TB scale-up & COVID-19

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SAHCS Continuing Medical Education Meeting
27 August 2020
Overview

1. Epidemiology of COVID-19 and TB

2. Impact of COVID-19 on TB services
   • Direct
   • Indirect
   • Opportunities

   • Findings from preliminary studies
     ▪ Outcome
     ▪ Clinic course
TB mortality & incidence in high burden countries

Nigeria
TB incidence: 219
Rates per 100,000 population: 64

Uganda
TB incidence: 201

South Africa
TB incidence: 520
Rates per 100,000 population: 37

Pakistan
TB incidence: 265

Mozambique
TB incidence: 551
Rates per 100,000 population: 72

India
TB incidence: 199
Rates per 100,000 population: 32

Indonesia
TB incidence: 316
Rates per 100,000 population: 35

Philippines
TB incidence: 554

China
TB incidence: 61

Russia
TB incidence: 54

Source: 2019 WHO Global TB Report

2018 Global TB Estimates
Cases: 10 million
Deaths: 1.5 million
Covid-19 mortality & incidence in high burden countries

FNB Stadium – Largest in Africa

Seating capacity ~ 95 000 people
SA COVID-19 Mortality

Deaths due to Covid-19 in 2020 ~ 13 000
SA TB Mortality

Deaths due to TB in 2018 ~ 63 000
TB has more than 4x the mortality rate of COVID-19
Unintended consequences of COVID-19 on the TB epidemic

**Transmission**
- Potential increase TB transmission from lockdown
- Impact on TB incidence still unknown

**TB services**
- Health workforce constraints
- ↓ Diagnostic testing and triaging of patients
- Challenges in sustaining essential TB care: access, monitoring, sustainable TB drug access

**Biological**
- TB impact on COVID-19 outcomes and vice versa
- Post-TB Lung Disease: increased COVID-19 acquisition risk, poor outcomes
- Co-morbidities: COPD, HIV, DM with TB → poor outcomes

**Resources**
- Diversion of TB funding, personnel, clinical and diagnostic infrastructure: towards COVID-19 response
- Interrupted supply of drugs and diagnostics
- R&D funding diverted from TB towards COVID-19 research
Improvements in TB outcome

- Profile of people dying from TB has changed:
  - Scale-up of ART programme resulted in fewer deaths in children <15 years, and in adults, especially women, in the reproductive age (15 - 49)
  - TB deaths in adults ≥50 years remain high

Source: SS Abdool Karim et al., NEJM. 2010, SS Abdool Karim et al., NEJM. 2011
COVID-19 Impact: Reversing gains TB elimination

- A rapid restoration of TB services critical
- Analysis predicts that 3-month lockdown and protracted 10-month restoration → additional 6.3 million cases & 1.4 million TB deaths between 2020 and 2025

COVID-19 Impact - TB testing & Diagnosis: Before & After Lockdown

Testing volumes declined more rapidly than the TB case detection rates resulting in an increase in weekly positivity rates during lockdown.

Source: NICD 10 May 2020
1. Prioritization of COVID-19 testing for DR-TB and TB in-patients

**DIRECTORATE:**

- Multi-month prescriptions and dispensing
- Decentralised, external TB pill pick up through the CCMDD programme
- WBOT for Tracking patients lost along the cascade of TB care
- Novel strategies for medication provision: WBOT, Uber, bicycle program etc

**SUBJECT:** Prioritization for COVID 19 test for diagnosed DS-TB patients who need inpatient care and MDR-TB patients by the use of a red sticker (Category 1)

**TO:** District directors, Laboratory Managers and TB coordinators, Hospital & CHC CEOs and Laboratory Managers

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**Turn-around time for Category 1 tests should be 24 hours.**

2. Prioritization of drug supply and retention in care for DR TB and TB patients

- **Multi-month prescriptions and dispensing**
- **Decentralised, external TB pill pick up through the CCMDD programme**

3. Re-aligning testing to run TB & COVID tests in parallel to each other
Harnessing COVID-19 opportunities for TB

1. Infection Prevention & Control will help limit TB and COVID-19 transmission
   • Hand hygiene, disinfection, social distancing and respiratory protection (mask wearing), isolation and quarantine measures

2. Health services
   • Diagnosis and testing
     ▪ Result SMS to reduced time and enhanced linkage
     ▪ Result communication with hours to patients
     ▪ Digital health technologies for accessing diagnostic services
   • Treatment, care and Triaging of patients
     ▪ Community-based diagnosis, care, monitoring
     ▪ Home-delivery/decentralized pick up of chronic medication
     ▪ Telehealth for medical triage, individualised counselling, support, referral

3. Public education and awareness
   • ↓ Social stigma + fear + discrimination

4. TB Surveillance on respiratory infections
   • Daily TB incidence surveillance systems → still referencing 2018 data
   • Daily/ monthly NICD reports stratified by province

5. Capacity building
   • Virtual training and support
   • Social media to disseminate key information
   • Clinical decision support groups

All tools, essential services and operations should be continued for long-standing diseases such as TB
COVID-19 & TB: Radiologic & clinical features in co-infected patients

Clinical characteristics of COVID-19 and active tuberculosis co-infection in an Italian reference hospital

Claudia Stochino  Simone Villa  Patrizia Zucchi  Pierpaolo Parravicini  Andrea Gori  Mario Carlo Raviglione

- 20 TB patients (19 PTB) diagnosed with COVID-19 within 30 days from TB diagnosis
- COVID-19 virus clearance - within 14 days in 63% and 5% (1/20) died
- TB lesions of chest radiographs after COVID-19 diagnosis
  - 12 patients (63%) TB lesions improvement
  - 1 patient with extrapulmonary TB - no change
  - 7 patients (35%) had worsening TB lesions
- Covid-19 associated lesions on chest radiographs
  - 4 patients developed new onset pneumonia
  - 3 patients (15%) had mild-to-moderate interstitial thickening
  - 1 patient had ground glass pattern on CT
- Modest impact of COVID-19 co-infection on clinical course of active TB
  - Fever occurred in most patients
  - No major clinical deterioration observed (except with 1 patient who died)
- Low rate of clinical and radiological deterioration observed
  - Likely due to young age (mean 39 years) & low frequency of other comorbidities (HIV, MDR-TB) and quality of healthcare services provided
COVID-19 & TB: Impact on Mortality

Impact of COVID-19 on TB clinical course and outcome is a major concern.

Data from WC South Africa shows a modest effect of current & previous TB on COVID-19 mortality:

- Cohort of 22,308 COVID-19 patients with 625 deaths
- Current TB increased COVID-19 mortality risk: aHR - 2.70 (95%CI:1.81; 4.04)
- Previous tuberculosis increased COVID-19 mortality risk: aHR - 1.51 (95%CI:1.18; 1.93)
- Similar impact of TB on COVID-19 mortality in rifampicin-sensitive and resistant TB, all deaths occurred in the intensive phase treatment
- COVID-19 TB deaths occurred mainly among older people

HIV and risk of COVID-19 death: a population cohort study from the Western Cape Province, South Africa.

Western Cape Department of Health with National Institute for Communicable Diseases, South Africa,

Mary-Ann Davies
COVID-19 & TB: Impact on clinical course & outcome

• Matched cohort of 530 COVID-19 patients, 106 with confirmed previous or current active TB
• TB vs no TB co-infection with COVID-19
  → R.R. Death: 2.2 fold higher (p=0.001)
  → Recovery 25% lower (p=0.003)
  → Time-to-death significantly shorter (p=0.0031)
  → Time-to-recovery significantly longer in patients with TB (p=0.0046)

Source: Sy et al., 2020
Increased susceptibility of TB patients to COVID-19 infection

Active or latent tuberculosis increases susceptibility to COVID-19 and disease severity

Yongyu Liu, Lijun Bi, Yu Chen, Yaguo Wang, Joy Fleming, Yanhong Yu, Ye Gu, Chang Liu, Lichao Fan, Xiaodan Wang, Moxin Cheng

Case-control study of 36 COVID-19 patients, 13 with MTB infection (IGRA pos)

Source: Liu et al., 2020
Clinical case study 1

COVID-19 and TB co-infection - 'Finishing touch” in perfect recipe to 'severity' or ‘death’

Letter to the Editor
R. Kumar, B. Bhattacharya, V. Meena, M. Soneja and N. Wig

A 38 year old man
• No medical history
• Attended large congregation during the Covid-19 pandemic

Presents with 1.5-month history of:
• Low-grade fever
• Expectorant cough and shortness of breath

Clinical Features:
• BP: 96/50 mmHg, PR: 92/min, SpO2: 84% (room air), respiratory rate: 28/min
• Chest X ray: diffuse bilateral infiltrates
• Laboratory abnormalities: anaemia, and mild transaminitis
Clinical course and outcome

• Severe acute respiratory illness → Tested for SARS-CoV-2 → RT PCR Positive

• Treated:
  • Intravenous antibiotics
  • Oxygen supplementation

• Clinical Course:
  • Remained symptomatic → evaluated for other causes including TB
  • Empirical anti-TB therapy started while awaiting test results
  • Clinical deterioration: ↑ dyspnoea and ↓ SpO2 → required mechanical ventilation → patient demised despite all measures

• TB diagnosis confirmed post-mortem

Key Learning Point: Overlapping non-specific clinical features of TB & COVID-19:
• Diagnosis of TB likely to be missed
• Lack of distinct radiological findings specific to TB
• Clinical and X-Ray features of TB disease may affect categorisation of COVID-19 severity
TB drug interactions with novel COVID-19 therapeutic agents

1. Use of immunomodulators, e.g., tocilizumab (TCZ) in moderate-severe COVID-19 may ↑ risk of latent TB reactivation, esp in TB endemic areas
   - TCZ competes with IL-6 at receptor level leading to ↓ TB specific immune response
   - Lack of consensus regarding the effect of IL-6 signal inhibitors on TB risk
   - TCZ should not be with-held in moderate-severe COVID – however consider risk of TB reactivation
   - Need for TB screening and TB preventive therapy prior to starting tocilizumab

2. Risk of additive toxicity with simultaneous use of anti-tuberculosis drugs and novel COVID-19 drugs
   - Hepatotoxicity: rifampin / isoniazid / pyrazinamide, and remdisivir/favipiravir/TCZ
   - Hyperuricemia: favipiravir and pyrazinamide,
   - Thrombocytopenia: TCZ and rifampin
   - QT prolongation: favipiravir and fluoroquinolones
Summary

• TB remains a long-standing public health challenge with > 800 new cases occurring each day in South Africa
• COVID-19 pandemic threatens progress made with ↓ TB incidence and mortality
• Programs need to be adapted; & resources prioritized to mitigate impact of COVID-19 on endemic chronic diseases incl TB
• Insufficient data to understand the contribution of COVID-19 to TB pathogenesis
• Clinically: in addition to COVID-19, always suspect TB co-infection, and vice versa
• Preliminary data suggests that COVID-19 in TB patients present with more severe symptoms, lower recovery rates & higher mortality – irrespective if latent infection, current active or previous TB disease
• The COVID-19 pandemic presents opportunities to strengthen our TB response – these opportunities must be seized!!
Acknowledgements

TB-HIV studies are funded by:

- South African MRC
- DAIDS, NIAID, National Institutes of Health
- President’s Emergency fund for AIDS Relief (PEPFAR)
- US Centers for Disease Control and Prevention (CDC)
- Fogarty International Center, NIH
- Doris Duke Charitable Foundation (DDCF)
- Howard Hughes Medical Institute (HHMI)
- The Global Fund to fight AIDS, Tuberculosis and Malaria
- EDCTP
- MRC - Newton Fund
- MRC-SHIPP
- USAID through BroadReach Health Care Africa
- NRF
- Gates Medical Research Foundation
- Merck/MSD
- UK MRC through Infectious Diseases Institute of Uganda

CAPRISA gratefully acknowledges all study participants