

COVID-19 Pandemic and Tuberculosis Control: A Narrative Review

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INTRODUCTION

Tuberculosis (TB), caused by *Mycobacterium tuberculosis*, is one of the leading infectious causes of death worldwide that is spread through the air (1-3). In 1993, the World Health Organization (WHO) announced TB as a global emergency (4); it is still a serious public health challenge, especially in low- and middle-income countries (5, 6), including Iran (7). TB is currently among the top ten causes of death and the first cause of death from a single

Background: The world is currently struggling with the COVID-19 pandemic. Measures to control the COVID-19 pandemic have affected other health problems and diseases, including tuberculosis (TB) and its control. The present narrative review aimed at reviewing published literature on the impact of the COVID-19 pandemic on TB control.

Materials and Methods: English language databases, including PubMed, ISI, Scopus, and Google Scholar, were searched using the keywords "Tuberculosis, COVID-19, and Coronavirus" to find relevant articles.

Results: Problems and limitations in financial and human resources, as well as medical and laboratory services caused by the COVID-19 pandemic, contribute to the reduction in the number of newly diagnosed patients with TB. More effort in identifying patients with TB is of great importance, and if the global number of newly diagnosed patients with TB decreases by 25% for three consecutive months due to the COVID-19 pandemic, the TB mortality rate will increase by 13%. An increase in the TB mortality rate means the failure of TB control programs to reach the targets of the Global End TB Strategy.

Conclusion: According to the latest statistics released by the Ministry of Health, the incidence of TB in Iran has not yet reached fewer than 100 cases per million population. On the other hand, being a neighbor with countries with a high risk of TB is a serious threat to Iran. Therefore, further effort to control TB during the COVID-19 pandemic is particularly important.

Keywords: Tuberculosis; COVID-19; Pandemic

infectious agent globally (ranking above HIV/AIDS since 2007) (8). About one-third of the world's population carries a latent TB infection (3, 9, 10). Hence, controlling TB is one of the top priorities of WHO (11).

Despite numerous efforts to eradicate TB, control of this disease has always been influenced by various events, including outbreaks of infectious diseases, such as severe acute respiratory syndrome (SARS) (12) and Ebola (13, 14).

The world is currently struggling with the coronavirus disease 2019 (COVID-19) pandemic, first reported in December 2019 in Wuhan, China, and spreading worldwide (15). Many countries took various measures to combat the COVID-19 pandemic, such as conducting extensive testing, rapid tracking of patients, mandating quarantine, applying travel restrictions, school closure, and social distancing. Although these measures have had a positive effect on the control of the disease (16), they also adversely have affected economic growth, poverty, food security, diseases (17), and other public health problems (16). There are many concerns in low- and middle-income countries about the impact of these preventive measures on the control of HIV, TB, and malaria (17). According to the Global Fund, in affected 106 countries, it is estimated that about 85% of HIV and 78% of TB control programs have been disrupted following the COVID-19 pandemic (18).

The present narrative review aimed at reviewing published literature on the effect of the COVID-19 pandemic on TB control. English language databases, including PubMed, ISI, Scopus, and Google Scholar, were searched using the keywords "Tuberculosis, COVID-19, and Coronavirus" to find relevant articles.

The impact of the COVID-19 pandemic on TB control:

The Stop TB Partnership Secretariat examines the impact of the COVID-19 pandemic and related measures on TB status through interviewing the officials of the National TB Programs (NTP) and key individuals in 20 high TB burden countries. The results showed that the measures taken for the COVID-19 pandemic have significantly disrupted TB control programs and affected communities and patients with TB, especially vulnerable groups. Officials of NTP in these countries reported that the number of people seeking TB-related health services has decreased during the COVID-19 pandemic (19).

Fei et al. in China evaluated the short-term impact of the COVID-19 pandemic on the incidence of TB, follow-up visits during treatment, and the outcomes of treatment. They used 2017-2019 data as basic information. The data on

the emergence of the COVID-19 pandemic were divided into three groups by time (control phase: 11 weeks before January 2020, with no measures taken to the COVID-19 pandemic; severe phase: 11 weeks from January 25 to April 8, 2020, with strict measures taken to control the pandemic; normal phase: four weeks from April 9, 2020, onwards with general measures to manage the pandemic). The results showed a dramatic decrease in identifying patients with TB in the first week of the severe phase. Also, the number of performed sputum culture tests has decreased by 8% compared to the control period (20).

Liu et al. in Jiangsu Province, China, reported a 50% decrease in the incidence of TB in 2020 compared to 2015-2019. Besides, the treatment outcomes and diagnostic screenings for multidrug-resistant TB decreased in 2020 (21).

Kwak et al. investigated the impact of the COVID-19 pandemic on the incidence of TB in South Korea, a country with a moderate incidence of the disease, and reported that the diagnosis of TB has decreased by 24% after the pandemic. Although TB incidence has followed a declining trend in South Korea since 2010, the reported decrease was beyond expectations (22).

In the study by Komiya et al. in Japan, the number of newly diagnosed patients with TB showed a declining trend following the COVID-19 pandemic (especially from March 2020 onwards). In addition, the number of sputum culture tests showed a significant decrease in April and from April to May 2020 compared to the same period in 2017-2019 (23).

In a study in Ethiopia, Mohammed et al. reported a dramatic decline in TB screening, care, and treatment programs after the COVID-19 pandemic. They reported that the diagnosis of TB after the pandemic onset significantly reduced (24).

Factors contributing to the influence of the COVID-19 pandemic on TB control:

Various studies have indicated that the number of performed sputum culture tests and TB-diagnosed cases has decreased dramatically. It can be hypothesized that the

rate of TB transmission has decreased due to physical distancing and facial masks. However, researchers have indicated that physical distancing could reduce the number of newly detected patients with TB by only 10% in countries with a high disease burden (25). On the other hand, TB is pathologically divided into two types primary and secondary (caused by reactivation of latent TB). The number of elderly patients with secondary TB has increased in recent years. Therefore, many TB cases, particularly among the elderly, are developed by the reactivation of TB after a long time (usually several decades after the primary infection). Hence, control measures to fight COVID-19 have not affected a reduction in the patient numbers diagnosed with TB (26). Therefore, a decline in the number of tests performed and patients diagnosed with TB can be influenced by factors mentioned as follows:

- Reduced access to medical centers and healthcare services (20,21,26,27), and postponement or cancellation of appointments (26)
- Lack of access to health centers due to restrictions on inter- and intra- city travels (16, 19,20)
- Lack of access to health centers due to poverty and economic problems caused by quarantine (28)
- Focus of laboratories on the diagnosis of COVID-19 (16, 20,21) and a decline in the number of TB diagnostic tests performed (20,29)
- Disruption in diagnostic practices due to the lack of human resources and even laboratory space (19)
- Allocation of health care workers to COVID-19 designated wards (16, 20, 24,29)
- Patients fear of getting COVID-19 by referring to medical centers (14, 16, 28)
- Patients' fear of social stigma (24, 25, 28)
- Disruption in the TB care system and cessation of screening programs and referral of patients (19, 20)
- Lack of TB contact evaluations and preventive treatment (22)
- Referral of patients developing new respiratory symptoms to COVID-19 screening clinics (22)
- Temporary closure of outpatient TB clinics (20)
- Suspension of research on TB (19)
- limited funds for TB programs (16)

Consequences of the impact of the COVID-19 pandemic on TB control:

Lockdown and preventive measures have greatly affected the control of the COVID-19 pandemic. However, restrictions imposed by these measures have extensive, unintended consequences (25), and encounter the world a health crisis (30). The effect of the COVID-19 pandemic and related interventions on TB control is significant. It should be noted that TB is a leading cause of death from an infectious disease worldwide (28). A total of ten million new cases of TB and 1.4 million deaths from it were estimated in 2019 (8); thus, the world still challenges the ancient pandemic of TB (27). Besides, the accumulation of patients with latent TB and the lack of treatment services during the COVID-19 pandemic has resulted in a vast reservoir of latent TB that may take years to neutralize (25). Lack of regular treatment for patients with TB may lead to failure and the rise of drug-resistant TB in the future (31, 32). Cilloni et al. evaluated the potential effects of COVID-19-related lockdown on TB status in three countries with a high TB burden, i.e., India, Kenya, and Ukraine- and indicated that even short-term lockdowns could cause long-term failures in TB control. According to the results of their study, if a fairly-strict lockdown is mandated, the TB incidence and mortality rate can increase by 1%-4% and 2%-6%, respectively. The figures would triple when a strict lockdown is scheduled (25). Studies and models have also indicated that if the global TB incidence decreases by 25% for three months following the COVID-19 pandemic, the TB mortality rate will increase by 13%, which is a decrease compared to that of 2015, indicating the failure and rollback of TB control programs (29, 30). Therefore, the

COVID-19 pandemic may hinder reaching the targets of the global end TB strategy (21).

CONCLUSION

TB is a preventable and curable disease; however, its control is cost-effective. A delay in the diagnosis and treatment of TB can increase the transmission of TB in the community, the spread of drug-resistant strains, and mortality (33). Given the importance of reaching the global end TB strategy target, governments and stakeholders should ensure the implementation of TB control programs during the COVID-19 pandemic (14, 16, 19) and take measures to diagnose, treat, and control TB (22, 30). Increasing awareness about TB, re-prioritizing TB control programs, prioritizing and allocation of sufficient funds and resources to screening for refractory multidrug-resistant TB, promotion of treatment adherence (21), research on the better diagnosis of TB, production of the vaccine, new therapies, equal access to modern care and interventions for social protection (27), protection of vulnerable groups, addressing economic problems, and protection of patients against isolation, stigma, and discrimination (14) should also be considered. Given the overlap of apparent signs and symptoms of COVID-19- i.e., fever, dry cough, fatigue, sputum, shortness of breath, sore throat, headache, body aches, cold sensation, hemoptysis, etc., with those of TB, physicians should always consider the differential diagnosis of TB (14, 24), and examine suspected individuals, especially the elderly with respiratory symptoms, in terms of TB (23).

Because according to the latest statistics released by the Ministry of Health, Iran has not yet reached fewer than 100 TB cases per million population (the first step of elimination) (34), which is a serious health threat to society, and because of neighboring countries with a high risk of TB, including Afghanistan, Pakistan, and Russia (35), unscramble effort to control TB during the COVID-19 pandemic is of particular importance.

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