Trends in mortality from pulmonary tuberculosis before and after antibiotics in the Portuguese sanatorium *Carlos Vasconcelos Porto* (1918-1991): archival evidence and its paleopathological relevance

Vítor M. J. Matos and Ana Luísa Santos

CIAS – Research Centre for Anthropology and Health,

Department of Life Sciences, University of Coimbra, Portugal

[vmatos@antrop.uc.pt; alsantos@antrop.uc.pt]

Corresponding author: **Vítor M. J. Matos**

E-mail: vmatos@antrop.uc.pt

CIAS – Centro de Investigação em Antropologia e Saúde

Departamento de Ciências da Vida

Universidade de Coimbra

Apartado 3046

P- 3001 401 Coimbra, Portugal

Phone + 351 239 854 108

Fax + 351 239 854 129

Abstract

The comparative study of patients' profiles and outcomes from pulmonary tuberculosis (TB), before and after the discovery of antibiotic therapy, using sanatoria archives is an unexplored approach in paleopathology. Although higher mortality rates are assumed before chemotherapy, scarce information exists regarding the disease's duration in institutionalized patients and to what extent tuberculous sufferers lived enough to develop skeletal lesions. To fill this gap, 315 clinical files from the former male Sanatorium *Carlos Vasconcelos Porto*, located in *São Brás de Alportel*,

Portugal, were studied. Two periods of hospitalization were considered: 1931-1944 (n=128, Group 1) and 1955-1961 (n=187, Group 2). The average duration of hospitalization (350.3 days for Group 1 and 371.8 for Group 2) and the crude mortality (18.2% and 11.2%, respectively in Groups 1 and 2) did not differ significantly between groups. However, Cox's regression revealed significant differences between survival curves, after adjusting for age at admission (14-74 years old), with pre-chemotherapy patients presenting a higher risk of dying during hospitalization (p=0.37, hazard ratio=1.94, IC95%=1.03-3.63). This study also confirms poorer prognoses for pulmonary tuberculosis sufferers hospitalized in sanatoria before antibiotics and reveals that a significant number of patients survived enough time to develop bone lesions.

Keywords

Pulmonary tuberculosis, Sanatoria, Mortality, Survival analysis, Antibiotics, Paleopathology.

1. Introduction

Clinical files from sanatoria are rich sources of both biological and sociocultural data. However these are poorly explored in paleoepidemiological and paleopathological studies [1]. Archival studies devoted to the comparison of the outcomes of pulmonary tuberculosis (TB) in patients interned before and after the medical use of antibiotics are virtually non-existent, nonetheless these sources can undoubtedly contribute to better understand the past history of these conditions. Yet, this issue encompasses not only the obvious historical interest but also has the potential to bring empirical evidence to the current debate around the claims for rebuilding the so-called "new sanatoria" to isolate patients affected by extensively and/or totally drug- resistant TB [2].

The main aim of this investigation is to test if before effective chemotherapy tuberculous patients presented poorer prognoses, namely higher mortality, when compared to those treated with

antibiotics. Additionally, the duration of the internment period is also analysed in order to transpose this unexplored data to the paleopathological context. Ultimately this approach also aims to evaluate if the profile of the institutionalized patients is analogous to the contemporary Portuguese population affected by TB.

These hypotheses were tested by studying clinical files from the first Portuguese private sanatorium, named *Sanatório Carlos Vasconcelos Porto* (SCVP) and located at *São Brás de Alportel*, a place recognized for its excellent climatic conditions to treat pulmonary TB [3]. The SCVP was inaugurated in 8th September 1918 and was active for 73 years. Firstly, between 1918 and 1952, it was exclusively for the internment of the male workers from the Portuguese Railway Company (*Companhia dos Caminhos de Ferro* [CP]) [1, 4-6] who, according to Cabanas [7], presented a high risk of contracting pulmonary TB due to the nature of their job. Later, from 1955 to 1991, it was integrated into the public health system under the supervision of the National Institute for Tuberculous Assistance (*Instituto Nacional de Assistência aos Tuberculosos* [IANT]). After its closure as a sanatorium, it was adapted into the Centre of Rehabilitation Medicine of the South (*Centro de Medicina de Reabilitação do Sul*) [6].

2. Material and Methods

This archival study was based on 315 clinical files preserved from the SCVP, which represent pulmonary TB patients interned during the two periods of activity: a) 128 files from 121 male railway workers interned between 1931 and 1944 (CP period); b) 187 files from 182 males interned between 1955 and 1961, mainly inhabitants of the Southern region of Portugal (IANT period). From the epidemiological point of view each of these periods represents distinct pulmonary TB patients groups: those treated before and after the discovery of antibiotics, and also those who lived before and after either the massive BCG vaccination or the epidemiologic transition in Portugal. This cleavage allows an interesting analytical approach by comparing the two groups of patients.

These files present detailed information collected by the medical doctors, namely the anamnesis and the patient´s history - including the clinical course of pulmonary TB and co-existence of other diseases. Additionally, the medical reports of radiographic exams and sputum bacilloscopy are also available as well as the schematic depiction and description of the pulmonary tuberculous lesions, including their location, extension, prognosis and treatments.

The methodological approach for the present investigation consisted of reading all the content of the clinical files and specific data regarding patient's personal, clinical, epidemiological and therapeutic aspects. These data were gathered and analysed statistically (SPSS Statistics, v. 19.0, IBM SPSS, Chicago, IL).

3. Results and Discussion

3.1. Age at admission

The age at admission in the sanatorium ranged from 14 to 74 years old with an overall mean of 39.28 years (Table 1). No statistical differences were found between the means of the two periods (t=1.120; df=273.34; p=0.26), respectively 40.20 years for CP patients and 38.77 years for IANT ones. This age span and mean age at admission do not correspond to the morbidity and mortality profiles of pulmonary TB in the Portuguese population since the majority of the SCVP patients, both from CP and IANT, were workers and, therefore, non-adults are clearly underrepresented. The Portuguese official statistics reveal that during the first half of the 20th century pulmonary TB had a predilection for young adults although individuals from all ages could be affected (contrary to some other forms of tuberculosis, e.g. tuberculous meningitis which had a higher incidence in non-adults). The high incidence of this disease in ages between 15 and 55 years old clearly represented a social problem, since this was the most active phase [8].

3.2. Duration of the internment

The duration of the internment at the SCVP ranged from 1 to 2509 days (Table 1). The longest stay lasted approximately seven years while short duration internments, corresponding to one week or less, occurred only in 6 patients: one from the CP period, who died 3 days after admission, and the remaining 5 belonged to the period after antibiotics (namely 4 patients who renounced the internment and the remaining one passed away 4 hours after his arrival). The sanatorium regime usually required a long period of internment and, in fact, the overall mean duration of the treatment was 363.22 days.

There are no significant differences regarding the duration of interment between the two periods ($U=10386.5$; $p=0.40$), however, the mean and median are both higher for IANT patients (respectively 371.8 and 249.0 days) when compared with CP ones (respectively 350.32 and 190.0 days). This finding is unexpected since antibiotics were already in use in the sanatorium during the IANT period and the global trend was that the care provided on sanatoria became more medicalized and less palliative [9]. There are a few possible explanations for this scenario: the patients usually were admitted in poor physical conditions and, despite the existence of antibiotics, only a long period of internment could be beneficial to their recovery; the better medical knowledge and diagnosis methods prevented false cures and in consequence shorter internment periods; and/or patients only left the SCVP after finishing the antibiotic treatment.

There are no comparative data from other Portuguese sanatoria regarding the duration of the internment. However, the official national statistics reveal that between 1909 and 1910 the majority of tuberculous patients under treatment at the Sanatorium Sousa Martins (the first public sanatorium for the treatment of pulmonary TB created in Portugal) stayed less than one year.

Developed by the end of the 19th century, the practice of the ‘hygienic triad’, comprising good air, good rest and good food, was still practiced at the SCVP in 1956 as depicted in the schedule of the patients. During the day, besides plenty of fresh air and sun exposure, patients rested a total of 7 hours distributed into 3 periods, one of these in absolute silence, and, additionally, 5 meals were served.

The benefits of the internment on the SCVP were variable although the general health status of some patients improved radically. The weight variation can be regarded as a proxy for the effectiveness of the sanatorium regime. This variable is available only for the patients from the CP period (Table 1). The weight variation ranged from the loss of 10.5 kg to the gain of 41.5 kg, and the overall mean was the gain of 7.50 kg [1]. Only 9.62% (10/104) of the patients lost weight. Before antibiotherapy the gain of weight during the internment was considered by physicians a promising sign of a future clinical cure from pulmonary TB [10]. Unluckily, there is no data about this parameter for IANT patients.

3.3. Mortality

The sanatorium treatment was not always successful as shown by the 14.0% (42/299) of the pulmonary TB patients who died during the internment (Table 1). The average duration of the hospitalization was not significantly different (t=-1.230; df=49.220; p=0.225) between patients who died (450.67 days) or who survived (350.18 days). Although it is impossible to know when these individuals became infected it is noteworthy that after admission the patients who died suffered longer from pulmonary TB. These data are very interesting for the debate around the osteological paradox [11] and the paleopathology of pulmonary TB, by showing that before antibiotics patients, even those who died, survived enough time to develop bone lesions such as new bone formation on the visceral surface of ribs, commonly found on identified skeletons with pulmonary TB recorded as the cause-of-death [12]. The development and wide use of antibiotics, such as streptomycin after 1943, may have contributed to reduced chronicity in TB and the subsequent possibility that bone may or may not be affected.

Non-significant differences were found between the mortality frequencies before and after chemotherapy (χ^2=2.332; df=1; p=0.127) with the proportion of deceased patients being higher for the period before antibiotics (18.2% [22/121] versus 11.2% [20/178]). However, logistic regression revealed statistical differences, after controlling for several variables including the age at admission

and the number of days of internment. The odds ratio of dying during the hospitalization were around 3.5 higher in the patients from the CP period (χ^2_{Wald}=8.370; OR=3.52; IC95%: 1.50–8.24), i.e. before the antibiotic era. Additionally, Cox's regression revealed significant differences between the survival curves (Figure 1) of the two groups after controlling for age at admission (p=0.37; hazard ratio=1.94; IC95%: =1.03-3.63).

These results confirm that pre-antibiotic patients (CP period) with pulmonary TB had worst prognosis, presenting lower survival probabilities during the internment at SCVP. This finding must be considered in the context of pulmonary tuberculosis mortality in Portugal during the 20th century (Figure 2). A tremendous decline in crude mortality from tuberculosis occurred at the end of the 1940's and beginning of the 1950's, related to the epidemiological transition that was taking place in the country [13,14] and to specific public health measures to fight against tuberculosis, including the reorganization of the sanatoria and dispensaries network, the regular use of antibiotics, the massive BCG vaccination of children and routine microradiographs screenings [15].

4. Conclusion

The preservation and study of medical archives from sanatoria is very important for the understanding of TB evolution since these contain relevant information regarding the history of these institutions as well as the paleoepidemiology and social history of tuberculosis. However, it is important to note that these data are biased by each sanatorium's admissions policy, by the partial preservation of archives, and do not represent the general population. Even so, the analyses of the clinical files from the SCVP provided useful information to the study of TB before the antibiotics era. The duration of hospitalization demonstrated that pulmonary TB patients, both before and after antibiotic therapy, can survive for long periods of time and eventually the disease had more time to leave pathological signs on their skeletons. Our results also confirmed the poorer prognoses for pulmonary TB sufferers hospitalized in sanatoria before antibiotherapy: i.e. a higher risk of a fatal

outcome. Moreover, the individuals who died during the internment were hospitalized longer than those who survived. The BCG immunization and a better health care assistance had a very positive effect on the decline of TB in Portugal and contributed to the epidemiological transition.

The study of clinical files from other sanatoria dedicated to the treatment of pulmonary and other forms of TB is necessary to confirm the trends revealed in this research. Moreover, the next step regarding the paleopathological investigation on the SCVP files will consist on the analysis of the distribution and patterns of the tuberculous pulmonary lesions and its correlation with the paleopathological findings derived from individuals with pulmonary TB cause of death from identified skeletal collections. This comparison is expected to provide new clues regarding the accuracy of rib lesions on the diagnosis of pulmonary TB in past human populations.

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Tables and Figures

Table 1. Demographical, clinical and epidemiological parameters compiled from the clinical files of the SCVP. Data for each administrative period (CP – *Portuguese Railways Company* – and IANT – *National Institute for Tuberculous Assistance*) are also presented.

	Total	**CP (1931-1944)**	**IANT (1955-1961)**
Clinical files (n)	**315**	**128**	**187**
Patients (n)	**303**	**121**	**182**
Age at admission (n)	282	100	182
Age range (years)	14-74	25-68	14-74
Mean	39.28	40.20	38.77
Median	39.0	39.00	38.00
Std. Deviation	11.8	8.36	13.03
Duration of internment (n)	303	121	182
Range of days	1-2509	3-2509	1-2147
Mean	363.22	350.32	371.80
Median	227.00	190.00	249.00
Std. Deviation	405.03	426.95	390.74
Weight variation (n)	104	104	-
Weight range (kg)	-10.5 to 41.5	-10.5 to 41.5	-
Mean	7.50	7.50	-
Median	6.25	6.25	-
Std. Deviation	7.98	7.98	-
Death (n)	299	121	178
Number of patients died	42	22	20
% within groups	14.0%	18.2%	11.2%

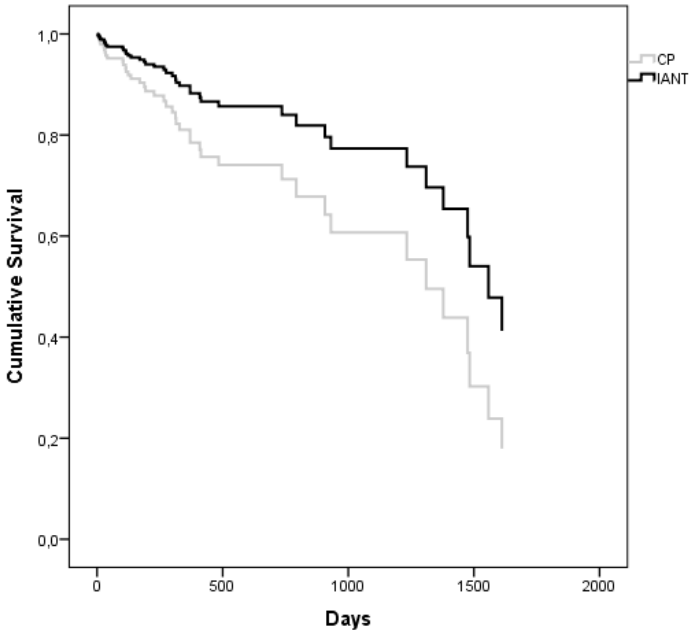

Figure 1. Cox regression analysis of survival amongst the SCVP pulmonary TB patients according to the periods before (CP) and after (IANT) the use of antibiotics.

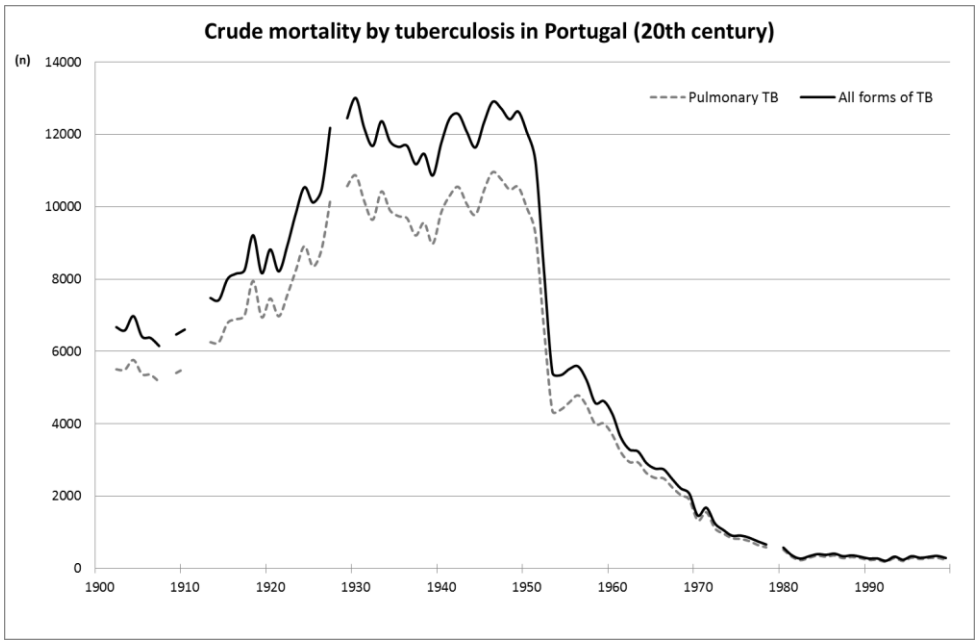

Figure 2. Crude mortality by tuberculosis in Portugal over the 20th century. Data compiled from Statistics Portugal (*INE – Instituto Nacional de Estatística*; http://www.ine.pt) and Pordata (*Base de Dados Portugal Contemporâneo*; http://www.pordata.pt).