INCIDENCE OF TUBERCULOSIS IN THE CITY OF CORDOBA AND ITS RELATIONSHIP WITH AREAS IN NEED OF SOCIAL TRANSFORMATION: A STUDY FROM 2015 TO 2021

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SUMMARY

Objectives: In 2022, about 17% of Andalusian population lived in disadvantaged areas, which accounted for 21% of tuberculosis (TB) cases. This concentration of cases resulted in TB rates in these areas being higher than both the regional and national averages. The aim of the present study was to understand the behaviour of TB in terms of person, time, and place in the city of Cordoba during the period 2015–2021 and its association with areas in need of social transformation (ANST).

Methods: A retrospective observational analytical study was conducted on cases reported to the Andalusian Epidemiological Surveillance System (Spanish acronym SVEA). Membership in ANST was determined by the SVEA.

Results: A total of 136 cases were reported, with 26.5% in ANST. The incidence rate (IR) in the city was 5.97 cases per 100,000 population per year, higher in ANST (11.82) compared to non-ANST (5.06), RR = 2.34 (95% CI: 1.60–3.42). In 2020, fewer cases were reported (IR: 3.99). The mean age was 44.82 years, lower in ANST (38.08) than in non-ANST (47.25), with a p-value < 0.05. Hospitalizations were more frequent in ANST (78% vs. 68%, $p = 0.3$). In ANST, the IR was highest in men over 60 years old and lowest in women of the same age. No significant difference was found between the groups regarding risk factors, except for HIV status ($p = 0.02$).

Conclusions: TB incidence rates in Andalusia vary by area of residence. To make better public health decisions, it is crucial to enhance the collection of socio-demographic and clinical data related to these cases.

Key words: tuberculosis, incidence, risk factors, health inequities, social determinants of health, epidemiology, Andalusia

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INTRODUCTION

Tuberculosis (TB) was declared a public health emergency by the World Health Organization (WHO) in 1993 and efforts to control the disease have continued since then (1). Currently, TB ranks among the top ten causes of death worldwide and was the leading cause by a single infectious agent until the SARS-CoV-2 pandemic, surpassing HIV/AIDS (2). One-quarter of the global population becomes infected at some point in their lives (1, 3).

In 2014, the WHO adopted the "End TB Strategy", aimed at ending the global TB epidemic by reducing deaths by 95% and the incidence rate by 90% between 2015 and 2035. The strategy also aims to ensure that no family faces catastrophic costs due to TB (1, 4).

The COVID-19 pandemic has had an impact on access to healthcare services, reflected in the number of diagnosed and reported TB cases and in mortality. According to the latest WHO report, it is estimated that the global number of deaths increased by 100,000 between 2019 and 2020, leading to a slowdown in the annual decline of the global TB incidence rate (5).

However, the measures implemented for COVID-19 can also aid in the control of respiratory diseases like TB (6–8).

Since 2008, the European Centre for Disease Prevention and Control (ECDC) and the regional office of the WHO have been coordinating TB surveillance in Europe (2, 9).

Since the year 2000, TB cases have consistently declined, but despite being the fastest decline among global regions, efforts must be accelerated to achieve the goals of the "End TB Strategy" (1, 4).

Nine out of the thirty countries with the highest rates of multidrug-resistant TB in the world are located in the European region (6).

In Spain, TB is a notifiable disease controlled by the National Epidemiological Surveillance Network (Spanish acronym RE-

NAVE). In 2019, the National Plan for the Prevention and Control of Tuberculosis in Spain was published (10).

In 2015, it was found that 28.7% of reported cases were born in countries other than Spain, with Morocco being the main country of origin, followed by Romania and Bolivia (11).

The number of cases in individuals born outside Spain continues to decrease, but at a slower pace than in Spanish-born individuals. The TB incidence rate in Spain has shown a downward trend in recent years. The greatest decline was observed in pulmonary forms at 6% annually, while other forms declined by 5% annually (11–14).

The elimination of TB requires early detection and prevention of secondary cases, which depend on diagnostic quality and therapeutic efficacy. However, social determinants such as social class, ethnicity, and geographical location influence the pathogenesis by determining exposure, diagnosis, and subsequent follow-up (15, 16).

Living and working in areas with high incidence (those with higher rates of incarceration, unemployment, and immigration) and overcrowded or poorly ventilated places entail higher risks, underscoring the importance of contact tracing (17, 18).

Directly observed treatment, vaccination, and early diagnosis have led to improved prognosis, but economic and social measures are also required. Therefore, the WHO advocates for a holistic approach that includes social determinants of health in the Sustainable Development Goals (4, 18–20).

In 2022, about 17% of Andalusian population lived in disadvantaged areas (areas with a higher risk of poverty and/or social exclusion), which accounted for 21% of tuberculosis (TB) cases. This concentration of cases resulted in TB rates in these areas being higher than both the regional and national averages (21). This disease is monitored by the Andalusian Epidemiological Surveillance System (Spanish acronym SVEA) for TB through periodic reports (21–25).

In Andalusia, the term "area in need of social transformation" (ANST) is employed to define clearly delimited urban spaces where the population faces structural situations of severe poverty and social marginalization, and where are significant problems related to:

- housing, urban deterioration, infrastructure deficit, and lack of public services and facilities;
- high rates of absenteeism and school failure;
- high levels of unemployment and significant deficiencies in professional training;
- serious hygienic and sanitary deficiencies; and
- social disintegration phenomena.

According to SVEA, 27 ANST in Andalusia exceed the low endemicity threshold set by the WHO (40 cases per 100,000 population per year), reaching maximum values of 182 cases per 100,000 population per year (21–25).

The aim of the present study was to understand the behaviour of TB in terms of person, time, and place in the city of Cordoba during the period 2015–2021 and its association with ANST.

MATERIALS AND METHODS

This study was designed as an observational, analytical, retrospective study.

Study Setting, Population and Sample

The study's setting corresponds to the city of Cordoba. The cases included in the sample are those registered, validated, and completed in the RedAlerta computer application by public health professionals from hospitals, districts, healthcare management areas, and the Spanish Ministry of Health. Inclusion and exclusion criteria were set as follows: all cases reported to SVEA were included; cases that lacked assigned home coordinates (X and Y) in previous instances were excluded. The study was conducted in the period from 1 January 2015 to 31 December 2021, based on the date of symptom onset or, if unavailable, the date of case registration in RedAlerta.

Analysis Variables

The variables analysed include those present in the RedAlerta case registration form, supplemented by the inclusion of the "ANTS" variable, which serves as an indicator of the socioeconomic context. The methodology used to obtain data involved collecting the home address from the mandatory declaration of the disease notification form. These addresses were then processed by SVEA for TB, which extracted the X and Y coordinates. These coordinates were subsequently mapped to determine whether the case was located in ANTS or not. This approach, known as the "social risk map", categorizes cases based on their geographical location relative to areas with social risk factors.

For case classification, we followed the definitions outlined in the 2013 version of the RENAVE Tuberculosis Surveillance Protocol (26), which include:

Clinical criteria

presenting one of the following characteristics:

- signs, symptoms, or radiological findings compatible with active TB at any site, along with a physician's decision to administer a complete course of anti-tuberculosis therapy;
- anatomopathological results at autopsy compatible with active tuberculosis that would have required anti-tuberculosis treatment.

Laboratory criteria

Confirmed case – meeting at least one of the following criteria:

- isolation in culture of a microorganism from the MTB complex (excluding the vaccine strain or Bacillus Calmette-Guérin – BCG) from a clinical sample;
- detection of nucleic acid from the MTB complex in a clinical sample along with positive bacilloscopy by conventional or fluorescent optical microscopy.

Probable case – meeting at least one of the following three criteria:

- positive bacilloscopy by conventional or fluorescent optical microscopy;
- detection of nucleic acid from the MTB complex in a clinical sample;
- granulomas on histology.

According to the same protocol (26), the classification of cases for reporting purposes is as follows:

Suspected case – person who meets clinical case definition criteria.

Probable case – person who meets both clinical and laboratory criteria for probable case.

Confirmed case – person who meets both clinical and laboratory criteria for confirmed case.

The microbiological and clinical variables studied were belonging to ANST (yes, no), type of diagnosis (confirmed, probable, suspicion), bacillary or not, isolated species (MTB complex and atypical, MTB complex, *M. africanum*, atypical mycobacterium, *M. bovis*, *M. tuberculosis*), location of TB (peripheral lymphadenopathy, meningitis, pleuritis, bones and joints, other organs, genitourinary system, lungs, miliary, unspecified respiratory, intrathoracic lymph nodes), contact tracing (number of contacts studied), and hospitalization (yes, no).

Other studied factors were age groups, gender (male, female), foreign origin (yes, no), risk factors (none known, addictions, clinical factors, HIV/AIDS), HIV status (positive, negative).

The "foreign origin" variable was recoded into two groups (yes/no), with the value "Spain" assigned to the "yes" group and all other values assigned to the "no" group. "Addictions" refers to alcoholism, injection drug use (IDU), or other drug addictions. The variable "clinical factors" refers to previous malnutrition, unstable diabetes or immunodeficiency.

Ethical Consideration

The information available in RedAlerta was received after undergoing an anonymization process carried out by a third party not involved in this study. There was no access to personal data of the registered cases, ensuring their confidentiality according to Regulation (EU) 2016/679 of the European Parliament and the Organic Law 3/2018 on Personal Data Protection and Guarantee of Digital Rights. This study was approved by the Provincial Research Ethics Committee of Cordoba on 25 January 2023 (study code TFG-TBZN-2022).

Calculation of Rates

To calculate incidence rates (IR), population data from the Municipal Register as of 1 January 2022, provided by the National Institute of Statistics (27), was used. The calculated rates are crude or age- and sex-specific and are expressed per 100,000 inhabitants. For the IR by sex and age, the population of 2021 is used as a reference. For the calculation of annual rates, it is provided as the average of the crude rate for each year and by ANTS or no-ANTS.

Statistical Analysis

Qualitative data were defined as numbers and percentages. Chi-square test and Fisher's exact test were used for comparison between categorical variables as appropriate. The quantitative data were summarized as follows: for variables with a normal distribution, descriptive statistics included the mean and standard deviation (SD); for non-normally distributed variables, the median and interquartile ranges (IQR) were provided, along with minimum and maximum values. Parametric and non-parametric tests were used for bivariate analysis depending on the normal distribution of the data (according to the sample size of the group or the result of the Shapiro-Wilk test). P-value < 0.05 was considered statistically significant. The collected data were introduced and statistically analysed by utilizing SPSS version 23.

RESULTS

During the period from 2015 to 2021, 170 cases of TB were reported to the SVEA in the city of Cordoba, of which 136 (80%) included geolocation in RedAlerta.

Out of the 136 cases, 100 (73.5%) were not located in ANST, and 36 (26.5%) occurred in residents of these areas. In the Sector Sur de Cordoba, there were 21 cases (15.5%), 11 in Barriada Las Palmeras (8.1%), and 4 in Las Moreras (2.9%).

The TB IR was 5.97 cases per 100,000 persons per year. Outside of ANST, the IR was 5.06 cases per 100,000 persons per year compared to 11.82 cases per 100,000 persons per year in ANST; 5.21 in Las Moreras, 10.56 in the Sector Sur de Cordoba, and 72.82 in Barriada Las Palmeras. Table 1 shows that there was significant difference found between the number of patients in non-ANTS group and those in ANTS group during the period from 2015 to 2021 ($p < 0.001$).

Table 2 compares the microbiological and clinical characteristics in non-ANTS group and those in ANTS group. No significant difference was found between the two groups.

In ANTS, tuberculosis incidence rates (IR) were the highest among men over 60 years old and the lowest among women in

Table 1. *Distribution of cases, population, and incidence rate per year and ANTS*

Year	City of Cordoba			Non-ANTS			ANTS		
	Cases n (%)	Population	IR[a]	Cases n (%)	Population	IR[a]	Cases n (%)	Population	IR[a]
2015	23 (17.0)	327,362	7.03	20 (20.0)	283,215	7.06	3 (8.3)	44,147	7.79
2016	31 (23.0)	326,609	9.49	20 (20.0)	282,524	7.08	11 (30.6)	44,085	24.95
2017	14 (10.0)	325,916	4.30	10 (10.0)	282,135	3.54	4 (11.1)	43,781	9.14
2018	22 (16.0)	325,708	6.75	18 (18.0)	282,034	6.38	4 (11.1)	43,674	9.16
2019	16 (12.0)	325,701	4.91	13 (13.0)	282,049	4.61	3 (8.3)	43,652	6.87
2020	13 (9.5)	326,039	3.99	6 (6.0)	282,419	2.12	7 (19.5)	43,620	16.05
2021	17 (12.5)	322,071	5.28	13 (13)	280,559	4.63	4 (11.1)	41,512	9.64
Total	136	325,629[b]	5.97	100 (73.5)	282,134[b]	5.06	36 (26.5)	43,496[b]	11.82

ANTS – areas in need of social transformation; [a]IR (incidence rate) – cases x 100.000/population-year; [b]mean population in 7 years

Table 2. *Distribution of microbiological and clinical characteristics resulting from descriptive study in ANTS and non-ANTS*

Variable	Cordoba (n = 136) n (%)	Non ANTS (n = 100) n (%)	ANTS (n = 36) n (%)	p-value
Type of diagnosis (n = 136)				
Confirmed	99 (73.00)	73 (73.0)	26 (72.0)	0.6
Probable	12 (9.00)	10 (10.0)	2 (6.0)	
Suspected	25 (18.00)	17 (17.0)	8 (22.0)	
Bacillary (n = 136)				
Yes	53 (39.00)	39 (39.0)	14 (39.0)	0.3
No	64 (47.00)	45 (45.0)	19 (53.0)	
Not applicable	2 (1.50)	2 (2.0)	0 (0.0)	
Not registered	17 (12.50)	14 (14.0)	3 (8.0)	
Isolated species (n = 96)				
MTB complex and atypical	1 (1.04)	1 (1.4)	0 (0.0)	0.8
MTB complex	67 (69.79)	49 (69.0)	18 (72.0)	
M. africanum	3 (3.12)	2 (2.8)	1 (4.0)	
Atypical mycobacterium	3 (3.12)	3 (4.2)	0 (0.0)	
M. bovis	4 (4.17)	4 (5.6)	0 (0.0)	
M. tuberculosis	18 (18.76)	12 (17.0)	6 (24.0)	
Location of TB (n = 136)				
Not registered	80 (58.80)	58 (58.0)	22 (61.1)	0.5
Peripheral lymphadenopathy	5 (3.70)	3 (3.0)	2 (5.6)	
Meningitis	1 (0.70)	1 (1.0)	0 (0.0)	
Pleurisy	2 (1.50)	2 (2.0)	0 (0.0)	
Bones and joints	2 (1.50)	1 (1.0)	0 (0.0)	
Other organs	3 (2.20)	3 (3.0)	0 (0.0)	
Genitourinary system	1 (0.70)	1 (1.0)	0 (0.0)	
Lung	19 (14.00)	13 (13.0)	6 (16.7)	
Miliary	4 (2.90)	4 (4.0)	0 (0.0)	
Unspecified respiratory	18 (13.20)	14 (14.0)	4 (11.1)	
Intrathoracic lymph nodes	2 (1.50)	0 (0.0)	2 (5.6)	
Total registered	56 (41.20)	42 (42.0)	14 (38.9)	
Hospitalized (n = 106)				
Yes	96 (71.00)	68 (68.0)	28 (78.0)	0.3
No	10 (29.00)	32 (32.0)	8 (22.0)	

IQR – interquartile range; SD – standard deviation
Source: own elaboration based on data from SVEA

the same age group. Additionally, IR was high in women under 20 years old.

Table 3 compares the risk factors in non-ANTS group and those in ANTS group. No significant difference was found between the two groups regarding the different risk factors, except for HIV status.

DISCUSSION

The current study aimed to understand the behaviour of tuberculosis in terms of person, time, and place in the city of Cordoba during the period 2015–2021 and its association with ANST.

The distribution of TB showed an important variation over the seven years. For the studied period (2015–2021), TB IR in the city of Cordoba was 5.97 cases/100,000 population per year, higher in ANTS (11.82) than in non-ANTS (5.06), RR = 2.34 (95% CI: 1.60–3.42), ($p < 0.001$). This was an expected finding considering the socioeconomic conditions related to the disease and the environment (20, 21), as previously demonstrated in another Spanish city (28), as well as in the autonomous community (21).

In 2020, there was a decline in the overall incidence of TB observed in the city of Cordoba, with similar trend seen in non-ANTS areas. Nationally, RENAVE reported similar findings, attributing this decrease to the impact of the pandemic, including measures like respiratory isolation and delays in diagnosis (13).

Table 3. Distribution of risk factors resulting from descriptive study by ANTS

Variable	Cordoba (n = 136) n (%)	Non ANTS (n = 100) n (%)	ANTS (n = 36) n (%)	p-value
Age (years), (n = 136)				
Mean (median, IQR)	44.82 (46.5, 34)	47.25 (48.0, 34)	38.08 (42.0, 35)	< 0.05
Gender (n = 136)				
Male	87 (64.0)	68 (68.0)	19 (53.0)	0.1
Female	49 (36.0)	32 (32.0)	17 (47.0)	
Foreign origin (n = 136)				
Yes	29 (21.3)	23 (23.0)	6 (16.7)	0.4
No	107 (78.7)	77 (77.0)	30 (83.3)	
Risk factors (n = 136)				
None known	84 (62.0)	63 (63.0)	21 (58.0)	0.4
Addictions	13 (9.5)	7 (7.0)	6 (17.0)	
Clinical factor	32 (23.5)	25 (25.0)	7 (19.5)	
HIV/AIDS	7 (5.0)	5 (5.0)	2 (5.5)	
HIV state (n = 136)				
Positive	2 (1.5)	0 (0.0)	2 (5.6)	0.02
Negative	37 (27.2)	28 (28.0)	9 (25.0)	
No realized	97 (71.3)	72 (72.0)	25 (69.4)	

IQR – interquartile range; SD – standard deviation
Source: own elaboration based on data from the SVEA

However, in ANTS areas, there was a notable increase in TB cases, believed to be driven by significant socioeconomic disparities exacerbated by the COVID-19 pandemic (21). Corresponding with national trends, the lowest IR in ANTS areas of Cordoba was recorded in 2021, while there was a surge in cases in 2020.

There was no significant difference between ANTS and non-ANTS regarding the type of diagnosis (confirmed, probable or suspected), bacillary status (yes, no), isolated TB species, and location of TB. In our study, there was no difference between ANTS and non-ANTS regarding hospitalization of TB patients. This contradicts previous reports from Andalusia and Spain, where more hospitalizations for TB patients from ANTS were observed (8, 10, 12, 13).

In our study, the mean age in ANTS areas (38.08 years) was significantly lower than in non-ANTS areas (47.25 years). This difference may be attributed to various factors, including real demographic differences, potential under-detection of cases in older individuals, or diagnosis without microbiological confirmation in younger people. Similar findings have been reported in studies conducted in other Spanish cities (28–30).

In our study, the highest IR in ANTS was observed in men over 60 years old and in women under 20 years old. These findings align with national publications (12), which have reported a higher average age in men compared to women.

The prevalence of non-imported TB cases in the present study was predominant in both ANTS and non-ANTS groups, accounting for 78.8% and 83.3%, respectively. There was no significant distinction between these groups (p = 0.4). Surprisingly, contrary to prevailing data, our study revealed that the majority of cases did not originate from foreign sources (12–14, 28, 30).

The majority of cases in our study, constituting 62% overall (58% in ANTS and 63% in non-ANTS), did not exhibit known risk factors, with no significant difference observed between the two groups (p = 0.4). Contrary to prevailing data, our study findings indicate that the majority of cases did not present with known risk factors (12–14, 29, 31).

Similar to previous studies conducted in Spain (31, 32), there has been a decrease in the number of TB cases among HIV-positive individuals compared to the previous years. It is worth noting that in our study, 71.3% of TB cases had an unknown HIV serological status, with 2 HIV-positive cases occurring in ANTS. This could be attributed to a low perception of risk among older individuals, while in young adults it may be due to inadequate data collection practices (13, 14). TB is a common opportunistic infection in HIV patients, highlighting the importance of comprehensive data collection for this variable. Previous studies have emphasized the increase in cases without proper testing, emphasizing the need for improved screening protocols (11, 12, 31, 32). A Spanish systematic review from 2022 stresses the importance of TB screening in all individuals diagnosed with HIV infection, and underscores the necessity of creating an integrated diagnostic service (29).

In our study, although differences were noted in the comparative analysis of certain variables based on their affiliation with ANTS, the analytical tests did not yield significant results. This could be attributed to the low TB incidence in Cordoba or the absence of actual disparities. The comprehensive data collection period has provided ample time to examine disease trends, and with the assistance of SVEA, we have been able to access a substantial number of variables. Nonetheless, we have been able to analyse a substantial population size and elucidate the social context that continues to be associated with TB.

CONCLUSION

In conclusion, TB incidence rates in Andalusia vary by area of residence. It is recommended that healthcare personnel should be encouraged to contribute to the accurate utilization of the surveillance system by enhancing precision in data collection before reporting to sustain the achievement of TB control objectives. To make better public health decisions, it is crucial to enhance the collection of socio-demographic and clinical data related to these cases. A potential future research endeavour could entail conducting a similar analysis across all cities in Andalusia to attain increased statistical power.

Conflicts of Interest

None declared

Data Availability

The datasets generated and/or analysed during current study are available from the corresponding author on reasonable request.

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