Racial and Ethnic Disparities in Pediatric Tuberculosis in North Carolina

Jason E. Stout, MD, MHS; Kapil K. Saharia, MD, MPH; Savithri Nageswaran, MD; Amina Ahmed, MD; Carol Dukes Hamilton, MD

Objectives: To investigate an increase in active pediatric tuberculosis (TB) cases in North Carolina from 9 cases in 2001 to 32 cases in 2002, and to pilot test a screening tool for detection of latent TB infection in children.

Design: Retrospective cohort and cross-sectional study.

Setting: State of North Carolina and a county public health department pediatric clinic.


Interventions: We reviewed medical records for 180 children (<15 years) with active TB reported in North Carolina. We subsequently initiated a screening project at a county public health department pediatric clinic.

Main Outcome Measures: Incidence of TB and prevalence of latent TB infection.

Results: One hundred eighty pediatric TB cases were reported from 1994 to 2002. Compared with 0.2 case per 100,000 non-Hispanic white children, the incidence rates were 3.0 cases per 100,000 non-Hispanic black children (P = .003) and 4.5 cases per 100,000 Hispanic children (P = .01); 88.3% of pediatric patients with TB were non-white. The screening project detected 2 cases of latent TB infection among 864 US-born children of foreign-born parents.

Conclusions: The burden of pediatric TB is almost entirely borne by black and Hispanic children in North Carolina. Tuberculin skin testing of US-born children of foreign-born parents is of low yield; more efficient screening strategies are necessary.


IN 2002, FOR THE FIRST TIME SINCE the inception of tuberculosis (TB) surveillance in 1951, foreign-born individuals accounted for most of the active TB cases in the United States.1 Because most new immigrants come from countries where TB is endemic, many enter the country with latent TB infection (LTBI) that becomes active after settling in the United States. The effect of immigration on national TB case rates has been well described.2,3 Epidemiological studies4-6 of pediatric TB in many US jurisdictions conducted in the 1990s indicated that the increasing pediatric TB incidence was associated with the growing immigrant population.

Between 1990 and 2000, North Carolina experienced a 274% increase in its foreign-born population, the greatest percentage increase of any state in the United States.7 The largest increase was observed in the Hispanic population, which rose almost 400% and by 2003 constituted more than 5% of the state’s population.8 Although the number of active TB cases in North Carolina children 0 to 14 years of age generally declined from 1994 to 2001, we observed a marked upsurge in reported pediatric TB cases, from 9 cases in 2001 to 32 cases in 2002. Given the recent demographic changes in North Carolina, we hypothesized that the state’s 2002 increase in pediatric TB was attributable to the growing Hispanic population.

We conducted a retrospective cohort analysis of all pediatric TB cases reported in North Carolina from 1994 to 2002 to test this hypothesis and to characterize the epidemiology and clinical characteristics of the pediatric cases. Based on our findings, we implemented a screening project in a county public health department pediatric clinic to determine whether we could improve detection of LTBI among children at risk.

Author Affiliations are listed at the end of this article.
and ethnicity were classified by public health nurses. Race/ethnicity were classified as having a foreign association if they were foreign born, non-Hispanic black children (13.9 cases per 100,000 person-years), compared with 3.0 cases per 100,000 person-years for non-Hispanic white children was 0.2 case per 100,000 person-years, corresponding to incidence rates ranging from 0.53 to 1.32 cases per 100,000 person-years for Hispanic black children (3.0 cases per 100,000 person-years). Sixty percent of children treated in the clinic are aged 0 to 4 years, 29% are aged 5 to 10 years, and 11% are aged 11 to 21 years. Sixty percent of children treated in the clinic are aged 0 to 4 years, 29% are aged 5 to 10 years, and 11% are aged 11 to 21 years. Thirty percent of children treated in the pediatric TB clinic had a TST performed on the initial visit. The screening project assessed the value of a TB screening questionnaire designed to identify the presence of any of the following TB risk factors: history of contact with a person with TB, foreign birth of the youth, foreign birth of the parent (if the child was <5 years), travel for longer than 1 month to a TB-endemic region, a compromised immune system, or exposure to high-risk individuals. The TB screening questionnaire was administered to all children aged 6 months to 5 years at each well-child examination and to all foreign-born children during their first visit, irrespective of age. If the answer to any question was affirmative, a TST was performed using the Mantoux method.

RESULTS

One hundred eighty pediatric TB cases were reported in North Carolina from 1994 to 2002 (Table 1). In 1994, 28 cases were reported (an incidence of 1.93 cases per 100,000), but from 1995 to 2001, the number ranged from 9 to 21 cases per year, corresponding to incidence rates ranging from 0.53 to 1.32 cases per 100,000 (Figure 1). In 2002, 32 cases were reported, resulting in an incidence of 1.84 cases per 100,000 subjects.

Tuberculosis rates were 15- to 23-fold higher among minority children compared with non-Hispanic white children, and 88.3% of pediatric patients with TB were nonwhite. The median incidence of TB among non-Hispanic white children was 0.2 case per 100,000 person-years, compared with 3.0 cases per 100,000 person-years for non-Hispanic black children (P = .003). The incidence of TB among non-Hispanic black children was 0.2 case per 100,000 person-years, compared with 3.0 cases per 100,000 person-years for non-Hispanic black children (P = .003) and 4.5 cases per 100,000 person-years for Hispanic children (P = .01). Although no TSTs were performed on the initial visit. The screening project assessed the value of a TB screening questionnaire designed to identify the presence of any of the following TB risk factors: history of contact with a person with TB, foreign birth of the youth, foreign birth of the parent (if the child was <5 years), travel for longer than 1 month to a TB-endemic region, a compromised immune system, or exposure to high-risk individuals. The TB screening questionnaire was administered to all children aged 6 months to 5 years at each well-child examination and to all foreign-born children during their first visit, irrespective of age. If the answer to any question was affirmative, a TST was performed using the Mantoux method.

RESULTS

One hundred eighty pediatric TB cases were reported in North Carolina from 1994 to 2002 (Table 1). In 1994, 28 cases were reported (an incidence of 1.93 cases per 100,000), but from 1995 to 2001, the number ranged from 9 to 21 cases per year, corresponding to incidence rates ranging from 0.53 to 1.32 cases per 100,000 (Figure 1). In 2002, 32 cases were reported, resulting in an incidence of 1.84 cases per 100,000 subjects.

Tuberculosis rates were 15- to 23-fold higher among minority children compared with non-Hispanic white children, and 88.3% of pediatric patients with TB were nonwhite. The median incidence of TB among non-Hispanic white children was 0.2 case per 100,000 person-years, compared with 3.0 cases per 100,000 person-years for non-Hispanic black children (P = .003) and 4.5 cases per 100,000 person-years for Hispanic children (P = .01). Although no TSTs were performed

Table 1. Demographic Characteristics of 180 Children Younger Than 15 Years With Tuberculosis in North Carolina From 1994 to 2002

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>96 (53.3)</td>
</tr>
<tr>
<td>Female</td>
<td>84 (46.7)</td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
</tr>
<tr>
<td>&lt;5</td>
<td>97 (53.9)</td>
</tr>
<tr>
<td>5-14</td>
<td>83 (46.1)</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>21 (11.7)</td>
</tr>
<tr>
<td>Non-Hispanic black</td>
<td>114 (63.3)</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>12 (6.7)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>33 (18.3)</td>
</tr>
<tr>
<td>Country of birth</td>
<td></td>
</tr>
<tr>
<td>United States</td>
<td>155 (86.1)</td>
</tr>
<tr>
<td>Foreign</td>
<td>25 (13.9)</td>
</tr>
<tr>
<td>Mexico</td>
<td>10 (40.0)</td>
</tr>
<tr>
<td>Other Latin America/Carribean</td>
<td>4 (16.0)</td>
</tr>
<tr>
<td>Asia</td>
<td>6 (24.0)</td>
</tr>
<tr>
<td>Africa</td>
<td>5 (20.0)</td>
</tr>
</tbody>
</table>

Downloaded From: http://archpedi.jamanetwork.com/pdfaccess.ashx?url=/data/journals/peds/5090/ on 06/18/2017
trend was observed in the incidence of TB among Hispanic children, they represented an increasing proportion of North Carolina TB cases over time (8.2% in 1994-1996 vs 25.4% in 2000-2002, *P* = .04). The increase in Hispanic pediatric TB paralleled the rise in the Hispanic pediatric population in North Carolina, which increased from 2.5% of all children younger than 15 years in 1994, to 7.3% of all children younger than 15 years in 2002.

The primary site of TB disease varied by age group. Although older and younger children experienced similar proportions of extrapulmonary disease (21.7% for both groups), 7 (7.2%) of 97 subjects in the younger group experienced severe TB (disseminated or meningeal) compared with 1 (1.2%) of 83 subjects in the older group (risk ratio, 5.99; 95% confidence interval, 0.75-47.69). Two children died of meningeal TB 6 and 8 days after starting TB treatment. Of the total 180 pediatric cases, specimens were sent for culture in 44 cases (24.4%), and 14 (31.8%) of these specimens were culture positive. More children had specimens sent for culture from 2001 to 2002 (19/41 [46.3%]) than from 1994 to 2000 (25/139 [18.0%]).

Foreign-born children accounted for 13.9% of pediatric TB cases. Another 13.9% were US born but had a parent or a source case who was foreign born. Therefore, foreign-associated children accounted for 27.8% of all cases reported during the study period, rising over time from 18.0% of all pediatric TB cases from 1994 to 1996, to 35.6% of all pediatric TB cases from 2000 to 2002.

Source cases were identified much less frequently for foreign-associated children aged 5 to 14 years compared with children in this age group without a foreign association (19.1% vs 72.6%, *P* < .001). Most (81.0%) of these older foreign-associated children were foreign born and likely represented reactivation of LTBI acquired in their country of origin. In contrast, children younger than 5 years who had a foreign association were usually US born (72.4%), and a source case was identified as frequently as in pediatric cases without a foreign association (62.1% vs 67.7%, *P* = .59). Figure 2 shows how the pediatric TB cases were identified. Children with a foreign association were less frequently identified through contact investigations than children without a foreign association (38.0% vs 56.9%, *P* = .03). No difference in the frequency of identification through contact tracing was noted when comparing non-Hispanic white children with minority children (42.9% vs 52.8%, *P* = .39).

**SOURCE CASE CHARACTERISTICS**

Eighty-two unique source cases were believed to have infected 113 (62.8%) of 180 pediatric cases. The source case was a parent, guardian, or relative of the subject in 89 (78.8%) of 113 cases. Source cases were household contacts in 60 children (53.1%). An additional 42 children (37.2%) had close contact with the source case, while 5 children (4.4%) had casual contact with the source case. The extent of contact between 6 children (5.3%) and their source case was unknown. Source cases were more likely to be female and to have more infectious forms of TB (smear-positive and cavitary) than other patients with pulmonary or laryngeal TB (Table 2).

**SCREENING FOR LTBI**

In the Wake County pediatric clinic, 1239 children (of 1917 initially seen for pediatric care) had a positive response to at least 1 of the 6 screening questions during the project period. Of these, 1213 (97.9%) had a TST placed, and 944 (77.8%) returned to have it read. Most subjects were younger than 5 years (73.2%) and Hispanic (87.5%); only 1.8% were non-Hispanic white, and 4.8% were non-Hispanic black. Seventeen (1.8%) of 944 subjects had new positive TSTs, and 1 child had a history of active TB. Foreign birth was the risk factor most highly associated with a reactive TST. Screening based on foreign birth alone would have identified 15 of 31 cases with a documented prior positive TST completed treatment for LTBI. In summary, 51 cases (28.3%) could have been prevented during the study period if all the tools available to treat and prevent TB had been used.

Thirty (16.7%) of 180 subjects were identified by contact investigations in which more than 1 subject with TB was presumably infected by the same source case. Two clusters with 4 children each involved adults who were symptomatic for more than 4 months before seeking healthcare.

**MISSION OPPORTUNITIES TO PREVENT TB TRANSMISSION OR DISEASE**

We identified several missed opportunities to prevent progression to TB disease in children. Contact investigations were delayed for more than 2 weeks for 13 (7.2% of all cases) of 93 children eventually identified through contact investigations. An additional 8 children (4.4% of all cases) younger than 5 years exposed to TB had a negative TST on initial evaluation but failed to take or were not prescribed isoniazid during the 3-month window period before retesting at 3 months. Finally, 4 children (2.2% of all cases) who had a positive TST but no known TB exposure failed to complete a course of isoniazid and subsequently developed TB.

Opportunities to prevent disease transmission were also identified. Twelve children (6.7%) were not initially named as contacts to an adult TB case but were later found to be contacts during further investigation. Disease might have been prevented in 21 children (11.7%) had 16 of 24 source cases with a documented prior positive TST completed treatment for LTBI. In summary, 51 cases (28.3%) could have been prevented during the study period if all the tools available to treat and prevent TB had been used.
17 children with positive TSTs, yielding a “number needed to screen” of 17.5. There was considerable overlap among foreign birth, foreign parentage, and foreign travel (Figure 3). Screening US-born children whose parents were born in TB-endemic countries and who had not traveled outside the United States required 628 TSTs to identify 2 children with positive TSTs, for a marginal yield of 0.32%. No TST-positive children were immunosuppressed (0 of 8 positive subjects), had contact with high-risk individuals (0 of 16 positive subjects), or had a history of contact with a person with TB (0 of 13 positive subjects), but few children with these risk factors were identified. The rate of reactive TSTs increased significantly with age, and among foreign-born children, the rate correlated with the incidence of TB disease in the region of the subject’s birth (Table 3).

The burden of pediatric TB in North Carolina is almost entirely borne by its minority population. Furthermore, the greatest burden falls on the youngest cohort and causes the most severe disease. In North Carolina, there are 2 separate but equally important phenomena driving ongoing disease in children. The first phenomenon is transmission among US-born non-Hispanic black adults, resulting in subsequent infection of non-Hispanic black children. The TB incidence among non-Hispanic black...
youth was 15-fold greater than that in non-Hispanic white children. Inequities in access to health care and declining familiarity with TB among health care providers may delay diagnosis, resulting in a higher likelihood of TB transmission by infectious adults.\textsuperscript{10} The 2 clusters identified in 2002 illustrate this failure, as the adult source cases were symptomatic for longer than 4 months.

The second phenomenon, TB in foreign-associated children, is the result of a large wave of immigration from Latin America, where TB remains endemic.\textsuperscript{13} The situation in North Carolina differs from the overall US situation because of the state's small population of non-Hispanic immigrants (who comprise a significant proportion of pediatric TB cases in states with high case-loads\textsuperscript{16}) and because most Hispanics in North Carolina are recent immigrants or are children of recent immigrants.\textsuperscript{11} Almost all Hispanic children with TB in North Carolina are foreign associated, whereas most pediatric patients with TB in the United States are US born and are likely to be a mix of foreign-associated and non–foreign-associated cases because of previously established Hispanic populations in many states.\textsuperscript{16} Older US children who immigrated with their parents were likely infected in their native country and developed reactivation disease after immigration; most children (81.0\%) aged 5 to 14 years with TB who had a foreign association were born foreign, and only 19.1\% of these children had a source case identified. Conversely, TB among younger children more likely reflects recent transmission. In our study, 72.4\% of children younger than 5 years with a foreign association were US born, and 62.1\% had a source case identified. Understanding this difference should focus our contact investigation efforts on the youngest cohort, as they represent ongoing community transmission.

Reporting of pediatric TB cases as foreign born vs US born underestimates the effect of immigration on TB incidence. The proportion of foreign-born pediatric TB cases in North Carolina ranged between 13\% and 15\% from 1994 to 2002, with no temporal trend. By contrast, the proportion of foreign-associated pediatric TB cases in North Carolina doubled from 18.0\% from 1994 to 1996, to 35.6\% from 2000 to 2002. Children acquire TB infection from adults, and the country of birth of the parent or guardian is an important factor that is not collected by the national TB surveillance system.\textsuperscript{16}

A source case was eventually identified in two thirds of our pediatric TB cases. Although most adults with TB in North Carolina (and in the United States in general) are male, source cases for children were more likely to be female adults and were more likely to be very infectious, as evidenced by a high rate of sputum smear–positive disease, a known risk factor for TB infection in youth contact.\textsuperscript{17-19} However, 7 children acquired TB from 6 smear-negative source cases, demonstrating that smear-negative adults can still be infectious\textsuperscript{20} and should be separated from contact with youth until the diagnosis of TB has been excluded or they demonstrate a response to treatment.

We identified several missed opportunities to prevent transmission or progression of disease in children. Twenty-eight percent of the pediatric TB cases could potentially have been prevented if the subjects or their adult sources had accepted and completed treatment of previously identified LTBI.\textsuperscript{21,22} In the present study, the proportion of cases not treated with isoniazid (6.6\%) was substantially less than others have reported\textsuperscript{23} but represents a significant missed opportunity to prevent TB in children. Furthermore, infectious adults failed to name 12 children whom they had exposed, pointing to weaknesses in contact investigation methods that others have noted.\textsuperscript{23-28} Better and continued training of TB field staff is needed to improve interviewing skills.

Compared with a recently published risk assessment questionnaire,\textsuperscript{29} our screening questionnaire detected a small number of additional children with LTBI. However, our approach was inefficient. Tuberculin skin test reactivity among these children (1.8\%) was lower than that among low-risk adults in North Carolina who received TSTs for “administrative” reasons (Table 4). Our highest yield came from screening children born in countries where TB is endemic, where we found 1 LTBI case per 17.5 children screened. Tuberculin skin test

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|}
\hline
Characteristic & Positive TST Result (n = 17) & Negative TST Result (n = 927) & Risk Ratio (95\% Confidence Interval) \\
\hline
Age, y & & & \\
0-4 & 5 & 686 & 1.0 (Referent) \\
5-14 & 7 & 224 & 4.19 (1.34-13.07) \\
15-21 & 5 & 17 & 31.41 (9.80-100.66) \\
Sex & & & \\
Male & 9 & 492 & 1.0 (Referent) \\
Female & 8 & 429 & 1.02 (0.40-2.62) \\
Race/ethnicity & & & \\
Hispanic & 13 & 813 & 1.0 (Referent) \\
Non-Hispanic white & 0 & 17 & 0.00 (0.00-13.39) \\
Non-Hispanic black & 3 & 42 & 4.24 (1.25-14.33) \\
Asian/Pacific Islander & 1 & 47 & 1.32 (0.18-9.91) \\
Offspring’s country of birth & & & \\
United States & 1 & 16 & 1.0 (Referent) \\
Mexico & 8 & 638 & 0.21 (0.03-1.59) \\
Other Latin America/Caribbean & 4 & 129 & 0.51 (0.06-4.31) \\
Sub-Saharan Africa & 2 & 36 & 0.89 (0.09-9.21) \\
Middle East & 1 & 11 & 1.42 (0.10-20.49) \\
Europe & 0 & 3 & 0 (0-108) \\
Asia & 1 & 3 & 4.25 (0.33-54.37) \\
\hline
\end{tabular}
\caption{Results of Tuberculin Skin Tests (TST) Among 944 Children With at Least 1 Tuberculosis Risk Factor on Screening Who Returned for TST Reading at Wake County Department of Health and Human Services From July 16, 2004, to December 8, 2004*}
\end{table}

*Data are given as number of youth unless otherwise indicated. Some characteristics do not sum to the heading totals because of missing data.
screening among US-born children of foreign-born parents was inefficient and was discontinued. More effective strategies must be developed and tested, such as screening US-born children who have foreign-born visitors in the household.

The study had several limitations. The TB case analysis was retrospective, which constrained the nature of questions that could be asked of the existing data set. Medical records describing source cases and their contact with children were often incomplete. In addition, genotyping of TB isolates was not done, so the epidemiological links could not be confirmed with molecular data. However, an emphasis in obtaining culture confirmation in pediatric cases during the past several years decreases the chance that the increased number of cases in 2002 was secondary to clinical misdiagnoses.

The questionnaire used in the LTBI screening project could not be validated because TSTs were not performed in subjects with no identified risk characteristics. However, data from the North Carolina Tuberculosis Control Program provide a credible benchmark (Table 4). The fact that the youngest children, who would have most recently been vaccinated with bacille Calmette-Guérin, had low rates of TST reactivity further supports the current Centers for Disease Control and Prevention guidelines to disregard a subject’s bacille Calmette-Guérin status when interpreting a TST.29

In conclusion, the pediatric TB caseload in North Carolina doubled in 2002 compared with the previous several years. Transmission among adults in poor communities, including US-born black citizens and a growing immigrant population, will likely contribute to new pediatric cases in the future. Additional public health resources are needed to identify and eliminate barriers to health care that delay evaluation and treatment of adults with TB. Effective TB education is needed among those likely to be exposed to TB, as well as among providers who may care for them. The public health community needs better tools for targeting socioeconomically disadvantaged communities in a culturally appropriate and supportive way to screen for LTBI and TB and to gain acceptance of proven treatment and prevention options.

Accepted for Publication: December 15, 2005.

Author Affiliations: Division of Infectious Diseases and International Health, Department of Medicine, Duke University Medical Center (Drs Stout and Dukes Hamilton), and Duke University School of Medicine (Dr Saharia); Durham; Tuberculosis Control Program, Wake County Department of Health and Human Services (Dr Stout); and North Carolina Tuberculosis Control Program, Communicable Disease Branch, Division of Public Health, Department of Health and Human Services (Dr Dukes Hamilton), Raleigh; School of Public Health (Dr Saharia) and Department of Preventive Medicine (Dr Nagaswaran), The University of North Carolina at Chapel Hill; and Division of Infectious Diseases, Department of Pediatrics, Carolinas Medical Center, Charlotte (Dr Ahmed), NC. Dr Saharia is now in the Internal Medicine–Pediatrics Residency Program at Yale University, New Haven, Conn.

Correspondence: Jason E. Stout, MD, MHS, Division of Infectious Diseases and International Health, Department of Medicine, Duke University Medical Center, Box 3306, Durham, NC 27710 (stout002@mc.duke.edu).

Funding/Support: This study was supported by grant K23 AI51409 (Dr Stout) and by grant K24 AI001833-02 (Dr Dukes Hamilton) from the National Institute of Allergy and Infectious Diseases, National Institutes of Health.

Acknowledgment: We thank the North Carolina Tuberculosis Control Program nurse consultants (Dee Foster, Elizabeth Zeringue, Myra Allen, and Julie Luffman) and the TB nurses in the North Carolina county public health clinics (Ellen Forthenberry and Elizabeth Tilson, MD), without whose cooperation this study would not have been possible.

REFERENCES


Call for Papers

Autism and Autism Spectrum Disorders. Archives of Pediatrics & Adolescent Medicine will publish a special theme issue in April 2007 on autism spectrum disorders including autism to foster a better understanding of the environmental and genetic risk (and protective) factors for autism; efficient and sensitive methods to screen for autism, especially in the primary care physician's office; confirmatory tools to accurately diagnosis autism and autism spectrum disorders; and information on the natural history of autism. We are especially interested in rigorously conducted studies on interventions for children with autism, as well as for their families. We will be happy to consider articles that consider policy implications of diagnosis and treatment of children with autism from the point of view of their families, communities, schools, and society as a whole. Papers submitted by September 1, 2006, will have the best chance for inclusion in this issue. Please consult our Web site at www.archpediatrics.com for submission information.