Original Article

Diagnostic Approach of Childhood Pulmonary Tuberculosis in Endemic Areas of Southeast Nigeria

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ABSTRACT

There is the need to ascertain the diagnostic approach on which medical doctors based their diagnosis of childhood pulmonary tuberculosis especially in tuberculosis endemic areas.

AIM OF THE STUDY: To determine the diagnostic approach used by medical doctors in the diagnosis of childhood pulmonary tuberculosis.

METHODOLOGY: A cross sectional study, using structured questionnaires to collect data from medical doctors whose daily routine include seeing sick children was carried out.

RESULTS: The common diagnostic approach or criteria were ranked by medical doctors in descending order of importance as follows; clinical features elicited from patients' history was ranked -1 by 56.4% (or 23 of 218); bacteriological investigation to isolate *Mycobacterium Tuberculosis* was ranked-2 by 22.5% or 49 of 218; radiological investigation to demonstrate typical changes consistent with active pulmonary tuberculosis was ranked -3 by 25.2% or 55 0f 218; therapeutic trial with standard anti tuberculosis drugs was ranked -4 by 52.3% or 114 of 218; immunological investigation using tuberculin skin testing was ranked -5 by 30.3% or 66 0f 218; and residual ranking of histological investigation using tissue biopsy was ranked -6 by 15.6% or 34 of 218. Therapeutic trial with standard anti tuberculosis drugs was consistently ranked as 4th by most groups of clinicians.

CONCLUSIONS: Most clinicians from different sub-groups studied followed a fairly similar order in the diagnosis of childhood pulmonary tuberculosis with a high premium placed on clinical features, bacteriologic, radiologic and therapeutic trial with anti tuberculosis drugs. The specialist in paediatric medicine relied more on clinical features and therapeutic trials for their diagnosis of childhood pulmonary tuberculosis.

KEY WORDS: Childhood Pulmonary Tuberculosis, Diagnostic Practice among Medical Doctors, Diagnostic Approach and Criteria.

INTRODUCTION

Morbidity and mortality from childhood tuberculosis has been on the increase due to the emergence of HIV/TB co-morbidity and multi-drug resistant strain of mycobacterium tuberculosis. This development has further compounded the diagnostic challenges of childhood tuberculosis. Research has shown that younger children do not usually produce good quality sputum and when they do it has been found to be paucibacillary even in those who have childhood pulmonary tuberculosis[1, 2,3]. The usual reference to positive sputum smear acid fast bacilli (AFB) (bacteriological confirmation) as gold standard does not apply in young children[4]. Some studies found that sputum smear microscopy was positive in less than 10 to 15 % of children with probable tuberculosis[4]. Similarly, low culture yields of 30 to 40% have been reported in children with probable tuberculosis[5,6].

Inspite of the expensive nature of bronchoalveolar lavage using flexible fiber optic bronchoscopy and nasopharyngeal aspirates, their bacteriological yields remain low and unavailable in resource poor TB endemic areas[7]. However, sputum smear microscopy has definite diagnostic value in children with adult-type TB disease (=10 years of age)[8].

The diagnosis of childhood TB in non-endemic areas is usually based on the triad of; history of contact with an adult index case (usually household contact), positive tuberculin skin test (TST), and suggestive signs on chest radiograph which provide fairly accurate diagnosis in settings where exposure to mycobacterium tuberculosis is rare. In endemic areas, by contrast, where exposure to *M. tuberculosis* is common, the accuracy of the triad is compromised as exposure frequently occurs outside the household [9,10].

Randomly selected healthy children in endemic areas have been found to have tested positive to TST[11]. This discovery has limited the diagnostic value placed on TST, and strengthened the suggestion of use of clinical features and chest radiograph for the diagnosis of pulmonary tuberculosis in children in endemic areas [12, 13].

Although, the specificity of the TST after Bacillus

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Calmette-Guaerin (BCG) vaccination and or exposure to environmental mycobacterium is low, a positive TST reaction remains a fairly accurate measure of *M. tuberculosis* infection in immune-competent children.

In the efforts to improve the case finding of childhood pulmonary tuberculosis, various clinical scoring systems have been developed over the years. However, reviewers have criticized them as being limited by a lack of standard symptom definitions and adequate validation[14].

OBJECTIVE OF THE STUDY: To determine the diagnostic approach on which medical doctors based their diagnosis of childhood pulmonary tuberculosis.

SUBJECTS & METHODS

Study design: A descriptive cross sectional study design was used.

Study setting: Private and public health facilities involved in routine childcare within the five southeastern states of Nigeria, (i.e. Abia, Anambra, Ebonyi, Enugu, and Imo states) were visited for recruitment of medical doctors for the study.

Study population: Medical doctors whose practice routine included providing clinical care services to children in both private and public health institutions in Abia, Anambra, Ebonyi, Enugu, and Imo States were recruited for the study.

Inclusion criteria: Medical doctors who provided clinical services to children and who consented to participate in the study.

Exclusion criteria: Medical doctors who were not providing clinical care services to children were excluded. Also excluded were medical doctors undergoing their internship training.

Sample size determination: Sample size was estimated using the formula $N = \underline{Z^2pqd^2}$

where N = desired sample size; Z =standard normal deviation at 1.96 (corresponding to 95% confidence interval); P= proportion in the target population estimated to have the desired characteristics; q = 1- p; d = degree of accuracy. $N = \frac{(1.96)2 \times 0.15 \times .85}{(0.05)^2}$

= 174 (minimum required sample size), which was increased to 230 to make provision for non response, attrition and other factors that tended to introduce bias in the study.

Sampling method: Purposive sampling of doctors whose routine included giving clinical care to sick children.

Study period: The study period spanned through five weeks from 25th August to October 2008.

Data collection: Self administered well structured questionnaire was used to collect data from the subjects. The information sought included demographic characteristics, academic qualification, practice experience, area of specialization, and location of practice, minimum number of children attended to in a typical day, indication as to working in a TB / DOTS centre, ranking of approach by the doctor when confirming the diagnosis of childhood PTB.

The questionnaire was tested on 10 subjects (medical doctors) working at Nnamdi Azikiwe University Teaching Hospital, Nnewi to ensure reliability and validity. However, these questionnaire and information were not included in the analysis.

Five assistant investigators were recruited and given one day training on data collection to ensure completeness in the questionnaire filling.

Data Analysis: Statistical analysis was done using SPSS for windows version 15.

Descriptive statistics such as means, frequency distribution, confidence interval and standard deviation were used to describe the results. Appropriate statistical test were used to analyze and test the significance of associations and differences in findings. Ranking of the diagnostic approach was done to determine the approach most commonly used by doctors in childhood pulmonary tuberculosis.

Ethics: The informed consent of the subjects was obtained orally before their inclusion in the study. Every attempt was made to keep the content of the questionnaire confidential and anonymous. Subjects were made to understand that they were free to withdraw from the study at any time they wished to do so before its conclusion.

REPORT

A total of 230 questionnaires were distributed to the study subjects in the southeastern zone of Nigeria, and 223 were returned. 221 questionnaires were analyzed after rejecting two questionnaires that were found to be incomplete, giving 96.1% response rate.

Table 1: The distribution of respondents by state and type of hospital

Variable	*Frequency*	Percent
State		
Anambra	81	36.7
Abia	58	26.2
Imo	38	17.2
Enugu	34	15.4
Ebonyi	10	4.5
Type of hospital		
Public	127	57.5
Private	84	38.0
Faith based	10	4.5
	221	100

The distribution of respondents from each of the five southeastern states show that slightly more than one third (36.7%) of the respondents were from Anambra state while respondents from Ebonyi (4.5%) constituted

the fewest (see table 1). Nearly 58% of these doctors work in public hospitals and less than 5% work in faith based hospital, while 38% work in private hospitals.

Table 2: Age and sex distribution of the doctors in this study

Age group	Male	Female	Total (%)	χ^2 - value	P-value
Years	Frequency (%)	Frequency (%)			
<30	13 (7.6)	9 (18.0)	22 (10.0)		
30-34	50 (29.2)	19 (38.0)	69 (31.2)		
35-39	34 (19.9)	12 (24.0)	46 (20.8)		
40-44	19 (11.1)	2 (4.0)	21 (9.5)	11.428	0.076
45-49	22 (12.9)	4 (8.0)	26 (11.8)		
50-54	13 (7.6)	1 (2.0)	14 (6.3)		
55+	20 (11.7)	3 (6.0)	23 (10.4)		
Total	**171(77.4)**	**50 (22.6)**	**221 (100.0)**		

The age and sex distribution show a preponderance of males with a sex-ratio of 3.4:1.0. The males, with a (mean ± SD) 40.6±10.43 years, were statistically significantly older than the females 25.9 ± 8.2 years (t = 2.938, P = 0.004). Majority of the female respondents (80%) were less than 40 years of age, while only 56% of their male counterparts were in that age category.

Table 3: The distribution of respondents by number of consultations per day.

	Frequency (%)	χ^2 - *2 value*	P-value
No of children consulted per day			
≤2	41(18.6)		
3-5	71(32.1)		
6-9	34(15.4)	76.498	0.000
≥10	75(33.9)		
Total	**221(100.0)**		

Similarly, one third of respondents saw =10 sick children per day, another one third saw 3-5 children, while less than one fifth saw =2 and 6-9 children.

Table 4: The distribution of respondents by their years of practice

Years of Practice	*Frequency*	Percentage
<5	75	33.9
5-9	57	25.8
≥10	89	40.3
Total	**221**	**100.0**

A majority of the respondents had =10 years, while one quarter had 5-9 years and about one third had <5 years experience in practice.

Table 5: The Frequency of consultation in relation with working in a TB/DOT centre

No of Consultation per day	Work in a TB/Dot Centre			
	Yes Frequency (%)	No Frequency (%)	Total (%)	P-value
<2	13 (5.9)	28 (12.7)	41 (18.6)	
3-5	19 (8.6)	52 (23.5)	71 (32.1)	0.648
6-9	8 (3.6)	26 (11.8)	34 (15.4)	
e 10	16 (7.2)	59 (26.7)	75 (33.9)	
Total	56 (25.3)	165 (74.7)	221(33.9)	

Approximately, three quarters of the respondents worked in non TB/DOTS centers, while one-quarter worked in a TB/DOTS centre. Those who attended to children =10 years and 3-5 years in a typical day were 33.9% and 32.1%, respectively. The pattern of consultations per day appears similar in both group of doctors working in a TB/DOT centre and those not (P > 0.05). The difference was not statistically significant.

Table 6: The ranking of diagnostic approach by respondents.

Diagnostic Approach	Rank 1	Rank 2	Rank 3	Rank 4	Rank 5	Rank 6
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Clinical features	123 (56.4)	41 (18.8)	29 (13.3)	11 (5.0)	2 (0.9)	13 (6.0)
Bacteriology-SSM	28 (12.8)	49 (22.5)	81 (37.2)	7 (3.2)	22 (10.1)	32 (14.7)
Radiology-chest X-ray	30 (13.8)	44 (20.2)	55 (25.2)	12 (5.5)	45 (20.6)	31 (14.2)
Histology-biopsy	13 (6.0)	40 (18.3)	42 (19.3)	28 (12.8)	62 (28.4)	34 (15.6)
Immunology-TST	12 (5.5)	26 (11.9)	8 (3.7)	46 (21.1)	66 (30.3)	59 (27.1)
Therapeutic trial with anti-TBdrug	12 (5.5)	18 (8.3)	3 (1.4)	114 (52.3)	21 (9.6)	49 (22.2)
Total	218(100.0)	218(100.0)	218(100.0)	218(100.0)	218(100.0)	218(100.0)

Clinical features elicited from patients' history had the highest percentage on the first rank, while bacteriologic investigation was highest in the second rank (see table 6). The third rank was bacteriologic investigation followed by radiologic investigation, which was second to the highest in rank 3. Therapeutic drug trial with standard anti TB drug was ranked fourth, while immunologic investigation was ranked fifth and sixth. Histological investigation received residual ranking.

Table 7: Summary of ranking using different characteristics of the respondents

Doctors	Rank 1	Rank 2	Rank 3	Rank 4	Rank 5	Rank 6
All Doctors	Clinical features (56.4%)	Bacteriology (22.5%)	Bacteriology (37.2%) (Radiology 25.2%)	Therapeutic trial (52.3%)	Immunology (30.3%)	Immunology (27.1%) (Therapeutic trial 22.2%)
In TB/DOT Centre	Clinical features (49.1%)	Clinical features - 29.1%) (Bacteriology - 23.6%)	Bacteriology (40%) (Radiology - 27.3%)	Therapeutic trial with anti TB drug (49.1%)	Immunology (29.1%)	Immunology (27.3%)
In Public Hospitals	Clinical features (47.6%)	Bacteriology (23.8%)	Bacteriology (37.3%) (Radiology - 23.8%)	Therapeutic trial with anti TB drug (51.6%)	Histology (32.5%)	Immunology (28.6%)
In Private Hospitals	Clinical features (68.3%)	Radiology (28%)	Bacteriology (37.8%)	Therapeutic trial with anti TB drug (56.1%)	Immunology (39%)	Immunology (24.4%)
In Faith based hospital	Clinical features (70%)	Radiology (30%) (Clinical features 30%)	Histology (50%)	Therapeutic trial (30%) (Immunology 30%)	Bacteriology (30%) (Radiology 30%)	Immunology (30%) (Therapeutic trial 30%)

Clinical feature was ranked first by all medical doctors scoring it highest (table 7). In the second rank respondents generally scored bacteriologic investigation as second. However, there were variations in their individual scoring depending on the respondents' background. Those working in TB/DOTS centres preferred clinical features to bacteriologic investigation and those in private and faith based hospitals preferred radiologic to bacteriologic

approach. Those in faith based hospitals ranked bacteriologic approach fifth. Therapeutic trial with anti TB drugs was scored consistently highest in rank 4 by all categories of respondents.

The pattern in rank 3 score was generally double ranking for bacteriology followed by radiology. However, doctors in faith based hospitals ranked histology third. Therapeutic trial with anti-TB drugs was consistently ranked 4 by all categories of respondents (see table 7). Immunology was generally ranked fifth with some variations; respondents in public hospitals and those in faith based hospitals preferred histologic, bacteriologic and radiologic investigation, respectively. The residual ranking of six, varied between immunologic test and therapeutic trial with anti TB drugs.

Table 8: The ranking of diagnostic approach by medical doctors who hold fellowship qualification in paediatrics.

Approach	*Rank 1*	*Rank 2*	*Rank 3*	*Rank 4*	*Rank 5*	**Rank 6**
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Clinical Features	14(77.8)	1(5.6)	1(5.6)	1(5.6)	0(0.0)	2(11.1)
Bacteriology (SSM)	1(5.6)	1(5.6)	13(72.2)	0(0.0)	1(5.6)	2(11.1)
Radiology (CXR)	2(11.1)	1(5.6)	3(16.7)	3(16.7)	8(44.4)	1(5.6)
Histology (Biopsy)	1(5.6)	5(27.8)	1(5.6)	3(16.7)	6(33.3)	2(11.1)
Immunology (TST)	0(0.0)	3(16.7)	0(0.0)	4(22.2)	2(11.1)	8(44.4)
Anti TB drug trial	0(0.0)	7(38.9)	0(0.0)	7(38.9)	1(5.6)	3(16.7)
Total	18(100.0)	18(100.0)	18(100.0)	18(100.0)	18(100.0)	18(100.0)

Table 8 shows that an overwhelming majority of the respondents (77.8%) who hold fellowship qualification in Paediatrics ranked clinical features first. Good clinical response to anti-TB drug trial was ranked second, bacteriological investigation third, while good clinical response to anti-TB drug trial, radiological investigation and Immunologic investigation as fourth, fifth and sixth, respectively.

DISCUSSION

Majority of the respondents worked in public health facilities with a preponderance of males who were on the average older in age than the female 40.6±10.43 years and 25.9±8.2 years, respectively.

This study found that majority of medical doctors ranked clinical features as first in the diagnosis of childhood PTB. This ranking was consistent for all categories of doctors who attended to childhood pulmonary tuberculosis. Although, extensive literature search by the authors failed to reveal studies that ranked approaches or criteria for the diagnosis of childhood PTB in other centers, Marias et al described well defined symptoms as a prime diagnostic tool that could improve the chances of diagnosing childhood PTB, even in resource limited settings[3]. The finding in this study tended to agree with that statement.

Bacteriologic and radiologic investigations were probably used for definitive diagnosis of childhood PTB following a high index of suspicion raised by the presence of well defined clinical features (symptoms and signs). Bacteriologic investigation with sputum smear AFB was regarded as the gold standard in the diagnosis in PTB, while radiologic investigation showed abnormal changes consistent with active pulmonary tuberculosis and the potentials of the patient to spread the infection to others.

Therapeutic trial with anti TB drug and immunologic investigation (tuberculin skin testing) were ranked fourth and fifth, respectively by respondents. These tests appear to be useful when the first three criteria with high predictive values[3] could not be relied upon or when the results of the bacteriologic tests were unequivocal.

Histologic investigation using biopsy of lymph nodes and tissues was given residual ranking probably because often times the lymph node enlargement or tissue involvement occur in extra pulmonary tuberculosis.

The study showed a slight variation in the order of ranking between different categories of doctors. However, clinical features and therapeutic trial emerged the most consistent of all the criteria in the ranking order among the different categories of respondents.

This study found that respondents in public practice ranked bacteriologic investigation twice ie. rank 2 and 3, while those in private practice ranked radiologic investigation 2 and bacteriologic investigation 3. The impact of this slight difference in the diagnosis of childhood pulmonary tuberculosis may be great when it is considered that about 93.2% of respondents belong to these two categories, therefore a slight change in either of these two criteria could affect the predictive value of the approach which may be misleading to the doctor. However, no attempt was made to study the predictive value of these diagnostic criteria.

The study showed that the specialists in the field of

paediatric medicine had a different ranking; clinical features -1, therapeutic trial -2, bacteriologic investigation -3, therapeutic trail (again) -4 (followed by Immunologic investigation), radiologic investigation -5 and Immunologic investigation -6. This study showed that paediatric specialists relied more on clinical features and therapeutic trials in the light of evidence of poor yield by other approaches (investigations) to confirm a diagnosis of childhood PTB. This finding agreed with the recommendations by WHO and showed that well defined clinical features supported by therapeutic trials had the potentials of improving the case finding of childhood PTB. A study is therefore required to validate the clinical algorithm in this environment for use by all doctors who attend to sick children.

CONCLUSION: the authors conclude that most clinicians follow a fairly similar approach in the diagnosis of childhood PTB; clinical features, bacteriologic investigation, radiologic investigation, therapeutic trial, immunologic investigation (TST), and histologic investigation. The specialist in paediatric medicine relied more on clinical features and therapeutic trials for their diagnosis of childhood PTB and this was in agreement with WHO's recommendation.

RECOMMENDATION: A study is needed to validate the use of clinical features and other approaches found in this study for the diagnosis of childhood PTB.

LIMITATION

A non probabilistic survey design was used in this study with all the possible biases. Although, efforts were made to limit the potential bias, caution should be exercised in the generalization of the conclusions of this study. Paucity of literature on this topic allowed only restricted comparative analysis in the discussion despite important findings in this study.

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REFERENCE

1. Marais BJ, Obihara CC, Gie RP, Schaaf HS, Hesseling AC, Lombard C et al. The prevalence of symptoms associated with pulmonary tuberculosis in randomly selected children from a high-burden community. Arch Dis Child 2005; 90: 1166-1170.
2. Marais BJ, Gie RP, Obihara CC, Hesseling AC, Schaaf HS, Beyers N. Well-defined symptoms are of value in the diagnosis of childhood pulmonary tuberculosis. Arch Dis Child 2005; 90:1162-1165.
3. Marais BJ, Gie RP, Hesseling AC, Shaaf HS, Lombard C, Enarson DA et al. A refined symptom-based approach to diagnose pulmonary tuberculosis in children. Pediatrics. 2006; 118 (5):e1350-9.
4. Eamranond P, Jaramillo E. (2001) Tuberculosis in children: reassessing the need for improved diagnosis in global control strategies. Int J Tuberc Lung Dis; 5:594-603.
5. Zar HJ, Hanslo D, Apolles P, Swingler G, Hussey G. Induced sputum versus gastric lavage for microbiological confirmation confirmation of pulmonary tuberculosis in infants and young children: a prospective study. Lancet 2005; 365:130-134.
6. Starke JR. Pediatric tuberculosis: time for a new approach. Tuberculosis (Edinb) 2003; 83: 208-212.
7. Singh M, Moosa NVA, Kumar L, Sharma M. Role of gastric lavage and bronchoalveolar lavage in the bacteriological diagnosis of childhood pulmonary tuberculosis. Indian Pediatrics 2000; 37:947-951.
8. Marais BJ, Gie RP, Hesseling AC, Beyers N. Adult-type pulmonary tuberculosis in children aged 10-14 years. Pediatr Infect Dis J 2005; 24: 743-744.
9. Schaaf HS, Michaelis IA, Richardson M, Booysen CN, Gie RP, Warren R et al. Adult-to-child transmission of tuberculosis: household or community contact? Int J Tuberc Lung Dis 2003; 7: 426-431.
10. Verver S, Warren RM, Munch Z, Richardson M, van der Spuy GD, Borgdorff MW et al. Proportion of tuberculosis transmission that takes place in households in a high-incidence area. Lancet 2004; 363: 212-214.
11. Obihara CC, Kimpen JL, Gie RP, Lill SW, Hoekstra MO, Marais BJ et al. Mycobacterium tuberculosis infection may protect against allergy in a tuberculosis endemic area. Clin Exp Allergy 2006; 36: 70-76.
12. Weismuller MM, Graham SM, Claesens NJ, Meijnen S, Salaniponi FM, Harries AD. Diagnosis of childhood tuberculosis in Malawi: an audit of hospital practice. Int J Tuberc Lung Dis 2002; 6: 432-438.
13. Enarson PM, Enarson DA, Gie RP. Management of tuberculosis in children in low-income countries. Int J Tuberc Lung Dis 2005; 9: 1299-1304.
14. Hesseling AC, Schaaf HS, Gie RP, Starke JR, Beyers N. A critical review of diagnostic approaches used in the diagnosis of childhood tuberculosis. Int J Tuberc Lung Dis 2002 ;6 :1038-1045.