Leptospirosis and COVID-19 co-infection case in Bangladesh

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1. Introduction

Leptospirosis is a rodent-borne acute febrile illness that is one kind of zoonotic infection caused by Leptospira species [1]. Leptospirosis mainly occurs in tropical or subtropical countries [2]. Globally, the annual incidence is estimated at 0.1–1 per 100,000 in hot climates and 10–100 per 100,000 in moist climates, but the worldwide prevalence rate is still underestimated [3]. It usually occurs when water or soil contaminated with the urine of an infected animal meets human skin or mucous membranes. In tropical settings, leptospirosis can be likened to other febrile illnesses such as scrub typhus, malaria, or dengue [1, 4]. It is not easy to characterize and is little researched. Various strains of Leptospiira may exist in nature and have different survival abilities, but the pathophysiology and causes of Leptospiroa in the environment are unknown. On the other hand, the world is still fighting against COVID-19. The rising number of COVID-19 cases, which can be confused with other diseases during hospitalization because COVID-19 presents with acute febrile illness, is a significant threat to public health [5]. The majority of new illnesses in humans are zoonotic. COVID-19 is an excellent example of a newly discovered emerging zoonotic disease generating a worldwide outbreak. COVID-19 has affected more than 48 million people worldwide, and more than 6 million people have died due to it as of April 02, 2022 [6]. There is no official record found globally or in Bangladesh mentioning the number of deaths in non-ovid patients who suffered from fatalities from COVID-19. Co-infection is described as the infection of more than one infection in the same host simultaneously, resulting in various diseases. Co-infection can hasten the progression of a condition [7]. In contrast to mono-infections, they can have a wide range of effects on the host's well-being. The number of pathogens and complex interactions could considerably impact infection processes by modifying host susceptibility and increasing the likelihood of many infections [8]. This co-infection is frequently misdiagnosed, worsens the disease, and can even be advantageous to the causative organism [9]. In leptospirosis care, co-infection with any other condition can pose extra hurdles if the coinfection's symptoms are similar to those of other infections [10]. Exposure to the environment and similar nature among other bacteria present in the environment may double the chance of coinfection and be wrong or undiagnosed [8].
The co-infection of *Leptospira* with other diseases has been underreported due to a lack of knowledge. The occurrence of leptospirosis coinfection might confound identification and lead to neglect, resulting in death. This might be the first case reported in Bangladesh regarding leptospirosis and COVID-19 co-infection in the same person.

2. Case report

A 47-year-old non-diabetic, normotensive male arrived with a high-grade, persistent fever, headache, cough, and weakness. He was admitted to Chittagong government hospital on 05 January 2022 and assigned to the medical unit, complaining of a one-week-long fever that was high grade in nature. It was coupled with 4 days of shortness of breath that steadily progressed and was accompanied by coughing and vomiting. For the past four days, he has had a severe headache. He had no history of joint or back pain, conjunctivitis, or bleeding manifestations associated with this fever. He did not drink alcohol or use illegal substances. He was not on any antibiotic medication before being admitted to this hospital. He resided in a rural part of Chittagong and had no recent travel or street food history, nor had he had any operations or blood transfusions. His residence, including his bedroom, is infested with rats occasionally. He also works as day a labour, and last one month back, he worked on the lake as day labour. His physical examination indicated mild jaundice, a temperature of 101 degrees Fahrenheit, a pulse of 110 beats per minute in a regular manner, blood pressure of 140/80 mm of Hg, and a GCS of 15/15 (Using criteria for eye movement [4], verbal ability [5], and motor function [6], the Glasgow Coma Scale/Score (GCS) gives a general approximation of the severity of coma present.). On room air without oxygen, his saturation was 98 per cent at the time of evaluation. Despite initial therapy, he experienced significant abdominal pain, vomiting, and persistent fever. His urine intake and output were both within the usual range. Because the COVID-19 pandemic raised the probability of COVID-19-related respiratory distress, RT-PCR tests for COVID-19 were sent and found to be positive on 06 January, 2022. The routine blood test was also sent, CBC, Hb% was 13.0 gm/dL, WBC 12000/cu mm, neutrophil 80 per cent, platelet count 350000/cu mm, bilirubin 10.2 mg/dL, Aspartate transaminase (AST)- 89 U/L and Alanine transaminase (ALT)- 112 U/L both were raised. He went for a rapid test for IgM and IgG antibodies to *Leptospira* (by OnSite *Leptospira* IgG/IgM Combo Rapid Test) and became positive on 09 January 2022. Then he was advised by the physician to start Tab Doxycycline 100 mg 12 hourly, Tab Azithromycine 500 mg once at night, Tab. Paracetamol 500 mg 8 hourly, Inh. Salbutamol and Ipratropium Bromide 12 hourly. After one week of observation and under treatment, he was discharged from the hospital with medication and advice.

3. Discussion

COVID-19 is a new infectious disease that has spread over the world. **Leptospirosis** is a zoonotic illness that is primarily found in tropical regions. Most affected persons are asymptomatic or have just moderate lung infection in both circumstances. Acute respiratory distress syndrome (ARDS) and multiple-organ failure develop fast in those who become critical, with a high mortality rate. Leptospirosis is a zoonosis caused by spirochetal bacteria excreted in the urine of various animals, including dogs, livestock, and rodents. Contact with infected urine is the most common mode of transmission. Farmers, agriculture workers, individuals participating in outdoor activities, physical contact with inland natural waterways, and sewage men, miners, and fish workers are all susceptible to leptospirosis [11]. In comparison, he had a history of working in the pond, and the rat was also found on occasion in his inhabitant. Even though COVID-19 and leptospirosis are two separate diseases, cytokine storm is a common element in their etiology [12]. The involvement of the cytokine storm in leptospirosis pathogenesis is well understood. An inflammatory response is triggered during infection, mainly through the generation of cytokines, which is critical for the early eradication of organisms. On the other hand, unregulated cytokine release can cause a cytokine storm, resulting in multi-organ failure and death [12]. In the long run, most human leptospiral infections, including COVID-19, are mild to severe. The ailment usually starts with a sudden onset of fever, rigor, myalgias, and headaches in people who have it. The very first phase is characterized by acute fever and bacteremia that lasts 2-9 days, followed by a period of low or no fever and apparent recovery. Phase two is an ‘immune’ phase marked by recurrent fever and the emergence of problems [13]. Leptospirosis, also called Weil’s disease, can cause renal failure, liver failure, or heart failure if it is not treated. Occasionally, it can be fatal. Weil’s illness affects approximately 5%-15% of individuals, and pulmonary involvement is a prominent aspect of condition (20%-70%). Lung involvement can range from a mild cough to ARDS. ARDS has a significant fatality rate, over 50% [14, 15]. Age (>40 years), oliguria, respiration insufficiency, pulmonary haemorrhage, cardiac arrhythmias, and impaired mental status have been proven to be poor prognostic markers for leptospirosis [16]. Age and respiratory distress were both risk factors in our leptospirosis case. Routine laboratory blood test for a moderate form of leptospirosis is frequently non-specific. Significantly raised blood bilirubin and a moderate increase in hepatic transaminases may develop in icteric leptospirosis, which is defined by a quickly progressing clinical presentation. Weil’s illness is characterized by jaundice and renal failure [17]. Our patient’s liver enzymes were likewise elevated (ALT-112 U/L, AST-89 U/L), but they returned to normal without causing any severe liver damage or failure.

Antimicrobial therapy for leptospirosis is still debatable. The role of antibiotics (penicillin) in leptospirosis, independent of severity, was unclear in a Cochrane review of seven randomized clinical studies [18]. Nearly 90% of cases are minor, and oral doxycycline or amoxicillin can also be used to treat them. In severe cases, parenteral high-dose penicillin G or ceftriaxone is indicated [19]. Because of the challenges, our patient was treated appropriately with oral doxycycline and quickly improved. He was given conservative therapy for COVID-19. The most common method for diagnosing Leptospirosis is to use serological tests. Because most serological tests are only positive after 5–7 days, the study only included people who had been sick for more than 5 days. The serological gold standard, the microscopic agglutination test, is resource-intensive [20]. Our patient had a one-week history of fever and other symptoms, and a rapid test for IgM antibodies to *Leptospira* was available, which was positive for this patient. IgM ELISA is the most commonly used [21]. A single sample taken during the acute phase of the disease can provide a provisional diagnosis of leptospirosis [21]. The sensitivity of the *Leptospira* IgM-ELISA ranges from 35–76% and the specificity ranges from 76–98% in various endemic settings. The performance of commercial ELISA assays varies by geographical region [22]. These ELISAs detect genus-specific anti-*Leptospira* IgM/IgG antibodies by using whole-cell lysates of pathogenic *L. interrogans*, *L. interrogans*, *L. fainei*, or saprophytic *Leptospira biflexa* as antigens. The test that the immune system of the host reacts differently to native antigens has been a big problem with ELISA tests. This may be why they are often not sensitive to local serovars [22]. Anti-Leptospira interrogans IgM and IgG in human serum, plasma, or whole blood were detected by the diagnostic rapid combo kid in this patient (*L. interrogans*). Comparing this quick test to a market-standard reference method, it shows identical levels of specificity and sensitivity [23]. The samples that were tested for tuberculosis, human immunodeficiency virus, dengue fever, typhoid, hepatitis B surface antigen, hepatitis C virus, hepatitis E virus, hepatitis A virus, human adenovirus, human chorionic gonadotropin, human adenovirus, human adenovirus, and hepatitis B surface antigen did not show any false positive results [23]. As COVID-19 expands over the globe, it will have more repercussions in tropical areas, where it will battle as a confounder with other well-known tropical ailments, making clinical identification more difficult. When a patient appears with an acute febrile-like illness (AFI) or an inconsequential respiratory tract infection. Primary care doctors and family doctors, especially those who work in tropical areas, may need to do another diagnostic test.
The percentage of leptospirosis patients with elevated CRP and procalcitonin was similarly more significant. CRP is an acute-phase reactant that rises quickly when inflammation begins. CRP levels are significantly greater in people who have a bacterial illness. CRP levels helped discriminate between dengue and leptospirosis upon admission in research from French Guiana [24].

Furthermore, while leptospirosis is mistakenly thought to be a rural infection, doctors may fail to identify it can be transmitted in an urban setting. As a result, diagnosis relies on laboratory studies rather than just clinical symptoms. Despite the high frequency of the condition, laboratory facilities in developing nations may be insufficient for diagnosis. Although our patient’s domicile was rural in this case, many persons who are at risk for leptospirosis should be evaluated, and physicians should be aware of the co-infection in this particular setting. As a result, diagnosis relies on laboratory studies rather than just clinical symptoms.

In both urban and rural Bangladesh, leptospirosis was a frequent source of fever, resulting in hospitalization. One study found that 2–4 percent of feverish outpatients had leptospirosis in Bangladesh. Sarmin, Mini, Australis, Icterohaemorrhagiae, Cynopteri, Autumnalis, Shermani, Javanica, Djatisman, Pyrogenes, Sejroe, Gelledoni, and Pamana were among the species of the genus discovered in Bangladesh [25]. According to a study, undifferentiated serovars may be circulating in Bangladesh, resulting in an underreporting of the leptospirosis epidemic. Only a well-established monitoring system can prove leptospirosis in other species, risk factors, transmission patterns, human-animal interfaces, environmental causes, and disease effects [25, 26].

Limitation. Due to his financial difficulties, neither a CT scan nor USG of the entire abdomen was not available, and other markers such as chest x-ray, CRP, Procalcitonin, or other biochemical tests (hepatitis, S. Creatinine) were not performed.

Leptospirosis has a wide range of clinical manifestations, with most cases remaining mild while others become severe and even fatal. The current strategy of isolating all patients with fever in COVID-19 suspect wards until COVID-19 reports are negative has resulted in a considerable delay in diagnosed leptospirosis infections. In this case, leptospirosis was also identified following the COVID-19 diagnosis, and this infection can be lethal if not diagnosed and treated promptly.

4. Conclusion

The symptoms of leptospirosis can range from mild fever, headache, and abdominal pain to more severe versions such as jaundice and renal failure. Identifying a leptospirosis consequence in the context of a COVID-19 pandemic is frequently ignored. Clinicians should be aware of these COVID-19 with leptospirosis co-infections, which are frequently ignored due to the COVID-19 pandemic. COVID-19 is not going away anytime soon, and while these are two distinct diseases, one of which is caused by a virus and the other by a bacterium, both have some clinical features in common. Their co-infection can cause one of them to be misdiagnosed; medical doctors in tropical areas should be knowledgeable of the commonalities between these two diseases, particularly the early diagnostic presentation and pathogenesis. It is also necessary to highlight how critical it is to distinguish between these two disorders during the condition’s early stages.

Declarations

Author contribution statement

All authors listed have significantly contributed to the investigation, development and writing of this article.

Funding statement

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