Comparison between childhood and adult tuberculosis in a rural tuberculosis unit of West Bengal: A retrospective study

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ABSTRACT

Background and Objectives: Tuberculosis (TB) is an important cause of childhood morbidity and mortality with different clinical presentations and outcomes as compared to TB in adults. The present study was designed to compare these differences and to determine if childhood TB was an important predictor of adverse outcome following treatment under the Revised National Tuberculosis Control Program (RNTCP). Materials and Methods: Retrospective record based study of cases registered between January 2008 and December 2011, at the Amdanga TB Unit (TU), West Bengal. Results: Of the total 1,508 cases notified, 3.4% were childhood TB. Differences with adult TB were noted in the number of cases categorized as cat II and III in children (P = 0.012 and 0.000, respectively). New smear positive pulmonary TB was significantly lower (21.6%, P = 0.000), while new extra-pulmonary TB (39.2%, P = 0.000) was significantly higher in children. Smear negative cases comprised 7.8 and 11.4% of the childhood and adult cases of TB, respectively. Retreatment cases were significantly higher in adults (P = 0.012). Among the registered new smear positive cases, the differences in favourable and adverse outcomes did not have a significant statistical difference (P = 0.000). Childhood TB was not a significant risk factor for adverse outcome following treatment (adjusted odds ratio [AOR] = 0.80, 95% confidence interval [CI] = 0.28–2.32). Conclusions: The registration of childhood TB under the RNTCP in the TU was low. There were differences in the clinical presentation and treatment outcomes of TB among children and adults. Childhood TB was not a significant predictor of adverse treatment following treatment.

KEY WORDS: Childhood, RNTCP, tuberculosis

INTRODUCTION

Tuberculosis (TB) is an important cause of childhood morbidity and mortality.1 The younger the child, the more are the chances of complications and death from the disease. Prevalence of childhood TB has been reported to be between 3 and 25% in different countries.2,3 It remains underreported in developing countries like India due to diagnostic difficulties and poor reporting and recording systems.4 Estimates of childhood TB in these countries put the figures at 1.3 million new cases and 450,000 deaths per year.5 Most cases in children are sputum smear negative and considered to be relatively minor contributors to the transmission of the disease.6 Consequently lower public health priority is given to childhood TB as it rarely presents with smear positive disease.7

In the absence of clear cut guidelines, the diagnosis of childhood TB during the initial years of the RNTCP in India was difficult. Management was physician specific and unstandardized. Pediatric medicines were either proprietary or doses had to be reconstituted from adult medicines supplied under the program. Since the formulation of specific guidelines for diagnosis (in collaboration with the Indian Academy of Pediatrics, IAP) and the introduction...
of weight based pediatric patient wise boxes in 2004, the management of childhood TB has been streamlined. However, even after 8 years since the introduction of these guidelines, studies on childhood TB cases under the RNTCP in West Bengal are rare. The present study was undertaken to compare the differences in clinical presentation, treatment outcome of new smear positive cases between childhood and adult TB and to determine if childhood TB was an important predictor of adverse outcome following antitubercular drug treatment under the RNTCP.

**MATERIALS AND METHODS**

**Setting**

Amdanga TB Unit (TU), North 24 Parganas in West Bengal is a predominantly rural TU serving a population of approximately 0.47 million (2001 census). Most of the population work in the agricultural sector and belong to the lower socioeconomic strata. The TU is located 12 km from the district headquarters at Barasat and 29 km from Kolkata, the capital of West Bengal.

**Study design, study variables, and definitions used**

The present study was a retrospective record based study. Data on age, sex, diseases type, disease classification, category of treatment, human immunodeficiency virus (HIV) status, as recorded on the TB register of the TU between January 2008 and December 2011, were collected for analysis.

The diagnosis of pulmonary TB in children and adults was done according to the RNTCP guidelines. Categorisation and treatment were in accordance with the RNTCP guidelines and under direct observation of the field level workers of the government healthcare system. Monitoring and supervision of treatment and follow-up were done as per the protocol laid down by the RNTCP.

In the present study, a child was defined as being 14 years or less in age as specified by the RNTCP definition. Cure, treatment completed, default, death, failure, and transferred out were also been defined in accordance to the RNTCP definitions. In addition the following definitions were used for the present study.

**Favourable outcome**

Cured and treatment completed taken together.

**Adverse outcome**

Default, death, failure, transferred out, chronic and shifted to category IV were together considered as adverse outcomes.

The ethical clearance for the present study was obtained from the Institutional Ethical Committee of the R.G. Kar Medical College and Hospitals, Kolkata.

**Statistical analysis**

Collected data were tabulated on the MS Excel Worksheet (Microsoft, Redwoods, WA, USA). Data analyses were done using MS Excel, and Statcalc 2000. Categorical data were expressed in proportions, while continuous data were expressed in mean values. Dispersion of data was expressed in terms of standard deviation (SD). In contingency tables, significance of association between categorical data was analyzed using Pearson’s chi-square (χ²) test. Fisher’s exact chi-square test was used in appropriate situations. Difference between two mean values was tested by unpaired Student’s t-test.

SPSS software version 16.0 IBM (Statistical Package for the Social Sciences Inc, Chicago, IL, USA) was used for bivariate regression and multivariate logistic regression using the Enter method to determine the predictors of adverse outcome of treatment. Result was expressed in terms of odds ratio (OR) and adjusted odds ratio (AOR). A P-value less than 0.05 was considered statistically significant.

**RESULTS**

Over the study period of 4 years 1,508 cases of TB patients were registered under the RNTCP at the Amdanga TU.

**Differences in childhood and adult tuberculosis**

The proportion of childhood TB cases among all cases of TB recorded in the TB register during the study period was 3.4% (51/1,508). Males constituted 62.7% of the childhood cases and 73.9% of the total adult TB cases. There was no statistically significant difference in the sex distribution of childhood and adults TB cases. More adults were categorized under cat II (18.9%) than children (3.9%) and the difference was statistically significant (P = 0.012). Statistically significant difference (P = 0.000) was noted in the number of cases categorized as cat III in children (31.4%) than in adults (11.0%). Statistically significant differences (P = 0.000) were seen in the proportion of smear positive TB cases in children (21.6%) and adults (55.5%). However, the proportion of smear negative cases among the two groups was not different (P = 0.574). The number of cases where sputum examination was not done was higher in children (14, 27.5%) than adults (2, 0.10%) and the difference was statistically significant (P = 0.000). Among new extra-pulmonary TB, proportions of tubercular lymphadenitis (children = 21.0%, adults = 4.4%) and skeletal TB (children = 7.8%, adults = 1.2%) were higher in children with significant statistical differences (P = 0.000 and 0.001, respectively) [Table 1].

**Treatment outcome**

Treatment outcomes were analyzed for the 741 patients registered as new smear positive pulmonary TB (adults = 730, childhood = 11) in the TB register. Overall favourable outcomes (cured and treatment...
completed taken together were 81.8% in children and 86.4% in adults and the difference was not statistically significant \((P = 0.1000)\). Outcomes of died, default, and failure analyzed separately did not show any significant statistical difference. However, there was a statistically significant difference in the rates of transferred out among the two groups [Table 2].

**Predicting adverse outcome on treatment**

Univariate analysis of the predictors for adverse outcome following treatment (considering all cases together) revealed that childhood TB was not a risk factor for adverse outcome \((OR = 0.48, 95\% CI = 0.17–1.35)\). Childhood disease was not found to be significantly associated with an adverse outcome even after adjusting for other factors \((AOR = 0.80, 95\% CI = 0.28-2.32)\) [Table 3].

**DISCUSSION**

The proportion of childhood cases in the present study was 3.4% of the total registered cases of TB; while the national average was 7% for 2011.\(^8\) It was lower than that found in other studies from India\(^9\) and other countries in the region.\(^10\) In the absence of an actual decrease in the number of adult cases from the area over the following years, the total number of childhood TB cases registered under the RNTCP is a reflection of the program related low notification of cases.

TB in children is difficult to diagnose, especially at the primary levels of government healthcare, due to lack of specialized pediatric departments and the nonavailability of chest radiography, aspiration cytology, and culture facilities for the diagnosis. Children attending these centers tend to remain underdiagnosed. The guidelines for diagnosis of childhood TB established by the RNTCP in conjunction with the IAP are more useful for the diagnosis of TB in children capable of providing sputum for microscopy. But younger children can rarely expectorate sputum, making diagnosis difficult.\(^11\) In addition, many children are diagnosed and treated outside the government healthcare settings and are not registered under the RNTCP.

| Characteristics | Total (n=1508) | Pediatric patients (n=51) | Adult patients (n=1457) | \(P\)-value |
|-----------------|---------------|--------------------------|------------------------|------------|
| Age (Mean±SD)   | 38.1±17.8     | 8.5±4.1                  | 39.2±17.2              | —          |
| Category \#      |               |                          |                        |            |
| I               | 1054 (69.9)   | 33 (64.7)                | 1021 (70.1)            | 0.505      |
| II              | 277 (18.4)    | 2 (3.9)                  | 275 (18.9)             | 0.012*     |
| III             | 176 (11.7)    | 16 (31.4)                | 160 (11.0)             | 0.000*     |
| Disease type and classification |               |                          |                        |            |
| Retreatment     | 277 (18.4)    | 2 (3.9)                  | 275 (18.9)             | 0.012*     |
| Smear not done  | 16 (1.1)      | 14 (27.5)                | 2 (0.1)                | 0.000*     |
| New smear positive | 820 (54.4)  | 11 (21.6)                | 809 (55.5)             | 0.000*     |
| New smear negative | 170 (11.3) | 4 (7.8)                  | 166 (11.4)             | 0.574      |
| New extrapulmonary | 225 (14.9) | 20 (39.2)                | 205 (14.1)             | 0.000*     |
| TB lymphadenitis | 75 (5.0)      | 11 (21.6)                | 64 (4.4)               | 0.000*     |
| TB skeletal | 21 (1.4)      | 4 (7.8)                  | 17 (1.2)               | 0.001      |
| TB abdominal     | 15 (1.0)      | 0 (0.0)                  | 15 (1.0)               | 0.992      |
| TB meningitis    | 6 (0.4)       | 1 (2.0)                  | 5 (0.3)                | 0.501      |
| TB pleural       | 92 (6.1)      | 4 (7.8)                  | 88 (6.0)               | 0.817      |
| Other forms of TB | 5 (0.3)   | 0 (0.0)                  | 5 (0.3)                | 0.412      |
| NA              | 11 (0.7)      | 0 (0.0)                  | 11 (0.8)               | 0.803      |
| HIV status       |               |                          |                        |            |
| Positive        | 9 (0.6)       | 0 (0.0)                  | 9 (0.6)                | 0.717      |
| Negative        | 428 (28.4)    | 6 (11.8)                 | 422 (29.0)             | 0.012*     |
| Unknown         | 1071 (71.0)   | 45 (88.2)                | 1026 (70.4)            | 0.009*     |

\#1 non-DOTS, *Statistically significant. TB: Tuberculosis, SD: Standard deviation, HIV: Human immunodeficiency virus, NA: Not applicable

**Table 2: Treatment outcome of new smear positive cases of childhood and adult TB (n=741)**

| Treatment outcome | Total No. (%) | Children No. (%) | Adults No. (%) | \(P\)-value |
|-------------------|---------------|------------------|---------------|------------|
| Favourable outcome | 640 (86.4)    | 9 (81.8)         | 631 (86.4)    | 0.100      |
| Cured             | 631 (85.2)    | 9 (81.8)         | 622 (85.2)    | 0.909      |
| Treatment completed | 9 (1.2)      | 0 (-)            | 9 (1.2)       | 0.309      |
| Adverse outcome   | 101 (13.5)    | 2 (18.2)         | 99 (13.5)     | 0.100      |
| Died              | 27 (3.6)      | 1 (9.1)          | 26 (3.6)      | 0.872      |
| Default           | 61 (8.2)      | 1 (9.1)          | 60 (8.2)      | 0.654      |
| Failure           | 12 (1.6)      | 0 (-)            | 12 (1.6)      | 0.439      |
| Transferred out   | 1 (0.1)       | 0 (-)            | 1 (0.1)       | 0.006*     |

*Statistically significant, TB: Tuberculosis; Outcomes were available up to 2nd quarter 2011, hence the number of cases included in the analysis was 1,340. Outcome of retreatment cases not compared as there were only two retreatment cases in the childhood tuberculosis group. Cases with smear not done were included under smear negative pulmonary tuberculosis
Table 3: Univariate and multivariate analysis to determine if childhood tuberculosis was an important predictor of an adverse outcome (n=1340)

| Variables       | Types               | Total | Number | Adverse outcome | OR    | 95% CI     | P-value | AOR | 95% CI     | P-value |
|-----------------|---------------------|-------|--------|-----------------|-------|------------|---------|-----|------------|---------|
|                 |                     |       |        |                 |       |            |         |     |            |         |
|                 |                     |       |        |                 |       | Reference  |         |     | Reference  |         |
| Sex             | Male                | 989   | 172    | 17.39           | 1.40  | 0.98-1.98  | 0.062   | 1.29 | 0.90-1.84  | 0.167   |
|                 | Female              | 351   | 46     | 13.11           |       | Reference  |         |     | Reference  |         |
| Age group       | Children (0-14 years)| 46    | 4      | 8.70            | 0.48  | 0.17-1.35  | 0.166   | 0.80 | 0.28-2.32  | 0.681   |
|                 | Adults >14 years    | 1294  | 214    | 16.54           |       | Reference  |         |     | Reference  |         |
| Age group       | Retreatment         | 248   | 80     | 32.26           | 7.18  | 3.78-13.65 | 0.000*  | 7.11 | 3.66-13.82 | 0.000*  |
| Disease type and classification | NSP | 741 | 101 | 13.63 | 2.380 | 1.28-4.43 | 0.006* | 2.34 | 1.24-4.41 | 0.008* |
| Disease type and classification | NSN | 158  | 25    | 15.82           | 2.835 | 1.38-5.85  | 0.005*  | 2.71 | 1.30-5.62  | 0.008*  |
| Disease type and classification | New extrapulmonary | 193 | 12 | 6.21 | Reference |       |         |         |     | Reference  |         |
| Disease type and classification | Positive | 8 | 1 | 12.50 | 0.766 | 0.09-6.36 | 0.805   | 0.98 | 0.11-8.47 | 0.988   |
| Disease type and classification | Unknown | 1014 | 167 | 16.47 | 1.057 | 0.75-1.49 | 0.753   | 1.14 | 0.80-1.62 | 0.468   |
| HIV             | Negative            | 318   | 50     | 15.72           |       | Reference  |         |     | Reference  |         |

OR: Odds ratio, AOR: Adjusted odds ratio, HIV: Human immunodeficiency virus, CI: Confidence interval, *Statistically significant, NSP: New sputum positive, NSN: New smear negative

Antitubercular drugs, based on weight bands, supplied under the RNTCP, do not have provisions for children with body weight less than 6 kg. These children are prescribed proprietary medicines even after being diagnosed by the physicians at the government health facilities, and are thus not registered under the RNTCP. This is also evident from the fact that only 1.96% of the total children registered during the 4 years under study are less than one year old with body weight less than 6 kg.

Differences in childhood and adult tuberculosis
The higher notification of males in both the groups reflects either a differential access to healthcare or biological reasons,[12] causing a reduced incidence of TB in females. Gender based differences in the notification pattern under the RNTCP have been seen in other studies. The proportion of male patients among childhood TB cases in the present study, were much higher than reported in other studies on childhood TB from India.[13]

The lack of sputum smear results in the large number of children in the present study reflects the difficulty in the collection of sputum samples in children. To overcome the difficulties involved in bacteriological confirmation of pulmonary TB in infants and young children, sputum induction techniques, that provide satisfactory and more convenient specimens for bacteriological confirmation of pulmonary TB even in HIV infected cases, are being used.[14] Some of these techniques can be used in the primary care setup for better yield of sputum in children.

Tubercular lymphadenitis was the most commonly diagnosed extra-pulmonary TB in children in the present study as well as in other studies from India.[19,15,16] The availability of well-defined diagnostic algorithms under the RNTCP for the diagnosis of TB lymphadenitis, but its absence for the diagnosis of other forms of pediatric TB may be the reason for this selectively increased number of TB lymphadenopathy cases.

In the present study, most childhood (96.1%) and adult (81.1%) TB cases were ‘new’, that is, never treated or treated for less than 1 month with anti-tubercular drugs before registration. In their study on childhood TB cases from Delhi, Satyanarayana et al., found that 93.1% of childhood TB cases were new, with the remainder being retreatment TB cases. Ninety percent of childhood TB cases from a record based study in Ahmedabad[17] were new cases. Ramos et al., reported a significantly higher number of relapses in adult TB cases compared to cases from the childhood patients from a rural hospital in Ethiopia.[18]

Treatment outcome among smear positive cases of childhood tuberculosis
Smear positive TB was associated with a high treatment success rate both in children and adults. A high treatment completion rate of 76% was also seen in retrospective studies of childhood TB from hospital records in Malawi.[19] In their study on children with TB in Delhi, Sharma et al., reported high cure rates of 92.4% in new cases among children with a mean age of 11.2 years.[20]

TB and HIV
Despite the publication of guidelines regarding screening for HIV in all patients with TB under the “intensified TB/HIV package” since 2008, these recommendations have come to be strictly followed only since the end of 2010. Before that only high risk cases or patients with other opportunistic infections were sent to the voluntary counseling and testing center (VCTC) for counseling and testing for HIV. This is the reason for the high number of cases with an unknown HIV status.

The prevalence of HIV co-infection among patients with TB in the present study is much lower than that found in studies on outpatient and inpatients TB cases at the All India Institute of Medical Sciences (AIIMS) or those reported form sub-Saharan Africa.[21] This low prevalence of HIV co-infection in patients with TB probably reflects the low level (0.31%) of HIV prevalence in the state of West Bengal.[22]

Adverse outcomes on treatment
Under the RNTCP, success rates of TB treatment have been seen to be similar among childhood and adult cases of TB[24]
The findings of the present study also reveal that childhood TB was not significantly related to treatment outcome either independently or after adjustment for other factors.

Limitations
1. Information about HIV co-infection was available for very few cases, which might have affected the likelihood of the outcome.
2. Only those variables recorded on the TB register were considered for predicting adverse treatment outcome. There may be several other important factors that may be related to the treatment outcome.
3. From 2011, there has been a modification in the classification of TB cases under the RNTCP with the abolishment of category III. No special adjustments were made in the calculations for this change.

CONCLUSIONS
The registration of childhood TB under the RNTCP was low. There were differences in the clinical presentation of TB among children and adults. Treatment outcomes were similar in both the groups, signifying the effectiveness of the RNTCP regimens in the treatment of childhood TB. Childhood TB was not a significant predictor of adverse treatment outcome either independently or after adjusting for other factors.

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