

# Comparison of Diagnostic BCG and Mantoux Tests in Detection of Tuberculosis in Children

Haroon Rashid Khan <sup>1</sup>, Muhammad Imran Sohail <sup>2</sup>, Muhammad Farooq Haider <sup>3</sup>, Muhammad Afzal <sup>4</sup>

## Author's Affiliation

<sup>1</sup>Senior Lecturer, Department of Community Medicine,

<sup>2</sup>Lecturer, Department of Community Medicine,

<sup>3</sup>Demonstrator, Department of Pathology,

Islamabad Medical and Dental College, Bahrakahu Islamabad.

<sup>4</sup>Biostatistician, Shaheed Zulfiqar Ali Bhutto Medical University, PIMS, Islamabad.

## Author's Contribution

All the authors contributed significantly to the research that resulted in the submitted manuscripts

## Article Info

Received: Dec 29, 2016

Accepted: Mar 29, 2017

## How to Cite this Manuscript

Khan HR, Sohail MI, Haider MF, Afzal M. Comparison of Diagnostic BCG and Mantoux Tests in Detection of Tuberculosis in Children. *Ann. Pak. Inst. Med. Sci.* 2017; 13(1):68-72.

Funding Source: Nil

Conflict of Interest: Nil

## Address of Correspondence

Haroon Rashid Khan  
drharoon.clinix@gmail.com

## ABSTRACT

**Objective:** To compare the accuracy of diagnostic BCG and Mantoux tests for detection of Tuberculosis in Children.

**Study Design:** Cross Sectional Survey

**Place and Duration:** The study was conducted at outpatient department of Pediatrics, Panjab Social Security Hospital, Ahmed medical complex, Islamabad Medical and Dental College Islamabad, from August 2014 to November 2016.

**Materials and Methods:** Patients having tuberculosis on the basis of Kenneth Edwards Criteria (scoring >7) at time of presentation were selected for the study. Guardians of all the children were described about the study protocol and informed written consent was taken. In all the patients (0.1 ml of fresh solution of freeze, dried BCG vaccine was administered intradermally in right deltoid region) and results were recorded after 48–72 hours. Similarly, all these patients were administered Mantoux test (0.1 ml of 5 TU of PPD) and results were noted after 48–72 hours. The standard criteria for results by both Mantoux test and BCG was followed.

**Results:** The mean age of the children was  $7.65 \pm 5.32$  years. There were 59 (52.21%) male and 54 (47.79%) female children in the study sample. Majority of the children presented with fever (85.84%), productive cough (71.68%) and weight loss (60.18%). Only 34 (30.09%) children in study group were normal and about 70% children presented with malnutrition. The results showed that the diagnostic BCG was positive in 77 (68.14%) children and in 49 (43.36%) children both the tests BCG and Mantoux tests gave positive results and in 36 (31.86%) children both BCG and Mantoux tests were negative. In 28 (24.78%) children the diagnostic BCG was positive and Mantoux test was negative. There was significantly ( $p$ -value < 0.05) higher rate of positive results on the basis of BCG test (68.14%) as compared with Mantoux test (43.36%).

**Conclusion:** BCG skin test gives superior results in comparison to Mantoux test to diagnose tuberculosis infection in children. About 70% children in the study sample presented with malnutrition. The diagnostic BCG was positive in 68.14% children and in 43.36% children both the tests BCG and Mantoux tests gave positive results and in 31.86% children both BCG and Mantoux tests were negative.

**Keywords:** Tuberculosis, BCG skin Test, Mantoux test, Accuracy

## Introduction

Pulmonary tuberculosis is a leading contagious infection affecting about one third of the world population. Main burden of this disease is in developing countries where 75% of the worlds infected population is residing. Pakistan like other Asian countries also has a very high prevalence of the tuberculosis and an estimated 2.5 million active cases of tuberculosis are present in Pakistan. This high incidence rate is major contributing factor of tuberculosis to be highly prevalent among pediatric age groups.<sup>1,2</sup>

This incidence is more prevailing in backward areas of the country. The reason might be the lack of awareness and facilities in these areas. Malnutrition due to poverty and ignorance with repeated infections make children more susceptible for tuberculosis by weakening their immunity. According to the estimates of world health organization Pakistan is 6<sup>th</sup> most prevalent country of the world for tuberculosis infection with a prevalence rate of 44% and among them 4% are registered pediatric cases of TB, 2.5% are at risk to get infection among which only 5-10% children progress to active disease, while remaining 80-90% children get latent tuberculosis infection (LTBI). The mortality rate of these tuberculosis children is 8%-20% of all deaths in children.<sup>3</sup>

This infection rate can be controlled by early and proper diagnosis with prompt treatment. For correct diagnosis, main helping factors are histopathological detection of granulomatous lesions, identification of bacilli and chest x-ray along with clinical findings.<sup>4</sup>

One of the main and established screening method for TB is tuberculin skin test which detects the cell-mediated response to inoculation of a mixture of Mycobacterium tuberculosis antigens, some of which are common to bacille Calmette-Guerin (BCG) and non-tuberculous mycobacteria.<sup>5</sup>

Several other diagnostic tests are in use for detection of TB, including Mantoux test which is a simple and easily available test for initial screening test of TB. But this test has some limitations in situations when a child has malnutrition, immunodeficiency stat or post measles infection, this test give biased results. Another diagnostic test, very commonly used for TB among pediatric age groups is BCG reaction test, is considered best available test for screening of tuberculosis infection. Many studies from Pakistan and India has found its results comparatively very satisfying in children.<sup>6</sup>

The mechanism of BCG skin test among non-immunized patients is based on reaction of BCG reactivity. After

intradermal injection at 2-3 weeks indurations appear, in 4-6 weeks pustule is formed and it heals at 8-12 weeks.<sup>7</sup> In a study conducted at Dera Ghazi Khan, the BCG diagnostic was found more helpful than Mantoux test as a diagnostic tool in patients suffering from various forms of tuberculosis. The comparison of mantoux test and BCG test of tuberculosis showed that BCG positivity rate (75%) was significantly higher than mantoux (45%).<sup>8</sup> Previous literature shows that BCG diagnostic is more helpful than Mantoux test as a diagnostic tool in patients suffering from various forms of tuberculosis in children. But its efficacy has not been tested in our population. The researches on its efficacy in diagnosing the tubercluis are limited. So this present study has been planned to compare the efficacy of BCG diagnostic in comparison with routinely used method Mantoux test in our target population.

## Methodology

The approval of the study was taken from hospital ethical committee prior to the study. Patients having tuberculosis on the basis of Kenneth Edwards Criteria (scoring >7) at time of presentation visiting to outpatient department of Pediatrics department, Panjab Social Security Hospital, Ahmed medical complex, Islamabad Medical and Dental College Islamabad. Guardians of all the patients selected for study were described about the study protocol and informed written consent was taken by the researcher. In this present study all the pediatric patients having age range from 4 months to 15 years and of both genders presenting with tuberculosis on the basis of Kenneth Edwards Criteria (scoring >7) were included. Pulmonary tuberculosis was diagnosed in these children on the basis of history, physical examination and nonspecific lab tests like ESR. The diagnosis was confirmed by chest X-Ray and positive sputum samples.

The patients who had respiratory illness lasting < 2 weeks, with immune deficiency, asthma, bronchiolitis, foreign body, viral or bacterial meningitis, malignancies and patients on anti-tuberculosis therapy, were excluded from the study. The sample size of the study was calculated by using WHO sample size calculator taking confidence level, 5 %, Anticipated population proportion (positive proportion by BCG) P (75 %) <sup>6</sup> and absolute precision level of 8%. And sample size turned out to be 113 patients. In all the patients (0.1 ml of fresh solution of freeze, dried BCG vaccine was administered intradermally in right deltoid region) and results were recorded after 48-72 hours. Similarly, all these patients

were administered Mantoux test (0.1 ml of 5 TU of PPD) and results were noted after 48-72 hours. The criteria for results by both Mantoux test and BCG was as follows

**Mantoux tests:** Criteria for Mantoux test with 15 TU of PPD

48-72 hours	mm-5 mm	Non-significant
48-72hours	mm-9 mm	Doubtful
48-72hours	>10 mm	Positive

**Diagnostic BCG:** Criteria for positive BCG will be an accelerated reaction to complete healing in 10-15 days instead of normal reaction in 7-10 weeks. Criteria will be as follows. <sup>7</sup>

48-72 hours	5 mm-9 mm	Mild (+1) (non-significant)
48-72 hours	10 mm-20 mm	Moderate (+2)
48-72 hours	21 mm-30 mm	Severe (+3)
05-08 days	Pustule formation	10-15 days healing and scar formation

All the information will be recorded on a predesigned performa. Data will be entered and analyzed with the help of statistical package for social sciences (SPSS v 16). Mean and standard deviation will be computed for quantitative variables. Frequency and percentage will be presented for qualitative variables. Chi-square test will be used to compare the results of Mantoux and BCG tests. A p-value < 0.05 will be considered as significant.

## Results

In this cross-sectional study, a total of 113 children clinically on the basis of symptoms have pulmonary tuberculosis were included. The mean age of the children was  $7.65 \pm 5.32$  years with majority of the children belonging to 12-15 years age group followed by 6-9 years age group. There was a bit male dominance in the study sample with 59 (52.21%) male and 54 (47.79%) female children in the study sample. Majority of the children presented with fever (85.84%), productive cough (71.68%) and weight loss (60.18%).

The main radiological finding in study sample was cavitation (25.66%), infiltration (25.66%) followed by consolidation (23.01%) and consolidation with cavitation (18.58%) as elaborated in table 1.

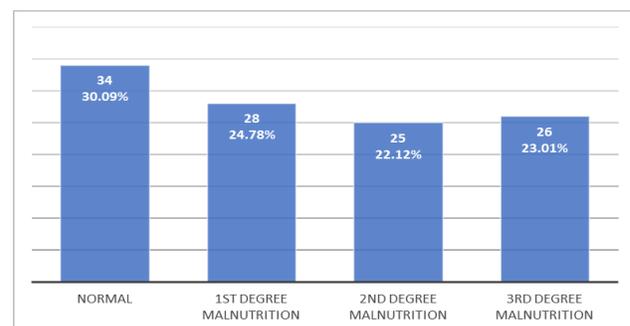
The malnutrition status shows that there were only 34 (30.09%) children in study group who were normal and about 70% children presented with malnutrition. Most of the children who had malnutrition, 28 (24.78%) had 1<sup>st</sup> degree, 25 (22.12%) children had 2<sup>nd</sup> degree and 26 (23.01%) had 3<sup>rd</sup> degree malnutrition as shown in figure 1.

The results showed that the diagnostic BCG was positive in 77 (68.14%) children and in 49 (43.36%) children both

the tests BCG and Mantoux tests gave positive results and in 36 (31.86%) children both BCG and Mantoux tests were negative. In 28 (24.78%) children the diagnostic BCG was positive and Mantoux test was negative as given in table 2.

The comparison of diagnostic BCG test with Mantoux test showed that there was significantly (p-value < 0.05) higher rate of positive results on the basis of BCG test (68.14%) as compared with positive results of Mantoux test (43.36%). That is the positivity of BCG test is significantly higher as compared with Mantoux test in clinically suspected cases of pulmonary tuberculosis in pediatric age group (Table 3).

Characteristics	No. of patients	Percentage
<b>Age of Patients</b>		
Mean $\pm$ SD	7.65 $\pm$ 5.32 years	
< 3 year	11	9.73%
3-6 years	22	19.47%
6-9 years	28	24.78%
9-12 years	19	16.81%
12-15 years	33	29.20%
<b>Gender of patient</b>		
Male	59	52.21%
Female	54	47.79%
<b>Presenting Complain</b>		
Fever	97	85.84%
Productive cough	81	71.68%
Weight loss	68	60.18%
Hemoptysis	33	29.20%
<b>Radiological findings</b>		
Cavitation	29	25.66%
Infiltration	29	25.66%
Consolidation	26	23.01%
Consolidation with cavitation	21	18.58%
Bronchiectasis	8	7.08%



**Figure 1: Malnutrition status of the children in study group**

Test Results	No. of Cases	Percentage
Diagnostic BCG positive	77	68.14%
Both BCG and Mantoux Positive	49	43.36%
Both BCG and Mantoux Negative	36	31.86%
BCG Positive and Mantoux Negative	28	24.78%

The main cause of chronic tuberculosis infection is gram positive acid fast bacilli, whose main source of transmission from person to person is through inhalation of droplets containing infectious germs. The diagnosis of pulmonary tuberculosis has been a challenge especially in children, because of unavailability of sputum for identification of acid fast bacilli, which is considered as gold standard for detection of tuberculosis.<sup>13</sup>

Test Result	Diagnostic BCG		Mantoux tests		P-value
	No. of Cases	Percentage	No. of Cases	Percentage	
Positive	77	68.14%	49	43.36%	0.000
Negative	36	31.86%	64	56.64%	
Total	113	100.00%	113	100.00%	

## Discussion

Childhood morbidity and mortality is very high in developing countries as compared to developed world. There are many causes of this elevated morbidity and mortality including poverty, ignorance and lack of facilities. There are different types of infections which significantly contribute to this morbidity and mortality in childhood like tuberculosis. The cases with TB is increasing gradually after start of 21<sup>st</sup> century. It is estimated that one third of world's population has mycobacterium tuberculosis infection and is considered a major cause of deaths. It is estimated that 1.7 million deaths throughout the world occurs due to tuberculosis infection. Annually a large number of cases are suffering from tuberculosis in pediatric age group. It is estimated that more than one million children younger than 15 years of age are diagnosed with tuberculosis and 400000 deaths occur due to TB in this population.<sup>9</sup>

In this present study, it was noted that there was no significant effect of age on tuberculosis reactivity. Same results were found by Carmina M et al, who also found insignificant effect of age on tuberculosis reactivity. But some authors have documented the increasing effect of age on tuberculosis reactivity that is this reactivity increases as age increases.<sup>10</sup>

In this present study, there was a bit male dominance with 52.21% male and 47.79% female children in the study sample. This high prevalence among male population of children is explained by the fact that they may have more chances of exposure to tuberculous patients in their surroundings due to their more freedom of movement as compared to the female patients who are mainly confined within their homes. These results are supported by previous studies.<sup>11, 12</sup>

Tuberculosis infection is most prevalent in backward communities and similar results has been found in Pakistan where different studies have shown that in poor areas of the country like Hazara, TB infection is quite common. The main causes can be poverty, malnutrition and ignorance. The immunity can be reduced due to repeated infections in growing children and put them on more risk to be infected with tuberculosis.<sup>14</sup>

In developing countries like Pakistan health facilities are not up to the mark and early and proper diagnosis of TB remain challenging because of limited facilities in backward areas. Pakistan is on 7<sup>th</sup> number among countries having highest tuberculosis disease burden in the world. Tuberculosis in children is completely different from tuberculosis in adult age group because children do not present with specific signs and symptoms of TB. Microbiologically it is also difficult to confirm or diagnose the tuberculosis.<sup>15, 16</sup>

A main contribution factor for tuberculosis is considered as malnutrition and in this present study 30.09% children presented without malnutrition, and majority of the children (70%) presented with any type of malnutrition. Among malnutritional children main bulk 24.78% had 1<sup>st</sup> degree malnutrition, 22.12% were 2<sup>nd</sup> degree malnourished and 23.01% had 3<sup>rd</sup> degree malnutrition. Same results have been found by most of the previous workers. Malnutrition has been observed among tuberculosis patients with prevalence of 60 to 100%.<sup>14, 17</sup> This study confirms that BCG skin test is much more sensitive as compared to the Mantoux test in the detection of tuberculin allergy in pediatric patients suffering from pulmonary tuberculosis. Our observations are exactly in line with those made in earlier studies carried out at Peshawar 9, and India.<sup>18,19</sup>

In our study The results showed that the diagnostic BCG was positive in 77 (68.14%) children and in 49 (43.36%) children both the tests BCG and Mantoux tests gave positive results and in 36 (31.86%) children both BCG and Mantoux tests were negative. Similar results were found by Mazhar et al, who found 81% positive patients with BCG skin test and 50% positive cases with mantoux test. All the patients having positive Mantoux test were positive with BCG skin test.<sup>20, 13</sup>

Previously it was assumed that already BCG vaccinated persons result of BCG skin test can be pretentious, depending upon the duration between test and vaccination interval. But studies have shown that the tuberculosis reactivity is not affected by the presence of BCG vaccination. The results form community based studies have elaborated that there was no difference in outcomes of BCG skin test in persons who were BCG vaccinated in infancy or later and those who were never vaccinated.<sup>10, 21</sup>

Form the results of this present study it can be concluded that the positive diagnosis on the basis of BCG test is more important as compared to Mantoux test positive result because the proportion of false negative results of Mantoux test was very high in contrast to BCG test. These findings are in very much accordance with previous researches.<sup>22,23</sup>

## Conclusion

The results of this study reveal that BCG skin test gives superior results in comparison to Mantoux test to diagnose tuberculosis infection in children. About 70% children in the study sample presented with malnutrition. The diagnostic BCG was positive in 68.14% children and in 43.36% children both the tests BCG and Mantoux tests gave positive results and in 31.86% children both BCG and Mantoux tests were negative. In 28 (24.78%) children the diagnostic BCG was positive and Mantoux test was negative. There was significantly (p-value < 0.05) higher rate of positive results on the basis of BCG test (68.14%) as compared with Mantoux test (43.36%). That is the positivity of BCG test is significantly higher as compared with Mantoux test in clinically suspected cases of pulmonary tuberculosis in pediatric age group.

## References

1. Ciesilski SD. BCG vaccination and PPD test: what the clinician needs to know? *J Fam Pract* 2013; 40: 76-80.
2. Beguin T, Khattak AA, Khan FM. Tuberculosis: a major threat to child health. *Pak Pediatr J* 2012; 3: 28-30.
3. Zafar M. Prevalence of latent tuberculosis and associated risk factors in children under 5 years of age in Karachi, Pakistan. *J Assoc Chest Physicians* 2014;2(1):16-24.
4. Khalil KF, Ambreen A, Butt T. Comparison of Sensitivity of QuantiFERON-TB Gold Test and Tuberculin Skin Test in Active Pulmonary Tuberculosis. *J Coll Physicians Surg Paki* 2013;23(9):633-6.
5. Pan W, Matizirofa L, Workman L, Hawkridge T, Hanekom W. Comparison of Mantoux and Tine Tuberculin Skin Tests in BCG-Vaccinated Children Investigated for Tuberculosis. *PLoS One* 2009;4(11):e8085.
6. Udani PM. Tuberculosis in children. *Pediatr Clin India* 2010; 18:143-56
7. Imran M. BCG – a diagnostic tool in childhood tuberculosis. *J Post grad Med Inst* 2012; 2: 181.
8. Channer MS, Qadri MSK, Khichi GQK, Masood Z, Birmani SA. Sensitivity of BCG inoculation and tuberculin skin test in active pulmonary tuberculosis in under-5 children. *JUMDC* 2015;6(2):26-8.
9. Onur H, Hatipoglu S, Arica V, Hatipoglu N, Arica SG. Comparison of Quantiferon Test with Tuberculin Skin Test for the Detection of Tuberculosis Infection in Children. *Inflammation* 2012;35(4):1518-24.
10. Carmina M, Reyes Ad, Sanchez L, Onglim AL, Gonzales LM. A paired comparison of tuberculin skin test results in children with clinical manifestations of tuberculosis using 2 TU and 5 TU tuberculin. *PIDSP J*. 2011;12(2):56-66.
11. Udani PM. Tuberculosis in children. *Pediatr Clin India* 2010; 18:143-56
12. Beguin T, Khattak AA, Khan FM. Tuberculosis: a major threat to child health. *Pak Pediatr J* 2012; 3: 28-30.
13. Usman M, Aleem A, Raza H. Frequency of positive results of Bacille Calmette Gurein and Mantoux skin tests in suspected cases of childhood pulmonary tuberculosis. *Annals* 2016;22(4):257-63.
14. Rashid A, Qayum S, Anjum R. Evaluation of BCG test in diagnosis of tuberculosis in BCG vaccinated children and its comparison with Mantoux test. *Int J Contemp Pediatr* 2016;3:1339-43.
15. Kabra SK, Lodha R, Seth V. Some current concepts on childhood tuberculosis. *Indian J Med Res* 2004, 120(4):387-397
16. Loeffler AM. Pediatric tuberculosis. *Seminars in respiratory infections* 2003, 18(4): 272-91
17. Kumar R, Dwivedi A, Kumar P, Kohli N. Tuberculous meningitis in BCG vaccinated and unvaccinated children. *J Neurol Neurosurg Psychiatry*. 2005;76(11):1550-4.
18. Barenholz A, Hovav AH, Fishman Y, Rahav G, Gershoni JM, Bercovier H. A peptide mimetic of the mycobacterial mannosylated lipoarabinomannan: characterization and potential applications. *J Med Microbiol* 2007;56:579-86.
19. Channer MS, Qadri MSK, Khichi JQK, Masood ZM, Birmani SA. Sensitivity of BCG inoculation and tuberculin skin test in active pulmonary tuberculosis in under-5 children. *J Uni Med Dent Coll*. 2015;6(2):26-9.
20. Mazhar MI, Sultan MA. Comparison of diagnostic BCG test with Mantoux in children with suspicion of Tuberculosis: *Pak Paed J*. 2006;30(1): 23-7.
21. Lucas M, Nicol P, McKinnon E, Whidborne R, Lucas A, Thambiran A, et al. A prospective large-scale study of methods for the detection of latent Mycobacterium tuberculosis infection in refugee children. *Thorax* 2010;65:442-8.
22. Bokhari SNH. Accelerated BCG response: Diagnostic value in adults in an endemic area. *Spectrum* 1999;15: 181-4
23. Anis-ur-Rehman, Idris M. Comparison of Mantoux's test with diagnostic BCG in pediatric patients with pulmonary tuberculosis. *J Ayub Med Coll Abbottabad*, 2005;17(2):6-8.