

Similarities between COVID-19 and Leptospirosis Signs and Symptoms May Lead to a Delay in Diagnosis and a Misleading Increase in Reported Cases of COVID-19

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Dear Editor

COVID-19 and Leptospirosis

Pathogenic serotypes of *Leptospira* cause a zoonosis infectious disease named Leptospirosis, also known as “farm fever” in Iran.¹ Any animal can be a reservoir for this infection; however, rodents are considered the primary reservoir; thus, human Leptospirosis more commonly occurs in rural communities with direct or indirect contact with infected animals, their urine, and contaminated water, food, or soil.² Coronaviridae (Coronavirus family) is the cause of 15% of respiratory diseases. SARS-COV-2 causes a novel respiratory infection seen both in humans and animals. This infection was first detected in December 2019, initiating the devastating COVID-19 pandemic.³ In the case of Leptospirosis infection (water-based, rodent-borne, and livestock/pet-borne), the bacterium enters the body via the mucosal membrane or abrasions on the skin. Based on the mode of transmission, one of the efficient prophylactic measures is focused on the safety training of farmers in endemic and agricultural environments.²

Leptospirosis is an occupational disease and is more commonly seen in farmers of rice and sugarcane fields, veterinarians, laboratory and slaughterhouse staff, and ranchers.⁴ *Leptospira* can enter the body through skin insults or scratches, mucosal membranes, conjunctiva, aerosols, or liquids that contain bacteria.⁵

The ongoing COVID-19 pandemic has affected the lives of most people around the world tremendously. The new coronavirus is extremely transmissible and has a long latency period of 2 to 14 days until clinical signs are apparent; therefore, these features increase the disease spread rate and make it more challenging to prevent and control the disease wave. The transmission mode is via respiratory droplets or exposure to secretions containing the virus (human to human).⁶ On the other hand, human-to-human transmission of leptospirosis is rarely reported. The incubation phase for leptospirosis, from the day of the exposure and symptom onset, averages from 7 to 12 days, with the lowest and highest period of 3 days and a month, respectively;⁷ however, for COVID-19, studies predict a mean serial interval from 4.2 to 7.5 days.³

Regarding the symptoms of COVID-19, the following can be mentioned: The COVID-19 virus infection is initially associated with non-specific and general symptoms such as nausea, fatigue, body aches, fever, and dry cough. Some patients may initially have nausea and diarrhea preceding fever, and a few patients may have headaches or hemoptysis. A large number of infected patients may be completely asymptomatic.⁸ Approximately 81% of patients with affirmed coronavirus infection show mild symptoms and improve at home. In 14% of cases, the patient develops severe symptoms, including pneumonia and shortness of breath. In 5% of cases, the patient's condition worsens, resulting in septic shock, respiratory, and other body systems failure.⁹ Although most patients with COVID-19 have a mild disease course, this disease

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is extremely contagious, and an infected person can infect at least three other people.¹⁰

In contrast, Leptospirosis can cause widespread symptoms such as fever, abdominal pain, kidney failure, meningitis, pulmonary hemorrhage, respiratory failure, and jaundice, sometimes leading to death.¹¹ In general, leptospirosis can present a broad spectrum of findings, from asymptomatic to severe and lethal. The mild course of leptospirosis presents with influenza-like symptoms, such as headaches and myalgia. The severe form of leptospirosis presents with jaundice, liver dysfunction, coagulopathies, and kidney dysfunction.¹

The wide range of signs and symptoms of Leptospirosis leads to difficulties in diagnosis. Due to the lack of laboratory resources, attention to the history of attendance in high-risk conditions is essential in primary history taking. The main reason that encouraged us to write this letter is the remarkable similarity of symptoms between Leptospirosis and the new pandemic outbreak of COVID-19. This disease causes annually 1.03 million infection cases and 58,900 deaths worldwide² according to a comprehensive review of the status of Leptospirosis in Iran, its seroprevalence as an endemic disease in Iran was 9.71% (95% CI: 6.78–32.65%) based on modified agglutination test (MAT) (12). Mazandaran as one of the three northern provinces (Guilan, Mazandaran, and Golestan)¹³ has high seroprevalence and a high incidence of this disease. The COVID-19 pandemic that can present itself similar to this disease make it necessary to prevent misdiagnosis and delay in treatment of Leptospirosis. Treatment of leptospirosis is highly influenced by its severity, and to date, there is no golden time for treatment; however, doxycycline has reduced the severity and duration of the disease. When Leptospirosis is not treated, it can lead to kidney damage, meningitis, liver failure, respiratory distress, and even death. Due to the pandemic, the general population is advised to restrict their referral to hospitals to reduce the transmission cycle; this may lead to delayed diagnosis and treatment of Leptospirosis.¹⁴ CRP, a marker known to be helpful in confirmation of COVID-19 infection, has helped diagnose leptospirosis when more than 50 mg/L is used with more sensitivity and specificity.¹⁵

Due to the overlap of the signs and symptoms of Leptospirosis and COVID-19, the devastating outcomes of undiagnosed leptospirosis, the unresponsiveness of COVID-19 to medical therapy in severe cases, and the unknown future of this pandemic, there should be specified diagnostic measures to distinguish these to medical issues, particularly in endemic areas.

We believe that in the current situation, some strategies must be considered:

1- Inform first healthcare providers and physicians about the high incidence of Leptospirosis in this season

2- Health officials should choose chemoprophylaxis against Leptospirosis, most specifically with doxycycline or azithromycin because both strongly inhibit inflammation and viral replication by blocking protein synthesis. It can be an effective treatment for both Leptospirosis and COVID-19 and should be strongly considered.¹⁴

3- Educating Rice farmers about self-care to prevent leptospirosis infection in this challenging time of a pandemic is crucial.

4- Considering the social background of the patients is important in history taking as Leptospirosis is mostly an occupational infection.

5- Since Leptospirosis is highly common in tropical and humid environments with high rainfall, place of living and travel history should be considered to try and distinguish COVID-19 viral infection and Leptospirosis.

6- The mild form of Leptospirosis can present itself with influenza-like symptoms, but the fulminant variant presents with kidney dysfunction, jaundice, and bleeding disorder; the latter kind is distinct from COVID-19.

7- Human-to-human transmission of leptospirosis has been reported rarely; however, COVID-19 is a highly contagious disease with an average transmission from an infected person to three more people.¹⁰ Thus, it is essential to take note of family history as well.

8- Lastly, it is challenging to diagnose leptospirosis based on clinical signs and symptoms since its clinical picture is similar to most acute viral and bacterial infections.¹⁶ However, due to high sensitivity and conclusive results, its laboratory diagnosis is recommended through serological methods, such as ELISA.⁷

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