HIV-TB co-infection in children: associated factors and access to HIV services in Lagos, Nigeria

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Background: Human immunodeficiency virus (HIV) and tuberculosis (TB) are the leading causes of death from infectious disease worldwide. The World Health Organization estimates that the prevalence of HIV among children with TB in moderate to high prevalence countries ranges between 10% and 60%. This study aimed to determine the access to HIV services of HIV-TB co-infected children.

Methods: A retrospective review of data of children diagnosed with TB in Lagos State, Nigeria from 1 January 2012 to 31 December 2013.

Results: A total of 1199 children aged between 0 and 14 years were diagnosed with TB. Of 1095 (91.3%) who underwent testing for HIV, 320 (29.2%) were HIV seropositive. The male-to-female ratio of HIV-TB positive outcomes was 1:0.9. Of the 320 HIV-TB co-infected children, 57 (17.8%) were aged <1 year, 86 (26.9%) 1–4 years and 186 (58.1%) 5–14 years; 186/320 (58.1%) began cotrimoxazole preventive therapy (CPT), and 151 (47.2%) were put on antiretroviral treatment (ART). ART uptake was not significantly higher in facilities where HIV-TB services were co-located ($P > 0.05$).

Conclusion: The uptake of CPT and ART was low. There is a need to intensify efforts to improve access to HIV services in Lagos State, Nigeria.

In 2012 there were an estimated 8.7 million new cases of active tuberculosis (TB) globally,¹ of whom 1.1 million (13%) were estimated to be co-infected with the human immunodeficiency virus (HIV).² In the same year, an estimated 490 000 active cases of TB and 64 000 deaths occurred in children, excluding those co-infected with HIV.³ It is estimated that about 79% of the HIV-TB co-infected cases occurred in Africa, making TB the leading cause of death due to a single infectious agent in the continent.³ In high TB burden countries, children are said to account for 15–20% of all TB cases, compared with 2–7% in low-burden countries.⁴ The interaction between TB and HIV is well described in the literature.^{5–9} HIV has made the diagnosis of TB in children more difficult due to overlapping clinical and radiographic manifestations with other lung diseases,¹⁰ resulting in missed or delayed diagnosis of TB in children. The manifestations of TB are more severe and progression to death more rapid in HIV-positive than HIV-negative children. Conversely, TB accelerates the progression of HIV disease by increasing viral replication and reducing the CD4 count.^{7,11} TB is a common cause of acute pneumonia in African chil-

dren and a common cause of death in HIV-infected children.^{11,12}

The introduction of antiretroviral treatment (ART) has greatly improved the survival of HIV-TB co-infected children. However, studies have shown that coverage of antiretroviral (ARV) drugs is low, particularly in children.¹³ It is estimated that about 34% of children aged <15 years needing ART in low- and middle-income countries receive treatment compared with about 68% of adults.¹³

This study was conducted to determine the prevalence of HIV among children diagnosed with TB and to assess the uptake of HIV services such as cotrimoxazole preventive therapy (CPT) and ART in Lagos State, Nigeria.

METHODOLOGY

Study design

This is a retrospective review of programme data of all children diagnosed and treated for TB between 1 January 2012 and 31 December 2013 in Lagos State, Nigeria. Lagos State has a population of 9.3 million (2006 national census). Health care services in Lagos State are provided by both the public and the private sectors. In the public sector, services are organised at the primary, secondary and tertiary level. The Lagos State Tuberculosis and Leprosy Control Programme (LSTBLCP) commenced in 2003 as a collaboration between the state government, the International Union Against Tuberculosis and Lung Disease (The Union), the World Health Organization (WHO), the Canadian International Development Agency (CIDA) and the United States Agency for International Development (USAID). By the end of 2013, 218 TB treatment facilities under the LSTBLCP were offering the DOTS strategy.

TB diagnosis and treatment

Nigeria's National TB Programme (NTP) has defined childhood TB as TB occurring in children aged <15 years.¹⁴ Any child with cough of ≥ 2 weeks is classified as having presumptive TB. For older children who can produce sputum, two sputum samples are collected for acid-fast bacilli (AFB) testing. If the result is positive, the patient is classified as having sputum smear-positive pulmonary tuberculosis (PTB). If the result is negative, other diagnostic tests, including chest X-ray, tuberculin skin test (TST) or erythrocyte sedimentation rate, are performed to aid in the diagnosis of TB. The child is diagnosed as having sputum smear-negative PTB if the radiographic findings are consistent with TB. For younger children who cannot produce spu-

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KEY WORDS

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TABLE 1 Sociodemographic characteristics of children diagnosed with TB

Variable	Frequency (<i>n</i> = 1199) <i>n</i> (%)
Age group, years	
<1	141 (11.8)
1–4	313 (26.1)
5–14	745 (62.1)
Age mean, $\pm$ SD	7.0 $\pm$ 4.7
Type of facility	
Public	1149 (95.8)
Private	50 (4.2)
Sex	
Male	621 (51.8)
Female	578 (48.2)
Classification of patients	
New	1142 (95.2)
Others	57 (4.8)
Type of TB	
Pulmonary	1086 (90.6)
Extra-pulmonary	113 (9.4)
HIV status	
Positive	320 (26.7)
Negative	775 (64.6)
Not determined	104 (8.7)

TB = tuberculosis; SD = standard deviation; HIV = human immunodeficiency virus.

tum, gastric aspiration is rarely performed, and a diagnosis is usually made using a score chart, according to national TB guidelines. The score chart takes into consideration parameters that include chest X-ray abnormalities, a history of close contact with a smear-positive PTB patient, failure to thrive, poor or no response to antibiotics and TST readings where available. A score of >7 is suggestive of TB. Children with extra-pulmonary TB are usually diagnosed in secondary and tertiary health facilities where there are facilities for histological and radiological diagnosis depending on the organ affected.

Smear microscopy and the treatment of childhood TB notified to the programme are at no cost to the patients because the facilities and reagents needed for the diagnosis and drugs are supplied by the LSTBLCP to the DOTS facilities. The treatment regimen consists of a 2-month intensive phase of rifampicin (RMP), isoniazid (INH) and pyrazinamide (PZA) as a fixed-dose combination and loose tablets of ethambutol, followed by a 4-month continuation phase of RMP and INH given as a fixed-dose combination.

The revised national HIV-TB guidelines in 2012 stipulated that HIV-TB co-infected persons should be commenced on CPT immediately after diagnosis and on ART 8 weeks after starting anti-tu-

berculosis treatment. The preferred ART for HIV-TB co-infected children regimen is lamivudine, tenofovir and efavirenz.

Data collection and analysis

All children diagnosed and treated for TB from 1 January 2012 to 31 December 2013 were included in the study. Information on age, sex, HIV status, type of TB, facility of referral, etc., were extracted from the TB register. HIV testing for children aged <2 years was performed using polymerase chain reaction. Older children underwent HIV testing using rapid test kits Determine HIV-1/2 (Alere Medical Co, Ltd., Chiba-ken, Japan) and Unigold (Trinity Biotech PLC, Wicklow, Ireland), with confirmation undertaken at designated specialised laboratories in the state.

Data were analysed using the Statistical Package for the Social Sciences version 19 (IBM Corp, NY, USA). Frequency, mean and standard deviation of numerical and categorical variables were determined. The χ^2 test was used to compare categorical variables and 95% confidence intervals (CIs) were set for all statistical tests. A statistical test was considered significant when the *P* value was <0.05 .

As data for the study were retrieved from secondary data routinely collected by the LSTBLCP, no ethical clearance was needed.

RESULTS

Of 1199 children diagnosed and treated for all forms of TB during the study period, 11.8%, 26.1% and 62.1% were aged <1 year, 1–4 years and 5–14 years, respectively. The male-to-female ratio was 1:0.9. Most (95%) of the childhood TB cases notified were new cases and 90.6% had PTB. HIV testing was conducted for 1095/1199 (91.3%) childhood TB cases (Table 1); 320 (29.2%) were seropositive. The age-specific HIV-TB co-infection rate was 42.1%, 29.3% and 26.7%, respectively, for children aged <1 year, 1–4 years and 5–14 years (Table 2). Of the 320 HIV-TB co-infected children, 186 (58.1%) were initiated on CPT, and 151 (47.2%) were on ART. The proportion of HIV-TB co-infected children on ART and CPT was respectively 44.6% and 60.7% for children aged <1 year, 45.3% and 65.1% for those aged 1–4 years and 48.9% and 60.1%, for those aged 5–14 years (Table 2). The uptake of ART and CPT among HIV-TB co-infected children treated in centres where TB and ART services coexist was respectively 48.3% and 63.3% vs. 34.6% and 42.3% in centres where there were no ART services (Table 3). There was no association between the uptake of ART and the co-location of ART and TB services ($P > 0.05$), but the uptake of CPT was significantly higher in facilities where ART and TB services were co-located compared with facilities where they were not ($P = 0.035$).

Among the different age groups, the rate of HIV-TB co-infection was significantly higher in children aged <1 year (42.1%) compared with those aged 1–4 years (29.3%) and 5–14 years (26.6%) (Table 4). Sex, type of TB and site of TB were not associated with HIV-TB co-infection. Of the 994 pulmonary TB cases, 297 (29.9%) were HIV-positive. The proportion of smear-positive cases was sig-

TABLE 2 Age-specific HIV positivity rates among children diagnosed with TB in Lagos State, Nigeria

Age, years	Diagnosed with TB <i>n</i> (%)	Underwent HIV testing <i>n</i> (%)	HIV-positive <i>n</i> (%)	Age-specific HIV rates %	HIV-TB co-infected children on ART <i>n</i> (%)	HIV-TB co-infected children on CPT <i>n</i> (%)
<1	141 (11.8)	133/141 (94.3)	56 (17.5)	42.1	25 (44.6)	34 (60.7)
1–4	313 (26.1)	294/313 (93.9)	86 (26.9)	29.3	39 (45.3)	56 (65.1)
5–14	744 (62.1)	668/744 (89.8)	178 (55.6)	26.7	87 (48.9)	107 (60.1)
Total	1198 (100)	1095/1198 (91.4)	320 (100)	29.2	151 (47.2)	197 (61.6)

HIV = human immunodeficiency virus; TB = tuberculosis; ART = antiretroviral treatment; CPT = cotrimoxazole preventive therapy.

TABLE 3 Uptake of ART in facilities where both TB and HIV services are co-located

Variable	Co-location of ART and TB services		χ^2	P value
	Yes n (%)	No n (%)		
On ART				
Yes	142 (48.3)	9 (34.6)	1.79	0.180
No	152 (51.7)	17 (65.4)		
Total	294 (100)	26 (100)		
On CPT				
Yes	186 (63.3)	11 (42.3)	4.43	0.035
No	108 (36.7)	15 (57.7)		
Total	294 (100)	26 (100)		

ART = antiretroviral treatment; TB = tuberculosis; HIV = human immunodeficiency virus; CPT = cotrimoxazole preventive therapy.

nificantly higher among HIV-negative patients (95.7%) than among HIV-positive patients (4.3%) ($P < 0.001$) (Table 4).

DISCUSSION

About one third (29.7%) of the study population was co-infected with HIV. This is lower than reports from studies conducted in eastern and southern Africa, where the HIV prevalence rate ranged between 48% and 56%,^{16–19} and higher than the national HIV prevalence rate of 3.4%.²⁰ The increased risk of TB in HIV-positive children may be a result of the high TB burden among adults in the general population. The WHO estimated the TB prevalence rate at 326 per 100 000 population in Nigeria, but only about a quarter of these are notified to the NTP.²¹ This means that many people with active TB disease are undiagnosed and remain a continued source of infection in the community. HIV-infected children are at higher risk of developing active TB when exposed to adults with smear-positive TB.²² Infants of mothers with active TB have been reported to be at higher risk of acquiring tuberculous infection and developing active disease.²³

The age-specific HIV rates among the children with TB show that HIV-TB co-infection was highest in children aged <1 year. This is consistent with other studies showing that the risk of the progression of TB from infection to disease is higher in children aged <5 years.^{10,11,22} Children aged <1 year are likely to have been infected by their mothers during pregnancy, labour or delivery. It has been reported that mother-to-child transmission (MTCT) of HIV accounts for over 90% of all paediatric infections.²³ HIV MTCT is high in sub-Saharan Africa, with rates as high as 25–40% without intervention.²³ The rate of MTCT has been reduced significantly in industrialised countries due to the implementation of prevention strategies,²⁴ and such strategies need to be vigorously pursued in Nigeria and other African countries to reduce the burden of HIV among children, and particularly infants.

As has been reported in earlier studies, the majority of the children diagnosed with TB were smear-negative.^{16–19} Diagnosing TB in children is challenging, especially in low-income countries where facilities for accurate diagnosis are limited.²⁵ This situation is further compounded by the high burden of HIV-TB co-infection among children in many African countries, including Nigeria. Studies have shown that the clinical overlap between PTB and HIV could result in the misdiagnosis and eventual overdiagnosis of TB.^{16,25}

TABLE 4 Association between HIV status and sociodemographic and clinical characteristics of patients

Variable	HIV status		χ^2	P value
	Positive n = 320 n (%)	Negative n = 775 n (%)		
Age group, years				
<1	56 (42.1)	77 (57.9)	12.81	0.002
1–4	86 (29.3)	208 (70.7)		
5–14	178 (26.6)	490 (73.4)		
Age, mean $\pm$ SD	5.6 $\pm$ 4.2	7.3 $\pm$ 4.8		
Sex				
Male	179 (31.7)	385 (68.3)	3.55	0.059
Female	141 (26.6)	390 (73.4)		
Type of facility				
Public	318 (30.1)	740 (69.9)	10.50	0.001
Private	2 (5.4)	35 (94.6)		
Classification of patients				
New	307 (29.4)	738 (70.6)	0.26	0.608
Others	13 (26.0)	37 (74.0)		
TB site				
Pulmonary	297 (29.9)	697 (70.1)	2.24	0.135
Extra-pulmonary	23 (22.8)	78 (77.2)		
Pulmonary TB cases				
Smear-positive	10 (4.3)	224 (95.7)	95.77	<0.001
Smear-negative	287 (37.8)	473 (62.2)		

HIV = human immunodeficiency virus; SD = standard deviation; TB = tuberculosis.

The proportion of HIV-TB co-infected children commenced on ART in this study was 48%, higher than the 38% reported globally in 2008.²⁶ The introduction of ART into the management of HIV-TB co-infection has led to a significant reduction in the pattern of morbidity and mortality.^{27–30} Without ART, it is estimated that a third of HIV-infected children would die by the age of 1 year and about 50% by the age of 2 years.^{28,29} It is therefore imperative to scale up efforts to provide access to HIV treatment for infected children. The 2013 WHO guidelines on ART recommend initiating ART at weeks 2–8 of anti-tuberculosis treatment in HIV-TB co-infected children, especially those with moderate to severe immunosuppression.³¹ A study from South Africa reported that delaying the initiation of ART by more than 8 weeks after the initiation of TB treatment was associated with increased mortality and poor virological outcome in children infected with HIV.³² The WHO also recommended that all HIV-TB co-infected children should be provided with CPT, which has been shown to improve survival in patients with HIV-TB co-infection.^{33–35} However, in this study only 58.1% of the children were on CPT. This was slightly higher than the uptake of CPT among HIV-TB co-infected adults reported in other studies.^{36,37}

Adherence to the WHO recommendation on CPT use in HIV-TB co-infected children has been poor in sub-Saharan Africa due to erratic drug supplies, poor knowledge amongst health care workers about the benefits of CPT, poor training and supervision, and a lack of proper recording and reporting of CPT utilisation in health facilities.^{36,37} Evidence on the increased uptake of ART among HIV-TB co-infected patients when HIV and TB services are co-located are inconsistent.³⁸ Our study shows that co-location of TB and HIV services does not significantly improve the uptake of ART. The reason for this is not known, but the belief on the part of some HIV care providers in the older, stringent eligibility crite-

ria for commencement of ART, the fear of immune reconstitution syndrome, which is common among HIV-TB co-infected patients, and poor record keeping at the health facility may be responsible for this finding.³⁸ HIV services are located in specialised clinics in secondary and tertiary health facilities, where there is staff trained in paediatric ART. There is a need for provision of trained staff in primary health care clinics.

CONCLUSION

The prevalence of HIV-TB in children was high and the uptake of CPT and ART was low. There is a need to intensify efforts to reduce HIV transmission in children and improve access to HIV services in Lagos State, Nigeria.

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Contexte : Le virus de l'immunodéficience humaine (VIH) et la tuberculose (TB) sont les causes majeures de décès dû à une maladie infectieuse dans le monde. L'Organisation Mondiale de la Santé estime que la prévalence du VIH parmi les enfants atteints de TB dans des pays à prévalence modérée à élevée va de 10% à 60%. Cette étude a eu pour but de déterminer l'accès aux services VIH pour les enfants coinfectés par TB-VIH.

Méthodes : Une revue rétrospective des données d'enfants ayant eu un diagnostic de TB dans l'état de Lagos au Nigeria entre le 1^{er} janvier 2012 et le 31 décembre 2013.

Résultats : Un total de 1199 enfants âgés de 0 à 14 ans ont eu un diagnostic de TB. Parmi eux, 1095 (91,3%) ont eu un test VIH, dont

320 (29,2%) ont été positifs. Le ratio garçon/fille de coinfection TB-VIH a été de 1:0,9. Sur les 320 enfants coinfectés TB-VIH, 57 (17,8%), 86 (26,9%) et 186 (58,1%) respectivement avaient <1 an, 1–4 ans et 5–14 ans. Sur les 320 enfants coinfectés TB-VIH, 186 (58,1%) ont débuté le cotrimoxazole (CPT) tandis que 151 (47,2%) étaient sous traitement antirétroviral (ART). La mise sous ART n'a pas été significativement plus élevée dans les structures où les services TB-VIH se trouvaient au même endroit ($P > 0,05$).

Conclusion : La mise sous CPT et ART a été faible. Il est nécessaire d'intensifier les efforts d'amélioration de l'accès aux services VIH à Lagos, Nigeria.

Marco de referencia: La infección por el virus de la inmunodeficiencia humana (VIH) y la tuberculosis (TB) son las principales causas de muerte por enfermedad infecciosa en todo el mundo. La Organización Mundial de la Salud considera que la prevalencia de infección por el VIH en los niños con TB de los países con prevalencia moderada o alta oscila entre 10% y 60%. El presente estudio tuvo por objeto determinar el acceso de los niños coinfectados por el VIH y la TB a los servicios relacionados con el VIH.

Método: Se llevó a cabo un examen retrospectivo de los datos sobre los niños con diagnóstico de TB en el estado de Lagos en Nigeria del 1^o de enero del 2012 al 31 de diciembre del 2013.

Resultados: Se estableció el diagnóstico de TB en 1199 niños de 0 a 14 años de edad, de los cuales 1095 contaban con una prueba

diagnóstica del VIH (91,3%) y 320 habían obtenido un resultado positivo (29,2%). La proporción entre el sexo masculino y femenino fue 1:0,9 en los niños coinfectados. De los 320 casos de coinfección, 57 eran menores de un año de edad (17,8%), 86 tenían entre 1 y 4 años (26,9%) y 186 entre 5 y 14 años de edad (58,1%). De los 320 niños coinfectados, se inició tratamiento preventivo con cotrimoxazol (CPT) en 186 (58,1%) y 15 niños comenzaron el tratamiento antirretrovírico (ART) (47,2%). La aceptación del ART no fue significativamente más alta en los establecimientos donde los servicios contra la TB y el VIH compartían la ubicación ($P > 0,05$).

Conclusión: La aceptación del CPT y el ART fue baja. Es preciso intensificar las iniciativas tendientes a mejorar el acceso a los servicios relacionados con el VIH de Lagos, en Nigeria.