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SHORT COMMUNICATION

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Coinfection of leptospirosis and coronavirus disease 2019: A retrospective case series from a coastal region in South India

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Abstract

During the monsoon season of 2020, the coastal areas of South India were endemic to both leptospirosis and coronavirus disease 2019 (COVID-19). This study aimed to investigate the clinical features and outcomes of patients infected with both infections. A retrospective review of charts of all patients with COVID-19 who were also diagnosed with leptospirosis by immunoglobulin M enzyme-linked immunosorbent assay was undertaken. The clinical features, laboratory report, treatment details, and outcomes of all the included patients were recorded. The collected data were summarized as the frequency with percentage for categorical data and the mean or median for continuous data. Twenty-four cases of coinfections were admitted between July and November 2020. Most of these patients were categorized as severe COVID-19 ($n = 15$, 62.5%). Acute kidney injury was seen in 79.2% ($n = 19$) patients, while raised bilirubin was present in 79.2% ($n = 19$) of the patients. All patients had raised C-reactive protein, while all but one had raised procalcitonin. Thrombocytopenia, leucocytosis, and leukocytopenia were seen in 91.7% ($n = 22$), 45.8% ($n = 11$), and 12.5% ($n = 3$) of the patients. The median duration of hospital stay was 11 (8.25–15) days. A total of 79.2% ($n = 19$) of the patients improved and were discharged, while 20.8% ($n = 5$) died during the hospital stay. In conclusion, patients with fever and atypical manifestations such as hepatic dysfunction, renal dysfunction, and thrombocytopenia should be evaluated for leptospirosis even if they are COVID positive.

KEYWORDS

acute febrile illness, COVID-19, leptospira, Weil's disease

1 | INTRODUCTION

Since December 2019, coronavirus disease 2019 (COVID-19) has resulted in a global increase in hospitalizations and mortality.[1] Most of these deaths occur in elderly or comorbid patients.[2] Although the negative impact of noninfectious comorbidities, such as diabetes, hypertension, and chronic kidney disease has been widely studied, comorbid infections have primarily been neglected.[3] Amongst infections, chronic infections such as human immunodeficiency virus infection in the context of COVID-19 have been discussed in many reports, but tropical infections such as leptospirosis have been largely neglected.[4,5] Although there are some reports of leptospirosis during the COVID-pandemic, the complex interplay between COVID and leptospirosis has not been evaluated in detail to the best of our knowledge.[6] Leptospirosis is a febrile zoonotic disease with rodents and other small mammals serving as reservoirs. These animals shed the bacteria in their urine and contaminate the water sources of humans.[7] There is increased exposure to leptospirosis in coastal areas

with heavy rainfalls and floods in the monsoons.[8] Therefore, a patient presenting with fever in the monsoon season may have concurrent COVID-19 and leptospirosis in such an area. This report discusses the clinical features and management of patients who were coinfected with COVID-19 and leptospirosis.

2 | METHODOLOGY

This is a retrospective review of charts of all patients admitted with COVID-19 in 2020. The study was conducted after taking approval from the Institute's Ethical Committee. Those patients with COVID-19 who were also diagnosed with leptospirosis were included in the study. The diagnosis of leptospirosis was made routinely by a positive immunoglobulin M (IgM) enzyme-linked immunosorbent assay (Lepto IgM Microlisa; J. Mitra). All the patients' demographic, clinical, and laboratory details were entered in a clinical case record form. The month of presentation, comorbidities (diabetes mellitus, hypertension), and severity of COVID-19 were recorded for all the patients. History of fever, headache, fatigue, myalgia, and symptoms suggestive of systemic involvement were noted. General physical examination details comprising rash, icterus, and organomegaly were also recorded. The hematological and biochemical parameters of all the patients were reported. Acute kidney injury (AKI) was defined as an increase in serum creatinine by >0.3 mg/dl within 48 h or increased serum creatinine to >1.5 times the baseline. Oliguria was described as a urine volume of <0.5 ml/kg/h for 6 h. Patients with electrocardiographic or echocardiographic changes and elevated troponin were classified as myocarditis. All patients' antimicrobial treatment details were recorded. The hospital stay's outcome (death or alive) was also recorded.

2.1 | Data analysis

The collected data were entered into an excel workbook and summarized as the frequency with percentage for categorical data and mean (±standard deviation) and median (interquartile range) for continuous data.

3 | RESULTS

During the year 2020, a total of 24 cases were diagnosed with coinfections of leptospirosis and COVID-19. The month-wise distribution was as follows: July (n = 3), August (n = 6), September (n = 6), October (n = 7), and November (n = 2). The patients were categorized into mild (n = 4, 16.7%), moderate (n = 5, 20.8%), and severe COVID-19 (n = 15, 62.5%). Diabetes and hypertension were present in 20.8% (n = 5) and 16.7% (n = 4) patients, respectively. The key clinical and laboratory features along with outcomes have been summarized in Table 1.

All patients were febrile at presentation, and the median duration of fever at presentation was 3 (1.5–4.5) days. Fatigue, myalgia, and rash were present in 33.3% (n = 8), 37.5% (n = 9), and 8.3% (n = 2) patients, respectively. Diarrhea and abdominal pain were seen in 29.2% (n = 7) and 45.8% (n = 11) of the patients. Haemoptysis and hematemesis were seen in one patient each. The median Brixia score was 5 (2.25–10.75). Hepatomegaly and splenomegaly were seen in 4.2% (n = 1) of the patients each.

At presentation, the median creatinine value was 4.4 (1.5–7.3) mg/dl. The median procalcitonin and C-reactive protein (CRP) were 5.6 (3.2–13) and 115.6 (92–259.7). The median leukocyte count and platelet counts were 10 300 (8050–14 300) per cubic millimeter and 36 000 (12 500–61 750) per cubic millimeter. Raised bilirubin (≥2 mg/dl) were

TABLE 1 Comparison of leptospirosis-COVID-19 infection with published series on patients with leptospirosis without COVID-19 and patients with severe COVID-19 from the same hospital

Parameters	Leptospirosis-COVID coinfection (n = 24)	Leptospirosis without COVID-19 (n = 63) [8]	Severe COVID (n = 50) [9]
Dyspnea	66.7% (n = 16)	79% (n = 50)	100% (n = 50)
Myocarditis	12.5% (n = 3)	31.7% (n = 20)	4% (n = 2)
Acute kidney Injury	79.2% (n = 19)	76.2% (n = 48)	26% (n = 13)
Dialysis	37.5% (n = 9)	23.8% (n = 15)	6% (n = 3)
Thrombocytopenia	91.7% (n = 22)	77.8% (n = 49)	12% (n = 6)
Leukocytosis	45.8% (n = 11)	63.5% (n = 40)	28% (n = 14)
Leukocytopenia	12.5% (n = 3)	7.9% (n = 5)	0%
Median bilirubin (mg/dl)	5.5 (2.2–13)	4.54 (1.26–13.5)	
Raised CRP	23/24 (95.8%)	100% (n = 63)	90% (n = 45)
Raised procalcitonin	19/20 (95%)	94.5% (n = 60)	22% (n = 11)
Death	20.8% (n = 5)	6% (n = 4)	2% (n = 1)

Abbreviations: COVID-19, coronavirus disease 2019; CRP, C-reactive protein.

present in 79.2% ($n = 19$) of the patients. A total of 62.5% ($n = 15$) of the patients had transaminitis. The median aspartate aminotransferase and alanine aminotransferase levels were 66 (35.5–98.5) IU/L and 55.5 (40–95.5) IU/L, respectively. Chest X-ray was normal in nine patients. In the rest of the 15 patients, nine had unilateral involvement, while six had bilateral involvement. The lesions were primarily restricted to the middle and lower zones (Figure 1).

The patients were treated variously with the following antimicrobials: ceftriaxone ($n = 17$), doxycycline ($n = 16$), piperacillin–tazobactam ($n = 11$), meropenem ($n = 3$), and azithromycin ($n = 5$). The median duration of hospital stay was 11 (8.25–15) days. A total of 79.2% ($n = 19$) of the patients improved and were discharged.

4 | DISCUSSION

From July to November 2020, the COVID pandemic coincided with an outbreak of leptospirosis in Udupi, Karnataka, India.[8] Since these diseases have similar manifestations, it is often difficult to differentiate the two entities.[6] It becomes all the more challenging in patients where there is a coinfection of COVID and leptospirosis. In this report, we discuss those few COVID patients with atypical manifestations who were evaluated and found to be positive for leptospirosis.

It is essential to differentiate the patients with COVID and leptospirosis coinfection from either of these diseases alone.[6] Comparing the present cohort to a published study of severe COVID alone admitted to our hospital around the same time, it was noticed that AKI, bilirubinemia, leucocytosis, and thrombocytopenia were more common in patients with coinfection (Table1).[9] Although CRP gets elevated in both groups, patients with coinfection are more likely to have raised procalcitonin when compared to severe COVID alone (Table1). Similarly, when comparing the patients with coinfection to patients from another published study with leptospirosis alone who were admitted at the same time in our hospital, it was noticed that dyspnea was significantly commoner in patients with coinfection (Table 1).[8] Although respiratory involvement is noted in leptospirosis alone due to increased vascular permeability, bacterial invasion, or pulmonary hemorrhage, concurrent COVID-19 seems to increase the severity.[10] Chest X-ray abnormalities in moderate to severe COVID-19 range from consolidation to ground glassing. The location is also variable with a predilection to peripheral lower lung distribution.[11] Similarly, nodular opacities progressing to consolidation or ground glassing can be seen as leptospirosis. It is difficult to practically differentiate leptospirosis from COVID-19 on X-ray alone.[12]

The presence of coinfection was also associated with poor outcomes in coinfected patients compared to either infection in isolation (Table 1).[8,9]

It is difficult to ascertain whether the patients were infected with leptospirosis before or COVID. It is also possible that they got coincidentally infected with both infections. However, in the authors' opinion, it is more likely that they got infected with leptospirosis first and got infected during their visits to hospitals or clinics flooded with COVID-19 patients. Considering the high mortality rate in coinfected patients, it seems prudent that patients with features of suspected

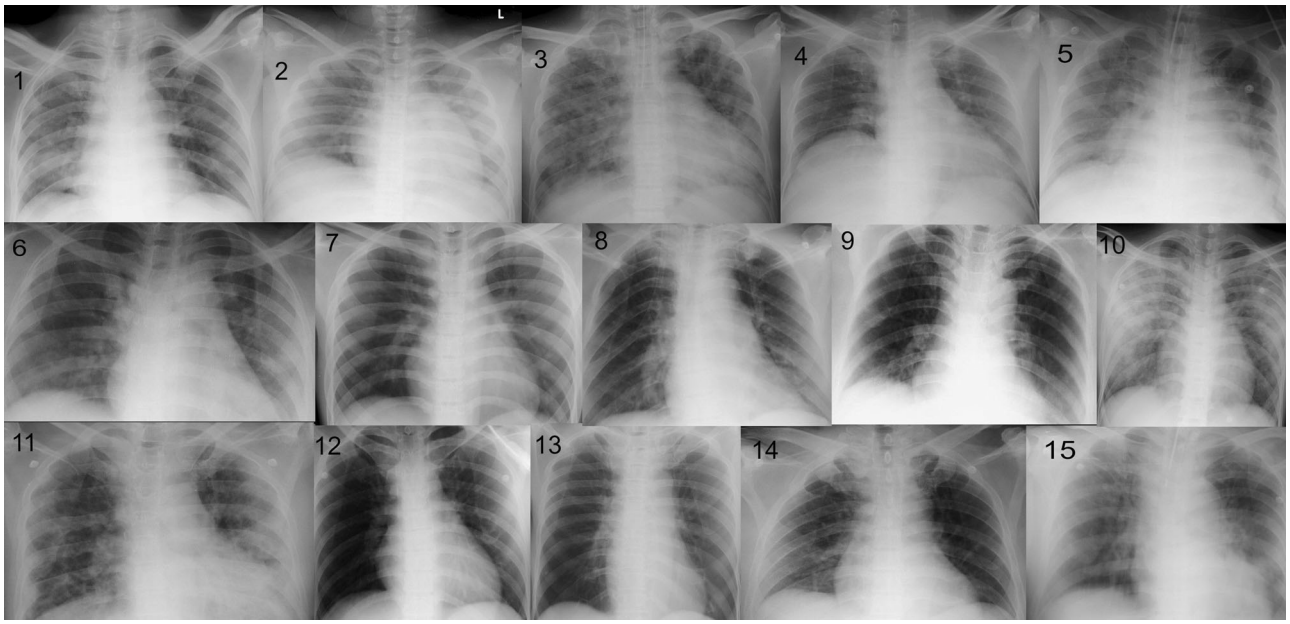

FIGURE 1 Chest X-ray findings in patients with COVID-19 and leptospirosis coinfection. 1—Ill-defined opacity in the right lower zone, 2—ill-defined opacity in the left lung field, 3—ill-defined opacities in bilateral lung fields, 4—homogeneous opacities in left lung field, 5—perihilar opacities in both lung fields, 6—reticular opacities in bilateral lower zones, 7—ill-defined opacities in the left lung field, 8—ill-defined opacity in the left lower zone, 9—reticular opacities in bilateral lower zones, 10—peripheral opacities in bilateral lung fields, 11—reticular opacities in bilateral mid and lower zones, 12—ill-defined opacity in the left middle zone, 13—ill-defined opacity in the left middle and lower zones, 14—ill-defined opacity in the left middle and lower zones, and 15—ill-defined opacities in the left lower zone.

leptospirosis should be cohorted separately so that they do not acquire COVID infection while in hospitals.

4.1 | Limitations

The study's retrospective nature is associated with its inherent limitations. Also, the historical controls used in the discussion may not have been a perfect comparison group.

In conclusion, this report indicates that not all patients with fever should be labeled as COVID alone. Patients with fever and atypical manifestations such as hepatic dysfunction, renal dysfunction, and thrombocytopenia should be evaluated for leptospirosis even if they are COVID positive.

AUTHOR CONTRIBUTIONS

Nitin Gupta: Conceptualization, data collection, data analysis, and manuscript writing. **William Wilson:** Conceptualization, methodology, and manuscript review. **Prithvishree Ravindra:** Data collection, analysis, and manuscript review. **Roshini Raghu:** Data collection and manuscript review. **Kavitha Saravu:** Methodology review, resources, and manuscript review.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data will be made available on reasonable request to the authors

ETHICS STATEMENT

We conducted the study after receiving institutional ethical committee clearance.

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