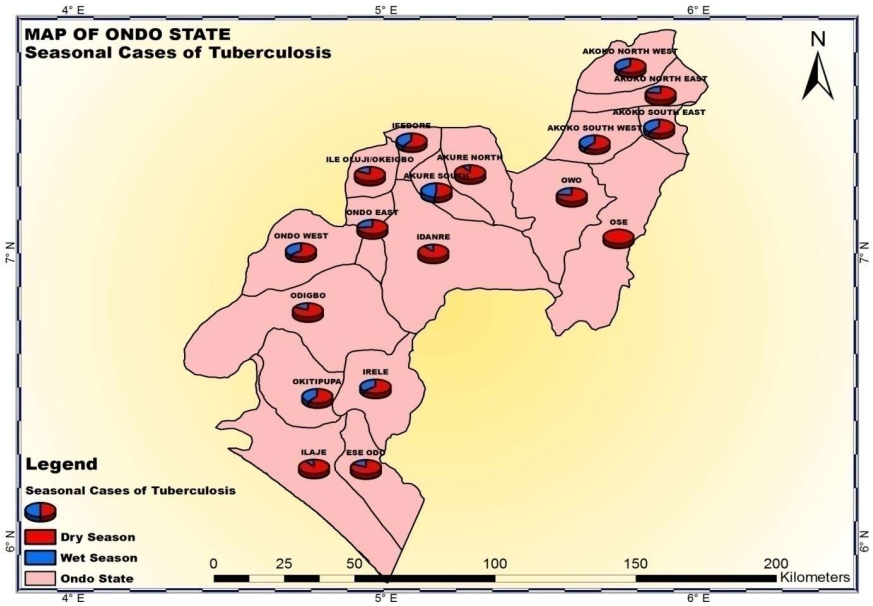

Figure 2. Seasonal prevalence of tuberculosis according to LGAS.

The microbial load in the patients revealed that those with moderate microbial load was 45%, followed by those with high microbial load 29.9%, very high microbial load 8.8% and 5.2% for patients with low microbial load (Fig. 3). Figure 4 shows the risk mapping of TB infection in the study area. The very high-risk areas include Odigbo and Okitipupa LGAs (OSSD), Ondo West, Ifedore, Akure South, Idanre and some parts of Akure North (OCSD). Owo (ONSD) and parts of Akure North LGAs (OCSD) are at high risk of TB infection. The LGAs at low risk of TB infection are Ilaje, Irele, Ese-Odo (OSSD) and all the LGAs in ONSD except a few communities in Owo LGA (Figure 4).

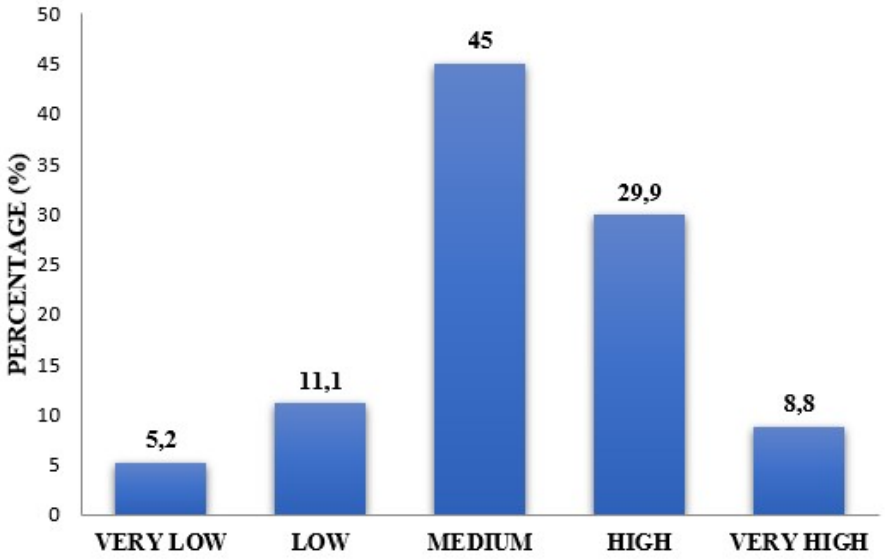

Figure 3. Microbial load of tuberculosis among patients in the study area. χ^2 =65.764, df = 2, P = 0.000.

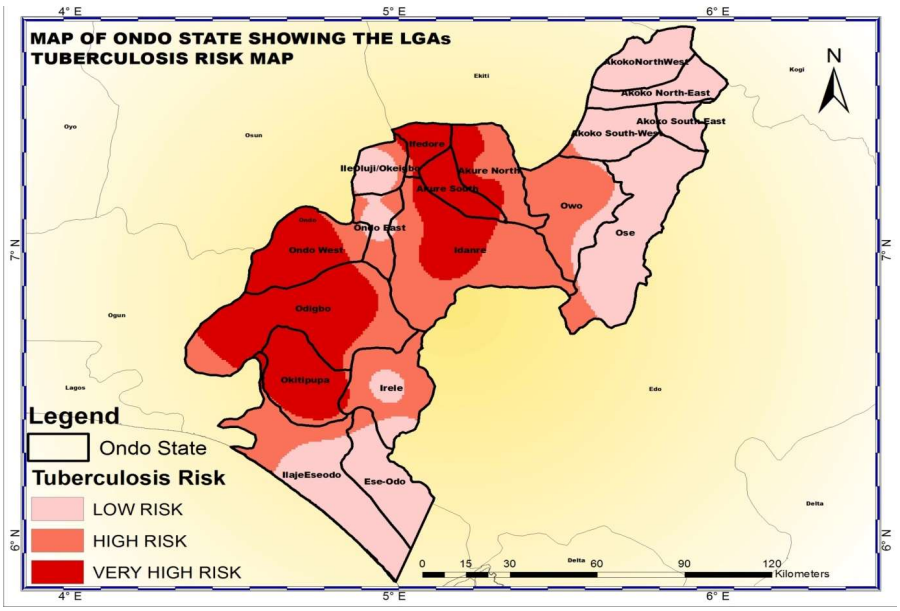

Figure 4. Tuberculosis risk mapping in the study Area.

4. DISCUSSION

This study clearly shows that TB is still an important health problem in the study area despite government-sponsored mass awareness and control programs. Akure South LGA (OCSD) stood out as the most highly infected area with high prevalence (Table 1). The high prevalence in Akure South LGAs could be due to the presence of a high population being the capital of Ondo State, city markets, and center of commercial activities for people from different urban and rural areas, thereby enhancing TB importation. A large proportion of TB patients in rural areas remained undiagnosed because of a lack of access to healthcare services which made them seek alternative care from non-licensed providers, pharmacies and private practitioners. In addition, the long distances traveled by patients seeking care together with the attendant transportation cost to health facilities may serve as a barrier to TB diagnosis [12]. This finding is in agreement with the report from the first National TB prevalence survey in the country where TB prevalence was almost twice in urban compared to rural areas [13, 14] reported that urban residence was a strong predictor of TB irrespective of the effect of poverty or the interaction of poverty on urban residence.

The relatively low prevalence (3.5%) in Ose LGAs (ONSD) can be attributed to the spacious environments and smaller population, which is a predisposing factor for the spread of TB infection as previously reported by [15]. The significantly high prevalence of TB in males recorded in this study when compared with females has been previously reported by other researchers. Globally, more males than females have been reported to be TB-positive [3]. This has been attributed to their often more risky activities, which include high social interactions, love for overcrowded environments, drinking, and smoking which enhance the spread of TB.

In the present study, more TB cases were recorded in the age group 55 years and above, closely followed by the age group 46-55 years and the least cases in the age group 16-25 (Table 3). This has been attributed to the reactivation of the latent infection acquired many years earlier [1]. TB is still known to be most prevalent in the elderly. This shift in trend to young adults and the middle aged as also reported in other studies [16] has been attributed to the advent of HIV/AIDS, which is most prevalent in people in these age brackets [3]. The BCG vaccination of newborn babies has been widely practiced in Nigeria and offers protection against the disease [17]. This could explain why individuals less than fifteen years old in this study recorded a low prevalence of TB. For the prevalence according to education status, the illiterate patients recorded the highest prevalence which could be that they do not have an awareness of the disease, mode of infection, symptoms etc. The traders presented the highest number of TB cases which may be a result of their commercial activities involving going from one place to another and having contacts with different categories of people in the process of their daily transactions. The income of the patients had no significant effect on the prevalence of TB infection (Table 4).

Among the 3200 patients tested for HIV, 513 were positive and 2687 were negative. The prevalence of TB among the 513 HIV subjects was 41.1% while for 2687 negative subjects, it was 15.3%. TB is the most common opportunistic infection associated with HIV/AIDS [18]. The problem of TB globally has been found to be worsened by HIV/AIDS, as people with HIV have a much higher risk of developing active TB. According to health reports, about 45% of HIV-negative people with TB and nearly all HIV-positive people with TB have a high risk of death without appropriate treatment [3]. HIV and TB co-infection has been described as a lethal combination, as each disease speeds up the other's progress, a realization that probably leads to death [1]. Also, intake of alcohol, smoking and diabetes accounted for the highest number of deaths and DALYs that could be attributed to TB.

The data from the study indicates strongly that the season influenced the epidemiological pattern of TB. The dry season presented a higher number of TB cases than the wet season. However, this finding is contrary to the report of [19] in Ethiopia where the prevalence of TB was higher during the rainy season. The patients with medium microbial load recorded the highest prevalence while the least prevalence was obtained from patients with very low microbial load with a statistically significant difference (Figure 2).

Ondo North and part of Ondo South Senatorial Districts have low risk while Ondo Central and some parts of Ondo South have a high risk of TB infection which could be a result of the differences in their population and commercial activities (sparse and dense population) respectively. High population density is associated with outdoor residential crowding experienced in cities, especially in urban slums and informal settlements characterized by lack of basic sanitation, poor housing and overcrowding, high levels of congestion and urban air pollution as a result of increased vehicular movements, industrial pollution, effluent from generating sets and household fuel combustion. These situations may contribute to increased respiratory illness including TB [20].

5. CONCLUSION

The outcome of this study confirmed that TB occurrence exhibits spatial heterogeneity in the distribution of TB across Ondo State with the identification of LGAs with the highest TB risk. The TB hotspots were detected in the central and southern parts of the State. This finding provided useful information that can assist policymakers and other stakeholders in targeting the scarce resources to the identified priority LGAs with high TB risk above the national average and the deployment of targeted specific interventions such as active case search which may be helpful in rapidly finding more TB cases in these priority LGAs with prompt treatment. Also, the implementation of preventive strategies such as increasing BCG vaccination coverage for children at birth and administration of isoniazid preventive therapy (IPT) to households and people living with HIV (without active TB) to reduce the risk of acquisition of infection after exposure to an infectious TB case. Improving the uptake of antiretroviral drugs among TB/HIV co-infected patients will also decrease the reactivation of TB and therefore reduce overall TB incidence in the state. As a result of the severity and consequences of the disease to public health, local control programs should be instituted and major educational efforts made to improve public awareness of the disease and the impact of HIV/AIDS on the spread of the disease. It would be important to consider the impact of seasonal changes in such evaluation strategies.

List of Abbreviations:

LGA: Local Government Area; TB: Tuberculosis; OCSD: Ondo Central Senatorial District; ONSD: Ondo North Senatorial District; OSSD: Ondo South Senatorial District.

Author Contributions: OO conceived the main idea, performed the data collection, practical part, analyzed the data writing and submission, IAS supervised and revised the work, wrote the manuscript and final editing. All authors read and approved the final version of the manuscript.

Conflict of Interest: The authors declare no potential conflict of interest.

Ethics Statement: The study has been approved by the Ministry of Health of Ondo State, with the issuance of an ethical clearance protocol number OSHREC/11/12/2018/079.

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