

The Relationship between Tuberculosis and Corona Virus

Saja A. Shareef¹, Mays K. Aldulaimy² and Walaa A. Mohammed³

¹Assistant lecturer, Molecular and Medical Biotechnology Department, College of Biotechnology, Al-Nahrain University, Baghdad, IRAQ.

²Assistant lecturer, Plant Biotechnology Department, College of Biotechnology Al-Nahrain University, Baghdad, IRAQ.

³Assistant lecturer, Microbiology department, College of science, AL-Karkh University of science, Baghdad, IRAQ.

¹Corresponding Author: saja.ali@nahrainuniv.edu.iq



www.sjmars.com || Vol. 3 No. 5 (2024): October Issue

Date of Submission: 21-10-2024

Date of Acceptance: 31-10-2024

Date of Publication: 01-11-2024

ABSTRACT

In 2020, COVID-19 and tuberculosis emerged as significant threats to global health, with increased mortality and decreased testing due to the pandemic's impact on the tuberculosis care system. Both diseases spread through respiratory system secretions and airborne particles, with the lungs being their primary target organ. Common remedies include addressing the spread of *Mycobacterium tuberculosis* and addressing the underlying causes of both diseases. COVID-19 diagnostics include quick antigen test kits and RT-PCR, while tuberculosis diagnostics include chest X-rays, sputum microscopy, and RT-PCR on sputum. These methods allow for same-day active TB diagnosis, compared to culture-based testing that could take up to eight weeks. Using a range of diagnostic tools ensures that COVID-19 and TB patients are identified and treated promptly. The combined danger of TB and COVID-19 presents a significant challenge to patient quality of life. To effectively combat this combined threat, cooperation, research funding, and policy changes are necessary.

Keywords- RT-PCR, COVID-19, Tuberculosis, corona virus.

I. INTRODUCTION

As ancient as mankind itself, tuberculosis (TB) has a long history. Skeletons from Egyptian mummies have been shown to have evidence of bone tuberculosis. The history of tuberculosis (TB) dates back to ancient China and India. The Vedas refer to tuberculosis as "Rajyakshama," which is Sanskrit for "to waste away." The effects of tuberculosis have affected every region of the planet. The "King's touch" was used for many years across Europe. Six The middle ages saw the development of a histological description of lesions, including tubercles and abscesses, the identification of extrapulmonary tuberculosis, and the recommendation for surgical excision of the afflicted gland, the scrofula. The observation that troops who remained inside in their barracks were more likely to have tuberculosis (TB) than those who were sent to combat zones was a commendable epidemiological relationship. This led to the establishment of a connection between disease transmission and overpopulation. Later, the condition known as tuberculosis (TB) was called "consumption," "phthisis," and "white plague" because the patient seemed to be consumed by the illness, becoming highly anemic and malnourished. The first known account of tuberculosis, "Rajyakshma," is comparable to these descriptions.

On March 24, 1882, Robert Koch isolated the TB mycobacteria, which completely changed our knowledge of tuberculosis. Thus, March 24 is designated as World TB Day. In addition to identifying *M. tb*, Robert Koch also cultured it and showed that it grows upon re-inoculation. Years later, isoniazid and a number of additional medications were created as antituberculars, with streptomycin being the first. Eleven TB was perceived as a treatable condition following the development of vaccines and treatments. Nevertheless, the World Health Organization (WHO) proclaimed a worldwide emergency in 1993 due to an increase in the number of patients with multi-drug resistance and an increase in the number of cases associated with an HIV epidemic. The globe is still at risk from tuberculosis. Within macrophages, the

mycobacterium prefers to remain latent and fends against death by blocking the phagosome-lysosome complex from forming. The illness has a protracted course and needs extensive care. The WHO advises multi-drug treatment (MDT) because to the TB mycobacterium's higher tendency to develop drug resistance. Relapse and the emergence of resistance are also caused by noncompliance. Globally, around 10 million individuals contracted tuberculosis in 2019; this figure has been steadily declining over the last several years. In underdeveloped nations, where poverty, malnutrition, and overpopulation are prevalent, the issue is more severe. China and India have the highest rates of tuberculosis. Differently, the Sustainable Development Goals (SDG) and the World Health Organization (WHO) want to reach this goal by 2030 and 2035, respectively. To meet this goal, decisive action was done right away. On March 16, 2018, TB notification became required, and noncompliance with these procedures became a crime. Additionally, active case finding has started in vulnerable groups. Every Indian district has a District Tuberculosis Officer (DTO) assigned to it. Incentives are being provided not just to patients and caregivers but also to private providers. On April 1, 2018, separate funding for dietary supplements was instituted. Despite all of these precautions, tuberculosis (TB) nonetheless killed 450,000 people in 2019—that is, more than 1000 people every day—and impacted 2.64 million people.

The SARS-CoV-2 epidemic has a major negative influence on all attempts to control tuberculosis. The β -coronavirus, which belongs to the Coronaviridae family, is the cause of SARS-CoV-2. Previously, this same family of viruses was responsible for the Middle East Respiratory Syndrome (MERS) in 2012 and the Severe Acute Respiratory Syndrome (SARS) in 2003. Once inside, the virus multiplies, creating virions that enter the bloodstream via using the golgi apparatus and endoplasmic reticulum of the host cell. The majority of illness manifestations are caused by an active host immune system.

On December 29, 2019, the Wuhan district of China reported the first case of SARS-Cov-2. Bats and pangolins were thought to be the intermediate hosts of the SARS-CoV-2 virus, which is a zoonotic illness. 2019nCoV (2019 novel corona virus) is the name given to the virus. Later, it was discovered that the two viruses shared roughly 80% of the same genome. The WHO subsequently dubbed the virus SARS-CoV-2 and the sickness COVID-19, and on January 30, 2020, they declared it an emergency, then on March 11, 2020, they proclaimed it a pandemic. The illness has a basic reproduction number that ranges from three to five, indicating its strong infectivity. Through aerosol and contaminated fomites, the infection is spread. More than a hundred million infections and more than two million deaths—a number that keeps rising—have been attributed to this deadly virus. The epidemic garnered international attention, and almost all medical resources were deployed to contain it, clouding the picture of other chronic illnesses, including tuberculosis.

India, the world's most populous nation with the highest rate of tuberculosis patients, is presently seeing a second wave of severe COVID-19 cases. Maybe the early nationwide shutdown prevented the virus from spreading too far last year, and the nation was spared severe damage. With almost 200,000 new cases of infection per day, the effects of this second peak are yet unknown. In the meanwhile, we want to highlight in this article the main connections between COVID-19 and tuberculosis, based on the experience of 2020.

Global healthcare systems have encountered unprecedented challenges as a consequence of the COVID-19 pandemic, which has caused significant disruptions in communities worldwide. Naturally, the struggle against COVID-19 has garnered the majority of attention; however, it is crucial to acknowledge that tuberculosis has been a persistent issue for an extended period. People have been sick with this very common disease for hundreds of years. People are likely to remember 2020 as the year that the coronavirus disease, or COVID-19, came to the forefront. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was initially identified in China in late 2019. This virus is the root cause of the current pandemic. While COVID-19 continues to be a topic of much discussion in academic journals and the public, it is important to remember about other infectious maladies, such as tuberculosis.

Because of the COVID-19 outbreak, fewer people are getting tested for and reporting TB. This has had a big effect on the TB care system. This is because of the cuts to TB services and limits on patients' ability to move around, which have led to more deaths from tuberculosis. In order to successfully fight these two contagious diseases, this review aims to show how COVID-19 and TB are related, how dangerous they are together, and how they can be fixed together.

II. EPIDEMIOLOGICAL OVERLAP

There are several interesting epidemiological similarities between tuberculosis and the COVID-19 epidemic. The primary method of transmission for these ailments is through respiratory particles, which is why close contact and congested environments are advantageous. Furthermore, individuals with compromised immune systems, the elderly, and those with underlying medical conditions are at an increased risk of contracting COVID-19 and TB.

A multifaceted impact of the COVID-19 pandemic has been observed on tuberculosis. Attempts to diagnose, treat, and control tuberculosis have been disrupted as a result of the diversion of health resources and the increased peril. Limited access to medical facilities, travel restrictions, and lockdowns have exacerbated the challenge of promptly diagnosing patients and identifying tuberculosis cases. It is imperative that prompt attention and comprehensive strategies be given to the complex situation that has resulted from the combination of these two infectious maladies.

There are numerous similarities between COVID-19 and TB, with the most notable being the transmission of Mycobacterium tuberculosis and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The transmission route for both infections is through respiratory system secretions. Both COVID-19 and tuberculosis (TB) have the potential to propagate through airborne particles and aerosols, with the lungs being their primary target organ. However, it is imperative to bear in mind that these maladies may affect various internal organs. In addition, the public health response to both ailments must include the protection of medical personnel and other vulnerable patients, as well as the identification and assessment of contact. In order to develop disease management strategies that are both effective and efficient, it is imperative to understand the routes and variables that influence transmission. A variety of data that can be employed to identify, prioritize, and evaluate contacts has been generated by numerous years of clinical and experimental research on tuberculosis. There is an ongoing debate regarding the relative functions of aerosols, fumites, and large respiratory particles, and it should be no surprise that additional research is required to gain a more comprehensive understanding of the manner in which SARS-CoV-2 spreads. It is interesting to note that the spread of both maladies has been associated with overextension phenomena. Following is a graphic that illustrates the most prevalent clinical symptoms and the multi-organ involvement: Figure 1.

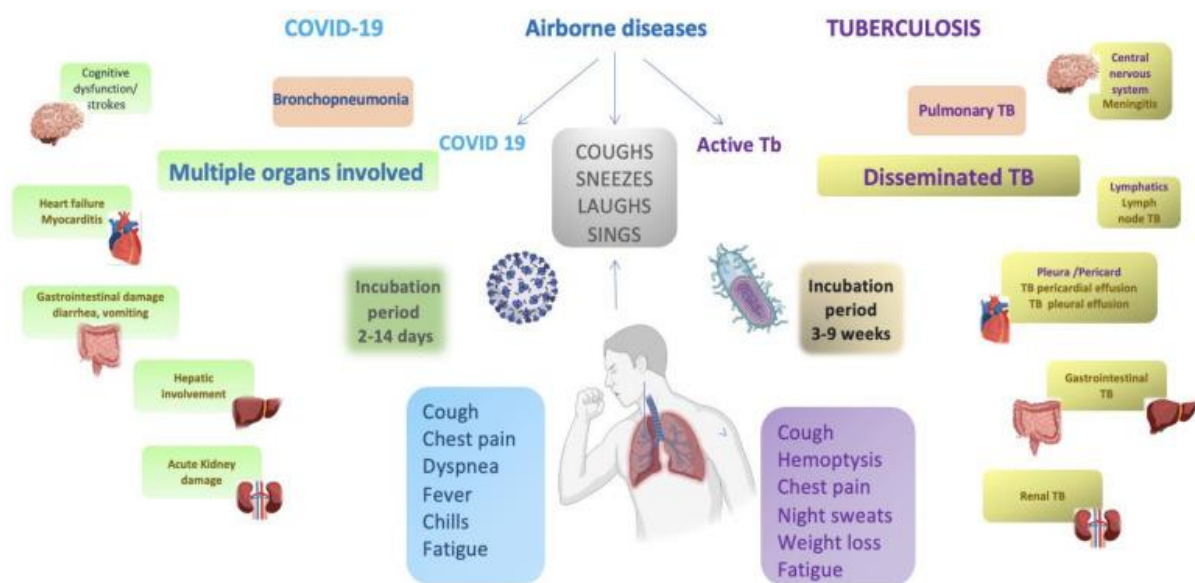


Figure 1: TB and COVID-19 have same symptoms and impact several organs.

The pulmonary system is heavily involved in both COVID-19 and tuberculosis (TB), making it a prominent site of conflict for both illnesses. The main organs affected by tuberculosis are the lungs, which result in increasing lesions, a persistent cough, and respiratory problems. It may lead to chronic coughing and the possible transmission of infected droplets by causing significant damage of lung tissue and the formation of caverns. In a similar vein, COVID-19 mostly affects the respiratory system, leading to acute respiratory distress syndrome (ARDS) and severe pneumonia. This virus impairs lung function by inducing inflammation and damaging lung cells. The respiratory symptoms of COVID-19 and TB overlap emphasize how crucial it is to comprehend and manage the respiratory dynamics of both illnesses in order to stop transmission, guarantee prompt diagnosis, and create efficient treatment plans.

Because their immune systems work in different ways, COVID-19 and TB both throw off the balance of defensive reactions. In other words, having two illnesses at the same time can make both of them worse. Some health problems, like chronic lung disease, diabetes mellitus, smoking, and liver failure, make it more likely that someone will get very sick and need to go to an intensive care unit or have forced breathing during COVID-19. When TB is found in a patient, smoking makes it more likely that they won't get enough medicine, which slows the start of sputum culture and treatment. There is more and more proof that people with diabetes are more likely to get COVID-19, a disease that can kill quickly, damage organs, and require treatment. People who have COVID-19 or tuberculosis are more likely to die early if they are malnourished or have a low body mass index (BMI).

The incubation period for TB can be anywhere from two weeks to many years before active TB appears. On the other hand, the incubation period for COVID-19 is shorter, lasting only one to fourteen days.

COVID-19 symptoms include fever, wheezing, sore throats, diminished or absent scent, taste loss, diarrhea, muscular soreness, and exhaustion. Typically, these symptoms manifest abruptly. Conversely, tuberculosis (TB) induces a persistently productive cough, fever, night chills, chest discomfort, exhaustion, appetite loss, and blood in the cough. Conversely, tuberculosis symptoms manifest gradually and with a subtle onset.

Those with comorbid maladies, such as HIV, diabetes mellitus, obesity, chronic pulmonary disease, chronic cardiac problems, and impaired immune systems, are more likely to experience severe presentations of COVID-19. The illness's progression may be exacerbated by these underlying medical conditions. On the other hand, it is known that having diabetes mellitus, sickle cell disease, chronic obstructive lung disease, HIV, or a weak immune system at the same time makes getting TB more likely and worse. If you want to avoid and treat serious COVID-19 and TB symptoms, you need to understand and be committed to treating these condition together. Figure 2 shows the most common things that put people at risk for both TB and COVID-19.

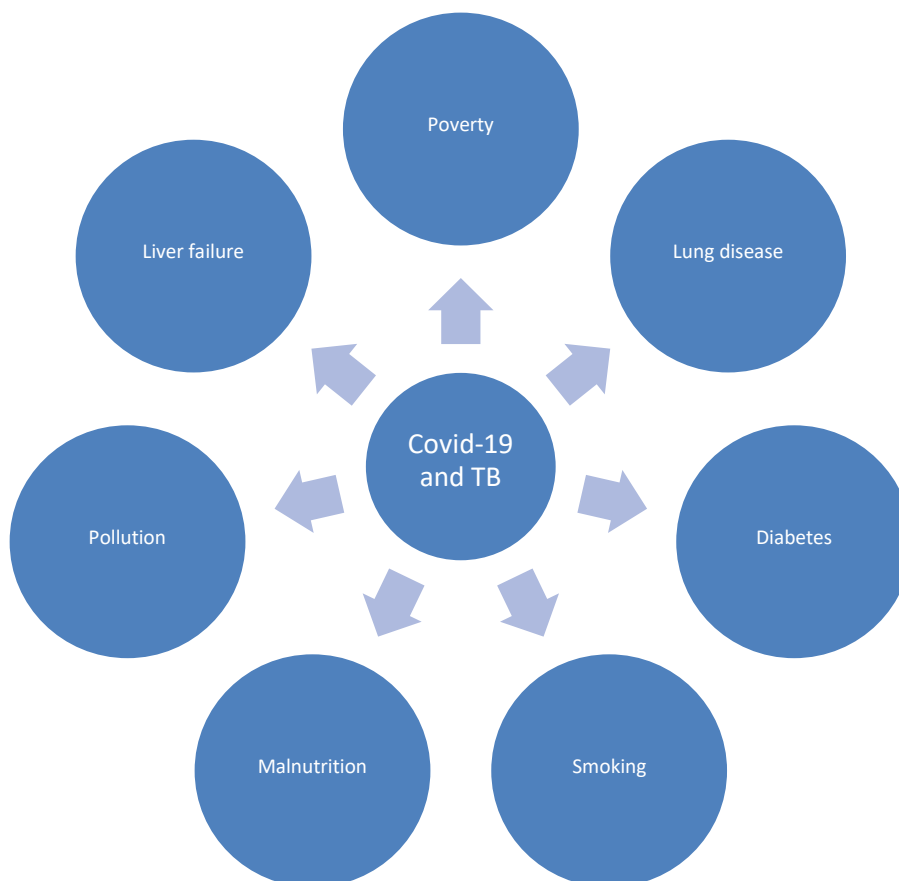


Figure 2: Common causes of TB and COVID-19 risk factors.

In terms of COVID-19 diagnostics, a number of techniques are available for quick and precise identification. These include quick antigen test kits, which provide results in a matter of minutes, and RT-PCR, which may yield findings in as little as two hours. Convenience is further improved by point-of-care self-testing availability. However, many methods are used for tuberculosis (TB) diagnostics in order to quickly detect active TB. These consist of chest X-rays, sputum microscopy, and sputum RT-PCR. Unlike culture-based testing, which may take up to 8 weeks, these approaches allow for the prompt identification of active TB on the same day. Using a variety of diagnostic instruments contributes to the prompt detection and treatment of COVID-19 and tuberculosis patients.

Saliva and nasopharyngeal swabs are the usual methods used to get COVID-19 samples, since they are very simple specimens to obtain. On the other hand, sputum or extrapulmonary samples are needed for a precise diagnosis in TB testing. For COVID-19 and tuberculosis cases to be successfully detected and diagnosed, the right samples must be collected.

Long-term consequences of COVID-19 sequelae might include diminished or absent smell, ageusia (loss of taste), mental health issues, pulmonary issues, and cognitive problems. When tuberculosis sequelae is present, it is not uncommon to observe persistent lung illness, which is defined by bronchiectasis, lesions, and cavities. Recurrent infections and diminished lung function may result from these aftereffects. In order to provide complete treatment to those impacted by COVID-19 and TB, it is essential to acknowledge and manage these long-term impacts.

In Figure 3, we have emphasized the most significant information to provide a succinct overview of this subject.

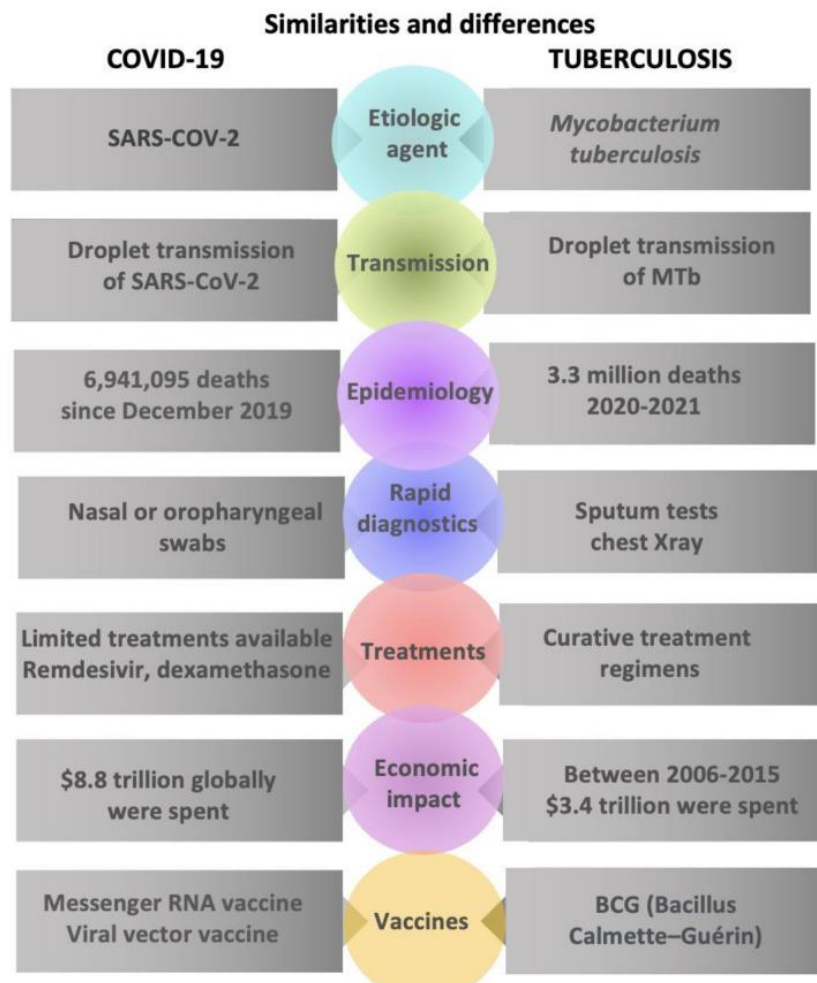


Figure 3: Overall, COVID-19 and TB have parallels and differences.

III. COVID-19 AND TUBERCULOSIS: INTERACTIONS

Infectious disorders that mostly affect the lungs include COVID-19 and tuberculosis. Aerosolized SARS-CoV-2 also spreads by droplet infection, as does tuberculosis. The spread of these illnesses is aided by overcrowding. Individuals who are immunocompromised, aged, malnourished, diabetic, or suffer from another chronic illness are at a higher risk of acquiring these illnesses. The pathophysiology of both infectious agents includes cell-mediated immunity. Because the host immune system may be weakened, it is likely that one infection raises the likelihood of contracting the other. Reactivation of an existing endogenous infection or exogenous TB infection is a risk associated with both acquiring COVID-19 and using corticosteroids for its therapy. Similarly, a higher risk of contracting COVID-19 is likely to exist among those with active tuberculosis or those with structural lung illness brought on by healed pulmonary Koch's disease. Meta-analysis, which found genetic signature overlap between COVID-19 and tuberculosis, details the interactions between the two drugs. It was determined that individuals with post-TB sequelae or latent/active TB are more susceptible to developing severe COVID-19. It was also suggested that people who had SARS-Cov-2 be watched for the growth of tuberculosis. Additionally, there was thought that the BCG injection might protect against SARS-CoV-2, but no solid proof was found.

Additionally, both illnesses are characterized by congestion, fever, fatigue, malaise, and hemoptysis, among other symptoms. The diagnosis of similar presentations may be challenging. In a restricted number of patients, The diagnosis of tuberculosis was facilitated while screening for SARS-CoV-19 infection. Larger investigations were necessary in order to assess the influence of one agent on the development of the other's illness. In a different investigation, out of 24 patients, 20 were found to be positive for active tuberculosis (TB), suggesting a potential greater vulnerability. The patients were all indoor patients. Despite reporting a mostly benign path, they issued a note urging further research to determine the effect on both sides. Numerous clinical investigations have shown a higher likelihood for tuberculosis patients to get coronavirus and have a severe course of the disease. Unfortunately, a significant flaw in the majority of these research is the small sample size and the ignorance of preexisting comorbidities.

However, more research will shed light on the relationship and long-term effects of these coexisting disorders.

IV. THE DIFFICULTIES IN ADDRESSING THE EFFECTS OF SARS-COV-2 ON TB

Nations all across the globe implemented lockdowns to control SARS-Cov-2. 45 There were many consequences from forcing people to remain indoors. Due to the similarities of symptoms between COVID-19 and TB, most patients may have chosen to wait it out rather than suspecting TB, which may have contributed to the delay in diagnosing TB. Additionally, individuals may not have been tested even after exhibiting symptoms similar to both COVID-19 and TB due to the pre-existing stigma surrounding both illnesses. Most of these individuals belonged to lower socioeconomic classes and were already having difficulty making ends meet and buying food. Therefore, in addition to their existing worries for their lives, the further worry of isolation or quarantine would have been a source of suffering. Due of the strong relationships that are encouraged by home confinement, spread among household contacts is also a significant risk. The suspension of most non-emergency services resulted in a delay in the identification of new tuberculosis among people who sought medical care. There was also less access to healthcare in the private sector. Overall, this led to a decline in illness identification and notification. The 2020 Global TB report, which showed a decrease in TB notifications, makes this clear. In the three nations with the biggest TB burden—India, the Philippines, and Indonesia—the notification rate decreased by almost 25% between January and June 2020 compared to the same period in 2019. Milgliory et al. obtained similar results. Long-term, TB-related fatalities may grow dramatically in the next years; a 13% increase in mortality is anticipated throughout this time. This is a significant setback to the progress achieved in the fight against tuberculosis worldwide so far.

Patients with diagnoses already made have also suffered. While labs have mostly been used to process COVID-19 patient samples, outpatient departments have not been operating. Sputum microscopy and culture growth are the main methods used for monitoring and assessing the response of pulmonary tuberculosis patients. Lockdown prevented this evaluation from being made. As a result, individuals who had treatment failure, relapse, or medication resistance might not have been promptly diagnosed, and their condition could have worsened. In addition, patients need a great lot of motivation and counseling to cope with the extended course of therapy, side effects, and stigma related to this illness. The imposition of lockdown brought the whole process to a halt. In India, the drug supply was abruptly halted, and medication treatments are disseminated under strict surveillance. The patient or caregiver is required to routinely retrieve the medications from the DOTS center. In the event of an emergency, there was no previous preparation to guarantee a continuous supply; still, patients were informed about the delivery of ATT medications at their doorsteps. No documentation exists on its use or efficacy. Long-term, premature medication withdrawal may have contributed to illness recurrence and the development of resistance in many individuals. As all funding were allocated by the WHO to battle COVID-19, financial restrictions also arose. India is now coping with the second SARS-CoV-2 outbreak. Curfews have been eased this time. Since there hasn't been a total lockdown, TB patients have been able to get healthcare; yet, this strategy could make it more difficult to control the presently spreading SARS-CoV-2. It is yet unclear how these encounters affect TB patients and how their care is affected.

V. CONCLUSION

Massive devastation has been wrought by the COVID-19 epidemic, which has had unforeseeable effects on the planet. Morbidity and death have significantly increased, affecting not just SARS-Cov-2 infected individuals but also those with pre-existing medical issues. The epidemic has brought attention to the deficiencies in healthcare that currently exist and provide a chance to fix them and clarify our objectives. Both patients and members of the general public now often use masks. It is now understood how important general cleanliness, physical distance, and cough etiquette are. Peripheral health facilities have been strengthened, which has improved treatment and reduced the mobility of tuberculosis patients. When digital consultations and appointments are used appropriately, the process of delivering healthcare has been improved. As the number of cases rises once again, the resources and efforts invested over the last year are finally paying off. It is now our responsibility to use the resources that are now available and seize the chance to improve our readiness going forward.

REFERENCES

- [1] Andom AT, Fejfar D, Yuen CM, Ndayizigiye M, Mugunga JC, Mukherjee JS. The impact of COVID-19 on tuberculosis program performance in the Kingdom of Lesotho. *Trop Med Infect Dis.* 2023;8(3):165. pmid:36977166
- [2] Berra TZ, Ramos ACV, Alves YM, Tavares RBV, Tartaro AF, Nascimento MCD, et al. Impact of COVID-19 on tuberculosis indicators in Brazil: a time series and spatial analysis study. *Trop Med Infect Dis.* 2022;7(9):247. pmid:36136658

- [3] Chiang CY, Islam T, Xu C, Chinnayah T, Garfin AMC, Rahevar K, et al. The impact of COVID-19 and the restoration of tuberculosis services in the Western Pacific Region. *Eur Respir J*. 2020;56(4):2003054. pmid:32978310
- [4] Dlangalala T, Musekiwa A, Brits A, Maluleke K, Jaya ZN, Kgarosi K, et al. Evidence of TB services at primary healthcare level during COVID-19: a scoping review. *Diagnostics (Basel)*. 2021;11(12):2221. pmid:34943458
- [5] Fuady A, Houweling TAJ, Richardus JH. COVID-19 and Tuberculosis-Related Catastrophic Costs. *Am J Trop Med Hyg*. 2020;104(2):436–40. pmid:33269683
- [6] Khan AW, Khan B, Shah SK, Kazi GN, Quadir A, Ghafoor A, et al. The impact of covid-19 on TB care in Pakistan during 2020. *Pak J Public Health*. 2022;12(1):8–11.
- [7] Khobragade RN, Kelkar RU, Sunilkumar M, Cency B, Murthy N, Surendran D, et al. Health system resilience: ensuring TB services during COVID-19 pandemic in Kerala, India. *Indian J Tuberc*. 2022;69(4):427–31. pmid:36460371
- [8] Kim B, Kang YA, Lee J. Heterogeneous impact of Covid-19 response on tuberculosis burden by age group. *Sci Rep*. 2022;12(1):13773. pmid:35962020
- [9] Klinton JS, Oga-Omenka C, Heitkamp P. TB and COVID—Public and private health sectors adapt to a new reality. *J Clin Tuberc Other Mycobact Dis*. 2020;21:100199. pmid:33163631
- [10] Manhiça I, Augusto O, Sherr K, Cowan J, Cuco RM, Agostinho S, et al. COVID-19-related healthcare impacts: an uncontrolled, segmented time-series analysis of tuberculosis diagnosis services in Mozambique, 2017–2020. *BMJ Glob Health*. 2022;7(4):e007878. pmid:35443938
- [11] Mihika FA, Jubayer Biswas MAA, Khan MMH, Islam SS, Haque MA, Banu S, et al. The effect of the COVID-19 pandemic on pulmonary tuberculosis control in the selected Upazila health complexes of Dhaka Division, Bangladesh. *Trop Med Infect Dis*. 2022;7(11):385. pmid:36422935
- [12] Min J, Kim HW, Koo HK, Ko Y, Oh JY, Kim J, et al. Impact of COVID-19 pandemic on the National PPM Tuberculosis Control Project in Korea: the Korean PPM Monitoring Database between July 2019 and June 2020. *J Korean Med Sci*. 2020;35(43):e388. pmid:33169559
- [13] Nhari LG, Dzobo M, Chitungo I, Denhere K, Musuka G, Dzinamarira T. Implementing effective TB prevention and treatment programmes in the COVID-19 era in Zimbabwe. A call for innovative differentiated service delivery models. *Public Health Pract (Oxf)*. 2020;1:100058.
- [14] Oga-Omenka C, Sassi A, Vasquez NA, Baruwu E, Rosapep L, Daniels B, et al. Tuberculosis service disruptions and adaptations during the first year of the COVID-19 pandemic in the private health sector of two urban settings in Nigeria—A mixed methods study. *PLOS Glob Public Health*. 2023;3(3):e0001618. pmid:36963094
- [15] Petersen E, Seif Al-Abr S, Chakaya J, Goletti D, Parolina L, Wejse C, et al. World TB Day 2022: Revamping and reshaping global TB control programs by advancing lessons learnt from the COVID-19 pandemic. *Int J Infect Dis*. 2022;124(Suppl 1):S1–3. pmid:35248715
- [16] Reid MJA, Silva S, Arinaminpathy N, Goosby E. Building a tuberculosis-free world while responding to the COVID-19 pandemic. *Lancet*. 2020;396:1312–13. pmid:34338198
- [17] Tran CH, Moore BK, Pathmanathan I, Lungu P, Shah NS, Oboho I, et al. Tuberculosis treatment within differentiated service delivery models in global HIV/TB programming. *J Int AIDS Soc*. 2021;24(Suppl 6):e25809. pmid:34713974
- [18] van Rensburg AJ, Petersen I, Awotiwon A, Bachmann MO, Curran R, Murdoch J, et al. Applying learning health systems thinking in codeveloping integrated tuberculosis interventions in the contexts of COVID-19. *BMJ Glob Health*. 2022;7(10):e009567. pmid:36316026
- [19] Cronin AM, Railey S, Fortune D, Wegener DH, Davis JB. Notes from the field: effects of the COVID-19 response on tuberculosis prevention and control efforts—United States, March–April 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69(29):971–2. pmid:32701944
- [20] Bouaddi O, Hasan MM, Sahito AM, Shah PA, Mohammed AZA, Essar MY. Tuberculosis in the middle of COVID-19 in Morocco: efforts, challenges and recommendations. *Trop Med Health*. 2021;49(1):98. pmid:34930506
- [21] Roberts T, Sahu S, Malar J, Abdullaev T, Vandeveld W, Pillay YG, et al. Turning threats into opportunities: how to implement and advance quality TB services for people with HIV during the COVID-19 pandemic and beyond. *J Int AIDS Soc*. 2021;24(4):e25696. pmid:33787058
- [22] Yadav P, Vohra C, Gopalakrishnan M, Garg MK. Integrating health planning and primary care infrastructure for COVID-19 and tuberculosis care in India: challenges and opportunities. *Int J Health Plann Manage*. 2022;37(2):632–42. pmid:34820907
- [23] Ruiz-Grosso P, Cachay R, De La Flor A, Schwalb A, Ugarte-Gil C. Association between tuberculosis and depression on negative outcomes of tuberculosis treatment: A systematic review and meta-analysis. *PLOS ONE*. 2020;15(1):e0227472. pmid:31923280

- [24] Loveday M, Cox H, Evans D, Furin J, Ndjeka N, Osman M, et al. Opportunities from a new disease for an old threat: Extending COVID-19 efforts to address tuberculosis in South Africa. *S Afr Med J*. 2020;110(12):1160–7. pmid:33403958
- [25] Ferrer JP, Suzuki S, Alvarez C, Berido C, Caballero M, Caraig B, et al. Experiences, challenges and looking to the future in a clinical tuberculosis cohort in the time of COVID-19 in the Philippines. *Trans R Soc Trop Med Hyg*. 2021;115(6):579–82. pmid:33693916
- [26] Malik AA, Hussain H, Maniar R, Safdar N, Mohiuddin A, Riaz N, et al. Integrated tuberculosis and COVID-19 activities in Karachi and tuberculosis case notifications. *Trop Med Infect Dis*. 2022;7(1):12. pmid:35051128
- [27] Zimmer AJ, Heitkamp P, Malar J, Dantas C, O'Brien K, Pandita A, et al. Facility-based directly observed therapy (DOT) for tuberculosis during COVID-19: a community perspective. *J Clin Tuberc Other Mycobact Dis*. 2021;24:100248. pmid:34189276
- [28] Sunjaya DK, Paskaria C, Pramayanti M, Herawati DMD, Parwati I. The magnitude of anxiety and depressive symptoms among tuberculosis patients in community health centers setting during the peak of COVID-19 pandemic. *J Multidiscip Healthc*. 2022;15:755–64. pmid:35422627
- [29] ACTION Global Health Advocacy Partnership et al. The impact of COVID-19 on the TB epidemic: a community perspective, 2020. Available from: <https://spark.adobe.com/page/xJ7pygvhrIAqW/>
- [30] Mandal A, Verma AK, Kar SK, Bajpai J, Kant S, Kumar S, et al. A cross-sectional study to determine the psychological distress among pulmonary tuberculosis patients during COVID-19 pandemic. *Monaldi Arch Chest Dis*. 2022;93(1) pmid:35593023
- [31] Millones AK, Lecca L, Acosta D, Campos H, Del Águila-Rojas E, Farroñay S, et al. The impact of the COVID-19 pandemic on patients' experiences obtaining a tuberculosis diagnosis in Peru: a mixed-methods study. *BMC Infect Dis*. 2022;22(1):829. pmid:36352374
- [32] Santos FLD, Souza LLL, Bruce ATI, Crispim JA, Arroyo LH, Ramos ACV, et al. Patients' perceptions regarding multidrug-resistant tuberculosis and barriers to seeking care in a priority city in Brazil during COVID-19 pandemic: A qualitative study. *PLoS One*. 2021;16(4):e0249822. pmid:33836024
- [33] Tinoco EM, Vasconcelos A, Alves F, Duarte R. Impact of COVID-19 on extrapulmonary TB and the benefit of decentralised TB services. *Int J Tuberc Lung Dis*. 2022;26(2):178–80. pmid:35086634
- [34] Togun T, Kampmann B, Stoker NG, Lipman M. Anticipating the impact of the COVID-19 pandemic on TB patients and TB control programmes. *Ann Clin Microbiol Antimicrob*. 2020;19(1):21. pmid:32446305
- [35] Zhang G, Yu Y, Zhang W, Shang J, Chen S, Pang X, et al. Influence of COVID-19 for delaying the diagnosis and treatment of pulmonary tuberculosis-Tianjin, China. *Front Public Health*. 2022;10:937844. pmid:36530737
- [36] Mwamba C, Kerkhoff AD, Kagujje M, Lungu P, Muyoyeta M, Sharma A. Diagnosed with TB in the era of COVID-19: patient perspectives in Zambia. *Public Health Action*. 2020;10(4):141–6. pmid:33437679
- [37] Beyene NW, Sitotaw AL, Tegegn B, Bobosha K. The impact of COVID-19 on the tuberculosis control activities in Addis Ababa. *Pan Afr Med J*. 2021;38:243. pmid:34104291
- [38] Buonsenso D, Iodice F, Sorba Biala J, Goletti D. COVID-19 effects on tuberculosis care in Sierra Leone. *Pulmonology*. 2021;27(1):67–9. pmid:32561353
- [39] Fatima R, Akhtar N, Yaqoob A, Harries AD, Khan MS. Building better tuberculosis control systems in a post-COVID world: learning from Pakistan during the COVID-19 pandemic. *Int J Infect Dis*. 2021;113(Suppl 1):S88–90.
- [40] Islam M. Extensively drug-resistant tuberculosis in the time of COVID-19-How has the landscape changed for Pakistan? *Disaster Med Public Health Prep*. 2020;14(4):e9–10. pmid:32635960
- [41] Kumar P, Goyal JP. Tuberculosis during Covid-19 pandemic: challenges and opportunities. *Indian Pediatr*. 2020;57(11):1082. pmid:32893833
- [42] Maroof M, Pamei G, Bhatt M, Awasthi S, Bahuguna SC, Singh P. Drug adherence to anti-tubercular treatment during COVID-19 lockdown in Haldwani block of Nainital district. *Indian J Community Health*. 2022;34(4):535–41.
- [43] Oga-Omenka C, Tseja-Akinrin A, Boffa J, Heitkamp P, Pai M, Zarowsky C. Commentary: Lessons from the COVID-19 global health response to inform TB case finding. *Healthc (Amst)*. 2021;9(2):100487. pmid:33607520
- [44] Soko RN, Burke RM, Feasey HRA, Sibande W, Nliwasa M, Henrion MYR, et al. Effects of coronavirus disease pandemic on tuberculosis notifications, Malawi. *Emerg Infect Dis*. 2021;27(7):1831–9. pmid:34152962
- [45] Uwishema O, Badri R, Onyeaka H, Okereke M, Akhtar S, Mhanna M, et al. Fighting tuberculosis in Africa: the current situation amidst the COVID-19 pandemic. *Disaster Med Public Health Prep*. 2022; June 8:1–3. pmid:35673793
- [46] Zimmer AJ, Klinton JS, Oga-Omenka C. Tuberculosis in times of COVID-19. *J Epidemiol Community Health*. 2022;76(3):310–6. pmid:34535539

- [47] Dheda K, Perumal T, Moultrie H, Perumal R, Esmail A, Scott AJ, et al. The intersecting pandemics of tuberculosis and COVID-19: population-level and patient-level impact, clinical presentation, and corrective interventions. *Lancet Respir Med*. 2022;10(6):603–22. pmid:35338841
- [48] Nkereuwem O, Nkereuwem E, Fiogbe A, Usoroh EE, Sillah AK, Owolabi O, et al. Exploring the perspectives of members of international tuberculosis control and research networks on the impact of COVID-19 on tuberculosis services: a cross sectional survey. *BMC Health Serv Res*. 2021;21(1):798. pmid:34384439
- [49] Chapman HJ, Veras-Estévez BA. Lessons learned during the COVID-19 pandemic to strengthen tb infection control: a rapid review. *Glob Health Sci Pract*. 2021;9(4):964–77. pmid:34933990
- [50] Anigbo AR, Gambhir L. Two years of the pandemic: Impact of COVID-19 on tuberculosis management in Nigeria. *J Appl Pharm Sci*. 2022;12(8):001–008.
- [51] Chen H, Zhang K. Insight into the impact of the COVID-19 epidemic on tuberculosis burden in China. *Eur Respir J*. 2020;56(3):2002710. pmid:32703778
- [52] Lipman M, McQuaid CF, Abubakar I, Khan M, Kranzer K, McHugh TD, et al. The impact of COVID-19 on global tuberculosis control. *Indian J Med Res*. 2021;153(4):404–8. pmid:34380784
- [53] Lungu PS, Kerkhoff AD, Muyoyeta M, Kasapo CC, Nyangu S, Kagujje M, et al. Interrupted time-series analysis of active case-finding for tuberculosis during the COVID-19 pandemic, Zambia. *Bull World Health Organ*. 2022;100(3):205–15. pmid:35261409
- [54] Hazra D, Chawla K, Shenoy VP, Pandey AK, S N. The aftermath of COVID-19 pandemic on the diagnosis of TB at a tertiary care hospital in India. *J Infect Public Health*. 2021;14(8):1095–8. pmid:34274858
- [55] Lakoh S, Jiba DF, Baldeh M, Adekanmbi O, Barrie U, Seisay AL, et al. Impact of COVID-19 on tuberculosis case detection and treatment outcomes in Sierra Leone. *Trop Med Infect Dis*. 2021;6(3):154. pmid:34449755
- [56] Lestari T, Kamaludin , Lowbridge C, Kenangalem E, Poespoprodjo JR, Graham SM, et al. Impacts of tuberculosis services strengthening and the COVID-19 pandemic on case detection and treatment outcomes in Mimika District, Papua, Indonesia: 2014–2021. *PLOS Glob Public Health*. 2022;2(9):e0001114. pmid:36962674
- [57] Loh FK, Thong PM, Ong CWM. The crucial need for tuberculosis translational research in the time of COVID-19. *Lancet Respir Med*. 2022;10(6):531–3. pmid:35338842
- [58] MacLean EL, Villa-Castillo L, Ruhwald M, Ugarte-Gil C, Pai M. Integrated testing for TB and COVID-19. *Med (N Y)*. 2022;3(3):162–6. pmid:35169763
- [59] Malik AA, Safdar N, Chandir S, Khan U. Tuberculosis control and care in the era of COVID-19. *Health Policy Plan*. 2020;35(8):1130–32. pmid:32832996
- [60] Mohammed H, Oljira L, Roba KT, Yimer G, Fekadu A, Manyazewal T. Containment of COVID-19 in Ethiopia and implications for tuberculosis care and research. *Infect Dis Poverty*. 2020;9(1):131. pmid:32938497
- [61] Muñoz-Salazar R, Le T, Cuevas-Mota J, González-Fagoaga JE, Zapata-Garibay R, Ruiz-Tamayo PS, et al. Impact of COVID-19 on tuberculosis detection and treatment in Baja California, México. *Front Public Health*. 2022;10:921596.
- [62] Nalunjogi J, Mucching-Toscano S, Sibomana JP, Centis R, D’Ambrosio L, Alffenaar JW, et al. Impact of COVID-19 on diagnosis of tuberculosis, multidrug-resistant tuberculosis, and on mortality in 11 countries in Europe, Northern America, and Australia. A Global Tuberculosis Network study. *Int J Infect Dis*. 2023;130(Suppl 1):S25–9.
- [63] Narita M, Hatt G, Toren KG. Narita M, Hatt G, Toren KG. Delayed tuberculosis diagnoses during the coronavirus disease 2019 (COVID-19) pandemic in 2020—King County, Washington. *Clin Infect Dis*. 2021;73(Suppl 1):S74–6. pmid:33956137
- [64] Nikolayevskyy V, Holicka Y, van Soolingen D, van der Werf MJ, Ködmön C, Surkova E, et al. Impact of COVID-19 on tuberculosis case detection and treatment outcomes in Sierra Leone. *Eur Respir J*. 2021;57(1):154.
- [65] Santos VS, Allgayer MF, Kontogianni K, Rocha JE, Pimentel BJ, Amorim MTP, et al. Pooling of sputum samples to increase tuberculosis diagnostic capacity in Brazil during the COVID-19 pandemic. *Int J Infect Dis*. 2023;129:10–4. pmid:36642209
- [66] Schiza V, Kruse M, Xiao Y, Kar S, Lovejoy K, Wrighton-Smith P, et al. Impact of the COVID-19 pandemic on TB infection testing. *Int J Tuberc Lung Dis*. 2022;26(2):174–6. pmid:35086632
- [67] Tovar M, Aleta A, Sanz J, Moreno Y. Modelling the impact of COVID-19 on future tuberculosis burden. *Commun Med (Lond)*. 2022;2:77.
- [68] Maurer FP, Shubladze N, Kalmambetova G, Felker I, Kuchukhidze G, Drobniewski F, et al. Impact of the COVID-19 pandemic on tuberculosis national reference laboratory services in the WHO European Region, March to November 2020. *Euro Surveill*. 2021;26(24):2100426. pmid:34142651
- [69] Awasthi AK, Singh PK. Tuberculosis management in India during COVID-19 crisis. *J Public Health Policy*. 2021;42(1):185–9. pmid:33235251
- [70] Apolisi I, Mema N, Tyeku N, Beko B, Memani B, Daniels J, et al. Supporting families with tuberculosis during COVID-19 in Khayelitsha, South Africa. *Lancet Respir Med*. 2022;10(6):542–3. pmid:35338838

- [71] Arega B, Negesso A, Taye B, Weldeyohans G, Bewket B, Negussie T, et al. Impact of COVID-19 pandemic on TB prevention and care in Addis Ababa, Ethiopia: a retrospective database study. *BMJ Open*. 2022;12(2):e053290. pmid:35135769
- [72] Benade M, Long L, Meyer-Rath G, Miot J, Evans D, Tucker JM, et al. Reduction in initiations of drug-sensitive tuberculosis treatment in South Africa during the COVID-19 pandemic: analysis of retrospective, facility-level data. *PLOS Glob Public Health*. 2022;2(10):e0000559. pmid:36962535
- [73] Caren GJ, Iskandar D, Pitaloka DAE, Abdulah R, Suwantika AA. COVID-19 pandemic disruption on the management of tuberculosis treatment in Indonesia. *J Multidiscip Healthc*. 2022;15:175–83.
- [74] Chilot D, Woldeamanuel Y, Manyazewal T. Real-time impact of COVID-19 on clinical care and treatment of patients with tuberculosis: a multicenter cross-sectional study in Addis Ababa, Ethiopia. *Ann Glob Health*. 2021;87(1):109. pmid:34824990
- [75] Coutinho I, Alves LC, Werneck GL, Trajman A. The impact of the COVID-19 pandemic in tuberculosis preventive treatment in Brazil: a retrospective cohort study using secondary data. *Lancet Reg Health Am*. 2023;19:100444. pmid:36818594