Original Research Article

Study of hematological and biochemical parameters in a cohort of Indian COVID-19 patients admitted in a tertiary care centre

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ABSTRACT

Background: In this study authors retrospectively analyzed the record of 102 patients with confirmed COVID-19 infection to determine factors associated with severity of disease.
Methods: Clinical, biochemical, radiological and hematological profiles of 102 patients with confirmed SARS-CoV-2 RNA testing were obtained and analyzed.
Results: A total of 102 patients were enrolled, with median age of patients of 32.5 years (range 10-85 years), of which 83.3% (85/102) were asymptomatic and 16.67% (17/102) symptomatic. Eighteen (17.6%) patients had co-existing illnesses. Clinical spectrum among COVID-19 patients varied from being asymptomatic to having symptoms like fever, dry cough, breathlessness with few progressing to respiratory failure and multi-organ failure. In our study, 97.05% (99/102) recovered while 2.94% (3/102) died. Mean age, total leucocyte count (TLC), neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), and lactate dehydrogenase (LDH) of severely ill patients were significantly higher than those of patients with non-severe illness.
Conclusions: Elevated NLR, TLC, PLR, LDH and lymphopenia were seen in the symptomatic patients especially manifesting severe disease. Early intervention and periodic monitoring of these parameters in patients, especially with severe disease may help in improving disease outcome.

Keywords: COVID-19, Neutrophil to lymphocyte ratio, Platelet to lymphocyte ratio, Symptomatic, Lymphopenia

INTRODUCTION

In December 2019, a cluster of patients presented with an unidentified form of viral pneumonia in Wuhan, China, with common history of visiting the Huanan seafood market. The virus was isolated from biologic samples and identified as genus betacoronavirus, placing it alongside other severe acute respiratory syndrome (SARS) and Middle east respiratory syndrome (MERS).[1] On the basis of a phylogenetic analysis of coronaviruses, it was designated as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the coronavirus Study Group (CSG) of International committee on virus taxonomy.[2] SARS-CoV-2 is an enveloped, non-segmented, RNA virus responsible for the 2019 coronavirus disease (COVID-19) pandemic.[3] Lung is considered to be the primary organ of involvement by COVID-19 infection, and most patients present with typical respiratory symptoms and signs. SARS-CoV-2 is mainly detected by nasopharyngeal/oropharyngeal swab of suspected case but it has also been isolated from blood, gastrointestinal tract, saliva and urine but these routes of potential transmission further need to be investigated.[4] The outbreak of COVID-19 has been arousing great global health concern, with the world still gathering information regarding the transmission dynamics and

spectrum of illness. The increasing number of COVID-19 infections may be attributable to the late identification of source of infection and the ability of host to shed the virus while being asymptomatic.[5]

The objective of our study is providing an assessment of biochemical, hematological profile and radiological features of 102 patients confirmed with SARS-CoV-2 infection admitted in a tertiary care hospital based on their symptomatology.

METHODS

Study design

We conducted a cross sectional observational study in a cohort of 102 patients with positive SARS-CoV-2 nucleic acid test results who were hospitalized in various COVID-19 facilities of SMS Hospital, Jaipur from 19th March to 15th April 2020. For SARS-CoV-2 confirmation, suspected cases underwent nasopharyngeal/oropharyngeal swab testing and WHO approved kits based on real time reverse transcription polymerase chain reaction (rRT-PCR) were used. 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. Informed consent was obtained from each registered patient or from his guardian. This study was reviewed and approved by the institutional ethics committee. The data is used in deidentified form and doesn't reveal identity of any subject.

Data collection

For each case, epidemiological history and information of other family members 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) and chest x-ray at the time of admission. Other investigations like 2D-echocardiogram, ultrasound of abdomen, computed tomography (CT) scan was done as indicated clinically. Data of investigation reports was gathered from electronic patient record system. Symptomatology of patients was recorded and patients were put on treatment according to their clinical condition, decided by the COVID-19 treatment protocol team of our institution. All the cases were given hydroxychloroquine (400 mg twice daily on first day and then 200 mg twice daily for four days) unless contraindicated. Other drugs like antihistaminics and antipyretics were given to patients on symptom basis. Patients with fever and leucocytosis and/or lung shadows on chest radiography were given azithromycin or cephalosporins. Patients who failed to maintain oxygen saturation (SpO2<94% on room air) were given oxygen via high flow mask or nasal prongs. Indian guidelines of COVID-19 management were followed according to

which, rRT-PCR for COVID-19 was done every third day till the report was negative and then it was repeated after 24 hours. A patient was considered COVID-19 recovered till he/she became asymptomatic along with two negative rRT-PCR tests 24 hours apart.[6] The patients were followed till any of the outcome of disease (cured/discharged with home isolation/death). All data was recorded in a predesigned proforma. Patients with incomplete records or who were transferred to other facilities before recovery were excluded from the study.

Statistical analysis

The data was systematically collected, compiled and statistically analyzed using IBM SPSS® 24.0 software to draw cross-tabs and make relevant conclusions. The normality test for continuous variables was done and data was found to be normally distributed. Results of continuous variables were expressed as mean±SD. The observations were tabulated and independent t test was applied to analyze variables between groups. The p value of <0.05 was considered significant <0.001 as highly significant and >0.05 as non-significant.

RESULTS

A total of 102 patients with confirmed SARS-CoV-2 infection were enrolled in this study and classified into two groups A and B based on clinical presentation to compare various biochemical, hematological and radiological parameters. The median age of all patients was 32.5 years (range 10-85 years).

There were 77 (75.49%) males and 25 (24.51%) females, sex-wise distribution of patients according to their symptomatology is mentioned in (Figure 1).

Group A had 85 (83.33%) patients which were asymptomatic while group B had 17 (16.67%) patients who had symptoms of virological illness ranging from fever, cough and breathlessness to worsening of symptoms leading to respiratory and multi-organ failure. In group A, all patients recovered without any adverse outcome while in group B, 14/17 (82.35%) patients were moderate to severely ill and recovered and 3/17 (17.65%) were critically ill and died (Table 1).

Table 1: Clinical profile and disease outcome in COVID-19 patients.

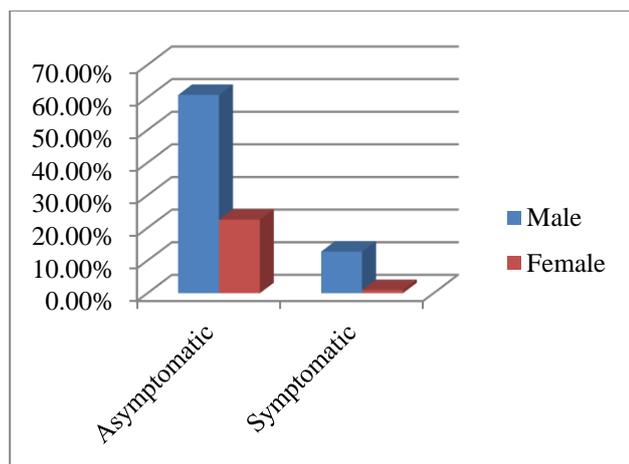| Outcome	Variables	
	Asymptomatic (Group A) (n=85)	Symptomatic (Group B) (n=17)
Recovered	85 (83.3%)	14 (13.7%)
Died	0	3 (2.94%)
Comorbidities (n)	12	6

Figure 1: Distribution of patients according to gender and symptomatology.

At the time of hospital admission and during the course of stay, the most common symptoms were fever (11/17), headache (9/17), dry cough (15/17), dyspnea (10/17), fatigue (9/17), running nose (7/17), nausea/vomiting (3/17), altered sensorium (3/17) and hemoptysis (1/17). Patients in group B had significantly higher mean age than patients of group A (p value<0.0001). Comorbidities were seen in 17.6% (18/102) patients, the most prevalent being diabetes mellitus 10.8% (11/102), hypertension 7.8% (8/102), chronic obstructive pulmonary disease (COPD) in 3.92% (4/102), chronic kidney disease (CKD) 0.98% (1/102), coronary artery disease (CAD) 0.98% (1/102) and cerebrovascular disease (CVD) 0.98% (1/102). Of these 18 patients, six were in the group B. All those who died were having one or more comorbidities. The presence of comorbidities was found to be significantly associated with the occurrence of severe disease (p=0.0365).

Table 2: Comparison of hematological and biochemical parameters among COVID-19 patients based on their symptomatology.

Variables	Group A (asymptomatic)	Group B (symptomatic)	P value
Mean age (in years)	35.05±16.52	53.5294±14.98	<0.0001
Sex			
Male	62 (60.78%)	15 (12.74%)	-
Female	23 (22.54%)	2 (0.98%)	
Mean Hb (gm/dl)	13.85±2.04	13.12±1.58	0.16
Mean TLC (/mm³)	7121.06±1782.17	8671.76±3925.70	0.011
Mean neutrophil (%)	66.42±8.85	74.47±11.89	0.001
Mean lymphocytes (%)	28. 60±8.65	20.58±10.87	0.001
Mean NLR	2.67±1.32	6.17±6.11	<0.0001
Mean PLR	115.47±47.88	146.29±88.90	0.043
Mean platelet count (lacs/μl)	2.14±0.79	1.82±0.59	0.119
FBS (mg/dl)	93.21±18.32	106.53±49.27	0.055
S. Bilirubin (mg/dl)	0.95±0.87	0.86±0.28	0.675
AST (U/l)	30.62±23.98	66.06±59.68	<0.0001
ALT (U/l)	37.02±36.53	68.71±52.94	0.003
Blood urea (mg/dl)	27.98±22.17	35.06±13.98	0.210
Serum creatinine (mg/dl)	1.19±1.71	1.21±0.48	0.976
Mean QTc interval			
% patient with baseline	423.88±35.78	441.89± 39.64	
QTc >440 in males	11 (10.78%)	4 (3.92%)	0.066
QTc >460 in females	1 (0.98%)	0	
Serum LDH (U/l)	410.32±124.74	583.18±260.45	<0.0001
ICU stay			
Non-intubated	0	9 (8.82%)	
Intubated	0	3 (2.94%)	
Time to covid negative (in days) during the hospital stay.	6.23±1.69	6.07±2.92	0.765

Table 2 summarizes comparison of hematological and biochemical parameters among COVID-19 patients based on their symptomatology. Hematological profile revealed significantly higher mean total leukocyte count (TLC), neutrophil (%), neutrophil lymphocyte ratio (NLR) and platelet lymphocyte ratio (PLR) in group B than group A.

Lymphocyte count was significantly lower in group B when compared to group A (p=0.001). Serum bilirubin

values in the two groups were insignificant on comparison (p=0.675) while mean AST, ALT and LDH values were significantly higher in symptomatic patients (p values<0.0001, 0.0033 and<0.0001 respectively). Fasting blood sugar (FBS) levels were higher in group B than in group A (p=0.055). Ninety out of 102 (88.2%) patients were kept in isolation wards while 11.76% (12/102) patients were severely ill and transferred to intensive care unit (ICU) of which 8.82% (9/102) maintained saturation on oxygen via high flow mask or required non-invasive mode of ventilation while 2.94% (3/102) patients were critically ill and on mechanical ventilator. In our study, three (2.94%) patients died during the hospital stay, of which two died of multi organ failure and one died of intracranial hemorrhage. Sixteen (15.68%) patients had baseline QTc prolongation above normal reference range (>440 msec in males and>460 msec in females) due to which, hydroxychloroquine was withheld in these patients.

However, mean QTc interval values did not differ significantly between the two groups (p value 0.065). ECG changes in the form of ST elevation was seen in two (1.96%) patients. Chest X-ray abnormalities were seen in 15.68 % (16/102) patients in the form of bilateral lung field infiltrates 12.74% (13/102), unilateral lung infiltrates 1.96% (2/102) and unilateral pleural effusion 0.98% (1/102). Prevalence of X-ray abnormalities was significantly higher in patients with symptomatic disease, group B 35.29% (6/17) patients when compared to group A 10.58% (9/85) patients (p=0.0015). The mean time in which patients were declared COVID-19 recovered (from the day they tested positive till two negative nucleic acid reports) was found to be statistically insignificant (p=0.7648).

DISCUSSION

SARS-CoV-2 has spread rapidly across many countries and has a wide spectrum of severity. Although most of the COVID-19 patients have mild to moderate course, up to 5–10% can have severe, potentially life-threatening disease.[7] Isolating confirmed COVID-19 cases and extensive tracing of contacts with their early testing can help in breaking the chain of transmission among population and control this pandemic. However, asymptomatic cases may also be capable of transmitting SARS-CoV-2, which is causing difficulties in COVID-19 prevention and control. The present study is unique in the fact that extensive sampling was done in identified "hotspot" areas and with contact tracing of confirmed COVID-19 cases we were able to identify and isolate many COVID-19 patients at an early stage and control further spread of disease. In our study, 83.33% (85/102) cases were asymptomatic while 16.67% (17/102) were symptomatic. Huang et al provided valid evidence demonstrating efficient local human-to-human-transmission with strong infectivity of SARS-CoV-2 within the cluster of youngsters during the incubation-period and asymptomatic-phase of COVID-19 with an attack-rate of 40%.[8]

The median age of patients enrolled in the study was 32.5 years (range 10-85 years). 18 (17.65%) patients had comorbidities, most common was diabetes mellitus followed by hypertension and COPD. Comorbidities were seen in all 3 patients who died. Similarly, in a study by Richardson et al, the most common comorbidities were hypertension, obesity, and diabetes.[9]

Liver injury in patients with COVID-19 might be due to viral infection in liver cells or due to other causes like drug-induced liver injury and systemic inflammation induced by cytokine storm or hypoxia.[10] Guan et al observed that 18.2% patients with non-severe disease and 39.4% patients with severe disease had elevated AST level, whereas elevated ALT levels were observed in 19.8% of patients with non-severe disease and 28.1% of patients with severe disease.[11] In our study, patients with symptomatic COVID-19 disease course had statistically significant elevated liver enzymes (AST, ALT and LDH) with much higher values in patients who were critically ill. However, rise in liver enzyme levels was transient and no case of liver failure was reported. In a study by Terpos et al elevated LDH was reported in 41% of patients. Increased LDH has also been associated with higher risk of acute respiratory distress syndrome (ARDS), ICU support and mortality.[12] Monitoring liver function tests is important during the course of COVID-19 especially in patients with higher disease severity.

In our study, chest x-ray abnormalities were seen in both symptomatic as well as asymptomatic COVID-19 patients. Nine asymptomatic, 10.58 % (9/85) and six symptomatic 35.29% (6/17) patients had radiological abnormalities most common being bilateral lung field infiltration. Similar findings were observed by Shi H et al, that every case of viral pneumonia did not had radiological abnormalities and the predominant pattern of involvement was bilateral lung infiltrates, they also reported that asymptomatic patients can have abnormal radiological findings.[13]

In our study, lymphopenia was seen in 52.94% (9/17) symptomatic and 11.76% (10/85) asymptomatic patients. 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.[14]

In our study, higher NLR and PLR was seen in symptomatic patients especially those manifesting severe disease. NLR and PLR may also have prognostic value in determining severe cases. In our study, mean NLR and PLR in the patients who were symptomatic and died was 14.23±9.92 and 255.55±113.34 respectively while Yang AP et al15 demonstrated mean NLR 20.7±24.1 and PLR 436.5±329.2 in severely ill patients.

Li et al reported that older age, leucocytosis, and high LDH level were associated with poor disease outcome.[16] In our study, three (2.94%) patients died, all of them were above 65 years of age with coexisting illnesses, lymphopenia, higher NLR, PLR and LDH levels.

Hydroxychloroquine was given to all patients while azithromycin was given only to symptomatic patients and it was observed that 99 (97.05%) patients recovered from infection. Gautret et al provided evidence of beneficial effects of co-administration of hydroxychloroquine and azithromycin to COVID-19 patients and its potential effectiveness in reduction of contagiousness and the mean duration of hospital stay was reduced to 5 days.[17]

Antiretroviral drugs, lopinavir (200mg)/ritonavir (50mg) 2 tablets BD were given to only two patients who met the criteria mentioned in Indian guidelines,6 both patients recovered without any adverse disease outcome. In our study, eight patients (7.84%) had positive repeat test after one negative report.

This phenomenon may be attributable to false negative results of assays or due to operational errors involving sample collection, reagents and possible intermittent viral shedding, hence two consecutive negative samples at least 24 hours apart should only be taken as a criterion for discharge.[18] There were no cases of readmission among the discharged patients till date.

Currently, our understanding of the spectrum and natural history of SARS-CoV-2-infection remains limited. Our study is unique in the aspect that it involved comparing hematological, biochemical and radiological parameters in a study group involving both asymptomatic and symptomatic COVID-19 patients which provides better assessment regarding disease course and severity of illness. 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. Close monitoring of confirmed COVID-19 cases and administration of hydroxychloroquine led to early recovery and better disease outcome. Therefore, early diagnosis, isolation and management of COVID-19 cases will not only help to contain this pandemic but also might collectively contribute to the reduction in morbidity and mortality from COVID-19.

CONCLUSION

The values of various biochemical, hematological and radiological were less deviated from the normal range in asymptomatic patients. Presence of comorbidities, lymphopenia, elderly age, elevated NLR, TLC, PLR and LDH have been associated with increased morbidity and mortality. Early intervention and periodic monitoring of these parameters in patients, especially with higher disease severity may help in improving disease outcome.

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