

## ANNUAL RISK OF TUBERCULOUS INFECTION IN ANDHRA PRADESH, INDIA

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### Summary

**Background:** There is paucity of information on epidemiological situation of Tuberculosis (TB) in Andhra Pradesh. The DOTS strategy under the Revised National Tuberculosis Control Programme (RNTCP) was introduced in the year 2000 to cover the entire State by 2005.

**Objectives:** To estimate the prevalence of tuberculous infection among children 5-9 years of age and to compute the average Annual Risk of Tuberculosis Infection (ARTI) from the estimated prevalence.

**Methods:** A cluster-sample house-based tuberculin survey was carried out in a representative sample of children between 5-9 years of age. The clusters were selected by a two-stage sampling procedure. At first stage, five districts were selected by probability proportional to population size (PPS) method. Depending upon child population ratio, 32 clusters allocated to each district were further sub-divided into rural and urban clusters selected by simple random sampling. A total of 3636 children, irrespective of their BCG scar status, were tuberculin tested using one TU PPD RT23 with Tween 80 and the maximum transverse diameter of induration was measured about 72 hours later.

**Results:** The prevalence of infection estimated by mirror-image technique using observed mode of reactions attributable to infection with tubercle bacilli at 20mm was 9.6% (95% CI: 8.0-11.2). The ARTI was computed at 1.4% (95% CI: 1.1-1.6).

**Conclusion:** Survey findings indicate a fairly high rate of transmission of tubercle bacilli.

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**Key Words:** Tuberculosis, Infection, Prevalence, Annual Risk, Tuberculin test, India.

## INTRODUCTION

Andhra Pradesh, situated in the southern region of India, is the third largest State in the country in terms of area and has a long coastal line bordering the Bay of Bengal<sup>1</sup>. In the last national census in 2001, it had 22 districts with a population of 75.73 million and population density of 275/sq.km<sup>1</sup>. The sex ratio in the state was 978 females for every 1000 males<sup>1</sup>. About 70% of the population is engaged in agrarian occupation, with annual per capita income of 17,642 Indian Rupees (about 400 US \$) in the year 2001-02 and the literacy rates of 71% among males and 51% among females<sup>2</sup>.

Tuberculosis (TB) is a major public health problem in the State as in all other parts of India. After pilot testing, the expansion of DOTS strategy under Revised National Tuberculosis Control Programme (RNTCP) was initiated in the State from

year 2000 and complete DOTS coverage was achieved by 2005. The case detection and treatment outcomes have improved over the years to achieve 74% case detection rate in the year 2006 against the estimated incidence of new sputum smear positive cases and treatment success of 87% for the cohort of patients registered during 2005<sup>3</sup>.

Hitherto, little information has been available on the epidemiological situation of TB in the State. During 2001-2002, a tuberculin survey was carried out among children 5-9 years of age in Khammam, a tribal district and the ARTI was estimated at 1.5%<sup>4</sup>. Another district (Medak) had earlier been included in the zonal level survey (south zone, 2000-01)<sup>5</sup>. However, its scope and objectives were not designed to meet the requirements of the State. It was, therefore, felt necessary, to obtain reliable information on epidemiological situation of TB in the State as a whole, which could also be considered as the baseline

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information to elicit changes at desired intervals. Carefully designed tuberculin surveys yield the desired information on epidemiological situation of TB in terms of prevalence of infection which is further converted into Annual Risk of Tuberculous Infection (ARTI), defined as the proportion of the population under study which is primarily infected or re-infected in the course of one year<sup>6</sup>. ARTI is the culmination of various factors responsible for the transmission of tubercle bacilli viz., load of infectious cases in the community and efficiency of TB control programmes in terms of case finding and treatment activities. These surveys are generally carried out among children since the results obtained among them reflect on the recent disease situation in the community. Thus, a cross-sectional tuberculin survey was carried out in the State during September 2005 to March 2006 in a representative sample of children between 5-9 years of age with the objective to estimate the prevalence of infection and compute the average ARTI.

## MATERIAL and METHODS

### Study population and sampling

Most of the tuberculin surveys in India in the past were carried out among BCG unvaccinated children. However, exclusion of BCG immunized children not only makes tuberculin surveys operationally difficult but also raises concerns about the study sample being representative. A recent meta-analysis revealed that tuberculin reactivity after BCG vaccination in infancy wanes rapidly in most individuals. During the zonal level tuberculin surveys in 2000-03, prevalence of infection estimated by mirror-image technique was found to be similar among children with and without BCG scar in 5-9 year age group<sup>8</sup>. Therefore, the present survey was carried out among children between 5-9 years of age irrespective of their BCG status, residing in a selected sample of rural and urban clusters in the State.

The sample size was estimated at 3200 to obtain the estimate of prevalence of tuberculous infection within 15% of the true value at 5% level

of significance, considering the expected prevalence of infection at 10% based on the earlier survey in Khammam district<sup>4</sup>. Design effect of two was considered to account for the sampling design based on the experience in zonal level tuberculin surveys during 2000-2003 (unpublished data). The size of a cluster was to be 20 satisfactorily test-read children and thus the number of clusters was 160. It was planned to register 24 children in each cluster to account for exclusions due to refusals, subcutaneous tuberculin injection or leakage of tuberculin during injection and to take care of reading absentees.

A two-stage sampling procedure was adopted for selection of clusters – first for selection of districts and second for rural and urban clusters (denoted by a village in rural area and census enumeration block in urban area). While selecting districts, five districts were excluded from the sampling frame - Warangal, Adilabad, Karimnagar deemed unsafe due to security reasons; and Khammam and Medak

**Table:** Study population

No. Satisfactory test-read	3636
<b>By district</b>	
Hyderabad	673 (18.5%)
Kurnool	741 (20.4%)
Prakasham	749 (20.6%)
Visakhapatnam	721 (19.8%)
Chittoor	752 (20.7%)
<b>By Place of residence</b>	
Rural	2197 (60.3%)
Urban	1439 (39.6%)
<b>By age</b>	
5 yrs	765 (21%)
6 yrs	800 (22%)
7 yrs	732 (20.1%)
8 yrs	663 (18.3%)
9 yrs	676 (18.6%)
<b>By gender</b>	
Female	1862 (51.2%)
Male	1774 (48.8%)
<b>By BCG scar status</b>	
With scar	2098 (57.7%)
Without scar	1521 (41.8%)
Doubtful scar	17 (0.5%)

where recently conducted tuberculin surveys might interfere with the interpretation of present survey results. From the remaining 17 districts, five were selected on population proportion to size (PPS) method. The districts thus selected were Hyderabad, Kurnool, Prakasham, Visakhapatnam and Chittoor (Fig.1).

One hundred and sixty clusters were equally divided between five selected districts. Therefore, 32 clusters in each district were further allocated to rural and urban areas depending upon their ratio of child population. Within the rural and urban areas, clusters were selected by simple random sampling.

### Field Procedures

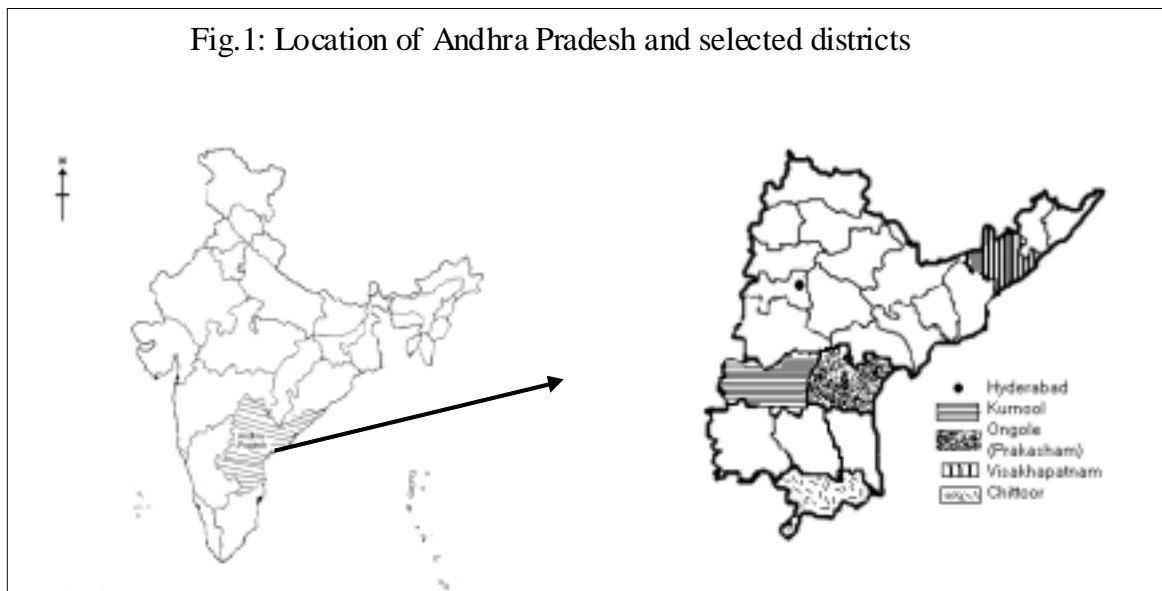
The fieldwork was carried out jointly by officials of National Tuberculosis Institute, Bangalore, (NTI) and State TB Demonstration and Training Centre, Hyderabad (STDC) with support of district health authorities. The officials selected for performing the field work were imparted a five week intensive training on all tasks involved in the survey. All were evaluated towards the completion of three-phase training course and a preferential list was prepared to allocate the specific tasks to best performers.

Fieldwork began in September 2005 and

concluded in March 2006 after methodically covering the selected clusters. Highest standards were maintained in carrying out all tasks as per the protocol without deviation. Support and assistance for fieldwork of the district selected for survey work was requisitioned through the Chief District Medical Officer. The services of the multi-purpose health workers were made available to the teams on appointed days of field work in the selected clusters. Three visits were made to each cluster for purposes of i) planning, ii) testing and iii) reading.

On the day of planning visit, community leaders and health workers of the cluster were apprised of the purpose of the survey and requisitioned for assistance and support. A rough map of the cluster was drawn and the lane to start registration work was selected using a random number table.

On the testing visit, registration of the eligible children began from the first household of the selected lane and proceeded to contiguous houses following a particular direction till 24 children (between 5-9 completed years on the date of visit) were registered. All available children in the last household were registered. Each household was numbered and individual child card was prepared for each child. The child was sent with the card along with the parents or guardian to the temporarily



set-up tuberculin testing centre. A designated tuberculin tester identified the child, verified the age, and inspected both shoulders for presence of BCG scar. After taking consent from the parent/guardian, he administered the tuberculin skin test with 1TU PPD RT 23 with Tween 80 on the mid-volar aspect of the left forearm slowly to achieve an accurate intradermal test (tuberculin dilutions were prepared by BCG laboratory, Chennai, in April 2005 from the original seed lot of PPD-Statens Serum Institute, Copenhagen). The testing status was recorded as unsatisfactory if the dose, depth, or testing procedure was not accurate. A designated tuberculin reader made the reading visit at about 72 hours (3rd day) after administration of tuberculin test. He measured the largest transverse diameter of induration appearing at the test site with a millimeter transparent scale and also recorded the unpleasant reactions if any - vesicle, bulla or necrosis. If a child showed a reaction size of  $\geq 15$  mm (chosen arbitrarily), he queried with parent or guardian on the current health status, especially about chest symptoms and contact history with a known case of TB.

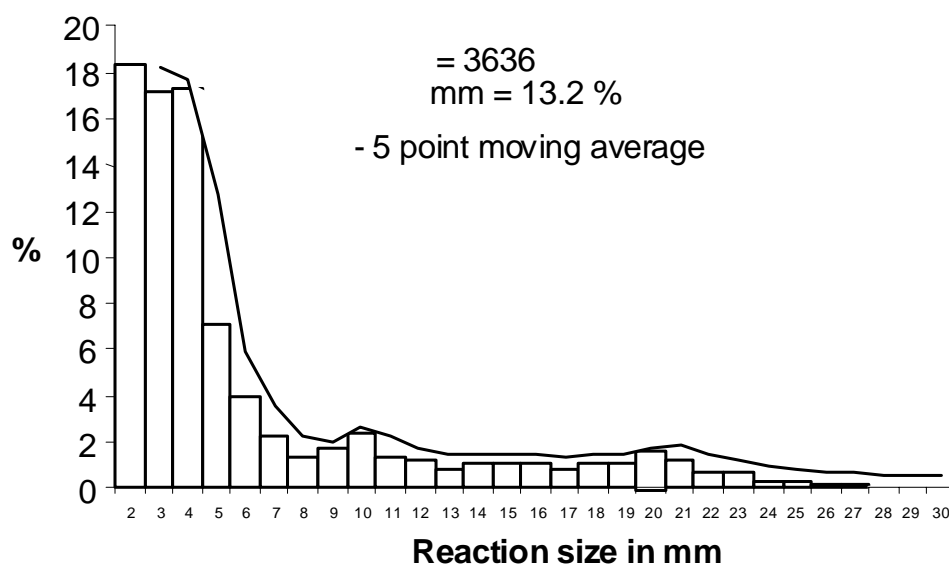
Children showing signs of ill-health, chest symptoms or history of contact with known case of TB were referred to the nearest health facility for further medical assistance.

Data recording during fieldwork was undertaken in prescribed formats. The data was double entered using EPI-INFO and validated. SPSS (Statistical Package for Social Sciences) 10.0 for windows was used for analysis.

### Statistical Methods

Tuberculin reaction sizes were plotted in the form of a histogram to identify the mode of reactions attributable to 'infection with tubercle bacilli'. Weighted prevalence of infection was estimated using mirror-image technique (weight was assigned to each district as the ratio of the numbers originally allocated to the numbers investigated). In this technique, the proportions of the reactions larger than the second mode observed on the frequency distribution curve is doubled and added to the frequency at the second

**Fig.2: Frequency distribution of reaction sizes (age 5-9 yrs), Andhra Pradesh, 2005-06**



mode<sup>10</sup>. The rationale of this approach is that tuberculin reactions due to infection with tubercle bacilli are distributed normally around the mode. On the other hand, the cut-off point (anti-mode) method for estimating prevalence of infection has been found to be less specific when BCG vaccinated children are included in the study sample<sup>8,9</sup>.

The 95% Confidence Interval (CI) of the estimate was obtained using the appropriate formula<sup>11</sup>.

ARTI was computed from the estimated prevalence of infection using the following equation<sup>11</sup>:

$$R_{b+a/2} = 1 - (1 - P_{b+a})^{1/a}$$

(b indicates calendar time of birth of study cohort, a the mean age of the cohort,  $P_{b+a}$  denotes prevalence of infection during the mid-point of survey period

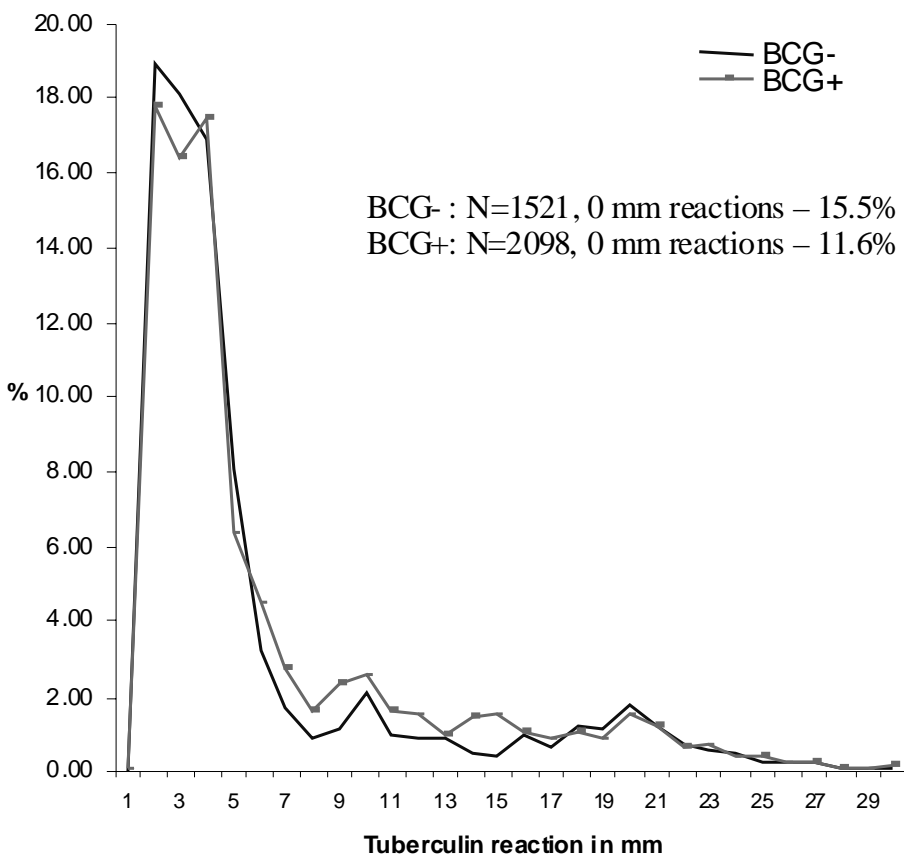
and  $R_{b+a/2}$  denotes ARTI at mid-point between the birth of the cohort and mid-point of the survey).

**RESULTS**

Of 4090 children registered, 4062 were subjected to tuberculin testing (satisfactory-3933, unsatisfactory-129). Of satisfactorily tested, 3636 (92.4%) were read. In all, 89% of the registered children were satisfactorily test read and were utilized for analysis. Distribution of study population by district, place of residence – Rural/urban, age in years, sex and BCG scar status is given in the table.

The frequency distribution of reaction sizes for the overall study group is plotted at figure 2. Though a clear bi-modal distribution could not

**Fig. 3: Frequency distribution of tuberculin reaction size by BCG scar status**



be appreciated on the histogram, the mode of reactions attributable to tuberculous infection could be considered at 20 mm. Therefore, the prevalence of infection was estimated by mirror-image technique using the mode at 20 mm. It was estimated at 9.7% (95% CI: 8.1-11.3). The ARTI was computed from the estimated prevalence at 1.4% (95% CI: 1.1-1.6).

To study the influence of digit preference if any, 5-point (including 2 points before and 2 points after the digit of reference) moving averages for each mm of reaction range were calculated. The prevalence of infection was estimated at 9.6% (CI: 8.0 - 11.2) using such averaged values while considering the mode at 20 mm.

Fig.3 presents the distribution of tuberculin reaction sizes by BCG scar status. A higher proportion of reactions are observed between 6-17 mm among children with BCG scar compared to those without scar. The estimated proportion of reactions attributable to tuberculous infection using the mirror-image technique as above was 10.0% (CI: 7.9 - 12.1) among children without BCG scar and 9.3% (CI: 7.4 - 11.2) among children with BCG scar. Since an anti-mode could be clearly made out at 15 mm among children without BCG scar, prevalence of infection was also estimated among these children considering all reactions =15mm as attributable to tuberculous infection and was computed as 9.7% (CI: 8.1 - 11.3).

Thirty-six children (1%) showed some form of unpleasant reactions: vesicle- 30 and bullae- 6.

## DISCUSSION

The present survey was the first ever scientifically planned and methodically conducted state level survey in Andhra Pradesh to obtain necessary information on the prevailing tuberculosis scenario in terms of ARTI.

Though a clear bi-modal distribution could not be appreciated on the histogram of tuberculin

reaction sizes, the mode of reactions attributable to tuberculous infection could be considered at 20 mm. Similar modes have been observed in smear +ve cases in a series of studies conducted in recent years in the country<sup>12-14</sup>.

**The present survey findings provide a baseline estimate of ARTI against which the impact of TB control measures can be assessed in future by repeat survey after an interval of 5-7 years. The ARTI of 1.4%, computed for the area included in the present survey, indicates a fairly high rate of transmission of tubercle bacilli. Considering the mean age of the children tested, the estimated ARTI of 1.4% would most closely correspond to the year 2002. Therefore, the computed ARTI would most closely pertain to the year 2002. During an earlier district level survey in Khammam in 2001-02, the ARTI estimated from the prevalence of infection in the same age group was 1.5%. In the zonal level tuberculin survey (2000-01), ARTI in south zone as a whole when computed from prevalence of infection in 5-9 year age group was 1.1%<sup>9</sup>.**

**In the present survey, the proportions infected were similar among children with and without BCG scar. Similarly, among children without BCG scar, the proportion of infected as estimated by mirror-image technique was similar to the proportion when estimated by anti-mode method, thereby justifying the inclusion of children with BCG scar as well as the analytical method.**

**To conclude, a fairly high level of transmission of tuberculous infection observed in the present survey suggests further intensification of tuberculosis control efforts.**

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