UNIVERSIDAD SAN FRANCISCO DE QUITO

# DIAGNOSIS AND TREATMENT DELAYS OF PULMONARY TUBERCULOSIS IN A TERTIARY HEALTH CARE CENTRE IN A SOUTH AMERICAN COUNTRY (Guayaquil – Ecuador)

Proyecto de tesis requerido por el Colegio de Ciencias de la Salud para obtener el titulo de Doctor en Medicina y Cirugía.

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**Diagnosis and Treatment Delays of Pulmonary Tuberculosis in a Tertiary Health Care Centre in a South American Country**

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There was no financial support for this study.

**ABSTRACT**

**Study objectives:** To determine the causes for delays in diagnosis and treatment of pulmonary tuberculosis, and the causative factors of such delays in an Ecuadorian population.

**Design:** Retrospective study

**Setting:** Pulmonology Department of the Second Division Hospital of the Ecuadorian Armed Forces, "Hospital de Division II –D.E. – LIBERTAD". Guayaquil-Ecuador

**Patients :** This observational study included 110 patients with confirmed diagnosis of pulmonary tuberculosis attended by the hospital's Pulmonology department

**Intervention**: none

**Results:** A total of 125 delays occurred, 56 of them were attributed to the patient and 69 to the health care system. Delays attributed to the patient were composed of longer time intervals than those related to the health care system (53 days ± 40.19 SD vs. 10.20 days ±13.73 SD). The factors most significantly related to delays were low educational level OR 2.4 (p=0.04), fever OR 2.7 (p= 0.03), hemoptisis OR 2.6 (p=0.04) and dyspnea OR 2.9 (p=0.01).

**Conclusions:** Delays attributable to the health care system occurred more frequently, but those attributable to the patient involved longer time periods. The factors most significantly related to delays were, paradoxically, those that provide strong evidence of respiratory impairment and disease.

**KEY WORDS**

Symptomatic pulmonary tuberculosis

Delays attributable to the patient

Delays attributable to the health care system

Factors related to delays

**ABREVIATION LIST**

**SD:** Standard deviation

**OR:** Odds ratio

**AFB:** Acid Fast Bacilli

**ANOVA:** Analysis of variance

**HIV:** Human Immunodeficiency Virus

**COPD:** Chronic obstructive pulmonary disease

# Diagnosis and Treatment Delays of Pulmonary Tuberculosis in a Tertiary Health Care Centre in a South American Country

## INTRODUCTION

Tuberculosis is a major health problem throughout the world. It is the second leading cause of death, affecting approximately 1 million people each year (1-2).

Ecuador is a South American country located in the pacific coast of the continent. It is and divided into four main regions, the coast, highlands, rainforest and the Galapagos Islands, and it has 13 026 891 inhabitants (3). Guayas is the province where this study was performed, it is located in a coastal region, its capital is Guayaquil. The city and its surrounding rural areas have 2 515 146 inhabitants. In 2004, 2 318 new cases of AFB + tuberculosis were reported in Guayaquil. This represents 53,41% of the nationwide reported cases (6).

Data from 2004 show that 41.5% of the Ecuadorian population is poor while 8.5% is extremely poor (4). The country's health care system only covers an average of 30% of its inhabitants. Tuberculosis in Ecuador is common, with variable reported incidences in the last ten years. Reports in 2004 show an incidence of 62/100 000 new cases; being 5 789 new cases of all forms of tuberculosis of which 78% were AFB (+) (4).

The prevalence of the disease is 210/100 000 habitants with a mortality rate of 28/100 000 habitants per year (6). However, the true impact of tuberculosis in Ecuador is unknown because of a poor national disease reporting system. Only 3 of the 19 provinces of Ecuador , Pichincha, Guayas and Azuay, had a government sponsored tuberculosis treatment and follow-up program, this leaves approximately 47.3 % of the

country's population unattended. As a result of Canadian cooperation, three more provinces will be included in the program this year (5).

Pulmonary tuberculosis is a disease transmitted by airborne droplets; patients with active disease (vs. carrier patients) release the microorganism by coughing and speaking. The probabilities of infection depend mainly on the duration of exposure and the immune status of the subject. Therefore early diagnosis and treatment are essential for prevention of transmission and spread, as well as progression to the deadly outcome of the disease (7) (8).

The early diagnosis of pulmonary tuberculosis is a process that depends on patients, health care personnel, and also on correct guidelines that assure that this is a quick and effective process (9).

This study's objective is to determine the factors related to delays in diagnosis and treatment of pulmonary tuberculosis in untreated symptomatic patients in a tertiary health care centre in Guayaquil-Ecuador.

## MATERIALS AND METHODS

The present study was performed at the Second Zone Armed Forces Regional Division Hospital in Guayaquil, Ecuador.

Medical records of the Pulmonology Department from January 1$^{st}$ 2000 to June 30$^{th}$ 2004 were reviewed for Acid Fast Bacilli (AFB) positive pulmonary tuberculosis cases. The following data from these cases was retrieved: age, sex, educational level (elementary, high school, college), socio-economic status (high, medium, low), ethnic

group (indigenous, caucasian, african-american, mestizo), medical insurance type (active military, passive military, military family member, civilian), alcohol, tobacco and tuberculosis exposure (yes/no), co-morbidity, pulmonary tuberculosis related symptoms (cough, expectoration, fever, weight loss, hemoptisis, chest pain), date of symptoms appearance, date of the first suspicion of pulmonary tuberculosis, date of the beginning of the diagnostic procedure, and date of initiation of treatment.

Case definition.-

A case was defined as the patient from whom *Mycobacterium tuberculosis* was isolated and had any of the following: cough, expectoration, fever, hemoptisis, chest pain, dyspnea, radiologic signs, positive sputum baciloscopy, gastric juice or bronchoscopy with positive *M. tuberculosis* results.

New cases were defined as those who had never been diagnosed or received treatment for tuberculosis.

Delay and intervals definitions.-

Interval and delay attributable to the patient: time elapsed between the first symptom appeared and the first medical appointment. A delay was considered more than 30 days.

Reference interval and delay attributable to the doctor: time elapsed between the first medical consult and AFB stain demand. A delay was considered more than 2 days.

Diagnostic interval and delay: time elapsed between culture demand and sample collection. More than 1 day was considered a delay.

Treatment interval and delay: time elapsed between diagnosis and beginning of treatment. More than 1 day was considered a delay.

Interval and delay attributable to the health care system: time elapsed since the first medical consult and the beginning of treatment. More than 4 days was considered a delay.

A final outcome, or total delay, was considered as the delays attributable to the patient and health care system together.

Statistical Analysis.-

Continuous variables with normal distribution are shown as means ± standard deviation, and percentages for categorical variables. Variables that do not follow a Gauss distribution were shown as medians. Student's t test and ANOVA were used to compare arithmetic means that follow a Gauss distribution, and Kruskall – Wallis for means. Kolmogorov-Smirnov's test was used to compare normality of data and Levene's test to compare homogeneity of variances.

Chi-square and Fisher's test were used to compare qualitative variables with dicotomic answers. The dependent variables (delays attributable to the patient and health care system) were analysed with each independent variable.

A multiple logistic regression model was applied, using as dependent variable delays attributable to the patient, health care system and total delay. A p value $< 0.05$ was considered as statistically significant.

## RESULTS

Sample description and Socio-economic characteristics.-

110 patients living in the urban and rural regions of Guayaquil were analysed, their characteristics are shown in table 1.

Tuberculosis, alcohol and tobacco exposure.-

39 (35.5%) had a history of alcohol consumption. 13 (12.8%) patients had previous exposure to pulmonary tuberculosis patients. 20 (18.2%) patients were active smokers.

Comorbitiy and nutritional status.-

24 (21.8%) patients had other coexistent diseases, diabetes was the most common with 13 (11.8%) cases. Others were COPD 4 (3.6%), asthma 3 (2.7%), HIV 1(0.9%), others 3 (2,7%). Nutritional state was approximated with the calculation of the Body Mass Index. 50 (45.5 %) patients fell within normal ranges, 44 (40%) were malnourished, 7 (6.4%) were overweight and 9 (8.2%) were obese.

Signs, symptoms and radiologic findings.-

The main symptoms presented by the patients were: cough 106 (96.4%), expectoration 81 (73.6%), weight loss 62 (56.4%), dyspnea 41 (37.3%), chest pain 30 (27.3%), fever 57 (52.8%) and hemoptisis 34 (30.9%). Of all the patients, 73 (66.4%) of them presented abnormal physical examinations. These abnormalities were: rales 44 (40%), decreased breath sounds 42 (38.2%), wheezing 15 (13.6%), ronchi 14 (12.7%), heart murmur 9 (8.2%). Radiologic findings were as follows: none 4 (3.6%), unilateral 71 (64.5%) and bilateral 35 (31.8%) Their distribution was interstitial 74 (67.3%),

condensation 9 (8.2%), cavitary 5 (4.5%), interstitial and cavitary 9 (8.2%), interstitial and condensation 9 (8.2%).

Delays.-

The number of times delays occurred was 125. Of those, 56 (50.9%) were attributable to the patient and 69 (62.7%) to the health care system.

The total interval delay mean was 63.27 days ± 43.92 SD, with a median of 59 (range 5-212) days. Total interval delay is composed of the interval delay attributable to the patient 53.06 ± 40.19 SD, median 38.5 days, and the interval delay attributable to the health system was 10.20 ±13.73 SD, median 7 (range 1-97) days. These elements are shown in figure 1.

Multivariate analysis showed that educational level OR 2.4 (CI 1-5.7) p=0.04, fever OR 2.7 (CI 1-6.9) p=0.03, hemoptisis OR 2.6 (CI 1-6.9) p=0.04 and dyspnea OR 2.9 (1.2-6.6) p=0.01 were the variables that most influence had on the model. Female patients had a mean delay of 58.7 ±40.3 SD compared to male patients 48.3 days ±39.8 SD (p=0.001). People 45 years old or older had greater delays in seeking medical attention (62.7 ± 44.1 SD vs. 46 ± 35.8 SD) (p=0.001). People living in rural areas had a mean of 51.2 ± 39.6 SD days in delay compared to 5.9 ± 41.3 SD days of those who lived in urban areas (p=0.001). Finally, a factor associated with delays between the symptom appearance and medical attention seeking was a low educational level (p=0.005).

## DISCUSION

We found that delays were more frequently attributable to the health care system, but that higher delay intervals were significantly attributable to the patient. That is, it was more common for the health care system to provoke a delay, but when patients provoked delays, they involved a significantly higher number of days.

The interval delays we report, both for patients and health care system, are similar to those presented by other studies (10-11-12-13).

Statistical analysis showed that the factors most related to delays attributable to the patient were: sex, age, rural origin, socio-economic status, co-morbidity and, paradoxically, the presence of classical pulmonary tuberculosis signs.

Female patients had a mean delay of 58.7 ±40.3 SD compared to male patients 48.3 days ±39.8 SD (p=0.001). Other studies have also found this difference (14-15-21). It has been suggested that women may receive inferior health care because of doctor's attributable delay in diagnosis (14). Males and females show comparable health-seeking behaviour (14), however, differences in the access and utilization of health care services between both sexes have also been acknowledged (23). In the rural setting, women have important roles in the agricultural work and in the household, which leaves them less time to seek medical attention (11). Also women may be more likely to visit traditional healers first, increasing the time delay before going to a health care provider (21). Further research is needed to clarify this issue, not only for reducing the delays in women, but also for decreasing the serious secondary impact on the incidence of tuberculosis in children attended by those women at home (14).

We found that people 45 years old or older had greater delays in seeking medical attention (62.7 ± 44.1 SD vs. 46 ± 35.8 SD) (p=0.001). Two possible explanations have been proposed to account for this difference. First, the active economic role of these subjects is of major importance for family income, and only a very debilitating condition, possibly that interferes with work, would be a reason to seek medical attention (11). The second reason is that many elderly patients have other associated diseases, and the symptomatology could have been interpreted as being part of the "actual disease" already diagnosed and in or to other illness. Studies in industrialized countries have also shown significant delays in diagnosis and treatment related to advanced age, and also attributed them to co-morbidity in this age group, where both the patient and the physician have decreased suspicion of chronic symptoms such as cough (13) Co-morbidity in these patients can also have an effect in the measured delay because of a recall bias, where mistaken symptoms of the pre-existing condition could have altered the reported dates of symptom onset (13).

People living in rural areas had a mean of 51.2 ± 39.6 SD days in delay compared to 5.9 ± 41.3 SD days of those who lived in urban areas (p=0.001). This was mainly attributed to poor availability of proper diagnostic equipment in the rural health care setting.

A Ghanaian study stated that despite having less access to health care centres and more likely to seek alternative medicine, people living in rural areas had no increased delays in seeking medical attention when compared to urban people. The rural people in this study had a longer overall delay, but this was attributable to the doctor's delay. The authors attribute this to poor diagnostic skills, low rates of sputum smear microscopy and over-reliance on central hospital referral (14).

Another factor associated with delays between the symptom appearance and medical attention seeking was a low educational level ($p=0.005$). These patients usually have other accompanying factors such as low socio-economic status and poor access to health services, which along with scarce knowledge of the disease and its consequences, increase the time for seeking medical attention (17-22). When taken together, instruction level and socio-economic status, these factors had a major role in overall delay ($p=0.04$). This is the reason why the improvement of both conditions would be the most influencing policy in diagnosing and treating pulmonary tuberculosis (29)

The symptoms most commonly found in our patients were cough, weight loss, fever and hemoptisis, these are comparable to those found in other studies (18-19). Paradoxically the signs and symptoms most related to total delays were the most debilitating: dyspnea, hemoptisis and fever. This finding could be analysed in the context of the poor educational level and socio-economic status mentioned previously, in which patients wait for their condition to be sufficiently advanced and debilitating in order to seek medical attention.

On the other hand, delays attributable to the health care system ($10 \pm 13.7$) were lower than those found in other studies. This could have occurred by the following reasons. First, a high index of suspicion in patients with pulmonary symptoms and who came from areas of high pulmonary tuberculosis prevalence. Second, the patients in our study were attended by pulmonologists, who as a routine request a chest x-ray. This is not done by general clinicians. S. Paynter (13) observed a delay in the diagnosis of patients first seen by general physicians as compared to those seen in an emergency room. This was attributed the fact that chest x-rays are immediately taken in the latter.

Also on the side of delays attributable to the health care system is the presence of co-morbidities. The signs and symptoms presented by diabetic patients, as well as their radiographic manifestations are atypical. This sometimes requires further diagnostic steps, gastric lavage and bronchoscopy, that increase the delays. In relation to this issue some authors favour empiric treatment for patients with pulmonary tuberculosis suspicion (20). Pulmonary tuberculosis has been highly associated with HIV (27), we only had 1 HIV(+) patient in our study, so statistical significance could nor be achieved or further conclusions drawn.

Variables that were found not to have any significant relation with delays, neither attributable to the patient nor the health care system, were ethnic group, medical insurance, or radiologic evidence of cavitary lesions. This is the same as reported by other studies (24-25-26)

One limitation of this study is that it is retrospective. Because of this some variables could not be considered for analysis. One of them was self-medication, a common practice in Latin-American countries, due to poor control of prescription medication availability (28).

Depending on individual and environmental conditions, one patient with active pulmonary tuberculosis could infect 10 persons annually, and become a reservoir for *Mycobacterium tuberculosis*. The spread and evolution of the disease are proportional to the time patients remain undiagnosed and untreated. Early detection and treatment of

pulmonary tuberculosis are the cornerstones of disease control, both at individual and comunitary levels.

Therefore we suggest that public health interventions that target the patient before he reaches the health care system should include symptom awareness campaigns targeted at specific sex and age groups, and non-medical interventions to improve overall economic and educational levels. Policies to improve the health care system should include decentralisation of tuberculosis management, increasing suspicion and improving diagnostic equipment in the rural setting.

## REFERENCES


1. Enarson DA, Rieder HL, Arnadottir T, et al. Tuberculosis guide for low income countries 4 th ed. Paris, France: International Union Against Tuberculosis and Lung Disease, 1996; pg 1

2. Frieden TR, Sterling TR, Munsiff SS, et al. Center for Disease Control and Prevention. Estimates for future global tuberculosis morbidity. MMWR Morb Mortal Wkly Rep, 1993; 42:961-964. Tuberculosis. Lancet 2003; 362:887-899.

3. United Nations Cartography Section. Geographic Resources and information. List of territories. April 2003. www. Org/Depts/Cartographic/english/geoname/pdf.

4. Pan-American Health Organization in the Americas. Republic of Ecuador. http://www.opsecu.org/orhs.ecuador

5. Guideline Manual for the control of Tuberculosis in Ecuador. DOTS Strategies. July 2005; pg 3.

6. Local conditions and situation of the environmental department of Guayaquil-Ecuador. Technical Assistance. PAHO/WHO. 2001

7. Pío A, Chaulet P. WHO Global Tuberculosis Program. Tuberculosis. Handbook. Geneve: WHO/TB/98. 253

8. Centers for Disease Control and Prevention. Estimates for future global tuberculosis morbility. MMWR Morb Mortal Wkly Rep, 1993; 42:961-964.

9. Raviglione MC, Snider DE, Kochi A. Global epidemiology of tuberculosis: morbidity and mortality of a worldwide epidemic. JAMA 1995; 273:220-226.

10. Guneylioglu D, Yilmaz A, Bilgín S, et al. Factors affecting delays in diagnosis and treatment of pulmonary tuberculosis in a tertiary care hospital in Istanbul, Turkey. Med Sci Monit 2004; 10:62-67.

11. Cheng G, Tolhurst R, Li Rz, et al. Factors affecting delays in tuberculosis diagnosis in rural China: a case study in four counties in Shandong Province. Medicine and Higiene 2005; 99:355-362.

12. Alter-Gómez MN, Alcaide J, Soler C, et al. Study of diagnostic delay in systemic pulmonary tuberculosis. Arch Bronconeumology 2003; 39:146-152.

13. Paynter S, Hayward A, Wilkinson P, et al. Patients and helth service delays in initiating tretment for patients with pulmonary tuberculosis: retrospective cohort study. Int J Tuberc Lung Dis 2004; 8:180-185.

14. Lawn SD, Afful B, Acheampong W. Pulmonary tuberculosis: diagnostic delay in Ghnaian adults. Int J Tuberc Lung Dis 1998; 2:635-640.

15. Sherman LF, Fujiwara PI, Cook SV, et al. Patients and health care system delays in the diagnosis and treatment of tuberculosis. Int J Tuberc Lung Dis 1999; 3:1088-1095

16. Liam CK, Tang BG. Delay in the diagnosis and treatment of pulmonary tuberculosis in patients attending a university teaching hospital. Int J Tuberc Lung Dis 1997; 1:326-332

17. Greenaway C, Menzies D, Fanning A, et al. Delays in diagnosis among hospitalized patients with active tuberculosis: predicts and outcome. Am J Respir Crit Care Med 2002; 165:927-933.

18. Puertas A, Baruque M, Burgos A, et al. Evolución de la tuberculosis en Palencia. Atención Primaria 2001; 27:637-641.

19. Okutan MO. Delays in the diagnosis of Turkish Serviceman with Pulmonary Tuberculosis. Military Medicine 2005; 170:211-213

20. Mathur P, Sachs L, Auten G, et al. Delayed diagnosis of pulmonary tuberculosis in city hospitals. Arch Intern Med 1994; 154:306-310.

21. Yamasaki-Nakagama M, Ozasa K, Yamada N, et al. Gender difference in delays to diagnosis and health care seeking behavior in a rural area of Nepal

22. Cantwell MF, MicKenna MT, McCray E, et al. Tuberculosis and race/ethnicity in the United States. Impact of socioeconomic status. Am J Resp Crit Care Med 1997; 157:1016-1020.

23. Lang NH, Johanson EJ, Lonnroch K, et al. Long delays in tuberculosis diagnosis among, women in Vietnam. Int J Tuberc Lung Dis 1999; 3:399-393.

24. Odusanya O, Babafemi J. Patterns of delays amongst pulmonary tuberculosis patients in Lagos, Nigeria. BMC Public Health 2004; 4:1-5.

25. Wandwalo ER, Morkve O. Delay in tuberculosis case – finding and treatment in Mwanza, Tanzania. Int J Tuberc Lung Dis 2000; 4:133-138

26. Guneylioglu D, Yilmaz A, Bilgin S, et al. Factors affecting delays in diagnosis and treatment of pulmonary tuberculosis in a tertiary care hospital in Istanbul, Turkey. Med Sci Monit 2004; 10:62-67.

27. Ausina V, Riutirt M, Vinado B, et al. Prospective study of drug-resistant tuberculosis in a Spanish population including patients at risk for HIV infection. Eur J Clin Microbiol Infect Dis 1995; 14:105-110.

28. Muñoz D, Ríos G, Villalva C, et al. Factors related to late diagnosis of pulmonary tuerculosis in eastern Lima, Perú. Rev Peru Med Exp Salud Publica 2004; 21:18-22

29. Caminero JA, Caylá J, Lana N, and the Working Group on the Current Status of Tuberculosis in Spain (SEPAR). Evaluation of Tuberculosis trends in Spain 1991-1999. Int J Tuberc Lung Dis 2003: 7:236-242.

30. Rodger A, Jaffar S, Paynter S, et al. Delay in the diagnosis of pulmonary tuberculosis, London, 1998 – 2000: analysis of surveillance date. BMJ 2003; 326:909-910.