

# COVID-19 coinfection in patients with active tuberculosis: First case-report in Iran

Nasrin Ghodrati Fard<sup>1</sup>, Mansoor Khaledi<sup>2</sup>, Hamed Afkhami<sup>2</sup>, Molood Barzan<sup>3</sup>, Hamed Eraghiye Farahani<sup>4</sup>, Fatemeh Sameni<sup>2</sup>, Omid Gholizade<sup>5</sup>, Fatemeh Maghsoudi<sup>1</sup>, Reza Farhadi Nezhad<sup>1</sup>, Sara mobarak<sup>1</sup>, Seyed Ali Nojourni<sup>6</sup>, and Sheida Mohammadi<sup>7</sup>

<sup>1</sup>Abadan University of Medical Sciences

<sup>2</sup>Shahed University Faculty of Medical Sciences

<sup>3</sup>Islamic Azad University of Tehran

<sup>4</sup>Iran University of Medical Sciences

<sup>5</sup>Tabriz University of Medical Sciences

<sup>6</sup>Pasteur Institute of Iran

<sup>7</sup>Urmia University of Medical Sciences

February 2, 2021

## Abstract

The pandemic of severe acute respiratory syndrome virus 2 (SARS-CoV-2) is a serious threat to global health. Since tuberculosis-COVID-19 co-infection is a great risk for tuberculosis patients. This is the first report from Iran. Rapid screening of respiratory infections caused by COVID-19, isolation, and treatment of tuberculosis patients is vital.

# COVID-19 coinfection in patients with active tuberculosis: First case-report in Iran

Nasrin Ghodrati Fard<sup>1</sup>, Mansoor Khaledi<sup>2</sup>, Hamed Afkhami<sup>2</sup>, Molood Barzan<sup>3</sup>, Hamed Eraghiye Farahani<sup>4</sup>, Fatemeh Sameni<sup>2</sup>, Omid Gholizade<sup>5</sup>, Fatemeh Maghsoudi<sup>1</sup>, Reza Farhadi Nezhad<sup>1</sup>, Sara mobarak<sup>1</sup>, Seyed Ali Nojourni<sup>6</sup>, Sheida Mohammadi<sup>7\*</sup>

<sup>1</sup>Abadan faculty of Medical Sciences, Abadan, Iran,

<sup>2</sup> Department of Microbiology, Faculty of Medicine, Shahed University, Tehran, Iran

<sup>3</sup> Msc of Molecular Cell Biology\_Microbiology, Islamic Azad University of Tehran Branch of Pharmaceutical Sciences, Tehran, Iran

<sup>4</sup> Department of Microbiology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran

<sup>5</sup> Department of Virology, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

<sup>6</sup> Microbiology Research Center, Pasteur Institute of Iran

<sup>7</sup> Department of Microbiology, Urmia University of Medical Sciences, Iran

Correspondence to: Mohammadi Sheida, Department of Microbiology, Urmia University of Medical Sciences, Iran; Tel: +984432752300, Email: university.ac33@yahoo.com

## Abstract

The pandemic of severe acute respiratory syndrome virus 2 (SARS-CoV-2) is a serious threat to global health. Since tuberculosis-COVID-19 co-infection is a great risk for tuberculosis patients. This is the first report from Iran. Rapid screening of respiratory infections caused by COVID-19, isolation, and treatment of tuberculosis patients is vital.

## KEYWORDS

TB, COVID-19, coinfection, SARS-CoV-2, pandemic

## Key Clinical Message

Considering the result of this study and other studies done on this subject, rapid screening of respiratory infections caused by COVID-19, isolation, and treatment of tuberculosis patients is vital.

## 1. INTRODUCTION

The first case of the 2019 novel coronavirus (2019-nCoV) was reported in December of 2019 in Wuhan, China<sup>1,2</sup>. According to the world health organization (WHO), since the outbreak of COVID-19 until December 6th, 2020, the pandemic has affected 66.6 million people worldwide and has claimed 1.3 million victims. The first cases of the novel coronavirus from 19th to 23rd of February 2020, was reported to be 43 infections and 8 deaths<sup>3</sup>. As numerous retrospective studies state, pandemics of respiratory diseases like Influenza are among the most important causes of mortality and their association with mortality rates of tuberculosis patients have been studied<sup>4-6</sup>. Co-infections of tuberculosis with other coronaviruses including SARS-CoV-1 in 2003 and MERS-CoV in 2012 are documented<sup>7-9</sup>.

Tuberculosis is a bacterial infection that targets the lungs. Its symptoms include respiratory problems and lung involvement which are similar to symptoms of the COVID-19 infection therefore it's a big concern during the pandemic. It is estimated that 1.7 billion people are infected by tuberculosis worldwide and according to WHO, 10 million people got infected by tuberculosis in 2019 thus tuberculosis infection is among the 10 leading causes of mortality in the world<sup>10</sup>. Tuberculosis patients are at high risk for COVID-19 infection since their symptoms are diagnosed and reported later. Hence, evaluation and screening of tuberculosis patients are important for their quick diagnosis and treatment. This study was conducted in tuberculosis center of Abadan, Iran to investigate SARS-CoV-2 in tuberculosis patients for a timely diagnosis of the co-infection and its treatment.

## 2. METHODS

This recent study was conducted to investigate COVID-19 among 96 tuberculosis patients from February to September 2020. 27 of these patients were suffering from extrapulmonary tuberculosis and 69 patients had pulmonary tuberculosis. Nasopharyngeal swabs were taken from patients and sent to the microbiology laboratory to test for SARS-CoV-2. Molecular detection and identification of SARS-CoV-2 were carried out using kit (DAAN GENE Ltd, <http://www.daangene.com>) through Real-Time polymerase chain reaction (RT-PCR) assay<sup>11-13</sup>.

## 3. RESULTS

96 tuberculosis patients with an average age of 38.3 years old (2 -24 years old) were inquired for this study. patients consisted of 68 (78.2%) men and 26 (29.9%) women. 3 (3.1%) of the mentioned tuberculosis patients were diagnosed with co-infection COVID-19 infection. The average age of these three patients with SARS-CoV-2-TB co-infection was 35.6 years old, all three of them were men and their history is as followed. These results highlight the importance of investigating COVID-19 co-infections during the pandemic.

## 4. CASE REPORT

### Case 1

A 49-year-old man from Shadegan, Iran with active extrapulmonary tuberculosis who was diagnosed in September 2019. After detecting the COVID-19 virus in his nasopharyngeal swabs sample via RT-PCR, the patient was analyzed through the course of his disease and treatment. The clinical symptoms of this patient included cough, fatigue, and body aches. Due to the importance of underlying diseases in the course of COVID-19, it was taken into consideration and the patient was inquired on this subject. It was found that he had an underlying kidney disease and was on dialysis. His weight was reportedly normal (BMI=21.3). According to the reports, the patient had no prior or recent contact with COVID-19-infected patients. Since this patient was in good overall condition and the viral infection was not severe, he did not need to be hospitalized. After the prescription of Sovodak, the patient was quarantined at home and fully recovered eventually.

### Case 2

A 43-year-old man who was diagnosed with active pulmonary tuberculosis in February 2020 in Khoramshahr, Iran. After identifying the virus in his swab sample, using the RT-PCR method, the patient was examined for further evaluation. The clinical symptoms of this patient consisted of cough, myalgia, fatigue, and fever. This patient had underlying diabetes and was overweight (BMI=28.3). Reportedly, he had no history of contact with COVID-19-infected patients but he reported traveling abroad to Basra, Iraq. Since the patient's condition was not severe, he was quarantined at home after a prescription of sovodak. The patient's recovery and treatment were monitored and he recovered completely.

### Case 3

A 30-year-old man living in Abadan, Iran with active pulmonary tuberculosis diagnosed in July 2019 was evaluated after detecting COVID-19 virus RNA in his swab sample via RT-PCR. The clinical symptoms of this patient were fever, fatigue, myalgia, cough, and high blood pressure. He had underlying Dyspnea and displayed severe weight loss (BMI= 13). The patient also had HIV co-infection. He did not report any recent contact with COVID-19-infected patients. Due to favorable conditions, he was not hospitalized and was quarantined at home after the prescription of Sovodok. This patient's course of the disease was evaluated and controlled. Eventually, he passed away due to TB-HIV-SARS-CoV-2 co-infection, high blood pressure, and disease progression.

## 5. DISCUSSION

COVID-19 causes severe diseases that mainly target the respiratory system. This epidemic has affected many countries around the world and respiratory transmission among people has made it a huge threat to human health<sup>14</sup>. The main clinical symptoms of COVID-19 are similar to the other disease that involve the respiratory system so prompt and accurate diagnosis of COVID-19 is essential to quarantine and treat the patients.

In this study, the first series of patients study in Iran, we aimed to investigate SARS-CoV-2 in tuberculosis patients (pulmonary and extrapulmonary) to detect the virus, quarantine, and treat the patients.

Limited information is available on if tuberculosis patients whether active, latent, or those who have recovered are at higher risk of COVID-19 consequences<sup>15</sup>. However, one study has shown that the long-term effect of COVID-19 may activate latent tuberculosis<sup>16</sup>.

According to a recent study, COVID-19 infection can be observed before, during, and after tuberculosis infection (both pulmonary and extrapulmonary) and the mortality rate of tuberculosis is higher in patients with advanced age. In the same study, HIV co-infection was reported in some patients<sup>17</sup>. Following an inquiry conducted on 24 patients with active tuberculosis in Italy to investigate COVID-19, 20 patients with TB- COVID-19 co-infection were observed. The average age of these 20 patients was 39 years old, 60% of them were men and their BMI was reportedly lower than 18.5 kg/cm<sup>2</sup>. 8 out of 20 patients with TB- COVID-19 co-infection had underlying conditions but HIV infection was not present in any of them<sup>18</sup>.

One Chinese research into this subject reported that patients with tuberculosis infections (active or latent) are more susceptible to COVID-19 infections due to rapid spread and severe involvement<sup>19</sup>.

## 6. CONCLUSION

Considering the result of this study and other studies done on this subject, the need for COVID-19 screening in tuberculosis patients is deemed essential. Given that limited studies have been performed in this regard, further and extensive studies are required, in other countries as well, to examine COVID-19 and tuberculosis co-infection to evaluate the severity of the disease and subsequently treat the co-infection.

## ACKNOWLEDGMENTS

The authors would like to express their sincere gratitude to the honorable officials of the Deputy of Health, Abadan University of Medical Sciences.

## CONFLICT OF INTEREST

The authors have declared that no competing interests exist. All authors have approved this manuscript.

## AUTHOR CONTRIBUTIONS

All Authors have contributed to the drafting and the critical revision of the article. The final version approved by all authors.

## DATA AVAILABILITY STATEMENT

Data are available on request from the authors.

## ORCID

Sheida Mohammadi <https://orcid.org/0000-0002-6510-5589>

## Funding statement

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

## Ethics approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of national research committee. The study was approved by the Ethics Committee of Abadan faculty of Medical Sciences, under code IR.ABADANUMS.REC.1399.175.

## Informed consent

Informed consent was obtained from all individual participants included in the study.

## REFERENCES

- 1 Wang, C., Horby, P. W., Hayden, F. G. & Gao, G. F. A novel coronavirus outbreak of global health concern. *The Lancet* **395**, 470-473 (2020).
- 2 Saberian, M. *et al.* An Overview on the Common Laboratory Parameter Alterations and their Related Molecular Pathways in Screening for COVID-19 Patients. *Clinical laboratory* **66** (2020).

- 3 Tuite, A. R. *et al.* Estimation of coronavirus disease 2019 (COVID-19) burden and potential for international dissemination of infection from Iran. *Annals of Internal Medicine* **172** , 699-701 (2020).
- 4 Oei, W. & Nishiura, H. The relationship between tuberculosis and influenza death during the influenza (H1N1) pandemic from 1918-19. *Computational and Mathematical Methods in Medicine* **2012**(2012).
- 5 Walaza, S. *et al.* Excess mortality associated with influenza among tuberculosis deaths in South Africa, 1999–2009. *PloS one***10** , e0129173 (2015).
- 6 Zürcher, K. *et al.* Influenza pandemics and tuberculosis mortality in 1889 and 1918: analysis of historical data from Switzerland. *PLoS One* **11** , e0162575 (2016).
- 7 Wong, C.-Y. *et al.* Tuberculosis in a SARS outbreak. *J Chin Med Assoc* **67** , 579-582 (2004).
- 8 Liu, W. *et al.* Pulmonary tuberculosis and SARS, China. (2006).
- 9 Alfaraj, S. H., Al-Tawfiq, J. A., Altuwaijri, T. A. & Memish, Z. A. Middle East respiratory syndrome coronavirus and pulmonary tuberculosis coinfection: implications for infection control. *Intervirology***60** , 53-55 (2017).
- 10 Jain, V. K., Iyengar, K. P., Samy, D. A. & Vaishya, R. Tuberculosis in the era of COVID-19 in India. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews* **14** , 1439-1443 (2020).
- 11 Corman, V. M. *et al.* Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. *Eurosurveillance* **25** , 2000045 (2020).
- 12 Nalla, A. K. *et al.* Comparative performance of SARS-CoV-2 detection assays using seven different primer-probe sets and one assay kit. *Journal of clinical microbiology* **58** (2020).
- 13 Jiang, F.-C. *et al.* Detection of severe acute respiratory syndrome coronavirus 2 RNA on surfaces in quarantine rooms. *Emerging Infectious Diseases* **26** , 2162 (2020).
- 14 Patel, A. & Jernigan, D. B. Initial public health response and interim clinical guidance for the 2019 novel coronavirus outbreak—United States, December 31, 2019–February 4, 2020. *Morbidity and Mortality Weekly Report* **69** , 140 (2020).
- 15 Singh, A., Prasad, R., Gupta, A., Das, K. & Gupta, N. Severe acute respiratory syndrome coronavirus-2 and pulmonary tuberculosis: convergence can be fatal. *Monaldi Archives for Chest Disease***90** (2020).
- 16 Pathak, L. *et al.* Coronavirus activates a stem cell-mediated defense mechanism that reactivates dormant tuberculosis: implications in COVID-19 pandemic. *bioRxiv* (2020).
- 17 Tadolini, M. *et al.* Active tuberculosis, sequelae and COVID-19 co-infection: first cohort of 49 cases. *European Respiratory Journal* (2020).
- 18 Stochino, C. *et al.* Clinical characteristics of COVID-19 and active tuberculosis co-infection in an Italian reference hospital. *European Respiratory Journal* (2020).
- 19 Liu, Y. *et al.* Active or latent tuberculosis increases susceptibility to COVID-19 and disease severity. *Medrxiv* (2020).