Clinical features and mortality in COVID-19 SARI versus non COVID-19 SARI cases from Western Rajasthan, India

Ankur Sharma¹, Nikhil Kothari², Akhil Dhanesh Goel³, Balakrishnan Narayanan², Shilpa Goyal², Pradeep Bhatia², Deepak Kumar⁴, Gopal Krishna Bohra⁴, Nishant Kumar Chauhan⁵, Ramniwas Jalandra⁵, Naveen Dutt⁵, Pankaj Bhardwaj³, Mahendra Kumar Garg⁴, Sanjeev Misra⁶

¹Departments of Trauma and Emergency (Anaesthesiology), ²Anaesthesiology and Critical Care, ³Community and Family Medicine, ⁴General Medicine, ⁵Pulmonary Medicine, ⁶Surgical Oncology, All India Institute of Medical Sciences (AIIMS), Jodhpur, Rajasthan, India

ABSTRACT

Background: In March 2020, the Indian Council of Medical Research (ICMR) issued guidelines that all patients presenting with severe acute respiratory infections (SARI) should be investigated for coronavirus disease 2019 (COVID-19). Following the same protocol, in our institute, all patients with SARI were transferred to the COVID-19 suspect intensive care unit (ICU) and investigated for COVID-19. Methods: This study was planned to examine the demographical, clinical features, and outcomes of the first 500 suspected patients of COVID-19 with SARI admitted in the COVID-19 suspect ICU at a tertiary care center. Between March 7 and July 20, 2020, 500 patients were admitted to the COVID-19 suspect ICU. We analyzed the demographical, clinical features, and outcomes between COVID-19 positive and negative SARI cases. The records of all the patients were reviewed until July 31, 2020. Results: Of the 500 suspected patients admitted to the hospital, 88 patients showed positive results for COVID-19 by reverse transcription-polymerase chain reaction (RT-PCR) of the nasopharyngeal swabs. The mean age in the positive group was higher (55.31 ± 16.16 years) than in the negative group (40.46 ± 17.49 years) (P < 0.001). Forty-seven (53.4%) of these patients in the COVID-19 positive group and 217 (52.7%) from the negative group suffered from previously known comorbidities. The common symptoms included fever, cough, sore throat, and dyspnea. Eighty-five (20.6%) patients died in the COVID-19 negative group, and 30 (34.1%) died in the COVID-19 positive group (P = 0.006). Deaths among the COVID-19 positive group had a significantly higher age than deaths in the COVID-19 negative group (P < 0.001). Among the patients who died with positive COVID-19 status had substantially higher neutrophilia and lymphopenia (P < 0.001). X-ray chest abnormalities were almost three times more likely in COVID-19 deaths (P < 0.001). Conclusion: In the present article, 17.6% of SARI were due to COVID-19 infection with significantly higher mortality (34.1%) in COVID-19 positive patients with SARI. Although all patients presenting as SARI have considerable mortality rates, the COVID-19-associated SARI cases thus had an almost one-third risk of mortality.

Keywords: Coronavirus Disease 2019, SARS-CoV2, severe acute respiratory infection

Introduction

Coronavirus Disease 2019 (COVID-19) is a contagious illness primarily affecting the respiratory tract. This disease was not known before the Wuhan outbreak in December...
Given its worldwide distribution, the World Health Organization (WHO) declared this disease a pandemic in March 2020.

Symptomatic COVID-19 infection is characterized primarily by fever, cough, dyspnea, and infiltrations in the chest. Although many of the observed infections are not dangerous, about 15–20 percent of confirmed COVID-19 patients may have a severe illness, including respiratory failure, shock, and multiple organ dysfunction that require admission to the critical care unit.

As per the WHO, severe acute respiratory infection (SARI) is described as an acute respiratory infection with fever or temperature ≥38°C and cough, onset since the last 10 days, and necessitating admission to the hospital. In the era of the current pandemic, all SARI patients need to be viewed with a high index of suspicion of COVID-19. Taking all COVID-19 patients thus provides a sound denominator to study the clinical pattern in all COVID-19 and non-COVID-19 patients.

In March 2020, the Indian Council of Medical Research (ICMR) issued guidelines to investigate all the patients presenting with SARI for COVID-19. In compliance with ICMR protocols at our institute, any patient presenting with SARI from March 7, 2020, was admitted first in the COVID-19 suspect intensive care unit (ICU) and tested for COVID-19. After confirmation of his COVID-19 status, the patient is shifted to a designated area accordingly. If the patient remains stable (not require high oxygen (more than 15 L/min of oxygen to maintain SpO2 > 94%) with a positive COVID-19 report, he is moved to COVID-19 ward; in case, the patient deteriorates (requirement of high oxygen or ventilator support) with a positive COVID-19 report, he is shifted to COVID-19 critical care unit; and with a negative report to the adult intensive care unit [Figure 1].

Studies have mentioned the clinical features of pneumonia incurred by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). This is the first report from western Rajasthan, a dry-arid region, describing the clinicodemographic and management profile of SARI patients in the initial days of COVID-19. Furthermore, this article also compared the mortality between COVID-19 SARI versus non-COVID-19 SARI cases. The plethora of clinical features and laboratory investigations described here give an important insight into the early indicators of disease severity. These should be on the radar of not only the intensivists but also primary care physicians to timely diagnose a potential case of SARI and channelize towards appropriate management.

The objective of the present study was to examine the clinical and laboratory as well as comorbidities and outcomes of the SARI patients admitted in the COVID-19 suspect ICU.

Materials and Methods
This was a hospital-based cross-sectional study done after approval from the institutional ethical committee (AIIMS/IEC/2020–21/2053). Five hundred suspected patients of COVID-19 with SARI were admitted in the COVID-19 suspect ICU from March 7 to July 20, 2020, at a tertiary care center in India. The records of all the patients were reviewed until July 31, 2020.

The data of the first 500 patients with SARI admitted in COVID-19 suspect ICU during this pandemic were analyzed. The information included demographic data, known comorbidities, clinical presentation (signs and symptoms), laboratory investigations, X-ray-chest, mechanical ventilator requirements, and outcomes.

All the suspected COVID-19 patients with SARI enrolled in this study were tested with reverse transcription-polymerase chain reaction (RT-PCR) of the nasopharyngeal swabs. The specimen was obtained for the SARS-CoV-2 RT-PCR examination on the day of admission. The nasopharyngeal swabs were placed into a vial that contained a viral transport medium. The specimens were stored and transported at 4°C to the laboratory. In the present study, the RT-PCR test was done only on admission.

The laboratory investigations collected were hemoglobin, total leukocyte counts, including neutrophil and lymphocyte percentage, platelet counts, serum urea, serum creatinine, serum procalcitonin, and serum D-dimer. Chest radiography was also performed for all inpatients.

Statistical analysis
The data were inserted using Microsoft Excel, and all statistical analyses were done utilizing Windows IBM SPSS statistics software version 21.0. Descriptive analyses were performed and presented as numbers and percentages for the study participants. Comparisons between nominal data were made.
using the Chi-square test, and between continuous data were done using an independent sample t-test. Ordinal data were described using the median and interquartile range and analyzed using the Mann-Whitney U test. A P value smaller than 0.05 was the cutoff for statistical significance.

Results
In the present study, 500 suspected patients of COVID-19 with SARI admitted in the COVID-19 suspect ICU were enrolled in the study. Among them, 318 (63.6%) were male, and 182 (36.4%) were female. The RT-PCR test for COVID-19 revealed 88 (17.6%) patients positive, and 412 were negative. The mean age in the positive group was 55.31 ± 16.16 years, and in the negative group was 40.46 ± 17.49 years (P < 0.001). Out of the 500 patients with SARI, 264 (52.8%) had comorbidities. Hypertension [n = 127 (25.4%)] and diabetes [n = 79 (15.8%)] were the top two comorbidities in these patients. Others were respiratory (n = 45), neurological (n = 39), renal (n = 32), cardiac (n = 20), and various types of cancers (n = 21). However, there was no statistically significant association of these comorbidities with COVID-19 positive patients [Table 1].

The common symptoms included dyspnea [71 (80.7%) in positive group; 331 (80.3%) in negative group], fever [69 (78.4%) in positive group; 327 (79.4%) in negative group], cough/sore throat [27 (30.7%) in positive group; 135 (32.8%) in negative group] at the time of admission [Table 1]. Less common symptoms were chest pain, headache, vomiting, loose stools, abdominal pain, nasal discharge, anosmia, and altered sensorium.

The mean total leukocyte count (TLC) in the positive group was 11.6 ± 4.5 × 10³/μL, and in the negative group was 13.3 ± 3.0 × 10³/μL. Most patients had neutrophilia and lymphopenia in both groups. The percentage of neutrophils in the positive group was (mean ± SD) 79.12 ± 17.49% and in the negative group was 75.64 ± 14.81% (P = 0.056). The percentage of lymphocytes was 13.81 ± 8.60% in the positive group and 15.62 ± 12.52% in the negative group (P = 0.231). In positive group, 66 (94.3%) and in negative group, 180 (94.8%) patients had raised D-dimer ≥0.5 (μg/mL) (P = 0.505) [Table 2]. The median procalcitonin (normal value < 0.02 ng/mL) at the time of admission in the positive group was 0.23 [0.08–1.23] ng/mL, and in the negative group was 0.67 [0.10–4.85] ng/mL (P = 0.035).

Sixty-six (75.9%) patients in the positive group showed bilateral chest infiltrates, and 45 (11%) had abnormal X-ray findings in the negative group (P < 0.001). The various patterns on chest X-rays of positive COVID-19 patients were bilateral patchy nodular or interstitial shadows, bilateral peripheral and basal nodular interstitial infiltration, bilateral peripheral interstitial infiltration, and bilateral basal nodular-interstitial infiltration [Figure 2].

Twenty (22.7%) patients in a positive group and 66 (16.0%) in the negative group required invasive mechanical ventilator support in COVID-19 suspect ICU (P = 0.318). Three (3.4%) patients in the positive group and 15 (3.6%) in the negative group were on high flow nasal oxygen (HFNO) support at the time of admission. The rest of the patients required no or minimal oxygen support in both groups at admission. There was notably greater mortality in COVID-19 positive patients (34.1%) relative to negative patients (20.6%) (P = 0.006). On adjusting the age differences, death continued to be associated with COVID-19 positive status, [aOR = 1.93, 95% CI = 1.14–3.29] [Figure 3]. The cause of mortality in these patients ranged from acute respiratory distress syndrome (ARDS), multiple organ dysfunction syndrome (MODS), and refractory shock.

Analysis of all deaths in SARI patients (n = 115)
Of the 500 SARI patients, 115 died. Of these, the COVID-19 positive patients (n = 30) had a significantly higher age as compared to the COVID-19 negative (n = 85) patients (P < 0.001). There were no differences with respect to gender, presenting symptoms, or any comorbidities. X-ray chest abnormalities were almost three times more likely in COVID-19 deaths (P < 0.001). Among the laboratory parameters, COVID-19 positive patients had a significantly higher median neutrophils percentage [88.2 [85.5–90.5] in COVID-19 positive patients who died; 78.5 [68.5–87.6], P = 0.003] in COVID-19 negative patients who died], lower median lymphocyte percentage [67 [4.8–10.2] in COVID-19 positive patients who died; 11.4 [6.2–19.9], P = 0.017] in COVID-19 negative patients who died] and a lower median procalcitonin value [0.5 [0.1–1.3] ng/mL in COVID-19 positive patients who died; 2.0 [0.4–19.7] ng/mL, P = 0.017] in COVID-19 negative patients who died }

Analysis of the COVID-19 positive patients (n = 88)
Of the 500 SARI patients, 88 were positive COVID-19 patients, of whom 30 died. There were no significant differences in age (P = 0.204) or gender (P = 0.359) or the presenting symptoms between the positive COVID-19 patients who had died compared to those who were alive. Similarly, none of the comorbidities evaluated had any significance with the mortality of COVID-19 patients. Among the laboratory parameters, dead COVID-19 patients were found to have a higher median total leucocyte count [16.6 [11.8–18.0] ×10³/μL in patients who died; 9.1 [6.2–13.0] ×10³/μL, P < 0.001 in alive patients] with significantly higher median

Figure 2: Various patterns of chest X-rays found in COVID-19 positive patients (a), (b) bilateral basal nodular-interstitial infiltration (c) bilateral patchy nodular-interstitial shadows (d) bilateral peripheral interstitial infiltration (e) bilateral peripheral and basal nodular interstitial infiltration

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neutrophils percentage \(88.2 \% \) in patients who died; \(77.0 \% \) in alive patients) and lower median lymphocytes percentage \(15.5 \% \) in patients who died; \(6.7 \% \) in alive patients) than alive COVID-19 patients.

### Analysis of SARI patients requiring ventilator support or HFNO (n = 104)

Of the 500 SARI patients, 104 required ventilator support or HFNO at admission [Figure 4]. There were no significant differences in age or the presenting symptoms between the patients who required ventilator support compared to those who did not need it during admission. Patients who required ventilator support had more comorbidities (65.7\%) in comparison to patients who did not (49.2\%) require ventilator support at admission \(P = 0.002\). There were more deaths in patients who required ventilator support (34.3\%) in comparison to those who did not need ventilator support (19.9\%) at admission \(P = 0.002\).

### Discussion

In the present study, the RT-PCR test revealed 88 SARI patients positive for COVID-19. The previous survey, conducted by the ICMR in India of SARI patients in March 2020, showed COVID-19 positivity of 1.8\%. Our study has shown that this number has dramatically increased to 17.6\% due to the progression of the transmission of the disease. In a retrospective case series of 82 patients with SARI, Aggarwal, et al. found 39% positivity for COVID-19. The higher rate of positivity in their case series may be due to their sampling for COVID-19 on the day of admission, and again on the day 5 of admission in case, the first sample was negative. In the present study, the RT-PCR test was done only on admission.

The patients diagnosed as COVID-19 positive were older than COVID-19 negative patients \(P < 0.001\), which was similar to earlier studies. Of the total dead SARI patients, the COVID-19 positive patients had a significantly higher age than the COVID-19 negative patients \(P < 0.001\).
The current study found that patients with various comorbidities had SARI and required hospitalizations. Hypertension (25.4%) and diabetes (15.8%) were the top two comorbidities in patients presenting with SARI. This was similar to previous studies.[15-18] There was no significant difference between COVID-19 positive and negative groups for these comorbidities. However, patients who required ventilator support had more comorbidities (65.7%) in comparison to patients who did not (49.2%) require ventilator support at admission \((P=0.002)\). It can be explained by higher chances of progression to multiple organ dysfunction syndrome because of these comorbidities, which necessitated ventilator requirements in these patients.[15-22] Yang et al.[16] in their study on 200 patients with COVID-19, found a mortality rate in the ICU as 51.7%. Agarwal et al.[9] observed COVID-positive subject’s death rate of 28.4% during the study of 281 SARI patients. Suresh et al.[21] in their study on 116 COVID-19 patients, concluded that lower SpO\(_2\) and Glasgow Coma Scale (GCS) were the main parameters that showed a significant association with mortality and the requirement for mechanical ventilation. Similarly, we also observed 34.1% of mortality in COVID-19 positive patients with SARI. A total of 104 out of 500 patients required ventilator or HFNO support. This pattern of utilization can be used for resource planning and allocation.

Like other studies,[8,14,15] most of our patients had cough, fever, shortness of breath, and bilateral chest infiltrates in chest X-rays. Most of our patients had lymphopenia, which was similar to the finding in the studies done by Bhandari et al.[23] and Zaboli et al.[24] It has been suggested that lymphocytes may be the principal target of SARS-CoV-2 and can be linked to disease progression and mortality. Neutrophilia and lymphopenia were significantly higher in COVID-19 positive patients who died. This result can be explained by the fact that neutrophils are triggered by inflammatory factors associated with viruses, such as interleukin-6, interleukin-8, and tumor necrosis factor.[23] Human immunological response from a viral infection, however, relies primarily on lymphocytes. Systematic inflammation depresses cellular immunity by reducing CD4+ T lymphocytes. Thus, virus-triggered inflammation causes neutrophilia and lymphopenia.[24] In a low–middle-income country like India, resources for the management of COVID-19 patients are limited. These barriers may occur at the infrastructure level (limited number of isolation beds), testing level (a smaller number of certified test laboratories, particularly in suburban and regional hospitals.), treatment level (inadequate ICU ventilators, oxygen supply, medications, personal protective equipment (PPE), and staff), information level (inconsistency and ambiguity about testing, triage, and management), and transport-level (insufficient transport choices for sufferers). These shortcomings may be overcome by using existing resources optimally. Some examples are utilizing exhaust fans to transform normal pressure rooms to negative pressure rooms to improve isolation, open field hospitals in large public spaces, focused testing on symptomatic patients, enrolling paramedical personnel, and re-use some forms of PPE after disinfection, etc.[27]

There are a few limitations to this study. First, this was a single-center study. Multicenter studies with a bigger sample size will help better understand the clinical and outcome profiles of COVID-19 patients. Secondly, the RT-PCR test was used to diagnose COVID-19 in nasopharyngeal swabs. This test, however, has a false negative rate of 38%, which could have missed the diagnosis of COVID-19 in some patients.[28] We did not use computer tomography (CT) of the chest for these patients. Patients with PCR negative could be considered to be COVID-19 based on the CT.[29,30]

**Conclusions**

In conclusion, of the 500 suspected patients of coronavirus disease 2019 with severe acute respiratory infection admitted at our hospital, the mortality of COVID-19 positive patients was considerably high.

**Key points**

This study examined the first 500 suspected patients of COVID-19 with SARI admitted at our center. Out of them, 104 required ventilator support or HFNO at admission. Of the 500 SARI patients, 88 patients showed positive results.
for COVID-19 by reverse transcription-polymerase chain reaction (RT-PCR). Eighty-five (20.6%) patients died in the COVID-19 negative group, and 30 (34.1%) died in the COVID-19 positive group ($P = 0.006$). Although all patients presenting as SARI have considerable mortality rates, the COVID-19 associated SARI cases thus had almost one-third risk of mortality.

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Conflicts of interest
There are no conflicts of interest.

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