

## Burden and outcome of Childhood Tuberculosis at a Tertiary Health Facility in North-Central, Nigeria

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### ABSTRACT

**Background:** Tuberculosis (TB) remains a disease of public health importance owing to its contribution to morbidity and mortality. It is a chronic infectious respiratory disease that is vaccine preventable and therapeutically curable. Besides, TB is a leading cause of death across all age groups but worse among children. Malnutrition has been shown to be a common risk factor of childhood tuberculosis. **Objectives:** The burden and treatment outcome of childhood TB was determined. **Methods:** A retrospective study of childhood tuberculosis using purposely kept register at both the Emergency Paediatrics Unit (EPU) and the Directly Observed Treatment Short course (DOTS) centre of the Hospital. We included children aged < 18 years either admitted at the EPU or seen at the Paediatric and or General outpatient department of the Hospital from 1<sup>st</sup> January 2019 to the 31<sup>st</sup> December 2019, with presumptive TB and sent to the DOTS centre for treatment. **Results:** The mean age of the children was  $7.7 \pm 3.2$  years. Childhood TB accounted for 88 (7.1%) of the 1243 EPU admissions and accounted for 25.2% of the TB cases managed at the DOTS unit in 2019. Of the 88 children, males were 49. More of the patients (84.1%) had pulmonary tuberculosis. Gene Xpert TB detection rate was 60.2%. Two - third (65.9%) of the cohort were successfully treated. One – quarter (26.1%) of the cases were loss to follow - up, while 8% died on treatment. **Conclusions:** One quarter of the burden of tuberculosis at our facility occurred in childhood, and two – third had pulmonary affection. Approximately two third of these study population were successfully treated. One quarter was loss to follow-up, while one out of every twelve died during the course of treatment.

**Keywords:** Burden, Childhood tuberculosis, Tertiary health facility, Outcome.

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and mortality<sup>1</sup>. It is a chronic infectious respiratory disease that is vaccine preventable and therapeutically curable<sup>2</sup>. Tuberculosis is caused by mycobacteria tuberculosis complex that includes the bovis, avium complex and africanus<sup>3</sup>. This disease is a leading cause of death across all age groups, but worse among children<sup>4</sup>.

The dearth of data on childhood tuberculosis is a common knowledge and it is heightened by the challenge in its diagnoses<sup>5,6</sup>. Diagnosis of tuberculosis in children is not as straight - forward as in adults, because of the non-specificity of the symptoms, pauci-baccillary nature of their sputum and non-classical radiographic features<sup>7</sup>. The relatively newer technique for diagnosis of TB, through the use of Gene Xpert which act via polymerase chain reaction amplification of the organism's genome offer a promising diagnostic outcome<sup>8</sup>. It is useful in the diagnosis of TB, and in detecting Rifampicin resistance, using sputum or other body fluids<sup>8</sup>.

Globally, about 1.5 million people died from TB in 2018, Nigeria is one of the eight nations that

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### Introduction

Tuberculosis (TB) remains a disease of public health importance owing to its contribution to morbidity

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website: www.bornomedicaljournal.com

DOI: 10.31173/bomj.bomj\_2108\_18



contributed to two – third of the global TB epidemics in 2018<sup>9</sup>. Children aged < 15 years accounted for 8% of tuberculosis burden in Nigeria<sup>10</sup>. Garba et al (2) reported 18.3% childhood TB, and pulmonary TB accounted for 76.3% of all cases seen in Gusau North – Western Nigeria. Attah et al<sup>11</sup> in Nasarawa Western senatorial district reported a prevalence of 32% in a multi – centre study of childhood TB risk factors.

Ogbudebe et al<sup>12</sup> found TB amongst 30.4% of under five children and 58.0% of the cases were pulmonary TB. In contrast, Mado et al<sup>13</sup> in Gusau reported a much lower TB prevalence of 4.8% among children admitted with a slightly preponderance (50.7%) of disseminated tuberculosis.

An earlier study had shown malnutrition as a major risk factor for childhood tuberculosis with one in every eight (12.5%) found to be severely malnourished<sup>11</sup>. This study was carried out to assess the burden and the treatment outcome of childhood tuberculosis managed at our facility using the DOTS strategy. We also evaluated their nutritional status and the possible effect(s) of HIV on the outcome of treatment.

### Materials and Methods

This was a retrospective descriptive study of childhood tuberculosis using purposely kept register at both the Emergency Paediatrics Unit and the Directly Observed Treatment Short-course (DOTS) centre of Dalhatu Araf Specialist Hospital (DASH) Lafia.

Children aged < 18 years with complete medical records that where either admitted at the Emergency Paediatrics Unit or seen at the Paediatric and or General outpatient department of DASH Lafia from 1<sup>st</sup> January 2019 to the 31<sup>st</sup> December 2019, with presumptive TB and sent to the DASH DOTS centre for treatment were studied.

#### Procedure for Recruitment

The record of patients with tuberculosis aged less than eighteen years seen between 1<sup>st</sup> of January to 31<sup>st</sup> of December 2019 were retrieved. Names and hospital numbers from the register were used to trace the folders / electronic medical record, and we extracted relevant information including the age, sex, socio-economic and anthropometric parameters. Other information extracted included the form of tuberculosis, site(s) of involvement, Gene Xpert results, duration and outcome of treatment. Missing folder was not a problem as the hospital has both the electronic medical record (EMR) and the physical folder as it is working towards phasing out of the folders and going fully electronic.

The Human Immunodeficiency Virus (HIV) status of the children recruited was also noted. HIV screening was done serially. A negative test to Determine® kit implies HIV negative. A positive Determine® test is confirmed with either the Stat Pak® or Unigold®.

Body Mass Index (BMI) was calculated from the weight and height of the children recorded in the register prior to commencement of anti-tuberculosis. Healthy BMI is from 5<sup>th</sup> to less than 85<sup>th</sup> percentile, less than 5<sup>th</sup> percentile is under-weight, greater than 85<sup>th</sup> to less than 95<sup>th</sup> percentile is overweight while 95<sup>th</sup> percentile and above is obesity. The Z scores for BMI-for-age, height-for-age and weight-for-age was calculated for each child. These was compared with the reference standard using WHO anthro-plus based on age and sex. Z score < -2 is undernourished, < -3 or < -4 is moderate and severe under-nutrition respectively, while ≥+2 is over-nutrition.

The confirmation of TB was done using Gene Xpert testing on sputum sample. Sputum for Gene Xpert was collected in a sterile container with a lid provided by the DOTS centre.

For younger children that cannot produce sputum, a nasogastric tube was passed in the early hours of the day after fasting for at least two hours. A gastric lavage done on an empty stomach and aspirate taken for Gene Xpert analysis. Results are gotten within few hours.

We classified the treatment outcome based on the guidelines by the National Tuberculosis and Leprosy Control Programme (NTBLCP): In brief;

**Cured:** Individual with detected Gene Xpert result before commencing ant - TB, whose sputum smear result became negative at the end of treatment<sup>14</sup>.

**Treatment completed:** Children who completed treatment but who did not meet up with the criteria of being classified as either cured or failed.

**Died:** Those that died during the course of treatment irrespective of the cause of death.

**Loss to follow – up:** Children whose treatment was interrupted for at least two consecutive months.

Those who were either cured or completed treatment were considered as “treatment successful” whiles others were “treatment unsuccessful”.

#### Funding

There was no a grant or support for this study, rather the researchers bear the cost of the study.

#### Conflict of Interest

There is none to be declared

#### Ethical Consideration

The research ethics committee of DASH Lafia gave Ethical approval for this study and waived the



informed consent been a retrospective study. Extracted data were anonymous and absolute confidentiality maintained.

### Data Analysis / Statistics

The data was coded and enter into an excel spreadsheet before transferring to a Statistical Package for Social Sciences (SPSS) version 20. We summarized the age with mean and standard deviations. Categorical variables (gender, site of disease [site of affection / involvement], HIV status and outcome of treatment) were presented using frequency and percentages. Association between categorical variables was determined using chi square test. Results were presented as tables. The p value was considered significant at < 0.05.

### Results

Childhood TB accounted for 88 (7.1%) of the 1243 total Emergency Paediatrics Unit (EPU) admission for the year 2019. Similarly, childhood tuberculosis accounted for 25.2% of the TB cases managed at the DOTS unit in the year 2019. The mean age of the study population was  $7.72 \pm 3.24$ . Of the 88 clients,

males were 49 with a male to female ratio of 1.3:1. Most of the patients (84.1%) had pulmonary tuberculosis. Approximately, two - third (65.9%) of the cohort in this study were successfully treated. More than half (51.1%) of the study population were under-nourished and fourteen (31.1%) had severe form of under-nutrition (**Table 1**).

### Distribution of treatment outcome and disease sites by Age grouping

There is a statistically significant differences in the site of childhood tuberculosis as more children aged 5 years and above had more of extra - pulmonary or disseminated TB  $p = 0.007$ . There are no statistically significant differences on the Gene Xpert results or treatment outcome (**Table 2**).

### Relationship between HIV status, Gene Xpert, site of disease and disease outcome

There is no significant difference between the Gene Xpert result, site of disease and or the treatment outcome of HIV infected compared with their negative controls (**Table 3**).

**Table 1:** Distribution of the children based on disease site, Gene Xpert result, nutritional status and treatment outcome

Variables	Male n (%)	Female n (%)	Total N (%)
Site of Disease			
Pulmonary	41 (55.4)	33 (44.6)	74 (100)
Disseminated	7 (63.6)	4 (36.4)	11 (100)
Extra-pulmonary	1 (33.3)	2 (66.7)	3 (100)
Total	49 (55.7)	39 (44.3)	88 (100)
Gene Xpert Result			
MTB Detected	29 (54.7)	24 (45.3)	53 (100)
MTB Not detected	20 (57.1)	15 (42.9)	35 (100)
Total	49 (55.7)	39 (44.3)	88 (100)
Nutritional status			
Over - nutrition	1 (33.3)	2 (66.7)	3 (100)
Normal	19 (54.3)	21 (45.7)	35 (100)
Under - nutrition	29 (64.0)	16 (36.0)	50 (100)
Mild to moderate	19 (61.3)	12 (38.7)	31 (100)
Severe	10 (68.4)	4 (31.6)	19 (100)
Total	49 (55.7)	39 (44.3)	88 (100)
Treatment Outcome			
Cured	7 (87.5)	1 (12.5)	8 (100)
Treatment completed	27 (54.0)	23 (46.0)	50 (100)
Died	4 (57.1)	3 (42.9)	7 (100)
Loss to follow up	11 (47.8)	12 (52.2)	23 (100)
	49 (55.7)	39 (44.3)	88 (100)

Site of disease = site of affection/involvement, Disseminated = Pulmonary + other sites. Non of the MTB detected was Rif resistant.



**Table 2:** Distribution of treatment outcome and disease sites by Age grouping

Variables	< 5 years n (%)	≥ 5 years n (%)	Total N (%)	$\chi^2$	p value
Treatment outcome				4.495	0.343
Cured	3 (37.5)	5 (62.5)	8 (100)		
Treatment completed	26 (52.0)	24 (48.0)	50 (100)		
Died	4 (57.1)	3 (42.9)	7 (100)		
Loss to follow up	7 (30.4)	16 (69.6)	23 (100)		
Disease site				9.935	0.007
Pulmonary	39 (52.7)	35 (47.3)	74 (100)		
Disseminated	1 (9.1)	10 (90.9)	11 (100)		
Extra - pulmonary	0 (0)	3 (100)	3 (100)		
Gene Xpert Result				0.228	0.633
M.TB Detected	23 (43.4)	30 (56.6)	53 (100)		
M.TB Not Detected	17 (48.6)	18 (51.4)	35 (100)		

Site of disease = site of affection/involvement, Disseminated = Pulmonary + other sites. Non of the MTB detected was Rif resistant

**Table 3:** Relationship between HIV status, Gene Xpert, site of disease and disease outcome

Variables	HIV STATUS		$\chi^2$	p value
	Positive	Negative		
Site of disease			0.868	0.648
Pulmonary	16	58		
Disseminated	2	9		
Extra - pulmonary	0	3		
Gene Xpert result			0.206	0.650
M.TB Detected	10	43		
M.TB Not Detected	8	27		
Treatment outcome			7.319	0.120
Cured	2	6		
Treatment completed	8	42		
Died	3	4		
Loss to follow up	5	18		

Site of disease = site of affection/involvement, Disseminated = Pulmonary + other sites. None of the MTB detected was Rif resistant.

## Discussion

The mean age of this study population is lower than the  $9.12 \pm 4.66$  found by Attah et al<sup>11</sup> across six selected health facilities within the same state. This is equally higher than the  $5.60 \pm 3.20$  reported by Mado et al<sup>13</sup> in Gusau Northwestern Nigeria among children aged 4 months to 13 years. The age variability with the studies cited probably reflects the differences in the study age and sites.

The prevalence of childhood tuberculosis among the overall admission in the present study is higher than the 4.8% reported by Mado et al<sup>13</sup> in Gusau. The

difference may be due to the variation in study population, while theirs was limited to children aged 4 months to 13 years, the present study is for all children aged < 18 years. Similarly, cases of childhood tuberculosis managed within the study period in our facility is higher than the 18.3% and 6.3% reported in Gusau and Lagos by Illah<sup>2</sup> and Adejumo<sup>1</sup> et al respectively. The differences may be explained by the differences in methodology vis - vis the study duration, while the current hospital-based



study was done over 12 months period, the Gusau study spanned 30 months period and the Lagos study was multi - centre community based in nature<sup>1,2</sup>. It is also higher than the 5.9% found in Accra in a study conducted over 4 years<sup>4</sup>. Regional variations with these mentioned studies may also account for the observed differences.

There are more males than females in this study, comparable to the finding of 1.5:1 in Gusau by Mado et al<sup>13</sup>. This is in contrast to higher females of 1:1.5 observed by Illah et al<sup>2</sup> in the same Gusau. The reasons for these findings are not clear.

Proportion of children aged less than five years in the current study is lower than the 56.2% reported by Ohene et al<sup>4</sup> in Accra, the variation may be attributed to geographical differences across different countries. It is also higher than the 38.2% reported by Illah et al<sup>2</sup> in Gusau as well as the 30.4% reported by Ogbudebe et al<sup>12</sup> in Lagos. The observed differences may be due to the wider study population in the present study compared with theirs.

Pulmonary TB is the commonest disease site found in this study. The proportion is higher than the 76.3% reported by Illah et al<sup>2</sup> in Gusau, 58.0% by Ogbudebe et al<sup>12</sup> in Lagos and the 26.9% by Mado et al<sup>13</sup> also in Gusau. This high figure found in the present study may be due to the greater proportion of the patients being under-nourished as reported in earlier studies<sup>15</sup>.

Two third of cases in the current study completed treatment comparable to the 67.1% found by Illah et al<sup>2</sup> and 59.7% by Mado et al<sup>13</sup> in Gusau, as well as the 76.3% reported by Adejumo et al<sup>1</sup> in Lagos. It is lower than the 83% found by Ogbudebe et al<sup>12</sup> also in Lagos. In the current study, the cure rate found is similar to the 9.4% found by Ohene et al<sup>4</sup> in Accra.

A third of subjects in this study failed treatment, this is slightly lower than the 40.3% earlier reported in Gusau among a slightly different study population<sup>13</sup>. The Gene Xpert was positive in more than half of subjects in this study, this is comparable to the 46.5% reported in Accra, Ghana<sup>4</sup>, 28% in a study in Lagos Nigeria<sup>12</sup> and only 9.2% in another study in Gusau Nigeria<sup>2</sup>.

The observed variation is possibly due to the relative non-availability of Gene Xpert in these earlier studies compared with the present study.

One out of every five subjects in the present study have TB/HIV co-infection compared with the lower value of 9.0% reported by Mado et al<sup>13</sup> in Gusau and

the higher 29% found in Lagos by Adejumo et al<sup>1</sup>. Approximately, one out of every four cases in this current study were loss to follow up, which is similar to the 22.4% reported by Mado et al<sup>13</sup> in Gusau. Almost one out of every twelve subjects died during the course of treatment in this study, similar to the 8.4% found by Ohene<sup>4</sup> in Accra Ghana and the 10.4% reported by Mado<sup>13</sup> in Gusau Nigeria. The reason for the observed similarity is not clear.

### Conclusion

This study shows that one out of four of the burden of TB at our facility occurred in childhood and two-third had pulmonary affection.

Approximately two third of this current study population were successfully treated. Besides, HIV status was not related to the outcome of TB treatment in this study.

More than half of the study populations were under-nourished, with a third in the severe category.

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Cite this Article as: Bello S, Ogunkunle T, Hassan I, Ibrahim O, Audu ES. Burden and outcome of Childhood Tuberculosis at a Tertiary Health Facility in North-Central, Nigeria. **Bo Med J** 2021; 18(1):1-6. **Source of Support:** Nil, **Conflict of Interest:** None declared

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