Original article

Challenges for tuberculosis elimination: knowledge and practices on latent tuberculosis infection among general practitioners in Havana

Desafíos para la eliminación de la tuberculosis: conocimientos y prácticas sobre la infección tuberculosa latente entre los médicos generales en La Habana

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ABSTRACT

Introduction: Preventive treatment in high-risk groups is a key but poorly implemented tuberculosis control strategy. Despite resource limitations, Cuba -a low tuberculosis-incidence country- aims at elimination. General practitioners identify individuals at risk of tuberculosis/latent tuberculosis infection, refer for testing and follow-up treatment.

Objective: We explored general practitioners' knowledge and practices on latent tuberculosis infection.

Methods: Randomly selected general practitioners in a municipality in Havana answered a self-administered questionnaire that assessed their knowledge on 19 essential latent tuberculosis infection concept and management items. General practitioners having managed tuberculosis/latent tuberculosis infection answered six questions on practices.

Results: Among 62 general practitioners, 24% had managed tuberculosis and 20% latent tuberculosis infection cases. Overall, respondents correctly identified a median of 12 of the 19 knowledge items. There was no association between knowledge and general practitioners' characteristics. Still, only 31% and 26% mentioned tuberculosis contacts as high-risk group and correctly conceptualised latent tuberculosis infection, respectively. On average, general practitioners discerned 3 out of the 5 items related to test execution for latent tuberculosis infection diagnosis and 2 out of the 4 on the indication of TST testing, but only 11% and 3% ascertained all the corresponding items. Respondents determined on average 2.5 of 4 items on isoniazid as preventive drug, with 14% working out all 4. Among general practitioners having managed tuberculosis/latent tuberculosis infection, 87% reported supervising isoniazid administration and 53% declared that patients not always completed treatment.

Conclusions: Tuberculosis elimination poses challenges to the health system: as incidence declines knowledge of the disease and its management dwindles, as illustrated here for latent tuberculosis infection. Continuous, effective training and improving communication between the different levels of care and the Tuberculosis program are needed.

Keywords: tuberculosis; latent tuberculosis infection; tuberculosis elimination; primary health care; general practitioners; knowledge and practices.

RESUMEN

Introducción: El tratamiento preventivo en grupos de alto riesgo es una estrategia clave, pero poco implementada para el control de la tuberculosis. A pesar de las limitaciones de recursos, Cuba -un país con baja incidencia de tuberculosis- tiene como objetivo la eliminación. Los médicos generales en la atención primaria identifican a las personas con riesgo de tuberculosis/infección tuberculosa latente, y las remiten para la realización de pruebas y el tratamiento de seguimiento.

Objetivo: Explorar los conocimientos y prácticas de los médicos de la familia sobre la infección tuberculosa latente.

Métodos: Médicos de la familia seleccionados aleatoriamente en un municipio de La Habana respondieron a un cuestionario autoadministrado, que evaluaba sus conocimientos sobre 19 conceptos esenciales y manejo de la infección tuberculosa latente. Los médicos de cabecera que habían manejado la tuberculosis/infección tuberculosa latente respondieron seis preguntas sobre prácticas.

Resultados: De 62 médicos de la familia, el 24 % había manejado casos de tuberculosis y el 20 %, personas con infección tuberculosa latente. En general, los encuestados identificaron correctamente una media de 12 de los 19 ítems de conocimientos. No hubo asociación entre los conocimientos y las características de los médicos de la familia. Sin embargo, solo el 31 y 26 % mencionaron los contactos de tuberculosis como grupo de alto riesgo y conceptualizaron correctamente la infección tuberculosa latente, respectivamente. Como promedio, los médicos de familia discernieron tres de los 5 ítems relacionados con la realización de pruebas para el diagnóstico de la infección tuberculosa latente y dos de los cuatro sobre la indicación de la prueba de la tuberculina. Solo el 11 y el 3 % acertaron todos los ítems correspondientes. Los encuestados determinaron una media de 2,5 de los 4 ítems sobre la isoniacida como fármaco preventivo, un 14% resolvió los 4. Entre los médicos de la familia que habían tratado tuberculosis/infección tuberculosa latente, el 87 % declaró haber supervisado la administración de isoniacida y el 53 % declaró que los pacientes no siempre completaban el tratamiento.

Conclusiones: La eliminación de la tuberculosis plantea retos al sistema sanitario: a medida que disminuye la incidencia, se reduce el conocimiento de la enfermedad y su manejo, como se ilustra aquí para la infección tuberculosa latente. Se necesita una formación continua y eficaz para mejorar la comunicación entre los distintos niveles asistenciales y el programa de TB.

Palabras clave: tuberculosis; infección tuberculosa latente; eliminación de la tuberculosis; atención primaria de salud; médicos generales; conocimientos y prácticas.

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Introduction

The World Health Organization (WHO) End TB Strategy envisions “a world free of tuberculosis (TB)” by 2035.[1,2] In low TB-burden countries the epidemic tends to concentrate in high-risk groups and reactivation of latent TB infection (LTBI) contributes to a higher proportion of cases than recent transmission.[3] As the disease becomes “rare”, its visibility among health policy-makers decreases, as well as clinical TB expertise and general public awareness.[4]

Besides timely case identification and treatment, a key TB elimination strategy is preventive treatment of people with LTBI at high risk of TB.[2] A systematic review and meta-analysis[5] documented losses at all stages of the cascade of care (the process going from identification of eligible individuals to treatment completion) with only 19% of people completing LTBI treatment. Differences between settings exist: in low and middle-income countries 52% complete the started treatment *vs.* 70% in high-income countries.[5] Improving LTBI management requires knowing

where losses occur, their determinants and designing cost-effective interventions for national TB control programs (NTP).[6]

Cuba is a resource-limited, low TB-burden country (the incidence was 6.8/100,000 inhabitants in 2021).[7] Despite favourable conditions for and political commitment towards disease elimination,[4] TB incidence is stagnating in the last decade and to achieve further decrease the Cuban NTP will have to fine-tune its strategies.[8] Primary health care (PHC) is at the heart of health system setup in Cuba and, supported by the NTP, general practitioners (GPs) are in the frontline for identifying and managing individuals at risk of TB or LTBI.[9] TB is eliminated at the local level, neighborhood by neighbourhood,[10] but it is essential ensure adequate skills of the professionals who lead the programmatic actions to control the disease.

This study explored LTBI knowledge and practices of GPs in Havana, Cuba. The results will help pinpoint reasons for losses along the LTBI cascade of care and provide evidence and handles for quality improvement efforts.

Methods

Study setting

Cuba has 82 medical doctors/10,000 inhabitants, free of charge healthcare services and universal population coverage.[11] GPs are the first contact point of the population with the health system, conduct individual and community risk-assessment and provide preventive and curative care.[12] Polyclinics offer specialized care and support GPs through basic working groups (small groups of GPs interacting with and supervised by specialists in, amongst other, internal medicine and paediatrics from the polyclinic). The Cuban National Tuberculosis Programme (NTP) is well established, with a national laboratory network and TB treatment provision under direct supervision since 1971.[13] GPs are responsible for identifying individuals eligible for TB/LTBI screening, organising their diagnostic work-up, and prescribing and supervising treatment.[9]

According to NTP guidelines, high-risk groups needing LTBI screening are: contacts of pulmonary TB cases, child contacts of confirmed or presumptive TB cases, recently diagnosed people living with HIV (PLHIV), health workers and resident foreigners from high TB-burden countries. LTBI is diagnosed with tuberculin skin test (TST). Upon identification and referral by their GP, TST is performed at the municipal level by public health nurses trained to administer, read and interpret the result. After active TB is ruled out, LTBI patients are referred back and treated with isoniazid preventive therapy (IPT) by their GP.[9]

In 2017 Havana accounted for 29% of Cuba's TB case notifications.[11] The study was conducted in one of the 15 municipalities of Havana, Boyeros, with 195,301 inhabitants,[14] seven health areas and 188 GPs. It notified 20 TB cases in 2017 (unpublished NTP data). The municipality exemplifies Havana and was selected for formative research in preparation of an intervention to improve the management of LTBI.

Study design and data collection

We selected, proportionally allocated by health area, a stratified random sample of 62 GPs (one third of all the GPs practising in the chosen municipality). This allowed to estimate a prevalence of 50% of an attribute in the GP population with an error of 10% and 95% confidence and any lower or higher prevalence with more precision.

In September 2018 consenting participants answered, outside their workplace, an anonymous self-administered, semi-structured, pre-tested questionnaire. Reporting demographic data and other personal characteristics was optional. The questionnaire covered knowledge and practices regarding all steps of the LTBI cascade of care. Knowledge was assessed on essential items dealing with four themes: groups at risk for TB according to NTP guidelines (one open question probing into 3 items); LTBI conceptualization (one multiple-choice question covering 3 items); diagnosis (test execution: 5 open questions corresponding to 5 items; indications of TST testing: one multiple-choice question covering 4 items); and treatment (3 multiple-choice questions corresponding to 4 items). Practices

were assessed among GPs that had managed TB or LTBI cases in the last two years. They answered six questions on a Likert scale that explored starting IPT in people with a positive TST, IPT availability, administering IPT (to people), monitoring liver function, IPT adherence and treatment completion.

Data analysis

Data were entered in a Microsoft Excel™ 2010 file and analysed using SPSS v.20. We calculated medians with 95% confidence intervals (95%CI) and interquartile ranges (IQR) for numerical variables and proportions and 95%CI for nominal variables. The association between the number of correctly identified essential items and GPs' characteristics was assessed with correlation coefficients for numerical variables and by testing differences in medians for categorical variables (at alfa <0.05).

Ethics approval and consent to participate

The Ethics Committees of the Institute of Tropical Medicine (ITM) "Pedro Kourí" (Havana, Cuba) and University Hospital Antwerp (Belgium) and the Institutional Review Board of ITM Antwerp (Belgium) approved the study protocol. Participants gave written consent for participation in the study.

Results

All 62 sampled GPs accepted to participate. Not all fully reported their personal characteristics (table 1). Participants were either residents or specialists in General Medicine; of the 25 GPs who were posted in their current office for ≤18 months, 18 (72%) were ≤30 years old; 24% of GPs had managed TB and 20% LTBI cases in the last two years.

Table 1 - Characteristics of the surveyed general practitioners. Latent tuberculosis infection knowledge and practices survey. Havana, Cuba, 2017

Characteristic	%, (95%CI) or median (95%CI) (IQR)
Female sex (n = 62)	66% (56-76%)
Age (years) (n = 61)	33 (29-39) (28-46)
Work experience (years) (n = 54)	9 (5-18) (4-24)
Appointment in current GP office (month) (n = 49)	18 (12-48) (8-156)
Managed TB case in the past two years (n = 62)	24% (15-33%)
Managed LTBI in the past two years (n = 61)	19% (11-27%)

Legend: N: number of GPs providing information (see text for clarification); CI: confidence interval; IQR: interquartile range; TB: tuberculosis; LTBI: latent tuberculosis infection; GP: general practitioner.

Participants correctly ascertained a median of 12 (IQR 11-14) (95%CI: 12-13) out of the 19 essential knowledge items (table 2). The highest number of correctly identified items was 17, the lowest seven, by two GPs in either case. There was no association between the number of ascertained items and sex, age, years of professional experience, duration of appointment in the current GP office and having managed TB and LTBI cases.

Table 2 - Number and percentage of general practitioners correctly recognizing essential latent tuberculosis infection knowledge items. Havana, Cuba, 2017

Essential items grouped by theme	GPs correctly recognising item n (%, 95%CI)
I. Identification of risk groups for TB	**10 (16, 9-24)***
1. TB contacts	19 (31, 21-40)
2. PLHIV newly enrolled in HIV care	49 (79, 71-87)

3. Prisoners/ex-prisoners	38 (61, 51-71)
II. Conceptualization of LTBI	**16 (26, 17-35)***
4. LTBI is the viable persistence of *Mycobacterium tuberculosis*, immunologically controlled, without clinical evidence of active TB	50 (81, 73-89)
5. The probability of developing active TB in people with LTBI is 5%-15%	25 (40, 30-50)
6. LTBI treatment is a strategy of the NTP	31 (50, 40-60)
III. LTBI diagnosis	**0***
III.a. Test execution	**7 (11, 5-18)**
7. Test (TST)	59 (95, 91-100)
8. Time to reading (72 hours)	40 (65, 55-74)
9. Measured reaction (dermal induration)	11 (18, 10-26)
10. Unit of measurement of induration (millimetres)	46 (74, 65-83)
11. Cut-point for positive test in immunocompetent people (10 mm)	37 (60, 50-70)
III.b. Indications of TST testing	**2 (3, 0-7)***
12. PLHIV newly enrolled in HIV care	55 (89, 82-95)
13. Health workers	47 (76, 67-85)
14. Contraindicated in very ill patients	8 (13, 6-20)
15. Indicated only if positive result leads to an intervention	3 (5, 0-9)
IV. LTBI treatment	**14 (23, 14-31)***
16. Drug used in preventive treatment (isoniazid)	59 (95, 91-100)
17. Contraindications (active TB)	23 (37, 27-47)
18. Indication in PLHIV	32 (52, 41-62)

19. Indication in contacts of positive sputum smear pulmonary TB case	46 (74, 65-83)

Legend: *: participants correctly recognizing all essential items in a (sub-)theme; GP: general practitioner; CI: confidence interval; TB: tuberculosis; TST: tuberculin skin test; PLHIV: people living with HIV; LTBI: latent tuberculosis infection; NTP: National Tuberculosis Control Program; HIV: Human of Immunodeficiency Virus.

When asked to list high-risk groups for TB, only 10 GPs (16%) mentioned all three groups most prioritized by the Cuban NTP (TB contacts, PLHIV and prisoners/ex-prisoners) (table 2). Most (79%) mentioned PLHIV and more than half (61%) prisoners/ex-prisoners (table 3), but only 31% specified TB contacts, which barely ranked seventh in order of cited frequency. The second most mentioned group was alcoholics; nobody mentioned miners or foreign-born residents from high TB burden countries.

Table 3 - Number and percentage of general practitioners mentioning a particular tuberculosis high-risk group. Havana, Cuba, 2017

Rank	Risk groups (ordered by frequency of mention[+])	n	% (95%CI)
1	PLHIV or immunosuppressed patients	49	79 (71-87)
2	Alcoholics	47	76 (67-85)
3	Prisoners and ex-prisoners	38	61 (51-71)
4	Children ≤ 5 and adults ≥ 60 years old	37	60 (50-70)
5	Diabetics	25	40 (30-50)
6	People living in congregate settings (residential institution for the elderly, the physically or mentally impaired)	20	32 (23-42)
7	Contacts of bacteriologically confirmed pulmonary TB case	19	31 (21-40)
8	Socio-economically vulnerable persons (drug addicts, homeless, living in precarious settlement)	19	31 (21-40)

9	People with chronic diseases (asthma, chronic obstructive pulmonary disease, chronic renal impairment)	15	24 (15-33)
10	Undernutrition	13	21 (13-29)
11	Health care workers	13	21 (13-29)
12	Smokers	13	21 (13-29)
13	People with fibrotic image on chest radiography	10	16 (9-24)
14	Cuban workers returning from high TB burden country	6	10 (4-16)
15	Foreign-born residents proceeding from high TB incidence country	0	-
	Miners	0	-

Legend: CI: Confidence Interval; PLHIV: people living with Human of Immunodeficiency Virus; TB: tuberculosis.

Only 16 GPs (26%) correctly ascertained all three LTBI conceptualization items (table 2). While most were aware of the definition, only half knew that LTBI treatment is a strategy of the NTP and even less could determine the order of magnitude of the probability of developing TB with LTBI.

No GP ascertained all 9 items related to LTBI diagnosis. Regarding diagnostic test execution, the median number of correctly ascertained items was 3 (IQR 2-4) (95%CI: 2-4) out of 5; 7 GPs (11%) ascertained all essential items and 1 (2%) none. Most (95%) were aware that TST is used for LTBI diagnosis in Cuba. However, only 18% knew the nature of the measured reaction. Regarding TST indication, the median number of correctly ascertained items was 2 (IQR 1.75-2) (95%CI: 2-2); two GPs (3%) recognized all four items and six (10%) missed all. Fifty-nine (95%) failed to recognize that TST should only be performed if a positive result leads to treatment (Table 2).

As for LTBI treatment, the median number of correctly ascertained items was 2.5 (IQR 2-4) (95%CI: 2-3); 14 GPs (23%) identified all four items and one (2%) missed all. Most GPs correctly mentioned the drug used in Cuba (isoniazid), but only 37%

recognized that it is contraindicated in case of active TB and 24 (39%) that PLHIV and TB contacts should start treatment irrespective of TST results.

All the 15 GPs that reported having managed TB or LTBI in the last two years could indicate in which facility in their health area TST is performed and 80% could describe the administrative procedures for receiving the test results. Ten (67%) stated to always start IPT if a TST is positive and active TB has been excluded, and for most (93%) IPT had never been out of stock. 13 GPs (87%) reported supervised IPT administration, as NTP recommends, eight (53%) declared that all patients missed isoniazid doses during treatment and that people did not always complete IPT.

Discussion

This exploratory study, the first of its kind in Cuba, points at major knowledge gaps on LTBI and its cascade of care and sub-optimal practices concerning LTBI management amongst most of the surveyed GPs. Our sample size is relatively low, but we attain sufficient power and precision, and random selection of participants assured internal validity. Furthermore, TB-incidence is comparably low nationwide, the country's health system is homogeneous and non-fragmented, and all GPs receive similar training and continuous education. Our findings ought to approximate the situation in other parts of the territory and, in particular, reflect the state of affairs in the different municipalities of Havana.

Because of allowing anonymity and self-administration of the study questionnaire, which guaranteed minimising bias, not all GPs reported their full personal characteristics, but this does not affect the validity of our main results. Half of participants had been appointed to their current GP office for not more than 18 months and over two thirds of them were ≤ 30 years old. The short time in office is partly explained by their age structure, compounded by the mobility of GPs, many of whom contribute to the Cuban medical internationalism project in more than 60 countries.[15] Continuity of care is guaranteed by replacing outgoing doctors,[16] but

incoming GPs face the challenge of learning to know their catchment population and territory's health determinants.

Information on specialist or resident status was not elicited, but part of the GPs ≤ 30 years old were probably residents in training as general medicine specialist, which lasts two years.[12] There are no studies on Cuban residents' TB/LTBI knowledge, but in Havana important deficiencies were documented in TB knowledge in final year medical students, amongst whom 65% failed to correctly define LTBI.[17] A study in China also revealed poor TB knowledge among medical students[18] and in the United States the major knowledge deficiencies among resident physicians was related to LTBI diagnosis and management.[18] This highlights the importance of reinforcing the subject in the undergraduate and resident curriculum, particularly in low to medium incidence settings.

Being alert for and identifying in the population individuals at high-risk for TB should trigger actions for prevention, diagnosis and treatment.[5] However, TB contacts ranked only seventh amongst the 16 risk groups GPs mentioned in our study. For German physicians, they ranked 10th out of 16[20] and in three cities in Brazil with high TB incidence, 51% of PHC doctors and nurses were not aware of the need for TB prevention in contacts.[21] Possibly, when secondary case identification and management is prioritized in contact investigation, it is challenging to also maintain a focus on LTBI management.

The vast majority of GPs in Cuba mentioned that PLHIV should be tested for LTBI, as recommended by the NTP. This reflects successful TB/HIV programmatic collaboration and recognition of PLHIV as a TB high-risk group. It may be useful to delve into the strategies deployed to this end and to consider extending them to other risk groups such as diabetic patients. In contrast, no GP mentioned residents proceeding from high TB-burden countries, despite their high probability of harbouring LTBI. Maybe, because most foreign residents in the country are students housed in training site accommodation with dedicated health staff. Neither did GPs mention miners, probably because mining is not a significant economic activity in Cuba.[14]

Many knowledge gaps on LTBI diagnosis were related to technical aspects of test execution, possibly because GPs themselves only prescribe TST. Specialized staff in municipal level polyclinics performs the test, GPs receive the results and are then responsible for follow-up and, possibly, treatment.[9] However, knowledge of technical aspects is still essential to facilitate communication with patients and ensure compliance. As for treatment, only a good third of interviewees knew the contraindications of IPT and just over half mentioned its indication for PLHIV. In Australia, difficulties of health personnel in explaining LTBI to patients and discussing treatment were partly attributable to the vagueness of the corresponding national guidelines.[22] Another study in Australia and in New Zealand documented variable LTBI management practices and highlighted the need for strengthening physicians' education, for implementing strategies to standardize practice and for improving existing guidelines.[23] Similarly, information on LTBI management is currently scattered throughout the Cuban NTP Guidelines[9] and, in addition, the most recent WHO recommendations,[24,25] issued after the Guidelines' publication, have not been incorporated yet.

Few GPs had recently managed TB/LTBI, in line with the country's low TB burden, which is a major challenge to disease elimination.[26] This is exemplified by a study in North Carolina, where more TB management experience was associated with better quality TB contact investigation.[27] However, as disease incidence decreases, clinical case management becomes more specialized, while preventive activities must still reach the whole community. This requires close links and division of tasks between PHC and higher levels of care. Furthermore, in an elimination contexts, TB disproportionately affects population groups living in precarious conditions, who hardly utilise specialized health services and for whom PHC is more accessible.[28] Providers at this level are key to expanding the reach and coverage of LTBI testing and treatment interventions[29] and must be familiar with new approaches to TB prevention and care.[30]

One of the obstacles to successful implementation of tuberculosis preventive therapy is the availability of adequately trained staff.[31] However, in a British study on the acceptability and feasibility of decentralizing LTBI treatment to PHC,[32] the

main barrier perceived by GPs themselves was insufficient expertise and practise, which could be compensated by adequate training together with support of specialists. The Cuban health system's setup, with basic working groups formed by GPs supervised by other specialists, is conducive to providing such an approach. Orientation and training of health care workers involved in TB elimination must be frequent, attractive and convenient[33] and WHO recommends training and participation of all health personnel in LTBI care.[4,34] Distance-based learning and self-teaching are attractive, affordable strategies that could perhaps facilitate this.[33] Cuba has mounted successful short face-to-face training cycles for improving programmatic activities related to TB diagnosis,[35] but an integrated PHC training strategy covering LTBI has still to be developed. Our results are a first step towards the comprehensive identification of challenges for LTBI management in Cuba. Other studies should further identify the underlying determinants of the problem. Replicating the present study among health care providers that attend specific vulnerable groups (e.g. prisoners, foreign students from high TB-burden countries) would also be useful. Once gaps and their causes are identified, strategies can be designed to improve the LTBI cascade of care and accelerate progress towards TB elimination. At any rate, continuous and effective training must be implemented already now, together with actions for improving communication and relationship between different levels of care and between the NTP and GPs.

Data Availability

Cuban regulations prevent making data sets publicly available. However, the Ministry of Health will allow data sharing for research purposes. Requests in this regard should be directed to the direction of the Institute of Tropical Medicine "Pedro Kourí" (email: secredirector@ipk.sld.cu)

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