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Early View

Research letter

Gauging the impact of the COVID-19 pandemic on tuberculosis services: a global study

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Gauging the impact of the COVID-19 pandemic on tuberculosis services: a global study

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Summary: This global study of 43 TB centres from 19 countries demonstrates the impact of COVID-19 pandemic on TB services. Newly diagnosed TB disease, drug-resistant TB, TB deaths, outpatient clinic attendances and newly diagnosed TB infection were reduced.

Keywords: COVID-19, Tuberculosis, TB infection, health services

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Dear Editor,

The effects of the COVID-19 pandemic on tuberculosis (TB) disease and TB services emerged in the beginning of 2020 [1, 2]. Epidemiological and clinical studies, including mortality rates of the first cohort of patients with COVID-19 and TB co-infection were described [3, 4]. Several reports from individual countries suggested that the COVID-19 pandemic significantly affected TB services [5-9], including validation by modelling studies [10]. The Global Tuberculosis Network (GTN) reported that the COVID-19 pandemic affected TB services in 33 TB centres from 16 countries in the first four months of 2020 [11]. An increased use of telehealth during the COVID-19 pandemic was observed in some TB centres [11]. The major limitations of that study were the short period of observation (January-April 2020 compared to the same period in 2019) and the limited number of variables analysed [11-14].

The current study aims to describe the effects of the COVID-19 pandemic on TB services and TB-related activities during the entire first year of the pandemic in 2020 compared to 2019.

Invitations were sent to the centres previously involved [11], with the addition of Virginia in the USA, Lithuania, Oman, and Paraguay. State-wide and /or regional data were collected from Australia (Victoria State), Oman, Paraguay, Portugal (Northern Portugal), Russia (Moscow and Arkangelsk Region/Oblast) and USA (Virginia State). The coordinating centre and the participating centres had ethics clearance in abidance with their institutional regulations [11]. Data was collected from January 1st 2019 to December 31st 2020.

The following variables were collected monthly: total number of TB disease of patients with a new diagnosis or a recurrence; number of newly diagnosed TB disease managed in

outpatient clinics; number of TB patients discharged from hospital; number of drug-resistant TB; number of new TB infections; number of tests performed to diagnose TB infection encompassing tuberculin skin test (TST) and interferon-γ release assays (IGRAs); number of TB-deaths; telehealth services provided for TB disease management (*i.e.*, video Directly Observed Therapy - DOT- or face-to-face teleconsultation). Data quality check was performed in dialogue with the participating centres under the guidance of two methodology experts.

As TB centres from Moscow and Paraguay only provided TB infection tests and newly diagnosed TB infections on an annual basis, these data were excluded from the monthly data analysis. Details of lockdown and other social restrictions were collected, including dates and whether they were fully or partially implemented (data not shown). Mean ± s.d were computed per month for each year. Analysis was performed using Mann-Whitney U test and a p-value of <0.05 was deemed statistically significant. All computations were performed using Graphpad Prism 7 (version 7.04, GraphPad Software)

Forty-three TB centres located in 19 countries of 5 continents provided epidemiological data (Figure 1, panel 1, individual country data not shown). Eight TB centres were enrolled in Spain, 6 in Oman, 5 in Italy, 3 in Brazil, 4 in Niger, 2 in Mexico, 2 in Russia, 2 in Australia, 2 in Philippines, and 1 from each of 9 other countries. Data on TB disease and infection were provided by all centres, except India, Netherlands, and Niger which did not have information on the number of TB-infected individuals and diagnostic tests provided.

Lockdowns were implemented in all countries at different times. The earliest lockdown was on February 1st, 2020, in Australia, and the latest on April 7th in Singapore. The majority of the countries implemented multiple lockdowns with partial or full reopening.

TB disease decreased from 32,898 (mean 2,742 ±177 s.d./month) in 2019 to 16,396 (1,366 ± 308/month; $p<0.0001$) in 2020 with a sudden decline in March 2020, concomitantly with the commencement of lockdown in majority of the countries (Figure 1, panel 2A). This epidemiological change was observed in all countries, except the TB centres in Australia, Singapore and Virginia (USA). The number of patients with TB disease discharged from hospitals increased in February and March 2020 compared to the same period in 2019, before a drastic drop commenced in April 2020 (Figure 1, panel 2B)(492 ± 37/month in 2019 vs 365 ± 105/month in 2020; $p=0.0007$). Only two TB centres located in Australia and Virginia (USA) showed a modest increase.

The number of drug-resistant TB disease decreased from 4,717 in 2019 to 1,527 in 2020 with the decrease starting in March and April 2020 (Figure 1, panel 2C)(393 ± 31/month in 2019 vs 127 ± 32 /month in 2020 ; $p<0.001$) . Although the number of drug-resistant TB in some countries was small, an evident decline was observed in Argentina, Brazil, India, Mexico, and Russia. Similarly, the overall TB deaths decreased from 795 in 2019 to 622 in 2020, but subsequently increased in May 2020 (Figure 1, panel 2D)(66 ± 9/month in 2019 vs 52 ± 9 /month in 2020; $p = 0.0006$).

Newly diagnosed TB disease in outpatient clinics reduced from 7,364 in 2019 to 5,703 in 2020, with a significant decline in March 2020, except the centres in Australia and Virginia (USA) (Figure 1, panel 2E)(613 ± 57/month in 2019 vs 475 ± 90/month in 2020; $p= 0.0005$). Despite substantially lower number of newly diagnosed TB disease in outpatient clinics during the pandemic year, the number of telehealth activities was much higher in 2020, with two peaks in April and September 2020 (Figure 1, panel 2F)(13 ± 7/month in 2019 vs 102 ± 54/month in 2020; $p<0.0001$).

Fewer individuals were diagnosed with TB infection, with a decrease in April 2020 (Figure 1, panel 2G)(363 ± 51/month in 2019 vs 248 ± 76/month; p=0.0007). There were less tests performed globally in 2020 with two major troughs in April 2020 and in November/December 2020 (Figure 1, panel 2H)(2,413 ± 269/month in 2019 vs 1,755 ± 412/month/month; p = 0.0002). Centres in the Russian Federation performed more TB infection tests in 2020, compared to 2019 which were done on recommendations by the Russian Department of Health.

The impact of the COVID-19 pandemic on TB services was investigated in 19 countries during 2020 compared with the pre-pandemic year 2019. For the first time we provided evidence that the overall number of patients with TB disease and drug-resistant TB identified at these centres substantially decreased in the first COVID-19 pandemic year compared to 2019, possibly due to difficult access to TB care, lockdown measures and delayed reporting. A similar trend was observed in the majority of the selected countries, mainly in those with higher TB burden. The peak of hospital discharges in March 2020 may be attributed to the need to make space for COVID-19 patients, while outpatient attendances may have increased in February 2020 due to a surge in outpatient prescriptions to tide patients over subsequent months.

A modest increase in TB notifications occurred in Australia and Virginia (USA) in 2020. Given the advanced health systems in these countries, this is likely due to enhanced surveillance to both TB and COVID-19 [12, 14, 15]. A reduction of identified TB disease cases was observed even in low TB incidence countries (e.g., Italy, France, and Spain), which were considerably affected by the COVID-19 pandemic. The reduction of identified drug-resistant TB

in countries with considerable burden of disease (e.g., Argentina, Brazil, India, Mexico, and Russia) raises concerns of future rebounds.

Although TB deaths in 2020 was lower than in 2019, an increase in May and July 2020 was possibly due to deaths misattributed to COVID-19, although other factors such as under-diagnoses or under-reporting are issues in some centres.

Despite decreased patients with TB disease in outpatient clinics, the use of telehealth services was considerably higher in 2020, driven by COVID-19 distancing measures and in keeping with programmatic innovations to address the challenges during the pandemic [16]. The peaks observed in April and October 2020 were temporally related to the first and the subsequent COVID-19 waves. Newly diagnosed TB infection and TB infection tests were also generally lower in 2020 relative to 2019.

Although the large number of countries and collected variables are strengths of the present study, the heterogeneity of the collected information (eg. hospital discharges and drug-resistant TB numbers which may themselves be affected by multiple factors), the reliance on individual TB centres and not on TB national programmes, and the under-representation of some geographical areas e.g., Africa, are limitations. The data that we collected were not available to national TB programmes at the time of data collection and the trends shown here may also be biased by the occurrences in countries with the largest amount of observations. However, our observations tie in with other substantive disruptions in TB care and notification that have been reported by WHO [17].

In summary, this study showed the severe impact of the COVID-19 pandemic on TB services across many countries. There is an urgent need to re-prioritise resources to manage an expected TB resurgence in future.

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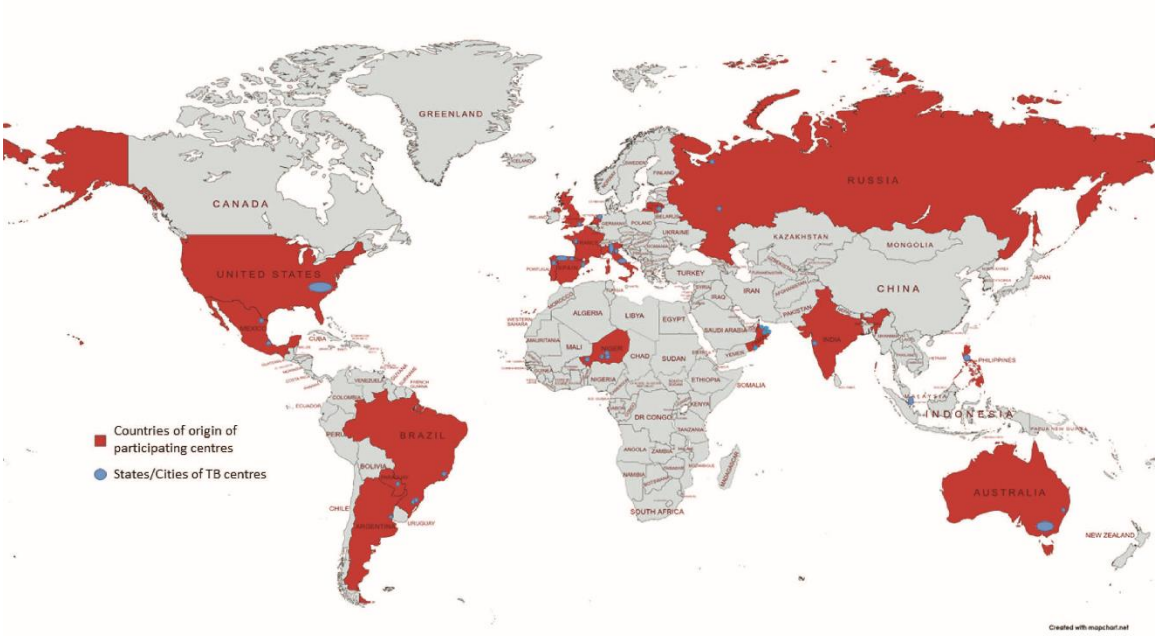

Figure 1, panel 1. Countries of the participating centres of the study.
State-wide and /or regional data were collected from Australia (Victoria State), Oman, Paraguay, Portugal (Northern Portugal), Russia (Moscow and Arkangelsk Region/Oblast) and USA (Virginia State).

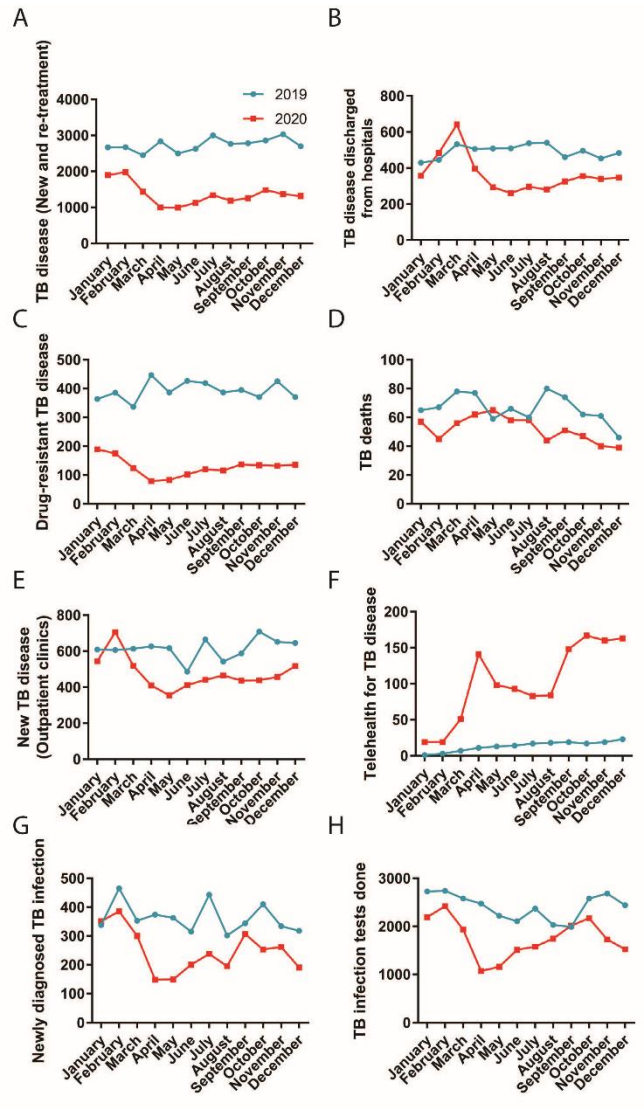

Figure 1, panel 2: **TB disease and infection trends in 2019 and 2020.** (A) TB disease. (B) TB disease discharged from hospital. (C) Drug-resistant TB disease diagnosed. (D) TB deaths. (E) Newly diagnosed TB disease in outpatient clinics. (F) Telehealth use for TB disease in outpatient clinics. (G) Newly diagnosed TB infection across centers. (H) Latent TB tests comprising of tuberculin skin tests and interferon-γ release assays performed.

*Data from Moscow and Paraguay are excluded from (G) and (H) as only annual data are available from these two centers.