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Early View

Correspondence

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Responding to SARS-CoV-2 in South Africa: What can we learn from drug-resistant tuberculosis?

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Introduction

The novel coronavirus strain, SARS-CoV-2, was first reported from China in December 2019[i]. As of the 14th May 2020, more than 4.4 million individuals have tested positive for SARS-COV-2 globally[2]. More than 300,000 individuals have died globally due to SARS-COV-2[ii]. In South Africa (SA), cumulatively at the same time point, 12739 individuals were infected and 238 deaths reported[2]. Tuberculosis is the leading infectious disease cause of death with 1.4 million deaths in 2018[iii]. Drug-resistant tuberculosis (DR-TB) is a threat to tuberculosis control globally. Over the last decade, several interventions have improved the outcomes of DR-TB patients and reduced the burden of disease. We discuss lessons from DR-TB interventions in South Africa that could be helpful in the fight against SARS-COV-2.

Lessons from DR-TB

1. Rapid adoption of new diagnostics.

Early awareness, testing and diagnosis are important factors in successful management. The use of GeneXpert MTB/RIF brought about a revolution in diagnosing DR-TB reducing time to detection from weeks to days. The recommended primary diagnostic for SARS-COV-2 detection is molecular using polymerase chain reaction method. Several rapid molecular diagnostic methods are available and should be rapidly evaluated and implemented. South Africa has adopted several and recently also introduced the GeneXpert Xpress SARS-CoV-2 cartridge diagnosing COVID-19 within 45minutes, leveraging the GeneXpert platform that is decentralised and extensively used for TB diagnosis.

2. Parallel process of research and implementation: The Bedaquiline Clinical Access Programme (BCAP) provided access to a novel drug for DR-TB patients, generated local evidence to support decision-making, led to rapid adoption, bolstering the fight against an infectious disease[iv]. We managed to reduce mortality among DR-TB patients after updating our clinical guidelines using local data[v]. Death rate decreased from 45 % (2010 cohort) to 21 % (2016 cohort) among XDR-TB patients and treatment success rate improved from 9 % to 58 % during the same period in this group of patients. Importantly outcomes were monitored closely after introduction of novel regimens and ensured that data is put in the public domain timeously. The BCAP model is a good example and we encourage rapid referral to COVID-19 clinical trials being conducted, the Solidarity clinical trial is an example and will evaluate new and repurposed agents to treat COVID-19. Another example of a research project that helped drive development of country-specific policies is the surveillance of adverse events conducted by Borisov et al[6].
3. Decentralization of complex services for easy access for community members. Bringing screening, testing and treatment close to where people live has proved to produce better treatment outcomes for DR-TB patients in South Africa and helped reduce cost of DR-TB care[7]. Such interventions are key to success in the fight against SARS-COV-2. Effective decentralization facilitates contact tracing important for both conditions and has been well resourced for COVID. It is a missed opportunity however not to test for TB when investigating COVID-19 and vice versa. This is recommended by WHO, local adoption is now planned and should be considered in high burden TB settings.
4. The use of personal protective equipment (PPE) by health care workers and patients:
   The use of PPE especially in clinical environments has been associated with reduction of DR-TB transmission among health care workers (HCWs) in various settings. Administrative and environmental factors are also critically important for DR-TB. The major challenge has been scarcity of PPE in various areas where they are needed to manage unsuspected, undiagnosed infectious patients and this is being adequately addressed.
5. Strong partnership and collaboration
   This is a central to the response and led to improvement of DR-TB treatment outcomes. Government officials, academia, non-governmental organizations, and civil society worked together in coalition driving the successes observed[8].
6. Management of TB and COVID-19 co-infection: as both conditions affect the respiratory system with overlapping symptoms, clinicians are urged to test for both. This is particularly important to prevent nosocomial spread when hospitalisation is needed for either. A total of 776 beds have been identified out of 3798 beds at 33 DR-TB treatment sites. Although, the first TB-COVID-19 cohorts reported did not show a high death rate in this group[9,10]; HIV co-infection among TB is 59% in SA and is dual risk. Integrating COVID-19 activities in the TB (and HIV) programmes is important.

<u>Conclusion</u>

The fight against SARS-COV-2 can be won if we continue to make effective use of rapid diagnostic tools, effective contact tracing, decentralize treatment services, and strengthen the use of personal protective devices in areas that need them most. Equally importantly partnership between government and private sector, political commitment and learning implementation may go a long way to defeat SARS-COV-2.

References

iWorld Health Organization (WHO). Rolling updates on Coronavirus disease (COVID-19). Accessible on https: www.who.int/emergencies/diseases/novel-coronavirus-2019/events-as-they-happen Accessed on 20/04/2020

ii Johns Hopkins University. Johns Hopkins Coronavirus Dashboard. Track the coronavirus outbreak on Johns Hopkins Live Dashboard. Accessible on *https://coronavirus.jhu.edu/map.html* . Accessed on 14/05/2020.

iii World Health Organization (WHO). Global TB report 2019, Geneva. Accessible on https: www.who.int/tb/global-report-2019 Accessed on 04/04/2020.

iv Ndjeka N, Schnippel K, Master I, Meintjes G, Maartens G, Romero R, et al. High treatment success rate for multidrug-resistant and extensively drug-resistant tuberculosis using a bedaquiline-containing treatment regimen. European Respiratory Journal. 2018;52(6):1801528.

v Schnippel K*, Ndjeka NO*, Maartens G, Meintjes G, et al. Effect of bedaquiline on mortality in South African patients with drug-resistant tuberculosis: a retrospective cohort study. Lancet Respir Med 2018. http://dx.doi.org/10.106/S2213-2600 (18)30235-2*These 2 authors are first authors.

6 Borisov S et al. Surveillance of adverse events in the treatment events in the treatment of drug-resistant tuberculosis: first global report. Eur Respir J 2019; 54:1901522.

7 E Sinanovic, L Ramma, A Vassall, V Azevedo, L Wilkinson, N Ndjeka, K McCarthy, G Churchyard, H Cox. Impact of reduced hospitalisation on the cost of treatment for drug-resistant tuberculosis in South Africa. The International Journal of Tuberculosis and Lung Disease 02/2015; 19(2):172-178.

8 Conradie F, Meintjes G, Hughes J, Maartens G, Ferreira H, Siwendu S, Master I, Ndjeka N. Clinical Access Program for Bedaquiline for the treatment of drug-resistant tuberculosis. SAMJ 03/2014 ; 104(3) :164-6.

9 Tadolini M, Codecasa LR, Garcia-Garcia JM, et al. Active tuberculosis, sequelae and COVID-19 co-infection: first cohort of 49 cases. Eur Respir J 2020; in press.

10 Motta I, Centis R, D'Ambrosio L, et al. Tuberculosis, COVID-19 and migrants: preliminary analysis of deaths occurring in 69 patients from two cohorts. [published online ahead of print, 2020 May 14]. Pulmonology 2020; doi:10.1016/j.pulmoe.2020.05.002