Toxocariasis and Co-infection With COVID-19: A Cross-sectional Study

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Abstract

Background: Toxocara infection is one of the most neglected tropical diseases that has remained undiagnosed in developing countries. The disease leads to many signs and symptoms such as fever, coughing or wheezing, belly pain, hepatomegaly, loss of appetite, rash, lymphadenopathy, red and painful eyes, strabismus, blurred or cloudy vision, and the like.

Objective: The present study aimed at investigating the seroprevalence and other demographic parameters of toxocariasis among hospitalized patients diagnosed with coronavirus disease 19 (COVID-19) in Karaj district, Alborz province, Iran.

Materials and Methods: This study was undertaken between March and September 2021. Ninety-two sera samples obtained from COVID-19 patients and 56 seemingly healthy individuals were tested for anti-Toxocara immunoglobulin G via an immunological assay (enzyme-linked immunosorbent assay, ELISA). The demographic characteristics of the participants were collected through a questionnaire.

Results: The findings indicated that during the study period, the seroprevalence of toxocariasis in the case group was significantly higher than in the control group (15.2% vs. 3.6%). Among the 92 seropositive COVID-19 patients, 35.7% (5/14) were males and 64.3% (9/14) were females.

Conclusion: Toxocariasis is a worldwide zoonotic parasitic infection in developing countries. The findings of the present study revealed the importance of toxocariasis in COVID-19 patients, and simple empirical treatment can be life-saving in such positive cases.

Keywords: Toxocariasis, COVID-19, Seroprevalence, ELISA

Background

Human Toxocara infection has been recognized as one of the worldwide zoonotic diseases caused by the Toxocara species larva stage.¹ Although the asymptomatic form (covert toxocariasis) of infection predominates and the migration of larvae to different organs and tissues can cause a variety of symptoms in the human host, the visceral larva migrans, ocular larva migrans, and neurotoxocariasis are the chief symptomatic forms.²

Concomitant helminthic infections, co-infections, and mixed infections, are the most common types of infections caused by helminthic parasites. Studies reveal that the coinfection with helminths is more frequent than the monoinfection; therefore, it is necessary to diagnose and treat these diseases.³ Toxocariasis has been considered one of the most common parasitic infections with a high seroprevalence rate in Iran.⁴,⁵

Coronaviruses (CoVs), enveloped positive-sense RNA viruses, are a large family of viruses that usually cause mild to moderate upper-respiratory tract illnesses in humans.⁶ The coronavirus disease 19 (COVID-19) caused by CoV is a respiratory disease that was first identified and reported in 2019 and then was acknowledged as a pandemic by the World Health Organization.⁷ Currently, the number of confirmed COVID-19 cases worldwide has exceeded 627 million, with over 6.5 million deaths; the main cause of death of this disease is inflammation, which can complicate the host’s condition if it is combined with another infection.⁸

Approximately 1.5 billion people worldwide suffer from helminth infections, and those living in resource-poor tropical regions are disproportionately affected. Interactions between helminths and their hosts lead to systemic effects on immunity responses and profound consequences on the host’s immune condition.⁹,¹⁰ The relationships between parasitic diseases and viral infections such as COVID-19 are still unclear. In fact, COVID-19 may contribute to the increase of pre-existing parasitic diseases. Recently, the role of CD + cell lymphopenia, which occurs in severe COVID-19 infection, has been hypotized as a facilitator in parasitic infection.¹¹ On the other hand, according to the conducted research, the involvement of type II responses in COVID-19 immunopathology when accompanied by helminthic co-infection does not benefit the host’s...
health. Considering that helminthic infections are among the major threats to human health and due to the lack of information about their prevalence in COVID-19 patients, the purpose of this study was to evaluate toxocariasis in COVID-19 patients and related demographical and epidemiological aspects of this infection.

Materials and Methods
Sample Collection
Karaj, the capital of Alborz province is positioned in the northwestern of Iran, neighboring with Qazvin, Tehran, Mazandaran, and Markazi provinces (Figure 1). This cross-sectional study was conducted between March and September 20201 in educational and therapeutic centers, Alborz University of Medical Sciences, Iran. Approval from the University Ethics Committee was obtained prior to the study. All the patients attending the infectious disease division and hospitalized were included in the study. The clinical symptoms of the patients were evaluated and recorded, along with the results of serology tests and CT scans. The exclusion criteria were confirmed cases for other febrile illnesses such as malaria and typhoid a negative polymerase chain reaction (PCR) test result for COVID-19 (COVID-19 testing by one-step real-time quantitative PCR). Informed consent, which is an inevitable step, was observed in this study; therefore, in cases where there was no informed consent from the participants, they were excluded from the study.

Serological Testing Protocol
Five milliliters of the blood sample was taken in a plain vial without anticoagulant, and the serum was separated after centrifugation at 2500 rpm for 5 minutes. This serum was used for further testing. Immunoglobulin G (IgG) antibodies to Toxocara were detected in all the cases and control groups of COVID-19 patients by ELISA kit (NovaTec Immunodiagnostica GmbH, Dietzenbach, Germany) for the confirmation of toxocariasis. The test steps were performed according to the manufacturer’s protocol, and the 450 nm was considered for the optical density (OD) reading of the examined wells. The result interpretation included values < 9.0 OD units = Negative, 9.0-11.0 OD units = Equivocal, and >11.0 OD units = Positive. Equivocal samples were subjected to repeat testing after 1 week.

Patient Follow-up
Information on patient demographic characterization, underlying diseases, and other outcomes was kept in the computer database and underwent analysis.

Data Analysis
The SPSS statistical analysis software (version 20) was used to analyze the obtained data. Descriptive statistics were calculated, and data are presented as proportions and percentages. The significance of differences was investigated using the chi-square test, and a level of \( P < 0.05 \) was considered statistically significant.

Results
A total of 92 patients diagnosed with COVID-19 and 56 cases as the control group were enrolled in this study between March and September 2021. Of the patient group, 47 (51.1%) cases were females and 45 (48.9%) of them were males. Their age range was between 9 and 95 (47.15 ± 3.04) years. Of the 56 subjects in the control group, 39 (69.6%) and 17 (30.4%) cases were females and males, respectively. They were in the age range of 5-83 years (36.11 ± 4.64, Table 1).
In the study of the clinical features and symptoms of patients hospitalized in our clinical environment, fever was mentioned as the most common presenting feature (100.0%), followed by chills and rigor (44.6%), rash (38.7%), and abdominal pain (60.0%). Other symptoms included cough, headache, pallor, lymphadenopathy, and hepatosplenomegaly.

Fourteen COVID-19 patients (15.2%, 95% CI: 11.1-35.60%) were positive for anti-Toxocara IgG Abs versus the control group (2 (3.6%)). This was statistically significant ($P=0.046$). Of the 14 patients with positive anti-Toxocara antibodies, 5 (35.7%) cases were males ($P=0.02$, (Figure 2)).

**Discussion**

As a pandemic respiratory infection, COVID-19 can be self-limiting or cause a wide range of symptoms in the infected host. However, older people and those with underlying medical conditions require more medical attention. Human toxocariasis occurs with the larval stage of Toxocara spp. The dogs, puppies, and cats are known Toxocara spp.-definitive hosts. This disease is zoonosis and is common between humans and animals. The present study investigated the seroprevalence of toxocariasis in people with COVID-19.

Helminthic parasitic infections are generally chronic and cause modulation of the host’s immune system in the long term, aiming at reducing immune responses. It is worth mentioning that the modulation of the host's immune system can also have protective effects. Thus, the parasitic helminths elicit modulated Th2-responses in their vertebrate hosts, resulting in an immune response with a well-controlled inflammatory component, including the inhibition of pro-inflammatory cytokines and induction of hypo-respondent state by interleukin-10, and produces Treg cells. In the present investigation, the seroprevalence of Toxocara spp. in the case group was higher than in the health group (15.2% vs. 3.6%). Although the seroprevalence of toxocariasis in the Iranian general population is estimated at 6.3%-37.7%, the relatively high prevalence of toxocariasis in the patient group has been significant and worthy of consideration.

Among the fourteen Toxocara seropositive patients (COVID-19), 64.3% (9/14) were females, indicating a higher prevalence in the studied women with COVID-19. Toxocariasis is more common in early middle age, which is probably due to the child’s exposure to soil or potentially contaminated sources, as well as the lack of proper hygiene. A relatively gradual increase in age-related seroprevalence suggests the consumption of embryonated eggs in water, raw or undercooked meat of

![Figure 2. Frequency of Toxocara Among COVID-19-positive and -negative Patients. Note: COVID-19: Coronavirus disease 19.](image-url)
paratenic hosts, which has the highest rate among young adults. Therefore, considering that this infection is mainly transmitted through the oral route (contaminated water and food), it is easy to control and prevent the infection by avoiding contaminated food and water.

In their study, Singh et al investigated the simultaneous infection of *Strongyloides* and *Ascaris* with Coronavirus in the form of a case report. They showed that in the era of COVID-19, there is a need for a lot of skepticism about parasitic infection from the attending physician and parasitologist. Thus, in addition to diagnosis, it helps in better understanding the pathogenesis of the disease, as well as the prognosis of the patients’ conditions.

In another study, researchers focused on fascioliasis in people with coronavirus disease and evaluated the simultaneous infection of *Fasciola* in patients with COVID admitted to the hospital, and the fascioliasis prevalence in COVID-19 patients was lower than its rate in healthy people, and there was no statistically significant difference between cases and the control group. In this test, 14 positive samples of toxocariasis were found in people with COVID-19, and there was a meaningful relationship between these two groups. Considering that parasitic infections can modulate the host’s immune system, a meaningful relationship can be found between these issues.

**Conclusion**
In general, toxocariasis as a parasitic infection can be prevented and treated based on evidence. The findings of the current research indicated a possible association between toxocariasis and viral infection. Of course, to confirm our results, there is a need for more studies with a larger sample size and evaluation of more variables.

**Author Contributions**

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**Conflict of Interest Disclosures**

The authors declare that they have no competing interests.

**Ethical Approval**

This study was approved by Alborz University of Medical Sciences, Karaj, Iran (Ethical code: IR.ABZUMS.REC.1401.149).

**References**


