

Original Research Article

Study of clinical parameters, diagnostics and outcome in patients with acute respiratory illness in a tertiary care centre during COVID-19 pandemic

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Received: 26 January 2021

Accepted: 16 March 2021

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ABSTRACT

Background: We retrospectively analyzed and compared 98 patients admitted in Intensive care unit (ICU) with symptoms of acute respiratory illness (ARI) during the era of COVID-19 pandemic.

Methods: We examined patients presenting in emergency department of SMS Medical College, Jaipur between 3rd and 20th May, 2020 with symptoms of ARI who were tested for SARS-CoV-2. Among those hospitalized, we compared symptoms, vital signs, comorbidities, biochemical and hematological parameters including viral diagnostics. We determined differences in outcomes (ICU admission, interventions, acute respiratory distress syndrome and cardiac injury).

Results: In a cohort of 98 patients with symptoms of ARI, 9 (9.183%) tested positive for SARS-CoV-2. Patients were divided into group A and B based on SARS CoV2 RNA testing. Among patients with additional viral testing, no co-infections with SARS-CoV-2 were identified by PCR. FDP and d-dimer was positive in 44.44% patients in group A and 68.53% in group B. 11.11% mortality was observed in group A and 14.606% in group B. The most common complication of ARI observed in both groups was coagulopathy 33.33% in group A and 42.696% in group B.

Conclusions: Presence of comorbidities, lymphopenia, elderly age and elevated NLR, TLC, PLR and LDH have been associated with increased morbidity and mortality. Tuberculosis was most common coinfection seen in patients presenting with ARI. ARI due to non-COVID-19 illness was more severe than due to COVID-19 and was accompanied by multiple respiratory and systemic symptoms and was associated with hospitalization.

Keywords: Acute respiratory illness, SARS-CoV-2, ICU, Coagulopathy, Coinfection

INTRODUCTION

A novel coronavirus was identified as the causative agent of an outbreak of pneumonia of unknown origin in Wuhan city, china and subsequently termed COVID-19 by the World Health Organization (WHO). COVID-19 is caused by a betacoronavirus named SARS-CoV-2 that affects the lower respiratory tract and manifests as pneumonia in humans.¹ Despite rigorous global containment and quarantine efforts, the incidence of COVID-19 continues to rise. SARS-CoV-2 is an enveloped, non-segmented, RNA virus responsible for the pandemic.² Lungs has been

considered as the primary organ of involvement in COVID-19 infection, and most patients present with typical respiratory symptoms and signs. The outbreak of COVID-19 has been arousing great global health concern, with the world still gathering information regarding the transmission dynamics and finding cure for the disease. The most common presenting symptoms are fever, cough, and dyspnea.^{3,4}

An acute respiratory illness (ARI) is defined as patient presenting with a measured temperature of $\geq 38^{\circ}\text{C}$ and cough, with onset of symptoms within the past 10 days.⁵

While many people recovered from Covid-19, reports from China, Italy, and the United States showed that approximately 5% of patients required intensive care and 1.7-7.2% died.^{6,7}

However, studies have predominantly focused on patients diagnosed with COVID-19 and have not described in detail the presentation of patients with acute respiratory illness (ARI) who did not have COVID-19. We herein provide an assessment of clinical spectrum, biochemical, hematological profile and radiological features of 98 patients admitted with acute respiratory illness in a tertiary care hospital at the outset of the COVID-19 pandemic.

METHODS

Study design

We conducted a cross sectional observation study/retrospective cohort study in 98 patients hospitalized in ICU from 3rd May to 15th May 2020 with symptoms of acute respiratory illness (ARI) like cough, fever, myalgia and dyspnea. We identified all patients who were 18 years or older, underwent nasopharyngeal/oropharyngeal swab testing for SARS-CoV-2 confirmation, by WHO approved kits based on real time reverse transcription polymerase chain reaction (rRT-PCR). Informed consent was obtained from each patient included in this study. The data has been used in anonymised form, without revealing identity of any subject.

Data collection

For each case, epidemiological history and information of other family members of each patient was obtained. Information regarding age, sex, previous medical history, clinical manifestations, and vaccinations was obtained. All patients were subjected to detailed clinical evaluation, routine hematological and biochemical investigations, electrocardiogram (ECG), chest x-rays and computed tomography (CT) scan at the time of admission. Other investigations like 2D-echocardiogram, ultrasound of abdomen, were done as indicated clinically. All patients were isolated from each other till covid-19 report was awaited. Confirmed covid-19 cases were shifted to Infectious disease hospital and patients with negative result were kept in the same ICU. The patients were followed till any of the outcome of disease (cured/discharged with home isolation/death) was achieved. All data was recorded in a predesigned Performa. The patients with incomplete records were excluded from the study.

Statistical analysis

Statistical analysis was performed using the IBM statistical package for social sciences (SPSS®) Statistics 24.0. The distribution of data was evaluated by the Kolmogorov-Smirnov test. Results of continuous variables were expressed as mean±SD. The data was expressed as

means, standard deviation, number and percentages. The observations were tabulated and data was analyzed using independent t test. The p value of <0.05 was considered significant, <0.001 as highly significant and >0.05 as non-significant.

RESULTS

We classified 98 patients admitted with acute respiratory illness (ARI) in ICU into two groups A and B based on SARS CoV2 RNA testing results to compare various biochemical, radiological, clinical and other parameters which have been compiled in Table 1. In our study, the median age of all patients was 50 years (range 18-90 years). There were 55/98 (56.12%) males and 43/98 (43.88%) females. 78/98 (79.59%) patients had comorbidities. The presence of comorbidities was found to be significantly associated with the occurrence of severe disease. Hematological profile revealed higher mean total leukocyte count (TLC), neutrophil (%), NLR and PLR in group B than group A but was statistically insignificant. Lymphopenia was prevalent amongst both groups but was statistically insignificant on comparison (p value=0.161). Aspartate transaminase, alanine transaminase and LDH were above normal reference range in both groups with ARI but statistically insignificant on comparison with p values 0.632, 0.928 and 0.734 respectively. FDP and d-dimer was positive in 44.44% patients in group A and 68.53% in group B. Serum procalcitonin values were higher in group B than group A but were statistically insignificant on comparison (p value= 0.497). Mortality was higher among group B (14.606%) than in group A (11.11%).

Co-infections

Among COVID-19 positive patients, dengue serology was positive in 3 patients while in COVID-19 negative, 4 patients were positive for dengue serology and 2 were positive for scrub typhus. None of the admitted patient was tested positive for chikungunya and H1N1. In COVID-19 negative patients, 14 cases were active case of tuberculosis on ATT.

Comorbidities

Among patients admitted with ARI, 3/9 (33.33%) COVID-19 positive patients while 72/89 (80.89%) COVID-19 negative had comorbidities. Co-morbidities among both groups have been tabulated in Table 2. Presence of comorbidities may be the contributing factor to higher mortality rates among patient with ARI among COVID-19 negative cases. Two patients were known case of rheumatological disorder and on steroids.

Radiological findings

Consolidation was seen in all cases with 100% patients presenting in emergency with ARI.

Table 1: Biochemical, hematological, radiological and clinical profile of patients admitted with acute respiratory illness (ARI) in ICU.

Variables	Group A (COVID-19 positive)	Group B (COVID-19 negative)	P value
Number of patients	9/98	89/98	
Mean age (in years)	52.444±13.1825	48.9101±16.4901	0.53672
Sex			
Male	4/9 (44.44%)	51/89 (57.303%)	
Female	5/9 (55.55%)	38/89 (42.696%)	
Mean Hb (gm/dL)	12.2667 ± 2.3415	18.3034 ± 6.895	0.81084
Mean TLC (/mm³)	9810± 6285.326	12186.5169±6889.774	0.32466
Mean neutrophil (%)	78.7778±13.2267	83.1573±8.2433	0.15596
Mean lymphocytes (%)	14.7778±11.6809	11.2022±6.6796	0.16177
Mean N/L ratio (NLR)	9.7256±7.5318	13.2047±14.063	0.46716
Mean P/L ratio (PLR)	243.0644±159.8389	267.2792±309.1879	0.81858
Mean Platelet count (lacs/μL)	2.0767±0.9331	2.0581±1.2246	0.96817
ESR	68.1111±42.1439	49.9101±36.9775	0.16774
CPK-MB	37.1111±22.1272	52.9438±46.5333	0.31503
S. Bilirubin (mg/dL)	0.8556± 0.654	1.7101±2.7533	0.35987
AST (U/L)	82.4444±135.4678	175.8764±588.821	0.63942
ALT (U/L)	118.8889±234.324	127.2921±280.414	0.92847
Serum LDH (U/L)	694.6667± 380.9521	810.191±1016.258	0.73459
Non-intubated	8/9 (88.88%)	72 (80.89%)	
Intubated	1/9 (11.11%)	17 (19.10%)	
D- dimer	4/9 (44.44%)	61/89 (68.53%)	0.2774
FDP	4/9 (44.44%)	61/89 (68.53%)	0.2774
Procalcitonin (PCT)	0.9088±2.048	4.8001±17.050	0.49795
Outcome			
Recovered	8/9 (88.88%)	76/89 (85.39%)	
Death	1/9 (11.11%)	13/89 (14.606%)	0.8231
Chest X-ray			
Consolidation	9/9 (100%)	89/89 (100%)	
Air bronchogram	4/9 (44.44%)	40/89 (44.94%)	
Unilateral lung involvement	0	9/89	
Bilateral lung involvement	9/9	80/89	
Pleural effusion	0/9 (0%)	5/89 (5.61%)	
Fever	8/9 (88.88%)	64/89 (71.91%)	
Cough	4/9 (44.44%)	55/89 (61.79%)	
Dyspnea	9/9 (100%)	83/89 (93.25%)	
Altered Sensorium	3/9 (33.33%)	27/89 (30.33%)	
Intubated	1/9 (11.11%)	17/89 (19.10%)	
Patients on steroids	1	4	

Pleural effusion was seen in 5/89 (5.617%) COVID-19 negative patients while none of the cases of COVID-19 positive patient. Air bronchogram was seen in 4/9 (44.44%) COVID-19 positive patients and 40/89 (44.94%) COVID-19 negative patients. B/L lung involvement was seen in 9/9 (100%) COVID-19 positive patients while among covid-19 negative patients 9/89 (10.11%) had unilateral and 80/89 (89.89%) had bilateral lung field involvement.

Complications

The most common complication of ARI observed in both groups was coagulopathy 33.33% in group A and 42.696% in group B. Cardiac injury in form of elevated cardiac enzymes and ECG changes was seen in 11.11% in group A and 11.23% in group B. AKI was seen in 11.11% in group A and 4.494% in group B. The complications observed among patients presented with ARI have been compiled in Table 3.

Table 2: Comorbidities in patients admitted with acute respiratory illness.

Co-morbidity	COVID positive	COVID negative
COPD	1/9 (11.11%)	25 (28.08%)
Tuberculosis	0 (%)	14 (15.73%)
Hypertension	1 (11.11%)	14 (15.73%)
Diabetes mellitus	1 (11.11%)	13 (14.60%)
Chronic Kidney Disease (CKD)	0 (%)	14 (15.73%)
Coronary artery disease (CAD)	0 (%)	10 (11.23%)
CVA	0 (%)	9 (10.112%)
Chronic liver disease	0(%)	4 (4.494%)
Hypothyroidism	0 (%)	4 (4.494%)
Cancer	0 (%)	3 (3.37%)

Table 3: Complications among patient presented with ARI.

Complications	COVID-19 positive	COVID-19 negative
Shock	4 (44.44%)	5 (5.617%)
Acute kidney injury (AKI)	1 (11.11%)	4 (4.494%)
Cardiac injury (Significantly raised cardiac enzymes) (upto 24 U/L)	1 (11.11%)	10 (11.23%)
Coagulopathy (Prolonged INR)	3 (33.33%)	38 (42.696%)

DISCUSSION

We compared acutely ill patients with and without COVID-19 presenting for emergency care. During this pandemic, a number of studies have described the clinical features of patients with COVID-19, few have compared directly the clinical presentation and outcomes of COVID-19 to other respiratory illnesses. After an incubation period, infection progresses from pre-symptomatic stage (1–3 days) through symptomatic infection (2–4 weeks) to a prolonged post-symptomatic or recovery stage (2–8 weeks). The spectrum of disease with SARS-CoV-2 ranges from asymptomatic infection to severe, often fatal disease. Patients with mild disease have fever, cough, sore throat, loss of smell, headache, and body-ache. Moderate illness is characterized by involvement of the lower respiratory tract. In addition to increased vascular permeability, the cytokine “storm” leads to high levels of fibrinogen and activation of the coagulation cascade on endothelial surfaces of small blood vessels, signaled by increased levels of a fibrin breakdown product called D-dimer.⁸

While most people with COVID-19 develop only mild or uncomplicated illness, approximately 14% develop severe

disease that requires hospitalization and oxygen support, and 5% require admission to an intensive care unit.⁹ In severe cases, COVID-19 can be complicated by the acute respiratory distress syndrome (ARDS), sepsis and septic shock, multiorgan failure, including acute kidney injury and cardiac injury.¹⁰ To control the spread of virus isolating confirmed COVID-19 cases and extensive tracing of contacts with their early testing can help in breaking the chain of transmission among population.

In the present study COVID-19 sampling was done in all patients admitted with acute respiratory illness. Nine (9.18%) patients admitted with symptoms of ARI tested positive for SARS-CoV-2, this was comparable to a study done by Shah SJ et al in which 10% patients tested positive for SARS-CoV2 and 16% tested positive for other respiratory virus.¹¹

Liver injury observed in patients with COVID-19 might be due to virus infecting hepatocytes or due to other causes like systemic inflammation induced by cytokine storm or hypoxia and drug-induced liver injury.¹² Guan et al observed that in patients with non-severe disease, 18.2% and 19.8% had elevated AST levels whereas in patient with severe disease 39.4% and 28.1% had elevated ALT levels respectively.¹³

In our study, patients with COVID-19 elevated AST, ALT were elevated more than 3 times in 1/9 patient and LDH was elevated in 2/9 patient. However, 1 case of liver failure was reported. In COVID-19 negative 14/89 patients had AST/ALT elevated more than 3 times and LDH was elevated 14/89. Increased LDH has been associated also with higher risk of ARDS, ICU support and mortality. In a study by Terpos et al elevated LDH was reported in 41% of patients.¹⁴ Monitoring of liver functions is important during the course of COVID-19 especially in patients with higher disease severity. 14.285% (14/98) patients died.

As opposed to community acquired bacterial pneumonia which tends to be unilateral and involving a single lobe, COVID-19 and other viral pneumonias typically produce lung opacities in more than one lobe.¹⁵ Identifying multifocal air-space disease on chest x-ray can be a significant clue to COVID-19 pneumonia. Early COVID-19 investigators have noted that the air-space disease tends to have a lower lung distribution and is most frequently bilateral.¹⁶

Similar findings were observed by Shi et al, with predominant pattern being bilateral lung involvement, they also reported that asymptomatic patients can have abnormal radiological findings.¹⁷

In our study, lymphopenia was seen in (84/98) 85.71% patients, 66.67% (6/9) COVID positive and 87.64% COVID negative (78/89). During hospitalization, non-survivors demonstrated a more significant deterioration in lymphocyte count. Similarly, lymphopenia was

documented in approximately 40% of the hospitalized patients with COVID-19 in Singapore.¹⁸

In our study, mean NLR and PLR was higher in both COVID-19 positive and COVID-19 negative patients especially those. NLR and PLR may also have prognostic value in determining severity of cases. Li et al reported that older age, leucocytosis, and high LDH level were associated with poor disease outcome.¹⁹ In our study, fourteen (14.28%) patients died, all of them were above 65 years of age with comorbidities, lymphopenia, higher NLR, PLR and LDH levels.

In our study, all patients with ARI were subjected to covid-19 testing, 9/98 (9.18%) patients were COVID-19 positive. None of the patient had history of contact with a confirmed case of COVID-19 neither anyone had travel history outside country. Biochemical parameters of all COVID-19 confirmed cases provide reliable information regarding disease course and assessing severity of illness.

Our study is unique in the aspect that all cases with ARI were admitted as COVID-19 suspects, isolated and subjected to COVID-19 testing as per ICMR guidelines and further their hematological, biochemical and radiological profile were compared on the basis of COVID-19 test reports. Currently, our understanding of the spectrum and natural history of SARS-CoV-2-infection remains limited. It was observed that close monitoring of biochemical and hematological parameters of all cases with ARI led to early recovery, understanding the disease course and better outcome. There is speculation that variations in the strains of SARS-CoV-2 may affect pathogenicity and contribute to geographic differences in case fatality rates.²⁰ There might be diversity of strains among the COVID-19 patients requiring ICU care without a predominant clade, larger studies are needed to assess any potential association.

Clinical characteristics of COVID-19 were difficult to distinguish from those characterizing influenza, at least in our influenza-vaccinated population. It is important to treat and cure patients at an early stage before irreversible severe respiratory complications take hold, this also further decrease duration of carriage and avoid the spread of the disease. Therefore, early diagnosis, isolation and management of cases will not only help to contain this pandemic but also might collectively contribute to the reduction in morbidity and mortality from COVID-19. An important issue with RT-PCR test is the risk of eliciting false-negative and false-positive results. It is reported that many 'suspected' cases with typical clinical characteristics of COVID-19 and identical specific computed tomography (CT) images tested negative on RT-PCR.²¹ Thus, a negative result does not exclude the possibility of COVID-19 infection and should not be used as the only criterion for treatment or patient management decisions. It seems that combination of RT-PCR and clinical features can facilitate management of SARS-CoV-2 outbreak. During this pandemic it is vital to presume every case presenting

with ARI as COVID-19, isolating the patient and testing for SARS Cov-2.

CONCLUSION

Presence of comorbidities, lymphopenia, elderly age and elevated NLR, TLC, PLR and LDH have been associated with increased morbidity and mortality. Tuberculosis was the most common coinfection among patients admitted with ARI. ARI due to non-COVID-19 illness was more severe than due to COVID-19 and was accompanied by multiple respiratory and systemic symptoms, and was associated with hospitalization. Coagulopathy was most common systemic complication among both groups presented with ARI.

ACKNOWLEDGEMENTS

We would like to thank the patients and contacts, all healthcare workers and hospital administration who provide care for patients with COVID-19 and are involved in the diagnosis and treatment of COVID-19 patients, staff involved in tracing and quarantine of contacts, members of the COVID-19 response teams at the local, city, province and national level.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Mahavar S, Tyagi P, Agrawal A, Banerjee S, Sharma R, Keswani P. Study of clinical parameters, diagnostics and outcome in patients with acute respiratory illness in a tertiary care centre during COVID-19 pandemic. *Int J Adv Med* 2021;8:530-5.