



## **Comparison of Mantoux Reactivity in Smear Positive Pulmonary Tuberculosis Adults and Controls in Yenagoa, Nigeria**

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### **Authors' contributions**

*This work was carried out in collaboration between all authors. Authors POI, JJ and IDE conceived and designed the study. Authors POI and IDE analysed the data while authors POI, JJ, IDE and EAS contributed to the literature search and writing of the paper. All authors read and approved the final Manuscript.*

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### **ABSTRACT**

**Background:** Tuberculin skin tests (TST) are long established screening methods for tuberculosis (TB). We aimed to compare Mantoux test (a TST) in smear positive pulmonary tuberculosis adults and control subjects. From January to December 2015, 131 patients with smear positive pulmonary (mean age 36.9 years) were given the Mantoux test. The results of the test group were compared with those of 121 control subjects (mean age 33.5 years).

**Methods:** Mantoux test results of all the 131 patients with smear positive pulmonary tuberculosis, aged above 15 years without HIV were collated and then analysed. These results were compared with results from 121 control subjects who were attending the chest clinic for other conditions, who were also smear negative with normal chest radiograph.

**Results:** Mean Mantoux reaction (mean±SD) for the test group was 9.31±10.6 mm while the mean reaction in the control group was 8.22±6.4 mm giving a p-value of 0.80 (Z-test). Thus there was no

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statistically significant difference between the test group and the control.

**Conclusion:** We conclude that the Mantoux test has limited usefulness as a screening or diagnostic tool.

*Keywords: Pulmonary tuberculosis; mantoux test; screening; tuberculosis skin test.*

## 1. INTRODUCTION

One third of the world's population is said to be infected with latent tuberculosis and that each year above eight million new cases arises and two million people die, mostly in low income countries as a result of this communicable disease [1]. Nigeria ranks 4<sup>th</sup> among the 22 high-burden TB countries in the world [2].

Tuberculin skin tests (TSTs) are long-established screening methods for tuberculosis (TB) infection that detects the cell-mediated response to inoculation of a mixture of *Mycobacterium tuberculosis* antigens, some of which are common to Bacilli Calmette-Guerin (BCG) and non tuberculous mycobacteria (NTM) [3,4]. Traditionally, TSTs have also formed part of the decision making pathway for the diagnosis of childhood TB disease [5]. In recent years, there has been intense research interest in diagnosis of latent TB infection by quantitative interferon - gamma release assays (IGRAs), which may offer rapid turn around and greater specificity [6]. Authorities in some developed countries have recommended that the TST be replaced completely by the IGRA, although the evidence supporting the use of IGRAs for diagnosis of active TB disease in young children is less than compelling [3,7,8,9]. Indeed, IGRAs have not yet been incorporated in TB control programmes in high burden developing countries where IGRA sensitivity may be lower, and where healthcare resources and laboratory capacity are most limited [10]. It follows that evidence to guide the use and interpretation of TSTs remain relevant to clinicians and public health programmes in high burden regions.

Mantoux reactivity may be subject to factor causing false positive or negative results, including BCG vaccination, NTM exposure, malnutrition and human immunodeficiency virus (HIV) infection [11]. It was our primary hypothesis that Mantoux reactivity will be significantly more in the smear positive pulmonary tuberculosis patients than in controls. We present a direct comparison of intradermal Mantoux test in proven pulmonary tuberculosis patients and controls in a South-South Nigeria community.

## 2. METHODS

A prospective analysis of Mantoux test results of all adult patients (>15 years) seen in the TB clinic of the Federal Medical Centre, Yenagoa between January 2015 and December 2015 was carried out. Those patients that had HIV infection, diabetes mellitus and malnutrition were excluded. The control subjects were adults (>15 years) who were attending our clinic but with no evidence of tuberculosis. They included patients attending the chest clinic for other conditions and consented, patients who were smear-negative for Acid Fast Bacilli (AFB) and patients who had a normal chest radiograph.

The study was undertaken in Federal Medical Centre, Yenagoa, a tertiary referral hospital in Bayelsa State, South-South Nigeria. The TB clinic is situated within the hospital premises and the program is supported by the United State Agency for International Development / Family Health International 360. (USAID/FHI 360) and the National Tuberculosis and Leprosy Control Program (NTBLCP). In the program a Comprehensive TB diagnosis, treatment and care is provided free of charge to the patients with pulmonary tuberculosis.

The diagnosis of smear positive tuberculosis required positive sputum acid fast bacilli using Ziehl-Neelsen (Z-N) stain at least two times in line with World Health Organisation (WHO) recommendation [2]. The Mantoux test was given using a needle and syringe to inject 0.1 ml of 5 tuberculin units of liquid tuberculin (BB-NCIPD LTD 1504 BULGARIA) between the layers of the skin (intradermally), on the left volar aspects of the forearm as recommended by the World Health Organisation (WHO) and the International Union Against Tuberculosis and Lung Disease (IUATLD) [2]. We made sure that the tuberculin solution was of the same batch number for the study. The patients arm was examined 48 to 72 hours after the tuberculin is injected. The area of induration (swelling that can be felt) around the site of the injection was then measured using a ruler. The diameter of the indurated area was measured across the forearm i.e. transversely, under the supervision of one of us.

The data were analysed using EPI-INFO 2012 Statistical program version 7.0.9.34. Continuous variables were described with mean and standard deviation, while discontinuous variable were described in percentages. The Mann-Whitney test was used when comparing groups of cohort. At 95% confidence, p-value less or equal to 0.05 were considered to be significant.

Approval for conducting the study was obtained from the Hospital Ethics Committee. Written consent for the study was obtained from the patients.

### 3. RESULTS

A total of 570 adult pulmonary tuberculosis patients were attended to in the period under review. Of this 131 met the inclusion criteria for the smear positive cohort. The mean age of this group was 31±15.86 made up of 67 males and 64 females with a mean±SD Mantoux reaction of 9.31mm±10.63. The control group were a total of 121 subjects of which 63 males and 58 were females giving a mean±SD Mantoux reaction of 8.22±6.43. When the Mantoux reaction in both cohorts were compared by Z-test, p value was 0.80. This was not statistically significant (Table 2) Table 1 shows the degree of Mantoux reactivity in both the test and control group.

Forty five percent (45%) of the smear pulmonary tuberculosis patient had reaction size of 0-4 mm, 8.40% had reaction size of 5-9 mm, 21.4% had reaction size of 10-14 mm, 13.0% had reaction size of 15-19 mm, 4.6% had reaction size of 20-24 mm and 7.6% had reaction size greater than 25 mm.

**Table 1. Classification of Mantoux Reaction in test group and the control group**

Mantoux category (mm)	Test group N (%)	Control group N (%)
0-4 mm	59(45.0)	37(30.6)
5-9 mm	11(8.4)	35(28.9)
10-14 mm	28(21.4)	29(24.0)
15-19 mm	17(13.0)	15(12.4)
20-24 mm	6(4.6)	2(1.7)
25 mm and above	10(7.6)	3(2.5)

In the control group 30.6% had reaction size of 0.4 mm, 28.9% had reaction size of 5-9 mm, 23.0% had reaction size of 10-14 mm, 12.4% had reaction size of 15-19 mm, 1.7% had

reaction size of 20-24 mm and 2.5% had reaction size of more than 25 mm (Table 2).

**Table 2. Age, gender and mantoux characteristics of study population**

Variable	Test group (n=131)	Control group (n=121)
Age (median and IQR)	31 (15.86)	29 (15.88)
<b>Gender (%)</b>		
Male	67 (51.1)	63 (52.1)
Female	64 (48.9)	58 (47.9)
Mantoux reaction Mean ±SD	9.31±10.63	8.22±6.43

\*Z-test for the comparison of Mantoux reaction of test and control group.  $p = 0.80$

### 4. DISCUSSION

Tuberculosis is a major public health problem in Nigeria. The prevalence is put at 512 per 100,000 population by NTBLCP [12]. With such prevalence any diagnostic tool becomes attractive and even desirable. Although it is imperfect, the gold standard for diagnosing latent tuberculosis injection remains the tuberculin skin test (TST) [13]. Although, the tuberculin skin test still continues to be a recognized tool in the screening and diagnosis of TB in more affluent countries, this and other studies in our setting has shown it is of limited usefulness [12].

Because the tuberculin skin test is imperfect, three different diameters of induration have been defined as indicative of latent tuberculosis injection in order to increase the predictive value of the test [14]. The lowest cut off value (5 mm) is used for persons who may not have a strong immunologic response, including persons who are infected with HIV or are being treated with immune suppressive drugs such as corticosteroids. A cut off value of 5 mm is also used for those with recent exposure to persons with infectious tuberculosis, who may not yet have mounted a full immunologic response. The same cut off value is used for persons with a high pretest probability of infection, as evidenced by abnormalities on a chest radiograph. A cut off value of 15 mm is used for persons at low risk for tuberculosis. For all other persons, the cut off value is 10 mm. A person with a negative initial tuberculin test and a subsequent test performed within two years that shows an increase of at least 10 mm in the diameter of induration is considered to have had a conversion to a

positive skin test, indicating recent infection and a high risk of progression to active disease.

From the results observed in our study, it can be inferred that Mantoux tuberculin reaction of any size from 0 mm to over 25 mm is possible in smear positive pulmonary tuberculosis. It could also be inferred that Mantoux reaction size of 0mm to over 25 mm is possible with apparently healthy Nigerian adults. Similar observations and inference were drawn by previous studies [15,16]. Thus Mantoux test is of very little diagnostic value in screening for pulmonary tuberculosis.

We assumed that since we were dealing with persons above the age of 15 years, that positive Mantoux test is rarely due to previous BCG vaccination [15]. This is one limitation of this study.

## 5. CONCLUSION

We concluded that the tendency to develop large tuberculin reaction is greater in patients with smear positive pulmonary tuberculosis but is not diagnostic since large reactions could also occur in normal (but previously infected but not active) Nigerians. However its routine use as a diagnostic tool should be downplayed.

## CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

## ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the authors.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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