

## ESTIMATION OF ANNUAL RISK OF TUBERCULOSIS INFECTION AMONG CHILDREN IRRESPECTIVE OF BCG SCAR IN THE SOUTH ZONE OF INDIA

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### Summary

**Objective:** To estimate the proportion infected and compute Annual Risk of Tuberculosis Infection (ARTI) among children irrespective of BCG scar and compare with that among children without BCG scar.

**Methodology:** Tuberculin survey was conducted in south zone of India as a part of the nation-wide survey to estimate the ARTI in different parts of the country and ARTI was computed among children without BCG scar excluding children with BCG scar. In this exercise, the tuberculin test results of children with BCG scar and irrespective of BCG scar were considered for analysis and the results were compared.

**Results:** The prevalence of infection and ARTI estimated among children irrespective of BCG scar aged 1-9 years were 5.7% and 1.0% (95% C.I: 0.8-1.3) respectively. The corresponding figures among unvaccinated children were 5.9% and 1.0% (95% C.I: 0.7-1.4) respectively. The ARTI among children irrespective of BCG scar were similar to that among unvaccinated children.

**Conclusion:** Estimation of proportion of children infected and computation of ARTI using mirror-image technique could be undertaken among children irrespective of BCG scar among children aged either from 1-9 years or 5-9 years. [*Indian J Tuberc* 2006; 53:7-11]

**Key words:** Prevalence of infection, ARTI

## INTRODUCTION

ARTI is an epidemiological index used to evaluate and monitor the tuberculosis situation in a community or country. It is derived from tuberculin surveys that measure the prevalence of tuberculosis infection. Conventionally, the estimation of this index is restricted to children without a Bacillus Calmette Guerin (BCG) scar. Usually, children with BCG scar are excluded from the analysis of prevalence of infection and subsequent estimation of ARTI. This is because BCG induces a tuberculin sensitivity causing cross-reaction with tuberculosis infection and complicates the interpretation of test results to identify natural infection with *Mycobacterium tuberculosis*<sup>1</sup>. The tuberculin surveys have got many other limitations like standardization and administration of tuberculin vials, reading of the test results and cross-reaction with environmental mycobacteria. Still, the tuberculin skin test is the only routinely available and comparatively cheap

method of detecting individuals infected with *Mycobacterium tuberculosis*. With an increase in the BCG vaccination under the Universal Immunization Programme (UIP), it is difficult to obtain sufficient children without BCG scar for conducting a tuberculin survey. The interpretation of the results becomes difficult when the BCG vaccination coverage is very high. Moreover, the children without BCG scar may not be representative sample because these children may be different from BCG vaccinated children with respect to accessibility, awareness of health care and socio-economic status. It also includes a proportion of children vaccinated at birth that do not leave behind a scar and in another proportion the BCG scar wanes in due course<sup>2</sup>. The ARTI estimated from test results among these children becomes difficult for interpretation. This report summarizes the results of estimating the ARTI from tuberculin test results among children irrespective of BCG vaccination included in the south zone of India as a part of the nationwide survey<sup>3</sup>

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conducted during 2000-2003 by National Tuberculosis Institute (NTI), Bangalore and Tuberculosis Research Centre (TRC), Chennai.

### MATERIAL AND METHODS

The whole country was divided into four zones namely; north, west, east and south. A random sample of children aged 1-9 years was selected from each of these zones and the survey was conducted meticulously and rigorously following the guidelines<sup>2</sup>. The tuberculin survey among children aged 1-9 years old was carried out in the south zone by TRC during 2000-02<sup>4</sup>. A total of about 53,000 children irrespective of BCG scar status were included in the survey. The estimation of sample size, study area, sampling procedure, data collection, analysis and interpretation of the data on test results among children without BCG scar and interpretation of the results are described in detail elsewhere<sup>4</sup>. The test results of children with BCG scar and those irrespective of BCG scar were considered for analysis in the present report. The prevalence of infection was calculated by weighted analysis using the mirror image method<sup>2</sup> after locating the mode in the right side of the frequency distribution of tuberculin test results of vaccinated children. ARTI was derived from the estimate of prevalence of infection and 95% confidence intervals were calculated for different estimates of ARTI.

### RESULTS

A total of 52,951 children aged 1-9 years were registered for the survey. Among these, 32,744 (64%) had BCG scar. The mode was located at 19 mm as seen from the distribution of reaction sizes of these children (Fig. a). Same was the mode located in the distribution of reaction sizes among children without BCG scar and irrespective of BCG scar (Figs. b & c). The prevalence of infection and ARTI estimated in BCG vaccinated children aged 1-9 years were 5.4% and 1.0% (95% C.I: 0.8-1.2) respectively (Table). The corresponding figures among unvaccinated children were 5.9% and 1.0% (95% C.I: 0.7-1.4) respectively as already reported<sup>4</sup>. The prevalence among children aged 1-9 years irrespective of BCG scar was 5.7% with an ARTI of 1.0% (95% C.I: 0.8-1.3). The proportion infected was 2.9% corresponding to an ARTI of 0.9% for 1-4 year age group and 7.7% for 5-9 year age group corresponding to an ARTI of 1.0% (95% C.I: 0.8-1.3). It could be seen that the ARTI computed among children irrespective of BCG scar was similar to that among children without BCG scar.

The proportion infected among vaccinated children was 4.7% for rural and 6.8% for urban strata and the corresponding estimates of ARTI were 0.9% and 1.3% respectively. For male and female children, the prevalence of infection was similar

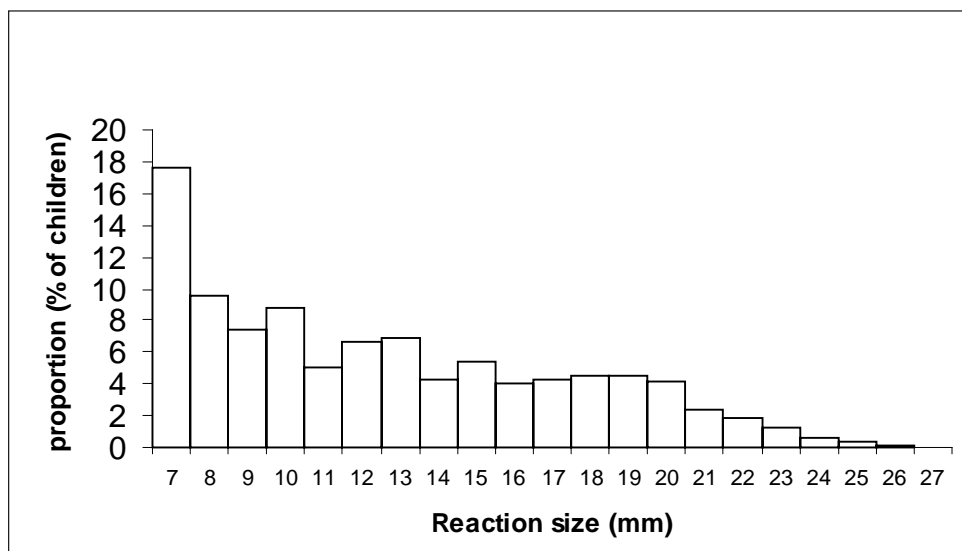


Fig (a) : Distribution of reaction sizes among children with BCG scar

namely; 5.1 % and 5.7% (ARTI: 1.0% and 1.1%) respectively.

**DISCUSSION**

The present study explored the possibility of estimating the ARTI among children irrespective of vaccination status and compared the findings with that among the unvaccinated children. The analysis showed that the tuberculosis infection was similar in all the groups, namely, unvaccinated, vaccinated and irrespective of vaccination status. In fact, tuberculosis infection among children refers to natural infection

with *M. tuberculosis* and hence is usually studied in unvaccinated children. When vaccinated children were also included, there could be a possibility of the skin test results contaminated by BCG induced tuberculin sensitivity. The possible contamination due to BCG vaccination in skin test results could be removed by applying mirror image method in estimating prevalence of infection and ARTI among children including those vaccinated. The analysis of the data showed that the proportion of children infected was 5.4% (ARTI of 1.0%) compared to 5.9% (ARTI of 1.0%) among the unvaccinated children aged 1-9 years using the mode at 19 mm on the right hand side of the frequency

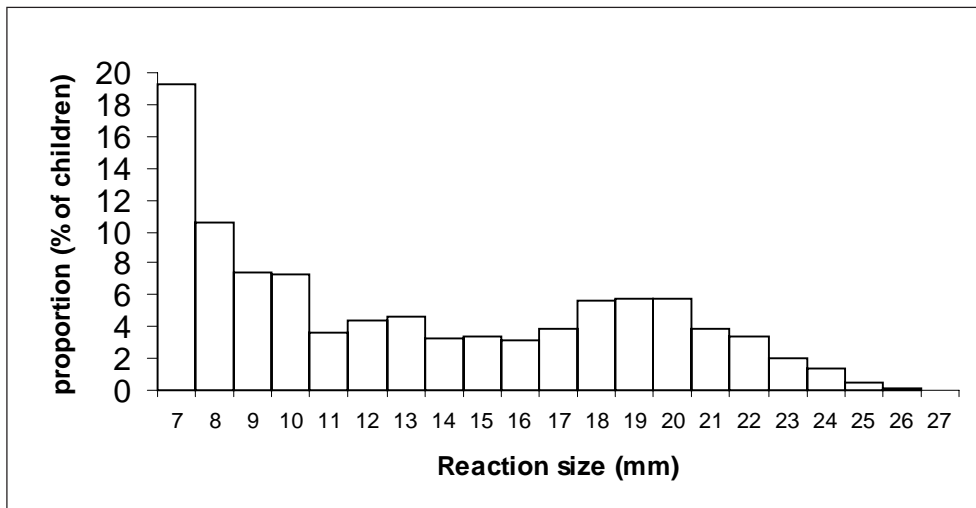


Fig (b) : Distribution of reaction sizes among children without BCG scar

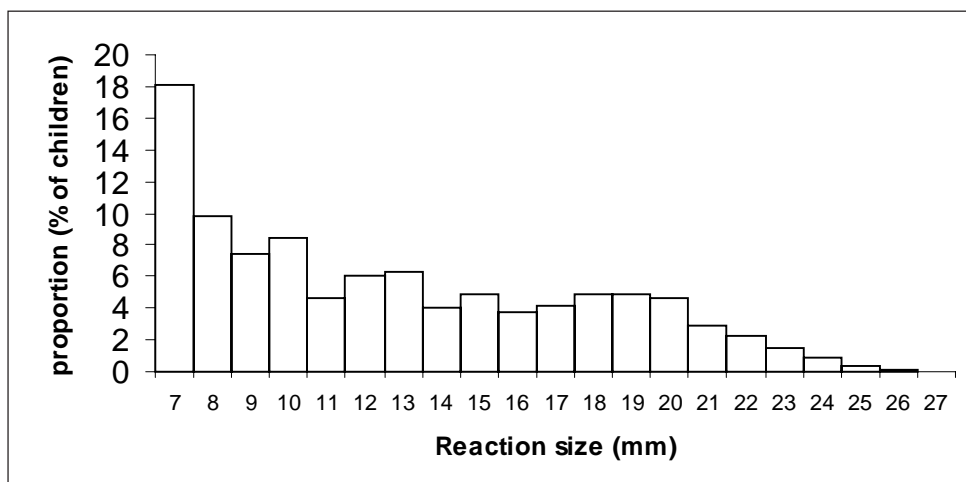


Fig (c) : Distribution of reaction sizes among children irrespective of BCG scar

**Table:** Prevalence of infection and ARTI among children without, with and irrespective of BCG scar

Age (in years)	Children without BCG scar		Children with BCG scar		Children irrespective of BCG Scar	
	P *(%)	ARTI (%)	P (%)	ARTI (%)	P (%)	ARTI (%)
1-4	2.3	0.7(0.5-1.0)	3.0	1.0(0.8-1.2)	2.9	0.9(0.8-1.1)
5-9	7.9	1.1(0.7-1.5)	7.3	1.0(0.7-1.2)	7.7	1.1(0.8-1.3)
1-9	5.9	1.0(0.7-1.4)	5.4	1.0(0.8-1.2)	5.7	1.0(0.8-1.3)

\*Prevalence of infection.

Figures in parenthesis indicate 95% Confidence Interval.

distribution of reaction sizes. This distribution was not unimodal; might be due to the BCG induced sensitivity showing a decline with time<sup>5</sup>. Moreover, the proportion infected was not influenced by the extent of BCG coverage<sup>6</sup>. Also, natural infection takes place irrespective of whether the child was vaccinated with BCG or not. The data showed that the estimation of infection in BCG vaccinated children is independent of the BCG induced tuberculin sensitivity. A study<sup>7</sup> on tuberculin sensitivity in BCG vaccinated children conducted by NTI showed that a large proportion of children with BCG scar did not develop a significantly high degree of tuberculin sensitivity and the effect of BCG induced sensitivity is insignificant if prevalence of infection is computed by mirror-image method. In another study<sup>8</sup>, NTI reported that under similar situation, the ARTI could be estimated among BCG vaccinated children. Of late, NTI has conducted another study<sup>9</sup> among school children and substantiated the earlier findings that the estimated prevalence among children with BCG scar was similar to that among children without BCG scar and suggested inclusion of BCG vaccinated children for the purpose of computing ARTI. NTI<sup>10</sup> has further analysed the data of the nationwide survey collected from the rural areas of the other three zones of the country namely; north, west and east and concluded that tuberculin surveys may be conducted irrespective of BCG scar status among children 5-9 years when BCG vaccination is given using Danish 1331 strain during infancy under UIP.

The present study included a very large sample size of about 53,000 children irrespective of BCG scar.

A large population of children is not required for estimation of ARTI if we combine children with and without BCG scar. The analysis was repeated by taking about 25% random sample of children irrespective of BCG scar status equivalent to size of the sample of unvaccinated children<sup>4</sup>. There was no difference in the prevalence of infection and ARTI compared to that among the total children studied (data not shown).

The prevalence of infection and ARTI were higher in urban children compared to that among rural children. This was similar to the findings in unvaccinated children already reported. There was no difference in the proportion infected among male and female children.

It should be borne in mind that the methodology of estimating children infected and the computation of ARTI is controversial and problematic<sup>11</sup>. When ARTI is used to measure the trend, it does not depend strongly on the proportion of children with BCG scar. Locating the mode in the distribution and calculating the ARTI using the mirror-image method substantiate this further because this eliminates the contamination in the tuberculin test results due to BCG vaccination<sup>2</sup>. In spite of the limitation of tuberculin survey, it remains an important epidemiological tool to assess the tuberculosis situation<sup>12</sup>.

**The findings of the analysis showed that in the event of non-availability of sufficient number of unvaccinated children (estimated**

sample size) especially when the BCG coverage is relatively high, the ARTI could be computed by including children irrespective of BCG scar. In conclusion, our data provides strong evidence that BCG vaccinated children may be included for tuberculin surveys and ARTI may be estimated either from children aged 1-9 years or 5-9 years. These estimates are comparable to that estimated from unvaccinated children and may be used to evaluate and monitor the tuberculosis situation in the community. The current estimate of ARTI can be used as baseline information and compared to that of any future ARTI survey(s) to measure the impact of tuberculosis control programme in the area.

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