Conformance contrast testing between rates of pulmonary tuberculosis in Ecuadorian border areas*

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Abstract

Objective. To estimate rates of cases of respiratory symptomatic subjects and the incidence rate of pulmonary tuberculosis in two border areas of Ecuador, and contrast them with official figures. **Materials and methods.** Cross-sectional survey in the southeastern (SEBA), and the Andean southern Ecuadorian border areas (ASBA), which were conducted, respectively, in 1 598 and 2 419 persons aged over 15 years recruited over periods of three weeks. In identified respiratory symptomatic cases, a sputum sample was taken for smear testing. The results (odds ratios and their respective 95% confidence intervals), were compared with local and national official figures using maximum likelihood contrasts. **Results.** The rates of respiratory symptomatic subjects (7.7% and 5.9% in the SEBA, and ASBA, respectively) and of pulmonary tuberculosis (cumulative incidence rates of 125 and 140 per 100 000 inhabitants, in the same order) were significantly greater than the official figures (of 0.98 and 0.99% for respiratory symptomatic subjects in the SEBA and ASBA, respectively; and of 38.23 per 100 000 inhabitants for pulmonary tuberculosis in Ecuador as a whole) (p<0.001). **Conclusion.** It is necessary to reinforce both active case finding for respiratory symptomatic subject cases, and epidemiological surveillance of pulmonary tuberculosis in Ecuadorian border regions.

Keywords: pulmonary tuberculosis; poverty; diagnosis; statistics; Ecuador

Ortiz-Rico C, Aldaz C, Sánchez-Pérez HJ, Mateo MM, Romero-Sandoval N. Pruebas de contraste de conformidad en tasas de tuberculosis pulmonar en zonas fronterizas de Ecuador. Salud Publica Mex 2015;57:496-503.

Resumen

Objetivo. Determinar las tasas de sintomáticos respiratorios y de incidencia de tuberculosis pulmonar en dos zonas fronterizas de Ecuador, y contrastarlas con cifras oficiales. **Material y métodos.** Encuesta transversal aplicada en comunidades fronterizas Sur Oriental (FSO) y Sur Andina (FSA) a 1 598 y 2 419 mayores de 15 años, respectivamente. A los sintomáticos respiratorios se les realizó una baciloscopía en esputo. Las tasas y razón de momios se compararon frente a cifras oficiales mediante contraste de verosimilitudes. **Resultados.** Las tasas de sintomáticos respiratorios (7.7 y 5.9% en FSO y FSA, respectivamente) y de tuberculosis pulmonar (incidencia acumulada 125 y 140 por 100 000 habitantes, respectivamente) discrepan de las cifras oficiales (0.98 y 0.99% de sintomáticos respiratorios, respectivamente; y, 38.23 por 10^5 habitantes para tuberculosis pulmonar en Ecuador) (p<0.001). **Conclusión.** Fortalecer la búsqueda de sintomáticos respiratorios y la vigilancia epidemiológica de la tuberculosis pulmonar en áreas fronterizas.

Palabras clave: tuberculosis pulmonar; pobreza; diagnóstico; estadísticas; Ecuador

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It is now over a decade since groups affiliated to the international network for health studies GRAAL (*Grups de Recerca d'Amèrica i Africa Llatines*), dedicated to the analysis of pulmonary tuberculosis (PTB), opted to tackle the problems represented by this disease through an approach differing from the usual population studies, i.e. which are based on representative general population samples. In this approach population groups analyzed are defined by their situation of marginality, and hence with a low likelihood of being selected in representative probability samples. This perspective of PTB focused on marginal groups, which are generally the ones facing greater difficulties to access health prevention, diagnostic and treatment services for PTB, has been used in the denominated *patchwork studies*.[1]

Studies of the prevalence of PTB in unofficial urban settlements in Lima, Peru, as well as in areas inhabited by Mayan ethnic groups in Chiapas, Mexico, and areas inhabited by Panzaleo ethnic groups in Cotopaxi, Ecuador, have reported high rates of respiratory symptomatic individuals (RS) and of PTB sufferers, not identified by the health services.[2,3] This illustrates a problem of invisibility regarding the magnitude of this disease in highly marginalized areas, whether in terms of official statistics, or in terms of population studies using representative samples in particular regions or countries, whereby these "global" rates smooth over, or make invisible, these realities.

Although the relationship between risk of suffering PTB and residing in localities of low socio-economic conditions has been extensively described,[4,5] as well as the patterns of geographical variability in relation to prevention of PTB associated to socioeconomic determinants (life expectancy, educational level, income, among others),[6,7] insufficient attention has being paid to analysis of the PTB situation in socially vulnerable areas.

Borders constitute one such area; in other words, adjacent territories between countries, which come to be a space of shared actions at economic, cultural and social levels; spaces of interaction in terms of circulation of people, goods and products;[8] and in a very particular way, in terms of health.

In this context, population movements in border areas ought to be taken into consideration for surveillance, follow up and recording of communicable diseases,[9] since the failure to do so when planning and implementing actions to control, for example, PTB leads to an increased risk of failing to detect and cure cases, as well as leading to more defaulting from treatment, more multi-drug resistant TB cases (MDR TB) and more deaths associated to the disease.

In Ecuador it has been noted that although conditions of extreme poverty have diminished notably, there are important inequalities in demographic and socioeconomic indicators, particularly in areas of medium and low population densities.[10] This suggests the existence of clearly differentiated population groups for which global rates are concealing serious problems in the prevalence of PTB. Thus the unmet health needs of certain population groups, such as those in marginal areas, go unnoticed and consequently receive no care or resources.

In 2012, according to figures of the Ecuador National Tuberculosis Control Program (PNCT) the incidence of PTB for the country as a whole was 38.23 per 100 000 inhabitants; the groups aged 15 to 64 years were the most affected, and the rate of detection of RS, was 0.78%, although the PNCT estimates the rate of RS among persons spontaneously attending health units to be 4%.[11]

In one south-eastern Ecuador border region (Morona Santiago), the incidence rate of PTB in 2012 was 37.07 per 100 000 inhabitants (population in 2010: 147 940) and the proportion of RS cases was 0.98%, whereas in the Andean southern border region (Loja) the incidence of PTB was 7.73 per 100 000 inhabitants (population in 2010: 448 966) and the proportion of RS was 0.99%.[11]

In the present study, it was proposed, first, to contextualize the characteristics of the social indicators for the Ecuadorian regions of the southeast border and the Andean southern border, based on information available in the 2010 Population and Housing Census;[12] and, second, via active case-finding of RS in both these border regions, conduct a conformance contrast analysis, with respect to the official figures. The participating communities, due to their small population size, very probably would not be represented in a national-level study, or even in a regional study, based on representative samples of this level of population breakdown.

Materials and methods

Study area

In order to contextualize the characteristics of the socio-economic indicators of the southeast border and Andean southern border regions, as well as for Ecuador as a whole, we used data files published by the 2010 Ecuador Population and Housing Census (CPVE-2010) (table I). The CPVE-2010 was a multi-objective national survey carried out by the Ecuador National Statistics and Census Institute, designed to provide information about a broad range of demographic and socioeconomic aspects of the Ecuadorian population.

The survey consists of three sections. 1. Dwelling: poor quality dwelling, get water from well or river, electricity, rubbish collection, kitchen, wood or kerosene as fuel for cooking, house has no toilet. 2. Household: overcrowding,

Table I
Dwelling, household and population characteristics for Ecuador, Southeast and Andean southern border, 2010

Indicator	*Ecuador*	*Southeast border (Taisha)*	*Andean southern border (Alamor)*
Dwelling characteristics			
Dwellings*	3 280 491	1 166	2 476
Poor quality housing‡	0.13	0.07	0.05
Get water from rain, well or river‡	0.21	0.82	0.38
No electricity‡	0.05	0.70	0.04
No rubbish collection‡	0.23	0.83	0.43
No kitchen‡	0.18	0.23	0.13
Wood or kerosene as fuel for cooking‡	0.07	0.76	0.13
House has no toilet‡	0.11	0.70	0.14
Household characteristics			
Households*	3 119 762	1 174	1 962
Overcrowding‡	0.34	0.44	0.35
Average persons per bedroom*	1.42	2.15	2.17
No household member has mobile phone‡	0.24	0.96	0.18
Population characteristics			
Inhabitants*	14 483 499	5 949	8 296
Population density (inhabitants/Km^2)	51.08	3.58	12.90
People living in rural areas‡	0.37	0.83	0.46
Self-describe as indigenous‡	0.07	0.88	0.02
Cannot read or write‡	0.06	0.13	0.07
Does not contribute to Social Security‡	0.73	0.78	0.76
Total number of general physicians[a] (physicians per 1 000 inhabitants)	6 968 (0.48)	7 (1.18)	8 (0.96)

* Absolute frequency
‡ Proportion

Source: reference 12 and 14[a]

average persons per bedroom, no household member has mobile phone. 3. Population Data: inhabitants, population density per km^2, people living in rural areas, self-describe as indigenous, cannot read or write, do not contribute to Social Security.[13] For total number of general practitioners, the information used was provided by the 2010 edition of Statistics on Health Resources and Activities.[14] The databases are accessible via the INEC website as data files for the Statistical Package of Social Science (SPSS). The symptoms of PTB were obtained through a survey applied by interviewers, for all the participants, and were analyzed for the entire study group.

Design

Cross sectional study in two temporal steps: First, in the southeast border area (SEBA), the study was conducted in one area (Taisha) with approximately 100 widely dispersed and remote communities, which can take three days to reach, travelling on foot and by canoe, or 30 minute flight from the nearest town. According to the 2011 census, the region has over 5 949 inhabitants. Second, in the Andean southern border area (ASBA) the study was carried out in two localities, a marginal urban neighborhood (Motupe) with a population of approximately 19 000 inhabitants, and in the Alamor area, with an approximate population of 8 296 inhabitants.[15]

Fieldwork was planned to take advantage of visits programmed by the Ministry of Public Health to the studied communities. The ministry's operational units provided the necessary transport facilities to reach the communities. The periods of stay in each area to collect data and samples were established, in accord with the logistic support provided by the Ministry, as periods of three weeks; the visits took place in November 2013 (Taisha), March 2014 (Motupe) and July 2014 (Alamor). The survey team consisted mainly of resident doctors of the Family and Community Medicine Specialty of the Central University of Ecuador and National University of Loja.

Study population

Recruitment was carried out in Ecuadorian communities of the SEBA (1 598 participants) and the ASBA (2 144 participants). Individuals aged over 15 years were surveyed to identify RS (i.e. active case-finding), collecting socio-demographic, epidemiological and clinical information related to PTB.[2]

Laboratory analysis

Sputum samples for smear testing were collected and analyzed following regulations and procedures of the Ecuador National Tuberculosis Control Program, which defines as smear positive for PTB any person in whom at least one bacillus is detected in Ziehl-Neelsen tincture. The samples were examined in each PTB reference laboratories of the Control Program areas.

Statistical analysis

The results obtained are described, for RS, in terms of the hidden prevalence rates and for PTB the three-week cumulative incidence rates, with their respective 95% confidence intervals (95%CI). The contrast between the observed rates and those recorded in official statistics (local rate for RS and national rate for PTB) was performed using likelihood ratio (LR) contrasts and the corresponding statistic (G^2), the level of statistical significance being taken as $p<0.05$. Associations between study variables (sex, migration, PTB history, overcrowding, geographical accessibility, and number of PTB associated symptoms) and the condition of being RS were analyzed using prevalence ratios (PR), and their respective 95%CI. Multivariate analysis of RS in terms of these variables was performed via logistic regression modelling, crude and adjusted odds ratios (OR), and their respective 95%CI. The data were analyzed using the SPSS, version 21.

Ethical considerations

The research protocol was approved by the Ethical Committee of the Ecuador Central University, as well as by the Ecuador Ministry of Public Health Directorate of Research. The study was performed in compliance with relevant laws and institutional guidelines and in accordance with ethical standards of the Declaration of Helsinki. Written informed consent was obtained from all study participants or their parents/guardians.

Results

Socioeconomic indicators obtained by the CPVE-2010 reveal conditions of marginality in the studied regions, particularly in the SEBA: high proportion of rural population, high proportion of population who self-declare to be indigenous, high proportion of persons who obtain water from wells or rivers, use wood as fuel for cooking, do not have rubbish collection, and do not contribute to the Ecuador system of social security. The number of physicians per 1 000 inhabitants in these areas was different compared to the country as a whole; in the SEBA was 2.5 times higher than Ecuador, while in the ASBA was two times higher (table I).

Regarding the results from fieldwork, in the SEBA the 1 598 participants, from 82 different communities, presented a mean age of 31.5 years (SD 14.7), 58% were men, and 82% self-declared themselves to be indigenous; 70.8% declared that they continually moved their place of residence to other territories, of whom 33.2% did so for work-related reasons, 10.9% to seek medical care, 55.9% to visit family or friends. We detected 123 cases of RS (7.7%; 95%CI 6.4-9.0), the contrast of this rate with that officially recorded for this region for 2012 (0.98%) presented a statistically significant difference ($G^2 = 295.1$; p value <0.001).

Smear-testing was carried out in 119 (96.7%) cases of RS, of whom two were PTB-positive (three-week cumulative incidence rate of 125 per 100 000 inhabitants), one of them being multi-drug resistant (MDR). In this indicator the differences were markedly significant with respect to the national level (38.23 per 100 000 inhabitants) ($G^2 = 34.8$; p value <0.001).

In the ASBA, the 2 144 participants came from 28 different communities, their mean age was 37.2 years (SD 19.1), all self-declared themselves to be *mestizos*, and 50.2% were men; 33.1% habitually travel to other communities, of whom 66.6% reported doing so for work-related reasons, and 33.4% to seek medical care. We detected 127 RS, representing a proportion of 5.9% (95% CI 4.9 – 6.9) which is notably higher than the official figure for the region (0.99%) ($G^2 = 246.1$; p value <0.001).

Of the 72 (56.69%) cases of RS who were smear-tested, three were PTB positive (three-week cumulative incidence rate of 140 per 100 000 inhabitants). In this case also the differences with respect to national level figures were highly significant (G^2 de 39.1; p value <0.001).

Characteristics of RS cases in the two border regions studied

Variable categories accounting for the greatest numbers of RS were: male sex, migration to other communities, family history of PTB in the last two years, personal history of PTB, living in overcrowded conditions, having had more than two symptoms associated with PTB in the last two weeks (fatigue, fever, loss of weight, loss of appetite, haemoptysis), and living more than two hours travel-time away from the nearest health centre. Table II presents the results

Table II
Characteristics of respiratory symptomatic subject cases (RS) in the border regions studied, 2014*

Variable	*Value*	*RS n (%)*	*No RS n (%)*	*Prevalence rate (95%CI)*
Sex	Male	151 (8.04)	1728 (91.96)	1.51 (1.18-1.63)
	Female	99 (5.31)	1764 (94.69)	
Migrates from home	Yes	145 (7.88)	1695 (92.12)	1.42 (1.12- 1.82)
	No	105 (5.52)	431 (94.48)	
History of PTB in household in last two years	Yes	26 (22.80)	88 (77.20)	3.69 (2.58-5.30)
	No	224 (6.17)	3404 (93.83)	
He/she has been previously diagnosed with PTB	Yes	12 (35.29)	22 (74.71)	5.50 (3.43-8.81)
	No	238 (6.41)	3470 (93.59)	
Fatigue	Yes	110 (30.05)	256 (69.95)	7.25 (5.79- 9.08)
	No	140 (4.14)	3236 (95.86)	
Fever	Yes	67 (35.26)	123 (64.74)	6.85 (5.39-8.69)
	No	183 (5.15)	3369 (94.85)	
Loss of weight	Yes	101 (24.10)	318 (75.90)	5.38 (4.27-6.78)
	No	149 (4.48)	3174 (95.52)	
Loss of appetite	Yes	73 (27.23)	195 (72.76)	5.34 (4.19-6.81)
	No	177 (5.09)	3297 (94.91)	
Hemoptysis	Yes	25 (59.52)	17 (40.48)	9.79 (7.40-12.95)
	No	177 (5.09)	3297 (94.91)	
Overcrowding	Yes	107 (9.43)	1027 (90.57)	1.72 (1.35-2.19)
	No	143 (5.48)	2465 (94.52)	
More than two respiratory symptoms	Yes	130 (27.65)	340 (72.35)	7.51 (5.99-9.43)
	No	120 (3.67)	3152 (96.33)	
Travel-time from residence to health services	>2 hours	76 (11.86)	548 (88.14)	2.18 (1.69-2.83)
	<2 hours	174 (5.58)	2944 (94.42)	

* All relationships were significant (*p* value <0.001)
RS: respiratory symptomatic subjects

Table III
Univariable and multivariable relationship between respiratory symptomatic subjects and covariates, 2014*

Variable	*Univariable analysis unadjusted OR*	*95%CI*	*Multivariable analysis adjusted OR*	*95%CI*
Sex	1.56	1.20-2.02	1.66	1.24-2.22
Migrates from home	1.46	1.13-1.89	1.44	1.07-1.93
History of PTB in household in last two years	2.74	1.25-5.50	3.22	1.85-5.62
Been previously diagnosed with PTB	7.93	3.89-16.39	5.29	2.16-12.93
Overcrowding	1.79	1.38-2.33	1.94	1.46-2.60
More than two respiratory symptoms	10.04	7.65-13.18	12.35	9.25-15.62
Travel-time from residence to health services	2.35	1.76-3.12	2.67	1.94-3.65

Reference category: female, no migrates from home, no history of PTB in household in last two years, no been previously diagnosed with Tb, no overcrowding, less than two respiratory symptoms, <2 hours travel-time from residence to health services

* All the relationships were significant (*p* value <0.001)

obtained in the bivariate analysis (prevalence ratio, PR), while table III presents those for the multivariate analysis (unadjusted OR / adjusted OR). In both cases, PR and unadjusted OR / adjusted OR, the variables that showed a strong association with the condition of being SR were have more than two symptoms (PR 3.69 95%CI 2.58-5.30; unadjusted OR 10.04 95%CI 7.65-13.18; adjusted OR 12.35 95%CI 9.25-15.62) and history of PTB in household in last two years (PR 7.51 95%CI 5.99-9.43; unadjusted OR 10.04 95%CI 7.65-13.18; adjusted OR 12.35 95%CI 9.25 -15.62).

Discussion

The results found are in agreement with other studies of populations marginalized in socioeconomic terms and in access to health services, carried out not only in Ecuador[3] but also in México,[16] and in which the patchwork methodology was also used.

The differences in rates obtained of RS for the two regions analyzed, of 7.7% in the southeast border region and 5.9% in the Andean southern border region, contrast with the official figures for these regions (0.98 and 0.99% respectively), something which may possibly be due to failure to actively search for RS cases, to the fact that sputum samples are not properly collected by the health services, either a consequence of poor quality or insufficient samples, or not ensuring subjects meet criteria for the definition of RS (for example, in order to cover established quotas of samples, these are taken indiscriminately from subjects, whether they meet criteria to be RS or not), as well as to under-notification, despite being obligatory, of RS cases. The criteria to diagnose RS subjects in the study were the same used by the health services in their daily practice, and it is the same to whole Ecuador.

In regard to PTB, the rates found in the two regions, of 125 and 140 cases per 100 000 inhabitants over three weeks, respectively, were at least four times higher than those recorded at national level, of 38.23 per 100 000, but over the 52 weeks of the year. These marked differences could be due to the conditions of marginality in the studied regions, to the geographical inaccessibility to health services, to the high proportion of immigrants,[17] to weaknesses in the TB Control Program in terms of active seeking of RS cases, or to poor data quality of the TB surveillance system, among other aspects.[18]

The interest in the strategies of primary health care for early detection of chronic diseases and their prevention is indisputable. Tuberculosis, as chronic infectious disease, requires the use of proactive methods to search for the sick, which goes beyond the "adjustments to an average general practice"[19] estimated for identifying respiratory symptomatic individuals, conducting smear and allocation of budgets for treatments. It is important to keep strengthening the first care level technicians program in order to reinforce the public health system in communities with low accessibility and favour conditions to avoid the presence of PTB.

In this context, it is noteworthy that of the two PTB cases diagnosed in the SEBA, one was MDR. And this despite the fact that since 2011 Ecuador has a program of economic incentives as a strategy for improving MDR treatment compliance and prevention of transmission, something which has significantly reduced the economic burden on patients during their treatment.[20]

If we suppose that the studied areas were representative of the entire SEBA and ASBA, and meeting assumptions of the Poisson distribution (temporal and geographical homogeneity), we would be facing a situation requiring urgent reinforcement of the National Tuberculosis Control Program. The surprising data in terms of the number of general practitioners in the studied areas, with respect to Ecuador as a whole, show a decisive action by Ministry of Public Health to strengthen the public health system. However, given the small number of inhabitants, an increase of just a general practitioner entails a substantial change in terms of the indicator, but does not solve the problems of accessibility, neither search strategy of respiratory symptomatic subjects, among others.

Finally, the word "patchwork" implies a vision formed from "scraps" that aims to show the overall situation in marginalized areas with common characteristics. In this case, the common feature is to be border areas that pose an additional risk by the mobility of the population; and therefore, for the diagnosis, treatment and follow-up of the patients.

Regarding limitations of the study, these are related to 1) the short time in which field work had to be carried out (three weeks), which in its turn was conditioned by health unit scheduling; 2) possible problems in the quality and quantity of sputum samples obtained for the study (we took only one per patient); 3) cultures were not processed in strict accordance with National Tuberculosis Control Program norms.[21] This aspect could be considered particularly relevant if we take into account, on one hand, the low sensitivity of smear tests obtained in marginalized areas;[22] and on the other, the numbers of RS (at least one third of them) who in addition to expectoration, presented three or more symptoms associated with PTB, very probably implying that the PTB rates found were underestimates. Also, patchwork studies do not attempt to generalize results from particular vulnerable groups of populations, but

they deserve special attention under a broader conception of human rights.[17]

Conclusions

Active case-finding of RS and epidemiological surveillance of PTB in the areas studied, on the Ecuadorian border, require to be reinforced, as should also be done in other regions in a similar situation, in order to allow identifying and improve actions to combat the prevailing PTB conditions.

In this sense, carrying out *patchwork* studies allows us to visualize and understand the epidemiological situation of marginalized population groups, not represented in national or even regional level health rates. The results obtained show how important it is to broaden the scope of these studies to communities which, due to problems of marginalization and accessibility, tend to be excluded from health programs, and from official health statistics. As in other studies conducted under the patchwork concept, these results have been placed at the disposal of the different administrative levels of the Ministry of Public Health of Ecuador.

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