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Original Article

Tuberculosis/HIV Prevalence and Treatment Success among Children Receiving Care in Two Tertiary Health Facilities within Ogun State, Nigeria

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Abstract

Background: About 1 million children become ill with tuberculosis every year, representing 10-12% of all cases of tuberculosis notified globally. HIV infection in children is often due to transmission from mothers to children. HIV infection in children increases their risk of having tuberculosis. Sub-Sahara Africa has one of the highest TB incidences and HIV prevalence thus children in this region bear a huge burden of TB/HIV infection. In addition, the treatment success rate in many countries is rarely disaggregated to evaluate children. Thus, this study aims to determine the prevalence of TB/HIV coinfection and treatment success among children with tuberculosis attending clinics in two tertiary institutions in Ogun State, Nigeria.

Methodology: The study was a retrospective cohort study of routine programme data of all children diagnosed and treated for tuberculosis from January 2015 to June 2017 in two tertiary hospitals in OgunState, Nigeria. The hospitals were Olabisi Onabanjo University Teaching Hospital Sagamu and Federal Medical Centre Abeokuta, Ogun State. Data were retrieved from the facility TB register and analyzed using epi info.

Results: A total of 759 patients were registered for treatment at the two tertiary facilities between January 2015 and June 2017. Of these, 112(14.8%) were children 0-14 years of age. Most of the children (95.54%) had pulmonary tuberculosis. Treatment success was 81.3%. About half (46.4%) of the patients were HIV positive. Age, site of disease, bacteriological diagnosis, and weight at the commencement of treatment were significantly associated with HIV status while none of the socio-demographic variables were associated with treatment outcome

Conclusion: There is a need to look for ways to further improve the current treatment success rate of children with tuberculosis. There should be increased efforts also to find better ways of diagnosing childhood tuberculosis. The high HIV rate among children with TB is of concern and strategies should be put in place to prevent HIV transmission to children.

Keywords: Tuberculosis; HIV; Treatment Success; Coinfection; Prevalence.

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Introduction

Worldwide, tuberculosis infection still causes a high burden of disease. It is the ninth leading cause of death worldwide and the leading cause from a single infectious agent ranking above HIV/AIDS.1 In 2016, an estimated 10.4 million people fell ill with TB.1 Most of these new cases of tuberculosis occurred in the South East Asia region (45%) and Africa region (25%).1
About 1 million children become ill with tuberculosis every year. Children represent 10-12% of all cases of tuberculosis. In 2015, 170,000 children died of tuberculosis and there were an additional 40,000 tuberculosis deaths among children who were HIV positive.2 A child usually gets a TB infection from being exposed to a sputum-positive adult. Young children below ten years of age are at risk of becoming infected with TB bacilli. They are also at high risk of developing active tuberculosis because the immune system of young children is less developed.3It is known that tuberculosis in children can be treated and that most children tolerate the treatment well.2

The magnitude of the burden of childhood tuberculosis in most parts of the world is difficult to accurately estimate. This is because childhood tuberculosis is associated with dilemmas as regards diagnosis as well as the lack of precision with case definitions. Children rarely produce sputum and even when they do, examination of the sputum smear tends to produce negative results. Diagnosis is thus based on a combination of clinical symptoms and non-specific investigations.3Childhood tuberculosis is usually paucibacillary and so does not contribute significantly to disease transmission.4 However, it is a good pointer of recent or ongoing transmission in a community which may represent a failure of prevention measures to an extent.5

In addition, HIV infection is especially common in children due to transmission from mothers to children. As a result of the HIV infection children are at increased risk of tuberculosis.6 Sub-Saharan Africa has one of the highest TB incidences and HIV prevalence. As a result, children in this region bear a huge burden of TB/HIV infection.7 The major challenge to tuberculosis control programmes in Africa is HIV/AIDS. A rise in HIV prevalence increases tuberculosis rates. Hence, the control of tuberculosis is partly dependent on the control of HIV transmission.8

Though WHO estimates that about 10-12% of total tuberculosis case notification is expected to be in children, most national tuberculosis programme reported much less.9 In a study10 done in Nigeria, about 6-7% of the total tuberculosis case notification in Lagos were in children. This may be due to the difficulty in making a diagnosis of tuberculosis in children. Out of the children that were diagnosed, only 77.4% were successfully treated.10 In another study involving three states in Nigeria, it was found that childhood tuberculosis treatment success rate was 83%.8

Treatment success has been identified as an indicator for the performance of the national tuberculosis control programme. It is also very important in preventing the spread of tuberculosis infection because a successful treatment implies that transmission of the infectious agent by the affected individual has been halted.11 Therefore keeping surveillance on childhood tuberculosis is important and instrumental in defining its epidemiology of the disease in children and identifying the predictors of treatment outcome.12

Studies have shown that children with TB/HIV coinfection are more likely to experience higher morbidity and mortality7,13in addition to increased risk of rapid disease progression,14unsuccessful tuberculosis treatment15 and recurrence of tuberculosis infection15,16compared to those children who only had tuberculosis infection.

Though tremendous progress has been made to reach the global target of a 90% treatment success rate among tuberculosis patients in the country, this figure is rarely disaggregated by the national programme to evaluate the outcome among children. Therefore, the effectiveness of the fixed drug combination among children is rarely documented. Few studies have been done to document treatment outcomes in children within Nigeria8,10 and this study will contribute to this objective.

Thus, this study aims to determine TB/HIV prevalence and treatment success of children with tuberculosis attending clinics in two tertiary institutions in Ogun State, Nigeria, and to determine the factors associated with treatment success.

Materials and Methods

Study Area

The study was carried out in two tertiary hospitals in Ogun state. Ogun State is one of the 36 states in Nigeria. It was created in 1976 and has a total land area of 16,409.26sq.km. Its boundaries are Oyo and Osun states in the North, Ondo State in the east, Lagos State in the south, and the Republic of Benin in the West. The Capital is Abeokuta which lies about 100km north of Lagos, Nigeria's business capital. The projected population of the state is 3,728,098 according to the national census carried out in 2006. The state is divided into 3 senatorial districts and there are two public tertiary facilities located in the state.17

Olabisi Onabanjo University Teaching Hospital is a tertiary hospital located in Sagamu Ogun State, Nigeria. The town (Sagamu) is an urban area located about 50 km from the metropolitan city of Lagos with an estimated population of 253 421 as of the 2006 census. The teaching hospital was established in the year 1986 with the primary aim of providing healthcare

service to the indigene of Ogun State and Nigeria as a whole. It is a 247-bed capacity hospital that caters to patients referred from hospitals located within and outside the state.

Federal Medical Centre Abeokuta is a tertiary hospital in the state capital. It is a 250 bedded specialist hospital which was established on the 21st of April 1993. The hospital provides medical services to people of Ogun state and other neighboring states. It also serves as a referral centre for DOTS clinics in the state.

Study Design

The study was a retrospective cohort study of routine programme data of all children diagnosed and treated for tuberculosis from January 2015 to June 2017 in two tertiary hospitals in Ogun State, Nigeria. The hospitals are Olabisi Onabanjo University Teaching Hospital Sagamu and Federal medical Centre Abeokuta, Ogun State.

TB programme in Ogun State

The National Tuberculosis Programme defined childhood tuberculosis as Tuberculosis occurring in children less than 15 years of age, and any child with cough for ≥2 weeks is considered a presumptive Tuberculosis case. Samples were collected from children who could produce sputum on their own or through gastric lavage/washout for those who could not produce sputum for gene Xpert test or acid-fast bacilli (AFB) test (where gene Xpert test is unavailable). Where any of the tests was positive for Tuberculosis, the patient was classified as bacteriologically confirmed pulmonary Tuberculosis. However, where the result was negative, other diagnostic tests like chest radiograph, tuberculin test, erythrocyte sedimentation rate were performed to aid diagnosis of Tuberculosis. If the radiographic findings were consistent with the clinical signs and symptoms of Tuberculosis, the child was diagnosed as clinically diagnosed pulmonary Tuberculosis. For children who were too young to produce sputum for smear microscopy/gene Xpert test, the diagnosis was made by using a tuberculosis score chart according to the national Tuberculosis guideline. However, according to the guidelines, only a doctor is allowed to make a clinical diagnosis of tuberculosis where sputum results are unavailable.

Treatment of TB in children was free because drugs were provided by the State TB and leprosy programme. The duration of TB treatment was 6 months (except in children who had TB affecting the bone or the meninges). The treatment regimen consisted of 2 months intensive phase of Rifampicin, Isoniazid, Pyrazinamide, and Ethambutol followed by 4 months continuation phase of Rifampicin and Isoniazid. For children with tuberculosis of the bone or meninges, the treatment was extended for a duration of 12 months: 2 months intensive and 10 months continuation phase.

HIV test was conducted for all presumptive tuberculosis patients in line with the national guidelines on HIV testing and counseling. The HIV rapid test kit used first was Determine (determine HIV-1/2 Alere DetermineTM, Japan 2012) and if this was positive then Uni-GoldTM(Trinity Biotech PLC, Wicklow, Ireland 2013) rapid test kit was used in series. A concordance result was regarded as positive. In cases of a discordant result, STAT-PAKR was used as the tiebreaker. For children less than 18 months, a DNA PCR test was carried out to diagnose HIV infection.

The Nigeria National Tuberculosis guideline categorized tuberculosis treatment outcomes as follows.

Cure: This was the proportion of patients among bacteriologically diagnosed patients that completed treatment and had at least two negative smears with an interval of at least 1 month, one of which should be obtained at the end of treatment.

Treatment completed: This was the proportion of patients that completed treatment, but sputum examination results are not available.

Died: The proportion of patients that died before the completion of treatment.

Lost to follow up: This was the proportion of patients that did not take drugs for two consecutive months or more.

Treatment failure: This was the proportion of patients who were bacteriologically diagnosed at the beginning of treatment and whose sputum smear or culture is positive at month five or later during treatment.

Not evaluated: This was the proportion of patients for whom no treatment outcome was assigned. It also includes those transferred out to another treatment unit and where the treatment outcome is unknown to the reporting unit.

Treatment success: Defined as the sum of the cases that were cured and that completed treatment.

Ethical Consideration

Ethical approval for this study was obtained from the Health Research and Ethics Committee of the Olabisi Onabanjo University Teaching Hospital, Sagamu Ogun State. Permission was also sought from the heads of the relevant facilities and clinics that were used. Strict confidentiality was maintained throughout the study. Data obtained was entered into a secured computer where only the researcher had access to it.

Data collection and Analysis

Data were extracted from the facility TB registers and were checked for completeness and accuracy. Data were entered into excel and exported to epi info for analysis. The necessary descriptive and inferential statistics were calculated. The level of significance was taken at $p \leq 0.05$.

Results

A total of 759 patients were registered for treatment at the two tertiary facilities between January 2015 and June 2017. Of these, 112(14.8%) were children <15 years of age. Table 1 shows baseline characteristics of children treated for tuberculosis. About 43 % of the children treated for tuberculosis were less than 5 years of age. The mean age was 6.26± 4.3. Females made up 55.36% of the total number of children treated. Most of the children (95.54%) had pulmonary tuberculosis. However, only 6 (5.36%) of the patients were bacteriologically diagnosed. Table 2 shows the HIV status of children treated for tuberculosis. About half (46.4%) of the patients treated for tuberculosis were HIV positive. Of the positive patients, only 40.4% were on antiretroviral treatment. However, almost all of those who tested positive were on co-trimoxazole Preventive treatment (CPT). Table 3 shows factors associated with HIV status in children treated for tuberculosis. Age, site of disease, bacteriological diagnosis, and weight at the commencement of treatment were significantly associated with HIV status. Table 4 shows treatment outcomes of tuberculosis treatment in children. Treatment success in children treated for tuberculosis was 81.3%. A total of 7(6.3%) children died and 6.3% were not evaluated. Table 5 shows factors associated with the treatment outcome of tuberculosis in children. None of the variables were significantly associated with treatment success.

Table 1: Baseline Characteristics of children treated for tuberculosis

Variable	Frequency n=112	Percentage
Age group (years)		
0-4	48	42.9
5-9	37	33.0
10-14	27	24.1
Sex		
Male	50	44.6
Female	62	55.4
Year of diagnosis		
2015	36	32.1
2016	39	34.8
2017	37	33.1
Site of disease		
Pulmonary	107	95.5
Extrapulmonary	5	4.5
Bacteriologically diagnosed		
Yes	6	5.4
No	106	94.6
Weight at diagnosis (kg)		
4-7	13	11.6
8-11	18	16.1
12-15	30	26.8
16-24	29	25.9
⩾ 25	22	19.6
Mean weight = 18.1 ± 10.9		

Table 2: HIV status of children treated for tuberculosis

Variable	Frequency	Percentage
HIV status	**n=112**	
Negative	60	53.6
Positive	52	46.4
Antiretroviral treatment	n=52	
Yes	21	40.4
No	31	59.6
Cotrimoxazole Preventive Therapy	n=52	
Yes	51	98.1
No	1	1.9

Table 3: Factors associated with HIV status in children treated for tuberculosis

Variable n=112	HIV negative n=60	HIV positive n=52	p-value
Age			
0-4	20(41.7)	28(58.3)	
5-9	18(48.9)	19(51.4)	
10-14	22(81.5)	5(18.5)	<0.01
Sex			
Male	23(46.0)	27(54.0)	
Female	37(59.7)	25(40.3)	0.15
Year of diagnosis			
2015	23(63.9)	13(36.1)	
2016	21(53.9)	18(46.2)	
2017	16(43.2)	21(56.8)	0.21
Site of disease			
Pulmonary	55(51.4)	52(48.6)	
Extrapulmonary	5(100.0)	0(0.0)	*0.02
Bacteriological diagnosis			
Negative	54(50.9)	52(49.1)	
Positive	6(100.0)	0(0.0)	*0.02
Weight			
⩽ 18kg	32(43.8)	41(56.2)	
>18kg	28(71.8)	11(28.2)	<0.01

*Fischer's exact

Table 4: Treatment outcome of tuberculosis treatment in children

Variable	Frequency	Percentage
Cured	12	10.7
Treatment completed	79	70.5
Died	7	6.3
Loss to follow up	5	4.5
Treatment failure	2	1.8
Not evaluated	7	6.3
*Treatment success	91	81.3

*Treatment success is a sum of cured and treatment completed

Table 5: Factors associated with treatment outcome of tuberculosis in children

Variable n=112	Treatment not successful	Treatment successful n=91(%)	p-value
Age group			
0-4	10(20.8)	38(79.2)	
5-9	8(21.6)	29(78.4)	
10-14	3(11.1)	24(88.9)	0.503
Sex			
Male	12(24.0)	38(76.0)	
Female	9(14.5)	53(85.5)	0.201
Year of diagnosis			
2015	9(25.0)	27(75.0)	
2016	4(10.3)	35(89.7)	
2017	8(21.6)	29(78.4)	0.227
Site of disease			
Pulmonary	19(17.8)	88(82.2)	
Extrapulmonary	2(40.0)	3(60.0)	*0.235
Bacteriologically diagnosed			
Yes	2(33.3)	4(66.7)	
No	19(17.9)	87(82.1)	*0.313
Weight at diagnosis (kg)			
⩽18kg	15(20.6)	58(79.5)	
>18kg	6(15.4)	33(84.6)	0.504
HIV status			
Negative	13(21.7)	47(78.3)	
Positive	8(15.4)	44(84.6)	0.396
Total	21(18.7)	91(81.3)	

*Fischer's exact

Discussion

The proportion of children with tuberculosis out of all the notified tuberculosis cases from this study was found to be 14.8%. This finding is similar to what was found in a study carried out in Ethiopia where notified childhood tuberculosis cases made up 13% of all notified cases.18The proportion found from this study is however higher than what has been recorded in some other studies. Another study done to assess treatment outcomes among children in Lagos state showed that 6.3% of cases notified during the study period were childhood tuberculosis cases.10 The finding from this study is also above the 10-12% estimated by World Health Organization. This may be because this study was carried out in tertiary health facilities which have the capacity and technical skills to diagnose tuberculosis in children.

This study also found that only 6% of the children treated for tuberculosis were bacteriologically confirmed. This is lower than what was found in the study done in Thailand where 32% of the cases were bacteriologically confirmed.19 In Lagos state, 20.6% of the children were bacteriologically confirmed.10Another Nigerian study also recorded that 27.8% of the registered childhood tuberculosis cases were bacteriologically confirmed.8The low proportion of bacteriologically diagnosed tuberculosis may be because a large proportion of the study population were children below the age of 5 years. These children can hardly produce sputum which makes the diagnosis with sputum difficult. Also, the yield from samples collected via gastric lavage is low. Therefore, diagnosis of children relies on clinical presentation assisted by radiological and laboratory parameters. This also further highlights the challenge of diagnosing childhood tuberculosis in Nigeria.

From this study, the prevalence of HIV infection in children with tuberculosis was46.3%. Most of the children who were HIV positive were ≤ 5years.This possibly reflects the state of the prevention of mother-to-child transmission of HIV in the region since children who are less than 5 years of age and who are HIV positive are likely to have acquired the infection from their mothers. The prevalence found from this study is higher than what was recorded in a study carried out in Thailand and in Lagos state where the prevalence of TB/HIV coinfection was 27% and 29% respectively.10,19A study done across three states in Nigeria also showed a TB/HIV co-infection rate of 14.9% in these groups of patients.8This study also found that only 40.4% of the patients with TB/HIV coinfection were on antiretroviral treatment and 98.1% of them were on cotrimoxazole preventive therapy. The percentage of children with TB/HIV coinfection on treatment as found from this study is higher than what has been estimated in low and middle-income countries where only about 34% of children less than 15yearswho need antiretroviral treatment are estimated to be receiving treatment. Nevertheless, it should be noted that this value is improving.20,21 The low rate of patients on antiretroviral could be because the data obtained was from the tuberculosis registers which were possibly not updated as regards commencement of antiretroviral treatment by the patients at the retroviral disease clinics.

The treatment success rate in this study was 81.3%.This is higher than what was obtained in some other studies with a success rate of 77% in Sadama and 78.9% in Ethiopia.22,23This is lower than what was obtained in studies done in Russia and Addis Ababa where treatment success rates were found to be 95.1% and 85.5% respectively.4,24 Treatment success in HIV negative cases was 78.3% and 84.6% in HIV positive cases of childhood tuberculosis. This is similar to what was found in a study done in Lagos Nigeria which recorded a treatment success rate of 79.2% in HIV-negativechildren with tuberculosis and 73.4% in children who had TB/HIV coinfection.10 The finding is also similar to what was found in a Nigerian study which found a treatment success rate of 83%.8

This study found that children who were less than 5 years of age were more likely to be successfully treated. This is different from what was found in similar studies done in Ethiopia where children less than 5 years old had a lower treatment success rate.8,21A study done in Lagos showed that children <1 year had the worst treatment outcomes. However, this study did not find age as a significant factor for treatment outcome. This study like the study done in Lagos state found that HIV status, gender, and type of TB were not associated with treatment success.10

Implications

This study revealed that many of the patients had TB/HIV coinfection. There is therefore a need to intensify efforts for the prevention of tuberculosis among HIV-infected children. In addition, it was revealed that the majority of the children with TB/HIV coinfection were less than 5 years of age. This is highly suggestive of mother-to-child transmission of HIV with the implication of the need for more preventive programmesin the context of perinatal transmission of HIV. Although treatment success was 81.3% it may be argued that the clinics have not functioned optimally in ensuring clients' compliance with antituberculosis medications. More efforts, therefore, need to be put into patient care to ensure satisfactory outcomes for the patients.

Strengths and Limitations

The baseline information about the patients in this study was obtained from records. This could have eliminated the effect of recall bias as compared to when patients were asked directly at the time of the study. Multivariate analysis was also done to analyze factors associated with treatment success. However, the retrospective nature of the study makes it difficult to utilize any information which was omitted or not properly documented by the health workers in the different facilities.

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Conflict of interest: nil

Authors Contributions
The first, second, third, and seventh authors conceived the research idea and prepared the first draft. The first, second, third, fifth, and sixth authors collected and analyzed the data. All authors drafted, reviewed the manuscript, and approved the final submission.

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