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An ecological study of the factors associated with childhood tuberculosis in Nigeria

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Abstract

Background: Childhood tuberculosis (TB) account for about 6% of the global TB burden, but there is a paucity of data on childhood TB at the national and state level in many countries in Sub-Saharan Africa.
Objective: To assess the childhood TB case notification rates and explore associated factors at the state level in Nigeria.
Methods: A retrospective ecological study was carried out to determine the childhood TB case notification rates in the 36 states and the Federal Capital Territory (FCT) in Nigeria. TB data was retrieved from the National TB and Leprosy Control Programme (NTBLCP) 2014 Annual Report using a proforma. The association between TB case notification rate at the state level and the six selected explanatory variables (Human Development Index, Bacillus Calmette-Guerin [BCG] coverage, percentage underweight, HIV positivity rate, mean household size and population density) were carried out using negative binomial regression in R statistical software.
Results: A total of 91, 353 TB patients were notified to the World Health Organization (WHO) in 2014 by the NTBLCP. Of these, 5463 (6%) were children aged 0-14 years. The childhood TB notification rate was 6.99/100,000 population. The highest childhood TB case notification rate was recorded in Nasarawa State followed by Lagos and Oyo States. There were significant associations between childhood TB case notification rate and HIV positivity rate, percentage underweight, household size, population density and BCG coverage.
Conclusion: The study showed that childhood TB case notification rate in Nigeria was low. TB case notification rate was associated with high HIV rate, percentage underweight, household size, population density and BCG coverage. There is the urgent need to address the associated risk factors to effectively control childhood TB in Nigeria.

Keywords: Childhood; Ecological study; HIVV; Tuberculosis; Nigeria.

Introduction

Tuberculosis (TB) remains a major public health problem, particularly in Sub-Saharan Africa, with considerable morbidity and mortality despite the implementation of the Directly Observed Therapy, Short Course (DOTS) and the STOP TB strategies over the last two decades. [1] The implementation of these policies led to a significant reduction in TB prevalence and mortality rates in many regions of the world. [1] Of the 22 countries with high TB burden, nine are within Africa, and Nigeria is ranked 4th with TB prevalence of 330/100,000 population in the year 2014. [2] The persistent TB epidemic in Africa has been attributed to HIV infection, underdevelopment and poverty among other factors. [3]

TB in children is mainly acquired from adults with active TB as child to child transmission of TB is very rare. [4, 5] Therefore, childhood TB is a measure of recent transmission of TB in the community. The World Health Organization (WHO) estimated that children account for about 6% (approximately 530, 000 cases) of the global TB burden. [6] Despite this high burden, childhood TB has received little attention due to several factors. Some of these factors include the difficulty in the diagnosis of TB in children, emphasis on the national reporting of TB case notification on smear positives, misconception that childhood TB was a low public health priority and the misconception that childhood TB will be curtailed only by controlling the disease among adults. [7, 8]

TB is associated with poor living conditions within communities. The ecological risk factors such as overcrowding, low socioeconomic status, poor quality housing conditions, indoor air pollution and other measures of deprivation can provide the necessary environmental conditions required for the propagation and community spread of the TB bacilli. [9] The study of the contextual community level risk factors to the development of TB is critical in mounting an effective strategy for the control of the disease.

In spite of the report of 91,353 TB cases to the WHO by the National Tuberculosis and Leprosy Control Programme (NTBLCP), in 2014, [10] there is paucity of data on childhood TB in Nigeria as a whole as well as at the 36 states and the Federal Capital Territory (FCT). Therefore, this study was conducted to assess the burden of childhood TB in the 36 states of the federation and the FCT and its associations with state-level risk factors.

Methods

The study was an ecological study of TB cases in children aged 0 to14 years, notified by the 36 states and the FCT to the NTLCP between January 1st and December 31st, 2014.

Tuberculosis Control Programme in Nigeria

The NTBLCP was established by the Federal Government of Nigeria in 1988 with the mandate to reduce the morbidity and mortality associated with TB to a level where it will no longer be a disease of public health importance. [11] The DOTS management of TB and the STOP TB strategy were also adopted by the NTBLCP in 1933 and 2006 respectively for the control of TB. The TB data from each Local Government Area (LGA) are summarised at state level before transmission to the central unit of the NTBLCP. The data from the NTBLCP are further summarised annually and reported to the World Health Organization. [11]

Diagnosis of childhood TB in Nigeria

In line with the NTBLCP guidelines, [11] the diagnosis of TB in children is made from by both the general health care workers and the medical officers. In instances where sputum smear for Acid Fast Bacilli (AFB) is positive, the general health care worker can make a diagnosis of TB and initiate treatment, in particular among the older children. In situations where sputum AFB test result is negative, the diagnosis of childhood TB is exclusively made by the medical officers. Children who cannot produce sputum or who have negative sputum AFB test results and who present to a DOTS facility where there are no medical officers are usually referred to facilities where there are medical officers for specific diagnosis.

The national TB programme defined childhood TB as TB occurring in children below 15 years. Two sputum samples are usually obtained from children who are old enough to produce sputum or in some cases, gastric aspirates are obtained for AFB test. If any of the sputum or gastric AFB test is positive for TB, the child is classified as sputum smear-positive pulmonary TB. For children with negative AFB results, other diagnostic tests like chest radiography, tuberculin skin test, erythrocyte sedimentation rates are performed to aid the diagnosis of TB. If the radiographic findings are consistent with the clinical features of TB, the child is diagnosed as sputum smear-negative pulmonary TB. Children with extra-pulmonary TB are usually diagnosed in secondary and tertiary health facilities, where facilities for histological and radiological diagnosis are available, depending on the part of the body affected.

Definition of terms

a) TB case notification rate was calculated by dividing the number of TB cases notified by each state with the 2014 projected population x 100,000 population. The childhood TB cases reported per state were obtained from the annual TB case report of the NTBLCP. [12]
b) The Human Development Index (HDI) was obtained from the 2009 Human Development Report in Nigeria. [13]
c) The HIV infection rate was obtained from the HIV Sentinel Surveillance Report for the year 2010. [14]
d) The population for each state was obtained from the National Population Commission for the year 2006. [15] This was projected to the year 2014 at an annual rate of 2.8%. The population density was obtained by dividing the projected population in 2014 by the total area of the state in kilometres.
e) The percentage weight for age (WFA) was used as an indicator of malnutrition (underweight) while the percentage BCG coverage was obtained from the Millennium

Development Goal (MDG) document for Nigeria in 2010. [16]

f) The household size for each state for 2010 was obtained online from the National Bureau of Statistics website. [15] This was adopted as a measure of household overcrowding.

The explanatory variables were intentionally taken before the outcome variable (Childhood TB) to show a temporal relationship between the independent and the dependent variable.

Data analysis

The data were checked for collinearity by examining the correlation between the dependent (Childhood TB CNR) and the explanatory variables (Human Development Index, BCG coverage, percentage underweight, HIV positivity rate, mean household size and population density). The association between the outcome variable and state level independent characteristics was tested using negative binomial regression to account for the overdispersion in the data. The final model for the multivariate analysis included six covariates or explanatory risk factors. In this statistical analysis, the model [9] took the form of:

$$\log \lambda i = \beta_0 + \beta_1 x_{i1} + \beta_2 x_{i2} + \ldots + \beta_k x_{ik} + \sigma\varepsilon + \log(pop_i)$$

where:

i=1…… 37],

λ is the expected childhood TB cases in the 36 state and the FCT,

xi represents each standardised ecological measure (with its associated β_1, $\beta_{2\ldots}$

β_k represents the regression coefficients associated with the standardised ecological measure),

σε is the disturbance or error term

Pop is the projected 2014 population (age 0–14 years) in the states and FCT.

The log (popi) term has no regression coefficient because it served as an offset variable. The σε term represents error and dispersion in the form of a negative binomial distribution. The exponent of each βj 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 $P < 0.05$.

Ethical consideration

Permission was sought from the National Tuberculosis and Leprosy Control Programme for the use of the childhood TB data. Data for the covariates were obtained from the secondary data of the Federal Government of Nigeria which is openly and freely available. [13-16]

Results

A total of 91, 353 cases of TB were reported in Nigeria in the year 2014. Of this, 5, 463 (6%) were children aged 0 -14 years. There were slightly more male children (2780; 50.9%) reported compared to females (2,683; 49.1%). Overall, the females aged 0 – 14 years formed 7.3% of all the female cases reported, and this proportion was higher than the percentage of reported male cases formed by male children aged 0 – 14 years in the year 2014 (Table I).

The mean population was 2,112, 6 444 with a Standard Deviation [SD] of 995,498 while the mean number of childhood TB cases reported was 147.5 with SD of 136.69. The mean childhood TB case notification rate (CNR) was 6.99 with an SD of 4.11. The descriptive statistics of the independent state-level ecological variables are shown in Table II.

Table III shows that the national childhood TB case notification rate was 6.99/100,000 population. The childhood TB case notification rate ranged from 0.85/100,000 to 18.01/100,000 population. The childhood TB case notification rate was highest in Nasarawa State (18.01/100,000 population) followed by Lagos (17.45/100,000) and Oyo (17.04/100,000) States. Ekiti State had the lowest childhood TB CNR (0.85/100,000 population) in the country.

Table I: Age and sex distribution of childhood TB cases reported in Nigeria, 2014

Age group	Males	Females	Total
0-4 years	988	835	1823
5-14 years	1792	1848	3640
Total (Children)	2780	2683	5463
Total National 2014	54808	36545	91,353
% of childhood TB among total cases reported	2780/54808 =5.1%	2683/36545 =7.3%	5463/91,353 =6.0%

Table II: Descriptive statistics of the 36 states and the Federal Capital Territory in Nigeria

Characteristics	Mean	SD	Range
Population of children 0-14	2,112,644	995,498.3	718,070 - 5,895,715
Childhood TB Cases	147.6	136.6897	10.00-688.00
Childhood TB CNR	6.99	4.11	0.85- 18.01
HDI	0.4675	0.09	0.28- 0.72
HIV	4.819	2.80	1.00-12.70
Population Density	307.5	447.38	51 - 2695.
WFA (Underweight)	24.56	15.91	12.40- 51.50
HHS	5.154	1.648669	3.20-10.90
BCG vaccine coverage	80.0	19.71	29.10 - 99.00

HDI=Human development Index; HIV= Human Immunodeficiency Virus; WFA=Weight for Age; HHS Household Size.

Figure 1 displays the map of childhood TB CNR in Nigeria. The highest childhood TB CNR was found in Nasarawa State in the north-central geopolitical zone followed by Lagos and Oyo states both in the south-west geopolitical zone.

Table IV shows a multivariate analysis of the relationship between the six ecological variables and childhood TB in Nigeria. Five of the six ecological variables, namely HIV prevalence rates, population density, prevalence of underweight, household size and BCG vaccine coverage were significantly positively associated with childhood TB.

However, the Human Development Index, though negatively related to childhood TB, but the relationship was not statistically significant. The exponentiated risk estimate showed that one unit increase in HIV would increase childhood TB cases by 6%, while one unit increase in percentage underweight will increase childhood TB cases by 4.0%. Also, a unit increase in household size will increase childhood TB by 4.4% a unit increase in population density will increase childhood TB by 0.06% and one unit increase in BCG coverage will increase childhood TB by 1.2%.

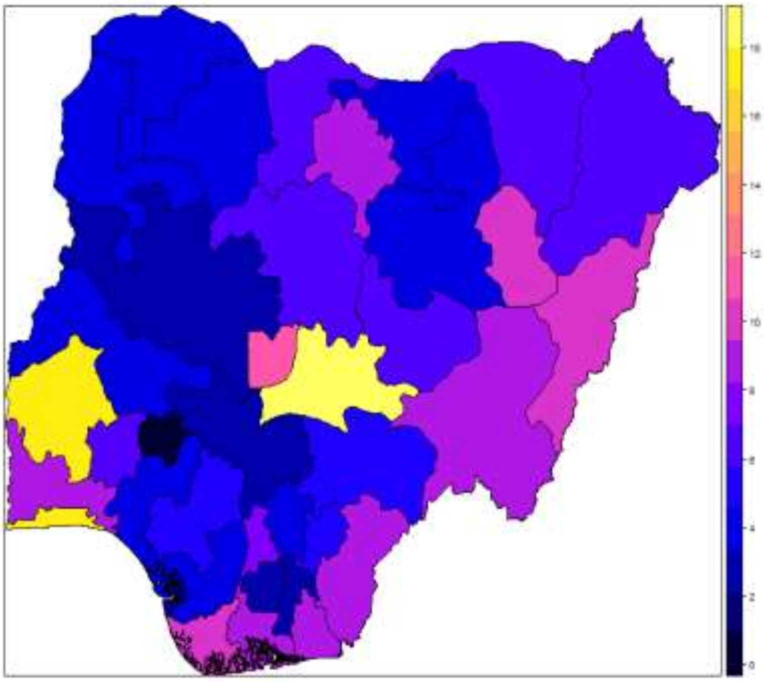

Figure 1: Childhood TB Case notification rate in Nigeria, 2014

Discussion

The present study showed that about 6% of the total TB cases notified in Nigeria in the year 2014 occurred among children aged 0-14 years. This observation was similar to the finding reported in Lagos state, Nigeria in 2015, [17] but lower than 11.9-39 % reported in other high TB burden African countries. [18-20]

Similarly, the childhood TB case notification rate of 7/100,000 population noted in the present study was relatively lower than the rates reported from other high TB burden countries in African which had reported childhood TB case notification rates between 51/100,000 and 300/100,000 population. [18-20] The low childhood TB case notification rate in Nigeria has brought into focus the challenges associated with TB case finding among children. The lack of appropriate and efficient diagnostic tool to confirm the diagnosis of TB among children has been one of the biggest challenges. [21] Majority of young children do not produce sputum, and when they do, they are often smeared negative. [21] In addition, the radiological diagnosis of childhood TB using chest x rays is usually non-specific. This diagnostic dilemma is further compounded by the HIV epidemic and low sensitivity rate of the new diagnostic tools such as the Gene Xpert. [21] In addition, the low case-finding rate may be due to under-reporting of childhood TB to the NTBLCP.

It is attractive to consider the situation as a reflection of the inequity in the distribution of health manpower resource and tools required for the confirmatory diagnosis of childhood TB in the country. Therefore, there is a need for innovative diagnostic techniques that will assist with the diagnosis of TB among children and strengthen the contact tracing of child contacts of bacteriologically-confirmed adults with TB. Furthermore, the capacity of the lower cadre staff at the primary health care facilities needs to be strengthened to enhance the recognition of presumptive childhood TB and referral for proper diagnosis. These efforts could increase childhood TB notification rates in the country.

The present study found that under-nutrition in the form of underweight was associated with TB and one unit increase in the percentage underweight will increase TB by 4.0%. Some evidence suggests that malnutrition affects the genetic expression and immune functions which predispose children to TB. Malnutrition affects the genetic expression of Vitamin D receptor which is important for the immune response against Mycobacterium tuberculosis and thus, impairs immune functions, thus predisposing children to TB. In addition, for children who already had latent TB, malnutrition leads to a progression or worsening of inflammatory response which can lead to TB disease. [22] The need for nutritional support for children in the country is an essential step in building the immunity of children against infections such as TB.

In the present study, HIV infection was also associated with TB. The global resurgence of TB has been attributed to the HIV pandemic, and the highest TB incidence and HIV infection prevalence are recorded in Sub-Saharan Africa. [23] Children bear the greatest burden of TB/HIV co-infection because of infection from their parents. [24] HIV-infected children are at increased risk of acquiring TB infection following exposure to an active TB case and such children have an increased risk of progression from latent TB infection to active TB disease. [23]

The study found that there were high childhood TB notification rates in states of the federation with high BCG vaccine coverage. The observed relationship is rather puzzling, bearing in mind that BCG vaccination is currently recommended as a strategy for the prevention of TB in children. However, several efficacy trials have suggested that the BCG vaccine has a 60-80% protection against severe forms of TB in children but its effect on pulmonary TB varies from one geographical region to another. [25, 26]

Table III: Distribution of childhood TB Case notification rate (CNR)/100,000 among the 36 states and the Federal Capital Territory in Nigeria, 2014

States	TB Cases (0-14yrs)	Population (0-14yrs)	CNR/100,000 pop.
Abia	40	1344118	2.98
Adamawa	187	1883947	9.93
Akwa Ibom	169	1935933	8.73
Anambra	139	1982134	7.01
Bauchi	105	2965463	3.54
Bayelsa	85	861623	9.87
Benue	120	2602551	4.61
Borno	150	2571619	5.83
Cross River	121	1472585	8.22
Delta	78	2045843	3.81
Ebonyi	57	1196266	4.76
Edo	74	1569411	4.72
Ekiti	10	1181061	0.85
Enugu	56	1547039	3.62
Federal Capital Territory	85	718070	11.84
Gombe	156	1490638	10.47
Imo	46	1884223	2.44
Jigawa	94	2754462	3.41
Kaduna	255	3750905	6.80
Kano	487	5895715	8.26
Katsina	253	3745801	6.75
Kebbi	78	2096427	3.72
Kogi	64	2000163	3.20
Kwara	60	1367270	4.39
Lagos	688	3943135	17.45
Nasarawa	205	1138464	18.01
Niger	75	2472268	3.03
Ogun	159	1884969	8.44
Ondo	78	1751243	4.45
Osun	104	1676342	6.20
Oyo	475	2788355	17.04
Plateau	117	1874305	6.24
Rivers	212	2499970	8.48
Sokoto	83	2340163	3.55
Taraba	118	1394745	8.46
Yobe	89	1444895	6.16
Zamfara	91	2095724	4.34
National	5463	78167845	6.99

In addition, the challenges of maintaining the cold chain and poor techniques of vaccine administration may contribute to the positive association between BCG vaccine coverage and childhood TB observed in the present study. Indeed, a systematic review and meta-analysis have suggested a protective effect of BCG. [27]

Though the present study is limited in providing a cause and effect relationship between BCG vaccination and TB in children at the individual level, further research will be required to ascertain the actual effect of BCG vaccination on childhood TB in the country.

Table IV: Multivariate negative binomial regression analysis of childhood TB case notification rate and state-level ecological factors in Nigeria

Characteristics	Estimate	Std Error	Z values	*P* values	Significance
HDI	-1.569e-01	3.546e-01	-0.367	0.7135	NS
HIV	5.708e-02	4.273e-01	4.621	3.82e-06	Sig ***
Population Density	6.258e-04	6.586e-05	9.502	< 2e-16	Sig ***
WFA	3.926e-02	4.462e-03	8.798	< 2e-16	Sig ***
HHS	4.304e-02	2.191e-02	1.964	0.0495	Sig *
BCG Vaccine Coverage	1.242e-02	2.432e-03	5.106	3.29e-07	Sig ***

Std Error – Standard Error Sig* - Significance at p<0.01 Sig* - Significance at p<0.0001**
HDI=Human development Index; HIV= Human Immunodeficiency Virus; WFA=Weight for Age; HHS = Household Size.
Residual deviance: 508.12 on 26 degrees of freedom
AIC [Akaike Information Criterion]: 5507.2

The study also found a positive association between population density and childhood TB notification rates in the country, similar to the findings in some previous studies. [28, 29] High population density increases the risk of spread of TB especially among children, due to their low immunity. Similarly, the present study found a positive association between childhood TB and household size. This finding was similar to previous reports from other African countries. [30, 31] The increased risk of childhood TB in states where household size is relatively large is possibly as a result of prolonged contact between children with low immunity and an index TB case within the household.

The Human Development Index, which is a measure of socioeconomic situation of the states, was not associated with childhood TB case notification rate in this study. However, some previous studies [32, 33] have shown that the socio-economic status of individuals can influence their rate of exposure to TB bacilli, vulnerability to infection, progression from infection to disease and the consequences or outcome of treatment for TB disease. [34] In addition, poverty influences access to health information concerning TB as well as access to diagnostic and treatment services. These factors culminate in delay in accessing quality treatment. The association between poverty and TB in Africa is not consistent. [35, 36] There is still a need for further research on the role of poverty in childhood TB.

This study is limited by its difficulty in extrapolating a cause and effect relationship between the childhood TB case notification rates and the six variables as they exist at the area level to the individual level as this will amount to ecological fallacy. However, this study is useful in providing a context to childhood TB and generating hypothesis which can be explored by a more analytical methodology. The use of multi-level analysis can be helpful in comparing the ecological and individual-level factors which can be explored in future research. In addition, the study analysed childhood TB data notified to the NTBLCP which may be confounded by several other factors such as the availability of skilled health manpower to diagnose childhood TB, health infrastructure for diagnosis and access to diagnosis. Unfortunately, the first national TB survey in the year 2012 did not include children. That was, indeed, a missed opportunity but there is an urgent need to estimate the actual burden of childhood TB and determine factors which may be responsible for the TB situation in the country.

Conclusion

The childhood TB case notification rate in Nigeria was low, and it was positively associated with HIV infection, underweight, household size, population density and BCG vaccine coverage. There is an urgent need to address these area-level determinants of childhood TB and improve case finding efforts, in addition, to prompt treatment of adults with TB to reduce the transmission of infection to children.

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