Tuberculosis in indigenous children in the Brazilian Amazon

ABSTRACT

OBJECTIVE: Assess the epidemiological aspects of tuberculosis in Brazilian indigenous children and actions to control it.

METHODS: An epidemiological study was performed with 356 children from 0 to 14 years of age in Rondônia State, Amazon, Brazil, during the period 1997-2006. Cases of TB reported to the Notifiable Diseases Surveillance System were divided into indigenous and non-indigenous categories and analyzed according to sex, age group, place of residence, clinical form, diagnostic tests and treatment outcome. A descriptive analysis of cases and hypothesis test ($\chi^2$) was carried out to verify if there were differences in the proportions of illness between the groups investigated.

RESULTS: A total of 356 TB cases were identified (125 indigenous, 231 non-indigenous) of which 51.4% of the cases were in males. In the indigenous group, 60.8% of the cases presented in children aged 0-4 years old. The incidence mean was much higher among indigenous; in 2001, 1,047.9 cases/100,000 inhabitants were reported in children aged < 5 years. Pulmonary TB was reported in more than 80% of the cases, and in both groups over 70% of the cases were cured. Cultures and histopathological exams were performed on only 10% of the patients. There were 3 cases of TB/HIV co-infection in the non-indigenous group and none in the indigenous group. The case detection rate was classified as insufficient or fair in more than 80% of the indigenous population notifications, revealing that most of the diagnoses were performed based on chest x-ray.

CONCLUSIONS: The approach used in this study proved useful in demonstrating inequalities in health between indigenous and non-indigenous populations and was superior to the conventional analyses performed by the surveillance services, drawing attention to the need to improve childhood TB diagnosis among the indigenous population.

TB in indigenous children in the Amazon  Gava C et al

INTRODUCTION

Brazil remains among the 22 countries responsible for approximately 80% of the world’s tuberculosis (TB) cases, despite reductions of more than 20% and 30% in the incidence and mortality for TB in Brazil from 1990 to 2007.1,5

High incidence of TB is generally linked to precarious living conditions; for this reason, the spatial distribution of the disease is not homogenous, and cases are concentrated in specific groups, such as homeless people, prisoners, health professionals and ethnic minorities.14,15

Approximately 50% of Brazil’s total indigenous population is concentrated in the North of the country. For reasons that remain unexplored, the incidence of TB among indigenous peoples in both Brazil and other Latin American countries is higher than the incidence in other segments of the population.6-8 Around 50% of TB cases occur in children and adolescents in certain locations where indigenous populations live.3,13

Data on the epidemiological situation of TB in children and adolescents are limited, largely because the disease does not manifest itself in the same way as it does in adults.12,16 Sputum samples are rarely obtained from children < 5 years old,20 and diagnostic confirmation by culture occurs in less than 50% of tested samples from children.16 Diagnostic difficulties are exacerbated in developing countries as a result of technical problems and limited resources.22 Most cases of pulmonary TB (PTB) in childhood are classified as smear-negative. The establishment of a correct TB diagnosis in children has emerged as one of the most important challenges in this area.

Information about the occurrence and distribution of TB in indigenous children in Brazil is scarce. Studies

RESUMO

OBJETIVO: Avaliar os aspectos epidemiológicos da tuberculose em crianças indígenas brasileiras e as ações para seu controle.

MÉTODOS: Estudo epidemiológico com 356 crianças de 0 a 14 anos de idade, em Rondônia, Amazônia, Brasil, de 1997 a 2006. Os casos, registrados no Sistema de Informação de Agravos de Notificação, foram classificados em indígenas e não indígenas, e analisados segundo sexo, faixa etária, local de residência, forma clínica, exames diagnósticos e resultado do tratamento. Foi realizada análise descritiva dos casos e teste de hipótese (χ²) para verificar se houve diferenças nas proporções de adoecimento entre os grupos investigados.

RESULTADOS: Foram identificados 356 casos de tuberculose (125 indígenas e 231 não indígenas), dos quais 51,4% em meninos. Nos indígenas, 60,8% dos casos foram notificados em < 5 anos. A incidência média foi maior entre os indígenas: 1.047,9 casos/100.000 habitantes < 5 anos, no ano de 2001. A forma pulmonar foi registrada em mais de 80,0% dos casos e a cura ultrapassou 70,0% em ambos os grupos. Cultura e exame histopatológico foram utilizados em apenas 10,0% dos pacientes. Houve três casos de coinfeção com HIV em não indígenas e nenhum em indígenas. A detecção dos casos foi classificada como insuficiente e/ou regular em mais de 80,0% das notificações em indígenas, mostrando que a maioria dos diagnósticos foi baseada na radiografia de tórax.

CONCLUSÕES: A abordagem empregada mostrou-se útil para ilustrar desigualdades em saúde entre indígenas e não indígenas, demonstrando-se superior às análises convencionais realizadas nos serviços de vigilância. Fica evidente a necessidade de um aprimoramento da investigação diagnóstica entre as crianças indígenas.

that deal with the subject are rare,5,13 and those that have been performed indicate failures in the detection and monitoring of reported cases. Investigations performed with native populations in Australia, Canada and the United States indicate a higher incidence of TB in individuals < 15 years old than in children from other ethnic groups.17,21,24 The lack of resources for TB control, poverty and diminished access to diagnosis and treatment also aggravate the epidemiological situation and can partly explain these discrepancies.

This study aimed to assess the epidemiological aspects of tuberculosis in Brazilian indigenous children and the actions for its control.

METHODS

An epidemiological study in reported TB cases with 356 children from zero to 14 years old in Rondônia, Northern Brazil, from 1997 to 2006.

The state of Rondônia is situated in the Brazilian Amazon region. It borders Bolivia (on the South and West) and the Brazilian states of Acre (West), Amazonas (North) and Mato Grosso (East). Rondônia has an area of 237,590 km², and 1,562,409 inhabitants are distributed over 52 municipalities. According to the 2010 IBGEb Demographic Census 0.4% (817,963 individuals) of the Brazilian population and 0.8% (12,015 individuals) of the population in Rondônia declared themselves as indigenous.

Data were obtained from the National Notifiable Diseases Surveillance System (SINAN), present in all of the country’s states and municipalities and managed by the Ministry of Health, Brazil. New TB cases reported from January 1, 1997 to December 31, 2006 were included and duplicate records were excluded.

The ethnicities of the cases were not available in the SINAN database and were inferred from the name and surname, home address and location of the health unit that reported the case. It is a traditional practice among the indigenous people of Rondônia to take the ethnic group as a surname (e.g., Antônio Oro Waran Xijein). This classification method has been applied in other contexts11 and has proven useful in revealing health inequalities in epidemiological research focusing on ethnicity and race. The classification used here was performed independently by one of the authors and a researcher who had prior experience working among the indigenous people of Rondônia. The inter-rater reliability was considered nearly perfect (Kappa statistic: 0.97).

Cases of TB were analyzed according to sex, age group (zero to four; five to nine; and ten to 14 years old), place of residence (urban; rural), clinical form (pulmonary – PTB; extrapulmonary – EPTB; both pulmonary and extrapulmonary – PTB+EPTB) and treatment outcome (cure; abandonment; death; transference; change of diagnosis).

The diagnostic tests for TB were included in the data analysis: I) direct observation of acid-fast bacilli (AFB) in sputum (positive; negative); II) culture for Mycobacterium tuberculosis in sputum (positive; negative); III) thorax radiography (normal; suggestive of TB; suggestive of another disease); IV) tuberculin skin test – TST (0 to 4 mm; 5 to 9 mm; or ≥ 10 mm); V) anti-HIV serology (positive; negative); and VI) histopathological slides (AFB-positive; suggestive of TB; not suggestive of TB).

Regarding the performance of the diagnostic tests described above, a classification system was created to compare the tests used for TB diagnosis among children in Rondônia with the national recommendations.14 The cases were classified into four categories:

- Insufficient (no diagnostic tests recorded or only one recorded)
- Fair (at least two tests recorded)
- Good (three tests recorded)
- Excellent (four or more tests recorded)

The sum of new TB cases in children (according to the three age groups shown, the year of occurrence and the ethnicity – indigenous or non-indigenous) was used as the numerator, and the sum of the populations (according to the same classifications) was used as the denominator to calculate the incidence rates; this quotient was multiplied by 100,000.

Population data were obtained from the IBGE Demographic Censuses performed in 2000 and 2010, which contained specific data on the indigenous and non-indigenous populations in the age groups of interest. Estimates of intercensal population were based on average annual growth rate of 2.9% and -1.2% for the indigenous and non-indigenous groups, respectively.

An electronic database was generated and the analyses were performed with the help of the Statistical Package for the Social Sciences version 9.0 (SPSS Inc., Chicago, IL, USA). The statistical significance of differences in proportions was assessed with the Chi-squared test ($\chi^2$), with a 5.0% significance level.

This study is part of a research project named “Tuberculose entre os povos indígenas de Rondônia” (tuberculosis among the indigenous peoples of Rondônia).
Rondônia), which was approved by the Research Ethics Committee of the Escola Nacional de Saúde Pública Sérgio Arouca (CEP/ENSP) (Process nº 14/07).

RESULTS

A total of 356 cases of TB were identified. Although indigenous people represented less than 1.0% of the state’s population, 35.1% of the total TB cases belonged to this ethnic group (Table 1).

Cases were slightly more common in boys in both groups (52.8% in the indigenous group and 50.6% in the non-indigenous group). Among indigenous people, 84.8% originated in the state’s rural areas, whereas among non-indigenous people, 87.9% came from urban areas (data not shown; p < 0.0001).

Most of the cases among indigenous children were concentrated in the zero to four age group (60.8%), and most of the cases among non-indigenous people were concentrated in the ten to 14 age group (46.8%). Despite marked fluctuations, a comparative analysis of the groups showed that, on average, TB incidence was higher among indigenous people over the whole period; largely among children zero to four years old. The incidence rate peaked at 1,047.9 cases/100,000 inhabitants in this group in 2001 (Table 1).

The pulmonary form of TB predominated, representing more than 80.0% of the notifications in both groups. The proportion of pulmonary cases was higher among indigenous children (93.6%) than among non-indigenous children (81.4%) (p = 0.006). The difference in the distribution of clinical forms was more accentuated in the zero to four age group, 94.7% of the indigenous cases had the pulmonary form, whereas the pulmonary manifestation was responsible for 80.3% of the reported cases in non-indigenous group (p = 0.008) (Table 2).

There was a higher concentration of extrapulmonary cases in the five to nine age group (22.1%), with pleural and peripheral lymph nodes affected in 44.0% and 24.0% of children, respectively (data not shown).

Overall cure rates for the whole period were above 70.0% except in non-indigenous children < 5 years of age (66.2%) in both ethnic groups. However, cure rates were higher in indigenous patients than in non-indigenous in all age groups (Table 2). Treatment compliance was better among indigenous patients, among whom there was a lower failure rate in all age groups (Table 2).

Except for sputum smear, thorax radiography and Tuberculin Skin Tests (TST), other complementary exams were not performed or were not reported in more than 88.0% of the cases in both groups (Table 3). Sputum smears were underused, especially in indigenous cases, among whom the test was performed in 26.4% of notifications (Table 3). Even in the group of children zero to four years old, where a greater availability of sputum samples would not be expected, there was a difference between the groups, with greater rates of sputum smears reported in non-indigenous people (9.9%) than in indigenous people (2.6%) (p = 0.009).

A high proportion of children underwent thorax radiographies (Table 3). Thorax radiographs of indigenous people presented results suggestive of TB more often than those of non-indigenous children in the zero to four year old age group (p = 0.047) (Table 3).

TST were not performed on most children in either group. The frequency of strong reactions (≥ 10 mm) was higher in non-indigenous subjects in the zero to four year old age group.

Culture of sputum and histopathological examination were not performed in more than 95.0% and 88.0% of the cases reported, respectively. Forty eight cases of extrapulmonary TB were reported, seven in indigenous and 41 in non-indigenous children. Histopathological exams should have been performed in all these cases. However, no record of histopathological exams were found in 85.7% of these cases in indigenous and 70.7% in non-indigenous children (data not shown). Histopathological exams were not performed for diagnostic confirmation among indigenous children zero to four years old (Table 3), and cultures were taken in two cases (2.6%); no record of the results was available for consultation.

There were three cases of TB/HIV co-infection in non-indigenous children, which corresponded to a prevalence of 1.3%; there was no record of co-infection among the indigenous children (Table 3).

Case detection methods were fair or insufficient for most subjects, but the utilization of diagnostic tests was lower among indigenous children. Around 6.0% of the total numbers of notifications were considered very good (Table 4).

DISCUSSION

Indigenous children, particularly those zero to four years old, present higher rates of tuberculosis than non-indigenous children in Rondônia. The diagnoses among children in this age group were almost entirely clinical. Pulmonary TB was also more common among indigenous children.

Case detection was considered insufficient among indigenous children in approximately half of the notifications. Most diagnoses were based on one diagnostic test, which fails to meet national guidelines for
childhood TB diagnosis. It is probable that the accuracy of many diagnoses were compromised.

Even if the incidence rate has been overestimated, the data indicate that TB constitutes a serious public health problem for indigenous children. Incidences of this magnitude have been recorded only in Brazilian prisoners and in native populations in Canada in the pre-chemotherapy era.

Table 1. Incidence (per 100,000 inhabitants) of tuberculosis cases, according to age group and background (indigenous or non-indigenous). Rondônia, Northern Brazil, 1997 to 2006.

<table>
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<th>Non-indigenous Cases</th>
<th>Incidence rates</th>
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Source: National Notifiable Diseases Surveillance System (SINAN) of Ministry of Health, Brazil

The high incidence of TB in children identified is consistent with the equally elevated incidence in indigenous adults in the Amazon region. These findings suggest that contact control must be intensified to facilitate opportune treatment of latent tuberculosis infection. As shown in non-indigenous people, BCG vaccine coverage above 90% in indigenous people appears to present limited utility for the prevention of TB (especially pulmonary TB) in children.
The large number of cases in the group of indigenous children zero to four years old suggests that a large number of children were infected and fell ill due to the active and continuous transmission of *Mycobacterium tuberculosis* in villages inhabited by indigenous people during the study period. Primary research data collected among different ethnicities in Rondônia and other Brazilian regions\textsuperscript{2,3,6} identified a high prevalence and
a high risk of TB infection and confirmed an elevated rate of transmission in indigenous areas in the country’s interior, particularly in the Amazon region. This scenario poses additional challenges for organizing health care services, especially with respect to early detection and opportune treatment of TB cases among indigenous Brazilian children.

This study may have included diagnostic errors, as underutilization of diagnostic tests suggested that, in many cases, diagnosis was based solely on a chest x-ray. Diagnoses in this age group should consider the clinical background, nutritional status, BCG scar and family history of contact with a sputum-positive patient from whom acid-fast bacilli were isolated. However, the available data did not include these elements.

Unlike TB cases in adults, children present a greater probability of developing primary TB, thus increasing the chance of extrapulmonary manifestations, especially pleural and lymphatic involvement. The enhanced proliferation of bacilli may lead to dissemination and neurological problems in small children or in subjects with impaired cellular immunity (e.g., HIV co-infection).

Most cases (94.9%) reported among indigenous children zero to four years old in Rondônia presented the pulmonary form of the disease. A sizable proportion of extrapulmonary forms (13.3%) was observed in the group of children five to nine years.

The low proportion of extrapulmonary forms of TB may indicate that other respiratory diseases were wrongly diagnosed as TB, illustrating the difficulties faced in correctly identifying the disease in children. According to Newton et al., TB can be confused with a great number of diseases prevalent in childhood, including pneumonia, viral and generalized bacterial infection, serious malnutrition and HIV. Communication difficulties can also contribute to classification errors, as many ethnic groups do not speak Portuguese.

A recent study of indigenous children and adolescents of the Suruí ethnicity in RO showed important differences between the approaches of the local health service and international recommendations, including the initiation of treatment without confirmation of the TB diagnosis.

According to Sant’Anna et al., TB diagnosis in childhood requires a distinct approach, integrating clinical, radiological and epidemiological data, as the identification of Mycobacterium tuberculosis in sputum is difficult. The symptoms of TB in children can be indicative of other diseases and radiological findings are non-specific factors that pose additional difficulties in arriving at a correct diagnosis.

Several regions of the world have implemented a scoring system based on clinical and epidemiological data to minimize mistakes in TB diagnosis in children. The Ministry of Health of Brazil has used a scoring system for childhood TB diagnosis since 2002. They recommend that every child suspected of having TB be evaluated with a combination of clinical and radiological findings, as well as interpretation of the tuberculin skin test, BCG vaccine status, nutritional state and history of recent contact with an adult suffering from tuberculosis. This system is validated at different times and shows a sensitivity of 86.0% and a specificity between 87.0% and 100.0%. The system is also operationally simple enough to be adopted in routine care for both indigenous and non-indigenous children.

Due to difficulties in diagnosis, it is reasonable to assume that children who were wrongly classified as TB cases were more likely to have a favorable outcome. This assumption could partly explain the high cure rates recorded over the study period, especially among indigenous children zero to four years old who showed an 86.8% cure rate following treatment.

Errors in the classification and/or codification of cases in information systems are known limitations of epidemiological analyses. Inadequate coverage of the health systems, in addition to limited access to health facilities, may contribute to low detection and the underreporting of cases in our data set. As a result of this and considering the small size of the Indigenous

### Table 4. Detection of cases according to background (indigenous or non-indigenous). Rondônia, Northern Brazil, 1997 to 2006.

<table>
<thead>
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<th>Case detection</th>
<th>Indigenous</th>
<th>Non-indigenous</th>
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<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
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<td>231</td>
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$\chi^2 = 37.886$

Source: National Notifiable Diseases Surveillance System (SINAN) of Ministry of Health, Brazil
population in Rondônia, there was a wide variation in the estimates of the incidence during this period. The difference in the proportion of Indigenous children affected by TB compared to non-Indigenous was high. However, caution is needed in interpreting these results due to the failings cited. Further studies are necessary to better address this issue.

Even with these limitations, the national health information systems constitute important bases for broad epidemiological studies in a population. The approach used in this study proved useful in revealing inequalities in health and surpassed the conventional analyses performed by health surveillance services, which aim to outline the epidemiological TB situation solely on the basis of absolute rates in a given location.

Improvement in health care for indigenous populations is needed, especially with respect to the conformity of TB case detection with national and international recommendations. Such improvements will also contribute to effective measurement of the burden of tuberculosis on the indigenous populations of the Brazilian Amazon and the impact of current control activities.
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