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Latent Tuberculosis Infection in School Children and Contact Tracing in Matlosana, North West Province, South Africa

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SUMMARY

This is a cross-sectional study to estimate the prevalence of latent TB infection (LTBI) and the annual risk of infection (ARTI) among a sample of children aged five and seven years in Matlosana, South Africa. LTBI prevalence was significantly higher in 7 children aged 7 years ($n = 704$) (19.7%, 95%CI 16.75–22.65) than in those aged 5 years (212/1401, 15.1%, 95%CI 13.23–16.97) ($P=0.0075$). The ARI was 2.9% (95%CI 2.2–3.6)

Keywords

TB; QGIT; children; TB Surveillance; South Africa

ALTHOUGH TUBERCULOSIS (TB) INCIDENCE and deaths due to TB have decreased worldwide, the disease remains a major public health problem.¹ South Africa has a high burden of both TB and human immunodeficiency virus (HIV), with an annual TB incidence of 715 per 100 000 population¹ and a reported 6.3 million HIV-infected individuals in 2013.² Apart from routine TB notifications and register data, data reflecting the impact of the TB control programme are limited.

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Surveys of latent tuberculous infection (LTBI) in young children reflect recent TB transmission and give a measure of the effectiveness of TB control programmes; however, they are seldom conducted in high HIV prevalence settings. We surveyed young children to ascertain the proportion with LTBI, and conducted active case finding in households of children with evidence of LTBI.

Matlosana Municipality, in the North West Province, South Africa, with a population of 708 000, is a peri-urban area with several gold and uranium mines and includes four towns and adjacent townships.³ HIV prevalence among pregnant women in the North West Province is 30%;⁴ estimated annual TB incidence in the Dr Kenneth Kaunda Health District, where Matlosana is located, was 1190/100 000 in 2011.³

POPULATION AND METHODS

We sampled children attending randomly selected schools and creches in townships in Matlosana, using lists generated by the Departments of Education and Health. The lists were randomly arranged and then stratified by township into groups of 10. Each decile was incrementally released to fieldworkers, based on attainment of planned sample size, ensuring that the number of schools sampled was approximately proportional to the total number of creches and schools in the township. The sample size of children tested was based on identifying a difference in prevalence of LTBI between the two groups.

Children had blood drawn for the QuantiFERON[®]-Gold In-Tube (QFT-GIT) assay (Cellestis, Melbourne, VIC, Australia) according to the information on the package insert, and shipped to the laboratory in Johannesburg within 8 h of sample collection for incubation and subsequent processing. Although the cost of a QFT-GIT test is higher than that of a tuberculin skin test (69 vs. 9 USD), QFT-GIT does not require an additional visit to the clinic, and the results are easier to read.

Hard copies of the results were obtained from the laboratory. QFT-GIT-positive children were referred to local clinics for further assessment and treatment. Children with indeterminate results were retested 6 weeks after their indeterminate result. The households of the QFT-GIT-positive children were visited to identify a possible index case of infectious TB. After obtaining individual informed consent and assent from the older children, a spot sputum specimen was obtained for auramine smear and MGITe liquid culture (BD, Franklin Lakes, NJ, USA).

We calculated the annual risk of LTBI using the following formula: $R = 1 - (1 - \text{prevalence})^{1/Ap0.5}$.⁵ All household contacts were offered on-site rapid HIV testing after counselling or a laboratory HIV enzyme linked immunosorbent assay on a saliva or blood specimen. Household members with actionable laboratory results were referred to their local clinic.

We engaged school principals and governing bodies to obtain written informed consent from parents before sampling. The study was approved by the ethics committees of the University of the Witwatersrand, Johannesburg, South Africa, and Johns Hopkins University, Baltimore, MD, USA. Approval was also obtained from local authorities at the district and sub-district levels.

RESULTS

A total of 2105 children were QFT-GIT-tested from 35 creches and 35 schools during February–October 2011. Of 1401 children aged 5 years, 212 (15.1%, 95% confidence interval [CI] 13.2–17.0) were QFTGIT-positive compared to 139/704 children aged 7 years (19.7%, 95%CI 16.8–22.7, $P = 0.0075$) (Figure). There were 10 indeterminate results; on repeat testing, 8 were negative, 1 was positive and 1 remained indeterminate, and for the purpose of this analysis, was assumed to be positive. Overall, the annual risk of tuberculous infection (ARTI) was 2.9% (95%CI 2.2–3.6).

We were able to study 292/351 (83.2%) households with a QFT-GIT-positive child; 1215 household contacts provided a sputum sample for smear and mycobacterial culture. Culture-positive TB was found in seven contacts (2.4%, 95%CI 1.5–3.3), of whom four were already on anti-tuberculosis treatment. Of the 780 household members who agreed to undergo HIV testing, 144 (18.5%, 95%CI 15.8–21.2) were HIV-infected, of whom 66/780 (8.5%; 95%CI 6.5–10.5) were newly diagnosed. Fourteen (9.7%) of the HIV-infected household contacts had a CD4 count of, 350 cells/mm³.

The ARTI among young schoolchildren in Matlosana was 2.9%, suggesting a high future disease burden, especially as HIV prevalence in sexually active adults is extremely high. The prevalence of LTBI reported here is similar to that of a smaller township in Cape Town where LTBI was reported in respectively 15% and 20% of 5 and 7 year olds.⁶ A study of children aged 1–9 years in India reported higher rates in urban than in rural areas (2.2% vs. 1.3%).⁷

We identified fewer cases of undiagnosed TB in household contacts than anticipated. Data from the same area studied showed that 8% of household contacts of an adult index case with TB had pulmonary TB,⁸ while 3.3% of household contacts of children aged, 7 years in Soweto with TB disease were found to have TB using the same testing strategy.⁹ The study was restricted to one high TB burden sub-district in South Africa, we were unable to survey all children in selected schools, and the study was cross-sectional. Moreover, we were not able to make direct comparisons, as we did not sample households of young schoolchildren who were QFT-GIT-negative. Although there are some data on the predictive value of QFT-GIT for future TB disease,¹⁰ the total burden of TB that could result from QFT-GIT positive children is not known, and our data suggest that children are continuing to be exposed to infectious cases of TB.

To interrupt intergenerational transmission of TB, more needs to be done to prevent and rapidly identify and treat patients with infectious TB. Serial national surveys of children need to be conducted to assess the effectiveness of national TB control programmes.

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Figure 1.
Flow chart of results of the TB prevalence using QGIT in School Children in Matlosana District.