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Scientific Letter

Analysis of the Evolution of Tuberculosis in Men and Women in Spain Between 2017 and 2022. Is There a Different Incidence Decline by Gender?

To the Director,

Historically, the epidemiological burden of tuberculosis (TB) has been larger in men than in women and, in many societies, exposure to infectious cases differs between both sexes.[1] Every year, more cases of TB are documented in men than in women worldwide,[2] and prevailing surveys show this disparity.[3]

The study's goals were: to identify the characteristics and risk factors associated with gender and tuberculosis (TB), assess the linear trend of the incidence of cases by over time, and determine whether there are differences in diagnostic delay and treatment compliance.

All TB cases included in the Integrated Programme of Research in Tuberculosis and Non-Tuberculosis Mycobacteria (PII-TB&MNT) of SEPAR between 2017 and 2022 were included in a cross-central multicenter study. The χ^2 test was used to analyze the gender differences, considering that they were statistically significant if *p*-value <0,05. A binary logistic regression was used and odds ratios (OR) and 95% confidence intervals (CI) were computed. The temporal trend of the variable was obtained using the χ^2 linear trend test. IBM SPSS Statistics 22 statistical software was used to conduct the analysis.

The processing of personal data was in accordance with Spanish Organic Law 3/2018, of 5 December, on the Protection of Personal Data and the Guarantee of Digital Rights and the European Data Privacy Directive.

A sample of 1769 cases included in the registration between 2017 and 2020 was studied, of which 1220 (69%) were men and 549 women (31%). Multivariate analysis showed significant gender differences associated with men in the following categories: aged >60; in confinement; living alone or in groups; homeless; consume tobacco or alcohol. However, extrapulmonary localization was more common in women. There were no differences in the rates of diagnostic delay. There were no differences in the rates of diagnostic delay. There were differences in treatment compliance and treatment outcome, but these were not statistically significant (Table 1). There were also no significant differences in the pre-Covid and post-Covid periods in the ratio of men and women (p = 0.59).

The annual incidence of cases has decreased significantly ($y = 14100 - 6.98x$), although the linear trend shows that it is decreasing in women ($y = 1330 - 0.66x$) while being positive in men ($y = 118 + 0.06x$) (Fig. 1).

There have not been many studies on the relationship between gender and tuberculosis in Spain; nonetheless, certain data from

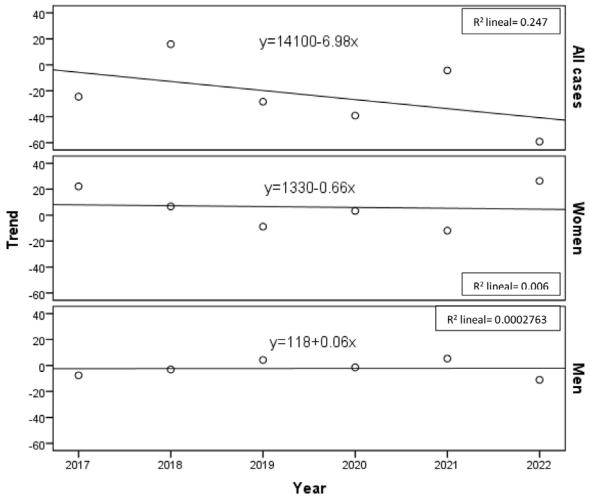

Fig. 1. Linear trend in the evolution of the incidence of cases in women and men (2017–2022).

national and autonomous TB control projects are accessible[4–6] showing numbers between 39.6% and 40% of women and between 60% and 60.4% of men between 2015 and 2017. However, they do not study the factors to which they may be related.

The SEPAR PII-TB&MNT evaluation, conducted between 2006 and 2016, showed that the population studied had a significant declining trend in the number of cases in women. The percentage of cases among women in the last two years of the evaluation (2015–2016),[7] was also lower than the figure reported in the World Health Organization's Global Tuberculosis Report 2019 (30.8% and 25.4% vs 32%),[8] and the figures in our current study are also lower than those in the World Health Organization's Global Tuberculosis Report 2023 (31% vs 33%).[9]

A constraint of this research is that, apart from the variables examined here, we also need to consider other studies that have identified additional characteristics related to gender. One of them at University College London[10] compared a short 4-month treatment to the 6-month standard and found gender differences in treatment outcomes without any objective biological causes. Others conclude that there is an urgent need for a greater understanding of gender-related barriers.[11] Another study found evidence that, in low- and middle-income countries, men are more at risk and have less access to screening and diagnostic services.[12] Some speculate that the development of tuberculosis may include a variety of physiopathological processes[13] and according to some authors, biological factors, such as sex hormones and genetic

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Table 1
Sociodemographic, Epidemiological, Clinical, Diagnostic and Treatment Characteristics and Risk Factors by Gender.

	Total N = 1769 (100%)		Men N = 1220 (69%)		Women N = 549 (31%)		Univariate analysis		Multivariate analysis	
	N	%	N	%	N	%	OR (95% CI)	p-Value	OR (95% CI)	p-value
Age (years)										
≤45	910	51.4	581	47.6	329	59.9		Ref.		Ref.
46–60	445	25.2	338	27.7	107	19.5	0.559 (0.433–0.722)	<0.001		0.154
>60	414	23.4	301	24.7	113	20.6	0.663 (0.514–0.856)	0.002	0.488 (0.349–0.681)	**<0.001**
Native country										
Natives	1056	59.7	737	60.4	319	58.1		Ref.		
Immigrant	713	40.3	483	39.6	230	41.9		0.361		
Living situation										
Confinement	37	2.1	30	2.5	7	1.3	0.391 (0.171–0.898)	0.027	0.340 (0.130–0.888)	**0.028**
Family	1301	73.5	815	66.8	486	88.5		Ref.		Ref.
Group	202	11.4	177	14.5	25	4.6	0.237 (0.154–0.365)	<0.001	0.153 (0.092–0.254)	**<0.001**
Homeless	60	3.4	57	4.7	3	0.5	0.088 (0.027–0.283)	<0.001	0.249 (0.074–0.834)	**0.024**
Alone	168	9.5	140	11.5	28	5.1	0.335 (0.220–0.511)	<0.001	0.288 (0.166–0.498)	**<0.001**
Unknown	1	0.1	1	0.1	0	0		–		–
Smoking										
Ex-smokers +6 months	238	13.5	198	16.2	40	7.3	0.223 (0.154–0.321)	<0.001	0.248 (0.158–0.389)	**<0.001**
Smokers	707	40.0	590	48.4	117	21.3	0.219 (0.172–0.278)	<0.001	0.349 (0.259–0.471)	**<0.001**
No smokers	824	46.6	432	35.4	392	71.4		Ref.		Ref.
Alcoholism										
No	1259	71.2	764	62.6	495	90.2		Ref.		Ref.
Yes	476	26.9	426	34.9	50	9.1	0.181 (0.132–0.248)	<0.001	0.304 (0.208–0.445)	**<0.001**
Unknown	34	1.9	30	2.5	4	0.7	0.206 (0.072–0.588)	0.003		0.287
Drug use										
No	1609	91.0	1080	88.5	529	96.4		Ref.		Ref.
Yes	160	9.0	140	11.5	20	3.6	0.292 (0.180–0.471)	<0.001		0.939
HIV infection										
No	1585	89.6	1090	89.3	495	90.2		Ref.		Ref.
Yes	52	2.9	43	3.5	9	1.6	0.461 (0.223–0.953)	0.037		0.822
Unknown	132	7.5	87	7.1	45	8.2		0.497		0.355
Immunosuppression										
No	1502	84.9	1033	84.7	469	85.4		Ref.		
Yes	184	10.4	129	10.6	55	10.0		0.712		
Unknown	83	4.7	58	4.8	25	4.6		0.833		
Previous treatment										
No	1652	93.4	1133	92.9	519	94.5		Ref.		Ref.
Yes	117	6.6	87	7.1	30	5.5		0.193		0.762
Localization of tuberculosis										
Pulmonary	1382	78.1	1003	82.2	379	69.0	0.482 (0.382–0.609)	<0.001		0.296
Pleural	241	13.6	166	13.6	75	13.7		0.975		
Disseminated	125	7.1	83	6.8	42	7.7		0.520		
Extrapulmonary only	185	10.5	90	7.4	95	17.3	2.627 (1.930–3.576)	<0.001	2.075 (1.395–3.084)	**<0.001**
Diagnostic delay (days)										
Median; IQR	62	30–120	61	30–115	64	31–134		0.075		0.623
Medical judgement										
Compliant patient	1558	88.1	1059	86.8	499	90.9		Ref.		Ref.
Non-compliant patient	78	4.4	67	5.5	11	2.0	0.348 (0.183–0.665)	0.001		0.123
Unknown	133	7.5	94	7.7	39	7.1		0.521		0.562
Treatment outcome										
Cured	634	35.8	467	38.3	167	30.4		Ref.		Ref.
Completed treatment	565	31.9	344	28.2	221	40.3	1.797 (1.407–2.294)	<0.001		0.523
Prolonged treatment	364	20.6	252	20.7	112	20.4		0.134		0.136
Default	1	0.1	0	0	1	0.2		–		–
Lost to follow-up	32	1.8	28	2.3	4	0.7		0.091		0.191
Covid periods										
Pre-Covid	1264	71.5	867	71.1	397	72.3		Ref.		
Post-Covid	505	28.5	353	28.9	152	27.7		0.591		

Values in bold: p-value < 0,05
IQR: interquartile range.

factors, could contribute to the host's immunity during tuberculosis.[14]

Despite the decline in the inclusion of cases during the Covid pandemic[15] (overload of medical services, possible reduction of cases due to the wearing of facemasks, decreased contact in public places or delayed diagnosis) and weakened TB control systems,[16,17] it can be concluded that there are significant gender differences in the incidence, age, living situation, tobacco and alcohol consumption and the localization of tuberculosis patients and that the trend in the number of cases in women continues to decrease.

Ethical Approval

The Biomedical Research Ethics Committees of the different participating centres approved this study.

Authors' Contributions

Teresa Rodrigo: conception and design of the study; acquisition, analysis and interpretation of data, and writing of the article.

Eva M. Tabernero, Luis Anibarro, José A. Gullón, Juan F Medina, Joan P. Millet, Marta M. García-Clemente, Joan A Caylà, José M. García-García: critical review of the intellectual content, final approval of the version presented.

Antonia Sáez: methodology design and statistical analysis of data. Working Group of the Integrated Tuberculosis and NMT Research Program (PII-TB & NMT): collection and contribution of data.

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Conflicts of Interest

The authors declare no conflicts of interest.

Appendix A. Integrated Tuberculosis Research Programme Working Group

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