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Impact of the COVID-19 pandemic on tuberculosis management in Spain

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ABSTRACT

Background: The impact of COVID-19 on the diagnosis and management of tuberculosis (TB) patients is unknown.
Methods: Participating centres completed a structured web-based survey regarding changes to TB patient management during the COVID-19 pandemic. The study also included data from participating centres on patients aged ≥18 diagnosed with TB in 2 periods: March 15 to June 30, 2020 and March 15 to June 30, 2019. Clinical variables and information about patient household contacts were retrospectively collected.
Results: A total of 7 (70%) TB units reported changes in their usual TB team operations. Across both periods of study, 169 patients were diagnosed with active TB (90 in 2019, 79 in 2020). Patients diagnosed in 2020 showed more frequent bilateral lesions in chest X-ray than patients diagnosed in 2019 ($P = 0.004$). There was a higher percentage of latent TB infection and active TB among children in households of patients diagnosed in 2020, compared with 2019 ($P = 0.001$).
Conclusions: The COVID-19 pandemic has caused substantial changes in TB care. TB patients diagnosed during the COVID-19 pandemic showed more extended pulmonary forms. The increase in latent TB infection and active TB in children of patient households could reflect increased household transmission due to anti-COVID-19 measures.

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Introduction

On 31 December 2020, China first reported a group of cases with atypical pneumonia caused by the SARS-CoV-2 (Lu et al., 2020). As of 8 December 2020, more than 68.5 million people were infected with the virus, and >1.5 million have died as a result of it (World Health Organization, 2020). In Spain, to date, >1.5 million people have been diagnosed with COVID-19 infection, and 47 624 people have died from the disease (Spanish Government, 2020). To reduce the risk of transmission, governments have launched urgent measures that include widespread use of facemasks, closure of public spaces and personal mobility restrictions. Health services have reduced to a minimum the number of daily outpatient visits to decrease the chance of nosocomial transmission. These strategies have allowed control of the first wave of SARS-CoV-2 infection; however, there is concern that we have paid a large toll in the control of other diseases (Saunders and Evans, 2020).

Tuberculosis (TB) is one of the top 10 causes of death globally and, since 2015, is the most frequent cause of death due to an infectious aetiology. In 2019, TB was responsible for an estimated 1.2 million deaths among people not infected with HIV and 251 000 deaths among HIV-positive patients (World Health Organization, 2019). TB has decreased significantly in high-income countries in recent decades; it is mainly diagnosed in immigrants from high incidence TB countries or immunosuppressed patients (Sánchez-Montalvá et al., 2018). Despite the global trend towards a progressive decrease in cases in recent years, recent research has concluded that new cases may increase by 6.3 million and deaths by 1.4 million over the next 5 years as measures taken to control SARS-CoV-2 infection prevent national TB programs from maintaining a minimum set of actions (Hogan et al., 2020). One of the measures adopted at the beginning of the pandemic is that anyone with mild symptoms related to COVID-19 (cough, fever) self-isolated for 14 days or longer if symptoms persisted. Symptoms and signs of pulmonary TB are similar to those related to respiratory viral infections, including COVID-19, which may cause delays in the diagnosis of TB. Moreover, close coexistence is a risk factor for transmitting TB among household contacts (Pienaar et al., 2010; Velen et al., 2020). Therefore, the control measures implemented during the peak of the first wave may have increased the number of TB infections. Additionally, difficulty accessing healthcare assistance may have delayed TB diagnosis, increasing transmission. Conversely, mask use and movement restrictions may positively affect TB transmission. We do not yet know the impact of COVID-19 on the diagnosis and management of TB patients.

Methods

Spanish healthcare providers with TB patient management programs were invited to participate in the study. A TB centre was defined as any healthcare facility with regular management of TB patients. A total of 90 TB centres were invited. Participating centres were asked to complete a structured web-based survey regarding the main changes in the management of TB patients during the COVID-19 pandemic. In addition, they were asked to provide data on all patients aged ≥18 years diagnosed with TB from March 15 to June 30, 2020 (pandemic case group) and the same period in 2019 (pre-pandemic control group). The study protocol was approved by the Vall d'Hebron Research Institute Ethics Committee, PR(AG)354/2020, Barcelona, Spain and local ethics committees as required. Informed consent was not considered necessary.

Data collection

The survey regarding changes at the organizational level and in management of TB patients was conducted using an electronic web-based tool (Google Form). The questionnaire consisted of 23 questions divided into 7 different sections: (1) modifications of the healthcare team working in the TB unit; (2) COVID-19 surveillance in TB patients; (3) modifications of the hospital wards where TB patients attended; (4) modifications in diagnostic tests for TB patients; (5) modifications in the follow-up of TB patients; (6) modifications in the treatment of TB patients; and (7) modifications in the household contacts screening program. The full version of the questionnaire is available as Online Appendix 1.

The patient data collection form included sociodemographic characteristics, comorbidities, radiological and microbiological and treatment variables. All data were retrospectively captured. Smear grade was defined by number of acid-fast bacilli (AFB) observed: 1+, 1–9 AFB/100 fields; 2+, 10-99 AFB/100 fields; 3+, 1–10 AFB/field; 4+, >10 AFB/field. Chest X-ray (CXR) was classified as normal if no parenchymal lesion was observed, unilateral lesions when only a lung field was affected, and bilateral lesions when both lung fields were affected. Presence of cavities was also collected. Time to diagnosis was defined as the number of days between symptoms onset and diagnosis date. Time to treatment initiation was defined as the number of days between symptoms onset and the date of first anti-TB treatment dose. Need for hospital admission, number and type of follow-up visits, adherence to treatment and smear conversion during the first month of treatment were also assessed. Information on number of household contacts assessed and diagnosis of these contacts was collected and classified as: not assessed, not infected, latent TB infection (LTBI), TB disease, and lost to follow-up. Not assessed was defined as a participant not undergoing symptoms evaluation, tuberculin skin test, or interferon gamma release assay and CXR. LTBI is defined as a participant without symptoms of active TB, CXR result not showing active signs of TB disease and positive tuberculin skin or interferon gamma release assay.

Data analysis

Anonymized patient data was entered into a database with a coding system and centralized at the lead hospital for the study, where database merge and cleaning was also carried out. Descriptive statistics are presented as number (percent) and median (interquartile range, [IQR]) or mean (SD) depending on variable normality. Smear grade and CXR classification was performed only in patients with a pulmonary form. To compare variables between patients diagnosed in 2019 and 2020, we used chi-square tests or Fisher's exact tests for categorical variables and t-test or Mann–Whitney U test for continuous variables.

Description of TB cases was summarized temporally by months and fortnights. The yearly incidence rate (IR) was calculated. Incidence was calculated over the total population covered by the hospital, considering the whole hospital-covered population had the same risk of acquiring TB disease. The incidence rate ratio (IRR) was used to compare if the number of cases had increased or decreased. Additionally, the IR for the lockdown (15 March to 30 April) and the post-lockdown period (1 May to 30 June) were calculated for 2019 and 2020 using the average of total cumulative cases per period to make the comparison. We used the IRR between the lockdowns in 2019 and 2020 and the post-lockdown periods in 2019 and 2020. We did not perform age or gender adjustment for the calculation of IRs. A P value <0.05 was considered significant. All analyses were performed using SPSS statistical software (IBM SPSS version 23, Armonk, N.Y.).

Results

Changes in the management of TB patients

A total of 13 Spanish centres answered the questionnaire regarding changes at organizational level and in the management

of TB patients; 10 had a specialized TB unit. The median (IQR) number of healthcare workers in the TB units was 3.5 (3–6.25). The number of healthcare workers was reduced due to the COVID-19 pandemic in 3/10 (30%) of the TB units and 7 (70%) reported changes in the usual operations of the TB team, mainly due to cancellation of meetings or substitution of face-to-face meetings for online/telephone meetings. SARS-CoV-2 screening was systematically performed in all TB patients in 3/13 (23.1%) centres, exclusively in patients with symptoms suggesting SARS-CoV-2 infection in 5 (38.5%), and not performed in 5 (38.5%).

Hospitalization wards where TB patients were admitted changed during the COVID-19 pandemic in 12 (92.3%) centres. The admission ward was determined based on whether the patient was concomitantly infected by SARS-CoV-2. However, the healthcare team attending TB patients was the same as before the pandemic with minimum modifications in 12 (92.3%) centres. Delays in performance of laboratory tests were reported by 3 (23.1%) centres and 11 (84.6%) reported difficulties in accessing other complementary exams, such as radiology exams or minimally invasive procedures (cancellation in 1, less test availability in 7, both in 3).

Follow up visits were either cancelled or delayed in 10 (76.9%) centres due to the pandemic. Changes in household contacts screening programs were described by 7 (53.8%) centres; screening was not performed in 1, delayed in 1 and both delayed and prioritized for vulnerable populations, such as the paediatric population and immunosuppressed contacts, in 5 (38.5%). None of the centres reported problems in drug supply.

Comparisons between patients diagnosed with TB 15 March to 30 June 2019 and 15 March to 30 June 2020

A total of 11 TB centres shared aggregated data on patients. The population covered by each TB centre is provided in Online Appendix 2. Across both study periods 169 patients were diagnosed with active TB (90 in 2019, 79 in 2020). The IR was 10.25 and 9.31 per 100 000 person-years in 2019 and 2020, respectively, IRR = 1.14 (95% CI (0.84–1.54); $P = 0.442$). The number of patients with active TB diagnosed per fortnight in both periods is represented in Figure 1. For the lockdown periods, the IR was 12.9 per 100 000 person-years in 2019 and 8.57 per 100 000 person-years in 2020 (IRR 1.61 (1.03–2.52); $P = 0.04$). In the post-lockdown period, we observed an IR of 10.43 and 9.86 in 2019 and 2020, respectively, with an IRR of 1.2 (95% CI (0.79–1.83); $P = 0.46$).

There were no significant differences in demographics between cohorts. In both years, approximately 40% of the patients were Spanish born. The World Health Organization regions of Europe and the Eastern Mediterranean accounted for approximately two-thirds of the cases. In 2019, 48/90 patients (53.3%) had a relevant comorbidity, in 2020, this was 48/79 patients (60.8%); the distribution did not differ significantly between the cohorts.

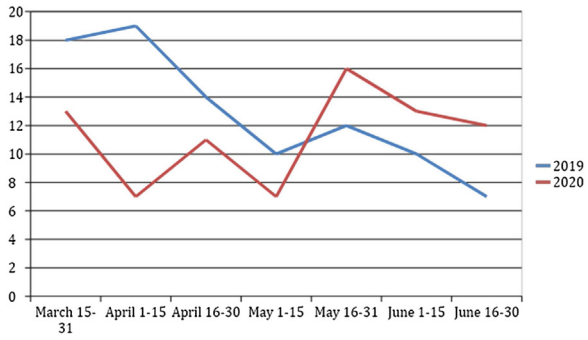

Figure 1. Number of patients with active TB diagnosed along both periods.

Extrapulmonary disease was frequent in both years, in 42/90 (46.7%) and 33/79 (41.8%) patients in 2019 and 2020, respectively. The most frequent extrapulmonary forms, in decreasing prevalence, were adenopathic, pleural and disseminated disease. Patients diagnosed in 2020 showed more frequent bilateral lesions in CXR compared with patients diagnosed in 2019 (56.5% vs 27.1%, $P = 0.004$).

Table 1
Demographics, clinical and microbiological characteristics of tuberculosis patients in both periods.

	2019 Cohort N = 90	2020 Cohort N = 79	*P* value
Sex, female	30 (33.3%)	27 (34.2%)	0.908
Age, years (mean, SD)	41.0 (31–59)	47.5 (34.5–65.7)	0.595
Country of birth			
Spain	35 (38.9%)	31 (39.2)	0.963
WHO region of origin			
Africa	6 (6.7%)	6 (7.6%)	0.628
America	8 (8.9%)	12 (15.2%)	
South-East Asia	7 (7.8%)	4 (5.1%)	
Europe	43 (47.8%)	38 (48.1%)	
Eastern Mediterranean	20 (22.2%)	17 (21.5%)	
Western Pacific	6 (6.7%)	2 (2.5%)	
Comorbidities	48 (53.3%)	48 (60.8%)	0.609
Chronic pulmonary disease	13 (14.4%)	15 (19.0%)	0.133
Cardiomyopathy	8 (8.9%)	8 (10.1%)	0.867
Liver disease	10 (11.1%)	5 (6.3%)	0.216
Renal disease	3 (3.3%)	2 (2.5%)	0.389
Diabetes	16 (17.8%)	6 (7.6%)	0.050
Hypertension	16 (17.8%)	13 (16.5%)	0.971
Psychiatric disease	10 (11.2%)	7 (8.9%)	0.348
HIV infection	5 (5.6%)	6 (7.6%)	0.845
Hepatitis B infection	1 (1.1%)	2 (2.5%)	0.770
Hepatitis C infection	4 (4.4%)	5 (6.3%)	0.857
Solid organ transplant	2 (2.2%)	2 (2.5%)	1.000
Immunosuppressive treatment	6 (6.7%)	6 (8.9%)	0.564
Current smoker	40 (44.4%)	23 (29.1%)	0.021
Alcohol use	19 (21.1%)	11 (13.9%)	0.066
Illegal drug use	6 (6.7%)	5 (6.3%)	0.639
Homeless	4 (4.4%)	3 (3.8%)	1.000
Pulmonary TB	48 (53.3%)	46 (58.2%)	0.523
Non-pulmonary TB	42 (46.7%)	33 (41.8%)	
Adenitis	12 (28.6%)	12 (36.4%)	
Pleural	10 (23.8%)	10 (30.3%)	
Abdominal	1 (2.4%)	2 (6.1%)	
Urinary	0	1 (3.0%)	
Bone	3 (7.1%)	1 (3.0%)	
Skin	1 (2.4%)	0	
Pericardic	1 (2.4%)	0	
Disseminated	11 (26.2%)	6 (18.2%)	
CNS	1 (2.4%)	0	
Radiological findings (CXR)			
Normal CXR	2/48 (4.2%)	0/46	0.495
Unilateral lesions	33/48 (68.8%)	20/46 (43.5%)	0.014
Bilateral lesions	13/48 (27.1%)	26/46 (56.5%)	0.004
Cavitation	14/48 (29.2%)	19/46 (41.3%)	0.218
AFB smear positive	29/48 (60.4%)	29/46 (63.0%)	0.611
Grade sputum smear			
1-9 AFB per 100 fields	11/29 (37.9%)	11/29 (37.9%)	0.891
10-99 AFB per 100 fields	4/29 (13.8%)	6/29 (20.7%)	
1-10 AFB per field	4/29 (13.8%)	4/29 (13.8%)	
>10 AFB per field	10/29 (34.5%)	8/29 (27.6%)	
NAAT positive in sputum	25/48 (52.1%)	29/46 (63.0%)	0.421
Culture positive for TB	65 (72.2%)	68 (86.1%)	0.078
RMP resistance	1 (1.1%)	0	
INH resistance	1 (1.1%)	4 (5.3%)	
PZA resistance	1 (1.1%)	1 (1.3%)	
ETB resistance	0	0	
SM resistance	1 (1.1%)	4 (5.1%)	
Days to diagnosis[a], median (IQR)	59 (22–134)	63.4 (29–116)	0.546
Days to treatment, median (IQR)	60 (21·2–134)	63 (25–116)	0.865

SD = standard deviation; WHO = World Health Organization; TB = tuberculosis; CNS = central nervous system; CXR = chest X-ray; AFB = acid fast bacilli, NAAT = nucleic acid amplification test; RMP = rifampin; INH = isoniazid; PZA = pyrazinamide; ETB = ethambutol; SM = streptomycin.

[a] Time from symptoms onset to diagnosis.

Table 2
Management and follow-up of patients with tuberculosis.

	2019 Cohort N = 90	2020 Cohort N = 79	P value
More than one consultation previous to diagnosis	44 (48.9%)	39 (49.4%)	0.982
Tested for SARS-CoV-2			
Home isolation due to SARS-CoV-2 suspicion	–	59 (74.7%)	–
Need for hospital admission during diagnosis	–	19 (24.1%)	–
Need for hospital admission during Follow-up[a]			
Initial treatment regimen	53 (59.6%)	52 (66.7%)	0.422
Rifampin based treatment			
Rifabutin based treatment	12 (13.3%)	11 (13.9%)	0.412
Quinolones supplemented treatment			
AFB conversion time (days), median (IQR)			
Treatment adherence (≥75%)	88 (97.7%)	73 (92.4%)	0.488
Adverse effects	0	1 (1.2%)	
Treatment interruption	2 (2.2%)	4 (5.1%)	
	33·5 (21.7–45.7)	34 (14–45)	0.306
	83 (92.2%)	75 (94.9%)	0.509
	24 (26.7%)	13 (16.5%)	0·212
	9 (10.0%)	5 (6.3%)	0.083
Number (median, SD) of FU visits[b]	2 (1–3)	1 (1–2)	0.002
Type of FU visits			
Face-to-face visit	58/71 (81.7%)	40/59 (67.8%)	0.006
Telephone	0	11/59 (18.6%)	
Both (face-to-face and telephone)	9/71 (12.7%)	4/59 (6.8%)	

RMP = rifampin; INH = isoniazid; PZA = pyrazinamide; ETB = ethambutol; Rb = rifabutin; Mx = moxifloxacin; Lx = levofloxacin; AK = amikacin.
[a] Patients who were admitted for diagnosis but could not be discharged during the first month of follow-up were also included.
[b] Patients who needed hospital admission during diagnosis were excluded.

Table 3
Household contacts with latent tuberculosis infection or active tuberculosis.

	2019 Cohort N = 68	2020 Cohort N = 51	*P* value
Total adult contacts	159	105	
Adult contacts screened	98/159 (61.6%)	89/105 (84.8%)	**<0.001**
LTBI among adult contacts	32/98 (32.7%)	33/89 (37.1%)	0.526
Active TB among adult contacts	2/98 (2.0%)	3/89 (3.4%)	0.670
LTBI or active TB adult contact	34/98 (34.7%)	36/89 (40.4%)	0.417
Total child contacts	24	31	
Child contacts screened	19/24 (79.2%)	26/31 (83.9%)	0.654
LTBI among children contacts	1/19 (5.3%)	7/26 (26.9%)	0.061
Active TB among child contacts	0	8/26 (30.8%)	**0.014**
LTBI or active TB child contact	1/19 (5.3%)	15/26 (57.7%)	**<0.001**

LTBI = latent tuberculosis infection; TB = tuberculosis.
Bold values are statistically significant values (<0.005).

Demographics, clinical and microbiological characteristics of patients diagnosed in both periods are summarized in Table 1.

In the 2020 cohort 59/79 patients were tested for SARS-CoV-2; none of the tests were positive, however, 19 (24.1%) patients were isolated at home due to suspicion of infection. The number of follow-up visits in 2020 was lower than in 2019 (median of 2 vs 1 follow-up visits, $P = 0.002$) and the type of follow-up visits differed between both periods, with more follow-ups by telephone in 2020. This information is summarized in Table 2.

Information from the household contacts screening program was available for 68 (75.6%) and 51 (64.6%) TB patients diagnosed in 2019 and 2020, respectively. More adult contacts were screened in 2020 than in 2019 (84.8% vs 61.6%, $P < 0.001$). We observed a higher percentage of LTBI and active TB among children who were household contacts of patients diagnosed in 2020 compared with patients diagnosed in 2019 (57.7% vs 5.3%, $P < 0.001$). See Table 3.

Discussion

To our knowledge, this is the first study describing changes in TB management and comparing the clinical variables of patients diagnosed with TB during the COVID-19 pandemic with the same period in 2019. We observed substantial changes in the clinical care of patients with TB during the COVID-19 pandemic. Moreover, we observed that patients diagnosed during 2020 showed more frequently bilateral lesions in CXR, and their children household contacts were more frequently diagnosed with LTBI or active TB.

During the COVID-19 pandemic both human and economic health resources have been re-allocated due to the high priority of this disease, causing disruption in the diagnosis and treatment of several health conditions (Raymond et al., 2020) and cancelling many outpatient activities and elective procedures (Ng et al., 2020). In addition, all community-based disease prevention and health promotion programs have been dramatically affected in many countries (Abdela et al., 2020). In our study, we observed that the number of healthcare workers usually taking care of TB patients was reduced due to the COVID-19 pandemic and most of the TB units reported organizational and operational changes. Moreover, most centres in the study reported difficulties in access to complementary tests, either cancellation or delay in follow-up visits, and changes in the household contact screening program. The impact of COVID-19 in the care of infectious, mainly pulmonary diseases might have been higher than in other disease areas, as the teams involved in their care were frequently mobilized to be part of the COVID-19 teams, often composed of infectious diseases or pneumology physicians, and specialized nurses. Global disruptions of TB services have been previously described (Migliori et al., 2020; Nikolayevskyy et al., 2020).

The restrictions imposed by governments (e.g., stay-at-home orders) to decrease the transmission of SARS-CoV-2 has changed the delivery of patient care, impacting negatively on the health of the patients through delayed care of acute emergencies, exacerbation of chronic diseases and psychological distress (Hamadani et al., 2020; Woolf et al., 2020). Across the United States a decrease in overall outpatient visits was observed during the first period of the pandemic and a rebound during the last months (Mehrotra et al., 2020). Similarly, we also observed a lower number of new TB diagnoses during the first months of the lockdown period, and a rebound during the last months. However, the overall number of patients with a diagnosis of TB has been lower in 2020 compared with the same period in 2019, as has been reported in other

countries (Lai and Yu, 2020; Kwak et al., 2020). The decrease in IR may be partially explained by the long-term trend of gradual TB incidence reduction in Spain. However, we also observed an upturn in diagnosed cases after the lockdown period, so the IR reduction may not be due to the historical trend in TB IR reduction but rather an effect of the lockdown itself. Notification of new TB cases during the next months will help to clarify this point.

The similarities in TB and COVID-19 symptoms may hinder the detection of TB, leading to a misdiagnosis impacting on community transmission. In our study, more than 24% of patients with active TB were isolated at home due to suspicion of SARS-CoV-2 infection. This home isolation may have increased household transmission. One of the most important strategies to fight against TB is early diagnosis, isolation and treatment of active TB patients so that they rapidly become non-infectious and secondary cases are avoided. Community TB transmission may have been reduced through population-wide wearing of face masks and social distancing measures. Studies on TB incidence during the next months and years will help us to better know the long-term epidemiological impact of COVID-19 measures.

The disruption of TB programs directed to highly vulnerable populations (e.g., economically disadvantaged, racial and ethnic minorities, homeless, people living with HIV, undocumented migrants) and restrictions to personal mobility combined with diagnosis delay may have negatively impacted vulnerable populations and household transmission, respectively (Amimo et al., 2020). In our study, patients diagnosed with TB during the COVID-19 pandemic showed more frequent bilateral lesions in chest radiographies, suggesting more advanced disease. We cannot be sure that there are no other variables involved in this finding and we did not observe a longer duration of symptoms in 2020 than in 2019. However, a relationship is likely to changes in health-seeking behaviours and delays in healthcare attention caused by difficulties in accessing healthcare facilities, overworked microbiology and other complementary laboratories, and patients' fears of interacting with other people and being infected (Jones et al., 2020). Moreover, during the pandemic, the only way to request an appointment with a medical practitioner was by phone or online. It is well known that TB usually affects people from low socioeconomic settings to whom remote medical consultation may be less suited, thereby increasing the barriers to healthcare assistance (Jones et al., 2020).

Our study did not observe differences between the cohorts in need for hospital admission or days to sputum smear conversion, indicating that TB units have been able to continue to manage TB patients with a high level of care during the pandemic. Reflecting on this finding may bring opportunities to implement new approaches to ensure TB programs remain successful and apply lessons learned from this emergency. Rapid restoration of TB services is essential to prevent long-term negative impacts (Cilloni et al., 2020), but we can also scale up successful initiatives such as the use of digital tools to cope with a TB epidemic (Chiang et al., 2020; Hopewell et al., 2021; Togun et al., 2020).

The participating TB units reported changes in TB household contact screening programs. Despite reported changes, the percentage of household contacts screened was higher than during the previous period; however, we also observed an alarming rise in child household contacts with either LTBI or active TB. One possible explanation is that during 2020 high-risk contacts had been prioritized. It is easy to understand that delays in diagnosis combined with stay-at-home orders are a dangerous combination in the household environment for airborne transmitted diseases such as TB. Preventing active TB disease through prompt screening and treating LTBI is a critical component of the World Health Organization's End TB Strategy (Uplekar et al., 2015) and one of the priority interventions required for countries with a low TB incidence to progress towards elimination of TB (Lönnroth et al., 2015).

Our study has some limitations. First, all variables were collected retrospectively with the inherent limitations of this study type. Second, we did not have data on household contacts for some patients. However, these were mainly patients with extrapulmonary TB in which contact studies aim to diagnose missing index cases. Third, our study cannot establish a causative effect between COVID-19 measures and delays in TB diagnosis and increased household transmission. However, it seems reasonable to conclude that the COVID-19 pandemic may have unknown consequences for the TB dynamic. Fourth, only 12% (effective response rate) of the centres returned the survey, and raw IRs were calculated without age or gender adjustment, so external validity could be compromised. However, the total population covered by the participating TB centres is >3 million people.

In conclusion, our study shows that the COVID-19 pandemic has caused substantial changes in TB care. TB patients diagnosed during the COVID-19 pandemic showed more extended pulmonary forms. The increase in LTBI infection and active TB in children who were household contacts of patients reflects increased household transmission due to anti-COVID-19 measures. More studies assessing the impact of the COVID-19 pandemic on TB dynamics both globally and locally are urgently needed. The situation may be an opportunity to implement lessons learned to ensure TB programs remain successful.

Ethical approval

The study protocol was approved by the Vall d'Hebron Research Institute Ethics Committee, PR(AG)354/2020, Barcelona, Spain and local ethics committees when needed.

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Conflicts of interest

None.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ijid.2021.04.075.

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