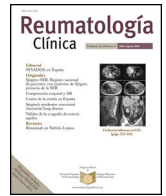




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## Brief Report

# Decrease in osteoarticular tuberculosis in Spain between 1997 and 2018<sup>☆</sup>

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## ABSTRACT

**Background and objective:** osteoarticular tuberculosis represents 2%–5% of the manifestations of tuberculosis. The objective was to calculate the incidence and describe the epidemiological characteristics of patients with osteoarticular tuberculosis who received hospital care in Spain between 1997–2018.

**Methods:** A retrospective study was conducted of patients treated with osteoarticular tuberculosis in Spanish hospitals between 1997 and 2018, using the data from the Minimum Basic Data Set at hospital discharge, using the ICD-9-CM and ICD-10 codes.

**Results:** 5710 patients with osteoarticular tuberculosis were detected over the 22 years in Spain. The mean annual incidence for the period was 6 cases per million inhabitants (95% CI 5.58–6.30). There was a significant difference between the mean annual incidence per million inhabitants of the first period (1997–2007) of 6.95 and that of the second (2008–2018) of 5.35 ( $p < .001$ ).

**Conclusions:** The incidence of osteoarticular tuberculosis in Spain is low, has reduced over 22 years and predominates in men.

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## Disminución de la tuberculosis osteoarticular en España entre 1997 y 2018

### RESUMEN

**Antecedentes y objetivo:** la tuberculosis osteoarticular representa el 2-5% de las presentaciones de la tuberculosis. El objetivo fue calcular la incidencia y describir las características epidemiológicas de los pacientes con tuberculosis osteoarticular que recibieron atención hospitalaria en España entre 1997-2018.

**Método:** Se realizó un estudio retrospectivo de los pacientes atendidos con tuberculosis osteoarticular en los hospitales españoles entre los años 1997 y 2018, a través del Conjunto Mínimo Básico de Datos al alta hospitalaria, usando los códigos del CIE-9-MC y CIE-10.

**Resultados principales:** Se detectaron 5710 pacientes con tuberculosis osteoarticular durante los 22 años. La incidencia anual media del periodo se situó en 6 casos por millón de habitantes (IC95% 5,58-6,30). Existió una diferencia significativa entre la incidencia media anual por millón de habitantes del primer periodo (1997-2007) de 6,95 y la del segundo (2008-2018) de 5,35 ( $p < 0,001$ ).

**Conclusión:** La incidencia de la tuberculosis osteoarticular en España es baja, se ha reducido a lo largo de 22 años y predomina en hombres.

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### Palabras clave:

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## Introduction

Tuberculosis (TBC) is a public health problem worldwide. The tuberculosis rates in Spain during recent decades have dropped but this reduction has been more pronounced in pulmonary forms and less so in extrapulmonary forms.<sup>1</sup>

Osteoarticular tuberculosis represents 2%–5% of tuberculosis manifestations.<sup>2</sup> Despite being known since antiquity few studies with a broad population base exist that report its incidence and epidemiological characteristics.<sup>3</sup> Most are reports of case series from one hospital centre or over a short period of time.<sup>4</sup>

The purpose of this study was therefore to analyse the incidence of osteoarticular TBC and its trend in Spain, from a hospital perspective, between 1997 and 2018, collecting data from most Spanish hospitals.

**Methods**

We conducted an observational study of patients treated in Spanish hospitals using data from the Minimum Basic Data Set at hospital discharge, whose main or secondary diagnosis included an ICD-9-CM or ICD-10 code which referred to bone and joint tuberculosis between 1997 and 2018.

Data were collected from the Health Information Institute, Ministry of Health, Consumer Affairs and Social Welfare, which receives information from most Spanish hospitals. The data, in addition to being anonymised, were treated with absolute confidentiality in accordance with Spanish legislation and the regulations of the Ministry of Health, Consumer Affairs and Social Welfare.

For the calculation of incidence, the first admission of the patient with the diagnosis and the population census of the National Institute of Statistics<sup>5</sup> were taken into account. The ages were distributed for some calculations by the following age groups: <1 year (infant), 1–14 years (child), 15–44 years (young adult), 45–64 years (adult), 65–74 years (senior) and >74 years (elderly).

Given the differences between ICD-9 and ICD-10 diagnostic coding, data on the location of osteoarticular tuberculosis were homogenised by classifying them into tuberculosis of the spine, tuberculous arthritis outside the spine, tuberculosis of other bones and other osteoarticular tuberculosis not specified/distinct from the above.

Statistical analysis was performed using SPSS® version 23 and Microsoft® Excel and fStats. Quantitative variables not adjusted to a normal distribution such as age were described with median and interquartile range. Inconsistent or missing data on each variable were excluded from the analysis.

**Results**

There were 8029 hospital attendances corresponding to 5710 patients. The mean annual incidence for the period was 5.95 cases

per million population (95% CI 5.58–6.30). When analysing the evolution of the annual incidence of osteoarticular TB, a progressive decrease was observed (Fig. 1).<sup>6</sup> There was a significant difference between the mean annual incidence per million population in the first period (1997–2007) of 6.95 and in the second period (2008–2018) of 5.35 (p < .001).

The sex distribution of the 5710 patients studied was: 3319 (58.1%) men and 2390 (41.9%) women (Table 1). The mean annual incidence in men was 7.01 (95% CI 6.72–7.32) cases per million compared to 4.89 (95% CI 4.69–5.11) in women. Both rates have declined over the study years, standing in 2018 at 5.45 cases per million for men and 4.11 for women. The relative risk male/female was 1.43 (95% CI 1.36–1.51) during the study period.

In the age distribution, a higher frequency was observed in the young adult group (15–44 years) with 1718 cases (30.1%) and in the elderly group (>74 years) with 1462 cases (25.6%) (Table 1). In men, the young adult group was the most frequent with 1220 cases (21.4%), while in women, the most frequent group was the elderly with 805 cases (14.1%).

Of the patients with bone or joint TB, 5.5% (336/5710) died. No deaths were observed in children under 14 years of age; 1% of young adults, 2.8% of adults, 6.3% of seniors and 11.7% of the elderly died. There was a significant difference in mortality rates between age groups (p < .001; V = .195).

The most frequent site of osteoarticular tuberculosis was the spine (Table 1). In our study it accounted for 3762 cases (65.9%), followed by tuberculous arthritis outside the spine with 1309 cases (22.9%).

The majority of patients (82.5%) did not present concomitantly with other TB sites. Pulmonary TB was present in 9.1% of cases, followed by miliary TB in 4.2%. Nervous system tuberculosis (2.6%) and urogenital tuberculosis (1.7%) were more rarely detected.

The most frequently occurring risk factors or comorbidities were diabetes mellitus (10.9%), followed by renal dysfunction (7.6%) (Table 1). HIV infection was detected in 7% of patients, and 5.6% of patients had acute respiratory failure. Other risk factors such as liver dysfunction, cardiovascular dysfunction or bone marrow failure occurred in less than 4% of patients (Table 1). Of the 622 patients with diabetes mellitus, 49 died (8.5%).

HIV infection was observed in 398 patients (7%), 314 males and 84 females. The age distribution of this group showed a higher frequency in the young adult group with 305 cases (76.6%). In addition, there was a decrease in HIV incidence over the years, from 37 cases in 1997 to 4 cases in 2018. Of the HIV co-infected patients, 4.5% died.

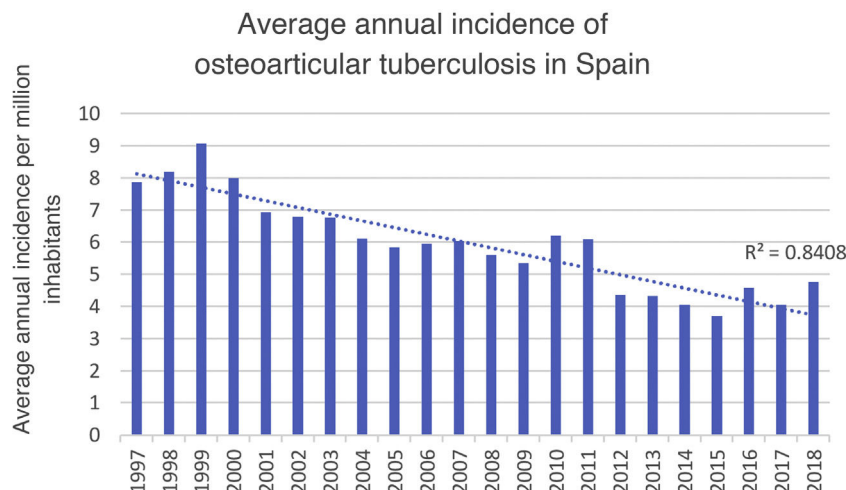


Fig. 1. Annual incidence per million population of osteoarticular tuberculosis in Spain.

**Table 1**  
Characteristics of the population admitted with osteoarticular tuberculosis and incidences between 1997 and 2018.

Variable	Frequency	Percentage
<b>Sex</b>		
Male	3319	58.1
Female	2390	41.9
<b>Age group</b>		
Infant (<1 year)	28	.5
Child (1–14 years)	136	2.4
Young adult (15–44 years)	1718	30.1
Adult (45–64 years)	1285	22.5
Senior (65–74 years)	1081	18.9
Elderly (>74 years)	1462	25.6
<b>Type of osteoarticular tuberculosis</b>		
T. spine	3762	65.9
Osteoarthritic tuberculosis outside the spine	903	15.8
T. of other bones	406	7.1
Other osteoarticular non specified or different tuberculosis	639	11.2
<b>Non associated osteoarticular tuberculosis</b>		
Tuberculosis of the nervous system	146	2.6
Miliary tuberculosis	239	4.2
Pulmonary tuberculosis	518	9.1
Urogenital tuberculosis	95	1.7
<b>Comorbidities</b>		
Diabetes mellitus	622	10.9
HIV	398	7
Acute respiratory failure	322	5.6
Chronic kidney disease	258	4.5
Neurological deficit	197	3.5
Renal dysfunction	176	3.1
Malignant neoplasms	147	2.6
Alcoholism	138	2.4
Rheumatic disease	138	2.4
Chronic liver disease	123	2.2
Cerebrovascular disease	112	2
Hepatic dysfunction	96	1.7
Transplant	94	1.6
Malnutrition	72	1.3
Acute ischemic heart disease	68	1.2
Spinal abscess	54	.9
Spinal cord failure/neutropenia	54	.9
Cardiovascular dysfunction	43	.8
Systemic steroids	22	.4
Immune disorders	11	.2
	Frequency	Annual average incidence (95% CI)
Spain	5710	5.95 (5.93–6.31)
Andalusia	752	4.59 (4.28–4.93)
Aragón	221	8.38 (7.35–9.56)
Asturias	209	9.44 (8.25–10.82)
Balearic Islands	91	4.45 (3.63–5.46)
Canary Islands	105	2.64 (2.18–3.20)
Cantabria	101	8.64 (7.11–10.50)
Castilla y León	424	8.20 (7.46–9.02)
Castilla la Mancha	193	4.90 (4.26–5.65)
Catalonia	1143	7.94 (7.50–8.42)
Community of Valencia	433	4.59 (4.18–5.05)
Extremadura	103	4.59 (3.79–5.57)
Galicia	479	8.41 (7.98–9.54)
Madrid	799	6.47 (6.04–6.94)
Murcia	124	4.53 (3.80–5.41)
Navarra	75	6.04 (4.82–7.57)
Basque Country	388	8.66 (7.85–9.58)
Rioja	49	8.00 (6.05–10.58)
Ceuta	13	7.97 (4.66–13.65)
Melilla	8	5.18 (2.63–10.23)

Significant differences ( $p < .001$ ) were observed in the distribution of incidence by autonomous community (Table 1). Asturias represented the community with the highest mean annual incidence per million inhabitants with 9.44 cases (95% CI 9.04–9.84), followed by the Basque Country with 8.67 (95% CI 8.15–9.19) and Cantabria with 8.64 cases (95% CI 8.37–8.91). The communities with the lowest incidence per million inhabitants were the Balearic

Islands with 4.45 cases (95% CI 4.27–4.63) and the Canary Islands with 2.64 cases (95% CI 2.49–2.79).

The mean length of stay of hospitalised patients was 24 days (+/– 30 days). The 25<sup>th</sup> and 75<sup>th</sup> percentiles corresponded to 7 and 30 days respectively, with an interquartile range of 23 days.

### Discussion

Analysis of the incidence of osteoarticular tuberculosis from a hospital perspective, based on data from most Spanish hospitals in the Specialised Health Care Activity Register, showed that the incidence has been low, at about 6 cases per million population per year, and has been declining for 22 years.

Since 2000, the prevalence of TB in the European population has been declining.<sup>7</sup> This fact could justify the decrease in osteoarticular tuberculosis. However, some articles warn of a slight increase in TB incidence in certain areas due to the immigrant population from countries with a high incidence of TB<sup>8</sup>. The heterogeneous incidence of osteoarticular TB by autonomous community may be explained by the different prevalence of tuberculosis and, in some areas, by the immigrant population.<sup>1,9</sup>

The disease was more prevalent in men with a relative risk of 1.43. Unpublished results from our research group have detected predominance in Spain in men with a relative risk of 2.6 for miliary tuberculosis and 1.9 for tuberculosis of the nervous system. One of the factors that may condition this predominance of extrapulmonary or disseminated tuberculosis in Spain is HIV co-infection, which is more prevalent in men. The age of presentation of osteoarticular tuberculosis is bimodal, with a peak in older people and another in the 15–44 age group associated with the higher frequency of HIV co-infected males.

The most repeated comorbidity was diabetes mellitus, followed by HIV infection, acute respiratory failure and chronic kidney disease, coinciding with other studies published in the literature.<sup>10</sup>

The most frequent location was the spine, coinciding with the existing literature<sup>11–13</sup> although some studies with a limited number of cases have suggested a predominance of other locations.<sup>14</sup>

The main limitation of the study is due to the retrospective nature of the Minimum Basic Data Set, which does not allow us to know the evolution of the patients if they are not re-admitted and which may include variability in the diagnostic criteria. In addition, there are differences between the ICD 9 and ICD 10 diagnostic codes that made it difficult to homogenise cases. Even so, our study provides complementary information to that from epidemiological surveillance studies.

In conclusion, this study, from the perspective of the Spanish population requiring hospital care, estimates that the incidence of osteoarticular tuberculosis has declined since the end of the last century, and is low in comparison with countries with a high incidence of tuberculosis.

### Conflict of interest

The authors have no conflict of interests to declare.

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