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Epidemiology and Clinical Features of Childhood Tuberculosis at Olabisi Onabanjo University Teaching Hospital, Sagamu

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Abstract

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Background: Tuberculosis (TB) is a major cause of childhood morbidity and mortality in most parts of the developing world.

Objective: To determine the epidemiological and clinical features of childhood tuberculosis in Sagamu.

Methods: Children aged 15 years and below, who were managed for tuberculosis in a Nigerian tertiary hospital between 2004 and 2009 were retrospectively studied for their clinical and laboratory features.

Results: Of 52 children with TB, 61.5 percent were males, 73 percent were aged ≤10 years and 94.2 percent belonged to socioeconomic classes IV and V. Most (65.3 percent) cases presented after three months of illness. Fever (73.1 percent), weight loss (69.2 percent) and cough (57.7 percent) were the leading features. Thirty (57.7 percent) had pulmonary disease while disseminated TB and spinal TB were the leading types of extra-pulmonary TB. History of BCG vaccination was elicited in 42.3 percent of cases. The mother was the contact in 71.4 percent of those who had a positive history of contact. HIV sero-positivity was present in 31 percent of the children who were screened for HIV. Only two (3.8 percent) of the children died and these two had TB/HIV co-infection.

Conclusion: Most of the children with tuberculosis were of school age and belonged to the lower socio-economic classes. Pulmonary TB was commoner than extra-pulmonary disease. Improved standard of living and routine HIV screening may be useful control measures.

Key words: Children; Epidemiology; Tuberculosis; HIV.

Introduction

ALTHOUGH accurate information on the global distribution of childhood tuberculosis is scarce,[1] children account for a major proportion of the global tuberculosis (TB) disease burden, especially in endemic areas.[2] Africa and South-east Asia have the largest number of TB cases and the situation in such places has been worsened by the Human Immunodeficiency Virus (HIV) epidemic.[3] Nigeria is currently ranked fifth worldwide among countries with high burden of TB.[4] Tuberculosis is a multi-system disease caused by *Mycobacterium (M) tuberculosis*.[3] In children, manifestations involving more than one system are common and extra-pulmonary forms of the disease are as common as the pulmonary ones, at least in hospital settings.[3] The symptoms and signs in children are so vague that diagnosis is often difficult, missed or over diagnosed.[3] Delay in case detection may worsen the disease and increase its transmission.[5] Hence, early case detection and prompt treatment of infectious TB cases is the basis for achieving the millennium development goals (MDG), which aim to halt and begin to reverse the incidence of TB by the year 2015.[6] To achieve this target in this part of the world, it is essential to examine the epidemiological characteristics of TB which can be explored to draw up effective

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preventive measures. In addition, the pattern of clinical features can be useful in early case detection which may facilitate prompt treatment, improve cure rate and reduce deaths due to TB.

There have been reports on childhood TB from different parts of Nigeria[7-9] as well as its resurgence in many parts of the developing world.[10] This resurgence has been attributed to the HIV pandemic, the emergence of multi-drug resistant strains of M tuberculosis, worsening state of poverty and the failure of the various tuberculosis control programmes.[10] Although there has been no previous study of TB in our centre, a previous study of childhood deaths in the centre showed TB as one of the important causes of death throughout childhood.[11] Therefore, TB is a major childhood illness which deserves attention in our population like other parts of the developing world.

The present study documents the epidemiology and clinical features of tuberculosis among children hospitalized in a Nigerian tertiary health facility.

Subjects and Methods

The Olabisi Onabanjo University Teaching Hospital, (OOUTH), Sagamu, southwestern Nigeria, provides general and specialized paediatric care for children in Ogun State and its neighbouring states of the federation. A retrospective review of hospital records of all children below the age of 15 years hospitalized with TB between January 2004 and May 2009 was carried out. Children with TB were hospitalized for the initiation of therapy to ensure compliance, when the illness was severe (overwhelming disease, disseminated or life-threatening extra-pulmonary forms) or complicated with intra-thoracic collections and cardio-respiratory failure. TB cases were managed with a combination of four drugs namely isoniazid, rifampicin, pyrazinamide and streptomycin (or ethambutol for children older than six years) in the initial phase, while only isoniazid and rifampicin were administered in the continuation phase of treatment according to the recommendations of the National Tuberculosis and Leprosy Control programme.[4]

Data extracted from the records included age, sex, clinical features including presenting symptoms, duration of illness prior to presentation in our hospital, history of BCG vaccination, history of contact with a suspected tuberculosis case, nutritional status, and results of relevant laboratory investigations such as packed cell volume (PCV), erythrocyte sedimentation rate (ESR) using the Westergren method, ELISA test for HIV I and II, and outcome of hospitalization. The nutritional status was derived by plotting the body weight of the children on the 2007 WHO Weight-for-Age reference charts (available only for age one month to 10 years).[12] Observed weights were converted to Z scores (SD) using the LMS method.[13] For the purpose of this study, weight-for-age less than 2SD defined underweight.

The diagnosis of TB was based on a constellation of suggestive historical and clinical features and one or more of the following:[7]

1. Demonstration of acid fast bacilli in direct smears of sputum or gastric washings.
2. Granulomatous lesions with caseous necrosis found on histological examination of aspirate or biopsy of lymph nodes.
3. Chest and/or vertebral column radiographic changes compatible with those of TB, plus a positive Mantoux test reaction.
4. Clinical and radiological improvement of presenting features on anti-TB drug therapy.

Socioeconomic background was ascribed based on the parental education and occupation using the method recommended by Ogunlesi.[14] Classes I and II constituted the upper class, class III formed the middle class while classes IV and V formed the lower class.

The data were analyzed with the SPSS 15.0 software using descriptive and inferential statistics. Proportions were compared using the chi-squared test with Yates' correction or Fisher's Exact test as appropriate. Mean values were compared using the Student t-test. P values less than 0.05 defined statistical significance.

Results

Fifty two children were managed for various forms of TB, out of the total admissions of 2,097. Thus the prevalence rate of TB in this cohort of children was 2.48 percent. Table I shows the age distribution of the patients. The age range of the children was four months to 14 years (0.33 to 168 months) and median age, 96 months. There were 32 males (61.5 percent) and 20 females (38.5 percent) with male-to-female ratio of 1.6:1. Majority (73.0 percent) were aged 10 years or less. The duration of illness prior to presentation ranged from one to 24 months (mean: 7.3 $\pm$ 5.9 months). Thirty four children (65.4 percent) presented after three months of onset of symptoms and 18 (34.7 percent) within three months. Forty-nine (94.2 percent) patients belonged to the lower socioeconomic classes IV and V and three (5.8 percent) to the middle class. III. None was in the upper socio-economic class.

Table II shows that the common presenting clinical features were fever (73.1 percent), weight loss (69.2 percent), and cough (57.7 percent). Excessive

Table IV

Comparison of the Clinical and Laboratory Features in Children with and without HIV-seropositivity

	Parameters	*HIV-Positive (n=8)*	*HIV-Negative (n=18)*	*p-values*
Clinical Features				
	Male sex	4 (50.0)	8 (44.4)	0.793
	Age < 5yrs	6 (75.0)	2 (11.1)	0.001
	Fever	8 (100.0)	10 (55.6)	0.023
	Cough	8 (100.0)	8 (44.4)	0.007
	Weight loss	4 (50.0)	14 (77.8)	0.157
	BCG	4/4 (100.0)	16 (88.9)	0.484
	Complications	4 (50.0)	0 (0.0)	0.001*
	PTB	6 (75.0)	8 (44.4)	0.149
	Weight <-2.0SD	4 (50.0)	12 (66.7)	0.420
Laboratory Features				
	ESR > 30mm/h	6 (75.0)	14 (77.8)	0.877
	PCV < 30%	2 (25.0)	14 (77.8)	0.011
	AFB Positivity	0/6 (0.0)	2/16 (12.5)	0.364
	Reactive Mantoux	2/8 (25.0)	4/14 (28.6)	0.856

Table V

Comparison of Children with Pulmonary and Extra-Pulmonary Tuberculosis

Parameters	*Extra-pulmonary TB(n = 22)*	*Pulmonary TB(n = 30)*	*p-values*
Age ≤120 months	16 (72.7)	22 (73.3)	0.90
Male sex	14 (63.6)	18 (60.0)	0.70
Underweight	12 (54.5)	10 (45.5)	0.13
BCG vaccination	8 (36.4)	14 (46.7)	0.46
History of contact	6 (27.3)	8 (26.7)	0.90
Complications present	10 (45.5)	14 (46.7)	0.92
HIV sero-positivity	4/16 (25.0)	4/10 (40.0)	0.7*
Positive Mantoux	8 (36.4)	12 (40.0)	0.72
Death	0 (0.0)	2 (6.7)	0.51**

Note: Figures in parentheses are percentages.
*Yate corrected chi-squared test **Fisher's Exact test

(P = 0.7), history of contact ($P = 0.9$) and nutritional status of children <five years ($P = 0.13$), and death as the outcome of hospitalization ($P = 0.5$).

Twenty eight (53.8 percent) patients had no medical or surgical complications. However, 10 (41.7 percent) of the remaining 24 had marasmus, severe anaemia occurred in eight (33.3 percent), septicaemia in four (16.7 percent) and failure to thrive in two (8.3 percent). There were no significant side effects of drugs to warrant discontinuation of any of the anti-tuberculous drugs in any patient. The duration of hospitalization ranged from five to 60 days (Mean: 16.8 $\pm$ 12.9 days). Forty eight (92.3 percent) children were discharged with clinical improvement and completed the course of treatment, two (3.8 percent) were discharged against medical advice and were lost to follow-up, while two (3.8 percent) with TB and HIV co-infection died.

Discussion

Although the features of tuberculosis in children had been reported from many parts of Nigeria,[7-9] there is no previous study that has been carried out to document the clinical features and epidemiology of tuberculosis in children in our centre, hence this study.

The preponderance of males in this study differs from some earlier reports from Nigeria.[8,9,15] The reason for the observed difference is unclear and it may simply be a reflection of differences in patient selection rather than sex-related predisposition to TB. The finding in the present study of a higher prevalence of tuberculosis among children aged five to 10 years is different from previous reports.[7,16] The reason for this observation is unclear and would require further studies. The long duration of illness prior to presentation in our health facility after the onset of symptoms, had also been noted in previous studies within and outside Nigeria.[5,17] This may be due to the non-specific nature of symptoms and signs in TB, poverty, ignorance and poor health care-seeking behaviour characteristic of the low socio-economic classes.[5] Although, there was no obvious relationship between delay in presentation and poor outcome of hospitalization in the children studied, possibilities of increased severity could not be excluded. This may contribute to the persistence of the disease in the populations despite the availability of effective therapies.

The clinical features observed in this study were similar to findings from earlier studies in Nigeria.[7-9] About two out of every five children with TB in the present study had received BCG immunization. This reinforces the known fact that the efficacy of BCG vaccine ranges from 0 percent to 80 percent.[18] This may also explain the dominance of non-severe respiratory diseases in the population studied since anecdotal reports have suggested that BCG vaccine protects more efficiently against the severe forms of the disease.[19]

The positive history of contact with a close member of the family who had TB is similar to other reports,[20,21] and highlights the importance of close proximity and risk of infection. The dominance of adults as the contacts of the affected children lends credence to the fact that children are mostly infected with M tuberculosis by adults and TB among children can only be successfully controlled when it is significantly controlled among adults.

The fact that most of the children in the present study belonged to the low socioeconomic classes supports the known fact that the strongest risk factors for childhood TB infection are socio-economic, mainly the effects of poverty, undernutrition, overcrowding and the resultant possibility of close contact with an infectious case.[22] This concurs with the diagnosis of underweight among more than half of the children studied. Poor nutrition may be a risk factor for the progression of tuberculous infection to disease as well as the effect of tuberculous disease.[19] Therefore, underweight children in areas where TB is endemic would benefit from extensive evaluation for TB. Socio-economic conditions have traditionally been cited as risk factors for developing TB.[23] Studies have shown a correlation between the rate of infection in households and poverty.[24,25] This study confirms this correlation for childhood TB. Poverty alleviation and improved standard of living for most families should reduce the transmission of TB in socially disadvantaged communities.

That most of the children in this study had pulmonary TB may be due to the fact that all the children had chest radiographs thus leading to a higher yield of diagnosis of pulmonary disease. Chest radiography remains the most widely used diagnostic test in clinical practice[26] providing an accurate diagnosis when interpreted by an experienced clinician.

Although HIV as a co-infection was found in less than one-third of those children whose HIV status were determined, incompleteness of these data makes generalization difficult. We observed difficulty in using AFB and Mantoux to diagnose TB in children with HIV. Although smear-positivity for AFB from sputum and gastric lavage in this study was low as the procedure was only carried out in about a third of the patients, nevertheless it is understood that the diagnosis of TB in children is a challenge as a result of the low yield of the mycobacterium. All the four children with cavitations

on chest X-ray were HIV-negative, contrary to expectation. It is not clear why severe anaemia was commoner among children without HIV co-infection compared to those with HIV co-infection. Tuberculin skin test was non-reactive in most of the children with TB in this study and this could have been due to a state of anergy.[19]

We acknowledge the incompleteness of data in some of the variables as a limitation of this study which made generalization difficult. Also, TB was not confirmed using microbiologic (AFB) detection. Nevertheless, the present study provides some baseline information about the current pattern of epidemiology and clinic-laboratory features of TB and also HIV co-infection in childhood as well as the diagnostic challenges in our centre. This information can be used in designing larger and prospective studies in the future.

Conclusion

Most of the children with TB in our study population were of school age and belonged to the lower socio-economic groups. Pulmonary TB was commoner than extra-pulmonary disease and outcome of treatment was generally good. TB/HIV co-infection deserves further, well-controlled research. Due to the non-specific clinical picture in TB, the use of adequately validated symptom-based diagnostic approaches and improved access to chest radiography and anti-tuberculous treatment seem to offer the most immediate benefit to children in tuberculosis-endemic countries with limited resources.

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