ORIGINAL ARTICLE

Clinical correlate of tuberculosis in HIV co-infected children at the University of Abuja Teaching Hospital, Gwagwalada, Nigeria

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Abstract

Background: Tuberculosis (TB) co-infection with HIV is becoming a global emergency especially in the sub-Saharan Africa. Its diagnosis is notoriously challenging in countries with poor resource settings with limited diagnostic facilities. Objective: To determine the prevalence, pattern, outcome, and clinical risk factors of TB in HIV co-infected children in Abuja, Nigeria.

Materials and Methods: An 18 months retrospective review of HIV-infected children diagnosed as having co-infection with TB was carried out at the special treatment clinic of the University of Abuja Teaching Hospital (UATH), Gwagwalada, from February 2007 to August 2008 for the above objectives.

Results: Of a total 210 HIV-infected children observed during the review period, 41 (19.5%) were diagnosed as having co-existing TB. Their mean age, weight, CD4 cell count and its percentage were 6.3 ± 2.4 years, 14.3 ± 3.4 kg, 262 ± 28.0 cells/ml, and 9.9%, respectively. Pulmonary TB accounted for 59% of all TB cases seen, while disseminated form was seen in 26.8%. Bone involvement was the least common form seen in only (2.4%) of cases. Confirmation of TB was only possible by positive smear and histology in 22.0% of cases, while 78.0% of cases remained unconfirmed. Co-infection was significantly higher in older children (>5 years) than in younger children <5 years (32 vs 9, $P < 0.05$). Severe weight loss was the only clinical feature found to have a fairly good sensitivity (88.9%) and specificity (88.6%) for TB in co-infected children, with a positive predictive value of 23.0%. While immune reconstitution syndrome (IRS) occurred in 2 (4.9%) of the patients, only one death (2.4%) was recorded among the co-infected children.

Conclusions: TB co-infection with HIV in children is common in this environment. Severe weight loss can be used as a clinical guide to identify HIV-infected children at risk of co-infection with TB who will require further evaluation.

Key words: Co-infection, human immunodeficiency virus, tuberculosis

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Introduction

At present, worldwide over one million children are infected with tuberculosis (TB) and 630,000 by HIV annually.[1,2] While TB alone is responsible for over 250,000 deaths every year, HIV is projected to cause more than 56,000 deaths worldwide annually[3,4] Co-infection with both organisms, also described as "cursed duet" or "deadly duo", is becoming an increasing global emergency especially in the sub-Saharan Africa [SSA], where between 10% and 60% of the children are co-infected.[5] While the highest cases of co-infection occurred in South Africa, the least ones were recorded in West Africa,[5,6] and people living with HIV/AIDS have six times greater risk of dying from active TB.[7]

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HIV infection has been known to weaken the immune system by depleting the CD4 cell counts and in turn giving room for opportunistic infections. TB itself can also lower the CD4 cell count in children and exacerbate the immunodeficiency caused by HIV infection.[7,8] Children infected with HIV have 50 times greater risk of developing primary progressive TB in a given year from severe immune suppression of young age and HIV infection,[5] Those with co-infection also have a higher case fatality rate.[9,10]

Diagnosis of TB in children has been notoriously challenging even before the HIV/AIDS pandemic; especially in resource-limited settings where culture proven facilities, polymerase chain reaction (PCR) test, and other newer diagnostic methods might not be feasible because of cost. Diagnosis is even more difficult with HIV pandemic because the affected children may have many other acute/chronic lung disease conditions that could mimic signs and symptoms of TB.[5] Most TB diagnostic criteria [chronic cough, hemoptysis, weight loss, night sweats, history of contact, positive Mantoux of >5 mm diameter, chest radiograph, high electrolyte sedimentation rate (ESR), and response to treatment] have low sensitivity and specificity in co-infected children due to overlap with common childhood diseases.[5,9] Studies of TB co-infection with HIV in children have been reported in both industrialized[10-12] and non-industrialized countries,[3,9,13] with proportions ranging from 5.5% in United Kingdom, to 17% in Peru. The true prevalence and magnitude of TB co-infection with HIV in children in Nigeria has remained under-reported. The aim of the present study is to determine the prevalence, pattern, outcome, and clinical risk factors of TB in HIV co-infected children. It is believed that such outcome will assist pediatric healthcare providers in identifying the risk of co-infected children, and possible referral for further evaluations.

Materials and Methods

The case records of HIV-positive children seen in pediatric outpatient special treatment clinic (POSTC) of UATH from February 2007 to August 2008 were retrieved from the medical records department of the hospital, and information collected were analyzed. Data extracted from the records included: HIV status of the child, diagnosis of TB in the patient, modalities used for the diagnosis, history of presenting complaint, clinical findings, sex, age, weight, whether admitted or not, outcome of the admission, CD4 cell count and its percentage, whether started on anti-TB drugs, and whether on highly active anti-retroviral therapy (HAART). The outcome of admission was classified as discharge with or without development of immune reconstitution syndrome (IRS), died, or absconded. Diagnosis of HIV infection in children less than 18 months was confirmed using DNA-PCR test after 6 weeks of age. For those aged greater than 18 months, the diagnosis was by double rapid antibody test [*STAT PAK by chembio diagnostic system INC New York, and DETERMINE by Abbot Laboratory Japan*]. POSTC is a specialized clinic for HIV/AIDS children, and an arm of the pediatric outpatient clinic of the department.

University of Abuja Teaching Hospital is a tertiary health institution located in Gwagwalada, one of the area councils in the Federal Capital Territory (FCT), Abuja in the North Central Zone of the country. The institution is sub-serving many states including Nassarawa, Kogi, Niger, Benue, parts of Kaduna and FCT, Abuja. It is also one of the first six centers in the country to provide free medical services to HIV/AIDS victims from 2005 till date, courtesy of the government of the United States through the President's Emergency Plan for AIDS Relief (PEPFAR).

Diagnosis of TB was made using combination of the following: History of chronic cough >1 month, history of contact with adult with chronic cough, positive mantoux test of >5 mm in diameter, chest radiograph, identification of acid fast bacilli (AFB) in sputum/gastric/body fluid, lymph node histology, history of ingestion of unpasteurized cow milk, history of night sweats, and non response to conventional antibiotics. No culture was carried out. A combination of more than two of the above findings was used for diagnosis of TB in our center.

Pulmonary TB was confirmed when the child has specific clinical and radiological criteria (fever, cough of >1 month duration, weight loss, history of contact with adult with chronic cough, night sweats, and at least one positive smear test of sputum or gastric aspirate). Confirmed extra pulmonary TB was diagnosed when the child had specific clinical criteria (lymph node enlargement, ascites, and history of ingestion of unpasturized milk, bone involvement, radiological features, meningitic signs, and lymph node histology confirming TB, or positive smear from other body fluid other than sputum). Non confirmed TB was considered when the child had specific clinical and radiological criteria mentioned above, and had no histological features suggestive of TB in the lymph node biopsy, or when AFB was not isolated in sputum or any other body fluid.

Sputum for AFB was obtained by expectoration (×3) for older children, and early morning gastric lavage (×3) for those less than 3 years who cannot expectorate. Sputum, gastric aspirate, and other body fluid aspirates were stained for acid-fast bacilli using Ziel-Nelson method. Tuberculin skin tests were performed by intradermal injection of 5 tuberculin units of purified protein derivatives (*Institut Merieux, Lyon France)*. Induration diameter was measured after 72 hours. Tuberculin test was considered positive when raised induration was greater than 5 mm in diameter. Complete blood count was performed using automated cell counter (*Coultronics TM, Margency, France*), while CD4 cell count was also carried out using automated Partec Cyflow easy Count Kit (*Partec Code No. 05-8401 Western Germany*).

The absolute CD4 cell number is age dependent in children, and the following percentage values was used to define the degree of immune suppression, (<15%) was defined as severe immunosuppression, (15–24%) as moderate suppression, and (>25%) as immunocompetent. WHO clinical staging,[14-16] an international four stage system that classifies the severity of HIV infection in children was used to classify the degree of immunosuppression in the study subjects [Appendix].

All patients received anti-tuberculous therapy (ATT), a combination of isoniazid, rifampicin, and pyrazinamide for six months, with additional steroid (prednisolone) for those having meningitic component. HAART was added to all patients 2–4 weeks after commencement of ATT. Combination of zidovudine or stavudine, lamivudine and efavirenz or abacavir were used.

Appendix: Revised WHO clinical staging of HIV/AIDS for infants and children

Clinical stage I	Asymptomatic stage with persistent generalized lymphadenopathy or hepatosplenomagaly.
Clinical stage II	Disease is manifested by papular puritic eruptions, seborrhea dermatitis, fungal nail infections, angular chelitis, lineal gingival erythema, extensive human papilloma virus (HPV) or mollscum infection (>5% of body area/face), recurrent oral ulceration (>2 episode/6 months), parotid enlargement, herpes zoster (>1 episode/12 months), recurrent or chronic upper respiratory infections (URTI): Otitis media, otorrhoea, sinusitis (>2 episodes/6 months).
Clinical stage III	Features include unexplained moderate malnutrition (-2 SD or Z score) not responding to standard therapy, unexplained persistent diarrhea (>14 days), unexplained persistent fever (intermittent or constant, >1 month), oral candidiasis, oral hairy leukoplakia, pulmonary tuberculosis, severe recurrent presumed bacteria pneumonia (>2 episodes/12 months), acute necrotizing ulcerative gingivitis/periodontal, lymphoid interstitial pneumonitis, unexplained anemia (<8 gm/dl), neutropenia (<1000/mm^3), or thrombocytopenia (<30,000/mm^3) for >1 month, HIV cardiomyopathy, and HIV-related nephropathy.
Clinical stage IV	Presence of unexplained severe wasting or severe malnutrition (-3 SD or Z score) not responding to standard treatment, pneumocystic pneumonia, recurrent severe bacteria infections (>2 episodes/12 months, excluding pneumonia), chronic orolabial or cutaneous herpes simplex virus (lasting >1 month), extra pulmonary TB, Kaposi sarcoma, esophageal candidiasis, central nervous system toxoplasmosis, cryptoccocal meningitis, any disseminated endemic mycosis, cryptosporidiosis or isosporiasis (with diarrhea >1 month), cytomegalovirus virus infection of organs other than the liver, spleen, lymph nodes (and onset age >1 month), disseminated mycobacterial disease other than tuberculosis, candida of trachea, bronchi or lungs, acquired recto-vesico fistula, cerebral or B cell non-Hodgkin lymphoma, HIV encephalopathy, and progressive multifocal leucoencephalopathy.

Adapted from 'Interim WHO Clinical Staging of HIV/AIDS Case Definitions for Surveillance. African Region'. WHO/HIV/2005.02. http://www. who.int/hiv/pub/guidelines/clinicalstaging. pdf

Data analysis was computed using Epi Info 6, and SPSS version 13.5 for statistical analysis.

Results

Of a total of 210 HIV-infected children reviewed during the 18 months period, 41 (19.5%) were co-infected with TB; 19 (46.3%) were males and 22 (53.7%) females giving a male to female ratio of 0.9:1. They had a mean age of 6.3 ± 2.4 years, weight of 14.3 ± 3.4 kg, and a mean CD4 cell count/percentage of 261.6 ± 28.0 cells/ml and 9.9%, signifying severe immune suppression [Table 1]. There was no statistical significant difference in the characteristics of male and female co-infected children at recruitment.

The site of TB co-infection with HIV and WHO clinical staging is shown in Table 2. Pulmonary TB (58.5%) and disseminated TB (26.8%) were the commonest form of TB seen in HIV patients in the study. Abdominal TB alone (7.3%), lymph node (4.9%), and bone (2.4%) were not very common. Though disseminated form of TB was not as common as pulmonary type, all presented with a mean CD4 percentage of less than 5.0%. One case of disseminated TB had meningitis component, and all the co-infected children were in WHO clinical stage 3 and 4.

Age distribution of various types of TB was shown in Table 3. TB was significantly commoner in older children >5 years than in those <5 years (32 vs 9, $P < 0.05$). All forms of TB were also seen to be commoner in older children. Table 4 shows the methods used in the diagnosis of TB as well as the sensitivity, specificity, and positive predictive values (PPV) of different methods used. History of chronic cough of >1month duration and history of contact with adult with chronic cough were

Table 1: Characteristics of the study population

	Male	Female	Total (%)	*P* value
Sex	19	22	41	>0.05
Age (years)	*6.6 ± 2.0	*6.0 ± 2.8	*6.3 ± 2.4	>0.05
Weight (kg)	*15.2 ± 4.3	*13.5 ± 2.4	*14.3 ± 3.4	>0.05
CD4 cell	*171 ± 30.2	*152 ± 25.7	*161 ± 28.0	>0.05
Count (cells/ml)	3-353	7-297	*7.3	>0.05
CD4 cell range	*8.2	*7.1	*54.3	>0.05
CD4%	*58.7	*49.8		
ESR (mm/hr)				

*Values are mean ± SD. ESR-electrolyte sedimentation rate

Table 2: TB sites and WHO clinical stage

Site of TB	n (%)	WHO clinical stage	CD4 cell count	CD4% age
Pulmonary	24 (58.5)	3	242	8.2
Disseminated	11 (26.8)	4	108	4.8
Abdominal	3 (7.3)	4	146	6.3
Lymph node	2 (4.9)	3	310	11.9
Bone	1 (2.4)	4	102	5.1
Total	41 (100)	4	161	7.2

Table 3: Age distribution and sites of TB in co-infected children

Age (years)	N (%)	Pulmonary	Disseminated	Abdominal	Lymph node	Bone
0-1	1 (2.7)	1	-	-	-	-
>1-2	2 (5.4)	2	-	-	-	-
>2-5	6 (16.2)	4	2	-	-	-
>5-10	15 (32.4)	8	4	2	1	-
>10-15	10 (29.7)	6	3	-	-	1
>15-17	7 (13.5)	3	2	1	1	-
Total (%)	41 (100)	24 (58.5)	11 (26.8)	3 (7.3)	2 (4.9)	1 (2.4)

TB co-infection in children <5 yrs vs >5 yrs [9 vs 32] $P > 0.05$

Table 4: Sensitivity, specificity, and positive predictive values for various methods used in diagnosis of TB in co-infected children

Modalities used for TB diagnosis	N (%)	Sensitivity (%)	Specificity (%)	PPV (%)
History of chronic cough >1month	10 (24.4)	44.4	92.5	21.1
Positive contact with adult with chronic cough	39 (95.1)	55.6	80.1	11.1
Chest x-ray suggestive	3 (7.3)	11.1	82.6	2.1
History of ingestion of unpasteurized cow milk	5 (12.2)	22.2	98.5	40.0
Mantoux test >5 mm indurations	0	-	-	-
Gastric lavage/Body fluid for AFB	4(9.7)	-	-	-
Sputum for AFB	5 (12.2)	-	-	-
Lymph node biopsy	32 (78.1)	88.9	88.6	23.0
Severe weight loss	29 (70.3)	100.0	80.0	18.4
Not responding to conventional AB				

seen in 70.3% and 24.4% of cases. While 95.1% showed radiological features suggestive of TB in their chest X-ray, AFB was difficult to identify in many body fluids, (9.7% from sputum, and none in any other body fluid. Mantoux test with indurations of >5 mm was also not very common (12.2% only). Confirmation of TB in the study was from lymph node histology, and identification of AFB in the sputum. While lymph node biopsy showed histological features of TB in 12.2% of cases, identification of AFB in the sputum was seen in 9.7% of patients, thus giving a total of confirmed TB as 21.9%, and 78.1% remained unconfirmed or suggestive.

The culture of respiratory specimens, often considers as gold standard for diagnosis of TB in adult population, performs poorly in children. Firstly, the collection of adequate specimen for bacteriological diagnosis from pediatric patients is difficult, secondly, the rapid confirmation by smear is achieved in less than 15%, with a positive culture generally in only 30–40% of cases after a delay of 4-8 weeks, and lastly, the natural history of disease in children demonstrate that positive Mycobacterium tuberculosis culture in a complete asymptomatic child recently exposed to TB likely reflects recent infection and not active disease.[17,18] Hence there is yet no established gold standard for children. However in the absence of gold standard method for children, identification of AFB in body specimen (sputum), and lymph node histology was used as a standard in this review. Going by the above, the sensitivity, specificity and PPV of the common clinical presentations, signs, and radiological/laboratory investigations were carried out in co-infected children were tested [Table 4]. The variable tested were history of chronic cough for >1 month, severe weight loss, history of contact with adult with chronic cough, mantoux test with induration of >5 mm, chest x-ray, and non response to conventional antibiotics. All showed low to moderate sensitivity and specificity with the exception of severe weight loss of >-3SD which showed sensitivity/specificity of 88.9%, 88.6%, and PPV of 23.0%.

The outcome showed that one patient (2.4%) died from disseminated TB, while 2 (4.9%) also having disseminated form of TB developed IRS. All patients received ATT, and were all started on HAART.

Discussion

TB co-infection with HIV in children is high in this environment (19.5%). This is comparable to 17% reported among HIV hospitalized children in Peru,[3] 15.2% from HIV infected children at Nnewi in Nigeria,[19] and 10% from studies from other West African countries.[5] It was however much lower than 48.0% report from South African study,[16] and also much higher than 5.5% report from United Kingdom.[10] Studies have shown that over 90% of 2.3 million world children living with HIV reside in the sub Saharan Africa.[2,20] Nigeria is one of the countries of sub region that have continued to bear the greatest burden of pediatric HIV/AIDS. Studies have also shown that more than 80% of people living with TB reside in the sub-region,[12] and those with HIV have 50 times more risk of developing TB in a given year than the none infected. TB is a contagious disease spread primarily by droplets nuclei expelled by someone who has infectious pulmonary or laryngeal TB when they cough or sneeze,[14] It can occasionally be contacted by ingestion of contaminated unpasturized animal milk. The number/concentration of the organism expelled into the air during coughing or sneezing, the duration of exposure to infected person, and the condition of the immune system of the host are the major factors that

predict the transmission of TB to another person.[14] Close contacts are at the highest risk of becoming infected, and children acquire this disease from infected adults. TB is equally a disease of poverty and easily acquired in over crowded environment with low standard of living. This is the true picture in most countries in the sub region, and other African countries,[19-22] and could explain the high prevalence seen in the country.[19,20,23,24] The much higher value (48.0%) however reported in South African study might not only be due to geographical location of the area, and the disease burden in the adult population, but most importantly, the culture proven diagnostic technique used in TB diagnosis in South African study, which was not applicable in the present study. This method appeared more realistic and probably responsible for the high figures obtained in their study.

Previous studies among HIV patients have shown great association between low CD4 cell counts and susceptibility to TB especially extra-pulmonary forms.[3,7] In the present study, all the TB co-infected are children were in WHO stages 3 and 4 diseases of severe imunosuppression. Other workers have reported association between low CD4 cell count and TB in HIV patients.[22,25] Cohen and co-workers[10] however made no such observation. In fact in their report, they noted many cases of TB in their co-infected children have relatively preserved T-cell function and found no association between CD_4 cell count and TB manifestation. They however attributed such observation to the small number of their study population. HIV is notoriously known to cause depletion and dysfunction of CD_4 cells.[5,8] Other immunological defects caused by this virus include lymphoid tissue destruction, CD_8 cell and thymic cell dysfunction, B cell abnormalities and auto-immune abnormalities.[5,8] The degree of depletion of CD_4 cell determines the degree of immune suppression. The two infections by having the capability of depleting the CD_4 cell count could explain the reason why the majority of patients in the present study had low CD_4 cell count.

Diagnosis of TB in HIV children has been very challenging especially in poor resource settings because of non-availability of newer modern methods of diagnosis, and overlap of TB and HIV symptoms and signs. In this present study, culture proven methods and newer techniques were not available. Diagnosis was mainly based on combinations of older methods. These include history of contact with adult with chronic cough (24.4%), history of cough of greater than 1 month duration (70.3%), chest x-ray suggestive of pulmonary TB (95.1%), Mantoux test of >5 mm indurations (12.2%). While most diagnosis of TB in the present study was on presumptive basis (78.0%) with therapeutic trial of anti-TB therapy, only 22.0% was confirmed by positive sputum and lymph node histology. Even in resource rich settings with newer diagnostic facilities, majority of TB in co-infected children were treated on presumptive basis, 80% by Cohen *et al*.[10] They did note that therapeutic response in all these cases justifies the approach, however, in the context of emergence of drug resistant TB, the presumptive or therapeutic trial becomes questionable.

Because of the difficulty encountered in the diagnosis of TB in poor resource settings like ours, sensitivity and specificity with positive predictive values of the common clinical presentations, signs, radiological and laboratory test for TB were carried out. The aim being to provide information that will guide healthcare providers in these areas with limited facilities predict infected children at risk of co-infection with TB. Severe weight of greater than 3SD below the mean weight for age was found to have greater sensitivity and specificity, though with lower predictive value, and can be used to predict HIV infected children at the risk of co-infection with TB, for further evaluation and quick intervention.

Many cases of IRS associated with TB in adult HIV patients occurs on commencement of HAART, and several have been reported in sub-Saharan Africa.[11,12] Little information is available on pediatric patients. Immune reconstitution syndrome, defined as paradoxical clinical deterioration after starting HAART, resulting from improving immune system interaction with organisms that have colonised the body during early stages of HIV infection.[5,14] was seen in 2 (4.9%) of patients in the presented study, and conforms with the rarity of this syndrome in pediatric patients. A wide range of pathogens have been known to cause IRS in both adults and children. This include *Mycobacterium tuberculosis*, Mycobacterium avium complex (the two organism causing TB), *Cryptococcus neoformans*, Aspergilla, *Candida albicans*, *Pneumocystis jiroveci*, Cytomegalovirus, Human herpes viruses and Hepatitis B. IRS usually presents within 2–6 weeks of commencement of HAART. The clinical presentation varies and depends on the causative organism. For patients in the present study, high fever, generalized lymphadenopathy, development of miliary shadows with pleural effusion radiologically were their presentation when HAART was introduced 2–3 weeks after commencement on ATT. All responded to steroids.

Conclusions

TB co-infection with HIV in children is common in this environment. Severe weight loss can be used as a clinical guide to identify HIV-infected children at risk of co-infection with TB who will require further evaluation and intervention.

References

1. Cotton MF, Schaaf HS, Hesselling AC, Madhi SA. HIV and Childhood Tuberculosis, the way forward. Int J Tuberc Lung Dis 2004;8:675-82.
2. UNAIDS. 2007 Report o the Global AIDS epidermic. Joint United Nations Programme on HIV/AIDS (UNAIDS) 2007.
3. Raminez- Cardich ME, Kawai V, Oberhelman RA, Bautista CT, Castillo ME, Gilman RH. Clinical Correlates of TB co-infection in HIV infected hospitalixed in Peru. Int J of Infect Dis 2006;10:278-81.
4. Selekman J. Changes in the screening for Tuberculosis in children. Pediatr Nurs 2006;32:73-5.

5. Tindyebwa D, Kayita J, Musoke P, Eley B, Coovadia H, Bobart R, *et al*. Handbook of Paediatric AIDS in Africa by the African Network for the Care of Children Affected by AIDS. p. 124. Available from: http://www.rcqhc.org.
6. WHO. Management of TB in the HIV-infected child. Int J Tuberc Lung Dis 2006;10;1331-6.
7. Swaminathan S. Tuberculsis in HIV-infected children. Paediatr Respiratory Rev 2004;5;225-30.
8. Martin DJ, Sim JG, Sole GJ, Rymer L, Shalekoff S, van Niekerk AB, *et al*. CD4 lymphocyte count in African patients co-infected with HIV and TB. J Acquir Immune Defic SynDr. Hum Retrovirol 1995;8;386-91.
9. Palme IB, Gudetta B, Bruchfeld J, Muhe L, Giesecke J. Impact of human immunodeficiency virus infection on clinical presentation, treatment, outcome and survival in a cohort of Ethiopian children with tuberculosis. Paediatr Infect Dis J 2002;21;1053-61.
10. Cohen JM, Whittaker E, Walter S, Lyall H, Tndor-Williams G, Kampmann B. Presentation, Diagnosis and Management of Tuberculosis in HIV infected Children in the UK HIV Med 2008;9;277-84.
11. Gutman LT, Moye J, Zimmer B, Tian C. Tuberculosis in human immunodeficiency virus-exposed United State children. Paeditr Infect Dis J 1994;13;963-8.
12. Wallers E, Cotton MF, Rabie H, Schaaf HS, Wallers LO, Marais BJ. Clinical presentation and outcome of tuberculosis in human immunodeficiency virus infected children on anti-retroviral therapy. BMC Paediatr 2008;8:1-6.
13. Sharma SK, Mohan A, Kadhiraran T. HIV-TB co-infection: Epidemiology, Diagnosis and Management. Indian J Med Res 2005;11:5-10.
14. Madhi SA, Huebner RE, Doeders L, Aduc T, Wesley D, Cooper PA. HIV-1 co-infection in children hospitalized with TB in South Africa. Int J Tuberc Lung Dis 2000;4;448-54.
15. Graham SM, Coutter JB, Gilks CF. Pulmonary disease in HIV infected African children. Int J Tuberc Lung Dis 2001;5:12-23.
16. Jean PM, Pillay T, Coovadia HM. Impact of HIV-1 co-infection on presentation and hospital related mortality in children with culture proven pulmonary tuberculosisin Durban, South Africa. Int J Tuberc Lung Dis 2002;6:672-8.
17. Stark JR. Paediatric tuberculosis: Time for a new approach. Tuberculosis 2003;83:208-12.
18. Zar HJ, Tannenbaum E, Apolles P, Roux P, Hanslo D, Hussey G. Sputum induction for the diagnosis of pulmonary tuberculosis in infants and young children in an urban setting in South Africa. Arch Dis Child 2000;82:305-8.
19. Ugochukwu EF. Clinical spectrum of Paediatric HIV infection in Nnewi. West Afr J Med 2006;25;10-4.
20. Federal Ministry of Health, Nigeria. Chap. 1. National guidelines for Paediatric HIV and AIDS Treatment and Care. 2007. p. 1.
21. Ramos JM, Reyes F, Tesfamariam A. Childhood and adult tuberculosis in a rural hospital in Southeast Ethiopia: A ten-year retrospective study. BMC Public Health 2010;10:215-9.
22. Palme IB, Gudetta B, Bruchfield J, Muhe I, Giesecke J. Impact of human immunodeficiency virus 1 infection on clinical presentation, treatment outcome and survival in a cohort of Ethopian children with tuberculosis. Paediatr Infect Dis J 2002:21:1053-61.
23. Ibadin MO, Oviawe O. Trend in childhood tuberculosis in Benin City, Nigeria. Ann Trop Paediatr 2001;21:141-5.
24. Mustapha MG, Rabasa AI, Ashir MG, Usman AB, Mohammed SY. Management of childhood tuberculosis: The experience in a tertiary health refacility in Nigeria. Nig Med Pract 2010;57:5-6.
25. Marais BJ, Graham SM, Cotton MF, Beyer N. Diagnostic and management challenges of childhood TB in the era of HIV. J Infect Dis 2006;196:576-85.

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