A decline in tuberculosis diagnosis, treatment initiation and success during the COVID-19 pandemic, using routine health data in Cape Town, South Africa

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Abstract

Background

Coronavirus disease (COVID-19) negatively impacted tuberculosis (TB) programs which were already struggling to meet End-TB targets globally. We aimed to quantify and compare diagnosis, treatment initiation, treatment success, and losses along this TB care cascade for drug-susceptible TB in Cape Town, South Africa, prior to and during COVID-19.

Methods

This observational study used routine TB data within two predefined cohorts: pre-COVID-19 (1 October 2018–30 September 2019) and during-COVID-19 (1 April 2020–31 March 2021). The numbers of people diagnosed, treated for TB and successfully treated were received from the Western Cape Provincial Health Data Centre. Pre and post treatment loss to follow up and cascade success rates (proportion of individuals diagnosed with an outcome of treatment success) were calculated and compared across cohorts, disaggregated by sex, age, HIV status, TB treatment history and mode of diagnosis.

Results

There were 27,481 and 19,800 individuals diagnosed with drug-susceptible TB in the pre- and during-COVID-19 cohorts respectively, a relative reduction of 28% (95% CI [27.4% - 28.5%]). Initial loss to follow up increased from 13.4% to 15.2% ($p<0.001$), while post treatment loss increased from 25.2% to 26.1% ($p < 0.033$). The overall cascade success rate dropped by 2.1%, from 64.8% to 62.7% ($p< 0.001$). Pre- and during-COVID-19 cascade success rates were negatively associated with living with HIV and having recurrent TB.

Conclusions

An already poorly performing TB program in Cape Town was negatively impacted by the COVID-19 pandemic. There was a substantial reduction in the number of individuals diagnosed with drug-susceptible. Increases in pre-and post-treatment losses resulted in a decline in TB cascade success rates. Strengthened implementation of TB recovery plans is vital, as health services now face an even greater gap between achievements and targets and will need to become more resilient to possible future public health disruptions.

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The COVID-19 pandemic became a public health crisis in 2020, with the SARS-CoV-2 virus accounting for nearly 7 million deaths worldwide by mid 2023 [1], making it the leading cause of death from a single infectious agent in 2020 and 2021, eclipsing TB, which had been the leading infectious agent since 2011 [2]. Global reductions in TB mortality and morbidity in the decade 2010–19 were insufficient to be on track to reach ambitious “End-TB strategy” and Sustainable Development Goal (SDG) targets [3], which has been exacerbated by COVID-19, with fewer people being tested, diagnosed and treated [4]. In countries supported by the Global Fund to fight AIDS, Tuberculosis, and Malaria, there was a decline from 2019 to 2020 in key TB program indicators, which was unprecedented since the inauguration of the fund in 2002 [5]. Globally, case notifications declined by 18%; from 7.1 million in 2019 to 5.8 million in 2020, a 9-year setback in plans as outlined by the Stop TB partnership to End TB [6, 7]. There have been some gains in finding and treating people with TB (PWTB), showing some degree of return to pre-COVID-19 figures in 2021 and a more substantial recovery in 2022; the number of people treated for TB had increased to 6.4 million in 2021 and 7.5 million in 2022 [8].

South Africa is one of the top ten high-burden countries for TB, HIV-associated TB and drug-resistant TB [6]. Under a South African National State of Disaster, various levels of lockdown were legislated from 26 March 2020 to 5 April 2022, resulting in limited access to public health services and negative impacts on health programs, including TB testing and diagnosis [9]. Initial COVID-19 restrictions resulted in a ~48% average weekly decrease in TB Xpert MTB/RIF testing volumes while the number of TB positive tests declined by 33% [10]. Early evidence suggested that the disruption of routine TB services would lead to suboptimal retention in care and poorer treatment outcomes for individuals with TB in South Africa [11], and globally [12].

South African provincial level data, while limited, showed considerable declines in TB testing and treatment patterns with much heterogeneity across provinces [13]. Using epidemiological data from a local context can inform and help prioritize key aspects within TB programs which require improvement [14]. The aim of this study was to quantify and compare the number of individuals diagnosed with drug- susceptible tuberculosis (DS-TB), treated for TB, successfully completed treatment; and the losses in the continuum of TB care in a large metropolitan district in South Africa (Cape Town), prior to and during the COVID-19 pandemic.

Methods

Study design

This was an observational study comparing two retrospective annual DS-TB cohorts; pre-COVID-19 (1 October 2018 to 30 September 2019) and during-COVID-19 (1 April 2020 to 31 March 2021) cohorts. Pre-COVID-19 reflected the most recent period possible while including sufficient time to record the 6-month TB treatment outcomes. The during-COVID-19 period was pragmatically defined to start from 1 April 2020, following the onset of the first lockdown on 26 March 2020 [15]. Using the TB care cascade as a conceptual framework [16–18], the study quantified and compared the number of people diagnosed with TB; treated for TB; and with treatment success across cohorts. We also calculated the treatment success rate and the cascade success rate for each annual period. In addition, we analysed the losses between diagnosis and treated for TB (initial loss to follow up, ILTFU) and between treated for TB and treatment success (post-treatment loss, PTL) comparing cohorts, and disaggregated by sex, age, HIV status, previous TB history and mode of diagnosis.

Setting

Cape Town is a metropolitan district within the Western Cape (WC) Province of South Africa. It is home to 4.7 million people (66% of the provincial population) [19]. Primary health care services are rendered by two health authorities, namely the Western Cape Government Health and Wellness Department (WCGHW) and the City of Cape Town (CCT) municipal government [20]. In the WC, 90% of the population access TB testing in the public sector services [20].

In 2019, there were 29,408 DS and 1,509 drug resistant (DR) TB diagnoses [21] in Cape Town. DS-TB treatment success was 76.3% in the 2018 cohort [22]. Antenatal HIV prevalence was 22% [23] with 54% ART coverage [20].

Unique to the WC, the Department of Health houses a Provincial Health Data Centre (PHDC), which links various primary sources of data (including laboratory, pharmacy, hospital and primary healthcare information and electronic disease-specific registers), using a unique patient identifier, into single patient level records [24], thus providing a more complete, integrated, person-level data set than any individual data system.

Data collection

Data was obtained from the PHDC (11 October 2022) for all individuals diagnosed with DS-TB in two predefined cohorts: the first was pre-COVID-19 and the second was during-COVID-19. All data received was de-identified; authors could not identify individual participants.

Variables, definitions

Data analysis

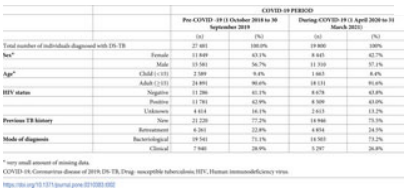
The PHDC undertook de-duplication of the data, using the unique patient identifier. Potential data anomalies were checked against source data. The numbers of individuals who were diagnosed with DS-TB, treated for TB and with treatment success within each cohort were quantified. Further, ILTFU and PTL were calculated and compared across the cohorts with Chi Squared tests using the IBM SPSS 29 software package. The open-source web tool OpenEpi was used to calculate the 95% confidence limits for proportions.

Ethics

Ethics approval for this study was obtained from the University of the Western Cape (UWC) Biomedical Research Ethics Committee (BM21/10/19). Study approval was also received from the Western Cape Provincial Health and City Health Departments (WC_202107_037; 9453). A waiver of informed consent was obtained for the routine health data received from the PHDC. All data received from the PHDC was anonymised.

Results

There were 27,481 individuals diagnosed with DS-TB in the pre-COVID-19 cohort and 19,800 individuals in the during-COVID-19 cohort. Demographics and disease characteristics were similar for individuals diagnosed with TB in both cohorts; men accounted for more than 50%, children <15 years accounted for 10% of the cohort, 40% of individuals were living with HIV, 75% were new TB diagnoses, and 70% were bacteriologically confirmed diagnoses (Table 2).



		COVID-19 PERIOD			
		Pre-COVID -19 (1 October 2018 to 30 September 2019		During-COVID-19 (1 April 2020 to 31 March 2021)	
		(n)	(%)	(n)	(%)
Total number of individuals diagnosed with DS-TB		27 481	100.0%	19 800	100%
Sex*	Female	11 849	43.1%	8 445	42.7%
	Male	15 581	56.7%	11 310	57.1%
Age*	Child (<15)	2 589	9.4%	1 663	8.4%
	Adult (≥15)	24 891	90.6%	18 131	91.6%
HIV status	Negative	11 286	41.1%	8 678	43.8%
	Positive	11 781	42.9%	8 509	43.0%
	Unknown	4 414	16.1%	2 613	13.2%
Previous TB history	New	21 220	77.2%	14 946	75.5%
	Retreatment	6 261	22.8%	4 854	24.5%
Mode of diagnosis	Bacteriological	19 541	71.1%	14 503	73.2%
	Clinical	7 940	28.9%	5 297	26.8%

* very small amount of missing data.

COVID-19: Coronavirus disease of 2019; DS-TB: Drug- susceptible tuberculosis; HIV: Human immunodeficiency virus.

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Table 2. Demographic and clinical characteristics of individuals diagnosed with DS-TB stratified by pre- and during-COVID-19 periods, in Cape Town, South Africa.

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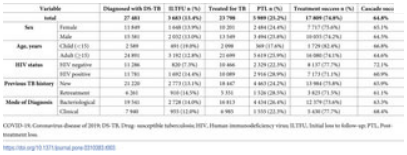
Pre-COVID-19 period

ILTFU was 13.4% and PTL was 25.2%. The collective losses resulted in a treatment success rate of 74.8% and a cascade success rate of 64.8% (Table 3).



Variable		Diagnosed with DS-TB	ILTFU n (%)	Treated for TB	PTL n (%)	Treatment success n (%)	Cascade succ
total		27 481	3 683 (13.4%)	23 798	5 989 (25.2%)	17 809 (74.8%)	64.8%
Sex	Female	11 849	1 648 (13.9%)	10 201	2 494 (24.4%)	7 717 (75.6%)	65.1%
	Male	15 581	2 032 (13.0%)	13 549	3 494 (25.8%)	10 055 (74.2%)	64.5%
Age, years	Child (<15)	2 589	491 (18.9%)	2 098	369 (17.6%)	1 729 (82.4%)	66.8%
	Adult (≥15)	24 891	3 192 (12.8%)	21 699	5 619 (25.9%)	16 080 (74.1%)	64.6%
HIV status	HIV negative	11 286	820 (7.3%)	10 466	2 329 (22.3%)	8 137 (77.7%)	72.1%
	HIV positive	11 781	1 692 (14.4%)	10 089	2 916 (28.9%)	7 173 (71.1%)	60.9%
Previous TB history	New	21 220	2 773 (13.1%)	18 447	4 463 (24.2%)	13 984 (75.8%)	65.9%
	Retreatment	6 261	910 (14.5%)	5 351	1 526 (28.5%)	3 825 (71.5%)	61.1%
Mode of Diagnosis	Bacteriological	19 541	2 728 (14.0%)	16 813	4 434 (26.4%)	12 379 (73.6%)	63.3%
	Clinical	7 940	955 (12.0%)	6 985	1 555 (22.3%)	5 430 (77.7%)	68.4%

COVID-19: Coronavirus disease of 2019; DS-TB: Drug- susceptible tuberculosis; HIV: Human immunodeficiency virus; ILTFU: Initial loss to follow-up; PTL: Post-treatment loss.

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Table 3. DS-TB diagnosed, treated, and treatment success during the pre-COVID-19 period (October 2018 to September 2019), in Cape Town, South Africa, disaggregated by demographic and clinical characteristics.

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ILTFU was significantly higher among children (<15 years) compared to adults (≥15 years), while PTL was significantly higher among adults compared to children. Both ILTFU and PTL were significantly higher among individuals living with HIV compared to HIV-negative individuals, individuals with TB retreatment. compared to those with new TB and those with a bacteriological diagnosis compared to those with a clinical diagnosis (Table 4). Overall cascade success was significantly higher among HIV-negative people compared to those living with HIV, those with new TB compared to those with retreatment and those who were clinically diagnosed

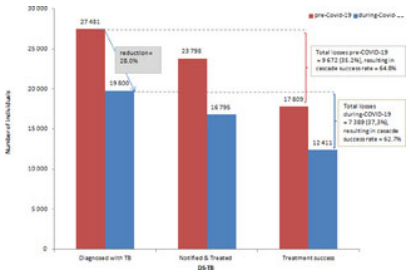

Fig 1. Pre- & during-COVID-19 individuals diagnosed with DS-TB, treated for TB and treatment success across Cape Town, South Africa.
COVID-19, Coronavirus disease of 2019; DS-TB, Drug- susceptible tuberculosis.
https://doi.org/10.1371/journal.pone.0310383.g001

Overall, ILTFU increased from 13.4% pre-COVID-19 to 15.2% during-COVID-19 ($p < 0.001$), a relative increase of 13.2%. ILTFU increased significantly irrespective of sex (males $p<0.001$, females $p = 0.002$), age (child $p = 0.007$, adult $p<0.001$) and HIV status (HIV-positive $p<0.001$, HIV-negative $p = 0.032$). The relative increase in ILTFU was higher for males (14.6%) compared to females (11.4%) and for those living with HIV (22.2%) compared to HIV-negative individuals (11.2%). ILTFU was significantly higher among new TB patients compared to retreatment ($p<0.001$) and those who were clinically diagnosed compared to those bacteriologically diagnosed ($p<0.001$) (Table 5).

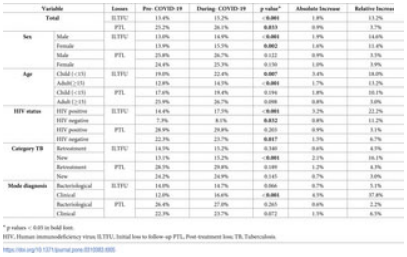

Table 5. Increases in initial loss to follow up (ILTFU) and post-treatment loss (PTL) between pre- & during-COVID-19 periods, disaggregated by demographic and clinical characteristics for all individuals diagnosed with DS-TB in Cape Town, South Africa.
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PTL increased from 25.2% pre-COVID-19 to 26.1% during-COVID-19 ($p = 0.033$), a relative increase of 3.7%. PTL in HIV negative individuals increased from 22.3% pre-COVID-19 to 23.7% during-COVID-19 ($p = 0.017$), a relative increase of 6.7% (Table 5).

The treatment success rate decreased from 74.8% to 73.9%, a relative reduction of 1.3%. The cascade success rate dropped from 64.8% pre-COVID-19 to 62.7% during COVID-19 ($p< 0.001$), a relative reduction of 3.3% (Fig 1).

Discussion

COVID-19 has had a substantial epidemiological impact on the TB program in Cape Town, a high TB burden district in South Africa. Comparing pre-COVID-19 to during-COVID-19, the number of individuals diagnosed with TB decreased by 28%. ILTFU increased by 13.2% and PTL by 3.7% during COVID-19. Treatment success decreased by 1.3% and cascade success by 3.3%.

Understanding the impact of COVID-19 at a sub-national level is vital to strengthen the district level TB program and allows for a focused implementation of the South African TB recovery plan [25, 26]. This will also provide opportunities to continue addressing gaps in the care cascade, which existed pre-COVID-19, and to address the losses experienced during COVID-19. Access to consolidated TB-related data through the PHDC in this setting provided the unique opportunity to comprehensively understand the changes in some of the steps in the TB care cascade in Cape Town, making this study practically relevant for health professionals.

We found that the relative increase in ILTFU was higher among males, and individuals living with HIV. Health seeking behaviour is typically poorer among males compared to females [35, 36] we know that a lower proportion of males compared to females seek TB care in South Africa [37]. It is plausible that COVID-19 exacerbated this problem.

Reasons for delayed linkage to care include lack of information and support from health care providers, unpleasant previous TB treatment episodes and being uncertain of their TB diagnosis [38]. Mortality is also a driver of ILTFU, as individuals who are sicker may die before they can link to care. Increasing age, HIV positive status, and a hospital-based TB diagnosis have been identified as predictors of mortality [39]. Males and individuals living with HIV have also been identified as sub-groups having a higher risk of mortality due to COVID-19 itself [40]. Strategies to find men specifically, early diagnosis and strengthening linkage of people diagnosed with TB to treatment, including the strengthening referral pathways from hospitals to mitigate ILTFU, are part of the TB recovery plan for South Africa [41] and are vital TB recovery strategies in South Africa.

PTL increased by 3.7% and the COVID-19 lockdown factors that impacted access to healthcare generally could have played a role in the reduced number of individuals completing their TB treatment. This reduction is relatively small, which may be explained by some of the interventions put in place to mitigate the impact of COVID-19-related factors and retain individuals in care, including policies to keep PHC services functional for essential services such as HIV and TB, in addition to the already established practice in Cape Town of monthly dispensing, following a 2 week treatment initiation phase, instead of daily directly observed therapy [42].

The proportion of individuals started on TB treatment with a successful TB treatment outcome (treatment success rate) decreased by 1.3%, from a below par success rate pre-COVID-19. TB treatment success is routinely reported for all individuals who are notified and started on treatment; however this study has additionally calculated a cascade success rate out of the diagnosed cohort. We found that the cascade success rate significantly declined by 3.3% during-COVID-19. Less than two thirds of those diagnosed with TB successfully completed treatment. Recording and reporting successful TB treatment outcomes as a proportion of those diagnosed, not only those initiated on treatment, can focus attention on addressing ILTFU [34] as well as the more routinely recognised PTL.

One of the main strengths of the study was the use of PHDC data (instead of data from stand-alone routine TB programmatic reporting systems). This allowed the inclusion of TB diagnoses made on clinical grounds and obviated modelling. Using PHDC data allowed for a cohort-based approach, with the same individuals followed from diagnosis to outcome, as has been recommended in constructing TB care cascades, to minimise risk of bias [16]. An additional strength of the study was that the data was extracted more than a year after the cohort periods, obviating the potential problem of missing data relating to reporting lags.

This study has limitations. We did not estimate TB incidence rates (i.e. the number of people diagnosed with TB in an annual period per 100 000 population). Population size decreases (e.g. due to COVID-19 mortality and out-migration) could theoretically have contributed to the reduction which was observed in the number of people diagnosed with TB between the two study-periods, however any population decrease is unlikely to have offset the trend of estimated annual population year-on-year increases [43] and highly unlikely to be on the same scale as the 28% decline in the number of people diagnosed with DS-TB in the annual period following the onset of the COVID-19 pandemic. Another limitation is that this study used data from only the public sector. While the vast majority of TB diagnosis and treatment is in the public sector [18], possible changes in sector use during the study period may be a confounder which could not be ascertained. Missing data can also be a limitation when using routine health data.

Conclusion

This study provides important findings on the impact of COVID-19 on TB services in a metropolitan district of South Africa. We found that COVID-19 negatively impacted TB health services, reducing diagnoses, and increasing pre- and post-treatment losses, resulting in a decline in individuals successfully being treated for TB.

During COVID-19, there was a substantial drop in the number of people diagnosed with DS-TB and an increase in losses along the DS-TB continuum of care, which was more marked for ILTFU than for PTL. This differential loss along the TB care cascade may reflect programmatic prioritisation of retaining people in care rather than focussing on linking newly diagnosed people to care. This highlights an important opportunity for mitigating risk in future service interruptions and the importance of TB programs designing interventions to ensure continuity of care across the cascade.

Within the research community, it remains important to determine what underlies the decrease in people diagnosed with TB. Within TB programmes, the priority is to ensure undiagnosed TB does not increase to prevent additional morbidity, mortality and onward transmission in communities. Focused implementation and attainment of local and national TB recovery plans are therefore of vital importance.

Supporting information

S1 Table. DS-TB diagnosed, treated, and treatment success in the during-COVID-19 period (April 2020 to March 2021), in Cape Town, South Africa

acknowledged in terms of conceptualisation of the study, ethical approval and application for access to PHDC data, as well as assistance with data validation. Prior and ongoing work in the Provincial and City of Cape Town Departments of Health using data to address gaps in the TB programme is acknowledged.

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