






ORIGINAL

Tuberculosis infection trend over 6 years. A retrospective analysis from 2011 to 2016

*Tendencia de la infección por tuberculosis a lo largo de 6 años.
Un análisis retrospectivo de 2011 a 2016*

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Received: 26 - VII - 2022**Accepted:** 12 - VIII - 2022**doi:** 10.3306/AJHS.2022.37.05.123**Abstract**

Introduction: Tuberculosis (TB) remains the leading cause of death from a single infectious agent and a major public health problem in Europe and worldwide. The present study pretends to characterize and evaluate the tendency of TB infections over a 6-year period.

Methods: We performed a retrospective study on patients admitted to a tertiary hospital with tuberculosis, from 2011 to 2016, through electronic medical files' data collection.

Results: We included 591 patients with a peak in 2013, as well as a slight increase in male gender prevalence and length of stay over the 6 years. There was a spike of comorbidities in 2012. A decrease in prevalence in white patients, due to increase in African and Asian was also reported, besides a decline in HIV status, homelessness and IV drugs use. This coincided with an increase in laboratory changes and radiological changes, along with a rise in microbiological resistance.

Discussion: Our data is in line with current health policy reports. It is of utmost importance the effort towards control and elimination of TB, through rapid diagnosis, prompt report and complete treatment.

Key words: Tuberculosis, risk factors, mortality.

Resumen

Introducción: La tuberculosis (TB) sigue siendo la principal causa de muerte por un único agente infeccioso y un importante problema de salud pública en Europa y en todo el mundo. El presente estudio pretende caracterizar y evaluar la tendencia de las infecciones de TB en un período de 6 años.

Metodología: Realizamos un estudio retrospectivo de pacientes ingresados en un hospital de tercer nivel con tuberculosis, desde 2011 hasta 2016, a través de la recolección de datos de historias clínicas electrónicas.

Resultados: Se incluyeron 591 pacientes con un pico en 2013, así como un ligero aumento en la prevalencia de género masculino y la duración de la estancia durante los 6 años. Hubo un pico de comorbilidades en 2012. También se informó una disminución en la prevalencia en pacientes blancos, debido al aumento en africanos y asiáticos, además de una disminución en el estado del VIH, la falta de vivienda y el uso de drogas intravenosas. Esto coincidió con un aumento en los cambios de laboratorio y cambios radiológicos, junto con un aumento en la resistencia microbiológica.

Conclusión: Nuestros datos están en línea con los informes de política de salud actuales. Es de suma importancia el esfuerzo por el control y eliminación de la TB, a través del diagnóstico rápido, el reporte oportuno y el tratamiento completo.

Palabras clave: Tuberculosis, factores de riesgo, mortalidad.

Introduction

Tuberculosis (TB) is an infectious-contagious disease, transmitted between humans through the respiratory route whose etiological agent is *Mycobacterium tuberculosis*¹. Pulmonary tuberculosis is the most frequent manifestation (~70%) and extrapulmonary TB occurs less frequently^{2,3}.

Despite misconceptions that TB is a disease of the past it continues to represent a public health threat even though there is an effective/curative treatment. TB is still the leading cause of death from a single infectious agent worldwide since 2007 and was responsible for 1.18 million deaths in 2017²⁻⁴.

It is a major public health problem in Europe and worldwide with a well-established association between public assistance spending, failure of antibiotic treatment and the rise of multidrug TB resistance and mortality. Despite implementation of control measures, active immunization and improvement in the socioeconomic state of the population in the last century have been achieved³⁻⁷.

In Portugal, the incidence in 2018 was 16.6 cases per 100.000 inhabitants, higher in Lisbon (23,7 cases/100.000 inhabitants)⁸. It has been reported an increase in the age of the TB patients, resulting in a reduction of community transmission⁸. Even though in Portugal, unlike other European countries, the majority of cases occurs in native population, the proportion of cases in people born outside of Portugal has increased (19,2% in 2017 and 20,2% in 2018)⁸.

The present study pretends, therefore, to characterize and evaluate the tendency in demographic, clinical and radiological features, treatment outcomes and mortality over a period of six years.

Methods

A retrospective study on patients admitted to a tertiary hospital from 2011 to 2016, with a tuberculosis (TB) infection diagnosis, was performed. Inclusion criteria were age over 18 years old and an ICD-9 code for TB (010-018). Considering the retrospective nature of the work, ethical approval was waived.

A revision of the electronic medical record was performed to obtain demographic data, length of stay, comorbidities (according to the Charlson Index), race (white, African and Asian) and risk factors for TB (HIV infection, immunosuppression, direct contact with patient with TB, homeless status or resident in a health care facility, intravenous drug use and health care professional status). TB was characterized according to site (lung, disseminated, etc), previous infection and clinical (local and systemic symptoms), analytical (leucocytes values higher than $11 \times 10^9/L$ and

below $4,5 \times 10^9/L$, and C-reactive protein (CRP) $>5 \text{ mg/mL}$, erythrocyte sedimentation rate (ESR) $>16 \text{ mm/h}$ and hyponatremia $<135 \text{ mmol/L}$) and radiological features (any of the TB radiological presentations was considered), microbiological isolate (and which), as dichotomous variables (presence/absence). Outcomes were in-hospital mortality, antibiotic complications and microbiologic resistance and were assessed for each year (2011-2016).

Data was analyzed as non-normal with median and Interquartile range (IQR). Trends throughout the years were evaluated by linear regression for continuous normal outcomes, test for trend for continuous non-normal variables, and standard correlation for the binary outcomes. A p-value of <0.05 was considered to be significant. Analysis was conducted in Stata (StataCorp. Stata statistical software: release 14. College Station, TX: StataCorp LP).

Results

A total of 591 patients were included, with a significant peak in 2013 (min 15- max 20%, p-value=0.001). Age was apparent stable over the years (42-48 median age, p-value=0.7). Although not statistically significant, there was a slight increase in male gender prevalence (65-79%, p-value=0.09), and length of stay (23-29 days, p-value=0.07). There was a trend with a peak of comorbidities by Charlson index score in 2012 (2-6, p-value=0.01) as well as a significant decrease in prevalence in white patients (from 80% to 52%) due to an increase in African (16%-38%) and Asian (3%-10%) (p-value=0.001). (**Table I**)

Regarding risk factors, there was a decrease in frequency regarding HIV status (from 34% to 23%, p-value=0.02), homelessness state (from 15% to 3%, p-value=0.005) and the use of IV drugs (from 19% to 3%, p-value=0.02). No tendency was observed in health care facility users or workers, direct contact with Tb patient or immunosuppression, regardless of the cause. (**Table I**)

Considering TB infection characteristics, there was an increase in laboratory changes detected (from 51% up to 98%, p-value=0.001) and in radiological changes (from 85% up to 99%, p-value <0.001). There was no difference regarding TB site, previous infection status, systemic or local symptoms or specimen positivity. (**Table II**)

As for clinical outcomes, there was a trend noticed, only in microbiological resistance with a significant increase from 5% up to 19% (p-value=0.02). No trend in treatment complications or mortality was found. (**Table III**).

Discussion

Mycobacterial infections have co-evolved with humans for thousands of years.

Table I: Demographic data and risk factor distribution: A total of 591 patients were included, which had a significant peak in. Age was apparent stable over the years. Although not statistically significant, there was a slight increase in male gender prevalence, and in length of stay. There was a trend with a peak of comorbidities by Charlson index score in) as well as a significant decrease in prevalence in white patients due to an increase in African and Asian patients. It was observed a decrease in frequency regarding HIV status, homelessness state and the use of IV drugs. No tendency was observed in health care facility users or workers, direct contact with TB patient or immunosuppression, regardless of the cause.

Demographics	2011	2012	2013	2014	2015	2016	Total	p-value
Age (median, IQR)	43 (34-52)	48 (38-58)	43 (36-55)	44,5 (32-56)	42 (34-56)	44,5 (34-57,5)	44 (35-56)	0.7
Gender (male)	62 (65%)	66 (72%)	90 (74%)	82 (75%)	67 (79%)	65 (74%)	432 (73%)	0.09
Length of stay (median, IQR)	23 (13-38)	28,5 (15,5-43)	28 (14-48)	28 (16-48)	29 (16-52)	27 (16-50)	27 (15-47)	0.07
Charlson index (median; IQR)	3 (0-7)	6 (1,5-8)	5 (1-6)	2 (0-6)	3 (0-8)	2 (0-6)	3 (0-6)	0.01
Race								
White	73 (80%)	61 (66%)	88 (74%)	80 (73%)	48 (64%)	41 (52%)	391 (69%)	0.001
African	15 (16%)	25 (27%)	28 (24%)	24 (22%)	21 (28%)	30 (38%)	143 (25%)	
Asian	3 (3%)	6 (7%)	3 (2,5%)	6 (5%)	6 (8%)	8 (10%)	32 (6%)	
Risk factors	2011	2012	2013	2014	2015	2016	Total	p-value
HIV status	32 (34%)	38 (41%)	44 (36%)	23 (21%)	30 (35%)	20 (23%)	187 (32%)	0.023
Homelessness status	14 (15%)	8 (9%)	12 (10%)	6 (5%)	7 (8%)	2 (3%)	49 (8%)	0.005
Health care facility user	1 (1%)	4 (4%)	6 (5%)	0 (0%)	4 (5%)	0 (0%)	15 (2,5%)	0.4
IV drugs user	18 (19%)	10 (11%)	28 (23%)	15(14%)	15 (18%)	3 (3%)	89 (15%)	0.02
Health care worker	2 (2%)	1 (1%)	0 (0%)	1 (1%)	1 (1%)	1 (1%)	6 (1%)	0.6
Direct contact	6 (6%)	7 (8%)	14 (12%)	18 (16%)	9 (11%)	10 (11%)	64 (11%)	0.1
Immunosuppression	18 (19%)	19 (21%)	32 (26%)	25 (23%)	13 (15%)	14 (16%)	121 (21%)	0.3
Immunosuppression cause								0.9
Autoimmune Disease	3 (18%)	0 (0%)	2 (6%)	0 (0%)	0 (0%)	0 (0%)	5 (4%)	
Immunosuppressive drugs	1 (6%)	0 (0%)	1 (3%)	0 (0%)	1 (8%)	0 (0%)	3 (2%)	
Diabetes	5 (29%)	10 (53%)	10 (31%)	12(46%)	7 (54%)	7 (50%)	51 (42%)	
Cancer	5 (29%)	4 (21%)	14 (44%)	9 (34%)	3 (23%)	6 (43%)	41 (34%)	
Hemodialysis	1 (6%)	1 (5%)	4 (13%)	0 (0%)	2 (15%)	0 (0%)	8(7%)	
Solid organ transplant status	2 (12%)	4 (21%)	1 (3%)	5(19%)	0(0%)	1(7%)	13(11%)	
Total	95 (16%)	92 (16%)	121 (20%)	110 (19%)	85 (14%)	88 (15%)	591	0.001

Table II: TB infection characteristics: There was an increase in and in radiologic changes. There was no difference in TB site, previous infection status, systemic or local symptoms or specimen positivity.

TB infection	2011	2012	2013	2014	2015	2016	Total	p-value
TB site								
Lung	67 (70%)	68 (74%)	86 (71%)	79 (72%)	68 (80%)	69 (78%)	437 (74%)	0.1
Other	28 (30%)	24 (26%)	35 (29%)	31 (28%)	17 (20%)	19 (22%)	154 (26%)	
Previous infection	12 (13%)	17 (18%)	27 (22%)	28 (25%)	15 (18%)	9 (9%)	107 (18%)	0.6
Systemic symptoms	79 (83%)	69 (76%)	117 (97%)	91 (83%)	66 (79%)	83(94%)	505 (85%)	0.1
Local symptoms	84 (88%)	68 (75%)	117 (97%)	98 (89%)	69 (82%)	81 (92%)	517 (88%)	0.2
Laboratory changes	71 (76%)	46 (51%)	117 (98%)	92 (84%)	54 (65%)	83 (94%)	463 (79%)	0.001
Radiological changes	85 (89%)	78 (85%)	117 (98%)	109 (99%)	78 (93%)	87 (99%)	554 (94%)	<0.0001
Specimen positivity	81 (85%)	87 (95%)	101 (83%)	100 (91%)	76 (90%)	84 (95%)	529 (90%)	0.07

Table III: Clinical outcomes: Only in microbiological resistance was a trend observed with a significant increase. No trend in treatment complications or mortality was noted.

Outcomes	2011	2012	2013	2014	2015	2016	Total	p-value
Microbiological resistance	5 (5%)	8 (9%)	8 (7%)	8 (7%)	14 (19%)	15 (17%)	58 (10%)	0.002
Treatment complications	8 (8%)	14 (15%)	23 (19%)	13 (12%)	20 (24%)	12 (14%)	90 (15%)	0.1
In-admission mortality	8 (8%)	4 (4%)	13 (11%)	7 (6%)	2 (2%)	5 (6%)	39(7%)	0.2

This infectious disease is generally transmitted through aerosols, although preventable and curable, remains to date a major public health problem and is one of the most common opportunistic infections in people living with HIV (PLHIV)^{9,10}.

Tuberculosis disease is a contagious infection that untreated or improperly treated has a significant fatality. WHO estimated that, in the last two decades, there has been a progressive increase in the number of cases of tuberculosis across the globe, due to an increase in incidence of human immunodeficiency virus (HIV), low economic status of nations, migration and emergence of resistant strains of tuberculosis bacillus¹¹. 8-9 million people develop the disease per year, and approximately two million people die^{10,11}.

Since TB resurgence peaked in the 90s, our data shows a steady number of reported cases although following a downward slope trend throughout the years.

This decrease in reports can be explained by the impact of financial and clinical resources to assist national and local TB control efforts, wider screening, and preventive therapy for high-risk populations and growing support for TB prevention programs among HIV-infected persons⁹.

Comparing to the WHO Global TB report, we confirm the same increase in the number of cases in foreign born populations^{8,9}, with significant decrease in prevalence in white patients (from 80% to 52%) due to an increase in African (16%-38%) and Asian (3%-10%). Migrants have several risk factors that make them more susceptible to

this disease. The migration process itself is complex, and a constant changing social phenomenon that can generate new social scenarios making the chains of transmission less predictable. The data analysis tends to reflect the sub-lineages prevalent in the patients' home countries, which suggests that they either brought their strains with them as latent infections, or acquired them in Portugal through social contact with people from their native country^{12,13}. It is important to see that the increase in the influx of immigrants into Portugal from high TB incidence countries may be a determinant for the persistence of TB locally¹³.

Taking in consideration widely known risk factors for TB, our study reported only a decrease in frequency regarding HIV status, homelessness state and the use of IV drugs. These data may reflect as stated previously the political, financial and social efforts in place in our country to reduce poverty, improve access to medical care and screening programs and also the national program against drug use.

TB as a clinical entity is the result of an immune imbalance. Immunological insufficiency may depend on different clinical factors, namely the presence of comorbidities such as diabetes mellitus¹⁰. We do report a trend with a peak of comorbidities by Charlson index score in 2012, reflecting the wider range of population affected by this disease and the need for proper screening programs amongst those with chronic diseases who have an increased risk for immunological insufficiency.

The increasing load of comorbidities is not only conditioning the tuberculous infection but it may also impact the morbidity and mortality amongst those infected.

Taking in consideration TB infection characteristics, there was an increase in laboratory changes detected

(from 51% up to 98%) and in radiological changes (from 85% up to 99%), reflecting the raised suspicion for the diagnosis in an earlier stage and a more accurate use of adequate diagnostic tests.

In line with the decline of HIV positive patients and immune compromised patients in our sample, there was no difference in TB site with a higher prevalence of pulmonary forms of disease. The same trend was noticeable in the inaugural symptoms and systemic manifestations which didn't differ from previous data collected in other studies at our center.

While analyzing clinical outcomes, the noteworthy data goes to the increase in microbiological resistance (from 5% up to 19%), keeping in mind the previous data about immigration and resurgence of cases in foreign born patients, this can be an explanation for the emerging number of resistant strains among the population of our study.

Maintaining the decline in TB morbidity and aiming towards the goal of eliminating TB requires sustained prevention and control efforts, especially rapid diagnosis, ensured completion of treatment, and prompt and complete reporting. Furthermore, establishing tuberculin-screening programs that target patients at higher risk may ensure the appropriate use of preventive therapy.

Disclosures

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Conflict of interest

The authors declare that they have no conflict of interest.

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