## Childhood Tuberculosis in a South-East Nigerian Tertiary Hospital: Treatment Outcomes and Determinants

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## Abstract

**Background and Objectives:** Tuberculosis (TB) is an important cause of childhood morbidity and mortality. Understanding the barriers to successful childhood TB treatment is vital to curbing the scourge of childhood TB. This study examined the outcomes and factors that influence the outcomes of childhood TB treatment in a South-East Nigerian tertiary hospital. **Methods:** A 10-year review of the medical records of under-15 year olds, who received anti-TB treatment at Nnamdi Azikiwe University Teaching Hospital, Nnewi, was carried out. Data were analyzed using SPSS version 20. **Results:** Majority of the 501 childhood TB cases were new (89.6%) and pulmonary (73.3%) TB cases. TB-HIV coinfection occurred in 42.5% of cases. The rate of successful treatment was 62.9%. About 57.5% completed treatment, 5.4% were cured, 7.0% were transferred out, 21.4% were lost to follow-up, 0.4% had treatment failure while 8.4% died. Majority (61.6%) of deaths or loss to follow-up occurred during the first 2 months of treatment. Factors significantly associated with treatment outcomes were ascertainment of HIV status (P = 0.049), disease site (P = 0.013), nutritional status (P = 0.039), Mantoux test result (P = 0.002), and period of treatment (P = 0.005). **Conclusion:** Findings indicate high rate of unsuccessful childhood TB treatment, as well as adherence to and completion of treatment. Special attention should be given to high-risk groups including those with unknown HIV status, extrapulmonary TB, and severe malnutrition. It is imperative to determine the HIV status of all childhood TB cases.

Keywords: Childhood tuberculosis, children, Nigeria, outcomes, treatment

## INTRODUCTION

Tuberculosis (TB) is a significant cause of childhood morbidity and mortality. Globally, TB is the 9th leading cause of death and the highest cause of death occurring from a single infectious agent.<sup>[1]</sup> In 2016, an estimated 10.4 million people became ill with TB, of whom about 1.67 million died.<sup>[1,2]</sup> Childhood TB accounts for 10%-11% of annual incidence of TB globally. Currently, Nigeria ranks 4th among the 30 countries with highest TB burden globally, and in 2016, about 56,000 children <15 years were estimated to have TB in the country.<sup>[1,3]</sup> Childhood TB is an important public health issue as it represents recent and ongoing transmissions as well as a potential reservoir for future epidemics if not treated properly.<sup>[4]</sup> One major factor that militates against successful childhood TB treatment, especially in developing countries, is difficulty with bacteriologic confirmation due to children's inability to produce quality sputum. Hence, many children suffering from TB may not benefit from timely and appropriate treatment

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which is vital for successful outcomes. Besides, children are more likely to develop more serious forms of TB and therefore at higher risk of death from TB.<sup>[4-6]</sup>

Despite efforts by World Health Organization (WHO)<sup>[5]</sup> and partners to scale up childhood TB management and achieve zero childhood TB deaths, TB continue to kill children in large numbers. Hence, childhood TB is now in global spotlight on account of its significant contribution to overall TB and childhood mortality.<sup>[1,5,7]</sup> In 2016, the global case fatality rate of childhood TB was approximately 25% as 250,000 out of the estimated one million incident cases

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died.<sup>[2]</sup> Notably, majority (>70%) of these deaths occur in Africa and South-East Asia, especially among under-fives.<sup>[6]</sup> The incidence of childhood TB deaths is highest in populous high-burden countries with India, Nigeria, China, Indonesia, and Democratic Republic of Congo leading in descending order.<sup>[6]</sup> To curb the menace of childhood TB, the barriers to successful treatment should be clearly understood and urgently addressed.

Surprisingly, there is paucity of data on childhood TB treatment outcomes, especially in Sub-Sahara African countries like Nigeria. Hence, this study was conducted to examine the outcomes as well as factors that influence the outcomes of children TB treatment at Nnamdi Azikiwe University Teaching Hospital (NAUTH), Nnewi, South-East, Nigeria. Results will guide stakeholders in adopting strategies that will ensure improved quality of care and outcomes of children suffering from TB.

## METHODS

A 10-years retrospective study was conducted to determine the outcomes of children <15 years of age, who received treatment for TB in NAUTH Nnewi, between April 2007 and May 2017, and had a documented final outcome. NAUTH is a tertiary teaching hospital located in Nnewi, one of the three largest commercial cities in Anambra State, South-East Nigeria. It serves as a referral center for Anambra and neighboring states. In NAUTH, TB treatment is provided and monitored by the Directly Observed Treatment short course (TB DOTS) Unit which is manned by adequately trained nurses and doctors. There was no separate Pediatric TB DOTS Unit in the hospital during the reviewed period. The NAUTH TB DOTS Unit provides services on every week day, and treatment for TB is free.

Data on date of presentation, age, gender, place of residence, weight, treatment supporter, disease category, HIV status, disease site, and treatment outcomes were abstracted from the treatment register and hospital records of eligible children.

The nutritional status of individuals aged 0–10 years of age was obtained by calculating the Z-scores of enrollment weight-for-age using the WHO growth chart. Children were categorized as normal if the Z-score of weight-for-age ranges between >-2 and <+2, moderate malnutrition if it ranges from  $\leq -2$  to >-3, severe malnutrition if it is  $\leq -3$ , and obese if z-score is  $\geq +2$ .

Statistical analysis was done using Statistical Package for Social Sciences (SPSS) version 20, (IBM Corp., Armonk, New York, U.S.A., 2011). Individuals' baseline characteristics were summarized using frequencies, percentages, means, and standard deviations. Chi-square test was used to determine the association between categorical variables. Kolmogorov– Smirnov test yielded P < 0.001 for both age and duration of treatment denoting that the data were not normally distributed. Thus, Mann–Whitney test, a nonparametric test, was used to determine the association between outcome and the continuous variables. Any P < 0.05 was considered as statistically significant.

#### Diagnosis, treatment, and definition of outcome variables

The diagnosis of TB was made according to standard guidelines.<sup>[8]</sup> Children with presumed TB, based on clinical suspicion and history of contact with TB case, were further evaluated using ancillary investigations such as tuberculin skin test (Mantoux test) and radiologic investigations, especially chest X-ray. Bacteriologic confirmation of diagnosis was done using Ziehl-Neelsen stain for acid-fast bacilli (AFB) on sputum samples of children who could expectorate. Where sputum was not obtainable, clinical specimens such as gastric aspirate, cerebrospinal fluid as well as lymph node fine needle, peritoneal or pleural aspirates were used depending on the site of infection. In 2015, the Nigerian National Tuberculosis and Leprosy Control Programme (NTBLCP) endorsed Gene Xpert test (Xpert MTB/RIF) as the initial diagnostic test for children with presumed TB. However, cassettes for nonsputum specimens became available shortly before the end of the reviewed period. Therefore, only few children benefited from Xpert MTB/RIF for isolation of AFB and rifampicin susceptibility testing. The NTBLCP guidelines approve clinical diagnosis of TB (smear-negative TB) based on the judgment of a competent clinician. The children were offered HIV counseling and testing as part of standard care.

The children were treated with standard regimen containing rifampicin (R), isoniazid (H), pyrazinamide (Z), ethambutol (E), and streptomycin (S), according to the NTBLCP guidelines. Before 2015, children with new and retreatment TB cases were treated with category 1 (2HRZ/4HR) and category 2 (2SHRZE/1HRZE/5HRE) anti-TB regimen, respectively. From 2015, children with pulmonary and some extrapulmonary TB (except TB meningitis, miliary TB, and osteoarticular TB) were treated with R6 regimen (2RHZE/4HR) irrespective of whether they were new or retreatment cases. On the other hand, those with TB meningitis, miliary, or osteoarticular TB were treated with R12 regimen (2RHZE/10RH) whether they were new or retreatment cases.

TB treatment outcomes were categorized according to the NTBLCP guidelines as follows:<sup>[8,9]</sup>

#### Cured

Pulmonary TB patient with bacteriologic confirmation of TB (smear, Xpert MTB/RIF or culture positive) at the beginning of treatment, who completed treatment and was smear or culture negative on two occasions (with an interval of at least 1 month), one of which should be in the last month of treatment.

## Treatment completed

TB patient who completed treatment but without evidence of cure or failure either because the smear or culture was not done or the results were not available.

## Died

TB patient who dies for any reason during the course of treatment.

## Lost to follow-up

TB patient with treatment interruption for 2 consecutive months or more.

## Treatment failure

Pulmonary TB patient with bacteriologically diagnosed TB, whose sputum smear or culture remains positive at 5 months or later after commencement of treatment, or who interrupted treatment for >2 months after completing 1 month of therapy, returned to treatment and is found to be smear or culture positive.

## Transferred out

Patients that moved out of the health facility catchment area.

#### Successful treatment

Sum of cases that were cured and those that completed treatment.

## Unsuccessful treatment

Sum of cases that were lost follow-up, died, or failed treatment.

## RESULTS

## **Baseline characteristics**

A total of 501 children commenced anti-TB drugs during the reviewed period. The age of the individuals ranged from 2 months to 14 years with a median and mean age of 5.0 and  $6.15 \pm 4.49$  years, respectively, and interquartile range of 8. Other baseline characteristics of the children are shown in Table 1. The male: female ratio was approximately 1:1. Majority of them had new TB cases (89.6%) and pulmonary TB (73.3%), received category 1 or R6 anti-TB regimen (90.2%), and had at least one parent (85.4%) as caregiver. The HIV status of majority of the individuals (91.2%) was known with more than a third of them (42.5%) being HIV positive.

#### **Treatment outcomes**

The treatment outcomes of the children are shown in Table 1. Approximately 7% were transferred out, 62.9% had successful treatment while unsuccessful treatment was documented in 30.1% of cases. Lost to follow-up accounted for majority (71.3%) of the 151 individuals with unsuccessful treatment outcome while 28.3% and 1.3% of them died or had treatment failure, respectively.

As shown in Figure 1, majority (61.6%) of death or lost to follow-up occurred within the first 2 months of treatment. The mean duration of treatment of those who were lost to follow-up or those who died were  $2.10 \pm 1.83$  and  $2.21 \pm 1.94$  months, respectively. Mann–Whitney test indicated that there was no statistically significant difference between the duration of treatment of those who died or were lost to follow-up (P = 0.970).

On the other hand, the mean duration of treatment among those who were transferred out was  $1.47 \pm 1.53$  months. Among the 35 individuals who were transferred out, majority lived outside Nnewi (91.4%), were new cases (94.4%), had pulmonary TB (77.1%), and were treated with either category

## Table 1: Baseline characteristics of the individuals and treatment outcomes

Characteristics         Number $(n=501)$ , $n$ (%)           Sex         Male         253 (50.5)           Female         248 (49.5)           Place of residence            Nnewi         79 (15.8)           Other towns in Anambra state         390 (77.8)           Other states         320 (77.8)           Other states         244 (48.7)           Positive         244 (48.7)           Positive         244 (48.7)           Positive         213 (42.5)           Unknown         44 (8.8)           Care giver            Parent (s)         428 (85.4)           Others         73 (14.8)           Disease site            Pulmonary         367 (73.3)           Extrapulmonary         134 (26.7)           Patient category            New case         449 (89.6)           Retreatment case         48 (9.6)           Transferred in         4 (0.8)           Treatment case         48 (9.6)           Rof         68 (13.6)           R12         5 (1.0)           Treatment outcome            Cured         27 (5.4)           Treatment					
Male       253 (50.5)         Female       248 (49.5)         Place of residence          Nnewi       79 (15.8)         Other towns in Anambra state       390 (77.8)         Other states       32 (6.4)         HIV status          Negative       244 (48.7)         Positive       213 (42.5)         Unknown       44 (8.8)         Care giver          Parent (s)       428 (85.4)         Others       73 (14.8)         Disease site          Pulmonary       367 (73.3)         Extrapulmonary       134 (26.7)         Patient category          New case       449 (89.6)         Retreatment case       48 (9.6)         Treatment regimen          Cat 1       384 (76.6)         Cat 2       44 (8.8)         R6       68 (13.6)         R12       5 (0)         Treatment outcome          Cured       27 (5.4)         Treatment completed       288 (57.5)         Transferred out       35 (7.0)         Lost to follow-up       107 (21.4)         Treatment	Characteristics	Number ( <i>n</i> =501), <i>n</i> (%)			
Female         248 (49.5)           Place of residence         248 (49.5)           Nnewi         79 (15.8)           Other towns in Anambra state         390 (77.8)           Other states         32 (6.4)           HIV status         244 (48.7)           Negative         244 (48.7)           Positive         213 (42.5)           Unknown         44 (8.8)           Care giver         200 (77.3)           Parent (s)         428 (85.4)           Others         73 (14.8)           Disease site         90 (77.3.3)           Extrapulmonary         367 (73.3)           Extrapulmonary         134 (26.7)           Patient category         86           New case         449 (89.6)           Retreatment case         48 (9.6)           Transferred in         408.           Treatment regimen         241 (48.8)           Cat 1         384 (76.6)           Cat 2         44 (8.8)           R6         68 (13.6)           R12         5 (1.0)           Treatment outcome         200.4           Cured         27 (5.4)           Treatment completed         288 (57.5)           Transfe	Sex				
Place of residence         Nnewi       79 (15.8)         Other towns in Anambra state       390 (77.8)         Other states       32 (6.4)         HIV status       213 (42.5)         Negative       244 (48.7)         Positive       213 (42.5)         Unknown       44 (8.8)         Care giver       200 (77.8)         Parent (s)       428 (85.4)         Others       73 (14.8)         Disease site       200 (77.3.3)         Extrapulmonary       367 (73.3)         Patient category       New case         New case       449 (89.6)         Retreatment case       48 (9.6)         Treatment regimen       200 (71.8)         Cat 1       384 (76.6)         Cat 2       44 (8.8)         R6       68 (13.6)         R12       5 (7.0)         Lost to follow-up	Male	253 (50.5)			
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Other towns in Anambra state $390$ (77.8)           Other states $32$ (6.4)           HIV status	Place of residence				
Other states $32 (6.4)$ HIV status	Nnewi	79 (15.8)			
HIV status       244 (48.7)         Negative       243 (42.5)         Unknown       213 (42.5)         Unknown       44 (8.8)         Care giver       213 (42.5)         Parent (s)       428 (85.4)         Others       73 (14.8)         Disease site       244 (48.7)         Pulmonary       367 (73.3)         Extrapulmonary       367 (73.3)         Putment sctees       48 (9.6)         Treatment case       48 (9.6)         R12       5 (1.0)         Treatment outcome       27 (5.4)         Cured       27 (5.4)         Treatment completed       288 (57.5)         Transfered out       35 (7.0)	Other towns in Anambra state	390 (77.8)			
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Positive $213$ ( $42.5$ )         Unknown $44$ ( $8.8$ )         Care giver $428$ ( $85.4$ )         Others $73$ ( $14.8$ )         Disease site $73$ ( $14.8$ )         Pulmonary $367$ ( $73.3$ )         Extrapulmonary $134$ ( $26.7$ )         Patient category       New case         New case $449$ ( $89.6$ )         Retreatment case $48$ ( $9.6$ )         Treatment regimen $Cat 1$ Cat 1 $384$ ( $76.6$ )         Cat 2 $44$ ( $8.8$ )         R6 $68$ ( $13.6$ )         R12 $5$ ( $1.0$ )         Treatment outcome $Cured$ Cured $27$ ( $5.4$ )         Treatment completed $288$ ( $57.5$ )         Transferred out $35$ ( $7.0$ )         Lost to follow-up $107$ ( $21.4$ )         Treatment failure $2$ ( $0.4$ )         Died $42$ ( $8.9$ )         Unsuccessful $315$ ( $62.9$ )         Unsuccessful $151$ ( $30.1$ )         Transferred	HIV status				
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Care giver       428 (85.4)         Parent (s)       428 (85.4)         Others       73 (14.8)         Disease site       9         Pulmonary       367 (73.3)         Extrapulmonary       134 (26.7)         Patient category       134 (26.7)         Patient category       8         New case       449 (89.6)         Retreatment case       48 (9.6)         Transferred in       4 (0.8)         Treatment regimen       2         Cat 1       384 (76.6)         Cat 2       44 (8.8)         R6       68 (13.6)         R12       5 (1.0)         Treatment outcome       27 (5.4)         Cured       27 (5.4)         Treatment completed       288 (57.5)         Transferred out       35 (7.0)         Lost to follow-up       107 (21.4)         Treatment failure       2 (0.4)         Died       42 (8.4)         Treatment success       315 (62.9)         Unsuccessful       151 (30.1)         Transferred out       35 (7.0)	Positive	213 (42.5)			
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Treatment failure2 (0.4)Died42 (8.4)Treatment success315 (62.9)Unsuccessful151 (30.1)Transferred out35 (7.0)	Transferred out	35 (7.0)			
Died42 (8.4)Treatment success315 (62.9)Unsuccessful151 (30.1)Transferred out35 (7.0)	Lost to follow-up	107 (21.4)			
Treatment successSuccessful315 (62.9)Unsuccessful151 (30.1)Transferred out35 (7.0)	Treatment failure	2 (0.4)			
Successful         315 (62.9)           Unsuccessful         151 (30.1)           Transferred out         35 (7.0)	Died	42 (8.4)			
Unsuccessful         151 (30.1)           Transferred out         35 (7.0)	Treatment success				
Transferred out 35 (7.0)	Successful	315 (62.9)			
	Unsuccessful	151 (30.1)			
Total 501 (100)	Transferred out	35 (7.0)			
	Total	501 (100)			

1 or R6 regimen (97.1%). Their HIV status was positive in 45.7% of cases.

## **Relationship between outcome and some factors**

Tables 2-4 show the relationship between some factors and treatment outcomes. The factors that had statistically significant relationship with treatment outcomes were ascertainment of HIV status, disease site, period of treatment, outcome of Mantoux test, and nutritional status. Those with unknown HIV status had the lowest proportion of successful treatment outcome compared to other groups (52.3% vs. 67.0% among HIV positive and 71.1% among HIV negative, P = 0.049). Likewise, those with pulmonary disease were more likely to have a successful treatment outcome compared to those with extrapulmonary disease (70.3% vs. 60.3%; P = 0.041).

Characteristics	Treatment outcomes		Total, <i>n</i> (%)	Р
	Successful, n (%)	Unsuccessful, n (%)		
Sex				
Female	155 (68.3)	72 (31.7)	227 (48.7)	0.758
Male	160 (67.0)	79 (33.0)	239 (51.3)	
Place of residence				
Nnewi	57 (76.0)	19 (25.0)	76 (16.3)	0.225
Other towns in Anambra	244 (66.7)	122 (33.3)	366 (78.5)	
Other states	14 (58.33)	10 (41.67)	24 (5.2)	
Care giver				
One or both parents	276 (68.8)	125 (31.2)	401 (86.1)	0.158
Others	39 (60.0)	26 (40.0)	65 (14.0)	
HIV status				
Negative	160 (71.1)	65 (28.9)	225 (48.3)	0.049*
Positive	132 (67.0)	65 (33.0)	197 (42.3)	
Unknown	23 (52.3)	21 (47.7)	44 (9.4)	
Disease site				
Pulmonary	239 (70.3)	101 (29.7)	340 (73.0)	0.041*
Extrapulmonary	76 (60.3)	50 (39.7)	126 (27.0)	
Patient category				
New case	282 (67.8)	134 (32.2)	416 (89.3)	0.893
Retreatment	30 (65.2)	16 (34.8)	46 (9.9)	
Transferred in	3 (75.00)	1 (25.00)	4 (0.9)	
Treatment period				
2007-2008	50 (61.7)	31 (38.3)	81 (17.4)	0.005*
2009-2010	63 (59.4)	43 (40.6)	106 (22.7)	
2011-2012	93 (67.9)	44 (32.1)	137 (29.4)	
2013-2014	66 (84.6)	12 (15.4)	78 (16.7)	
2015-2017	43 (67.2)	21 (32.8)	64 (13.7)	
Treatment regimen				
Cat 1	243 (67.7)	116 (32.3)	359 (77.0)	0.607
Cat 2	29 (67.4)	14 (32.6)	43 (9.2)	
R6	41 (69.5)	18 (30.5)	59 (12.7)	
R12	2 (40.0)	3 (60.0)	5 (1.1)	
Total (%)	315 (67.53)	151 (32.47)	466 (100.00)	

Table 2: Relationship	hetween some	characteristics	and	treatment or	utcomes
		0114140101101100	unu	u cauncii cu	

\*Statistically significant

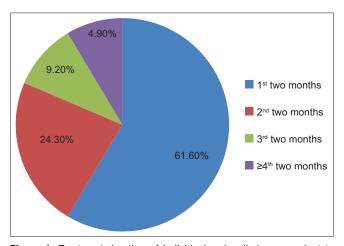


Figure 1: Treatment duration of individuals who died or were lost to follow-up

Treatment between 2013 and 2014 was significantly associated with higher rate of successful outcome compared to other periods (84.6% compared to <70% during the other periods, P = 0.005).

The rate of successful outcome decreased with increasing distance between home and hospital although the relationship was not statistically significant. Likewise, those who had at least one parent as their caregiver had a higher proportion of successful outcome but the relationship was not statistically significant.

Among the investigations done such as Mantoux test, X-ray, and bacteriologic confirmation of TB, only positive Mantoux test was significantly related to outcome. A higher proportion of individuals who had positive Mantoux test had successful treatment outcome compared to those who had negative Mantoux test (78.1% vs. 63.2%, P = 0.002).

Characteristic	Treatment outcomes		Total, <i>n</i> (%)	Р
	Successful, n (%)	Unsuccessful, n (%)		
Mantoux test				
Positive	107 (78.1)	30 (21.9)	137 (29.4)	0.002*
Negative or not done	208 (63.2)	121 (36.8)	329 (70.6)	
X-ray				
Suggestive	240 (67.8)	114 (32.2)	354 (76.0)	0.870
Not suggestive or not done	75 (67.0)	37 (33.1)	112 (24.0)	
Bacteriologic confirmation				
Yes	34 (68.0)	16 (32.0)	50 (10.7)	0.949
No	281 (67.6)	135 (32.5)	416 (89.3)	
Total	315 (67.6)	151 (32.4)	466 (100.0)	

Table 3: Relationshi	p between some	e investigations an	d treatment outcomes

Table 4: Relationship between nutritional status at enrollment and treatment outcome Weight-for-age Z-score (n=372) Successful treatment Р Defaulted Died Total >-2 to <+2 (normal weight) 167 (69.9) 53 (22.2) 19 (7.9) 239 (64.2) 0.039\* ≤-2 to>3 (moderate underweight) 42 (70.0) 12 (20.0) 6 (10.0) 60 (16.1)  $\leq -3$  (severe underweight) 42 (57.5) 20 (27.4) 11 (15.1) 73 (19.6) 372 (100.00) Total 251 (67.5) 85 (22.8) 36 (9.7)

\*Statistically significant

The mean age of individuals who had successful and unsuccessful treatment outcomes were  $6.16 \pm 4.41$  years and  $5.95 \pm 4.56$  years, respectively, while the median age for both groups was 5.00 years. There was no statistically significant relationship between the age of individuals and treatment outcomes, P = 0.506 (Mann–Whitney test).

Among individuals aged 0-10 years, a lower proportion of those who had severe malnutrition at presentation had successful treatment compared to others (57.5% vs. approximately 70% in other groups, P = 0.039).

## DISCUSSION

TB treatment was characterized by relatively poor outcomes during the reviewed period. The overall successful treatment rate (62.9%) was comparable to finding of a similar Tanzanian study.<sup>[10]</sup> However, this contrasts with higher rates (83% and 77.4%) reported by some Nigeria studies which used statewide programmatic data.<sup>[9,11]</sup> The variation may be attributed to the fact that the index study was conducted in a tertiary hospital which is a referral center for more severe TB cases. Similar studies in Northern Nigeria reported lower rates in Kano (52.5%) and Sokoto (53.5%).<sup>[12,13]</sup> This may be explained by higher prevalence of extrapulmonary TB in Kano study as well as other factors that may contribute to unsuccessful treatment outcomes such as malnutrition in Northern Nigeria.<sup>[12,14,15]</sup>

One disturbing finding of this study was the high loss to follow-up rate. This is consistent with previous reports from Thailand and other sub-Sahara African studies as well as the lost to follow-up rate of 21% previously reported among the general population in Anambra State.<sup>[13,16-20]</sup> Possible explanations for high rate of lost to follow-up in childhood TB treatment programs may include tendency of care givers to attribute sickness to other causes due to lack of bacteriologic confirmation of TB, dependence on third party for drug administration and follow-up visits as well as high risk of death (which may be counted as lost to follow-up if not reported). In Nigeria, unsuccessful TB treatment outcomes have been linked to misconceptions around the cause of TB, preference for alternative healthcare, fear of stigmatization, lack of transport fare to health facilities, poor attitude to work, and frequent strike actions by health workers.<sup>[20]</sup> However, further prospective studies are required to confirm these relationships. Children who default from TB treatment are potential reservoirs of multidrug-resistant TB which is associated with high risk of death and constitutes a formidable obstacle against effective TB control. To achieve the Global End TB targets, childhood TB treatment programs should adopt alternative treatment completion strategies such as the home-based (door-step) approach which was demonstrated to significantly improve treatment completion rate among South African children.<sup>[21]</sup>

The mortality rate in this study is consistent with previous reports from some low-income countries in Asia and Africa.<sup>[9,13,16-19,21]</sup> Higher rate of death was reported in Kano Nigeria which may be due to higher prevalence of extrapulmonary TB. Reducing mortality attributable to TB could be achieved by proactive search for TB cases through effective case contact management, early diagnosis, and timely treatment as well as intensified efforts to ensure adherence to and completion of treatment.

The low rate of treatment failure was not unexpected and agrees with previous reports.<sup>[10,12,13]</sup> However, this should be interpreted with caution since the definition of treatment failure in DOTS program is usually based on sputum smear positivity. However, the diagnosis of childhood TB treatment failure could also be made if there is no resolution or worsening of symptoms as well as poor weight gain or continuing weight loss.<sup>[8,22]</sup> To improve reportage of childhood TB treatment failure, such diagnostic criteria should be put into consideration.

The significant relationship between treatment outcome and disease site as well as determination of HIV status is in keeping with previous reports.<sup>[1,4,9-13]</sup> Higher proportion of children with unknown HIV status significantly had unsuccessful outcome compared to other groups. Similar finding was reported in southwestern and northern Nigeria.<sup>[13,16]</sup> Many of these children could have undiagnosed and untreated HIV that may increase their risk of death. Therefore, very strong collaboration is imperative between TB and HIV programs to ensure the ascertainment of the HIV status of every child on TB treatment. The lack of marked difference between the proportion of HIV-positive and HIV-negative individuals with successful outcomes, unlike previous reports, could be a positive fallout of the joint effort of both HIV and TB programs in ensuring adherence to treatment and retention in care.

The significantly higher rate of unsuccessful treatment among severely malnourished children highlights the need for utilization of anthropometric indices in predicting children with higher risk of unsuccessful outcomes. Such children should be nutritionally rehabilitated and closely monitored to forestall death.

The isolated statistically significant higher successful treatment rate in 2013 and 2014, compared to other periods, contrasts with a progressively increasing national trend. The explanation for the observation is not clear but may not be unconnected with repeated and prolonged industrial actions by health workers which has been previously identified as a serious threat to achievement of targets.<sup>[20]</sup> A strategy to ensure continued service delivery and provision of anti-TB drugs during periods of industrial strike actions should be identified and effectively implemented.

Contrary to expectation, there was no significant relationship between retreatment and childhood TB treatment outcomes in contrast to several previous reports.<sup>[1,8,12,22-25]</sup> This may be attributed to the limited number of retreatment cases which might have underestimated its impact on TB treatment outcomes. This can also explain the lack of significant relationship between treatment regimen and outcomes.

The significant relationship between outcome and positive Mantoux test as well as lack of significant relationship between outcome and suggestive X-ray agrees with report by Jiya *et al.*<sup>[13]</sup> This could be attributed to the difference in the specificity of the two tests. However, the lack of significant relationship between successful outcome and bacteriologic confirmation of cases was surprising and differs from previous reports.<sup>[10,11,16]</sup> This may be explained by the small proportion of

bacteriologically confirmed cases in the index study. Therefore, search for a more sensitive and specific nonsputum-based childhood TB diagnostic tool should be intensified.

The mean duration of treatment among those who had unsuccessful outcome corroborates with previous report that death occurs early in childhood TB treatment, especially within the first 2 months of treatment.<sup>[13]</sup> Children on TB treatment have been documented to have 8 times higher risk of death during the intensive compared to continuation phase of treatment.<sup>[13]</sup> This buttresses the need for early diagnosis and treatment as well as adequate patient monitoring, especially during the intensive phase.

## **CONCLUSION/RECOMMENDATION**

Findings of this study indicate a high rate of unsuccessful childhood TB treatment outcome with majority of deaths or loss to follow-up occurring within the first 2 months of treatment. Higher risk of unsuccessful treatment occurred among children with unknown HIV status, extrapulmonary TB, severe malnutrition, negative or no Mantoux test result, and those who were not treated between years 2013 and 2014.

Findings highlight the need for early diagnosis as well as effective monitoring and supervision of childhood TB treatment to ensure treatment completion and survival. Special attention should be given to those with higher risk of unsuccessful outcome. Efforts should be intensified to ensure ascertainment of the HIV status of all childhood TB cases. The NTBLCP should adopt strategies to ensure uninterrupted services and drug supply, especially during industrial strike actions.

## Limitations

This study was limited by the fact that it was a retrospective study conducted in a single tertiary health facility. Therefore, certain inferences cannot be drawn. For instance, mortality rate may be underestimated as deaths after exit from care were not accounted for. In addition, potential confounding factors such as BCG vaccination status, adherence to treatment, drug dosage, drug reactions, and interactions could not be adjusted for. Furthermore, the population may represent children with increased risk of unsuccessful outcomes which may not be so apparent in programme-level data. Therefore, findings may not be a true representation of what is obtainable in the general population. A larger prospective community-based evaluation of childhood TB treatment outcomes is recommended.

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### **Conflicts of interest**

There are no conflicts of interest.

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## ملخص المقال باللغة العربية

# السل في الطفولة في مستشفى ثالثي بجنوب شرق نيجيريا: نتائج العلاج والمحددات

المؤلفون:

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**الخلفية والأهداف**: السل (TB) هو سبب مهم لمراضة ووفيات الأطفال. فهم الحواجز لعلاج مرض السل الناجح في مرحلة الطفولة أمر حيوي لكبح آفة مرض السل في الطفولة. بحثت هذه الدراسة العوامل والمخرجات التي لها تأثير على نتائج علاج مرض السل في الطفولة في مستشفى ثالثي بجنوب شرق نيجيريا.

الطرق: هذه دراسة استيعاديه لمدة عشرة سنوات لسجلات أطفال أقل من 15 عاما والذين تلقوا العلاج المضاد للسل في مستشفى نامدي أزيكيوي الجامعي، نيني. تم تحليل البيانات باستخدام SPSS الإصدار 20.

النتائج: غالبية حالات السل (89.6 ٪) في مرحلة الطفولة كانت جديدة، (73.3 ٪) من الحالات كانت مصابة بالسل الرئوي. (42.5%) من الحالات كانت تعاني من السل وفيروس نقص المناعة البشرية. كان معدل نجاح العلاج (62.6٪)، في حين أن فقط (57.5٪) أنهوا العلاج. فقط (5.4٪) عولجوا، (7.0٪) تم نقلهم، (21.4٪) لم العلاج (62.6٪)، في حين أن فقط (5.5٪) أنهوا العلاج. فقط (5.4٪) عولجوا، (7.0٪) تم نقلهم، (21.4٪) لم يستمروا في المتابعة، (0.4٪) عانوا من فشل العلاج، بينما توفى (8.4٪). حدثت غالبية حالات الوفاة أو عدم الاستمرار في المتابعة (6.6٪) خلال أول شهرين من العلاج. كانت العوامل المرتبطة بشكل كبير بنتائج العلاج الاستمرار في المتابعة (6.6٪) خلال أول شهرين من العلاج. كانت العوامل المرتبطة بشكل كبير بنتائج العلاج الاستمرار في المتابعة (6.6٪) خلال أول شهرين من العلاج. كانت العوامل المرتبطة بشكل كبير التائج العلاج الاستمرار في المتابعة (6.6٪) خلال أول شهرين من العلاج. كانت العوامل المرتبطة بشكل كبير المالاج العلاج الاستمرار في المتابعة (6.6٪) خلال أول شهرين من العلاج. كانت العوامل المرتبطة بشكل كبير المالاج العلاج الاستمرار في المتابعة (6.60٪) خلال أول شهرين من العلاج. كانت العوامل المرتبطة التعليم العلاج العلاج الاستمرار في المتابعة (6.6٪) خلال أول شهرين من العلاج. كانت العوامل المرتبطة المركل العلاج العلاج الاستمرار في المتابعة المناعة البشرية (6.00) ، موقع المرض (6.000) ، الحالة التغذوية (=0)، موقع المرض (6.000) ، نتيجة اختبار مانتوكس (20.00)، وفترة العلاج (6.000) ، نتيجة اختبار مانتوكس (20.00) موقترة العلاج (6.000) ، نتيجة المتار مانتوكس (20.00) موقترة العلاج (6.000) ، نتيجة اختبار مانتوكس (20.00) موقترا العلاج (6.000) موقترة العلاج (6.000) موقت المرض (6.000) مالالي الماليم المناح المرامل (6.000) موقتران المرامل (6.000) ماليم موليم المرامل (6.000) ماليم موليم (7.000) موقترا العلاج (6.000) موقترا الماليم (6.000) ماليم موليم (6.000) موليم (6.000) موليم (6.000) ماليم موليم (6.000) موليم (6.000)

**الخلاصة**: تشير النتائج إلى ارتفاع معدل العلاج غير الناجح لمرض السل في الأطفال. ينبغي تكثيف الجهود لضمان تحسين النتائج من خلال البحث الاستباقي عن حالات السل في مرحلة الطفولة، التشخيص والعلاج في وقت مبكر، وكذلك الالتزام بالعلاج واستكماله. يجب إيلاء اهتمام خاص للمجموعات الشديدة الخطورة، بما في ذلك الفئات غير المعروفة بفيروس العوز المناعي البشري، والسل خارج الرئة، وسوء التغذية الحاد. لا بد من تحديد حالة فيروس نقص المناعة البشرية لجميع حالات السل في مرحلة الطفولة.

الكلمات المفتاحية: السل في الطفولة ، الأطفال ، نيجيريا ، النتائج ، العلاج.