Nigerian Medical Journal
NIGERIA MEDICAL ASSOCIATION
Print ISSN 0300-1652, E-ISSN 2229-774X

Original Article

An Audit of Tuberculin Skin Testing among Nigerian Children in a Tertiary Health Facility in Benin City, Nigeria

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Abstract

Background: This study objective was to describe the indications for the use of Tuberculin Skin Testing (TST) and the results in order to provide information that may be useful in defining the role of TST in the investigation and control of childhood tuberculosis.

Methodology: Through a Prospective cross-sectional study an audit of TSTs carried out over a one year period (2015-2016)in a tertiary hospital was done. The indications for the TST were extracted as well as the TST readings.

Results: Of the 1276 TST requests, 279(21.9%) were for children. Majority 112(40.1%) of the tests were carried out to investigate suspected cases of tuberculosis. The TST readings ranged between 0 and 20mm. Up to 68.2% (176) were negative (0-4mm). Majority 13(41.9%) of those with positive results (>10mm) were being investigated for tuberculosis. Of those diagnosed with tuberculosis 50% had a positive result.

Conclusion: TST is useful in providing supportive evidence for a diagnosis of tuberculosis. It is also useful in identifying children at school entry who are infected and may benefit from prophylaxis

Keywords: Tuberculin Skin Test; Role; Investigation; Control; Tuberculosis.

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How to cite this article: Sadoh AE, Eki-Udoko FE, Nwaneri DU, Uduebor S, Iguodala O. An Audit of Tuberculin Skin Testing Among Nigerian Children in a Tertiary Health Facility in Benin City, Nigeria. Niger Med J 2021;62;(6):305-311

Quick Response Code:

Introduction

Tuberculosis is a major cause of morbidity and mortality globally and the leading cause of death by a single infectious agent.[1] A quarter of the world population is estimated to be infected with Mycobacterium tuberculosis, the causative agent of tuberculosis.[1] Although only a minority of these infected persons progress to developing the disease (with a 5-10% life time risk of progression; the numbers of those who progress to disease are significant.[2,3] Globally, ten million persons were estimated to have developed TB in 2018 and of these, children accounted for 1.12 million representing 11%.[1] In the same year, mortality from TB was 1.4 million (1.2million in HIV negative persons and 250,000 in HIV positive persons) of which 205,000 were children.

Children are at a higher risk of progression from infection to disease with peaks of vulnerability in the under-fives and in adolescence.[4] One of the methods for preventing progression of disease is the use of prophylaxis for those known to be infected by the bacterium. However, such treatment entails risks and costs.[3] It is thus important to focus preventive therapy interventions on these children who are at the highest risk of progressing to active disease following documented TB exposure and/or infection.[2] The International standard of care also recommends that individuals in close contact with persons with infectious tuberculosis be evaluated and managed in line with international recommendations.[5]

Distinguishing between infection and disease in children is a challenge as is making a diagnosis of tuberculosis disease in children. The tuberculin skin test (TST) also known as the Mantoux test is one of the methods for determining the presence of infection with M. tuberculosis. A positive TST indicates that a person is or was infected with M. tuberculosis but does not necessarily indicate tuberculosis disease. There are however challenges in the interpretation of the TST. These accrue from the cross reactivity of the tuberculo proteins with proteins from other mycobacteria as well as with those of the BCG strain.[6] The fact that anergy occurs in disseminated TB and in malnourished and immunocompromised children also confounds the interpretation.[6] Despite these limitations the TST is useful in identifying persons with infections who might benefit from treatment to prevent progression.[7]Other uses of TST include- for providing evidence for and against tuberculosis when making a diagnosis,[7]for the assessment of children with suspected tuberculosis and in the screening of children exposed to tuberculosis.[8]However, the use of TST is discouraged in low risk population.[7]

Other tests like the gamma interferon used for determining exposure to M. tuberculosis are not readily available in low resource setting and require more sophisticated equipment.[3] Thus, the TST remains the major screening test for tuberculosis, in low resource settings.

The current Nigerian guideline for the control of tuberculosis lists TST as an ancillary test in the diagnosis of childhood tuberculosis.[9] This may be due to the fact that TST is not readily available in all settings. Several TST based studies have been carried out in Nigerian children. Mustapha et al [10] recorded high TST positivity among apparently healthy children and recommended that prior BCG vaccination be taken into consideration in the interpretation of TST. In another study on adolescents at school entry it was found that over two thirds of those studied were at risk of being infected.[11]

This study is an audit of TSTs carried out in a tertiary hospital over a one-year period to determine the indications for TST evaluation, the results of the TSTs and the association between different levels of TST and the indications for evaluation. The information from this study may provide the necessary background to define the role of TST in the management and control of tuberculosis in Nigeria and in other low resource settings.

Methodology

All requests for TST are attended to at the Department of Public Health Nursing, University of Benin Teaching Hospital, Benin City. A trained public health Nurse administers the TST every Friday apart from public holidays and the test read the following Monday morning. For in-patients, a public health nurse is assigned to administer the test at the patient's bedside and the result is also read at the bedside. Records of the TSTs and results are documented in a register. This study was a cross-sectional prospective audit of the TSTs carried out over a one-year period (January to December 2016).

A proforma was used to extract the following information from the register- age, gender, indication for the TST and the results of the TSTs. During the waiting period prior to the administration of the TST, other information such as symptoms suggestive of TB, BCG immunization status and presence of BCG scar were obtained from consecutive clients aged below 15years whose parents gave written informed consent. Assent was obtained from children older than 6 years. Ethical clearance for the study was obtained from UBTH Ethics and Research committee with protocol number ADM/E22/A/VOL.VII/1272.

The TST was administered according to standard procedure by injecting 0.1ml of PPD (5TU) into the volar aspect of the left forearm. The PPD was injected using a 1 ml syringe with a 25 G needle. With the bevel of the needle pointing upwards, it was inserted intradermally, and the injection administered to raise a wheal (Figure 1). The parents were instructed to ensure that the child does not scratch the site. The TST was read the following Monday (three days later) and the result recorded on the proforma.

As part of the National programme on tuberculosis, patients with tuberculosis and children requiring Isoniazid prophylaxis receive the drugs free from Directly Observed Treatment (DOT) centres. Using the DOT registers for children who were commenced on treatment during the study period, we also identified those who were commenced on anti-tuberculosis treatment or on Isoniazid prophylaxis.

The TST reading was reported as:negative if 0-4mm; intermediate if 5-9mm and positive if>10mm regardless of BCG immunization status.

The Data was entered into a Statistical Package for Social Sciences (SPSS) spreadsheet in a pass worded computer. Analysis was done using the same software and Graphpad Instat. Categorical variables are presented in simple percentages. Fishers Exact test and Chi square test where applicable were used for testing associations between variables. Multiple medians were compared using Kruskal wallis test.

Results

A total of 1,276 requests for TST were made during the study period and of these, 279 (21.9%) were among children aged 15 years and below. There were 153 (54.9%) females and 125(44.8%) males. The age and gender of the study population is shown in table 1. The mean age (SD) of the children studied was 7.48(±5.05) years. Referrals for TST were from the paediatric wards in 61 children, the internally displaced persons (IDP) camp in 5 children and from various outpatient clinics in 91 children. The source of referral was not indicated in 122 children. The indications for requesting TST are shown in Table 2. Majority of the children 112(40.1%) had TST done to investigate a suspicion of tuberculosis.

The TST results ranged between 0 and 20mm with a mean 3.27±4.50mm and a median of 0mm. Some 21(7.5%) had tests done but did not return for or died before reading could be done. The median TST reading for the different indications is shown in table 2. The median TST reading for those being investigated for tuberculosis was 0mm with an interquartile range (IQR) of 5.38. Those who had TST done as part of medical exams also had a median reading of 0mm with an IQR of 5.0. Those with no BCG scar and those being investigated as contacts had median TST readings of 3.0mm each with IQR of 5.0 and 10.0 respectively. The difference in median TST readings for the different indications were not statistically significantly different P=0.084.

Majority of the test results 176 (68.2%) were in the negative range of 0-4mm while 31(12.0%) had readings of >10mm. Majority 13(41.9%) of those who had TST readings in the positive range (>10mm), were among those being investigated for Tuberculosis followed by those being investigated as contacts of a tuberculosis case 9(29.0%). Others are as shown in table 3.

There were 12(10.7%) of the 112 children investigated for tuberculosis who were started on anti-tuberculosis therapy, of which 6 (50%) had positive Mantoux test. Of those investigated as contacts 6 were under-fives and only 3 of them were put on Isoniazid prophylaxis.

Table 1: Age and gender of children who had TST

Characteristics	n	%
Age		
<1 year	33	11.8
1-5 Years	73	26.2
6-10 years	82	29.4
>11years	88	31.5
Not indicated	3	1.1
Gender		
Male	125	44.8
	154	55.2

Table 2: Median TST reading of children with different indications for TST

Indication for TST	n	%	Median TST result	Interquartile Range
Investigation of TB	112	40.1	0.0mm	5.38
Medical Examination	77	27.6	0.0mm	5.00
Contact Investigation	35	12.6	3.0mm	10.00
No BCG scar	32	11.5	3.0mm	5.00
Did not receive BCG	6	2.2	2.5mm	7.75
Not indicated	17	6.1	4.5mm	8.00

Table 3: Distribution of TST results according to indication for TST

Indication for TST	TST Result in mm					
	0 – 4		5 -9		⩾10	
	n	%	n	%	n	%
Investigation for TB	71	74.0	12	12.5	13	13.5
Medical Examination	55	73.3	15	20.0	5	6.7
Contact Investigation	20	57.1	6	17.1	9	25.7
No BCG scar	19	61.3	10	32.3	2	6.4
Did not receive BCG	3	50.0	2	33.3	1	16.7
Not indicated	8	53.3	6	40.0	1	6.7
*Total	176	68.2	51	19.8	31	12.0

*The total for this table is 258 as 21 children did not come back for reading of the TST

Discussion

TST remains a popular investigative tool in the setting studied. More TSTs were done in the study setting compared to another teaching hospital setting where 5863 tests were done over a seven year period.[12]The difference may be due to the fact that they did not include tests that were done but not read or that there are differences in prevalence of the disease. The indications for the test in this were in line with identified scenarios in which the TST is considered beneficial. Majority of the tests were done as part of evaluation of children suspected to have tuberculosis. In this group of children 13.5% had a positive result. Among those who received treatment for TB in the DOTs centre 50% of them had a positive result. This suggests that the TST provided supportive result in half of the children treated for TB. This 50% positive rate in those treated for tuberculosis is higher than the 15% documented by Mustapha et al [13] among children diagnosed with tuberculosis and the 34.3% reported by Agrawal et al [14] amongst children with tuberculosis. However, this was lower than the 74% reported by Ewa et al. [15] The reasons for these differences are not exactly clear. However, 40% of those treated for tuberculosis in this study had a negative result. This is in keeping with known facts that a negative TST response does not exclude tuberculosis.[16]

The Mantoux test amongst child contacts of patients with tuberculosis represented only 12.5% of the Mantoux tests done. The low rate may reflect compliance with national recommendations which did not include the use of this test in the screening for tuberculosis (latent or disease) among children at the time.[8] It may, however, also suggest inadequate contact tracing among children. This is in keeping with reports that childhood tuberculosis is being under reported.[17] Evaluating child contacts for tuberculosis is one of the important methods of detecting cases as well as for determining those who should receive prophylaxis among children older than 5 years.[3]Recent recommendations does not include testing for contacts who are aged below five for latent tuberculosis before offering prophylaxis.[3]Current national guidelines recommend prophylaxis for under-fives who are contacts but have screened negative for tuberculosis.[8] Only 50% of the under-fives investigated as contacts were on INH prophylaxis in the DOTs register, further corroborating the possibility of inadequate contact tracing in children.

TST as part of medical exams was responsible for just over a quarter of the tests. Since the subjects are healthy children, positive results are likely to indicate latent tuberculosis and possibly a few cases of tuberculosis which will be detected on further examination. In this study only 5(6.7%) had a positive result which should prompt further investigation for the presence of tuberculosis disease by carrying out other investigations such as chest radiography. In a study in Mumbai, of 44 children (33 apparently healthy and low risk for tuberculosis and 11 high risk for tuberculosis) who had a positive TST, 25 on further investigation were found to have tuberculosis.[14] Current recommendation for testing does not include testing for medical examination. Most of the children in this category were those entering secondary school. These children are in the adolescent age group which is known to be a vulnerable age group for disease progression.[2] It may thus be recommended that those found to have positive results but do not have the disease should be offered prophylaxis to prevent future progression to tuberculosis. The positive rate in this group of children was slightly lower than the 7.9% by Mustapha et al[10] and much lower than the 12.2% reported by Ifezulike et al[18] among apparently healthy children; and also lower than the 18.3% recorded among 6-7 year old primary school entrants in Madagascar.[19] The differing prevalence of positive TSTs may be due to geographic differences in the burden of tuberculosis.
The TST results ranged between 0 and 20mm which is similar to the result obtained in a study that screened children living among adults with tuberculosis.[15] There was no significant difference between the median test results for the different indications. However, among those who had a positive result, majority were being investigated for tuberculosis. Majority of the children 68.2% had a negative result which may suggest absence of tuberculosis but up to 40% of those treated for tuberculosis also had a negative result. Malnutrition has been identified as one of the reasons for a negative reaction to TST.[20] In a population with high rates of malnutrition, negative TST may thus not reflect absence of TB. Nigeria has a stunting rate of 32%.[21] However, a positive result may likely be due to TB infection or disease. Thus, a positive result is more useful than a negative result. The low specificity of the TST has previously being highlighted.[22]

Of those who were evaluated as contacts of cases of tuberculosis, up to a quarter of them had positive TST results. This may reflect the known risk of exposure which is more certain for them than for other categories of children studied. This result is however considerably lower than 75.6% of children who were investigated as household contacts of adult cases of tuberculosis in a study that was carried out in a facility where adult tuberculosis cases were on admission and in which children had a high risk of potentially acquiring tuberculosis through contact with the tuberculosis cases.[15]

BCG is recommended to be given as soon as possible after birth. In Nigeria, many children do not start routine immunization early. [22,23] Being highly endemic for tuberculosis it is envisaged that young infants who do not receive BCG vaccination may already be infected before being presented for immunization. Since tuberculin conversion occurs between 6-12 weeks after infection our centre routinely requests TST testing prior to giving BCG vaccination to infants who present at 3 months or later for BCG vaccination. Among this category only one had a positive result that would warrant further screening for tuberculosis. In the absence of disease this child should receive prophylaxis while the others can safely be vaccinated without the fear of accelerated BCG reaction.
Amongst those who had received BCG but did not develop a scar, 12 had results above 4mm suggesting at least a response to the BCG and obviating any need for revaccination. Two of these though had results in the positive range which would require further investigation.

The current algorithm for the diagnosis of childhood TB in Nigeria requires any two of three criteria – a history of contact with a case of tuberculosis, presence of compatible symptoms and a chest radiograph with findings suggestive of tuberculosis.[9]It is pertinent to determine if TST should continue to be used as part of investigation for childhood TB. In this study TST provided supportive evidence in 13.5% of those being investigated for TB. However, amongst those in whom Tuberculosis was confirmed up to 50% had positive TST. The TST in our setting should probably still be considered an ancillary test.

Limitation

We were unable to get information on the HIV status of most of the children (most didn't know their status).

Conclusion

The TST remains an important investigative tool in low resource settings. Despite its poor specificity we can conclude from this study that it is useful as ancillary test in providing supportive evidence for a diagnosis of tuberculosis. In the investigation of contacts older than 5 years it is helpful in identifying children who should receive INH prophylaxis. As part of medical examinations, it may be useful in identifying those who require prophylaxis to help in reduction of adolescent cases. To deploy widespread use of the TST in medical examinations and in evaluation of contacts, cost effectiveness will need to be evaluated.

Conflict of interest

All authors declare no conflict of interest.

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