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Impact of the COVID-19 pandemic on contact tracing of patients with pulmonary tuberculosis

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Background: The COVID-19 pandemic could have negative effects on tuberculosis (TB) control. The objective was to assess the impact of the pandemic in contact tracing, TB and latent tuberculosis infection (LTBI) in contacts of patients with pulmonary TB in Catalonia (Spain). **Methods:** Contact tracing was carried out in cases of pulmonary TB detected during 14 months in the pre-pandemic period (1 January 2019 to 28 February 2020) and 14 months in the pandemic period (1 March 2020 to 30 April 2021). Contacts received the tuberculin skin test and/or interferon gamma release assay and it was determined whether they had TB or LTBI. Variables associated with TB or LTBI in contacts (study period and sociodemographic variables) were analyzed using adjusted odds ratio (aOR) and the 95% confidence intervals (95% CI). **Results:** The pre-pandemic and pandemic periods showed, respectively: 503 and 255 pulmonary TB reported cases (reduction of 50.7%); and 4676 and 1687 contacts studied (reduction of 36.1%). In these periods, the proportion of TB cases among the contacts was 1.9% (84/4307) and 2.2% (30/1381) ($P = 0.608$); and the proportion of LTBI was 25.3% (1090/4307) and 29.2% (403/1381) ($P < 0.001$). The pandemic period was associated to higher LTBI proportion (aOR = 1.3; 95% CI 1.1–1.5), taking into account the effect on LTBI of the other variables studied as sex, age, household contact and migrant status. **Conclusions:** COVID-19 is affecting TB control due to less exhaustive TB and LTBI case detection. An increase in LTBI was observed during the pandemic period. Efforts should be made to improve detection of TB and LTBI among contacts of TB cases.

Introduction

Tuberculosis (TB) is one of the main health care problem worldwide with 10 million cases and around 1.5 million deaths worldwide each year.[1,2] Provisional data collected by World Health Organization indicate a reduction in reported TB cases in 2020 of 1.3 million (5.8 million in 2020 and 7.1 million in 2019).[2] The COVID-19 pandemic may have negative effect on reporting and global TB control.[2,3] Policies widely implemented in most countries in 2020 in response to the pandemic, particularly reassignments of health staff and equipment, may have had a severe impact on the delivery TB services.[2–4]

COVID-19 has led to an overload of work in the health system that may have reduced the care of TB-associated comorbidities, such as diabetes, cancer and HIV infection. It may also be associated with greater diagnostic delay, increased exposure to transmission and an increase in the risk of progression of latent tuberculosis infection (LTBI).[4–6]

The specific effect of COVID-19 on TB transmission is difficult to estimate. The reduction in community contacts due to lockdowns and mass mask wearing may have led to a reduction in community transmission.[7] However, a less exhaustive TB and LTBI detection and diagnostic delays due to reductions in access to the health system, could have led to greater transmission.[8]

Overwork in the health system could lead to reductions in the detection of TB and LTBI, and in the mandatory reporting of notifiable diseases, which could worsen the future epidemiological situation of TB.[9] Some studies have indicated that there has been a significant diversion of resources from TB to COVID-19 during the pandemic[10] and, in this scenario, the study of contacts and the detection of new cases of TB and LTBI could be reduced and past errors in TB control reproduced.[11,12]

Catalonia, a region of northern Spain with 7.5 million inhabitants, presented in the last report an annual incidence of TB of 13.0 cases per 100 000.[13] Before the onset of the pandemic, TB control in this region was carried out by the TB clinical units of the main hospitals and by the Epidemiology Services. Since the beginning of the pandemic the surveillance and control of TB and COVID-19 in Catalonia has been carried out by the same units.[14] However, due to impact of COVID-19 the health workers of these units have been focused in the control of pandemic with an important decrease in the number of TB cases notified and in the number of TB contact tracing carried out.[15]

The objective of this study was to assess the impact of the COVID-19 pandemic in contact tracing and in LTBI in a cohort of patients with pulmonary TB in Catalonia (Spain).

Table 1 Results of contact tracing of pulmonary TB cases in the pre-pandemic and pandemic periods in Catalonia (Spain) (1 January 2019 to 31 May 2021)

Period	Pulmonary TB cases with contact tracing	Registered contacts	Contacts with result of LTBI study	LTBI proportion *n/N* (%)	Mean contacts per case	TB proportion *n/N* (%)
Pre-pandemic	503	4676	4307 (92.1%)	1090/4307 (25.3)	8.5	84/4307 (1.9)
Pandemic	255	1687	1381 (81.9%)	403/1381 (29.2)	5.4	30/1381 (2.2)
Total	758	6363	5688 (89.4%)	1493/5688 (26.2)	7.5	114/5688 (2)

Note: TB, tuberculosis; LTBI, latent tuberculosis infection.

Table 2 Characteristics of contacts of pulmonary TB cases in the COVID-19 pandemic and pre-pandemic periods in Catalonia (Spain) (1 January 2019 to 31 May 2021)

Variable	Study period			
	Pre-pandemic		Pandemic	
	n/N (%)	*P-value*	*n/N* (%)	*P*-value
Sex				
Male	652/2231 (29.2)	<0.001	203/677 (30.0)	>0.05
Female	438/2074 (21.0)	Reference	200/704 (28.4)	Reference
Age group (years)				
0–17	181/1006 (18.0)	Reference	88/427 (23.2)	Reference
18–29	188/880 (21.8)	<0.033	42/183 (23.0)	<0.259
30–44	300/1227 (24.5)	<0.001	69/296 (23.3)	<0.193
45–64	365/1010 (36.2)	<0.001	157/402 (39.0)	<0.001
≥65	56/184 (30.4)	<0.001	37/73 (50.7)	<0.001
Immigrant				
Yes	659/1777 (37.1)	<0.001	194/551 (38.3)	<0.001
No	431/2530 (17.0)	Reference	209/830 (25.2)	Reference
Household contact				
Yes	552/1392 (39.6)	<0.001	196/531 (36.9)	<0.001
No	538/2915 (18.5)	Reference	207/850 (24.2)	Reference
Smoking				
Smoker	301/527 (57.1)	<0.001	107/188 (56.9)	<0.001
Ex-smoker	20/53 (37.7)	<0.001	17/35 (48.6)	<0.001
No/Unknown	769/3727 (20.6)	Reference	279/1158 (20.1)	Reference
Alcohol				
Yes	44/89 (49.4)	<0.001	14/37 (37.8)	<0.001
No/Unknown	1046/4218 (24.8)	Reference	389/1344 (28.9)	Reference

Note: *n*, contacts with latent tuberculosis infection; *N*, contacts traced.

Methods

We carried out an epidemiological study of the prevalence of LTBI in contacts of pulmonary TB cases in Catalonia in the pre-pandemic (1 January 2019 to 28 February 2020) and pandemic (1 March 2020 to 30 April 2021) periods. The study population was the contacts of all new active pulmonary TB patients recorded by the epidemiological surveillance network of the Public Health Agency of Catalonia. The study inclusion criterion was being an active case of pulmonary TB residing in Catalonia with community (contact in indoor space, other than household, as working place, public transport, recreational settings or schools) or household contacts who could be located and studied.

Public health officers of Epidemiology Services carried out an epidemiological survey of cases of pulmonary TB that met the inclusion criteria and enlisted the household or community contacts through interviewing the TB patients and/or the health workers that had notified the active TB cases. In addition, all contacts recorded received the tuberculin skin test and/or interferon gamma release assay (IGRA) and a questionnaire on the migrant status, setting of the exposure to the index case, smoking status and risk of alcohol consumption [>4 standard alcohol units (40 g) daily in men and 2.4 units (24 g) in women or a medical record indicating risk of alcohol consumption].

Contacts with positive IGRA or tuberculin skin test (≥5 mm) results were considered infected.[16] All contacts with a positive test underwent a posterior–anterior chest X-ray to rule out active TB. Patients with lesions suggestive of active TB gave a sputum sample to determine the presence of acid-alcohol-resistant bacilli and make cultures.

The dependent variable was contacts presenting LTBI. The main independent variables investigated were the study period (before or after the pandemic onset), age, sex, household contact or non-household contact of the index case, migrant status, smoking status and alcohol consumption.

We compared the prevalence of LTBI in contacts between the pre-pandemic and pandemic periods by age group, sex, household and non-household contact, migrant status, smoking status and alcohol consumption. The chi-square, Fisher and Mantel–Haenszel test and the odds ratio (OR) were used to compare the proportion of TB and LTBI in the pre-pandemic and pandemic periods and the other variables of study, considering a level of $P<0.05$ as statistically significant.

A multiple logistic regression model was developed using the backward stepwise method (SPSS program. 27 version) to detect factors independently associated with the proportion of LTBI. Multiple logistic regression analysis allowed determination of the adjusted OR (aOR) and the 95% confidence intervals (95% CI) of

Table 3 Factors associated with LTBI in contacts of pulmonary TB cases in Catalonia (Spain) (1 January 2019 to 31 May 2021)

Variable	Latent tuberculosis infection % (*n*/*N*)	Crude odds ratio	95% CI	*P*-value
Total	26.2 (1493/5688)			
Period				
Pandemic	29.2 (403/1381)	1.2	1.1–1.4	0.002
Pre-pandemic	25.3 (1090/4307)	Reference		
Sex				
Male	29.4 (855/2908)	1.4	1.2–1.6	0.002
Female	23.0 (638/2778)	1.0		
Age group (years)				
0–17	19.6 (279/1425)	Reference		
18–29	21.6 (230/1063)	1.2	0.9–1.5	0.168
30–44	24.2 (369/1523)	1.4	1.1–1.7	0.003
45–64	48.9 (522/1067)	2.5	2.1–3.1	<0.001
≥65	36.2 (93/257)	2.5	1.8–3.5	<0.001
Immigrant				
Yes	36.2 (853/2328)	2.5	2.2–2.8	<0.001
No	19.0 (640/3360)	Reference		
Household contact				
Yes	38.9 (748/1923)	2.6	2.3–2.9	<0.001
No	18.8 (745/3765)	Reference		
Smoking habit				
Smoker	57.1 (408/715)	4.9	4.1–5.7	<0.001
Ex-smoker	42.0 (37/88)	2.7	1.7–4.1	
No/unknown	21.4 (1048/4885)	Reference		
Alcohol				
Yes	46.0 (58/126)	2.4	1.7–3.5	<0.001
No/unknown	25.8 (1435/5562)	Reference		

Note: 95% CI, confidence interval.

the ORs of the variables associated with the proportion of LTBI, considering a level of $P < 0.05$ as statistically significant.

The Ethics Committee of the Arnau Vilanova University Hospital approved the study (code: CEIC-2049) and conducted according to the principles expressed in the Declaration of Helsinki. All subjects included in the study received detailed information about the study aims before recruitment.

Results

We studied 6363 contacts of 758 cases of active pulmonary TB (mean contacts per case: 8.4). Possible active TB or LTBI was studied in 89.4% (5688/6363) of contacts (7.5 contacts/case). Of the 503 cases of active pulmonary TB in the pre-pandemic period, 4307 contacts (8.5 contacts/case) were studied and of the 255 cases in the pandemic period, 1381 contacts (5.4 contacts/case) were analyzed (Supplementary figure S1).

The proportion of active TB in contacts was 1.9% (84/4307) in the pre-pandemic period and 2.2% (30/1381) in the pandemic period ($P = 0.60$). The proportion of LTBI was 25.3% (1090/4307) in the pre-pandemic period and 29.2% (403/1381) in the pandemic period ($P < 0.01$) (table 1).

In the pandemic period, the proportion of household contacts was higher than that of non-household contact (38.4% vs. 32.3%; $P < 0.01$). With respect to the pre-pandemic period, the proportion of LTBI that were diagnosed increased in females (28.4% vs. 21.0%; $P < 0.01$), and in the <18 years (23.2% vs. 18.0%; $P < 0.01$) and ≥ 65 years (50.7% vs. 30.4%; $P < 0.01$) age groups (table 2).

The risk of LTBI was higher in the pandemic period (OR = 1.2; 95% CI 1.1–1.4), in males (OR = 1.4; 95% CI 1.2–1.6) and increased with the age of contacts (table 3). The proportion of LTBI was also higher in household contact (38.9% vs. 18.8%; $P < 0.001$) immigrants (36.2% vs. 19.0%; $P < 0.001$) smokers (57.1%) and ex-smokers (42.0%) compared with non-smokers (21.4%) ($P < 0.001$), and in risk consumers of alcohol (46.0% vs. 25.8%; $P < 0.001$) (table 3).

Table 4 Factors associated with LTBI in contacts of pulmonary TB cases in Catalonia (Spain): multivariate analysis

Variable	Adjusted odds ratio	95% confidence intervals		*P*-value
Period (pandemic/pre-pandemic)	1.3	1.1	1.5	0.007
Sex (male/female)	1.4	1.2	1.6	0.001
Age group (18–29/0–17)	1.0	0.8	1.2	0.790
Age group (30–44/0–17)	1.2	1.0	1.5	0.118
Age group (45–64/0–17)	2.7	2.2	3.4	0.001
Age group (≥65/0–17)	2.7	2.0	3.9	0.001
Immigrant (yes/no)	2.3	2.0	2.8	0.001
Household contact (yes/no)	2.2	1.9	2.6	0.001

In the multivariate logistic regression model, the risk of LTBI was higher in the pandemic period than in the pre-pandemic period (aOR = 1.3; 95% CI 1.1–1.5) and was also higher in males (aOR = 1.4; 95% CI 1.2–1.6), in the 30–44 years (aOR = 1.2; 95% CI 1.0–1.5), 45–64 years (aOR = 2.7; 95% CI 2.2–3.4) and ≥65 years (aOR = 2.7; 95% CI 2.0–3.9) age groups, in household contact (aOR = 2.2; 95% CI 1.9–2.6) and in immigrants (aOR = 2.3; 95% CI 2.0–2.8) (table 4).

Discussion

During the study period there was a significant reduction in cases of pulmonary TB and in contact tracing and an increase in the proportion of LTBI in the pandemic period, which started in March 2020 and included four pandemic waves (1 March 2020 to 30 April 2021) compared with the pre-pandemic period (1 January 2019 to 28 February 2020).

In the pre-pandemic period, Catalonia had an annual incidence of TB of 13.0 cases per 100 000[13] and a prevalence of LTBI among contacts of TB cases of 25.3%. In the pandemic period, there was an increased to 29.2% in the proportion of LTBI in contacts that may be explained by the differences in the characteristics of the contacts studied.[17,18] Multiple logistic regression analysis showed that the proportion of LTBI was associated with a statistically significant OR of 1.3 for the pandemic period vs. the pre-pandemic period, taking into account the effect on the proportion of LTBI of the other variables studied as sex, age, household contact and migrant status.

The reduction in the number of cases and contacts studied, as in other European countries,[19,20] might be attributed to the reduction in resources allocated to TB control due to COVID-19 pandemic, which has implied that most of health workers of the epidemiological units and clinical centers focused most of their work in COVID-19 patients. Studies have estimated a drastic reduction in TB reporting of 20–30% in the pandemic period.[9,21] Similarly, in Canada Geric et al.[22] in a study in two centers reported a fell of active TB treatment in the pandemic period of by 16% and 29%, respectively; and Louie et al.[8] in San Francisco showed a decreased of 60% for active TB evaluations compared to pre-pandemic levels. Other recent report by the USA. CDC TB program also found a relative reduction in TB cases, but the reduction is much more modest and less likely to be associated with a reduction in resources in disease detection and control.[23]

It is difficult to determine the relative importance of a possible decrease in incidence or a reduction in access to health services that may have led to a reduction in the reporting and diagnosis of active TB in the first few months after the start of the COVID-19 pandemic.[6] It has been suggested that the lockdown periods of the pandemic have led to a further reduction in community contacts and may have led to a reduction in the community transmission of

TB.[17,23] The mass use of masks may also have favored this reduction.[24] In contrast, the reduction in resources for the diagnosis and control of TB may have produced the opposite effect.[7,17,21] The higher proportion of LTBI in the pandemic period (29.2% vs. 25.3%; $P < 0.01$) may be attributed to the reduction in contact tracing in the pandemic period in work contacts, recreational settings and schoolchildren, where the prevalence of LTBL is relatively lower, and to the concentration of studies in household contacts, where the prevalence is comparatively higher. In both, the pre-pandemic and pandemic periods, there was a high proportion of LTBI in household contact (35.9% and 35.5%). The increased risk of infection in females, in the <18 years and ≥65 years age groups in the pandemic period has been observed in other studies.[21,23] All of this suggests that, in the pandemic period, most contact tracing was concentrated in the family where the transmission is usually higher. However, the smaller number of cases studied was not accompanied by an increase in the proportion of detected cases of active TB in contacts. Also, in the study as a whole, the higher prevalence of LTBI in immigrants, alcohol consumption and in smokers and ex-smokers should also be pointed out, as other studies have showed.[25,26]

Studies based on mathematical models have estimated an increase in TB incidence and mortality of 5–15%, but these models should be tested in forthcoming years by empirical data.[21,27] Some studies indicate that, during the pandemic, significant resources for TB programs have been eliminated and a reduction in cases has been attributed to a reduction in diagnoses and an increase in barriers to access to the health system.[6,27] Dara et al.[20] have estimated a decreased of TB notifications by 35.5% in the European Region and data gathered by the World Health Organization from 84 countries shows that an estimated 1.4 million fewer people received care for TB in 2020 than in 2019—a reduction of 21% from 2019.[3]

The study has some limitations. The coverage of the study of LTBI in registered contacts was high (89.4%), but the risk of infection in unstudied contacts could be higher and the proportion of LTBI could be underestimated. The reduction in the number of TB cases in the pandemic period is partly due to lower detection and reporting of cases by the health system.[3] The higher proportion of LTBI in the pandemic period could be explained by the restriction of tracing to cases with a higher risk of transmission, but the relative weight of these factors is unknown. The restrictions on economic activity to essential jobs and the closure of schools during the state of alarm in the COVID-19 pandemic could have reduced community transmission. Likewise, the mass use of non-pharmaceutical measures to prevent the transmission of SARS-CoV-2 may have had an impact on TB transmission in the community that the study did not capture. The strength of the study is that it was population-based, covers all Catalonia and had an inclusion period of more than 2 years.

We recommend that resources for COVID-19 should be reallocated to epidemiological surveillance and that TB surveillance and control activities (including contact tracing and screening of at-risk populations) be made a priority. Public health measures for the control of COVID-19 and TB should be assessed globally through the epidemiological surveillance system and be seen as an opportunity to improve the overall control of transmissible diseases.

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Supplementary data

Supplementary data are available at *EURPUB* online.

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Key points

- The COVID-19 pandemic has had negative effects on tuberculosis (TB) control in Catalonia.
- An increase in latent tuberculosis infection (LTBI) was observed during the pandemic period in Catalonia from 25.3% to 29.2%.
- COVID-19 is strongly affecting TB control due less exhaustive TB and LTBI case detection.

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