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**ORIGINAL ARTICLE**

# Social determinants of tuberculosis in Nigeria: an ecological approach

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## Abstract

**Background:** Nigeria is $4^{th}$ among 22 tuberculosis high-burden countries. However, TB is not evenly distributed in the country, presumably due to state-specific risk factors.

**Objectives:** This study maps TB and socioeconomic risk factors in Nigeria.

**Methods:** State-level age/sex standardized tuberculosis notification data was utilized in an ecological design to evaluate the spatial distribution of TB in Nigeria and its social and economic consequences between 2012 and 2015. Negative binomial regression analysis examined the relationship between TB and five state-level covariates: HIV, BCG coverage, GDP per capita, percentage underweight, and percentage treatment success rate. Global and Local Moran's I test statistics in R were used for spatial analysis.

**Results:** The mean age/sex TB CNR was 54.4/100,000. Non-spatial ecological regression analysis found that TB was greater in states with high HIV, low BCG, low GDP per capita, and low TB death rates. Three states—Nasarawa, Benue, and Taraba—had high TB rates and spatially auto-correlated TB CNRs.

**Conclusions:** TB case notification differed by age and gender. Economically-disadvantaged states exhibited higher TB case notification, HIV prevalence, lower BCG coverage, and lower mortality rates. The study found three TB hotspots. To reduce the national TB notification rate discrepancy, TB policies should incorporate social variables and target high-risk states with specific initiatives.

Keywords: Tuberculosis, spatial, inequality, ecological, social determinants.

## INTRODUCTION

Tuberculosis (TB) remains a significant public health problem of the 21st century. It is one of the top 10 causes of death globally and the leading cause of death from a single infectious disease agent.[1] In 2019 an estimated 10 million new TB cases and 1.2 million deaths occurred worldwide due to TB, and the majority of these infections and deaths occurred in sub-Saharan Africa.[1]

Nigeria is one of the 30 countries with a high TB burden with an estimated TB burden of 440,000 cases in 2019, the sixth worldwide and the first in Africa. However, only about a quarter of the estimate was notified by the country.[1] TB is differentially distributed both within and among countries due to the differences in socio-economic and other structural factors. The distribution of TB in the country especially at the sub-national level is uneven due to several epidemiological and social determinants that may be responsible for the differential TB incidence and case notification by the 36 states and the Federal Capital Territory.

The World Health Organization's Commission for Social determinant of Health described social determinants of health as the *conditions in which people are born, grow, live, work* that mostly contribute to health inequities which are the unfair and modifiable differences in health within and among countries.[2] The social determinants of health are shaped by upstream factors such as increasing economic inequities as a result of globalization, migration, rapid urbanization, demographic transition and population growth. These upstream factors give rise to unequal distribution of downstream factors such as food insecurity and malnutrition, poor housing, and environmental conditions. In addition, poor health behaviors that result in diabetes and tobacco use, barriers to health care access, including gender, geographic, financial and cultural factors, affect the distribution of diseases within and among countries.[2]

The health inequities in TB result from differences in risk exposure, vulnerability and progression of the disease once infected.[3] The downstream factors (social determinants of health) responsible for the uneven distribution of TB include the number of active TB cases in a community and the living conditions such as overcrowding, poor ventilation, tobacco use, indoor air pollution and the diseases that increases vulnerability to TB (such as HIV, diabetes, malnutrition, alcoholism and other lung diseases). These downstream factors interact with biological and genetic factors to increase the probability of exposure to TB infectious, the likelihood of acquiring the infection when exposed, the risk of progression to active disease when infected, and the consequences of TB when the individual has the disease.[3]

Spatial analytic tools have increasingly been used to study the role of social determinants of health in the non-uniform distribution of disease incidence in certain geographical areas.[4,5] These studies have demonstrated the clustering of TB in areas of high unemployment, high deprivation and poverty, high population density, overcrowding, low educational attainment and low-income status.[6−10] However, there is paucity of studies using spatial analysis tools to determine the spatial distribution and determinants of tuberculosis in Africa especially Nigeria. Therefore, this study was conducted to determine the spatial distribution of TB in Nigeria and assess the effect of some social determinants on TB distribution in Nigeria.

## MATERIALS AND METHODS

### Study design

An ecological design was used to determine the spatial distribution of TB in Nigeria and its social and economic correlates between 2012 and 2015 using state-level age/sex standardized TB notification data. The association between TB and five state-

**Supplementary information** The online version of this article (Tables/Figures) contains supplementary material, which is available to authorized users.

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level covariates such as HIV prevalence rate, BCG coverage, GDP per capita, percentage underweight and treatment success rate was done using negative binomial regression analysis.

### Study population

Nigeria is a relatively large country situated in West Africa bounded in the north by the Niger Republic, on the east by Chad and Republic of Cameroon, on the south by the Gulf of Guinea (approximately 800km of the Atlantic Ocean), and the west by the Benin Republic. It occupies an estimated 923,768 square kilometres area. The country has a population of about 200 million people with an annual population growth rate of 2.8 per cent.[11]

### Diagnosis of TB in Nigeria

In line with the National Tuberculosis and Leprosy Control Program (NTBLCP) guidelines,[12] the diagnosis of TB was made by both the general health care workers and medical officers. The diagnosis of TB in adults and older children was carried out using sputum for AFB microscopy and gene Xpert test. Diagnosis in adults who were sputum negative and in children were done clinically using the clinical presentation of the patients in addition to ancillary investigations such as Chest X-ray, Erythrocyte Sedimentation Rate, Mantoux test, Full Blood Count etc.

### Definition of terms

A) TB case notification rate was calculated by dividing the average number of TB cases notified over the four years (2012-2015) by the average population of each state multiplied by 100,000. The TB cases reported per state were obtained from the annual TB case report of the NTBLCP for the year 2012-2015.[13]The population for each state was obtained from the National Population Commission for the year 2006.[11]

B) Gross Domestic Product (GDP) per capita is a measure of each state's economic development. The distribution of GDP per capita for each state was obtained from the 2009 Human Development Report in Nigeria.[14] This indicator was used as a proxy for the status of the socio-economic development for each state.

C) The Human Immunodeficiency Virus (HIV) infection rate was obtained from the HIV Sentinel Surveillance Report for the year 2010.[15]

D) The percentage weight for age (WFA) was used as an indicator of malnutrition (underweight), while the percentage Bacillus Calmette Guerin (BCG) coverage rate was obtained from the Millennium Development Goal (MDG) document for Nigeria in 2010.[16]

E) Death during TB treatment: This is the percentage of TB patients in each state who died during treatment in the previous year. This indicator was used as a proxy for the quality of the TB programme in each state. The data was obtained from the annual TB report.[12]

### Spatial analysis

The 36 states and Federal Capital Territory (FCT) were used as the unit of geographical analysis. The Global Moran's I index was used to estimate the strength of the global spatial autocorrelation of average tuberculosis case notification. The values of Global Moran's I ranged from -1 to +1. A Moran value of +1 suggests a strong positive autocorrelation while a value of -1 suggests a strong negative spatial autocorrelation. The Global Moran I is expressed by the formula.[17]

$$I = \frac{N}{\sum_i \sum_j \omega_{ij}} \frac{\sum_i \sum_j \omega_{ij} (X_i - \bar{X})(X_j - \bar{X})}{\sum_i (X_i - \bar{X})^2}$$

Where N is the number of spatial units i.e. the 36 states and the Federal Capital territory indexed by i and j; X is the average tuberculosis case notification rate, while is the mean. $W_{ij}$ measures the spatial weights. A first-order adjusted connectivity matrix was used, in which region i is considered neighbor of region j, if they share a common boundary. $W_{ij}$ takes the value of 1 in contiguous location i and j and the value of zero (0) where areas are not contiguous.

The Local spatial autocorrelation (LISA) developed by Luc Anselin[17] was used to identify local clustering or hot-spots of TB cases in the states. It is expressed as

$\mathbf{I}_i = \mathbf{z}_{iij}\mathbf{z}_j$

Where $z_i$ is the original variable $x_i$ (average tuberculosis case notification rate) in standardized form and $w_{ij}$ is the spatial weight as described above for global autocorrelation.

A choropleth thematic map was drawn to visualize possible clustering of tuberculosis in states with significant spatial clustering. The false discovery rate (FDR) method by Benjamin and Hochberg's was used to adjust for the local Moran's I p values.[17] A final choropleth map of local Moran's FDR-adjusted p values was produced at P-value of $\leq 0.05$. The analysis of the data was carried out in R statistical package version 3.2.3.[18]

**Aspatial Data analysis**

Non-spatial analysis was done using negative binomial regression to assess the relationship between average TB notification and five explanatory variables (Gross Domestic Product (GDP) per capita, BCG coverage, percentage weight for age, HIV positivity rate and percentage death during TB treatment). In this statistical analysis, the model took the form of:

$$\log \lambda i = \beta 0 + \beta 1xi1 + \beta 2xi2 + \ldots + \beta kxik + \sigma\varepsilon + \log(popi)$$

where:

**i=1…… 37,**

$\lambda$ is the expected average TB cases notified in the 36 state and the FCT,

xi represents each standardized ecological measure (with its associated $\beta 1$, $\beta 2 \ldots \beta k$ represents the regression coefficients associated with the standardized ecological measure),

$\sigma\varepsilon$ is the disturbance or error term.

Pop is the projected average population between 2012-2015 in the states and FCT. The $\sigma\varepsilon$ term represents error and dispersion in the form of a negative binomial distribution. The exponent of each $\beta j$ regression coefficient provides the incidence rate ratio for a 1- standard deviation change in the corresponding ecological measure. All statistical analysis was carried out in R software version 3.2, and the level of significance was taken at P<0.05.

## RESULTS

The mean TB age/sex Case Notification rate (TB CNR) during the study period was of 54.4/100,000. The Male: Female ratio was 1:6 in 2012, 1.5:1 in 2013, 1.5:1 in 2014 and 1.6:1 in 2015. Table 1 shows a decline in the age/sex standardized TB Case Notification rate from 58.02/100,000 in 2012 to 49.9/100,000 in 2015. The peak age CNR/100,000 for males was in the age group 45-54 years and the age group 65 years, as shown in Figure 1. The peak age group in females was in the age group 25-34 years, as shown in Figure 2. Figure 3 shows the distribution of the average TB Case notification rate by states in Nigeria. Nasarawa state had the highest average case notification rate of 132/100.000, followed by Federal Capital Territory with a CNR of 127/100,000, Benue state with CNR of 122/100,0000 and Taraba 114/100,000. The lowest CNR/100,000 was in Ekiti state with a CNR of 19.8/100,000

Table 2 shows the relationship between TB case notification rates and five variables using a negative binomial regression analysis. The five state-level variables were HIV prevalence rates, BCG vaccine coverage rate, Gross domestic product (GDP), Weight for age and Death during TB treatment. The regression analysis showed that TB Case notification rate was significantly higher in states with low GDP per capita rates, high HIV prevalence rates, low BCG coverage rates, and in states with low TB death rates during treatment. There was global spatial autocorrelation of TB in the country. Figure 4 shows the adjusted false discovery rate (FDR) p values of the local Moran I test. The choropleth map identified significant clustering of TB at p<0.05 in three states namely Nasarawa, Benue and Taraba.

## DISCUSSION

The study showed a decline in the case notification rate between 2012 and 2015. The world health organization global TB reports 2019 suggests that the TB case notification for Nigeria is about a quarter of the expected notification rates. Low TB case notification rate has been a major challenge in the country despite significant progress by the National TB programme to increase facilities for diagnosis and treatment in the country. Several factors have been adduced for sub-Saharan Africa's TB low case finding. These include, among others, low awareness of TB and poor knowledge about the location where to seek care; limited community outreach by health facilities; limited human resources for health in terms of both quality and quantity of health care workers trained on TB; poor TB management information systems; barriers to diagnosis and treatment.[19−21] The National TB programme may need to complement existing passive case-finding strategies with more aggressive active case-finding efforts engaging all care providers, including the private sector and the community members, in the fight to end TB by 2035. The search for the missing cases within the health system and addressing barriers to accessing TB diagnostic and treatment services is imperative for successful TB control in the country.

The study showed that more males than females were notified during the study period. The finding is in keeping with the first TB prevalence survey carried out in 2012.[22] There has, however been an argument that the excess burden of TB in males may be as a result of social, economic and cultural barriers to diagnosis faced by women. However, a systematic review on sex differences in TB prevalence surveys showed that TB prevalence was significantly higher in men than women in low-and middle-income countries.[23] The study highlighted that men were significantly disadvantaged in seeking and accessing TB care and should be seen as a high-risk group to be targeted to reduce the burden of TB.

The peak age for women in this study was in the age group 25-34 years compared to men who had two peaks in the age group 45-54 years and over 65 years age group. A study conducted in Brazil found that TB infection among household contacts showed a significant difference in the risk of TB infection between males and females. Females had their highest risk of infection at a significantly younger age than males that had the highest risk of infection in the older age group. Some studies have suggested that the differences in TB infection between males and females may be due to biological differences in the susceptibility of TB infection.[25]Others have suggested that older males may have increased exposure due to their higher social contact and a higher risk from alcoholism and smoking, which increases their susceptibility to TB infection and that women are more likely to have a timely diagnosis compared to men who are more likely to be diagnosed later on in life.

The study found that states with low GDP per capita had a higher TB burden. The association between Poverty and TB notification has been reported in several studies.[27−30] Poverty predisposes individuals to malnutrition which makes them susceptible to tuberculosis infection. Likewise, poverty is associated with poor living conditions such as overcrowding that provides an enabling environment for the TB bacillus to thrive and be readily transmitted from one person to another.

Three states along the country's middle belt, namely Nasarawa, Benue and Taraba states were identified as high risk for tuberculosis. The states incidentally have the highest HIV prevalence rates in the country. The association between HIV and TB has been established in the literature.[31−33] In order to decrease the prevalence of TB in the country, close attention needs to be placed on the HIV situation in these states with the deployment of HIV prevention strategies such as HIV testing services, prevention of mother to child transmission, provision of Isoniazid (INH) preventive therapy, and increase the coverage of persons living with HIV to antiretroviral treatment.

The study found that states with a lower BCG vaccine coverage had a higher TB case notification rate. Though there is wide variability in the potency of BCG vaccine, the vaccine is recommended in many countries with a high prevalence of TB to prevent childhood tuberculous meningitis and miliary disease. The study reiterates the need for states to increase BCG coverage among children. Further studies need to be carried out to provide evidence on the continued use of BCG vaccine in low and middle-income countries.

The study used the death rate among TB patients on treatment as a proxy for the quality of TB services in the states. The study found that states with a lower death rate (high-quality programme) had a higher TB case notification rate. The states with good quality TB programs were likely to have better health infrastructure for early diagnosis of presumptive TB cases and effective management of diagnosed TB patients initiated on treatment. To strengthen TB management, efforts at the basic management units are required to bring TB diagnostic and treatment services closer to the community. Also, efforts to control TB and improve diagnosis and treatment services to the community should be with a specific focus on states and communities that are socially deprived.

## CONCLUSIONS

This study has some limitations. The dependent variable in this study is the TB case notification rate rather than the true TB prevalence rate in the LGAs. The information on the prevalence of TB was not available at the time of this study. The first national TB prevalence survey conducted in 2012 did not include all the 774 LGAs. Therefore, some LGAs may have a relatively higher TB risk compared with what was reported in this study because of the current passive case finding approach utilized by the NTBLCP where individuals infected with TB need to seek care in health facilities before they are captured and notified by the NTBLCP surveillance system. Consequently, poor socioeconomic factors and lack of access to TB diagnostic and treatment services may serve as barriers to TB patients becoming notified by the National TB surveillance system.

Secondly, the population figures used to calculate the denominator of TB CNR was projected from the last census conducted in 2006. This may not give an accurate reflection of the current population considering the fact that population growth may not be uniform across all LGAs in the country. Similarly, the data used to develop the socioeconomic index (SEI) was collected in 2006 and it is unlikely that the economic situations of the LGAs have remained the same since 2006. Therefore, the socioeconomic data may not adequately represent the present economic realities and the increasing income inequality in the country.

Lastly the findings from this study cannot be applied as a cause-and-effect relationship at the individual level as this may amount to committing ecological fallacy. Similarly, it was impossible to observe both the combination of the spatial and spatio-temporal changes in TB pattern because the study was done in a single year.

## INFORMATION

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Authors' contribution. Conceptualization and study design: OD, OA, KO. Data collection: OD, JB, AA, AG. Data analysis: OD, KO. Study supervision: OD, OA. Manuscript writing: OD, OA, JB, AG. Revision of manuscript: OD, OA, JB, AA, AG, KO.

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**Ethical Consideration:** Ethical clearance for this study was obtained from the Health Research Ethics Committee of the Olabisi Onabanjo University Teaching Hospital, Sagamu, Ogun State, Nigeria (NHREC 08/10/2012) dated 10$^{th}$ November 2015.

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**Table 1. TB cases notified in Nigeria, 2012-2015.**

| Year | National Population | Total number of TB cases notified | Age/sex standardized notification rate per 100,000 |
|---|---|---|---|
| 2012 | 170123740 | 97853 | 58.02 |
| 2013 | 174507539 | 100401 | 58.05 |
| 2014 | 178975125 | 85890 | 51.53 |
| 2015 | 183528798 | 90584 | 49.90 |
| Average | 176783801 | 93682 | 54.38 |

**Table 2. Factors associated with TB Case notification rate in Nigeria 2012-2015.**

| Factors | Estimate | Standard Error | Z value | P value |
|---|---|---|---|---|
| HIV | 7.86e-02 | 2.45e-02 | 3.21 | 0.0013 |
| BCG | -1.29e-02 | 6.35e-03 | -2.01 | 0.0427 |
| GDP per capita | -1.33e-04 | 4.74e-05 | -2.81 | 0.005 |
| Weight for Age | -7.59e-03 | 9.72e-03 | -0.43 | 0.435 |
| Death during TB treatment | -1.10e+01 | 3.61e+00 | -3.034 | 0.002 |

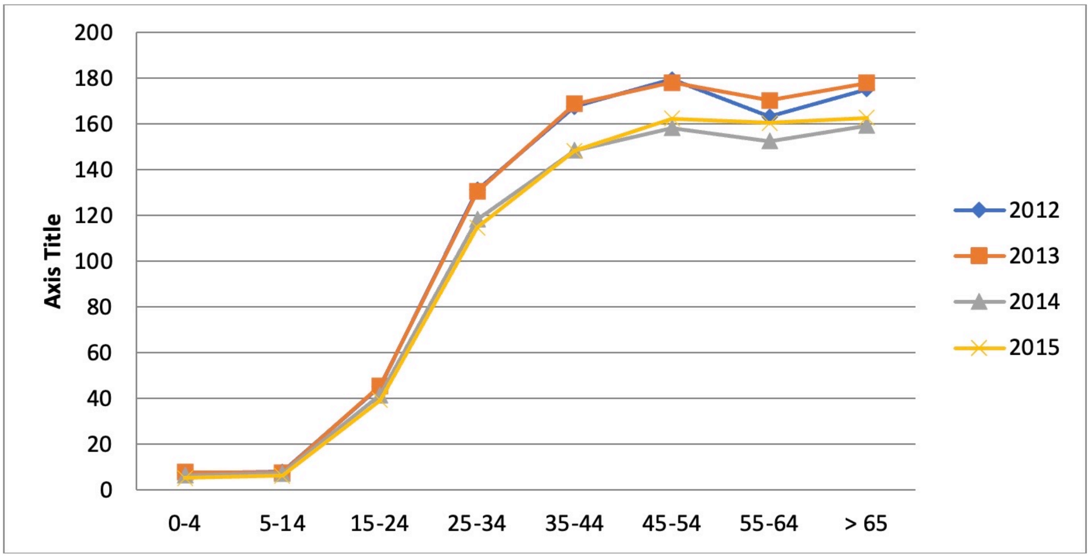


**Figure 1. Age-standardized case notification rate per 100,000 for males in Nigeria 2012-2015.**

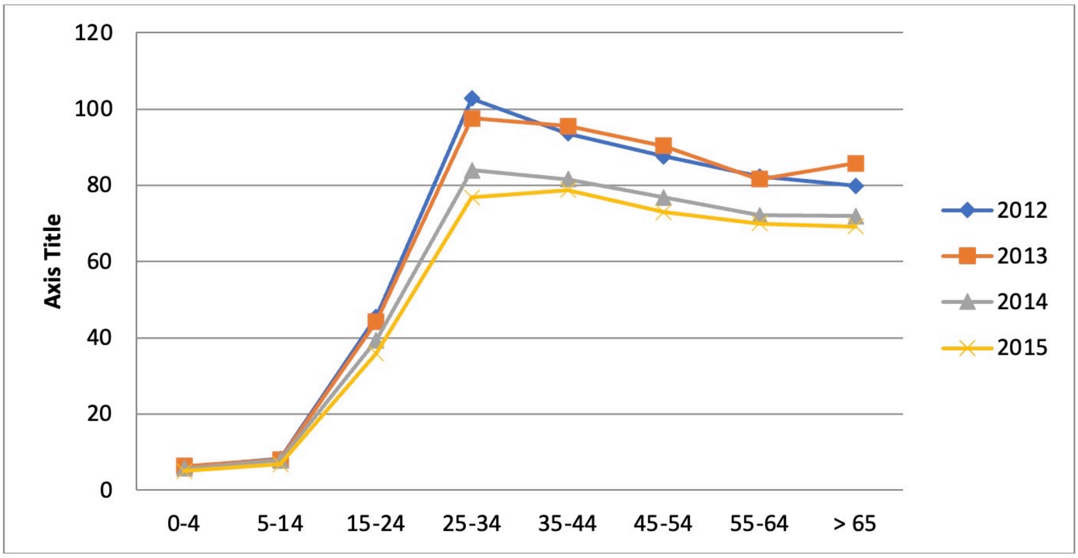


**Figure 2. Age-standardized case notification rate per 100,000 for females in Nigeria 2012-2015.**

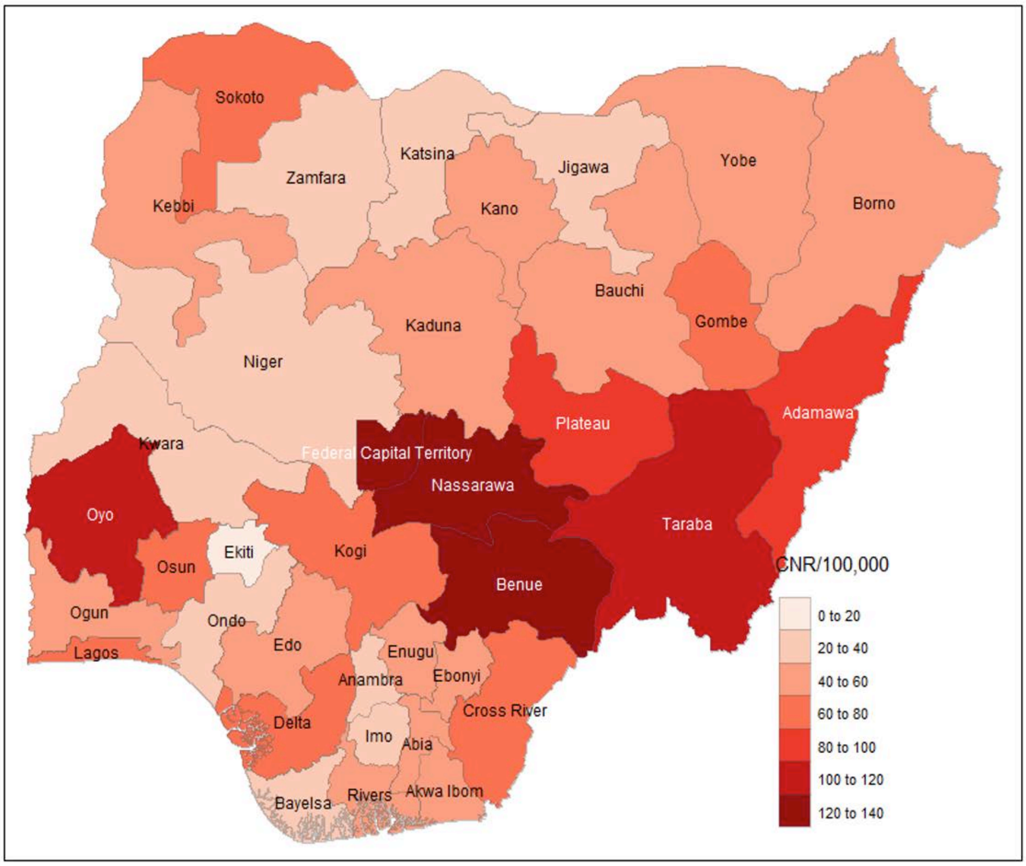


**Figure 3. Average TB Case notification rate per 100,000 2012-2015 in Nigeria.**

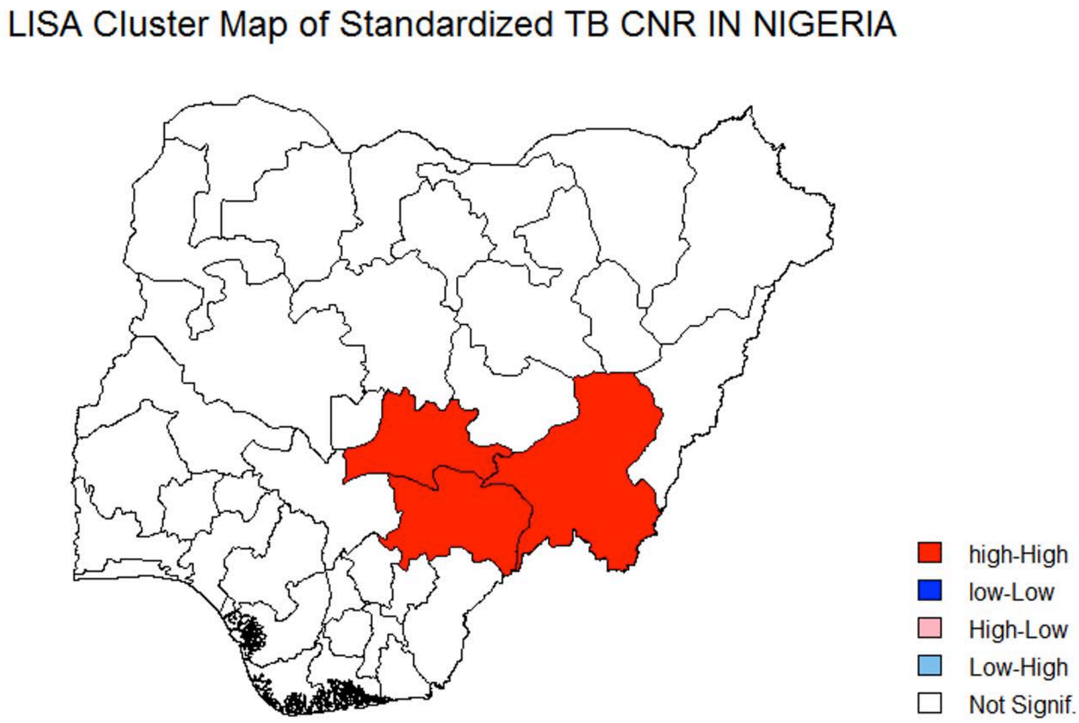


**Figure 4. Significant clustering of TB in states using Local Indicator Spatial Autocorrelation Moran I statistic.**