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Bacteriological Prevalence of Tuberculosis Among Children Seen in Health Facilities in Nasarawa State, Nigeria

Attah Caleb Joseph^{1*}, Oguiche Stephen², Egah Daniel³, Banwat Mathilda⁴,
Adgidzi Godwin¹, Nandi Ishaya Tokit⁵

Affiliation

¹Infectious Disease Unit, Department of Pediatrics, Federal Medical Centre, Keffi, Nasarawa State, Nigeria

²Infectious Disease Unit, Department of Pediatrics, Jos University Teaching Hospital, Plateau State, Nigeria

³Department of Medical Microbiology, Jos University Teaching Hospital, Plateau State, Nigeria

⁴Department of Community Medicine, Jos University Teaching Hospital, Plateau State, Nigeria

⁵Department of Family Medicine, Jos University Teaching Hospital, Plateau State, Nigeria

*Corresponding author: Attah Caleb Joseph, Infectious Disease Unit, Department of Pediatrics, Federal Medical Centre, Keffi, Nasarawa State, Nigeria, Tel: +234 8069 231690, E Mail: attah.caleb@yahoo.com

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Abstract

Background: Tuberculosis, a disease of significant public health importance remains a leading cause of childhood morbidity and mortality globally. Under-reporting of new cases is a major setback in the correct estimate of the global burden of pediatric TB. Data on pediatric TB from TB-endemic countries being limited. It is recommended that continuous research be conducted to ascertain and better understand the magnitude of the problem and to provide reliable, timely and cost-efficient information for action.

Objective: This study was undertaken to determine the bacteriological prevalence of tuberculosis and TB-HIV co-infection among children seen in health facilities in Nasarawa state, North-Central Nigeria.

Subjects and Method: The study subjects consisted of one hundred and fifty (150) children aged 18 months to 15 years who were selected using multi-stage sampling technique. Data, was obtained from their care-givers using interviewer administered questionnaires. The study subjects had their sputum or gastric aspirates samples collected for acid-fast bacilli microscopy and culture. Blood samples were taken for HIV screening. Data was analyzed using SPSS statistical software version 17.0.

Results: The ages of the subjects averaged 9.12 ± 4.66 years and majority of them were females with male to female ratio of 0.92:1. The prevalence of tuberculosis found among them by microscopy and culture are 16.7% and 30.0% respectively while the prevalence of definite TB case was 32% which is 5.5 times higher than the reported national average. The prevalence of 10.0% for TB-HIV co-infection was also found among the study subjects.

Conclusion: There is a high burden of pediatric TB in Nasarawa State (higher than average national prevalence). This study can be extended to six Geopolitical regions of Nigeria, to find out the true situation nationwide.

Introduction

Tuberculosis is the first health condition that was declared by World Health Organization (WHO) as a "Global Emergency". WHO gave a global estimate of TB incidence in the year 2008 to be 9 million cases annually, and of this, about 1 million (11%) occur in children (under 15 years of age) [1-3]. Of these childhood cases, 75% occur annually in 22 high-burden countries that together account for 80% of the world's estimated incident cases; Nigeria is listed among these countries. Under-reporting was the major setback in the WHO correct estimate of global burden of pediatric TB cases because of the diagnostic challenges and poor record keeping among high disease burden countries [1]. The diagnostic challenges are worsened by the undue reliance on sputum smear microscopy for diagnosis whose yield is poor

in children (<10-15%) due to the paucibacillary nature of their TB, and in most cases are unable to produce sputum. Thus, this inadvertently keeps out more than 95% of TB cases among children who are younger than 12 years from being diagnosed [2-4].

Approximately 2 million persons globally die each year from active TB despite the existence of effective treatments for both latent infection and active disease, and more than half of all deaths occur in Asia. Every 15 seconds, one of every three persons to die from TB is a child [2,3]. Second to Asia, Africa appears next on the list of continents with high prevalence of TB. The number of incident cases in the African Region is still on the increase with estimate of 2.6 million (29% of global burden) in 2013 compared with 2.3 million (25.5% of global burden) in 2008 [2-5].

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According to the 2014 WHO global tuberculosis report, Nigeria was ranked 3rd among the 22 high TB burden countries globally and the 1st in Africa with incidence of 340,000-880,000 [5]. This estimate is however approximately two times higher than the previous estimates of 2011 and this underscores Nigeria's high TB burden. Although over-diagnosis does occur, under-diagnosis is more frequent especially among children due to diagnostic challenges. This problem of under-diagnosis in children is clearly seen by the low national reported pediatric caseload of 1.4% in 2011 and 5.8% in 2013 [5,6]. The total number of cases and deaths are still rising due to population growth, therefore there is need to ascertain the present prevalence in our environment [7].

Materials and Method

This study was a health facility based carried out in Nasarawa State North-Central Nigeria. The climate is tropical and the vegetation is Guinea Savannah which is favorable for rearing of livestock with seven Game Reserves [8].

The central towns in the state have grown in the recent time into major urban centers with a high population influx as a result of ethno-religious crises and insurgents terrorist attacks in North-Eastern Nigeria. These towns are now major truck stops for long distance drivers and a beehive of social and commercial activities in the midst of low literacy and high fertility rate [9-12].

The study design was a facility-based cross-sectional descriptive study that was carried out over a period of six months; February 2012 to July 2012.

The sample size was calculated to be 150 children based on the 8.9% prevalence of TB in children taken from the reported percentage of smear positive microscopy in the bacteriology study of childhood TB in Ibadan, Nigeria [13].

A multistage sampling technique was used to select the study subjects. Stage one was the selection of 3 LGAs, one from each of the senatorial districts by simple random sampling (SRS) technique using a table of random numbers. The selected local governments were Lafia, Keffi and Akwanga. Stage two was the selection of six health facilities, two each from the 3 LGAs by SRS technique by balloting. Stage three involved the selection of the study subjects using systematic sampling technique in which the initial subject who met the eligibility criteria was selected using SRS by balloting, after which the sampling interval of 2 or 3 (as calculated for each LGA) was used to select eligible subjects until the predetermined sample size for the health facility was reached. A record was kept of the names, gender and hospital number of selected subjects so as to avoid reselection of subjects during the next clinic or hospital visits.

The inclusion criteria were children age 18 months to 15 years old seen in the six selected health facilities in three LGAs in Nasarawa state; written informed consent, including readiness to comply with the processes of sample collection. These included subjects who were receiving in-patient and ambulatory services. Children who are on Anti-tuberculosis chemotherapy were excluded from the study because it may affect the bacteriology giving false negative results.

Ethical clearance for the study was obtained from the Human Research and Ethical Committee of the Nasarawa state Ministry of Health.

A written informed consent was sought from parents/caregivers in addition to child assent. The nature of the study, aims and objectives were explained in detail to the parents/caregivers/subjects by the researcher and where necessary interpreter is used. Where they decided

to opt out at any stage of the study they were free to do so and they were not deprived of any consultation or treatment.

Counseling of subjects and caregivers on HIV/AIDS was done in two phases which are pre- and post-test. Where the result is positive, information like confirming the diagnosis, treatment options, care of the child, screening of parents/siblings for HIV, issues concerning disclosure and shared confidentiality were discussed with caregiver /subject to help them decide on a realistic course of action that is suitable for the family.

A designed questionnaire was administered to get information on personal data, medical, and family history from each subject in each of the selected health facility.

Specimens of either sputum for subjects ≥ 5 years or gastric wash-out for subjects < 5 were used for Bacteriological study which includes Acid Fast Bacilli (AFB) microscopy using Ziehl-Neelsen stain and mycobacterium culture on Egg-based media (Löwenstein-Jensen) in the reference laboratory in Jos University Teaching Hospital (JUTH). Results were recorded in the questionnaire form of each subject.

For the purpose of international standardization in line with WHO recommendation, a definite tuberculosis case definition was adopted for reporting TB cases in this study. This is simply defined as any subject with either culture positive or AFB microscopy positive in two of his/her samples or has the combination of positive results in both culture and AFB microscopy. In other words, a case of TB is reported in this study as AFB microscopy positive (in two smears)+culture negative, or culture positive+AFB microscopy negative, or AFB microscopy positive (in two smears)+culture positive [14].

All subjects' data in the questionnaire form were entered into the computer using Microsoft excel and analysed using the SPSS statistical software version 17.0. Categorical variables were cross tabulated using frequencies and percentages, whereas quantitative variables were summarized using mean, standard deviations, median or range as appropriate. The prevalence of TB and TB/HIV co-infection were expressed as proportion. Student t-test was used for comparison of means of variables. The chi square test was used for testing significance of association between categorical variables on contingency tables. All tests of significance were two-tailed. P-value < 0.05 was taken to indicate statistically significant difference.

Results

A total of 150 subjects were enrolled into the study with mean age of 9.12 ± 4.66 years and median age of 10.0 years. Of the 150 subjects studied 72(48%) were males while 78(52%) were females with male to female ratio of 0.92:1.

Sputum and gastric aspirates samples were collected from 110 and 40 of the study subjects respectively. Out of the 110 sputum samples 41 (37.8%) were found to have definite TB, whereas from 40 gastric aspirates samples 7 (17.5%) of them were diagnosed of definite TB and this is statistically significant ($p=0.022$).

The prevalence of tuberculosis in the study population by microscopy and culture were 25/150 (16.7%) and 45/150 (30.0%) respectively while the prevalence of definite TB case is 48/150 (32%). The prevalence of TB/HIV co-infection is 15/150 (10.0%).

Akwanga LGA has the highest TB prevalence among its population 15/39 (38.5%) followed by Lafia and Keffi LGA's with prevalence of 22/70(31.4%) and 11/41(26.8) respectively, but the difference is not statistically significant ($p=0.532$) as shown in Table 1.

Within the age groups, children between the ages 5 - < 10 years have the highest prevalence of definite TB (37.1%) compared to under fives



(20.0%) and the adolescents (35.0%) but this difference is not statistically significant ($p=0.215$).

For the age and sex distribution of definite TB Cases, equal number of males (24) and females (24) were diagnosed. Amongst the males with definite TB, the adolescents have the highest prevalence (60.7%) followed by the age group 5-<10 years (46.2%) and under-fives (14.3%). For the females under-fives have the highest prevalence (85.7%) followed by the age group 5 - <10 years (53.8%) and adolescents (39.3%). There was no statistical significance ($p=0.085$) in the differences of the age and sex distribution as shown in Table 2.

Age group (years)	Definite TB (%)	No TB (%)	Total
1.5 - <5	7(20.0)	20(80.0)	35(100.0)
5 - <10	13(37.1)	22(62.9)	35(100.0)
10 - 15	25(35.0)	52(65.0)	80(100.0)
Total	48(32.0)	102(68.0)	150(100.0)

Table 1: Prevalence of definite TB by age groups of study subjects.

Age group (years)	Male (%)	Female (%)	Total
1.5 - <5	1(14.3)	6(85.7)	7(100.0)
5 - <10	6(46.2)	7(53.8)	13(100.0)
10 - 15	17(60.7)	11(39.3)	28(100.0)
Total	24(50.0)	24(50.0)	48(100.0)

Table 2: Age and sex distribution of definite TB cases (n=48).

The correlation of results of AFB microscopy and culture for TB/HIV and TB/non-HIV among definite TB cases (n=48) is shown in Table 3. More Acid-fast bacilli were detected by culture 23/48 (47.9%) than microscopy 3/48 (6.3%). AFB culture had a higher yield amongst TB/HIV co-infected (22.9%) and TB/non-HIV infected (25.0%) compared to microscopy which had a yield of 2.1% and 4.2% respectively. These differences were statistically significant ($p=0.047$).

The validity testing of AFB microscopy (Ziehl Neelson) and culture (Löwenstein-Jensen) found in this study shows that culture has higher sensitivity (95.7%) and NPV (98.1%) than AFB which has sensitivity of 52.0 % and NPV of 81.6%. However, both have specificity and PPV of 100%.The differences were statistically significant ($p=0.0001$).

Method And Result	TB/HIV (%)	TB/non-HIV (%)	Total (%)
Microscopy positive + Culture positive	3(6.3)	19(39.6)	22(45.8)
Microscopy positive + Culture negative	1(2.1)	2(4.2)	3(6.3)
Microscopy negative + Culture positive	11(22.9)	12(25.0)	23(47.9)
Total Positivity	15(31.3)	33(68.8)	48 (100)

Table 3: Correlation of results of AFB microscopy and culture for TB/HIV and TB/non- HIV among definite TB cases (n=48).

Discussion

The thirty two percent prevalence of definite TB found among children in Nasarawa state, North central Nigeria is higher than the ones reported previously in other regions of the country which were 8.9%

(Ibadan, South-West), 22.1% (Benin, South-South) and 1.1% (Sokoto, North-West) [13,15,16]. The use of culture method of diagnosis in this study is a possible explanation for the higher prevalence obtained compared to the previous studies cited in that TB culture is known to increase the yield of acid-fast bacilli even when missed by microscopy [17]. Although Ibadan, as previously cited, included culture method of diagnosis; it was characterized by high culture contamination rate which resulted in low yield [14].

The TB prevalence in this study when compared with the reported 2013 national prevalence rate of 5.8% among children is 5.5 times higher [6,18]. This could be due to the inclusion of some DOTs centres in the study which have the capacity to diagnose pediatric TB, and are known to have contributed about 85% of reported TB cases seen in children in the state [19]. The strongest reasons however may lie in the fact that the risk factors for TB exist in high proportion in Nasarawa state. These factors includes the very high HIV infection sero-prevalence of 10.0% among pregnant women attending antenatal clinic in Nasarawa state making it second highest in the nation according to the 2010 national technical report [20]. Other prevailing risk factors are high level of poverty, unhealthy living conditions, low BCG immunization coverage, low maternal educational level; and the recent influx and increasing migrant settlements in Nasarawa state from conflicts areas of the North [10-12]. There has also been the report of increased consumption of unpasteurized milk and increased close contact of general populace with confirmed TB infected herds [8].

Also, the fact of national prevalence rate being lower when compared to the rate found in this study may have emanated from the undue reliance on the compilations of data solely from DOTs programme registry of different states which may not give a true reflection of the pediatric TB burden in the country [1,6,21,22]. Moreso, some of these DOTs centres are known to report low TB rates for children as a result of diagnosis challenges coupled with the paucibacillary nature of pediatric TB, inability of children to produce sputum for bacteriology, difficulties often encountered in obtaining other samples such as gastric washouts, lymph nodes biopsy etc and the inadequate number of trained personnel to make diagnosis of TB [3,4,19,23].

Similarly, the recommendation of national tuberculosis control programme (NTCP) for the use of CXR and TST (mantoux test) as basic tools for diagnosis especially among children with smear-negative TB disease, though widely used is not without its limitations [1,24]. These limitations are also possible strong factors responsible for the under diagnosis and under reporting of pediatric TB in the state and the nation at large, thus reducing the impact of DOTs services among children. The limitations can be traced to; firstly, the unavailability of tools in endemic rural areas with limited resources. Secondly, CXR interpretations are marked by inconsistencies (both inter and intra observer variability), and its reliability depends on expertise of the interpreter; who are mainly concentrated in tertiary health facilities in urban settings. For TST (mantoux test), the tool is not specific for M. tuberculosis infection, and not sensitive in immune-compromised children. Finally, NTCP recommendation for the use of clinical score charts has challenges nationwide due to poor knowledge on its use and application among primary health workers, its poor validity and poor performance particularly in children suspected of pulmonary TB (the



most common form) and in children who are also HIV infected [24,25]. These factors, coupled with poor attitude toward record keeping, contact investigation and routine surveillance have contributed remarkably to the problem of under-reporting of pediatric TB in Nigeria as reflected in the very low national prevalence rate despite the nation's ranking as the fifth among the twenty two high TB burdened countries globally and the second in Africa [5,6]. Therefore the exceptionally high prevalence of TB found in the present study supports the assertion that national average notification figures often may not reveal the disparity in case rates between other parts of the country [26].

The growing association between TB and HIV is globally recognized [17]. The prevalence of TB-HIV co-infection found in this study is 10.0%. This can be explained by the fact that the state is ranked second highest in terms of HIV prevalence in the country and therefore high rates of TB-HIV co-infection are not unexpected as TB is one of the common opportunistic diseases associated with HIV infection [17,27]. Comparing the prevalence of TB-HIV co-infection found in this study to that reported in Cape Town, South Africa by Schaaf et al (2007) [28], shows that the prevalence is approximately twice lower than what was reported from Cape Town where TB-HIV co-infection was found to be 22.3% amongst culture confirmed children. The probable reasons for this discrepancy could be higher prevalence of HIV infection in the general populace of Cape Town as demonstrated by HIV seropositivity of 15.7% amongst women attending public antenatal care facilities (Cape Town) compared to 10.0% in Nasarawa state, and also from declining rates of HIV in Nigeria from effective intervention programs [6,28]. Furthermore the use of more advanced culture medium (Middlebrook 7H9 broth based) in the study from Cape Town could account for higher yield for AFBs and therefore higher prevalence of TB/HIV co-infection.

It was also discovered that, the yield of AFB by sputum production is twice higher than gastric aspirate in this study. This finding is consistent with the report of the study on culture-confirmed childhood TB in Cape Town, South Africa by Schaarf et al. in 2007 [28]. The reason for this could be that sputum samples of TB infected children are heavily laden with AFBs in that it proceeds directly from the lungs without undergoing degradation along its route and few as 10 bacteria/millilitre can be detected by culture [29]. Also TB infected children with ability to produce sputum are usually older children who in most instances have adult form of TB (open TB) [18]. As for gastric aspirate, AFBs are degraded in the acidic environment of the stomach during the overnight fast thereby reducing the quantity of AFBs in the sample [30]. Also children in whom early morning gastric washings are performed usually have paucibacillary form of TB and couple with the fact of diluting samples with 10-20 ml of normal saline during procedure reduces the concentration of bacteria/milliliter thereby affecting the overall yield of AFBs from gastric aspirates [30,31].

Consequently, correlation of results of AFB microscopy and culture for TB/HIV co-infection and TB/non-HIV infected subjects show that more AFB are detected by culture alone than microscopy with approximately forty two percent of the AFB missed by microscopy being detected by culture. These data corresponds to observations recorded in a report by Onubugu et al. in 2010 [17]. Added to this fact, the high sensitivity of culture in contrast to microscopy found in this

study demonstrate the superiority of culture method of diagnosis over microscopy and therefore suggest that culture of Mycobacterium tuberculosis remains the gold standard in pediatric cases.

Summarily, the health implication of the high TB prevalence found in this present study shows that extra efforts and commitment are needed in our national tuberculosis control programme geared towards intensifying intervention and TB control measures in states with high prevalence based on data generated from periodic research, otherwise high case rates are likely to continue. The fact that more AFBs are detected by culture than microscopy is an indication that there is an urgent need for the country to increase capacity for culture facilities in TB laboratories and provision of long awaited GeneXpert MTB/RIF machine with appropriate cartridges for children's different samples such as Gastric washouts, Cerebrospinal fluids, pleural fluids etc. This will avert the consequences of undue reliance on microscopy that include delayed or misdiagnosed cases, contributing to delay in treatment and increased morbidity and mortality rates among children.

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