



## Childhood tuberculosis in Bhutan: profile and treatment outcomes

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**Setting:** All hospitals and health centres under the National Tuberculosis Control Programme (NTCP) in Bhutan.

**Objective:** To describe the number and proportion of childhood tuberculosis (TB) cases registered under the NTCP in 2010, their demographic and clinical characteristics and any associations with treatment outcomes.

**Design:** Retrospective cohort study involving a review of TB treatment cards and registers.

**Results:** Of 1332 TB cases registered, 187 (14%) were children aged <15 years, 75 (40%) were aged <5 years, and 180 (96%) were new cases; nearly half were extra-pulmonary TB, with lymphadenitis being the most common form. The overall treatment success rate was 93%, and none of the demographic and clinical characteristics were associated with treatment outcomes. A few recording deficiencies were identified.

**Conclusion:** TB in children is well recognised in Bhutan, and their treatment outcomes were excellent.

Tuberculosis (TB) is a major public health problem in Bhutan. The National TB Control Programme (NTCP) was established in 1986 and adopted the World Health Organization (WHO) recommended DOTS strategy in 1997. According to the Global TB Control Report 2012, the incidence is estimated at 191 per 100000 population.<sup>1</sup> The case notification rate of all forms of TB in 2011 was 174/100000, with a treatment success rate of 90%.<sup>1,2</sup> The first tuberculin survey in Bhutan in 1991 gave an infection rate of 1.5%, while a repeat survey in 2009 showed it to be 0.4–0.5%.<sup>3</sup>

Childhood TB (for children aged <15 years) is generally considered to be a good marker of transmission in the community. Globally, TB has been reported to be one of the major causes of death among children.<sup>1,4</sup> Traditionally, childhood TB has received limited priority due to the paucibacillary nature of the disease in children, limited infectiousness to others and perceived small numbers. Accurate numbers of childhood TB are difficult to obtain, mainly due to diagnostic difficulties and non-inclusion of children in most surveys. In 2011, of the estimated 8.7 million new TB cases in the world, approximately 0.5 million occurred in children aged <15 years.<sup>1</sup> The proportion of childhood TB ranges from 13.7% to 40% of total cases notified in high-burden countries, and is as low as 5% in low-burden countries.<sup>5–7</sup> TB in children aged <5 years, especially those aged <2 years, has been shown to cause high mortality and morbidity.<sup>7–9</sup> Most childhood TB cases occur in children aged <5 years;<sup>10–12</sup> these

children are at higher risk of developing TB after infection and of developing severe forms of TB.<sup>9,10,13</sup> Treatment outcomes vary. In one study from Malawi, treatment outcomes among children with TB were found to be poor,<sup>14</sup> while studies from India showed high treatment success rates among children.<sup>15,16</sup>

Although there are no representative data on the situation and burden of childhood TB in Bhutan, a 6-year retrospective study conducted in Phuentsholing General Hospital, a TB centre in Bhutan, found that children accounted for 12.4% of the total number of cases.<sup>17</sup> Routinely reported data do not capture comprehensive information on treatment outcomes and associated characteristics. This study was therefore undertaken to describe the number and proportion of childhood TB cases registered under the Bhutan NTCP in 2010, their demographic and clinical characteristics and any associations between these characteristics and treatment outcomes.

### METHODOLOGY

#### Study design

This was a retrospective cohort study involving a review of records routinely maintained under the NTCP of Bhutan.

#### Setting

Bhutan is a small, land-locked country in the South-East Asia region, with a population of approximately 708265 residing in an area of 38394 km<sup>2</sup>,<sup>18</sup> which is administratively divided into 20 districts. Bhutan provides free health care services to its population, and there are no private practitioners or private health facilities in the country. The NTCP is fully integrated into the three-tiered health system of Bhutan, which comprises one national referral hospital, two regional referral hospitals, 29 hospitals and 181 basic health units (BHUs) spread across the entire country. All hospitals and 15 of the total BHUs are staffed by at least one medical doctor. TB is diagnosed and treatment is initiated in these facilities. In other BHUs where there are no doctors, presumptive TB patients are referred to those facilities with doctors. All facilities are involved in follow-up and contact tracing and providing DOTS support.

For children, the approach to case finding remains passive and follows WHO recommendations, using clinical examination, Mantoux test, sputum microscopy and chest X-ray for diagnosis. Based on the severity of the disease, cases are either treated by the

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Medical Officer of the facility or are referred to regional hospitals for specialist review and management. Treatment is in line with the 2010 WHO recommendations.<sup>19</sup> Until 2010, patients were admitted to hospital for the first 2 months of treatment; however, recent policy recommends admission for only the first 2 weeks of treatment; cases are then followed up by the respective treatment centre and the BHUs. The NTCP Bhutan has followed the standardised international recording and reporting system since 2001.

### Data collection and validation

All hospitals and BHUs with TB registers were visited in July 2012 by seven trained researchers. Information on age-specific population was obtained from the Statistical Year Book of Bhutan 2011,<sup>18</sup> and data on the total number of TB cases registered in 2010 was extracted from the Annual Health Bulletin of the Ministry of Health, Bhutan, 2011.<sup>20</sup> Information and data on all childhood TB cases registered in 2010 were extracted from the TB treatment cards and TB registers into a structured data collection tool. The variables included: TB registration number, age, sex, type and category of TB, body weight at the initiation of treatment, treatment category and treatment outcome. Outcomes were categorised as favourable (cured and treatment completed) and unfavourable (loss to follow-up, died, failure and transfer out). Data from the treatment cards were cross-checked with the data in TB registers. In case of disparities, the information on the TB treatment card was verified.

### Data analysis

The data were double-entered into EpiData (The EpiData Association, Odense, Denmark) by two independent data operators, validated for inconsistencies and analysed using EpiData software. Age-specific case notification rates (for 0–14 years overall, and separately for 0–4 and 5–14 years) were calculated using population data. Relative risks with 95% confidence intervals (CI) were calculated to measure the strength of association between clinical and demographic factors and treatment outcomes. The  $\chi^2$  test was used to compare proportions and  $P < 0.05$  was considered statistically significant.

### Ethical issues

As this study was based on record review and did not involve any patient interaction, informed consent was deemed unnecessary. Ethical clearance was obtained from the Research Ethics Board of Health, Bhutan and the Ethics Advisory Group (EAG) of the International Union Against Tuberculosis and Lung Disease, Paris, France.

## RESULTS

Of the 1332 TB cases registered under the NTCP in 2010, 187 (14%) were children. This amounts to an age-specific case notification rate of 88/100 000 in the 0–14 years age group compared to a rate of 237/100 000 in adults. Among children, the age-specific case notification rate in the 0–4 years age group was 93/100 000, and it was 85/100 000 in the 5–14 years age group.

**TABLE 1** Demographic and clinical characteristics of childhood TB cases registered under the NTCP, Bhutan, in 2010 ( $N = 187$ )

Category	<i>n</i> (%)
Sex	
Male	107 (57)
Female	80 (43)
Age group, years	
<1	16 (9)
1–4	59 (31)
5–14	112 (60)
Weight bands, kg	
0–7	3 (1.6)
8–14	50 (27)
15–20	36 (19)
21–30	37 (20)
>30	21 (11)
Not recorded	40 (21)
Sites of TB	
Pulmonary	92 (49)
Extra-pulmonary	95 (51)
Extra-pulmonary sites ( $n = 95$ )	
Lymphadenitis	51 (54)
Abdominal	7 (7)
Pleural effusion	7 (7)
Miliary	5 (5)
Meningitis	2 (2)
Bone and joint	1 (1)
Eye	1 (1)
Not recorded	21 (23)
Patient type	
New pulmonary positive	10 (5)
New pulmonary negative/ unknown smear status	79 (42)
New extra-pulmonary	91 (49)
Retreatment	6 (3)
Not recorded	1 (1)

TB = tuberculosis; NTCP = National Tuberculosis Control Programme.

Demographic and clinical characteristics are described in Table 1. Of the 187 childhood TB cases, 57% were males, 40% were aged <5 years, 96% were new TB cases and nearly half of them had extra-pulmonary involvement, with lymph nodes being the most common site of involvement. Most weighed between 15 and 30 kg, but bodyweight at the initiation of treatment was not documented for 21% of cases. The overall treatment success rate (cured and treatment completion) was 93%; the death rate, all forms, was <1% (Table 2).

The associations of demographic and clinical characteristics with the treatment outcomes are given in Table 3. Treatment outcomes among retreatment cases

**TABLE 2** Treatment outcomes of childhood TB cases registered under the NTCP, Bhutan, in 2010

Treatment outcomes	<i>n</i> (%)
Treatment success rate	176 (93)
Loss to follow-up	3 (2)
Died	1 (1)
Failure	1 (1)
Transfer out	0
Not recorded	6 (3)
Total	187 (100)

TB = tuberculosis; NTCP = National Tuberculosis Control Programme.

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**TABLE 3** Association of demographic and clinical characteristics with treatment outcomes among childhood TB cases registered under the NTCP, Bhutan, in 2010

Category	Unfavourable outcome n (%) <sup>*</sup>	Favourable outcome n (%) <sup>†</sup>	RR (95%CI)	P value
Sex				
Male	6 (5.6)	101 (94.4)	Reference	
Female	5 (6.3)	75 (93.7)	1.1 (0.4–3.5)	0.85
Age group, years				
0–4	6 (8.0)	69 (92.0)	1.8 (0.6–5.6)	0.31
5–14	5 (4.5)	107 (95.5)	Reference	
Weight bands (n = 147), kg				
<20	5 (5.6)	84 (94.4)	1.1 (0.3–4.3)	0.91
>21	3 (5.2)	55 (94.8)	Reference	
Types of TB				
New smear-positive	1 (10.0)	9 (90.0)	2.3 (0.3–18.4)	0.44
New smear-negative	5 (6.3)	74 (93.7)	1.4 (0.4–5.2)	0.57
New extra-pulmonary	4 (4.4)	87 (95.6)	Reference	
Retreatment	1 (16.7)	5 (83.3)	3.8 (0.5–28.7)	0.19

<sup>\*</sup>Unfavourable outcome = loss to follow-up, died, failure and transfer out.

<sup>†</sup>Favourable outcome = cured and treatment completed.

TB = tuberculosis; NTCP = National Tuberculosis Control Programme; RR = relative risk; CI = confidence interval.

were worse than those in new cases, but this difference was not statistically significant. Of the five children with disseminated TB, one died.

## DISCUSSION

This is the first study from Bhutan describing the profile and treatment outcomes among childhood TB patients. We found that around 14% of all TB cases were children, mostly new TB cases, and that half of them had extra-pulmonary involvement. The treatment success rates were very high across age groups, weight bands, sex and type of TB, reflecting good programme performance. Although outcomes were poor among retreatment and new smear-positive TB cases, the associations were not statistically significant, primarily due to the small numbers.

The measured proportion of childhood TB of 14% of all TB could indicate good awareness of the disease by health care providers and community health workers. This may be because Bhutan provides free health care services to all citizens, with good health coverage through its three-tiered health care system spread across the entire country. As there were no private health care providers in the country until 2011, the public health services could be credited for the performance in TB case finding and management.

The case notification rate among children aged <5 years was higher than in those aged ≥5 years. This is in line with the expected epidemiology of TB, and allays fears of possible under-notification in the 0–4 year age group. This is in contrast to the findings of other studies from India, which have reported very low proportions of childhood TB cases in the 0–4 year age group.<sup>15</sup> This is possibly due to the presence of a dominant private health sector in India and the consequent undernotification of TB cases to the NTCP as compared to no private health sector in Bhutan. The proportion of extra-pulmonary TB (EPTB) was almost 50%, with lymphadenitis accounting for over half of these cases. This is consistent with findings of other studies.<sup>14,15,17,21</sup>

The NTCP in Bhutan applies a standardised daily treatment regimen throughout the country, and its policy guidelines require

directly observed treatment (DOT) to be practised throughout the course of treatment either by a health worker or by a trained DOT provider. Until the end of 2010, pulmonary smear-positive and severe TB patients were admitted to the treatment centres for the 2-month intensive phase of treatment, with a supervised continuation phase. The high treatment success rate can therefore be attributed to effective implementation of DOT through Bhutan's free health care system and to good treatment adherence achieved through educated patients and trained DOT providers, in addition to the absence of private health care providers. Human immunodeficiency virus (HIV) prevalence is estimated to be as low as 0.1%,<sup>22</sup> indicating low TB deaths associated with HIV. In the last 2 years, no TB-HIV co-infected cases have been reported by either the TB or the HIV programme; the high treatment success rate could thus also be associated to low HIV prevalence.

The strength of this study was that it covered health facilities throughout the country, and hence the findings are generalisable. In addition, data were collected from individual treatment cards, which meant that numbers and most data were accurate.

Our study had some limitations. First, several cases were diagnosed as tuberculous pneumonia, but there was no information to confirm the validity of this diagnosis. A weakness of the study was poor documentation of the results of diagnostic investigations. A study from Malawi found that the practice of TB diagnosis in children was poor.<sup>21</sup> A review of diagnostic procedures of childhood TB is therefore deemed essential to understand current practices and further improve diagnosis and management. Second, as a fifth of the children did not have their weight recorded at the start of treatment, the correct dose per body weight was not possible. Similarly, sites of extra-pulmonary involvement were not recorded for 21% of the EPTB cases. These deficiencies in the recording system need to be addressed by training and supportive supervision of the health care staff at the TB centres.

This study highlights childhood TB as a problem in Bhutan, and shows good treatment outcomes. It will hopefully serve to facilitate planning and policy development for better management of childhood TB.

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**Contexte :** Tous les hôpitaux et centres de santé appartenant au Programme National de Lutte contre la Tuberculose (PNLT) au Bhutan.

**Objectif :** Décrire le nombre et la proportion de cas de tuberculose (TB) infantile enregistrés par le PNLT en 2010, leurs caractéristiques démographiques et cliniques et toute association avec les résultats du traitement.

**Schéma :** Etude rétrospective de cohorte impliquant la revue des cartes et des registres de traitement de la TB.

**Résultats :** Sur les 1332 cas de TB enregistrés, 187 (14%) étaient des

enfants âgés de <15 ans. Sur ces 187, 75 (40%) étaient âgés de <5 ans, 18 (96%) étaient des nouveaux cas ; près de la moitié concernait des TB extra-pulmonaires, dont la lymphadénite était la forme la plus courante. Le taux global de succès du traitement a été de 93%, et on n'a trouvé aucune association entre les caractéristiques démographiques et cliniques et les résultats du traitement. On a identifié quelques déficiences d'enregistrement.

**Conclusion :** La TB infantile est bien dépistée au Bhutan et les résultats du traitement sont excellents.

**Marco de referencia:** Todos los hospitales y los centros de salud inscritos al Programa Nacional contra la Tuberculosis (PNT) en Bután.

**Objetivo:** Definir el número y la proporción de casos de tuberculosis (TB) en la infancia que se registraron en el PNT en el 2010, analizar las características demográficas y clínicas de los pacientes y determinar la asociación de estas características con los desenlaces terapéuticos.

**Método:** Fue este un estudio retrospectivo de cohortes, en el cual se examinaron las tarjetas de tratamiento y los registros de TB.

**Resultados:** De los 1332 casos de TB registrados, 187 ocurrieron en

niños <15 años de edad (14%); 75 de ellos eran <5 años de edad (40%) y se diagnosticaron 180 casos nuevos (96%); cerca de la mitad de los casos correspondió a una TB extrapulmonar y la forma más frecuente fue la linfadenitis tuberculosa. La tasa global de éxito terapéutico fue 93% y no se observó ninguna asociación entre las características demográficas o clínicas de los pacientes y el desenlace terapéutico. Se detectaron unas pocas deficiencias de registro.

**Conclusión:** En Bután se reconoce en forma adecuada la TB en los niños y se logran excelentes desenlaces terapéuticos.