Original article

Tuberculin Skin Test Positivity in Children in a Tertiary Care Hospital

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Abstract

Introduction: It is extremely challenging to make a correct diagnosis of tuberculosis (TB) in children because of the difficulty in isolation of Mycobacterium tuberculosis. The tuberculin skin test (TST) or theMantoux test (MT) is still an important modalityfor diagnosis.

Methods: We evaluated the TST positivity in 700 children;those without tuberculosis and with low risk for development of TB (groupA-400 children), those without tuberculosis but high risk eg. HIV positive children, those with severe malnutrition and those on steroids (group B - 100 children) and diagnosed cases of tuberculosis (group C - 200 children). We also studied the correlation between TST positivity and BCG vaccination.

Results: Overall Mantoux positivity was 16.6%; that ingroup A9.3%, group B9.1%, and group C 34.3%.In group C,the maximum cases of positive Mantoux were seen in pulmonary tuberculosis. BCG scar prevalence was 73.5% in the present study and was not associated with a higher incidence of positive Mantoux in any of the groups. In the patients with a positive contact, Mantoux was positive in 26.9% children in group A, 66.6% in group B and 36.6% in group C.The highest prevalence of Mantoux positivity was seen in group C, it being highest in pulmonary TB (67.5%)followed by lymph node TB (42.4%).Mantoux positivity was lowest in disseminated TB (9.5%).Of 44 cases with a positive Mantoux in groups A and B, 56.8 % were found to have tuberculosis on further testing.

Conclusion: TST still serves as a useful screening test for tuberculosis in children.

Keywords: tuberculin test; BCG vaccine; tuberculosis

Introduction

As per the World Health Organization estimates, the annual global burden of tuberculosis (TB) in children in 2012 was approximately 5,30,000 cases (or 6% of the global TB burden), with 74,000 children dying from TB that year.[1] The estimated lifetime risk of developing active disease for a child infected with mycobacterium tuberculosis as indicated by a positive tuberculin skin test (TST) is about 10-20%, of which 5% are likely to develop the disease in the first year after infection.[2] As TST is a cost effective test, most of the pediatric guidelines and the RNTCP programs use tuberculin skin test as an important modality to diagnose tuberculosis in children along with smear, culture and radiology. Other tests like Interferon Gamma Release Assay (IGRAs) are comparable to tuberculin skin test and have some advantages but are extremely expensive and not feasible in most countries where tuberculosis is a problem.[3]

Culture and smear should be the gold standard for diagnosis but the positive rates range from 20 to 40

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percent in children.[4]. A positive TST will mean either that the child is infected (asymptomatic) or diseased. Also, as children are exposed to tuberculosis very early in developing countries, the diagnostic utility of TST would probably diminish with age.

Aims and objectives

1. To study the prevalence of tuberculin positivity in children
2. To correlate tuberculin positivity with the presence of a BCG scar

Patients and methods

The study was conducted over a period of one and a half year from January 2013 to May 2014, in children more than 1 month and less than 12 years of age, who were admitted to the pediatric inpatient department or attending the outpatient clinics of the G.S.Medical College and KEM Hospital, a tertiary care teaching hospital in Mumbai .

Seven hundred children were enrolled. Four hundred were low risk childrenie.immuno- competent patients but without evidence of tuberculosis (group A).

A hundred were high risk children without evidence of tuberculosis but immunocompromised namelydiagnosed HIV positive children, children with Grade III or IV malnutrition and children on long term steroid therapy (>1mg/kg/day for > 1 month) (group B). Two hundred children diagnosed with tuberculosis (group C) were also included.

All patients meeting the inclusion criteria were included in the study after taking informed, written consent of parents and assent of children >7 years of age. All the enrolled patients underwent tuberculin skin testing. TST was given using 5TU of Purified Protein Derivative (PPD) with a 26 gauge needle and a tuberculin syringe to inject 0.1ml of PPD intra-dermally over the left forearm. The test was read after 72 hours by measuring the width of induration across the forearm by ball point method. Presence of erythema was not considered as a positive result. As per updated national guidelines guidelines for pediatric tuberculosis in India, a positive TST was taken as induration of more than 10 mm in low risk childenand more than 5 mm in HIV-positive children.[3] A detailed history regarding tuberculosis contact with an adult sputum positive patient was taken. All patients were examined for signs and symptoms of tuberculosis and presence of BCG scar. Cases were divided into upper and lower socioeconomic class as per the modified Kuppuswamy scale. Protein energy malnutrition (PEM) was graded from grade I- IV as per the Indian Academy of Pediatrics classification. Children with grade III and IV PEM were included in high risk group.Children receiving the tuberculin test on an outpatient basis were asked to report after 72 hours for the reading. All patients with a positive TST underwent further work up for diagnosis of active tuberculosis in the form of chest X ray, gastric lavage for acid-fast bacilli (AFB) in infants and young children and sputum in older children. Specimens were also sent for AFB culture.Fine needle aspiration cytology (FNAC) of lymph nodes,histopathology and computerised tomography brain/abdomen/chest were done, if indicated, to confirm the presence of active disease. The details of history and investigations were recorded in the case record form.

The study protocol was approved by the Institutional Ethics Committee.

Statistical analysis

As the data obtained in our study was qualitative data, proportions (%) were calculated Chi square test and Fisher Exact test were used for comparison of

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two groups. Data was analysed using the program Graph Pad Prism version 3.06.

Results

Among the 700 children studied, 351(50.14%) were males and 349(49.8%) were females with a male to female ratio of 1.005.Sixty-nine patients did not follow up for the Mantoux reading; 46 in group A, one in group B and 22 in group C. Table 1 shows the patients characteristics.A hundred and five children were Mantoux positive giving an overall prevalence of Mantoux test (MT) positivity of16.6 %. Amongst 44 children with a positive Mantoux in group A and B, 25children were found to have active tuberculosis on further investigation (chest X ray, gastric lavage for AFB or computerized tomography scan/magnetic resonance imaging as indicated).

Table 2 shows the relationship between Mantoux positivity and presence of a sputum-positive contact in the various groups. The relationship between Mantoux positivity and a sputum-positive contact was found to be highly significant in group A and B.

Overall BCG vaccination coverage rate as evidenced by presence of BCG scar was 73.8%. There was no significant association of Mantoux positivity with the presence of BCG scar in all three groups.

Eighty-one children with BCG scar were Mantoux positive. In Mantoux positive children without any evidence of tuberculosis but with BCG scar i.e. group A and group B, 81.8% had induration of 10-15mm and 18.8% had induration more than 15 mm. In group C ie.children with tuberculosis, 37.5% had induration more than 15 mm. However this was not found to be statistically significant (p = 0.08).

In patients with diagnosed tuberculosis ie. group C, Mantoux positivity was seen most in children with pulmonary tuberculosis followed by those with lymph node tuberculosis (see table 4).

Table1: Mantoux positivity in the various groups

	Total number	**Number showing Mantoux positivity**
Age		
<1year	159	28 (17.6%)
1-5 years	233	38(16.3%)
5-12 years	239	39 (16.3%)
P=0.91 by chi square test		
Groups		
Group A	354	33 (9.3%)
Group B	99	11(9.1%)
Group C	178	61(34.3%)
P<0.0001 by chi square test		
Socio-economic status		
Lower	405	75(18.5%)
Upper	228	30 (13.1%)
P<0.001 by chi square test		

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Table 2: Relation between contact with tuberculosis and a positive Mantoux

	Number with h/o TB contact	**Number of Mantoux positive**	**Number with no h/o TB contact**	**Number of Mantoux positive**
Group A (n=354)	78	21(26.9%)	54	12(3.7%)
P<0.0001 by Fischer's exact test				
Group B (n=99)	9	6(66.6%)	91	5(5.4%)
P<0.000 by Fischer's exact test				
Group C (n=178)	60	22(36.6%)	140	39(27.8%)
P=0.43 by Chi square test				

Table 3: Relationship of presence of BCG scar with Mantoux positivity

	Number with BCG scar	**Number of Mantoux positive**	**Number with no BCG scar**	**Number of Mantoux positive**
Group A (n=354)	272	27(9.9%)	82	6(7.3%)
P=0.404 by Fischer's exact test				
Group B (n=99)	63	6(9.5%)	26	5(19.2%)
P=0.28 by Fischer's exact test				
Group C (n=178)	130	48(36.9%)	48	13(27.0%)
P=0.20 by Chi square test				

Table 4: Relationship of Mantoux positivity to site of tuberculosis in group C

Site of TB	**Number of patients**	**Number with positive Mantoux**
Central nervous system	60	13 (21.7%)
Pulmonary	40	27 (67.5%)
Lymph node	33	14(42.4%)
Disseminated	21	2 (9.5%)
Miliary	13	2 (15.4%)
Abdominal	11	3 (27.3%)

Discussion

Prevalence of Mantoux positivity

Overall prevalence of Mantoux positivity was 16.6%; in low risk children it was 8.2%, high risk 9.1%, and children with tuberculosis 34.3 %. Prevalence of Mantoux positivity in children varies from 3.5% to 18.8%.[5,6,7]The lower prevalence of Mantoux positivity in low risk patients is similar to the study by Chadha et.[8]. In contrast, in developed countries the prevalence is low as BCG is not given and also TB is not a very common disease. Serwint in Baltimore USA reported a prevalence of 0.8%.[9]

As the child grows older he is likely to be infected with TB as the disease is common in the community. The diagnostic value of Mantoux in older children and adults is less as most of them by that age would have been infected with TB. Though the prevalence of Mantoux positivity was 9.3% in the low risk group, it was high (34.3%) in the cases with active tuberculosis. This reinforces the importance of the tuberculin skin test as an important screening test for the diagnosis of tuberculosis in children. This is especially so because of the low yield of AFB cultures in children.

Prevalence of Mantoux positivity in high risk group was included in the study because. tuberculosis is difficult to diagnose in such cases and the disease may spread rapidly. The national program also considers them as a special group. [3]The tuberculin skin test is useful for both making a diagnosis and for starting chemoprophylaxis. In our study,Mantoux positivity was 9.1% in the high risk group, which is lower than in most other studies. In a study in seropositive children by Kiwanuka et al, the Mantouxpositivity was reported as 19%.[10] Portu et al found a positive tuberculin test in 16.9% of HIV-infected intravenous drug abusers in comparison with 39.9% in HIV uninfected intravenous drug abuser.[11]

Mantoux positivity in children with diagnosed tuberculosis

In our study Mantoux positivity in the TB group was 34.3 %. The central nervous system was the most common site of tuberculosis followed by pulmonary and lymph node. Mantoux positivity was least in children with disseminated tuberculosis (9.5%)andmiliary TB (15.4%). It is likely that Mantoux positivity is low in children with disseminated and military tuberculosis as they have poor immunity.The clinical spectrum of tuberculosis in this study was found to be similar to a study by Vijayasekaraet al.[14] However studies by Kabra et al[15] and Garg et al[16]found a higher prevalence of pulmonary and lymph node tuberculosis than in the present study.

Prevalence of Mantouxpositivity and socioeconomic class

The prevalence of Mantoux positivity was found to be higher in the lower socioeconomic class in our study (p value 0.0001). The higher number of TB cases in this group may be due to overcrowding, poor sanitation and pollution. This was also reported byAddo et al in Ghanaian school children. [17]

Mantoux positivity and contact with a sputum-positive contact

Tuberculosis contact was present in 21% of all cases in our study. TB contact was present in 78(19.5%) out of 400 apparently healthy children, 9 (9%) of 100 immunocompromised children and 60(30%) of 200 children with tuberculosis. Similar findings were found by Vijayasekaran et al.[18]. Mantoux test was positive in 33% of theirchildren with positive contact. Mantoux positivity in our patients with a positive

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contact was 26.9% in group A,66.6% in group Band 36.6% in group C.

Mantoux positivity was higher in all three groups in those with a positive TB contact than in those without a TB contact. The children with a positive Mantoux may be infected with TB but are not symptomatic or having disease. The development of disease in an infected child depends on his immune status, nutrition and other stress factors. In group B Mantouxwas positive in 66.6% of those with a contact with tuberculosis. Since these children are immunocompromised, a positive Mantoux alone is adequate to start these children on chemoprophylaxis.

BCG vaccination rate was 73.8% in our study. BCG scar positivity in the three groups was 74% in group A, 68% in group B and 75% in group C. BCG is not a very effective vaccine as it only prevents severe forms of TB. In our study 75%of proven cases of TB had a BCG scar supporting this view. In all 9.9%, 9.5% and 36.9% children with BCG scar were Mantoux positive in group A, group B and group C respectively.The presence of BCG scar was not associated with a higher prevalence of a positive Mantoux in all the three groups.In all children in whom BCG scar was present ,Mantoux test positivity was highest in TB group (36.9%) as compared to the non TB group A (9.4%) and group B (9.5%). The results of the present study were similar to previous study done by Chadha et al who found that 70-80% of vaccinated subjects had indurations<10 mmie.wereMantoux negative. [19]Thus BCG vaccination does not interfere with the interpretation of tuberculin test.

In children in whom BCG scar was present, induration of > 15mm on Mantoux testing was seen in 37.5% of cases with TB and only 18.8% of cases without TB. Thus reaction of > 15mm is more likely to be due to tuberculosis rather than an effect of BCG vaccine. Though the correlation was statistically insignificant, more studies are required to be done .Our findings were consistent with the study done by Johnson et al. [20]In children without tuberculosis i.e. group A and B, out of 44 cases with a positive Mantoux, 56.8 % also had other evidence of tuberculosis onfurther investigation. This is comparable to the study done by Chauhan et al who found that 63-83% of children with a positive TST also had a CXR suggestive of tuberculosis.[19].This implies that it is worthwhile to evaluate every child with a positive Mantoux as children may be initially asymptomatic even when they have active tubercular disease. In children below 2 years of age (who are considered to be immune immature and have poor disease containment), a positive TST indicates high risk of disease progression. Hence if such children whether symptomatic or not must be considered to have active disease and treated accordingly.[21]

Conclusion

The highest prevalence of Mantoux positivity was seen in cases of tuberculosis. Overall Mantoux positivity was 16.6%. Mantoux positivity in low risk children was 9.3%, high risk 9.1%, and children with tuberculosis 34.3%. Out of 44 cases with a positive Mantoux in low and high risk children, 56.8 % also had other evidence of active tuberculosis on further investigation, indicating that TST still serves as a useful screening test for tuberculosis in children, and such children should be followed up closely for few months to rule out the development of tuberculosis.

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