Frequency of Positive Results of Bacille Calmette Gurein and Mantoux Skin Tests in Suspected Cases of Childhood Pulmonary Tuberculosis

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Abstract

Objective: To determine the frequency of positive results of Bacille Calmette Gurein and Mantoux skin tests in suspected cases of childhood pulmonary tuberculosis.

Patients and Methods: This prospective interventional study was conducted on 160 children from outpatient and inpatient departments of Pediatrics in Services institute of medical sciences, Lahore. An informed consent was taken from their parents for using their data in research and to keep the results confidential. Cases were diagnosed on the basis of history, examination and investigations. Each patient was given 0.1 ml BCG intradermally on left shoulder and 5 IU of PPD intradermally on volar aspect of right forearm. The results were observed after 48 hours of application in the form of induration (in mm). The diagnostic BCG >8 and Mantoux test >10 after 48hrs was taken as positive. All the information was recorded in a pre-designed proforma.

Results: Out of 160 patients, 83 (51.9%) were males and 77 (48.1%) were females. It was found that 72 (45%) patients showed positive response to both mantoux test and BCG. While alone BCG test was positive in 56 (35%) patients. Both BCG and mantoux tests were negative in rest of 32 (20%) patients. 131(81.9%) patients had variable degree of malnutrition. Severe malnutrition was present in 54 patients; out of these, 50 (92.6%) patients were BCG positive while only 10 (18.5%) patients showed positive response to mantoux test.

Conclusion: BCG is more reliable than the tuberculin test in the diagnosis of childhood pulmonary tuberculosis.

Keywords: Bacilli calmette gurein (BCG), Mantoux test, Tuberculosis (TB), Tuberculous meningitis (TBM), Antituberculous treatment (ATT).

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Contribution

All Authors have contributed in Study Design, Data Collection, Data Analysis, Data Interpretation, Manuscript Writing and Approval.

Introduction

Tuberculosis (TB) is a common chronic infection caused by weak gram-positive acid-fast bacilli that usually transmit from person to person by the inhalation of infective droplets. It basically refers to disease caused by a group of microbiologically similar bacilli, the most common of which is Mycobacterium Tuberculosis (M. TB). It can infect any part of the body, most common of which are the lungs. Tuberculosis is a major cause of illness and death worldwide especially in Asia and Africa, and it has an increasing trend in developed countries because of acquired immunodeficiency syndrome (AIDS). Annual infection rate in Pakistan is 231/100,000 people.[1] Worldwide 8.6 mil-

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lion new cases and 1.3 million people died from the disease (9,40,000 deaths in HIV negative and 3,20,000 in HIV positive). Among these deaths there were an estimated 1,70,000 from MDTRTB, a relatively high total compared with 450000 incident cases of MDR-TB.[2]

In most of the developing countries, including Pakistan, the risk of infection with TB is 20 – 25 times higher than the developed countries. There are many associated factors particularly poverty, malnutrition, overcrowding, illiteracy, lack of health awareness, inaccessibility to health care, lower vaccination rate and other communicable diseases. During the last 20 years or so mass migration of Afghan refugees, earthquakes and internally displaced persons (IDPs) have compounded the problem.

Young children (< 5 year old) have a high risk to develop progressive severe tuberculous disease.[3] WHO and most national tuberculosis programs (NTPs) advise that patients in these age groups with a positive test especially when they are in close contact with a smear positive pulmonary TB and no other clinical manifestations should receive INH prophylaxis.[4] The gold standard for diagnosis of tuberculosis is identification and isolation of mycobacterium tuberculosis either by staining or by culture of a sputum specimen. However it has a very low yield (< 30%) in children due to paucity of organisms and the non-availability of sputum specimen.[5] For this reason confirmation of diagnosis of tuberculosis is always a challenge in pediatrics population. In the absence of sputum smear and culture it is mainly based on the patient history, epidemiological data, clinical examination, chest X-ray and mantoux test.[6] This has been modified by Pakistan Pediatric Association (PPA) for diagnosis of childhood tuberculosis. By this method, tuberculosis can be diagnosed with a reasonable degree of accuracy in children.[7,8]

Mantoux test (intradermal skin test by PPD) has been traditionally used for many decades as skin test for detection of tuberculosis. It has its own limitations because it may give false positive and false negative results. Contrary to this, diagnostic BCG is positive in many conditions where Mantoux test is negative like malnutrition, tuberculous meningitis and disseminated tuberculosis. In a Pakistan based study by Rehman et al, the BCG test had shown 71% positive results as compared to 24% with Mantoux test.[9]

BCG (Bacille Calmette Guerin) is primarily a vaccine used to immunize children against tuberculosis. During immunization program it was found in India that it could be used as screening test like mantoux test. The same thing was later observed in Pakistan.[10] An induration of > 8mm is taken as positive and ≤ 8mm after 48 hours of BCG inoculation can be normal in Indian setting due to exposure to mycobacterium in environment or by BCG vaccine.[11]

Inspite of the superiority of the BCG test over Mantoux test, its use in the routine clinical practice is still controversial. It can be used as rapid diagnostic test for TB in situations where the condition of patient is serious and diagnosis has to be made rapidly so that the treatment has to be started at an early stage to reduce the sequalae and mortality rate in children with TB.

Field conditions in Pakistan lack advanced and expensive diagnostic facilities like PCR, BECTEC etc, especially in rural population. Majority of our patients belong to low socioeconomic group and can not afford these tests. These patients are usually malnourished where Mantoux test is expected to be inconclusive. In these circumstances, the BCG test can be used as an alternative tool which is rapid, reliable and cost-effective diagnostic test. Therefore this study was done to evaluate which test should be used preferably, either BCG or Mantoux, in suspected cases of childhood pulmonary tuberculosis.

Patients and Methods

We carried out a prospective and interventional study over six months period in departments of Pediatrics, Lahore. This study was approved by the institutional ethical committee. Following inclusion and exclusion criteria was followed:
Children up to the age of 15 years.

Patients with suspicion of tuberculosis having fever and cough for > 2 weeks, anorexia, subjective complaint of weight loss, contact with tuberculous patient and unvaccinated against tuberculosis.
Patients already on anti-tuberculosis therapy.

Patients on immunosuppressive drugs like steroids and chemotherapeutic agents.

A total of 160 children fulfilling the inclusion criteria were selected from outpatient and inpatient department of pediatrics. An informed consent was taken from their parents for using their data in this research and to keep the results confidential. Cases were diagnosed on the basis of history, examination and investigations. Each patient was given 0.1 ml BCG intradermally on left shoulder and 5 IU of PPD intrader-

mally on volar aspect of right forearm. The results were observed after 48 hours of application in the form of induration (in mm). The diagnostic BCG >8 and Mantoux test > 10 after 48 hrs was taken as positive. All the information was recorded in a pre-designed proforma.

Descriptive statistics including means ± SD was calculated for quantitative variables like age etc. Frequencies and percentages were calculated for qualitative variables including gender, BCG, Montox, and Malnutrition etc. Chi-square test was applied to see the significant association between age groups and malnutrition. P-value < 0.05 were taken as significant. The statistical packages SPSS (Version 20) and MS Excel (MS Office 2010) were used.

Results

A total of 160 patients fulfilling inclusion criteria were recruited in the study. There were 83 (51.9%) males and 77 (48.1%) females (Table 1). The age range was 8 months to 14 year and mean age of patients was about 6.1 ± 2.0 years.

According to nutritional status, out of total of 160 patients, 29 (18.1%) patients were well nourished and 131 (81.9%) had variable degree of malnutrition. Among malnourished, 50 (31.3%) were with 1st degree malnutrition, 27 (16.9%) with 2nd degree malnutrition and 54 (33.8%) had 3rd degree malnutrition. And out

of 83 male patients 20 (24.1%) were well nourished, 23 (27.7%) had 1st degree malnutrition, 13 (15.7%) were 2nd degree malnourished and 27 (32.5%) were 3rd degree malnourished. Out of 77 female patients 9 (11.7%) were normal, 27 (35.1%) were 1st degree malnourished, 14 (18.2%) were 2nd degree malnourished and 27 (35.1%) were 3rd degree malnourished (Table 2). Modified Gomez Classification was used to classify the nutritional status among the patients.

According to the age, patients were subdivided into four groups i.e. (0 – 1 year, 1 – 5 year, 5 – 10 year and > 10 years). It was found that in age group 0 – 1 year out of 36 patients, 21 (58.3%) were 3rd degree malnourished and in age group > 1 year – 5 year, out of 66 patients, 30 (45.5%) were 3rd degree malnourished. In age group of > 5 year – 10 year only two (5.1%) and in age group > 10 year out of 19 only one (5.3%) had 3rd degree malnutrition. The difference between younger age group (< 5 year) with malnutrition and elder age group (> 5 year) with malnutrition was found to be statistically significant (p value < 0.05).

When the results of accelerated BCG and mantoux test were studied it was found that out of 160 patients 72 (45%) showed positive response to mantoux test (induration > 10mm) applied intradermally on volar

Table 1: *Gender distribution of patients included in the study.*

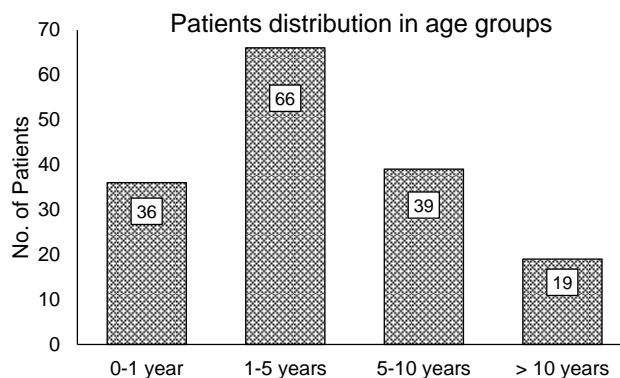| Sex	Frequency	Percentage
Male	83	51.9
Female	77	48.1
Total	160	100

Fig. 1: *Distribution of patients in different age groups.*

Table 2: *Nutritional status of study cases (n = 160).*

Sex	Total Patients	Normal	1st Degree Malnutrition	2nd Degree Malnutrition	3rd Degree Malnutrition
Male	83 (100%)	20 (24.1%)	23 (27.7%)	13 (15.7%)	27 (32.5%)
Female	77 (100%)	9 (11.7%)	27 (35.1%)	14 (18.2%)	27 (35.1%)
Total	160	29 (18.1%)	50 (31.3%)	27 (16.9%)	54 (33.8%)

Note: Modified Gomez Classification, for nutritional assessment was used.

aspect of right forearm and it was negative in 88 (55%) patients. While 128 (80%) patients showed positive response to BCG (induration 8 mm) applied intra-dermally on left shoulder and it was negative in 32 (20%) patients (Figure 2). All the 72 (45%) patients who had positive mantoux test, showed positive response to accelerated BCG. Apart from these 72 patients there were also 56 (35%) patients who showed positive response to BCG and in all these 56 patients mantoux test was negative. Both BCG and mantoux tests were negative in rest of 32(20%) patients.

The difference between BCG positivity and mantoux positivity in clinically suspected cases of pulmonary TB was found to be statistically significant (p value < 0.05).

When the results of mantoux test were compared with respect to malnutrition it was found that mantoux test was positive in 14 out of 29 (48.3%) normally nourished children, 36 out of 50 (72%) 1st degree mal-
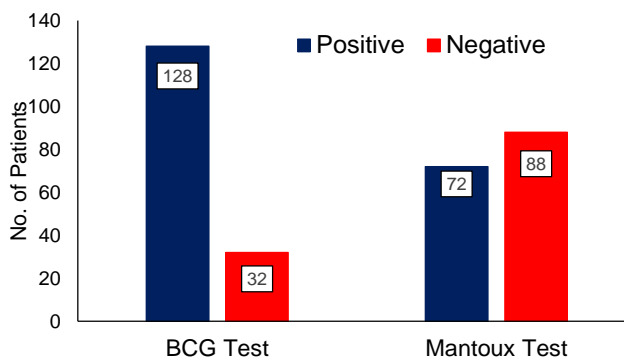

Fig. 2: *No. Of patients with results of two tests i.e. BCG and Mantoux.*

nourished, 12 out of 27 (44.4%) 2nd degree malnourished and 10 out of 54 (18.5%) in 3rd degree malnourished children (Table 4).

Table 3: *Malnutrition with age distribution.*

Age Groups	Malnutrition				Total
	Normal	1st Degree Malnutrition	2nd Degree Malnutrition	3rd Degree Malnutrition	
0 – 1 year	1 (2.8%)	5 (13.9%)	9 (25.0%)	21 (58.3%)	36 (22.5%)
1 – 5 years	16 (24.2%)	14 (21.2%)	6 (9.1%)	30 (45.5%)	66 (41.25%)
5 – 10 years	10 (25.6%)	19 (48.7%)	8 (20.5%)	2 (5.1%)	39 (24.38%)
> 10 years	2 (10.5%)	12 (63.2%)	4 (21.1%)	1 (5.3%)	19 (11.88%)
Total	29 (18.1%)	50 (31.3%)	27 (16.9%)	54 (33.8%)	160 (100.0%)

Note: The difference between younger age group (<5 year) and elder age group (> 5 year) with malnutrition was found to be statistically significant (P-value = 0.000)

Table 4: *Comparison of Mantoux test results in malnutrition and age groups.*

Age Groups	Normal n = 29		1st Degree Malnutrition n = 50		2nd Degree Malnutrition n = 27		3rd Degree Malnutrition n = 54	
	Mantoux +ve	Mantoux –ve	Mantoux +ve	Mantoux -ve	Mantoux +ve	Mantoux -ve	Mantoux +ve	Mantoux -ve
0 – 1 year	0	1	3	2	6	3	2	19
1 – 5 year	7	9	9	5	2	4	8	22
5 – 10 year	6	4	17	2	3	5	0	2
> 10 year	1	1	7	5	1	3	0	1
Total	14(48.3%)	15(51.7%)	36(72%)	14(28%)	12(44.4%)	15(55.6%)	10(18.5%)	44(81.5%)

Table 5: *Comparison of BCG results in malnutrition and age groups.*

Age groups	Normal n = 29		1st Degree Malnutrition n = 50		2nd Degree Malnutrition n = 27		3rd Degree Malnutrition n = 54	
	BCG +ve	BCG –ve	BCG +ve	BCG-ve	BCG +ve	BCG-ve	BCG +ve	BCG-ve
0 – 1 year	0	1	4	1	7	2	18	3
1 – 5 year	13	3	11	3	5	1	29	1
5 – 10 year	6	4	17	2	4	4	2	0
> 10 year	1	1	9	3	1	3	1	0
Total	20 (69%)	9 (31%)	41 (82%)	9 (18%)	17 (63%)	10 (37%)	50 (92.6%)	4 (7.4%)

When the results of accelerated BCG test were compared with respect to malnutrition, it was found that accelerated BCG was positive in 20 out of 29 (69%) normally nourished children, 41 out of 50 (82%) 1st degree malnourished, 17 out of 27 (63%) 2nd degree malnourished and 50 out of 54 (92.6%) in 3rd degree malnourished children (Table 5).

Discussion

Tuberculosis (TB) is a common chronic infection caused by weak gram-positive acid-fast bacilli that usually transmit from person to person by the inhalation of infective droplets. It has an increasing trend in developed countries because of acquired immunodeficiency syndrome (AIDS). The diagnosis of pulmonary tuberculosis in children has always been a problem due to non-availability of sputum for identification of acid fast bacilli, which is a gold standard in the diagnosis of tuberculous infection. Pakistan is a developing country where health facilities and the early diagnosis of tuberculosis (TB) remain difficult due to lack of advance investigation facilities. Therefore this study was done to evaluate, which test may be used preferably, either BCG or Mantoux, in suspected cases of childhood tuberculosis.

The present study compares the usefulness of accelerated BCG test with mantoux skin test in suspected cases of childhood pulmonary tuberculosis. Out of 160 patients there were 83 (51.9%) males and 77 (48.1%) females. This male predominance for pulmonary tuberculosis has also been shown by a similar study done by Rehman et al,[9] where 64% were males and 36% were females.

In our study, 102 (63.8 %) children were less than 5 years and 58 (36.2 %) children were greater than five years. This high prevalence rate of childhood tuberculosis is in conformation to a study conducted in India by chotmongkol, et al.[12] showing 54.3% studied population having tuberculosis were < 5 year of age. Similarly, another Indian study by Mtabho et al.[13] showed higher incidence of TB in younger children. This supported our evidence that a high prevalence of childhood tuberculosis is in the younger age group. The probable reasons for this may be due to low resistance of younger host, increased prevalence of moderate and severe malnutrition, close contact with infected adults and needing relatively small inoculum for infection.

In our study fever and cough for more than 2 weeks and history of contact with tuberculous patient was present in all the patients while weight loss was present in 51.9% of patients. These results are also in conformation with a study conducted by Mazhar et al.[14]

In our study out of 160 patients, 128 (80%) patients showed positive accelerated BCG response whereas 72 (45%) patients showed positive mantoux skin test. All these 72 patients who had positive mantoux response were also positive for accelerated BCG response. These results are comparable to a study done by Mazhar et al,[14] where BCG skin test was positive in 81% patients and mantoux test was positive in 50% patients. Mazhar et al, also reported that all the patients who showed positive mantoux results were positive for accelerated BCG response.

Similar results were also observed in another Pakistan based study by Rabia et al, the BCG test had shown 99% positive results as compared to 73% with Mantoux test.[15] A Turkish study done by Gocmen et al.[16] showed even more positivity of BCG test as

compared to the mantoux test in childhood pulmonary tuberculosis. In that study they found that BCG test was positive in 100% of patients as compared to 44.5% mantoux positive in clinically suspected cases of TB.

This shows a high yield for the accelerated BCG response as compared to mantoux skin test. As these tests were applied in clinically suspected cases of pulmonary TB, which is not a gold standard for the diagnosis of TB. So it is difficult to commit whether all those patients who showed positive response to accelerated BCG, actually had tuberculous disease. So, further studies should be carried out in the elderly patients in which a gold standard for diagnosis i.e. identification of mycobacteria, be used and both mantoux and accelerated BCG skin tests should be compared for accuracy of diagnosis.

Malnutrition is another important risk factor which decreases the immunity thereby making children more prone to infections. In this study 131 (81.9%) patients had variable degree of malnutrition, and among these 54 (33.8%) were severely malnourished (according to Gomez classification i.e. children having weight below 60% of the expected weight). Similar findings were observed in a study conducted in Karachi where 60% of the children with tuberculosis were malnutrition.[17]

In the present study, the ratio of malnutrition was high in females as compared to males. Out of 77 females, 27 (35.1%) and out of 83 male patients, 27 (32.5%) were having severe malnutrition. This relatively higher malnutrition in females might be due to cultural background and because of male dominating society. Better food and better education is offered to males as compared to females in our society.

Malnutrition also produces a state of energy giving rise to false negative mantoux test, thus making the diagnosis of tuberculosis even more difficult. In our study the comparison of BCG and mantoux test showed that accelerated BCG was positive in 50 out of 54 (92.6%) and mantoux test was positive in only 10 out of 54 (18.5%) severely malnourished children. Similar results were observed in a local study at Lahore done by Mazhar, et al,[14] where the BCG test was positive in 84% of severely malnourished children while Mantoux`s test was positive in only 4.8% of such patients. This probably indicates that state of energy is more in mantoux response as compared to accelerated BCG response. So accelerated BCG response seems to be more useful in the diagnosis of tuberculosis in malnourished children.

In this study, the Diagnostic BCG test gave a bet-

ter yield as compared to the Mantoux`s test. The difference was more obvious in children with respiratory tuberculosis having severe malnutrition. So, diagnostic BCG test has a definite edge over Mantoux`s test in the diagnosis of childhood pulmonary tuberculosis.

Conclusion

BCG was more sensitive than the tuberculin test in the diagnosis of tuberculosis. It was also more sensitive than the tuberculin test in malnourished children with pulmonary TB. It is still valuable in the diagnosis of tuberculosis especially in developing countries where the disease is still a major public health problem and where sophisticated methods such as rapid culture with BACTEC and demonstration of bacilli with DNA probes are not widely available.

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