Mycobacterium tuberculosis infection among community health workers involved in TB control*

Infecção por *Mycobacterium tuberculosis* entre agentes comunitários de saúde que atuam no controle da TB

Patrícia Marques Rodrigues, Tiago Ricardo Moreira, Andressa Karla Luz de Moraes, Rafael da Cruz Araújo Vieira, Reynaldo Dietze, Rita de Cassia Duarte Lima, Ethel Leonor Noia Maciel

Abstract

Objective: To evaluate the incidence of *Mycobacterium tuberculosis* infection, using tuberculin skin test, among community health agents (CHAs) monitoring TB patients in the city of Cachoeiro de Itapemirim, Brazil. **Methods:** We included 30 CHAs acting in the Family Health Program and 30 of their family members residing in the same household. The tuberculin skin test results of each CHA were compared with those of the corresponding family member. **Results:** Of the 30 CHAs, 27 (90.0%) were female, compared with 23 (76.7%) of the 30 family members (p = 0.299). The mean age of the CHA group and of the family member group was, respectively, 36.8 and 39.7 years. No statistically significant difference was found between the groups regarding the level of education. Regarding *M. tuberculosis* exposure, the same number of participants in the two groups reported having known or had contact with a TB patient (17 individuals; 56.7%). There was a statistically significant difference regarding positive tuberculin skin test results (26.7% in the CHA group and 3.3% in the family member group; p = 0.011). **Conclusions:** *M. tuberculosis* infection was significantly higher among CHAs than among their family members, fueling the debate on the occupational risk involved in the activities of these professionals.

Keywords: Community health aides; Tuberculosis; Tuberculin test.

Resumo

Objetivo: Avaliar a incidência de infecção por *Mycobacterium tuberculosis* através da prova tuberculínica em agentes comunitários de saúde (ACS) que acompanham pacientes em tratamento de TB no município de Cachoeiro de Itapemirim (ES). **Métodos:** Incluímos 30 ACS que atuam no Programa de Saúde da Família e 30 de seus familiares residentes no mesmo domicílio. Comparamos o resultado do teste tuberculínico de cada ACS e do membro familiar correspondente. **Resultados:** Entre os 30 ACS, 27 (90,0%) eram do sexo feminino, ao passo que entre os 30 familiares, 23 (76,7%) eram do sexo feminino (p = 0,299). A idade média do grupo ACS e do grupo dos familiares foi, respectivamente, 36,8 e 39,7 anos. Não houve diferença estatística no nível de escolaridade entre os grupos estudados. Na investigação da exposição ao *M. tuberculosis*, o mesmo número de indivíduos nos dois grupos afirmou conhecer ou já ter tido algum contato com paciente com TB (17 indivíduos; 56,7%). Houve diferença estatisticamente significativa quanto ao resultado positivo da prova tuberculínica nos dois grupos (26,7% no grupo ACS e 3,3% no grupo de familiares; p = 0,011). **Conclusões:** A infecção por *M. tuberculosis* entre os ACS foi significativamente maior que entre seus familiares, e isso contribui para o debate em torno do risco ocupacional envolvido nas atividades destes profissionais.

Descritores: Auxiliares de saúde comunitária; Tuberculose; Teste tuberculínico.

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* Study carried out at the Federal University of Espírito Santo Infectious Diseases Center, Vitória, Brazil.
Correspondence to: Ethel Leonor Noia Maciel. Laboratório de Epidemiologia, Núcleo de Doenças Infecciosas, Universidade Federal do Espírito Santo, Av. Marechal Campos, 1468, Maruípe, CEP 29040-090, Vitória, ES, Brasil.
Tel 55 27 3335-7210. E-mail: emaciel@ndi.ufes.br
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Introduction

Currently, TB is one of the leading causes of morbidity and mortality worldwide. From an epidemiological point of view, it has been observed that approximately one third of the world population is infected with *Mycobacterium tuberculosis*, the etiologic agent of TB, which is capable of promoting the development of the active form of the disease in the infected individual.[1,2] During the course of the active disease, each patient infects an average of ten other individuals, perpetuating the chain of TB transmission in the community.[2]

According to the Case Registry Database, 1,400 cases of TB are reported annually in the state of Espírito Santo, Brazil. In 2004, the incidence of new cases of TB was 39.4/100,000 inhabitants, and 25.3/100,000 were infectious cases. The directly observed treatment, short-course (DOTS) strategy has been implemented in 123 of the 1,097 health care clinics in the state, representing 11.2% of the total.[3]

In the city of Cachoeiro de Itapemirim, which has an estimated population of 198,150 inhabitants (according to the Brazilian Institute of Geography and Statistics), the incidence and prevalence of TB are high. Therefore, it is included on the Brazilian *Plano Nacional de Controle da Tuberculose* (PNCT, National Tuberculosis Control Plan) list of cities considered priorities for control of the disease.[4] In 2006, 80 new cases were reported in the city, with an incidence of approximately 40 cases/100,000 inhabitants.[3]

As a means of dealing with this situation, the PNCT has relied on the strategies of the Family Health Program (FHP) and of the Community Health Agent Program (CHAP), in the hope that this partnership will contribute to the expansion of the TB control interventions, since these strategies have the family and the home as the tools of their trade. With this in mind, emphasis is given to the FHP and CHAP team activities, which are aimed at increasing the detection of cases, improving treatment adherence and reducing treatment abandonment.[5] In this context, the CHAP representatives stand out. These professionals, in addition to residing in the community where they work, have shown themselves to be familiar with its values, habits and language, therefore being able to produce a mixture between the use of technology/biomedical knowledge and local beliefs. Acting as a liaison, the CHAP representative bridges the gaps between health care services and the community, readily identifying its problems, facilitating the prevention of diseases and the promotion of health.[6]

Although community health workers are definitively incorporated into the control of TB in many parts of the world, especially where there is broad DOTS high coverage,[1] little is known regarding the occupational conditions of CHAP representatives working within the PNCT in the state of Espírito Santo, or in Brazil in general.

It has long been known that TB patient care, an activity listed among those carried out by CHAP representatives, increases the risk of infection for the health professionals involved. This problem, long neglected, returns to current discussion, with many studies highlighting the elevated risk of *M. tuberculosis* infection for health professionals and students in this area when compared with the risk for the general population.[7,8] However, there are no reports in the literature that describe the risk of *M. tuberculosis* infection for CHAP representatives. Since these professionals play a fundamental role in TB control and are in close contact with the susceptible population, we felt that it would be useful to create an occupational profile of CHAP representatives working within the FHP in the city of Cachoeiro de Itapemirim.

The present study was designed to evaluate *M. tuberculosis* infection, using the tuberculin skin test, in the CHAP representatives who work under the auspices of the FHP to monitor patients undergoing TB treatment in Cachoeiro de Itapemirim. Since the CHAP representatives live in the same community as the TB patients, and exposure might also take place within the community (outside the work environment), the tuberculin skin test result for the CHAP representative was compared with that of a family member residing in the same household.

Methods

This was an observational hybrid study of prevalent cases with retrospective evaluation of the exposure. Two groups, defined by their exposure to the occupational risk, were identified at the beginning of the investigation: exposed (for a minimum of 3 months); and unexposed. Data on past exposure and on outcomes were collected after the study outset.

The study population was composed of all CHAP representatives who worked within the FHP in the city of Cachoeiro de Itapemirim, Brazil, and who had TB patients under treatment in the area served. At the time of data collection, the city had 40 working CHAP representatives. Since adherence to the study was voluntary, 9 CHAP representatives declined to participate in the study, and 1 left the job during this period. Therefore, the final sample was composed of 30 CHAP representatives. A non-health professional family member of each CHAP representative, residing in the same household, was selected for the comparison between the professional exposure and the prevalence of the tuberculin skin test. Therefore, 30 CHAP representatives and 30 CHAP representative family members who were not health professionals participated in the study, completing the questionnaire provided. All study participants gave written informed consent.

A self-report questionnaire was applied, and the tuberculin skin test was performed in all CHAP representatives and family members participating in the study between February and May of 2007. In the tuberculin skin test, PPD RT23 tuberculin was delivered intradermally in the middle third of the anterior face of the left forearm. The test was read 72 h after its application. The maximum transverse diameter of the area of palpable induration was measured with a millimeter ruler, in accordance with the Tuberculosis Control Guidelines.[2] An induration equal to or larger than 10 mm was considered a positive result to the tuberculin skin test, as recommended by the Brazilian National Ministry of Health (NMH).[9]

The questionnaire completed by the CHAP representatives contained questions designed to collect personal and demographic data (name, date of birth, gender and level of education), as well as questions related to clinical and occupational history. For the family member group, the questionnaire contained the same questions designed to collect personal and demographic data (name, date of birth, gender and level of education) and clinical history, but the remaining questions were related to the history of contact with any TB case. With the exception of the occupational contact data for the CHAP representatives, all data were collected in a similar manner in both groups.

The data obtained through the questionnaires were transferred to a Microsoft Excel T spreadsheet. In the statistical analyses, we used the Stata program, version 9.0 (Stata Corp., College Station, TX, USA). Means and standard deviations were calculated for the age and level of education of the CHAP representatives, whereas their length of professional service was expressed as the median. Absolute and relative values were calculated for each variable. In the comparative evaluation of the dichotomous variables studied between the groups, we used Fisher's exact test; Student's t-test was used for quantitative variables. The level of significance was set at 5% ($p < 0.05$) for both.

The project was previously authorized by the Cachoeiro de Itapemirim Municipal Health Department and was approved by Research Ethics Committee of the Espírito Santo Federal University Health Sciences Center, protocol no 127/06. All study participants gave written informed consent, and their anonymity was guaranteed. The study participants who were strong reactors to the tuberculin skin test (induration ≥ 10 mm) were investigated at the local referral facility for TB control.

Results

The results are presented in accordance with the categories of the instrument used, as follows: demographic data, clinical history and occupational history.

As for the gender of the interviewees, it was observed that, of the 30 CHAP representatives, 27 (90.0%) were female, as were 23 (76.7%) of their family members ($p = 0.299$). The mean age of the CHAP representative group was 36.8 ± 8.7 years (range, 20-58 years), compared with 39.7 ± 11.7 years (range, 16-73 years) in

Table 1 - Distribution of the subjects surveyed according to variables related to demographic data.

Demographic variable	CHA group	Family member group	p
Female, n/N (%)	27/30 (90.0)	23/30 (76.7)	0.299*
Age, years (mean ± SD)	36.8 ± 8.7	39.7 ± 11.7	0.272**
Schooling, years (mean ± SD)	10.8 ± 1.8	9.4 ± 3.3	0.073**

CHA: community health agent. *Fisher's exact test; and **Student's t-test.

the family member group. The mean level of education among the CHAP representatives was 10.8 ± 1.8 years of schooling, higher than the 9.4 ± 3.3 years of schooling among the family members (Table 1).

As for the clinical history, the presence of scarring due to the application of the BCG vaccination was detected in most participants of the study, and was present in 28 (93.3%) of the CHAP representatives and in 24 (80.0%) of the family members. There was no significant difference between the groups. When questioned about the application of a prophylactic BCG vaccination booster, 2 (6.66%) of the CHAP representatives and 4 (13.33%) of the family members responded affirmatively. As for previous tuberculin skin testing, 15 (50.0%) of the CHAP representatives and 4 (13.33%) of the family members had been submitted to the test, and the proportional differences were statistically significant between the groups (p = 0.002). None of those 19 participants had tested positive on the previous tuberculin skin tests. However, in the investigation of exposure to *M. tuberculosis*, we asked the participants whether they knew or had ever had contact with a TB patient, and the result was identical in both groups (17 in each group; 56.66%; Table 2).

As for the result of the tuberculin skin test carried out in the study, 8 (26.66%) of the CHAP representatives tested positive result (induration ≥ 10 mm), whereas it was positive in 1 family member (3.33%), the difference between the two groups being statistically significant (p = 0.011; Table 2).

It is important to highlight that, of the 8 CHAP representatives testing positive and referred for investigation, 1 was diagnosed with active TB and initiated the treatment during the study.

The variables related to the occupational history of the CHAP representatives are presented in Table 3, although they are not compared with variables of the family members group.

The median time of service as a CHAP representative was 23 months (range, 4-108 months). The proportion of CHAP representatives who had some degree of training in TB/DOTS was 26/28 (92.9%; Table 3). When asked about the means of transmission of the TB bacillus, all (100%) answered "saliva droplets" (airborne transmission); however, 2 (6.66%) answered that the transmission also occurred by means of contact with personal belongings of the patient. The participants were allowed to select more than one response to that question. At the time of the survey, 22/26 (84.6%) of the CHAP representatives were monitoring TB patients (Table 3), the number of patients per CHAP representative ranging from 1 to 3. Of those, 19/26 (73.1%) were applying the DOTS strategy (Table 3). As for the use of personal protective equipment during the performance of the activities and monitoring of the TB patients, the study revealed that none of the CHAP representatives wore masks during the visits. In addition, 12/29 (41.4%) reported that the locales where the visits or DOTS implementation took place were closed or stuffy (Table 3).

Discussion

The CHAP representative is a professional active in two important NMH programs: the CHAP and the FHP. As described in Law no. 10.507, issued on 10 July 2002, the CHAP representative is licensed to perform activities related to disease prevention and health promotion in the home and the community (individual and collective interventions), developed in accordance with the Brazilian Unified Health Care System guidelines and under the supervision of the local administrator of the latter. This professional instructs and monitors families in relation

Table 2 - Distribution of the subjects surveyed according to variables related to clinical history.

Clinical variable	CHA group	Family member group	p*
BCG scar	28/30	24/30	0.129
Prophylactic BCG booster	2/30	4/30	0.389
Previous tuberculin skin testing	15/30	4/30	0.002
Has known or had contact with a TB patient	17/30	17/30	1.00
Positive tuberculin skin test result	8/30	1/30	0.011

CHA: community health agent. *Fisher's exact test.

Table 3 - Distribution of the subjects surveyed according to variables related to occupational history.

Occupational history variable	CHAs evaluated, n/N	Values
Median time of service, months	30/30	23
Underwent training in TB/DOTS, %	26/28	92.9
Monitored TB patients, %	22/26	84.6
Performed DOTS, %	19/26	73.1
Wore a mask during visits, %	0/29	0.0
Performed visits/DOTS in closed or stuffy environments, %	12/29	41.4

CHAs: community health agents; and DOTS: directly observed treatment, short-course.

to cares with their own health and also with the health of the community.[6] The CHAP representatives undoubtedly present particularities, since they work within their own communities, becoming references for the populations served.

In the present study, females predominated, in the CHAP representative group as in the family member group. Surveys involving CHAP representatives in various other Brazilian cities have obtained similar results.[10,11] This can be intimately associated with the caretaker role that women play in society, being the ones primarily responsible for the upbringing and feeding of children, as well as for the care given to elderly family members.[12] Of the 170,000 CHAP representatives in Brazil, 140,000 are women, which confirms the result obtained in the present study.[13] One of the prerequisites of the NMH is that the agents be over 18 years of age, although there is no set maximum age.[13]

A determined level of education was not required by the NMH for the function of agent; it was only necessary that the candidate knew how to read and write.[13] However, Federal Law no. 10,507, which regulates the CHAP profession, requires that CHAP agents have completed junior high. Having a higher level of education, CHAP representatives are more apt to incorporate new knowledge and to instruct the families under their care. In the present study, the mean level of education of the CHAP representatives was higher than that of their family members, although the difference was not statistically significant. In other Brazilian cities, CHAP representatives have a high level of education. Among those working in the city of São Paulo, 36.7% have finished high school, and 27.3% are soon to graduate from high school.[14] The CHAP representatives working in the city of Porto Alegre have had 9-11 years of schooling.[10]

In Brazil, it is recommended that the primary BCG vaccination be administered as early as possible (as soon as the infant weighs more than 2,000 g), and it is obligatory that this vaccination be administered during the first year of life,[15] which explains the fact that most of the study participants presented the vaccination scar. However, the absence of the scar does not indicate that the vaccination was not administered. The presence of the vaccination scar represents a history of BCG vaccination, and there is no evidence in the literature of an association between the presence of the scar and protection or immunity against TB. However, the NMH, through the National Immunization Program, recommends the vaccination of children who do not present the vaccination scar, even of those with a history of BCG vaccination, due to the theoretical possibility that nonviable vaccination units were administered, resulting in the absence of skin reactivity.[16]

The World Health Organization recommends the use of one dose of BCG for protection against TB, considering the absence of evidence to justify the use of additional doses of BCG.[17] Some countries, such as Russia, Portugal, Chile and Hungary, have adopted the use of multiple doses of BCG for the control of pulmonary TB, based on the assumption that the protection provided by the BCG vaccination wanes over time. In a case-control study conducted in Chile, additional doses of BCG were not found to confer additional protection.[18] In Finland, the use of the second dose of BCG vaccination in PPD non-reactive children was discontinued in 1990, and no increase in the number of cases was subsequently observed, when compared with the cohort of children revaccinated with BCG.[19] Randomized controlled studies of the revaccination in schoolchildren in two Brazilian state capitals, Salvador and Manaus, showed the absence of protection of the second dose of BCG against pulmonary TB.[20,21] Consequently, the authors recommended the discontinuation of this practice. This explains the low percentage of people who were revaccinated for BCG in this study.

The proportion of individuals having previously undergone tuberculin skin testing was higher in the CHAP representative group than in the family member group, since most CHAP representatives submitted to the test already worked in the field, which was probably reflected in this finding. Although undergoing a tuberculin skin test is not obligatory in Brazil, its use as a parameter for the evaluation of the quality of the biosafety in the work environments is a routine practice in health care facilities.[9]

Although the same proportion of CHAP representatives and their family members had known or had contact with TB patients, there remain no doubts that the infection rate associated to the activities of the CHAP representatives was different from that observed for the family members. The difference resides in the frequency and intensity with which the contact takes place, since the family members had typically known a TB patient but did not maintain contact with the individual. This finding seems to show that, in smaller communities, the diagnostic condition of TB patients is known to the members of the community where they reside.

The fact that the median time of service of the CHAP representative was 23 months indicates a certain stability of employment. In Porto Alegre, turnover among these professionals is low, and some of those who worked there for a short time had initiated their activities in recently implemented services.[10] Knowing the time of service in the program is important to understanding the role of the agent, which is built in the everyday practice.[22]

In the present study, a highly significant finding was obtained regarding the number of individuals testing positive on the tuberculin skin test. The proportion of such individuals was considerably higher among the CHAP representatives than among their family members, who differed from the CHAP representatives primarily in professional terms. Since the controls were family members dwelling in the same place and having approximately the same age as the CHAP representatives, there is evidence that the difference found between the two groups in terms of the rate of infection is due to the greater level of exposure to the infectious agent promoted by the professional activity of the CHAP representative. Although the occupational risk of *M. tuberculosis* infection in other health professionals has generated considerable discussion,[7,8,23] there have been no studies evaluating the risk related to the activities performed by CHAP representatives.

Although our findings suggest a strong relationship between the CHAP representative activity and increased *M. tuberculosis* infection, they should be confirmed through prospective studies involving larger numbers of participants, in order to evaluate the tuberculin skin test conversion rate after entering the service, using more sophisticated diagnostic methods, such as those based on the liberation of IFN-γ.[24]

The proportion of CHAP representatives who had attended training programs was high, which is consistent with the epidemiological situation of the city and its classification as one of the eight PNCT priority cities in the state of Espírito Santo. Similarly, the fact that most CHAP representatives were monitoring TB patients is to be expected, due to the great number of existing cases in the city. However, the fact that the city was a priority and that the agents carried out the monitoring as well as having undergone training did not lead them to carry out their activities in accordance with the recommended norms of biosafety, since we observed that none of the professionals wore a mask during visits and monitoring, as has been recommended.[9]

Despite the recognition of the fact that DOTS is a highly effective strategy for the control of TB in the community, the NMH has not given the necessary attention or provided the resources required to allow the activities of the CHAP representatives, the professionals primarily responsible for the monitoring of TB patients, to be carried out appropriately in relation to the level of risk involved.

The fact that no studies referring to the occupational risk of the CHAP representatives was found in the literature reviewed can be explained by the short period of time for which TB control has been effectively incorporated. In this context, the central finding of this study was that the prevalence of TB infection was significantly higher among the CHAP representatives than among their family members, which contributes to the debate regarding the occupational risk involved in the activities of these professionals. The high proportion of CHAP representatives monitoring TB patients or performing DOTS without the use of individual

protection equipment underscores our evaluation and shows the need to formulate health care policies for this professional class.

References

1. World Health Organization. Global tuberculosis control: surveillance, planning, financing. WHO report 2007 [report on the Internet]. Geneva: World Health Organization 2007 [cited 2007 Jul 16] Available from: www.who.int/tb/publications/global_report/2007/pdf/full.pdf
2. Ministério da Saúde. Manual de Normas para o Controle da Tuberculose. 4 ed. Brasilia: Ministério da Saúde; 2002.
3. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Sistema nacional de vigilância em saúde: relatório de situação: Espírito Santo. Brasília: Ministério da Saúde; 2006.
4. Brasil. Ministério da Saúde. Secretaria de Vigilância Epidemiológica. Coordenação Geral de Doenças Endêmicas. Programa Nacional de Controle da Tuberculose. Brasília: Ministério da Saúde; 2004.
5. Muniz JN, Villa TC, Pedersolli CE. Tratamento supervisionado no controle da tuberculose em Ribeirão Preto: novo modo de agir em saúde. Bol Pneumol Sanit. 1999;7(1):33-42.
6. Nunes MO, Trad LB, Almeida BA, Homem CR, Melo MC. O agente comunitário de saúde: construção da identidade desse personagem híbrido e polifônico. Cad. Saúde Pública. 2002;18(6):1639-46.
7. Maciel EL, Viana MC, Zeitoune RC, Ferreira I, Fregona G, Dietze R. Prevalence and incidence of Mycobacterium tuberculosis infection in nursing students in Vitória, Espírito Santo. Rev Soc Bras Med Trop. 2005;38(6):469-72.
8. Sepkowitz KA, Schluger NW. Tuberculosis and the health care worker. In: Rom WN, Garay S, editors. Tuberculosis. New York: Browand Company: 1996. p. 935-43.
9. Brasil. Ministério da Saúde. Fundação Nacional de Saúde. Centro de Referência Professor Hélio Fraga; Sociedade Brasileira de Pneumologia e Tisiologia. Controle da tuberculose: Uma proposta de integração ensino-serviço. Rio de Janeiro: FUNASA/CRPHF/SBPT; 2002.
10. Ferraz L, Aerts DR. O cotidiano de trabalho do agente comunitário de saúde no PSF em Porto Alegre. Ciênc saúde coletiva. 2005;10(2):347-55.
11. Martins CL, Oliveira LS, Rodrigues MA, Watanabe HA, Jacomo YA. Agentes comunitários nos serviços de saúde pública: elementos para uma discussão. Saúde Debate. 1996; 51:38-43.
12. Ellis JR, Hartley CL, editors. Enfermagem contemporânea: desafios, questões e tendências. Porto Alegre: Artes Médicas; 1998.
13. Brasil. Ministério da Saúde. Secretaria Executiva. Programa agentes comunitários de saúde (PACS)/ Ministério da Saúde, Secretaria Executiva. Brasília: Ministério da Saúde; 2001.
14. Campinas LL, Almeida MM. Agentes Comunitários de Saúde e o acolhimento aos doentes com tuberculose no Programa Saúde da Família. Bol Pneumol Sanit. 2004;12(3):145-54.
15. Ferreira AA, Bunn-Moreno MM, Sant'Anna CC, Ferreira MF. BCG vaccination in low birth weight newborns: analysis of lymphocyte proliferation, IL-2 generation and intradermal reaction to PPD. Tuber Lung Dis. 1996;77(5):476-81.
16. Barreto Mauricio L., Pereira Susan M., Ferreira Arlan A. Vacina BCG: eficácia e indicações da vacinação e da revacinação. J Pediatr (Rio J). 2006;82(3 Suppl):s45-s54.
17. Global tuberculosis programme and global programme on vaccines. Statement on BCG revaccination for the prevention of tuberculosis. Wkly Epidemiol Rec. 1995;70(32):229-31. Erratum in: Wkly Epidemiol Rec. 1995;70(34):246.
18. Sepulveda RL, Burr C, Ferrer X, Sorensen RU. Booster effect of tuberculin testing in healthy 6-year-old school children vaccinated with Bacillus Calmette-Guérin at birth in Santiago, Chile. Pediatr Infect Dis J. 1988;7(8):578-81.
19. Lugosi L. Theoretical and methodological aspects of BCG vaccine from the discovery of Calmette and Guérin to molecular biology. A review. Tuber Lung Dis. 1992;73(5):252-61.
20. Barreto ML, Rodrigues LC, Cunha SS, Pereira S, Hijjar MA, Ichihara MY, et al. Design of the Brazilian BCG-REVAC trial against tuberculosis: a large, simple randomized community trial to evaluate the impact on tuberculosis of BCG revaccination at school age. Control Clin Trials. 2002;23(5):540-53.
21. Rodrigues LC, Pereira SM, Cunha SS, Genser B, Ichihara MY, de Brito SC, et al. Effect of BCG revaccination on incidence of tuberculosis in school-aged children in Brazil: the BCG-REVAC cluster-randomised trial. Lancet. 2005;366(9493):1290-5.
22. Viana AL, Poz MR. A reforma do sistema de saúde no Brasil e o Programa de Saúde da Família. Physis. 1998;8(2):11-48.
23. Harries AD, Nyirenda TE, Banerjee A, Boeree MJ, Salaniponi FM. Tuberculosis in health care workers in Malawi. Trans R Soc Trop Med Hyg. 1999;93(1):32-5.
24. Pai M, Riley LW, Colford JM Jr. Interferon-gamma assays in the immunodiagnosis of tuberculosis: a systematic review. Lancet Infect Dis. 2004;4(12):761-76.

About the authors

Patrícia Marques Rodrigues
Young Investigator Grant Recipient. Federal University of Espírito Santo, Vitória, Brazil.

Tiago Ricardo Moreira
Masters Student in Collective Health. Postgraduate Program in Collective Health, Federal University of Espírito Santo, Vitória, Brazil.

Andressa Karla Luz de Moraes
Young Investigator Grant Recipient. Federal University of Espírito Santo, Vitória, Brazil.

Rafael da Cruz Araújo Vieira
Researcher. Epidemiology Laboratory, Infectious Diseases Center, Federal University of Espírito Santo, Vitória, Brazil.

Reynaldo Dietze
Coordinator. Infectious Diseases Center, Federal University of Espírito Santo, Vitória, Brazil.

Rita de Cassia Duarte Lima
Professor. Postgraduate Program in Collective Health, Federal University of Espírito Santo, Vitória, Brazil.

Ethel Leonor Noia Maciel
Adjunct Professor of Epidemiology. Epidemiology Laboratory, Postgraduate Program in Collective Health, Federal University of Espírito Santo, Vitória, Brazil.