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ORIGINAL ARTICLE

ROLE OF ANTITUBERCULOSIS DRUGS IN COVID-19 INFECTION IN MOSUL CITY

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Summary

Introduction: Coronavirus (COVID-19)-patients with another critical ailment, such as tuberculosis need more effective care and therapy. This study aims to investigate the role of COVID-19 on active tuberculosis patients who are receiving directly observed therapy (DOT) for tuberculosis in Mosul.

Methods: In a seven-month prospective observational case-control unicenter-study at a chest and respiratory disease clinic and control and disease center in Mosul, we examined two groups of the population. (cases): considered 100 patients who attend the chest and respiratory diseases clinic with clinically, laboratory, radiology diagnosed active tuberculosis and receiving Directly Observed Therapy for tuberculosis. The control group includes one hundred individuals randomly selected from daily reported tuberculosis-free COVID-19 patients at the control and disease center. The two groups were compared for COVID-19 infection clinical investigations, radiology, and laboratory tests (polymerase chain reaction test) for the cases and control. The present study revealed that from a total of 100 active tuberculosis patients who received Directly Observed Therapy for tuberculosis only one got COVID-19 infection and 10 of 100 for the controls which are significantly 9.1 times at risk of COVID-19 infection than those with tuberculosis and on Directly Observed Therapy.

Conclusion: Patients with active tuberculosis and enrolled on Directly Observed Therapy appear to be at lower risk for COVID-19 infection.

Key words: COVID-19; tuberculosis; PCR; Directly Observed Therapy

Introduction

The epidemic of COVID-19-infection, in Wuhan (Hubei, China) announced in December 2019, drives awareness and concern of the World Health Organization (WHO). COVID-19 is a human infectious disease caused by a coronavirus, the virus strain changes rapidly, thereby the transmission of COVID-19 becomes influential and the infection rate is fast. Due to the unavailability of specific therapy for COVID-19, the treatment of admitted patients are mainly symptomatic supportive therapy (1). The severity of the illness is the most important determinant of the required treatment option. It has been postulated that COVID-19 when infects a patient with strong immunity may move smoothly and responds effectively to the treatment, but patients might suffer when they have another

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illness, the immune system may not respond strongly enough to fight the other bacteria or viruses effectively. Stress, poor diet, certain medications, being pregnant or elderly can also weaken the person's immune system (2). Many available drug options have been suggested to be used due to previous experience as prophylaxis or therapy (3, 4).

Clinically, COVID-19 infection has two phases, a mild-moderate phase, and a severe phase. The adaptive immune response is needed to eliminate the virus and to stop the disease progression to the severe stage and when a protective immune response is not well, the virus will propagate and massive destruction of the affected organ tissues will occur, especially in tissues or organ that have high ACE2 receptors, such as lung, intestine, and kidney. The damaged cells stimulate innate inflammation in the lungs that is largely mediated by macrophages and granulocytes (5). Therefore, general health may not be of benefit for patients who have an advanced stage, when severe lung damage occurs.

Patients with tuberculosis infection (any type of tuberculosis pulmonary, intestinal, bone, joint, skin, brain, lymph node, or genital system) are endemic with an average occurrence of the disease reaches 1 % yearly all over the world, and the highest average of it in the Philippines, Korea People's Republic (North) and African countries (6) their general health feature and their immune response to any other disease will be decreased. Patients with tuberculosis infection diagnosis will be clinical, laboratory, and radiology and those with active TB will have all the symptoms and signs or one of them like a persistent cough, loss of weight, fever, loss of appetite, weakness, shortness of breath, hemoptysis, also when the patient had extrapulmonary tuberculosis with general symptoms according to the affected organs. They should be treated until being latent tuberculosis after 180 days.

Usually, in these stages, the patients receive a course of treatment called Directly Observed Therapy (DOTS). For the first 60 days, they have four drugs which are isoniazid, rifampicin, ethambutol, and pyrazinamide then complete 120 days with 2 drugs rifampicin and isoniazid (4) this called category-1 used in Mosul city to all patients in 2021. While in the previous year's category-2 used also when rifampicin resistance develops.

The study aims to investigate the role of COVID-19 on tuberculosis patients who are receiving Directly Observed Therapy in Mosul city.

Methods

A seven-month prospective observational case-control study at chest and respiratory disease clinic and control and disease center in Mosul from the first of January to the 1st of august 2021 examined two groups of population:

The first group (Group 1): considered 100 patients who attend the chest and respiratory diseases clinic with clinically, laboratory, radiology diagnosed active tuberculosis and receiving Directly Observed Therapy for tuberculosis.

The comparison group (Group 2) considered one hundred of population taken randomly from the daily report for COVID-19 at control and disease center and in whom not tuberculosis was diagnosed clinically by specialist or laboratory and radiological finding.

The two groups were compared for COVID-19 infection clinically radiology and laboratory by doing polymerase chain reaction test PCR for the cases & control.

Data were analyzed by Minitab 17 using chi-square test p-value considering the value of Equal and <0.05 significant (Table1).

Table 1. This shows that the population in Mosul who were not tuberculosis significantly 9.1 times at risk of COVID-19 infection than those with tuberculosis and receiving DOT for tuberculosis.

COVID-19	Cases	Control	OR	p value	CI 95%
Present	1	10			
Absent	99	90	0.091	0.005	0.011 - 0724
Total no.	100	100			

Results

A total of 100 active tuberculosis patients and 100 not tuberculosis were enrolled in the study. All from both sexes.

Discussion

COVID-19 has been declared by the World Health Organization (WHO) as the latest pandemic in March 2020 (8). Then, three months later, the pandemic of COVID-19 has extended to our locality; Iraq (9), shortly thereafter COVID-19 covered the whole nation (10).

This study found the percentage of COVID-19 infection in non-tuberculosis patients was 10% while another population-based cohort study by Al-Ridhwany HH. In Mosul 2020 found it 6.1 in Mosul (11), Which is the second most populous Iraqi Governorate after the capital city; Baghdad. However, the difference in result may be due to an increase in the availability of PCR tests so more cases are diagnosed in 2021, at 2020 up to the end of the year total numbers of PCR done 117241 while in 2021 up to the first of August it's 688440 increasing 5.87 times or the virus become more infectious at 2021 the total number of positive PCR 47301 for seven months only comparing with total positive at 2020 which is 24493 (9).

The important result was that patients with active tuberculosis infection and enrolled on Directly Observed Therapy (DOTS) category 1 (isoniazid, rifampicin, ethambutol, and pyrazinamide) had a lower risk for COVID 19 infection (odds ratio=9.1) fold compared to those not tuberculosis with 95%CI=0.011-0724. For more interest, I deal with all the Tuberculosis patients in Mosul 2020 (237) patients who had completed their DOTS only one of them got COVID-19 during DOTS, and the active tuberculosis patient who acquired COVID-19 infection received category 2 at 2020 because of rifampicin-resistant. While other studies were done on patients with latent tuberculosis who complete their course of treatment with DOTS category 2. Valafar's lab confirmed an association between COVID-19 and TB remission, alongside increasing the possibility of the viral spreading presence of TB, TB increases the chance of producing resistance strains of the virus, moreover, the tuberculosis bacteria is an opportunistic micro-organism that lays dormant until people's immune systems become impaired, as in AIDS patients, or overwhelmed, as in the case of COVID-19, before it erupts (12).

Tadolini *et al*. discovered that in 49 patients 53.0 percent of patients had a previous of tuberculosis, 28.5 percent acquired COVID-19 initially, and 18.3 percent were treated with both TB and COVID-19 at the same time. COVID-19 emerged following TB therapy in 38.8 percent of patients, highlighting the possible danger of spread to caretakers. In two health care workers, TB facilitated COVID-19 infection (13). Another study conducted by Chen *et al*. proposed that COVID-19 infection was reciprocal to the presence of TB infection (14), with reports confirming their co-existence in the same patients in a research conducted by Motta *et al*. in Italy (15).

A series of experimental analyses based on information from the Philippines (16) reported potentially greater mortality in TB+COVID-19 patients than in non-COVID-19 patients, with a quicker time to death and lower chance of recovery (16). International research on TB and COVID patients is underway, with 132 centers from 27 countries/regions providing data for 597 individual patients. The study's major goal is to report the characteristics of patients with COVID-19 and TB (current or previous), encompassing tests and recommended medications (17).

The GTN worldwide study (18) compared the amount of TB-related healthcare actions during the first four months of the COVID-19 pandemic (January to April 2020) to the same time in 2019. During their nationwide shutdowns in the first four months of 2020, the bulk of the centers saw decreases in TB-related discharge from hospitals, newly diagnosed cases of active TB, total active TB outpatient care, and new latent TB infection detected. Employees nearly universally to TB service delivery became re-allocated to COVID-19 in some centers. Furthermore, lower enrollment at TB facilities was connected with patient anxiety of COVID-19 contamination in the population, service interruptions, or difficulty accessing health services during lockdown (18).

Research conducted in Sierra Leone evaluated the number of patients examined for presumptive tuberculosis, findings suggest a considerable decrease in diagnosed TB cases (19). Similar outcomes were obtained in a study

conducted in Brazil (20), China (21), India (22, 23) Iran (24), Nigeria (25), and the United States have all reported similar findings (26). Children in South Africa had a similar experience (27) In Korea, on the other hand, no effect of COVID-19 was detected on the effectiveness of the TB private sector project (28). Repeat lockdowns of different severity have been documented in nations with recurring COVID-19 waves, with serious ramifications for TB care predicted (29).

Conclusions

Patients with active tuberculosis and enrolled on Directly Observed Therapy category 1 (isoniazid, rifampicin, ethambutol, and pyrazinamide) appear to be at lower risk for COVID-19 infection. We do recommend that More experimental study should be done to identify the role of ant tuberculosis drugs in COVID-19 especially those with category used as a directly observed therapy, like rifampicin.

Acknowledgment

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Conflict of Interest

The authors declare that no conflict of interest exists for this research.

Adherence to Ethical Standards

The study was approved by the Bioethics Committee of the Iraqi Ministry of Health and Environment (No30034 and date of registration 24/8/2021).

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