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Original Article

Factors associated with tuberculosis-diabetes mellitus type 2 binomial in rural population of Oaxaca, Mexico

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Abstract

Introduction: Type 2 diabetes mellitus (T2DM) is a growing condition that hinders the treatment and control of tuberculosis (TB). Several factors promote this comorbidity showing variations according to characteristics of the population affected. The objective was to identify the factors associated with the comorbidity of TB-T2DM in a rural population of Oaxaca, Mexico.
Methodology: This was an unpaired case-control study. Descriptive statistics was performed for clinical and sociodemographic variables. Logistic regression was used to calculate odds ratio (OR) to identify associated factors with TB-T2DM binomial.
Results: 126 controls (TB+ T2DM-) and 69 cases (TB+ T2DM+) were included. 43% were considered as indigenous population. Significant differences were found according to the groups. Treatment failure was higher in individuals with binomial ($p = 0.015$), as well as a higher bacillary load (two crosses) and presence of pulmonary TB ($p \leq 0.001$). Association analysis showed that the risk factors of binomial were: female sex (OR = 2.47; 95% CI 1.24-4.92), age ≥ 45 years (OR = 2.90; 95% CI 1.42-5.92), body mass index ≥ 25 kg/m2 (OR = 2.69; 95% CI 1.25-5.77) and presenting > 6 symptoms (OR = 2.71; 95% CI 1.19-6.14).
Conclusions: This is the first report of this comorbidity in a rural Mexican population. The results highlight the growing problem of TB-T2DM, and the need to address the issue from an integral and gender perspective. Furthermore, mandatory screening is necessary in patients with T2DM to improve early diagnosis of TB and T2DM. This would promote better management of both conditions.

Key words: *Mycobacterium tuberculosis*; comorbidity; hyperglycemia; risk factors.

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Introduction

Tuberculosis (TB) persists as one of the most relevant public health problems worldwide. According to the World Health Organization (WHO), there were about 10 million new cases of TB and 1.4 million deaths due to this condition worldwide in 2019 [1].

In addition to sociodemographic factors associated with TB, such as poverty, overcrowding, and lack of access to health services [2], some factors that have hindered TB control are the presence of multidrug resistance (MDR) [3], and comorbidities, mainly HIV [4] and type 2 diabetes mellitus (T2DM) [5]. In recent years, the global T2DM pandemic has had an impact on the dynamics, and control of TB, mainly in endemic areas [6]. By 2019, 463 million people with T2DM were reported worldwide [7], and various investigations have described TB-T2DM comorbidity percentages ranging from 1.9% [8] to 45% [9].

Diabetes mellitus type 2 is one of the main public health problems in Mexico; the prevalence for 2020 was 10.6% in people older than 20 years of age. However, this percentage could be higher, as it is estimated that at least 30% of the population do not know their medical condition, and T2DM is frequently associated with being overweight and bad glycemic control, which aggravates the epidemiological situation of this pathology [10]. Additionally, the number of TB cases has shown a significant increase in recent years. In 2018 there were 17,433 TB cases, and by 2020 this was 31,724 cases [11], an increase of nearly 50% in just two years. In Mexico, the prevalence of TB-T2DM comorbidity is 27.6% [12], which is among the highest worldwide, with variations ranging from 19.2% [13] to 35.2% [14]. In this context, the Isthmus of Tehuantepec region has the second the highest prevalence of T2DM in the state of Oaxaca; in addition, TB-T2DM comorbidity is > 40%, and 35% of patients live without glycemic control [15]. These numbers are higher than the national statistics.

In this epidemiological context, one of the main emerging problems is the appearance of multidrug-resistant tuberculosis (MDR-TB), since evidence suggests that patients with TB-T2DM have higher probability of developing multidrug resistance (MDR) [16,17]. In 2019, 465,000 new cases of MDR-TB were reported worldwide. MDR-TB increases treatment failure and mortality, in addition to requiring a more expensive second-line treatment with side effects [1]. Bacterial resistance mechanisms have been described that aid pathogens in evading the effects of the drugs. The most important mechanisms are enzymatic degradation, target alteration, decreased uptake and overexpression of efflux pump proteins [18]. In patients with diabetes, this may be attributed to the effect of diabetes on concentration of antitubercular drugs, which would lead to a bacterial adaptation to the selective pressure of the drugs [19]. In Mexico it has been reported that up to 50% of MDR cases have been identified in patients with the binomial [13].

Several factors associated with the binomial have been described: male with age > 40 years, living in an urban residence, high body mass index (BMI), sedentary lifestyle, consumption of tobacco and alcohol, and belonging to an indigenous community. These variables have diverse effects according to the geographical area and the conditions of the population [20]. Nevertheless, there are no studies on the factors associated with the binomial in rural populations from Mexico. Therefore, the present study aims to identify the factors associated with the TB-T2DM binomial in the rural population of the Isthmus of Tehuantepec, Oaxaca.

Methodology

Study design

This was an unpaired cross-sectional case-control study, with a ratio of two controls for each case. The study population consisted of 195 patients with a diagnosis of TB, considering individuals with and without T2DM and residing in the region of the Isthmus of Tehuantepec, Oaxaca. The selection was done according to the Integrated Tuberculosis Epidemiological Surveillance System of the Health Jurisdiction No. 2, in Oaxaca, Mexico. The study period extended from July 2019 to July 2020.

Context of the study region

Health Jurisdiction No. 2 covers the Isthmus of Tehuantepec region, with an area of 20,755.26 km^2 (8013.651mi²), and a total population of 629,036 inhabitants. It is one of the eight regions in the state of Oaxaca and includes 41 municipalities. Sixty percent of its population are poor, with income less than 2700 pesos a month (127 USD), which is not sufficient for their basic needs; 61% of the population is indigenous, mainly represented by the Zapotec ethnic group. The main commercial activities are agriculture, livestock, fishing, and small-scale commerce, which is typical of rural areas [21]. This region is among the three areas that are most affected by TB in Oaxaca and is also an obligatory passage for Central American migrants seeking to reach the United States of America.

Participants and recovery of variables

The sample size was calculated according to previous recommendations by Pérez *et al.* [22], estimating a minimum sample of 126 controls and 68 cases. Participants were recruited by random sampling of all individuals included in the Tuberculosis Epidemiological Surveillance System database. Clinical and sociodemographic data were collected for each patient and included in the study. A case was considered a subject when there was a confirmed diagnosis of TB and a previous (15 days) or simultaneous diagnosis of T2DM (TB+T2DM+); while the control group consisted of subjects with a diagnosis of TB without T2DM (TB+T2DM-). Only people older than 18 years were included. Individuals with a HIV positive diagnosis or incomplete data were excluded.

Data processing and statistical analysis

The information was collected in a database and analyzed using IBM SPSS Statistics, version 27.0 software [23].Descriptive statistics were performed considering several sociodemographic, and clinical variables of the population such as gender, age, socioeconomic level, indigenous or not, tobacco, alcohol, and drug use, as well as the type of TB (pulmonary and extrapulmonary), type of case (new, relapse or failure), type of treatment (primary or retreatment), and the number of symptoms reported. Student's t-test was used to determine the difference in means of continuous quantitative variables and Mann-Whitney test was used to determine the difference in medians. Chi-square test or Fisher's test was used for differences in proportions of qualitative variables.

Factors associated with the TB+T2DM+ binomial were identified by OR estimation considering a 95%

confidence interval (CI), and *p* value < 0.05 as significant. Logistic regression was performed considering variables associated with the binomial according to the literature, and with significance in the previous binomial analysis. Considering the above, the variables included in the analysis were female gender, age ≥ 45 years, indigenous, tobacco, alcohol, or drug use, low socioeconomic status, number of symptoms > 6 and BMI ≥ 25kg/m^2. The Hosmer-Lemeshow test was used considering a value > 0.05 for the goodness of fit.

Ethical concerns

Strict adherence to ethical considerations was maintained. Given that the study was based on secondary sources, there was no contact with the participating patients, so informed consent was not considered. The information was completely anonymized, ensuring protection of personal data following national and international regulations.

Results

Sociodemographic characteristics of the patients

The population included in the study consisted of 195 patients, 69 of them were TB+T2DM+ cases, and 126 TB+T2DM- controls. The median age was 50 years (IQR: 35-60) and 59% of the population were men, showing significant differences between gender (*p* = 0.019). Forty-three percent were considered as indigenous population, and 76% belonged to low socioeconomic status. Only 15% consumed alcohol, 6% consumed tobacco, and 2% used drugs. Sixty-seven percent of the population reported a history of BCG vaccination, with significant differences (*p* = 0.008) between both groups. Regarding occupation, household activities predominated in 31%, with a higher proportion in the TB+T2DM+ group (*p* = 0.038) and agricultural activities in 25%, predominating in the TB+T2DM- group (*p* = 0.037). Sixty three percent were normal weight, 15%, were overweight, and 14% were underweight. Obesity was observed in 8.2%, showing significant differences between groups (*p* = 0.004). In the TB+DM+ group, 20% lacked glycemic control (Table 1).

Table 1. General characteristics of the populations TB+T2DM- and TB+T2DM+.

Characteristics	Total (n = 195)	TB+T2DM- (n = 126)	TB+T2DM+ (n = 69)	*p*
Gender				
Male	115 (59.0)	82 (65.1)	33 (47.8)	0.019[a]
Female	80 (41.0)	44 (34.9)	36 (52.2)	
Age in years				
Median age (IQR)	50 (35.0-60.0)	47 (30.5-59.0)	52 (47.5-65.5)	< 0.001[d]
Socioeconomic level				
Low	148 (75.9)	96 (76.2)	52 (75.4)	0.897[a]
Medium	37 (19.0)	23 (18.3)	14 (20.3)	0.729[a]
High	10 (5.1)	7 (5.6)	3 (1.5)	0.715[a]
Indigenous				
Yes	83 (42.6)	53 (42.1)	30 (43.5)	0.848[a]
No	112 (57.4)	73 (65.2)	39 (34.8)	
Occupation				
House wife	61 (31.3)	33 (26.2)	28 (40.8)	0.038[a]
Farmer	48 (24.6)	37 (29.4)	11 (15.9)	0.037[a]
Employee	21 (10.8)	13 (10.3)	8 (11.6)	0.783[a]
Worker	12 (6.2)	8 (6.3)	4 (5.8)	0.878[a]
Merchant	8 (4.1)	3 (2.4)	5 (7.2)	0.101[a]
[e]Others	34 (17.5)	24 (19.2)	10 (14.4)	0.423[a]
Unemployed	11 (5.6)	8 (6.2)	3 (4.3)	0.562[a]
BMI classification				
BMI mean ± SD	22.53 ± 4.68	21.63 ± 4.03	24.16 ± 5.34	< 0.001[b]
Underweight	27 (13.8)	19 (15.1)	8 (11.6)	0.187[a]
Normal	123 (63.1)	86 (68.3)	37 (53.6)	0.153[a]
Overweight	29 (14.9)	16 (12.7)	13 (18.8)	0.249[a]
Obesity	16 (8.2)	5 (4.0)	11 (15.9)	0.004[a]
Lifestyles factors				
Alcohol consumption	29 (14.9)	17 (13.5)	12 (17.4)	0.464[a]
Tobacco consumption	12 (6.2)	8 (6.3)	4 (5.8)	0.878[a]
Drug consumption	4 (2.1)	3 (2.4)	1 (1.4)	0.661[c]
Vaccination				
BCG vaccine	131 (67.2)	93 (73.8)	38 (55.1)	0.008[a]

[a] Chi-square test; [b] Student's t-test; [c] Fisher test; [d]Mann-Whitney test; [e] It includes students, drivers, nurses, doctors, inmates, retirees, carpenters, electricians, and teachers, each representing < 2% of the total. N/A: Not applicable. IQR: interquartile range.

Figure 1. Number of symptoms and differences in proportions between the TB+T2DM- and TB+T2DM+ groups.

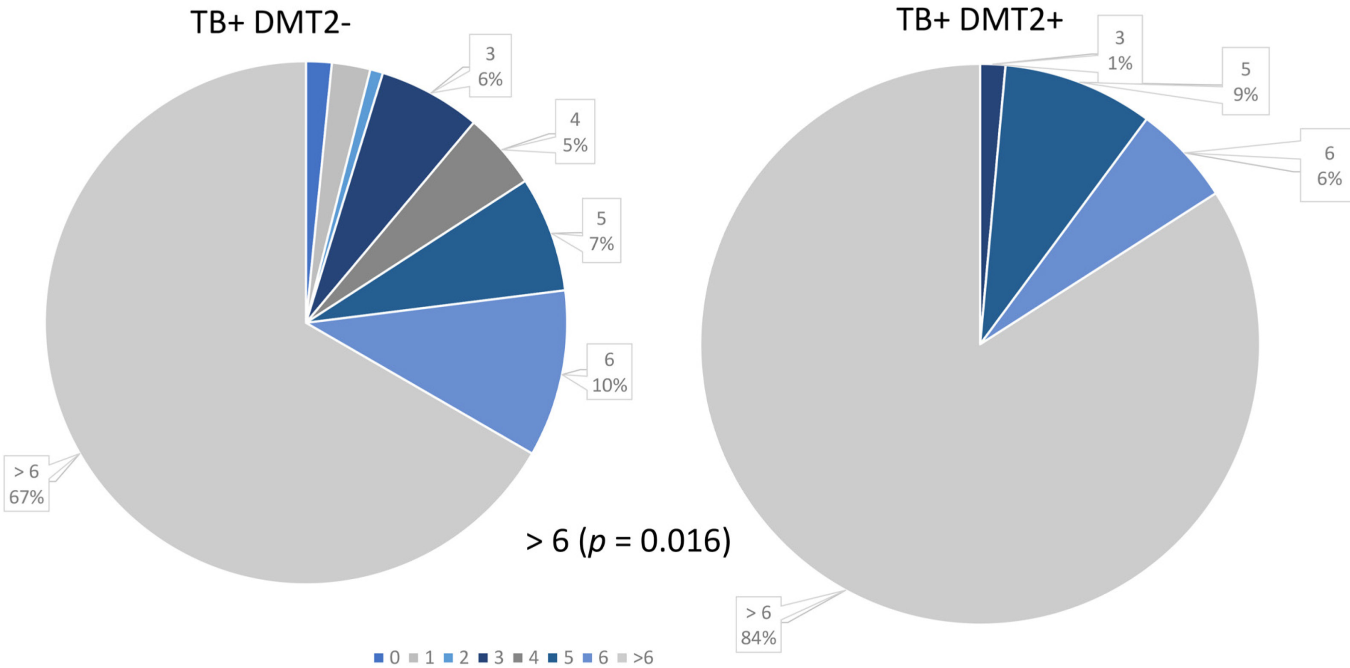

Table 2. Clinical characteristics of the population TB+T2DM- and TB+T2DM+.

	Total n = 195 (%)	TB+T2DM- n = 126 (%)	TB+T2DM+ n = 69 (%)	*p*
Diagnostic result				
(+++)	51 (26.2)	29 (23.0)	22 (31.9)	0.178[a]
(++)	52 (26.7)	16 (12.7)	36 (52.2)	< 0.001[a]
(+)	36 (18.5)	25 (19.8)	11 (15.9)	0.502[a]
Suggestive data of TB	54 (27.7)	54 (42.9)	0 (0.0)	N/A
MTB	2 (1.0)	2 (1.6)	0 (0.0)	N/A
Type of case				
New case	185 (94.9)	121 (96.0)	64 (92.8)	0.321[a]
Relapse	5 (3.1)	4 (3.2)	1 (1.4)	0.658[a]
Treatment abandonment	1 (0.5)	1 (0.8)	0 (0.0)	0.458[b]
Treatment failure	4 (2.1)	0 (0.0)	4 (5.8)	0.015[b]
Type of TB				
Pulmonary	172 (88.2)	103 (81.7)	69 (100.0)	< 0.001[b]
Extrapulmonary	23 (11.8)	23 (18.3)	0 (0.0)	
Type of treatment				
Primary	185 (94.9)	119 (94.4)	66 (95.7)	0.321[a]
Retreat	6 (5.1)	7 (5.6)	3 (4.3)	0.330[b]
Standardized	4 (2.1)	0 (0.0)	4 (5.8)	0.015[b]
Drug resistance	1 (0.5)	0 (0.0)	1 (1.4)	0.354[b]
Main reported symptoms				
Productive cough	162 (83.1)	102 (81.0)	60 (86.9)	0.275[a]
Weight loss	160 (82.1)	101 (80.2)	59 (85.5)	0.352[a]
Fever	143 (73.3)	90 (71.4)	53 (76.8)	0.416[a]
Muscular weakness	108 (55.4)	67 (53.2)	41 (59.4)	0.401[a]
Asthenia	118 (60.5)	68 (54.0)	50 (72.5)	0.012[a]
Adynamia	114 (58.5)	64 (50.8)	50 (72.5)	0.003[a]
6 symptoms	142 (72.8)	84 (66.7)	58 (84.1)	0.016[a]

* Chi-square test; † Fisher test; Tx: treatment; MTB: Xpert MTB/RIF diagnosis; CT: computerized tomography; N/A: Not applicable.

Clinical characteristics

Ninety six percent were new cases, and 71% were diagnosed by smear microscopy. Primary treatment predominated in 95%, only 0.5% were rifampicin-resistant TB (RR-TB). Of the 26 symptoms reported in the follow-up record, the most frequent were: productive cough in 83%, weight loss in 82%, and fever in 73%. Significant differences were found between the groups: treatment failure (p = 0.015), higher bacillary load (two crosses, ++) and presence of pulmonary TB ($p \leq 0.001$), were higher in individuals with binomial. The presence of more than 6 symptoms was more frequently described in TB+T2DM+ patients (p = 0.016) (Figure 1 and Table 2).

Bivariate and multivariate association analysis

Bivariate analysis showed that the risk factors associated with the binomial were: being female (OR = 2.03; 95% CI 1.11-3.69), age ≥ 45 years (OR = 3.01; 95% CI 1.55-5.82), BMI ≥ 25 kg/m2 (OR = 2.66; 95% CI 1.34-5.27), and presenting > 6 symptoms (OR = 2.63; 95% CI 1.25-5.64). This association was maintained in the adjusted logistic regression model; being female (OR = 2.47; 95% CI 1.24-4.92), age ≥ 45 years (OR = 2.90; 95% CI 1.42-5.92), BMI ≥ 25 kg/m2 (OR = 2.69; 95% CI 1.25-5.77), and the presence of > 6 symptoms (OR = 2.71; 95% CI 1.19-6.14). In contrast, smoking, alcohol, drug use, socioeconomic status, and being indigenous showed no association, and were used as adjustment variables in the regression model. (Table 3).

Discussion

Among the people studied, the majority belonged to low socioeconomic status and the main activities were housewives and agricultural work. In addition, a higher percentage of indigenous population were affected, indicating that it is an eminently rural population.

These characteristics differ from those observed in the predominantly urban population of Nepal [24], and Mexico [22] where a medium-high socioeconomic level and a relatively smaller presence of indigenous population were observed. However, our observations are similar to the results of the TANDEM study [25]. The main type of TB presentation was pulmonary with 88%, and 99.5% drug-sensitive cases, similar to a previous report from a population in the United States [26].

Table 3. Estimation of crude and adjusted OR of factors associated with the binomial TB+DM+.

	Subjects (%)	TB+DM- (%)	TB+DM+ (%)	Crude OR			ǂ Adjusted OR		
	195 (100)	126 (64.6)	69 (35.4)	OR	CI 95%	p^a	OR	CI 95%	p
Gender									
Female	80(41)	44 (34.9)	36(52.2)	2.03	1.11-3.69	0.019	2.47	1.24-4.92	0.010
Male	115(59)	82 (65.1)	33(47.8)		1			1	
Age in years									
≥ 45	119(61)	66(52.4)	53(76.8)	3.01	1.55-5.82	0.001	2.90	1.42-5.92	0.003
< 45	76(39)	60(47.6)	16(23.2)		1			1	
Indigenous									
Yes	83(42.6)	53(42.1)	30(43.5)	0.94	0.52-1.70	0.848	-	-	-
No	112(57.4)	73(57.9)	39(56.5)		1				
SE level									
Low	148(75.9)	96(76.2)	52(75.4)	0.95	0.48-1.89	0.897	-	-	-
Medium-High	47(24.1)	30(23.8)	17(24.6)		1				
Alcohol							-	-	-
Yes	29(14.9)	17(13.5)	12(17.4)	1.35	0.60-3.02	0.464	-	-	-
No	166(85.1)	109(86.5)	57(82.6)		1				
Tobacco									
Yes	12(6.2)	8(6.3)	4(5.8)	0.90	0.26-3.13	0.878	-	-	-
No	183(93.8)	118(93.7)	65(94.2)		1				
Drugs									
Yes	4(2.1)	3(2.4)	1(1.4)	0.60	0.06-5.90	0.661	-	-	-
No	191(97.9)	123(97.6)	68(98.6)		1				
BMI									
≥ 25 kg/m^2	45(23.1)	21(16.7)	24(34.8)	2.66	1.34-5.27	0.004	2.69	1.25-5.77	0.011
< 25 kg/m^2	150(76.9)	10(83.3)	45(65.2)		1			1	
Symptoms									
> 6	142(72.8)	84(66.7)	58(84.1)	2.45	1.16-5.17	0.016	2.71	1.19-6.14	0.017
≤ 6	53(27.2)	42(33.3)	11(15.9)		1			1	

[a] Chi-square test; ǂ OR: Odd ratio adjusted by logistic regression; SE level: socioeconomic level; Adjustment variables: indigenous, SE level, alcohol, tobacco, and drug consumption; 1: Reference category.

The variables that were identified with a significant association with comorbidity were age ≥ 45 years, BMI ≥ 25kg/m2, female gender, and presence of > 6 TB symptoms. It has been reported that age is a significant risk factor for the development of the binomial TB-T2DM [20]. This behavior was also observed in our study population, with a difference of almost 10 years between patients with TB, and those with the binomial. These results are similar to those reported in inhabitants from Ethiopia [27], Vietnam [28], and México [13], suggesting that it could be an associated factor independent of the type of population.

Body mass index ≥ 25kg/m2 was identified as a significant factor in patients with the binomial disease, and this coincides with the TANDEM study [24]. This issue is of particular importance for Mexico, considering that 75% of the population over 20 years old is overweight and obese. This increases associated conditions such as hypertension and T2DM [10]. In addition, constant increase in the prevalence of T2DM is an obstacle to TB control, as it is estimated that up to 25% incident TB cases worldwide are attributable to diabetes [29]. In addition, T2DM has been reported to have important implications in reactivating latent tuberculosis infection (LTBI) [30,31]; this implies a greater problem as it is estimated that a quarter of the world population has LTBI [32], nevertheless, the mechanisms of this reactivation are not well understood.

In the Isthmus of Tehuantepec, a higher proportion of women are overweight and have T2DM [33]. This could be due to the nutritional transition process that Mexico is undergoing that has led to an increase in obesity in women in the rural areas, and T2DM [10]. This would explain our observation that being female and obese resulted in significant association with the binomial. These data agree with those described in a study based in Iran [34], where women were more affected by the binomial. However, these data differ from those found in numerous studies where men predominated with the binomial [25,28,35]. Furthermore, most of the TB+T2DM+ cases in our study were housewives (p = 0.038) compared to TB+T2DM- controls who were mostly farmers (p = 0.037), and could reflect the influence of physical activity on glycemic control and the presence of TB [36]. This would place this variable as related to the specific characteristics of the population, and it should be further investigated in areas affected by the binomial and with this type of population.

The outcomes obtained showed no significant association with alcohol consumption, smoking, drug use, indigenous origin, socioeconomic level, and the development of the TB-T2DM binomial. These findings do not agree with reports from other populations [20], which could indicate variations resulting from differences in geographic area and type of individuals [25]. Nevertheless, it is important to consider that some variables in this study such as alcohol consumption, smoking, and drug use were reported in a dichotomous manner; therefore, it would be necessary to conduct more studies with better measures of consumption of substances.

The group of individuals with the binomial presented a higher number of symptoms, indicating a more symptomatic TB. This is consistent with findings in Indonesian population [37]. Likewise, the presence of a higher number of symptoms associated with a higher risk of mortality was reported in people from the Republic of Guinea [38]. Considering the above, an alternative for screening and clinical monitoring in patients with the TB-T2DM binomial is the use of the TBscore II to predict the risk of mortality. This tool allows assigning a score to the number of symptoms reported by the patient at the time of clinical monitoring, the maximum score is 8 points (3 symptoms and 5 signs) and those patients with a score > 2 have a higher risk of TB and are therefore candidates for confirmatory laboratory tests [39]; however, further studies will be required to confirm its usefulness. Likewise, follow-up studies will be necessary to determine the evolution of the symptoms in the individuals, considering that most of the population studied here was diagnosed with tuberculosis for the first time.

One of the limitations of the present study was derived from its design because it was not possible to identify whether T2DM preceded the development of TB. However, there is increasing evidence to support that T2DM is a preceding condition for the development of TB [40]. It has been shown that the presence of T2DM increases the risk of developing active TB up to 3 times [41], therefore, it would be expected that in most cases with the binomial, T2DM is the underlying condition. It should also be considered that Mexico has one of the highest rates of TB, and T2DM epidemic conditions in Latin America. Therefore, specific screening measures should be reinforced considering both diseases, to increase chances of early detection of both conditions, allowing adoption of control strategies that reduce the development of the comorbidity.

Furthermore, it has been reliably demonstrated that, in addition to the risks inherent to each disease, T2DM hinders the therapeutic control of TB, and increases the risk of developing resistance and treatment failure [42,43]. This is confirmed by observations in the population studied here where patients with the binomial presented larger therapeutic failures (p = 0.015), and increased number of crosses in the smear microscopy ($p < 0.001$). This reflects greater severity in the tuberculous disease. It has been reported that patients with TB-T2DM have a higher bacterial load, which would lead to a longer conversion time of the sputum culture, causing more frequent recurrence of TB [44]. A systematic review concluded that diabetes increases the risk of failed treatment and death among patients with tuberculosis; RR = 1.69 (95% CI 1.36–2.12) [45]. Furthermore, TB and the drugs used for its treatment can lead to worse glycemic control in people with T2DM, it has been observed that the efficacy of sulphonyl urea derivatives decreases up to 30% in combination with rifampicin [46], as the isoniazid antagonizes its action and worsens glycemic control [47]. On the other hand, dipeptidyl peptidase inhibitors (DPP), have a theoretical possibility of reducing immunocompetence because of their mechanism of action, and this effect could possibly worsen the outcome of patients with TB [48]. In addition, hyperglycemia has contributed to the reduction of plasma concentrations of anti-tuberculosis drugs, which would favor the survival of the bacteria and their adaptation [49,50]. Therefore, TB and T2DM could aggravate each other and this could produce effects equivalent to the mismanagement of drugs against TB, which is the most common cause for drug resistance [51]. In our study, 1.4% of TB+T2DM+ patients had RR-TB, while in the TB+T2DM- group no case was found. However, in this study there was no access to the treatment scheme for patients with the binomial. Therefore, it was not possible to assess whether the treatment of patients with TB + DM2 + influenced the results obtained. Likewise, all patients with the binomial presented pulmonary TB, which coincides with other studies [27,52,53], and could be related to defects in the immune functions and the lower capacity of alveolar macrophages to eliminate the infection in patients with T2DM [54].

One of the main limitations of this study was that the lack of direct access to the study population; so, it was not possible to obtain information on several variables such as blood glucose levels, physical activity, and years of T2DM evolution. This information would have allowed more accurate monitoring of the T2DM evolution, and its influence on the development of TB.

Conclusions

This is the first study that describes the TB-T2DM binomial behavior in rural Mexican populations. The variables with significant association were BMI $\geq$ 25kg/m2, and age $\geq$ 45 years, which also showed association in the urban population, except for gender, where women predominated in the population studied. Our analysis confirms that the TB-T2DM binomial should be addressed from an integral perspective, including the gender component. Furthermore, is necessary to mandatorily screen patients with T2DM to improve early diagnosis of TB, and vice versa, and promote better management of both diseases, to avoid the development of drug resistance and spread of TB. In addition, it is important to consider a longer treatment regime for TB in patients with the binomial. This would favor a lower prevalence of treatment failure and it already seems to be a common practice in other countries such as China. Therefore, it is necessary to reformulate the clinical practice guidelines for this type of patients. Despite the growing evidence of interaction between DM and TB, as well as their treatments, the schemes remain the same in most countries. Undoubtedly, this will have important implications in rural populations with high levels of obesity and the occurrence of T2DM.

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Authors' Contributions

Zaira Liz Yague-Santiago: data curation, investigation, writing -original draft; María del Pilar Ramírez-Díaz: supervision, data curation and methodology, formal analysis, investigation, writing, reviewing and editing; Doireyner Daniel Velázquez-Vázquez: writing, reviewing, supervision; Roberto Zenteno-Cuevas: conceptualization, methodology, formal analysis, writing, reviewing, supervision and editing; Jorge Fernando Luna-Hernández: supervision, methodology, formal analysis, writing, reviewing, editing, conceptualization.

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