Prevalence of *Mycobacterium tuberculosis* Infection in Children in Western Uttar Pradesh

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This study was conducted to estimate the prevalence of tubercular infection and compute the Annual risk of tuberculosis infection (ARTI) in Bijnor district of western Uttar Pradesh through a hospital-based tuberculin survey conducted at a pediatric hospital. A total of 1085 children below 18 years (0-4 years 866, 5-17 years 219), attending the out-patient department during October 2007 through September 2008 were included. Tuberculin skin test using standard PPD RT23 with Tween 80 was performed on every 4th child attending the out-patient department and induration was measured after 48 to 72 hours. Using a cut-off of 15 mm among 0-4 y aged children, the average prevalence rate was 7.4%, and using cut-off of 10 mm in 5-17 y age group the average prevalence rate was 26.9%. ARTI was 4.11% (95% CI 3.09-5.14) and 3.50 % (2.46-4.48), respectively in the two age groups.

Key words: *Annual rate of tuberculosis infection, Child, India, Prevalence, Tuberculin skin test, Tuberculosis.*

Tuberculin surveys help us to estimate the prevalence of tuberculosis (MTb) infection and to compute the annual incidence (annual risk) of MTb infection (ARTI)[1]. Tuberculosis control is defined as cumulative prevalence of <1% infection by age 14 years [2-7]. This translates to an average ARTI of about 0.07% below 14 years of age[2-7]. Currently ARTI is about 1% per year in many regions of India [5-9]. In the absence of any baseline data from western Uttar Pradesh, we conducted this tuberculin test survey.

METHODS

This study was conducted at a secondary-care pediatric hospital in Bijnor, western Uttar Pradesh. Ethical clearance was obtained from the ethics committee of the hospital. The study population consisted of children below 18 years, attending the out-patient department (OPD) during October 2007 through September 2008. Every 4th child attending the OPD was included, irrespective of the presenting complaints, avoiding bias or possible non-random clustering effect that might have occurred if all children had been tested at one point of time. Exclusion criterion was any illness that included TB in the differential diagnosis.

The tuberculin skin test (TST) was performed using the standard PPD RT23 with tween 80 (Span Diagnostics, Sachin, Gujarat; dose equivalent to 5 TU old tuberculin). However, it is to be understood that the 5 TU is equivalence value for standardization - 2 TU PPD with Tween 80 has potency equal to 5TU old tuberculin. Test result was read after 48 to 72 hours by one of the authors and recorded as the transverse diameter (in millimeters) of palpable induration[1].

The study children were grouped in two subsets, 0-4 years and 5-17 years. The prevalence rates in both the subsets were estimated at different cut-off values.

The annual risk of MTb infection (ARTI) was calculated from the prevalence of infection (P) by using the equation: $ARTI = 1 - (1 - P)^{1/A}$ where A is the mean age of tested children (6,9,10). Prevalence frequencies of infection were analyzed by Chi-sqare test to calculate *P* values.

Results

A total of 1137 children were recruited; 1085 (95.4%) of them were test-read. The age of tested children ranged from infants to 17 years (*Table* I). The distribution of tuberculin indurations (*Figure* 1) in the entire study children (Panel A) as well as in the age-group of 0-4 years (Panel B) appeared to be bimodal, with the first mode clearly at 4 mm. As the second mode was not clearly demarcated, the antimode could not be precisely identified. Visually the best fit antimode appears to be at 12 or 14 mm. The distribution of tuberculin indurations in the age group 5-17 years (Panel C) appeared to be trimodal, with the modes of the first 2 clusters at 7 and 9-10 mm, respectively and the 2 antimodes were at 8 and 12 mm, respectively.

The detection of the antimode for the determination of the cut off value is an important step in distinguishing MTb-specific response from non-specific response(6,7,9,11). Since the antimode was not clear, to measure the prevalence of MTb infection, we used 15 mm as a conservative cut-off value in the first subgroup (0-4 y), to minimize the

TABLE I Prevalence of Tubercular Infection in the Study Population

Age	0-4 years (*n*=866)	5-17 years (*n*=219)
Mean age	1.8 y	8.8 y
Median induration (IQR)	5 (4-7)	6 (4-10)
Mean induration (SD)	6.4 (4.5)	8.4 (6.1)
Prevalence (95% CI)	7.4 (1.8)	26.9 (6.9)
ARTI (95% CI)	4.1 (3.1-5.1)	3.5 (2.5-4.5)

ARTI: Annual risk of tuberculosis infection.

inclusion of responses induced by BCG or other environmental mycobacteria and to increase the confidence of identifying MTb infection(12). Similarly, we used 10 mm (midway between the 2 antimodes) as cut off for children in the second subgroup (5-17 y) to measure the prevalence of MTb infection.

The prevalence rates of MTb infection in different age groups was 6.1 to 6.7% (0-2 y), 12.7% (3-4 y), 20.5 to 27.8% (5-10 y), 47.6% (11-12 y) and 50% (13-16 y). There was no significant sex-wise difference.

Discussion

Our results show alarmingly high rates of MTb infection prevalence in children and consequently, very high ARTI values. However, our study has some limitations. Strictly speaking, the study subjects do not 'represent' children in the community. In order to minimize the potential for over-representation of MTb infected children, we selected a systematic sample of every fourth child. To maximize specificity, even at the cost of some sensitivity, we chose PPD reaction cut off values of 15 mm for children under 5, even though the antimode was 12 or 14 mm. Similarly, we chose a cut off value of 10 mm for children above 4 years, even though the first antimode was 8mm. Many other investigators have also used such cut off values(6,9,12). The study methodology was similar to that described for TST surveys(1,3,7). We did not attempt to correlate tuberculin sensitivity with a history of BCG vaccination as many studies have shown that it does not interfere with TST result in children at and above 5 years(6,7). As for children below 5, by using 15 mm as cutoff value we have avoided cross reactions to BCG(6,7).

There is paucity of data on Mtb prevalence and ARTI rates in various districts of Uttar Pradesh. One community based tuberculin survey had been conducted amongst 1-9 years old rural children in three districts of central and eastern UP(13). The ARTI computed from the prevalence of infection, using the cut off value of 14 mm, was 2.3% in rural areas of Rae Barelli, 1.9% in Hardoi and 1.5% in Jaunpur(13). These rates are among the highest

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WHAT THIS STUDY ADDS?

- The population studied showed an Annual rate of tuberculosis infection of >3%, which is higher than that in other regions of UP and other States in India.

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reported anywhere in India, showing relatively high intensity of transmission of MTb.

Our study results show even higher ARTI in Bijnor – 4.11% below 5 yr and 3.5% between 5 and 17 yr. There were 4 age intervals when the rise in infection frequency were relatively steep, namely during infancy (0 to 6%), during 2 to 3 yr (6.8 to 12.8%), during 4 to 5 yr (12.8 to 20.5%) and during 9/10 to 11/12 yr (27.8 to 47.6%). Whether this pattern is artifactual or real can only be settled by a larger survey of PPD response in children selected from the community.

The aim of Revised National Tuberculosis Control Program is to bring down the infection rate to <1% by 14 years of age, for an annual infection frequency of 0.07%(3,4,7,8). Against that goal, the frequency of 3.5-4.11% is 50 times higher. By 14 years the infection frequency had gone up to 50%, also clearly over 50 times higher than the goal of TB control(3,4,7,8).

Our findings should be taken as an alert to the National TB control programme and program officers should conduct systematic community based tuberculin surveys to independently measure the prevalence and incidence of MTb infection in Bijnor as well as in other populations in western UP.

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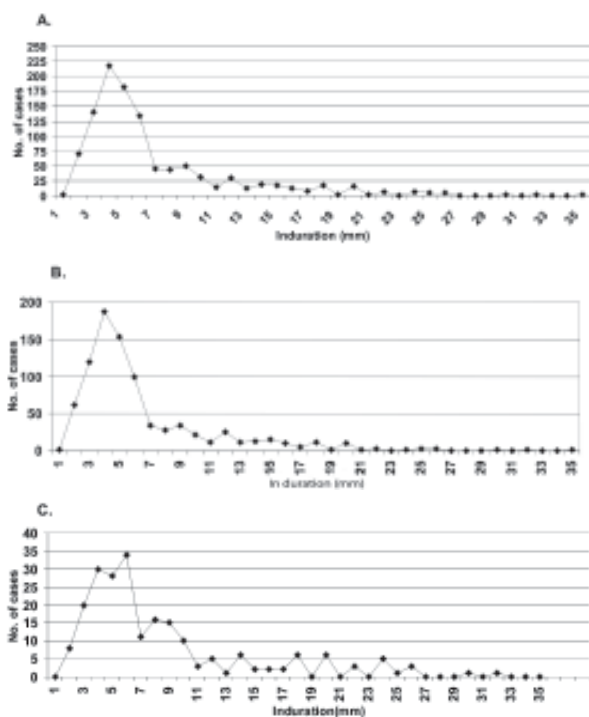8. Khatri GR. National Tuberculosis Control Program. J Indian Med Assoc 1996; 94: 370-375.

Fig. 1 *Frequency distribution of tuberculin reaction sizes among study children. **Panel A.** All children (0-17 yrs); **Panel B**. Children 0-4 yrs; **Panel C**. Children 5-17 yrs.*

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