Latent Tuberculosis Infection among Children under Five Years

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Abstract

Background
Latent tuberculosis infection (LTBI) is a significant public health problem. Despite the advanced diagnostic tools, the LTBI remains undiagnosed.

Objectives
To determine the frequency of LTBI and its predisposing factors in children under 5 years.

Methods
This cross sectional study was conducted in Out Patient Department (OPD) of National Institute of Child Health (NICH), Karachi from March 2014 to September 2014 after informed parental consent. All children under 5 year who attended OPD with symptoms like fever, cough of less than one week were screened. Children with strong suspicious of Tuberculosis (TB) were excluded. Medical factors contributing to LTBI such as family history of tuberculosis, BCG vaccination status and malnutrition on assessment were noted. Social factors including lack of parental education, passive smoking and overcrowding were also noted. All included children were given tuberculin skin test (TST) and an induration of ≥10 mm was considered positive TST.

Results
A total of 443 children were screened for LTBI during study period. Children's mean age was 3.40 ±0.96 years. Illiteracy (88%), passive smoking (65%) and over crowding (24%) were social factors where as malnutrition (53%), positive family history (35%) and lack of BCG vaccination (71%) were medical factors found among screened children. LTBI was strongly correlated with age, weight, nutritional status and passive smoking (*p*-value <0.05).

Conclusion
LTBI was found in 3.83% of screened children with important contributing factors of illiteracy, passive smoking, malnutrition and TB in family.

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Keywords
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Introduction
Latent Tuberculosis Infection (LTBI) represents a substantial public health burden and is among the leading cause of infectious disease worldwide. More than one third population of the world is affected with latent infection.[1] Tuberculosis is a leading cause of morbidity and mortality in all age groups in developing countries and Pakistan ranks 5th in the world among TB high-burden countries.[2]

Childhood tuberculosis accounts for 10-20% of all cases of TB and it accounts for 8-20% of all deaths among children of high TB burden countries.[3] Childhood TB is common but it is undetected and underreported, in many parts of the world particularly in South Asia.[4] Data regarding childhood TB in Pakistan shows that only 4% are registered and 2.5% of children are at risk of acquiring infection.[5] Among them 80-90 % of children develop LTBI and the risk of reactivation and development of primary progressive disease is 5-10%.[5] This risk of progression is even higher in infants (30-40%) and young children (24%) younger than five years of age.[6]

A close contact with active TB case, lack of BCG vaccination, undernutrition, small houses with large family size, under ventilated and poor sunlight exposure and smoking are possible predisposing factors among children with either LTBI or TB.[1,7,8]

Children with LTBI represent the future reservoir for cases of TB and mostly under diagnosed or under reported. Thus, detecting and treating children with LTBI would be an important strategy for prevention of progression and elimination of TB.[2] Establishing diagnosis of LTBI is problematic in children. Existence of active TB has

been used as a surrogate for LTBI and various tools has been used for detection of LTBI. Though interferon gamma release assay (IGRAs) tests have been found highly sensitive (83-100%) for detection of active TB disease.[2] But, TST is very inexpensive, easily available and commonly used screening testfor detection of LTBI in developing countries in comparison to IGRAs tests which are very expensive, not standardized yet not easily available.[1-3]

Thus, the purpose of this study was to screen children for LTBI and common factors associated with LTBI so that recommendation may be made for prevention and control of childhood tuberculosis in the country.

Patients and Methods

This cross sectional study was conducted in Out Patient Department (OPD) of National Institute of Child Health (NICH), Karachi from March 2014 to September 2014 after informed consent from the parents/guardians. Institutional Ethical approval was taken. All children of age less than 5 years who attended OPD with symptoms like fever, cough of less than one week were randomly selected. Selected children were screened using tuberculin skin test (TST) and children with an induration of >10 mm were diagnosed as LTBI.[9]

Physical Examination and Chest radiography was provided to all included patients. None of the children was reported for active pulmonary TB. Exclusion of active TB disease was done on basis of either symptoms or chest radiography or both. The presence of any symptom suggestive of TB (i.e. any one of cough >2weeks, low grade fever of >2 week, night sweats, weight loss, chest pain, shortness of breath and fatigue) plus any abnormality on chest radiography highly suggestive of active TB. Confirmed latent tuberculosis infections were also enrolled in TB Clinic for treatment.

All children were evaluated for medical and social risk factors for LTBI. Medical factors such as family history of tuberculosis and close contact, BCG vaccination status and malnutrition (as assessed by using Modified Gomez classification) were noted. Social factors like lack of parental education, passive smoking and overcrowding were also noted.

A structured questionnaire was used to collect demographic data and possible factors contributing to LTBI. There are some potential confounders which may be responsible for either false positive or false negative TST results. These include prior BCG vaccination during last one year, recent or old TB infections, age less than 3 months, recent viral infections (chicken pox, measles, mumps, HIV), severe malnutrition, recent use of immunosuppressive drugs like steroids, faulty technique of TST administration, insufficient dose of purified protein derivative (PPD) and inactive tuberculin PPD. These confounders were controlled through sample selection. To avoid non response bias we used simple and of brief duration questionnaire.

Statistical Analysis

Data was analyzed using SPSS version 21. Descriptive analysis was done for socio-demographic variables. Bivariate analysis was run to see any effect of socio-demographics information on LTBI. Fischer exact test was applied after stratification of age, gender and weight with respect to LTBI and common factors. *P*-value = 0.05 was taken as significant.

Results

A total of n=443 children were screened during study period. Anthropometric measurements are shown of screened children are shown in Table 1. It shows that mean age of the patients was 3.40 ±0.96 years with majority of the children n= 298 (67%) were >3 years of age. Mean weight of the children was 10.69 ±1.71 Kg with majority n= 331 (75%) were >10Kg. Mean height of the children was 94.39 ±9.64 cm and majority of the patients n=305 (69%) were >95 cm. Females n=229 (52%) were slightly more than males n=214 (48%).

Out of 443 children screened, n=17(3.83%) children had LTBI.Table 2 shows socio-demographic and medical factors contributing to LTBI. Parental illiteracy n=15 (88%), history of passive smoking n=11(65%) and overcrowding n=4 (24%) were social factors whereas protein calorie malnutrition (PCM) grade II n=9 (53%), family history of TB n=6 (35%) and lack of BCG vaccination n=12 (71%) were the important medical contributing factors for LTBI. There was significant correlation of LTBI with age, weight, nutritional status and passive smoking (*p*-value <0.05).

Discussion

LTBI is a substantial public health problem. Approximately >1/3rd world's population is infected with latent TB. Childhood LTBI is under diagnosed and under reported that may be due to lack of clinical symptoms and signs. In this study, we looked at the prevalence of latent tuberculosis infection in children younger than five years of age at our tertiary care hospital and possible risk factors attributable to LTBI.

Table 1: Age & Anthropometric measurements of 433 Children Screened for LTBI

Parameter		N(%)
Age (years)	*mean ±SD**	*3.40 ±0.96*
	≤3	145(32.70)
	>3	298 (67.30)
Weight (Kg)	*mean ±SD*	*10.69 ±1.71*
	≤10	112(25.28)
	>10	331(74.71)
Height (Cm)	*mean ±SD*	*94.39 ±9.64*
	≤95	138(31.2)
	>95	305(68.8)

*SD: Standard Deviation

Table 2: Factors Contributing to Latent TB in 443 Children

Variables		Latent TB Infection Yes (n=17)	No(n=426)	*p*-value
Anthropo-measurements		**N (%)**	**N (%)**	
Age	≤3	13(77)	132(31)	0.0002
	>3	4 (23)	294(69)	
Weight (Kg)	≤10	8(47)	104(24)	0.0460
	>10	9(53)	322(76)	
Height (Cm)	≤95	8(47)	130(30)	0.1816
	>95	9(53)	296 (70)	
Social Factors				
Over crowding	Yes	4(24)	128(30)	0.7876
	No	13(76)	298(70)	
Literacy	Illiterate	15(88)	368(86)	1.0000
	Literate	2(12)	58(14)	
Passive Smoking	Yes	11(65)	154(36)	0.0215
	No	6(35)	272(64)	
Medical Factors				
Family history of TB	yes	6(35)	123(29)	0.5901
	No	11(65)	303(71)	
Malnutrition	Grade II	9(53)	342(80)	0.0121
	Grade I	8(47)	84(20)	
BCG	Yes	5(29)	132(31)	1.0000
	No	12(71)	294(69)	

LTBI is defined as a state of persistent bacterial infection controlled by body's immune response in the absence of clinical symptoms of active disease.[1] It is very important because this is a state of long-term bacillary containment in alveolar macrophages and extracellularly in granulomas that limits further spread and adjacent tissue destruction. There is a balance between pathogen and host but the correlates and mediators of this immune balance are not fully understood.[10,11]

The LTBI has the highest prevalence in India, similar to that of active tuberculosis.[12]

In our study, frequency of LTBI in children under five at tertiary care center was found to be 3.83%. This is similar to reported prevalence of LTBI of 3.5% and 4.7% in 1-5 year and school age children from Iran and China respectively.[13,14]

The overall life time risk of LTBI reactivation is approximately 5-10% among older children but risk of progression to active disease is higher in younger children.[15, 16] Childhood infection establishes the reservoir for outbreaks in the future so it is important to make proper diagnosis and treatment of LTBI in the endemic region for Tuberculosis control.[17]

There are many socioeconomic and medical factors which predispose to latent TB such as low family income, illiteracy, poor housing and overcrowding, passive smoking, living in close contact with active TB patient, lack of BCG vaccination and access to medical access care. In addition, undernutrition, measles and HIV are also important medical conditions which predisposes a child to LTBI.[7,9,17,19]

In this study, we found high frequency of social factors like illiteracy (88%), passive smoking (65%) and overcrowding (24%). Nguyen TH *et al* highlighted the importance of contact tracing in remote settings with high TB prevalence.[9] Similarly den Boon *et al* from South Africa suggested that passive smoking may also be responsible for the increased risk of acquiring TB infection.[19]

We also found a high frequency of family history for TB (35%), PCM grade II (53%) and lack of BCG vaccination (71%) in screen children.

In this study, we used TST for the diagnosis of LTBI similar to Nguyen *et al*, Iskander *et al* and Okeda *et al*.[9,21,22]

Overall control of TB infection depends on the detection and preventive treatment of LTBI, thus halting the progression of LTBI to disease.[23,24] Rutherford M E *et al* has suggested that t there is underutilization of WHO guidelines in TB endemic areas, which promotes active screening and preventive therapy for children under 5 years of age.[25] In our study, the screening in children less than 5 years and their management is small step towards to WHO guidelines.

In this study, the identified factors including parental illiteracy, history of passive smoking, overcrowding, grade II PCM, family history of TB, lack of BCG vaccination were the social and medical contributing factors for LTBI. This information may facilitate policy makers for public health planning and policies in the community for control of TB in our country.

This study supports the importance of contact tracing activities in the control of TB in developing countries, associated with early case detection and treatment.

Limitation of Study

This is a small study from single tertiary care center over a short period in population below 5 years. It cannot be generalized since it has not been carried out in a community with large number of children and adolescent. However, we think that it is a good start to develop trends in screening and management of LTBI before development of active disease.

Conclusion

The prevalence of latent tuberculosis infection was 3.83%. We found a high prevalence of parental illiteracy (88%), malnutrition (53%), family history of TB or close contact (35%) and overcrowding (24%). These may be attributed to LTBI. However, further studies on prevalence of LTBI and implementation of WHO guidelines are required in our country for better control of LTBI and thus ultimately decreasing burden of active TB.

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