Original Article

Results of a tuberculin skin testing survey in Albania

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Abstract

Introduction: Tuberculosis affected about 8.5 million patients in 2011. Numerous efforts are needed to reduce the pool of individuals with latent TB infection (LTBI). The aim of the study was to describe a tuberculin skin testing (TST) survey carried out in Albania to estimate the LTBI burden; furthermore, knowledge of TB was evaluated through an *ad hoc* questionnaire.

Methodology: A TST survey was performed in three geographical districts of Albania: Tirana-Kamez, Vlora, and Dibra. Cluster sampling was carried out of young Albanian students. In addition, the same students were given a questionnaire to assess their knowledge, attitudes, and any misconceptions about TB. The mean (standard deviation) age of the individuals, according to their educational level, was the following: grade five, 11.03 (0.18) years; grade six, 12.02 (0.17) years; and grade seven, 13.02 (0.16) years.

Results: The TST induration size was read in 4,648 students. About 5.0% showed a reaction >5 mm, with a significant variability in the districts selected (12.1% in the district of Dibra). An induration diameter >15 mm was found mainly in those areas with high TB incidence (*i.e.*, Tirana-Kamez and Dibra). About 13% of the students had no knowledge of TB.

Conclusion: LTBI prevalent cases are estimated to be low in Albania, although there are areas where the TB management should be improved to reduce the probability of *Mycobacterium tuberculosis* transmission. The level of knowledge about TB disease is inadequate and new public health strategies should be implemented, focusing on educational TV programs.

Key words: TST; Albania; LTBI; questionnaire

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Introduction

Tuberculosis (TB) represents one of the most important life-threatening infectious diseases worldwide [1]. The last World Health Organization (WHO) TB report estimated a global incidence and mortality of 8.5 and 1.4 million in 2011, with an estimated prevalence of 170 cases per 100,000 population [2].

The public health WHO strategy of directly observed treatment short course (DOTS) has improved the global epidemiological scenario in recent decades, saving millions of individuals, particularly in high TB incidence countries [2,3,4,5,6].

The WHO Stop TB strategy, published a few years later, reinforced the previous strategy and addressed emerging serious epidemiological risks such as TB/HIV co-infection and multidrug resistant (MDR) TB [2,6,7,8,9].

However, several logistical, economic, and programmatic drawbacks are holding back the 2050 WHO TB elimination goal (< 1 sputum smear positive case per 1,000,000 inhabitants) both in developing and developed countries [2,10,11,12]. In particular, aside from the mismanagement of TB cases [10], in low and middle TB incidence countries, there is a persistent pool of latently infected cases that could be a source of new TB patients [13,14].

To better organize national economic and healthcare efforts to reach TB elimination, it is critical to assess the epidemiological impact of the reservoir of individuals with latent TB infection (LTBI) [14].

Unfortunately, the diagnosis of LTBI is indirect, relying on the identification of an immune response in individuals exposed to and infected by *Mycobacterium tuberculosis* strains [13]. The tuberculin skin test (TST) and/or interferon-γ release assays (IGRAs) represent the only diagnostic tools currently adopted for LTBI diagnosis [13,15]. Their diagnostic accuracy, however, is not 100%; it is influenced by several extrinsic and intrinsic factors [15,16].

On this basis, the National TB Program (NTP) in Albania, a Central European country characterized by a TB notification rate < 20 cases per 100,000 population in 2010 [2,17], decided to carry out a countrywide TST survey on young students to estimate the burden of LTBI. A questionnaire was administered to assess the knowledge, attitudes, and mistaken beliefs regarding TB in the enrolled young country-representative cohort.

Methodology

An observational, cross-sectional study was undertaken to estimate the prevalence of LTBI in Albania in 2010. During the TST survey, a questionnaire on the topic of TB was distributed to the majority of the included Albanian students.

Setting of the prevalence survey

The epidemiological TB indicators in Albania have considerably improved during the last decade [2,17] after the implementation and the scale-up of TB-oriented public health and clinical programs and the financial and technical support of several international organizations.

In 2010, WHO estimated a TB incidence and prevalence (including HIV-positive patients) of 14 (95% confidence intervals-CIs: 12-16) and 16 (95% CIs: 3.8-28) per 100,000 population, respectively, whereas in 2011 they were 13 (95% CIs: 11-15) and 14 (95% CIs: 4-31); the mortality rate was estimated to be 0.38 (95% CIs: 0.28-0.64 with the exclusion of the HIV-positive patients) and 0.21 (95% CIs: 0.15-0.29) per 100,000 population in 2010 and 2011, respectively [2,17,18]. The case detection rate of pulmonary and extra-pulmonary TB was 97% (95% CIs: 83-114) and 100% (95% CIs: 87-120) in 2010 and 2011, respectively. Treatment success rate in 2009 was 89%, 84%, and 76% in new smear-positive, new smear-negative/extra-pulmonary, and retreated cases, respectively. Treatment success rate in 2010 was 91% and 90% in the new smear-positive and retreated cases, respectively. The caseload of children under 15 years of age with TB was 18 in 2010. The proportion of TB patients who tested positive for HIV infection was 0% and 1% in 2010 and 2011, respectively.

The national TST survey was carried out in three districts selected on the basis of their geographical location, TB incidence and prevalence rates (figures were obtained from the NTP register), and migration patterns. The following districts were included:

1. Tirana District-Kamez (Bathore), which is located in the central part of the country and was characterized by a population facing complicated hygienic and socio-economic living conditions.
2. Vlora District (city and surrounding areas), which is situated in the south and had a low TB incidence.
3. Dibra District (town and surrounding rural areas), which is situated in the north and had a high TB incidence.

The estimated sample size for the TST survey, calculated on the basis of the above-mentioned parameters, was 4,967 students. The survey was designed so the majority of students were from the district of Vlora (n = 2,962; 59.6%), with sample sizes from the districts of Tirana-Kamez and Dibra of 1,113 (22.4%) and 892 (18.0%), respectively.

Operational procedures

Healthcare workers involved in the survey were trained on how to interact with and how to explain the scope of the study to the young Albanian students and their teachers. The field team was composed of two healthcare workers.

During the design of the survey, several parameters were considered, particularly the overall population, the cluster sampling procedure, the time period of the survey (during the school year calendar, avoiding overlapping with the holidays and the weekends), and the age groups (10-13 years of age, *i.e.*, students attending middle school in grades five, six, and seven). The choice of the latter parameter was influenced by a planned subsequent survey to take place after a five-year period. No specific exclusion criteria were considered.

Tuberculin skin testing

Two separate visits took place: one for the administration of the tuberculin and the other one for the TST reading after an average time of 48-72 hours. A PPD RT 23 SSI 2 T.U./0.1 mL was used and kept in special containers at -20°C to avoid light exposure [19]. The standardized Mantoux technique was used: tuberculin 0.1 mL was injected intradermally, usually

in the dorsal aspect of the left forearm until a wheel appeared. The diameter of the induration was evaluated in the second visit, and data on TB exposure in the family were recorded.

All the demographic and epidemiological variables were recorded in an *ad hoc* register and included in an electronic database for the analysis.

Questionnaire

A standardized questionnaire was given to a sample of students to assess the knowledge, misconceptions, and attitudes related to TB. Several items were included: knowledge of TB through television, internet, local newspapers or magazines; discussions with teachers, friends, parents, grandparents; transmission of *Mycobacterium tuberculosis* strains (foodborne, airborne, direct contact); health risk related to TB development; clinical symptoms of pulmonary TB; the possibility of treatment, treatment success, and complete recovery; and preventive measures against TB.

Statistical analysis

The qualitative and quantitative variables, collected through *ad hoc* designed forms, were inputted into an electronic database. The chi-square test was used for qualitative covariates, described with percentages, and parametric or non-parametric tests were applied for quantitative variables when appropriate.

P values < 0.05 were considered statistically significant.

All the descriptive and inferential analyses were performed using Stata statistical software (StataCorp, Stata Statistical Software Release 9, College Station, TX, USA, 2005).

Results

Characteristics of the enrolled cohort

The TST was performed in 4,722 young students; 49.9% (n = 2,359) of them were males and their educational levels were grade five (1,410; 30%), grade six (1,566: 33%), and grade seven (1,746; 37%) (Table 1). For grade five, the mean (standard deviation) age of the individuals was 11.03 (0.18) years; for grade six, it was 12.02 (0.17) years, and for grade seven, it was 13.02 (0.16) years.

The proportions of males were 50.3%, 49.8%, and 49.8% for grades five, six, and seven, respectively.

The questionnaire was administered and completed by 3,242 children; the calculated sample sizes were 979 (30.2), 998 (30.8%), and 1,265 (39.0%) in the districts of Dibra, Tirana-Kamez, and Vlora, respectively.

Tuberculin skin test survey

TST results were read in 4,649 out of 4,722 (98.5%) students because 73 (1.5%) individuals were absent during the visit (Table 1).

The percentage of individuals with a TST higher than 5 mm was 5.0% (233/4,649); 12.1% (114/938), 9.5% (88/926), and 1.1% (31/2,785) tested positive in the districts of Dibra, Tirana-Kamez, and Vlora, respectively. No statistically significant differences were found between the age groups evaluated ($p > 0.05$) or between males and females.

The percentage of individuals with a negative TST result was 95.0%. The proportion of individuals with a presumed LTBI (induration size > 10 mm) was 104/4,649 (2.24%).

Table 1. Distribution of children selected for tuberculin skin testing, stratified by Albanian district and educational level

Educational level, n (%)	District, n (%)			
	Tirana-Kamez	*Dibra*	*Vlora*	*Total*
Students enrolled for TST				
Grade 5	283/936 (30.2)	281/951 (29.6)	846/2,835 (29.8)	1,410/4,722 (29.9)
Grade 6	320/936 (34.2)	305/951 (31.8)	941/2,835 (33.2)	1,566/4,722 (33.2)
Grade 7	333/936 (35.6)	365/951 (38.4)	1,048/2,835 (37.0)	1,746/4,722 (37.0)
Total	936/4,722 (19.8)	951/4,722 (20.1)	2,835/4,722 (60.0)	4,722/4,722 (100.0)
Students evaluated for TST induration				
Grade 5	281/936 (30.0)	277/951 (29.1)	838/2,835 (29.6)	1,396/4,722 (29.6)
Grade 6	315/936 (33.7)	302/951 (31.8)	914/2,835 (32.2)	1,531/4,722 (32.4)
Grade 7	330/936 (35.3)	359/951 (37.8)	1,033/2,835 (36.4)	1,722/4,722 (36.5)
Total	926/4,722 (19.6)	938/4,722 (19.9)	2,785/4,722 (60.9)	4,649/4,722 (98.5)

Specifically, induration size was between 6 and 10 mm in 129/233 (55.4%), between 11 and 15 mm in 65/233 (27.9%), and > 15mm in 39/233 (16.7%) (Figure 1). The proportion of children with an induration size > 15 mm was higher in the districts of Tirana-Kamez (24/39, 61.5%) and Dibra (15/39, 38.5%).

Household contact with one or more TB patients was reported by 23 (9.9%) students among those who were PPD positive; more than 95% (n = 22) of these individuals reported having a contact who lived in the district of Dibra.

Questionnaire on TB knowledge

Of the 3,242 children who received the questionnaire, only 2,814 (86.8%) could adequately answer the item-related questions, because 428 (13.2%) had never heard of TB.

Students' knowledge about TB was deemed low, despite the fact that 87% had heard about TB. The positivity response rates were below 50% in all selected educational groups: 46.5%, 43.6%, and 48.2% for grades five, six, and seven, respectively. The lowest score was recorded in the district of Tirana-Kamez, while the highest was obtained in the district of Dibra, where the majoirity of the information was obtained from family members and television programs.

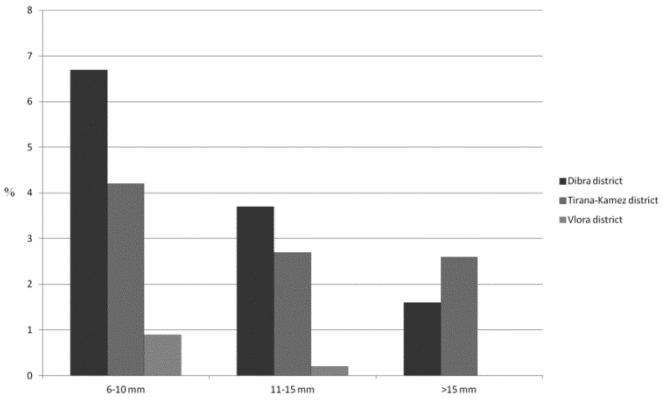
School programs and family members were identified as the less informative sources (45% and 26%, respectively).

Discussion

Prevalence of LTBI was estimated to be higher in the districts of Dibra and Tirana-Kamez (12.0% and 9.5%, respectively). It is likely that this finding could be significantly correlated to the TB incidence and prevalence of the districts included in the survey. TB case management, as well as the socio-economic conditions in some geographical areas (*i.e.*, Dibra) clearly need improvement. It was not possible to evaluate the influence of some risk factors (homelessness, imprisonment, HIV infection, etc.) overrepresented in adult males in the prevalence of LTBI in young students. The sample we enrolled showed a balance in gender, and the proportion of young males with LTBI was similar to that of young females when we stratified data using the gender variable.

However, it is noteworthy that the estimated relative frequency of those latently infected is significantly low owing to the adequate management

Figure 1. TST induration size in a country-representative sample of Albanian children.



of the infectious TB cases. The accurate implementation and scale-up of the DOTS strategy countrywide significantly improved the epidemiological trends of TB in Albania, reducing the probability of exposure of non-infected persons to TB cases and, consequently, the probability of transmission of *Mycobacterium tuberculosis* strains. Furthermore, the satisfactory diagnostic and therapeutic approach has decreased the probability of the emergence and spread of drug-resistant mycobacterial strains.

It is obvious that the low prevalence of HIV-infected cases favoured the positive epidemiological TB pattern, if compared, for instance, with patterns in African settings [6,7,9].

It was not possible to confirm the results obtained using the TST with the IGRAs; the cost would have been too high. Nevertheless, the burden of LTBI was estimated to be low, based on the lower specificity of TST and the existence of some TST-positive cases due to exposure to BCG vaccine and/or to non-tuberculous mycobacteria.

The weak relationship between household exposure and a positive TST may be explained by the higher age of TB cases. The frequency of contact between grandparents and children is not so high in Albania when compared with African settings. However, as TB is often associated with dishonour and stigma, it is not surprising that household exposure is underreported.

New public health measures are required to manage the latently infected cases in the near future in order to reduce the probability of new TB cases arising.

The cross-sectional survey on knowledge of TB demonstrates that the children living in high TB incidence areas, such as the Dibra district, showed

more knowledge of TB, probably due to the information received from television programs and family members.

It is clear that television programs should be used as a crucial tool to improve the knowledge of TB as well as to reduce the stigma.

The next LTBI survey will assess the epidemiological scenario and whether clinical and public health system performance can be improved.

Conclusions

LTBI prevalence is estimated to be low in Albania as demonstrated in the 2010 national survey, which selected a representative national sample. However, there was a significant geographical variation. Students' knowledge about TB disease was deemed inadequate, even though 87% of them knew that the disease exists.

Acknowledgements

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