

# Immune Response of Tuberculin test and Diagnostic BCG Test in Children Suffering from Tuberculosis

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## ABSTRACT

**Objective:** To compare the immunological response of tuberculin test and diagnostic BCG test inoculation given simultaneously to children suffering from tuberculosis.

**Study Design:** Comparative – Cross sectional.

**Place and Duration of Study:** This study was carried out at the Department of Paediatric Medicine, Nishtar Hospital Multan from 6 April 2011 to 5 Oct 2011.

**Materials and Methods:** Fifty patients with tuberculosis were selected. Relevant data of cases including personal data, presenting complaints, physical examination finding and results of all the relevant investigations were collected. We injected 0.1 ml tuberculin intradermally on ulnar surface of right forearm and 0.1 ml BCG vaccine intradermally on deltoid muscle of left side. Both the BCG and tuberculin tests were performed at the same time by the same doctor. All information was recorded in a specifically designed proforma.

**Results:** 26 patients were male and 24 female. Out of 50 patients; BCG test was positive 36 patients and was negative in 14 patients. Mantoux test was positive in 26 patients and was negative in 24 patients. Both BCG and mantoux tests were positive in 26 patients. Ten patients had a positive BCG test where Mantoux test showed negative results. Both tests were negative in 14 patients.

**Conclusion:** BCG skin test is more superior to Mantoux test as a diagnostic tool in paediatric age group patients suffering from various types of tuberculosis.

**Key Words:** Tuberculosis, Baccilus Calmette Guerin (BCG), Mantoux test.

## INTRODUCTION

Tuberculosis (TB) is one of the leading infectious disease,<sup>1</sup> responsible for 2.9 million deaths and 8 million new cases per year in the world.<sup>1,3</sup> Tuberculosis is one of the common infectious diseases of the developing world, resulting in high morbidity and mortality in these countries.<sup>3,4</sup> It is estimated that 95% cases occur in under developed world where diagnostic and treatment facilities are rudimentary or non-existent.<sup>5</sup>

Tuberculosis even today, remains a major cause of death throughout the world. Children under 3 years of age are more at risk. Almost 1.3 million cases and 450,000 deaths occur among children due to tuberculosis each year.<sup>6</sup>

In Pakistan it is estimated that 2, 68,000 new cases and 64,000 deaths occur due to tuberculosis each year.<sup>7</sup> Prevalence of tuberculosis in Pakistan assessed by tuberculin reaction is estimated as 2.8% in age group 0–4 years, 7.7% in age group 5–9 years while it is 12.9% in age group 10–14 years.<sup>8</sup>

Tuberculosis is caused by several species of mycobacteria often described as Mycobacterium tuberculosis complex which include; M. tuberculosis, M. microti, M. africanum, M. bovis and BCG. Out of them Mycobacterium tuberculosis is the most frequent

cause of the disease in human. Other members of this complex are rare causes of TB.<sup>9</sup>

The rapid diagnosis of infectious diseases, particularly those that represent a public health problem, like tuberculosis, is a challenging problem. Pediatricians and even general practitioners often document the presence of tuberculosis by using diagnostic techniques namely tuberculin skin test, chest roentgenogram, sputum examination, lymph node biopsy or serologic tests.<sup>10</sup>

The tuberculin test is often resorted to but it has limitations in tuberculin negative individuals. Host related factors such as age, nutrition, immune-suppression, viral infections or immunization with live viral vaccines and presence of disseminated tuberculosis may alter the tuberculin reactivity of a patient. Also, recent exposure to environmental non-tuberculous mycobacteria (NTM) can result in cross sensitization and false positive reaction to purified protein derivative (PPD). In children, sputum examination is difficult to obtain. Furthermore, gastric washing culture is expensive and takes time.

There is no gold standard for diagnosis of tuberculosis. In children diagnosis has to take into account history, clinical examination and investigations including radiology, gastric lavage along with a mantoux test.<sup>11-12</sup> Polymerase chain reaction (PCR) is an emerging

diagnostic tool for diagnosis of TB in children.<sup>13</sup>

- Accelerated response to BCG has been used as a screening test for TB in Asian countries where tuberculin test was less reliable. Although some comparative studies have demonstrated the superiority of BCG test over mantoux's test, its use in routine clinical practice is still controversial.<sup>11-12</sup>
- In patients who are malnourished, mantoux test is expected to be inconclusive.<sup>14-15</sup> In such situation, the diagnostic BCG test has been recommended as an alternative, rapid, reliable and cost effective diagnostic test.<sup>11-12</sup>
- Present study is designed to compare the diagnostic accuracy of the two methods (i.e. diagnostic BCG test and tuberculin test) for the diagnosis of children suffering from tuberculosis.

## MATERIALS AND METHODS

It was a cross sectional comparative study. Patients were selected from children suffering from TB admitted in ward or visiting outpatient department fulfilling inclusion criteria in the department of Paediatrics (Unit I and Unit II), Nishtar hospital Multan. Fifty patients with tuberculosis were selected using Kenneth Jone's criteria. Fifty patients with tuberculosis were selected using Kenneth Jone's criteria. Both BCG and Tuberculin test were performed at the same time by the same doctor.

Parents/attendants were informed about the risks and benefits of the study and informed consent was taken. Permission of Ethical Committee of institution was taken before start of study.

Relevant data of cases including personal data, presenting complaints, physical examination finding and results of all the relevant investigations were collected. We injected 0.1 ml tuberculin intradermally on ulnar surface of right forearm and 0.1 ml BCG vaccine intradermally on deltoid muscle of left side.

To reduce the bias, both the BCG and tuberculin tests were performed at the same time by the same doctor. Reading of tests was taken by the same observer. As both the tests were done on the same patient, no confounding variable was there (like age, sex, nutritional status, severity of disease).

Investigations including hemoglobin, TLC, DLC with ESR were done in all cases. Chest X-ray was done in all patients. CT scan brain and examination of CSF was done in patient with suspected TBM. Lymph node biopsy of accessible lymph nodes in suspected case of TB lymphadenitis was performed.

BCG test was carried out in all patients by injecting 0.1 ml of freeze dried BCG vaccine, over the deltoid muscle on the left shoulder intradermally. BCG test results were noted between 48-72 hours. The criteria used for positive BCG test was taken from various studies of Udani and Imran. If induration more than 5

mm in diameter, was taken as positive and results were graded as:<sup>11</sup>

- Mild positive 5-9 mm induration.
- Moderate positive 10-20 mm induration.
- Strongly positive > 20 mm induration.

Along with BCG test mantoux test was also applied in all patients they were given 0.1 ml of PPD (5 units) on the volar surface of right forearm interdermally. The criteria for positive mantoux test was used as described by Red book.<sup>16</sup> The results were read by me between 48-72 hours and were graded as:-

- Doubtful positive 6-9 mm induration.
- Positive 1+ 10-14 mm induration.
- Positive 2+ 15-19 mm induration.
- Positive 3+ 20-30 mm induration
- Positive 4+ >30 mm induration.

Data was analyzed by SPSS 10.0. Descriptive statistics were applied to calculate mean  $\pm$  SD for age of the patients. Frequencies and percentages were calculated for sex, presenting complaints (fever, cough, weight loss, loss of appetite, fits), history of contact, history of measles, tuberculin test findings, diagnostic BCG findings, x-rays, chest findings and clinical diagnosis. Chi-square test was used for comparison of positive response to Mantoux test and BCG test. P-value equal or less than 0.05 ( $p \leq 0.05$ ) was considered significant.

## RESULTS

Present study compares immune response of BCG test with mantoux test in children with suspicion of TB. A total of 50 patients were studied. Out of these, 26 patients were male and 24 female.

Majority of the patients were from 6-10 years. Regarding the various types of tuberculosis, 17 patients had involvement of respiratory system including 1 case of miliary TB and 2 cases of tuberculous pleural effusion. The TBM cases were 26 where as abdominal, pericardial TB was 4 and 1 case respectively. There was 1 case of disseminated TB. Five patients with pulmonary TB had measles at the onset of symptoms.

Out of 50 patients, BCG test was positive 36 patients and was negative in 14 patients. Mantoux test was positive in 26 patients and was negative in 24 patients.

Both BCG and mantoux tests were positive in 26 patients. Ten patients had a positive BCG test where Mantoux test showed negative results. Both tests were negative in 14 patients. All patients were fulfilling Kenneth Jone's criteria (Table-1). Fifteen patients had TBM with neurological deficit and hydrocephalous on CT scan brain (Table No. 2).

In pulmonary TB, BCG was positive in 10 (71%) as compared to mantoux test 9(64%). In miliary form, BCG test was positive in 1 case and mantoux in no case. In pleural tuberculosis, BCG test was positive in 2 (100%) and mantoux in 2 (100%) cases. Both tests were negative in patients who had measles at the onset of

symptoms.

In TBM, BCG test was positive in 17(65%) as compared to mantoux test which was positive in 13(50%) cases. The BCG test was also positive in cases where mantoux test was positive. These patients had

clinically suggestive for x-ray chest which was positive in 12(46%) cases. Tuberculous infection was also suspected due to contact with tuberculous patient which was present in 22 (85%) of cases.

**Table No. 1: Kenneth Jone's Criteria for the Diagnosis of Tuberculosis in Children Score Chart**

Features	1	2	3	4	Score
<b>I. History</b>					
Age	Les than 2 year	-	-	-	Score
Contact	With TB Pt.	With sputum +ve TB Pt.	-	-	
BCG Scar	Absent				
History of Measles or Whooping cough	Within 3-6 months	Within 3 Months	-	-	
Immunocompromised/ immunosuppressant	yes				
PCM III *	yes				

**II. Examination & investigations**

**Interpretation**

Physical examination	-	Suggestive of T.B.*		
Radiological Findings	Non-Specific ***	Suggestive of T.B.***	-	-
Tuberculin test	5-10 mm	-	>10 mm	-
Granuloma	Non Specific	-	-	Specific T.B
AFB				Positive

**Total Score**

0-2 Points	T.B unlikely
3-4 points	keep under observation
5-6 Points	Tuberculosis probable Investigations may justify therapy
7 or more Points	T.B unquestionable

**NOTE**

\*consolidation not responding to antibiotics/ For at least 3 months Gibbus/Meningitis etc.  
 \*\* Paratracheal/Mediastinal Lymphadenitis, military mottling, consolidation Pleural effusion etc.  
 \*\*\* III defined opacity/ infiltrations, marked PCM bronchovascular markings etc.

III=Protein Caloric Malnutrition (Wt<60% expected for age)

**Table No.2: Clinical Features at the Time of Presentation (n = 50)**

Symptom	No. of Patients	Percentage (%)
Fever	48	96.0
Cough	30	60.0
Loss of appetite	36	72.0
Weight loss	36	72.0
Fits	26	52.0
Altered level of consciousness	26	52.0
Diarrhoea	4	8.0
History of measles	5	10.0
History of contact	39	78.0
Malnutrition	33	66.0

**Table No.3: Comparison of BCG Test and Mantoux Test in Different Types of Tuberculosis (n = 50)**

Type	BCG +tive	Mantoux +tive	Both +tive	Both -tive	BCG positive, mantoux negative	Total
Pulmonary TB	10	9	9	4	1	14
TBM	17	13	13	9	4	26
Miliary TB	0	0	0	1	0	1
Abdominal TB	4	0	0	0	4	4
Disseminated TB	1	1	1	0	0	1
Pleural TB	2	2	2	0	0	2
Pericardial TB	1	0	0	0	1	1
Lymph node TB	1	1	1	0	0	1
Total	36	26	26	14	10	50

In abdominal TB, BCG test was positive in all cases where mantoux was negative in all cases. These patients were clinically suggestive. Chest x-ray was positive in all cases with abdominal tuberculosis. Contact with tuberculous patient was present in 1 case. In disseminated TB, BCG test and Mantoux test were positive in one case. In pericardial tuberculosis BCG was positive in one case where mantoux test was negative. In miliary tuberculosis, BCG and mantoux test were negative in one case. In lymph node tuberculosis BCG and mantoux test were positive in one case (Table No.3).

**Table No.4: Results (n=50)**

Response	No. of Patients	Percentage (%)
BCG Positive	36	72
Mantoux positive	26	52
Both positive	26	52
Both negative	14	28
BCG positive, mantoux negative	10	20

## DISCUSSION

The BCG test has been shown to have an edge over mantoux test for the diagnosis of TB. The present study also favours the superiority of BCG test over mantoux test in children.

Majority of patients in present study were of TBM (52%) and respiratory TB (34%). In a study by Imran at Postgraduate Medical Institute Peshawar, patients were mainly of respiratory TB (43.9%) and TBM (40%). This difference is probably due to methodology of recruitment of study cases by Imran, who included only admitted cases.<sup>18</sup>

BCG test was positive in 72% patients while mantoux test was positive in 52% patients. In other studies, Imran showed BCG test positivity of 70% and positive mantoux test in 49%.<sup>18</sup> Udani showed BCG test positive in 88.8% patients and positive mantoux test in 52.3% patients.<sup>19</sup>

Velhal et al had 81.5% BCG test positive and 52.3% has positive mantoux test but they used 10 tuberculin units of PPD while in present study 5 tuberculin units of PPD were used.<sup>20</sup>

Goceman et al shows 100% positive BCG test in various forms of TB and only 44.5% mantoux test positive in pulmonary TB but no positive mantoux test in TBM and miliary TB.<sup>21</sup>

Ten (20%) patients had BCG test positive where mantoux test was negative. Imran.<sup>18</sup> showed 100% BCG test positive where mantoux test was positive and

31.1% had positive BCG test where mantoux test was negative and patients were mainly of respiratory TB (43.9%) and TBM (40%).

In TBM, BCG test was positive in 17 (65%) as compared with mantoux test positivity 13 (26%). All patients with positive mantoux test also had positive BCG test. In study by Imran<sup>18</sup> in TBM BCG was positive in 35 patients as compared with mantoux test positive in 12 cases.

In respiratory TB, BCG test was positive in 12 (71%) cases as compared to mantoux test which was positive in 11 (65%) cases. All patients with positive mantoux test also had positive BCG test.

The results of various Indian studies<sup>22,20,19</sup> and a study, from Turkey<sup>21</sup> and a local study also have shown the better diagnostic value of BCG test over mantoux test.<sup>23</sup> This study showed a better positivity with the BCG test than mantoux test.

## CONCLUSION

BCG skin test is superior to Mantoux test as a diagnostic tool in paediatric age group patients suffering from various types of tuberculosis.

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