

# Incidence of Covid-19 Infection Among Tb Patients in Basrah City

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## Abstract

The fact that COVID-19 causes severe infection in lungs and general respiratory system, thus it shares the site of infection and pathogenicity mode with *Mycobacterium tuberculosis*, also, the fact that BCG vaccination is a mandatory approach in Iraq. These criteria directed our interest to detect the incidence rate of COVID-19 infection in tuberculosis patients in the city of Basrah (south of Iraq), depending on the weakness of their immune system, the similarity of the infection site and BCG vaccine effects. In this study data were collected from 215 tuberculosis patients who registered in T.B. and Respiratory Specialize Center in Basrah city, for both sexes and for all age groups, during a period extended from November 2020 to February 2021. All cases were surveyed for the presence of the COVID- 19 infection. Out of 215 patients, 8 (4%) patients were represented COVID- 19 infection associated with tuberculosis infection. All 8 patients were infected with extra pulmonary tuberculosis. The obtained results were showed that the incidence of tuberculosis patients with COVID- 19 is almost low and most of them were in extra pulmonary tuberculosis. Current study aims to correlate between lower level of COVID-19 infections and death rate among tuberculosis patients in Basrah with the national BCG immunization program in Iraq, in addition to correlate between BCG vaccine and innate immune memory or trained immunity.

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## Keywords

Keywords: COVID- 19 infection, tuberculosis, BCG vaccine, trained immunity

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Coronavirus disease 2019 (COVID-19) pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has emerged in Wuhan, China, in December 2019<sup>1</sup>. On 24 February 2020, an outbreak was detected in Iraq.

COVID-19 is a causative agent of a new form of viral respiratory tract infection that can be complicated by severe pneumonia and an acute lower respiratory system infection<sup>2</sup>. While co-infection between COVID-19 and many pathogens has been reported, there's limited published research interested in co-infection with *M. tuberculosis*<sup>3</sup>.

*M. tuberculosis* is an intracellular bacterium associated worldwide with high morbidity and mortality of tuberculosis infection<sup>4</sup>. Both COVID-19 and tuberculosis are infectious diseases that attack the lungs, they are airborne transmissible diseases that stress health systems, and have similar clinical findings like cough, fever and difficulty breathing<sup>5</sup>.

Bacillus Calmette-Guerin (BCG) is only available vaccine has protective role against tuberculosis and its complications. In general, vaccines provide protection to a particular pathogen by inducing effector mechanisms directed to that pathogen. However,

attenuated vaccines like BCG can also protect against unrelated pathogens, some of which cause acute respiratory tract infections<sup>6</sup>. BCG works by induction of non-specific protection mediated via enhancing of innate immune memory or "trained immunity"<sup>7</sup> that re-stimulated with different pathogens<sup>8</sup>. Actually, this vaccine has been designed and used against *M. tuberculosis*, different research and studies have shown cross-prevention against other non-relevant pathogens, including viruses such as yellow fever<sup>9</sup>, hepatitis B, and influenza (H1N1)<sup>10</sup>.

of the Ministry of Health according to Resolution No. 233\2022 dated 26\5\2022.

### Data Collection

Data were collected from T.B. and Respiratory Specialize Center in Basrah city, during a period extended from November 2020 to February 2021. 215 tuberculosis patients from both sexes and different age groups were registered for the presence of the COVID-19 infection among tuberculosis patients.

### Ethical Approval

A valid consent was achieved from Research Committee\Training and Human Development Center

### Results and Discussion

Among the 215 tuberculosis patients, were 78 (36%) males and 137 (64%) females. Table (1).

**Table (1):** Distribution of tuberculosis cases depending on sex.

Total No. of tuberculosis patient's	215
Male	<b>78 (36%)</b>
Female	<b>137 (64%)</b>

Tuberculosis cases were divided depending on types into:

1. pulmonary tuberculosis with 121(56%) cases that included 50 (23%) males and 71 (33%) females.

2. extra pulmonary tuberculosis with 94 (43%) cases that included 28 (13%) males and 66 (30%) females. Table (2).

**Table (2):** Distribution of cases according to tuberculosis types.

Pulmonary tuberculosis cases = 121 (56%)	
Male	female
50 (23%)	71 (33%)
Extra pulmonary tuberculosis cases = 94 (43%)	
Male	Female
28 (13%)	66 (30%)

According to the results obtained in this study, the infections of COVID- 19 were registered in patients with

extra pulmonary tuberculosis with 8 (4% from the total number of tuberculosis patient's) cases. Table (3).

**Table (3):** COVID- 19 infections associated with extra pulmonary tuberculosis cases.

Total No. of tuberculosis patient's	215
Extra pulmonary tuberculosis cases No.	<b>94 (43%)</b>
COVID- 19 infections	<b>8 (4%)</b>
Males	<b>Females</b>
2 (1%)	<b>6 (3%)</b>

Also, all tuberculosis patient's associated with COVID-19 tuberculosis patients were divided according to age

groups were summarized in Table (4):

**Table(4):** Distribution of tuberculosis cases depending on age groups.

Age groups No.	Age	Patient's No.	Male	Female	COVID-19 infection
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1	<1 y - 10 y	18	6	12	-
2	11 y – 19 y	32	10	22	-
3	20 y – 29 y	36	8	28	4 females
4	30 y – 39 y	32	12	20	-
5	40 y – 49 y	36	14	22	2 males 2 females
6	50 y – 59 y	28	12	16	-
7	60 y – 69 y	26	14	12	-
8	70 y – 79 y	6	2	4	-
9	80 y – 89 y	1	1	-	-

y = year

While all the data suggest an increase in the possibility of tuberculosis patients infecting with the Corona virus, due to the similarity of site of infection and the route of transmission between *M. tuberculosis* and COVID-19, beside tuberculosis patients are immunologically weakened, they are more susceptible to infection with COVID-19, but according to the obtained results in this study, we noticed that tuberculosis patients who infected with COVID-19 are only 8 (4%) patients they all share that they have extra-pulmonary tuberculosis infection (table 3), (table 4). These results showed a very low rate of infection for tuberculosis patients with COVID-19 that does not match the expectations.

The explanation of these results may be due to the fact that the immune system of tuberculosis patients is stimulated due to the presence of cell mediated immunity, in spite of the immune response to *M. tuberculosis* infection is poorly understood, the immune response to Mtb infection is predominantly cellular<sup>11</sup>, leading to the concept that pathogenesis of *M. tuberculosis* and related immunity are mediated by cell mediated immune response that have protective role of lymphocyte response<sup>12</sup>.

Tuberculosis is considered as contagious disease and Mtb is an intracellular pathogen that stimulate primary immune response by phagocytosis, so, this bacterium has the ability to enter the alveolar macrophages, forming phagolysosomes leading to intracellular infections<sup>13</sup>. Bacteria enter the body by infecting the body's immune cells and move through them in the bloodstream, due to their high virulence, they overcome the components of the immune system, and because these bacteria used immune cells to enter the body and caused the infection, which means that the immune system will remain stimulated continuously and thus will be able to confront any other bacterial or viral infection, including COVID- 19<sup>14</sup>.

On other side, there is an association between national BCG immunization program and a lower rate of COVID-19 infection<sup>2</sup>. Studies have been confirmed that the BCG vaccine can decreased several infectious diseases severity beside its essential target against tuberculosis. The non-specific boosting of immune response by BCG vaccine represents useful concept termed as trained immunity that may be prevent infection with COVID-19<sup>15</sup>.

BCG vaccine, a live attenuated vaccine that provide protection against tuberculosis, it decreased the rate of children's mortality that caused by infections of another causative agents not related to *M. tuberculosis*, this may be support the idea of induction of trained immunity<sup>16</sup>. Usually, the BCG vaccine provides protection for individual under to the age of sixteen, when tuberculosis infection occurs at the age up of sixteen, trained immunity provides protection against infection result from actual exposure to the *M. tuberculosis*, then stimulate and boost the nonspecific innate immune cells and autophagy<sup>17</sup>. Vaccination with the BCG vaccine plays a preventive role to combat COVID-19 mortality, by inducing innate immune response. According to estimates by the World Health Organization, a quarter of the world's population carries latent infections of tuberculosis, in which no clinical symptoms of tuberculosis are diagnosed or the tuberculosis not clinically active, however, the immune response remains stimulated by *Mycobacterium* antigens. Thus, latent infection of tuberculosis with BCG vaccine contributes to stimulate long-term immunity and may provide immune protection for the patients against infection with COVID-19<sup>18</sup>.

Inclusion of BCG vaccination in early stages of life may induce trained immunity that as a part, may confer protective effect for COVID- 19 infection. So, the COVID- 19 related positive cases and mortality rate were decreased in countries that used BCG in their

national vaccination program<sup>16</sup>. Trained innate immunity that enhanced by BCG vaccination, may clear up host tolerance against COVID-19 infection<sup>19</sup>.

In **Iraq**, BCG vaccine is a mandatory childhood immunization schedule, so, may be that explain the low rate of COVID-19 incidence among TB patients in **Basrah city**, these results compatible with<sup>20</sup>, 2020 who assumed that the countries that adopted BCG vaccine as a mandatory vaccination system were able to control or limit spread of COVID-19 better than countries that do not adopt it or stop using it as national vaccination program.

An accordance with available data, in countries that adopted BCG vaccine as mandatory approach of vaccination in childhood immunization schedule found that the level of COVID-19 prevalence was lower than the others<sup>21</sup>. Immunization with an unrelated bacterial antigens or vaccines may offer non-specific benefits against COVID-19 as well as other diseases<sup>19,21</sup>.

Immune memory is a distinctive characteristic of acquired immune response, lead to enhancement of innate immune system by subsequent triggers lead to innate immune cells responsiveness, in a process known as 'trained immunity' which is a de facto innate immune memory<sup>21</sup>.

Trained immunity represents non-specific memory-like immune response stimulated by pathogens and vaccines. BCG can confer antigen-independent protection against different pathogens. In the past decade, research pointed to advantages of trained immunity for improvement host defense, with the possibility of adverse effects in immune-mediated and chronic inflammatory diseases<sup>22</sup>.

Perhaps we should also give explanations for the eight 8(4%) cases of tuberculosis patients who infected with COVID-19, the data of these patients indicate that they have completed their treatment against tuberculosis or recovered from it, but they are registered in the T.B. and Respiratory Specialize Centre in Basrah city for the confirmatory periodic examination. All of the eight patients have extrapulmonary tuberculosis infection (extrapulmonary tuberculosis (EPTB): is an infection caused by *M. tuberculosis* that occurs in organ systems other than the lungs), according to<sup>23</sup>, *M. tuberculosis* infect type II pneumocytes cells of lungs which are the same type of cells that COVID-19 infects. Actually, these facts also compatible with<sup>24</sup>, who mentioned that *M. tuberculosis* and SARS-CoV-2

infections have some substantial similarities as cell entry, immune response and immune evasion, therefore competition between tuberculosis bacteria and COVID-19 may get the same receptors found in the lungs, when tuberculosis is in the lungs. In the case of the eight patients, the infection was limited to extrapulmonary tuberculosis, so may be the path was open for the COVID-19 to infect the lung cells without competition from the tuberculosis bacteria that are present in other organs except the lungs. In addition, the high virulence of the virus since the onset of the pandemic COVID-19, with high capability of virulence transmission and immune evasion, also differences in the efficiency of the immune system of the eight patients, and the disparity in the immune response of individuals against COVID-19, all these criteria may lead to immune dysregulation<sup>25</sup>.

The specific virulence factors related to COVID-19 are directed to escape detection by host immune cells, or to deregulate host immune responses like delaying of interferon (IFN) mediated protection and efficient production of neutralizing antibodies, or employment host cell machinery for viral replication<sup>25</sup>, therefore, from the aforementioned reasons, it may have contributed to the infection of eight patients with COVID-19.

## Conclusions

1. Data were collected from TB patients registered with T.B. and Respiratory Specialize Centre in Basrah city. All patients were screened to see whether they were infected with COVID-19 or not. Of 215 TB patients, there are only 8 patients who were infected with COVID-19.

2. We concluded that the BCG vaccine, which is a mandatory vaccine in Iraq, may have an important role in reducing or eliminating the infection from tuberculosis patients with the COVID-19 in the city of Basrah, despite the severity of infections and deaths caused by this virus in our city at the time of pandemic. The obtained results were supports the facts that the BCG vaccine has a protective role against many pathogens other than *M. tuberculosis*, the explanation about the gained results may be related to cell mediated immunity, BCG vaccine that induced trained immunity in TB patients, thus they exhibited a resistance against COVID-19 infection, and support the fact that a

percentage of peoples may carry a latent infection with tuberculosis, as they do not show symptoms of the disease, but their immune response remains stimulated by M. tuberculosis, therefore, both latent tuberculosis and the BCG vaccine induce lifelong immunity, non-specific memory-like innate immune response induced by some pathogens.

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

## Conflict of interest

We have no conflict of interest to declare.

## Ethical approval

The study protocol and the subject information and consent form were reviewed and approved by a Research Committee Training and Human Development Center of the Ministry of Health according to document No. 233\2022 dated 26\5\2022.

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انتشار اصابات فايروس كوفيد-19 بين مرضى التدرن الرئوي في مدينة البصرة  
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#### البصرة \ العراق

بسبب عدوى شديدة في الرئتين والجهاز التنفسي العام COVID-19 أن حقيقة كون فايروس ، وبالتالي فهو يشترك في موقع الإصابة ونمط الأمراض مع جرتومة يعتبر نظام BCG ، وكذلك حقيقة أن لقاح *Mycobacterium tuberculosis* تلقيح إلزامي في العراق، كل هذه المعايير وجهت اهتمامنا إلى الكشف عن معدل الإصابة بين مرضى التدرن الرئوي في مدينة البصرة (جنوب العراق) ، COVID-19 بعدوى اعتماداً على ضعف جهاز المناعة لدى المرضى ، وتشابه موقع الإصابة وتأثيرات لقاح BCG.

في هذه الدراسة ، تم جمع البيانات من 215 مريضاً من مرضى التدرن الرئوي الذين سجلوا في المركز التخصصي للأمراض الصدرية والتنفسية في مدينة البصرة لكلا الجنسين ولجميع الفئات العمرية خلال الفترة الممتدة من تشرين الثاني 2020 إلى شباط 2021. وتم مسح جميع الحالات بحثاً عن الإصابة بفايروس كوفيد-19.

من بين 215 مريضاً بالتدرن الرئوي ، تم تسجيل الإصابة بفايروس كوفيد-19 في 8 (4%) مرضى مصابين بالتدرن خارج الرئتين. أظهرت النتائج التي تم الحصول عليها أن اصابات مرضى التدرن الرئوي بفايروس كوفيد-19 تعتبر منخفضة وتكررت في المرضى المصابين بالتدرن خارج الرئتين.

تهدف الدراسة الحالية إلى الربط بين انخفاض مستوى الاصابات بفايروس كوفيد-19 ومعدل الوطني الإلزامي BCG الوفيات بين مرضى التدرن الرئوي في البصرة وبرنامج لقاح والذاكرة المناعية الفطرية أو المناعة BCG في العراق ، بالإضافة إلى الربط بين لقاح المدرية.