Original Article

Clinical profile of hospitalised moderate category COVID-19 patients: Short study from a Tertiary Care Centre in Delhi

Sachin Gautam[1], Rahul Kumar[1], Dharam Pal Bhadoria[1], Govind Mawari[2], Naresh Kumar[3], Mradul K. Daga[4], Sanjay Pandit[1], S. Anuradha[1], Gaurav Shanker Pradhan[5], Sandeep Garg[1], Gaurav Sharma[1], Raghu RV[1], Nupur Ritchie[1], Dasari Jayamsulekha[1]

[1]Department of Internal Medicine, Maulana Azad Medical College, New Delhi, India, [2]Department of Centre for Occupational and Environmental Health (COEH), Maulana Azad Medical College, New Delhi, India, [3]Department of Pulmonary Medicine, Maulana Azad Medical College, New Delhi, India, [4]Department of Internal Medicine and Infectious Disease, Institute of Liver and Biliary Sciences, New Delhi, India, [5]Department of Radiodiagnosis, Maulana Azad Medical College, New Delhi, India

Abstract

Background: The clinical profile of hospitalized moderate-category COVID-19 patients has been understudied globally and in India. **Aim:** The present study was conducted to study the clinical profile and assess the proportions of patients who progressed to severe disease and its predictors among moderate COVID-19 patients. **Materials and Methods:** In this single-center observational study, 100 moderate-category COVID-19 patients as per Ministry of Health and Family Welfare (MoHFW) criteria of age ≥18 years of either sex, excluding pregnant females from February to November 2021, were studied by analyzing their clinical profiles and assessing Quick Sequential Organ Failure Assessment (qSOFA), National Early Warning Score 2 (NEWS-2), and chest computed-tomography severity score (CTSS) to predict progression to severe disease. Severe disease was defined as per MoHFW criteria. **Results:** Out of 100 moderate-category COVID-19 patients, progression to severe disease was seen in 11 patients (11%), among which eight patients had expired, three patients were discharged, and the rest of the 89 patients (89%) who did not progress to severe disease were discharged. A higher age (62.2± 19.5 vs 54.8 ± 14.6 years), along with multivariate analysis revealing male sex (1.25 times), chronic kidney disease (2.86 times), leukocytosis (6.10 times), thrombocytopenia (1.04 times), anemia (9.3 times), a higher qSOFA score (3.6 times), and a higher NEWS-2 score on admission (1.56 times) had higher odds of progression to severe disease. A significant correlation ($P < .05$) of qSOFA score with serum LDH, ferritin, and hs-CRP levels; CT severity score with the serum ferritin, IL-6, and LDH levels; and NEWS-2 with serum LDH, hs-CRP, and ferritin levels were found. Moreover, the NEWS-2 score was found slightly better than qSOFA on receiver operating characteristic (ROC) curve analysis, with an area under the curve of 85.8% and 83.2%, respectively, predicting progression to severe disease. **Conclusion:** Our study revealed male gender, chronic kidney disease, leukocytosis, anemia, thrombocytopenia, a higher qSOFA and NEWS-2 score on admission, and further, NEWS-2 score better than qSOFA on ROC curve analysis, with an area under the curve of 85.8% and 83.2%, respectively, in predicting severe disease among hospitalized moderate COVID-19 patients.

Keywords: CTSS score, inflammatory markers, moderate category COVID-19, MoHFW COVID-19 criteria, NEWS-2, qSOFA

Address for correspondence: Dr. Sachin Gautam, Post Graduate Resident, Department of Medicine, Maulana Azad Medical College and Associated Lok Nayak Hospital, New Delhi - 110002, India.
E-mail: sachingautam26273@gmail.com

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Introduction

During the first wave of COVID-19, India had the second highest number of confirmed cases, and during the second wave, around April and May 2021, there was a massive surge in hospitalization that overwhelmed the healthcare system and led to resource shortages.[1] MoHFW in India categorizes COVID-19 patients based on their clinical severity as mild, moderate, and severe. Patients with pneumonia and symptoms such as dyspnea and/or hypoxia, fever, cough, and a respiratory rate of 24 or more per minute or with SpO_2 <94% (range 90%-93%) on room air with no sign of severe disease are classified as the moderate cases.[2]

Although severe COVID-19 patients have been the focus of attention in many studies, investigators have assessed the clinico-epidemiological characteristics, various risk factors, and predictors of mortality in such patients.[3,4] A systematic review revealed several demographic, laboratory, and radiological features crucial for predicting the severity and mortality in COVID-19 patients.[5] Furthermore, risk stratification scores like the National Early Warning Score 2 (NEWS-2), Quick Sequential Organ Failure Assessment (qSOFA), and CT severity score (CTSS) have also been used to identify patients who are at a high risk of early clinical deterioration, particularly in severe disease.[6-10] Another retrospective study found that NEWS-2 was superior to qSOFA in determining the need for intensive care support and/or mortality.[11] Similarly, a high CTSS had been found to correlate with severe COVID-19 infection, inflammatory markers, and hospital stay.[12,13]

Literature shows different definitions of moderate COVID-19 patients; initials were from China, where studies assessed progression risk factors in mild to moderate cases, differentiating moderate cases from severe ones based on hematology parameters and mild ones based on clinical laboratory and radiological parameters.[14-16] Hence, it becomes equally important to assess the clinical profile and the performance of risk stratification scores like NEW-2, qSOFA, and CTSS to predict COVID-19 disease progression among hospitalized moderate COVID-19 patients, especially in Indian settings, wherein data pertaining to these are sparse. Moreover, NEWS-2 and qSOFA scores do not use any laboratory or radiological parameters, making them convenient to use during patient admission for better triage. Therefore, timely identification of such patients could help, especially family and primary care physicians, in proper triaging, timely patient referral, and planning intensive medical care. It could further enhance clinical management protocols and resource allocation pertaining to Indian settings.

Thus, it is imperative to identify such patients at risk of progressing to a severe or critical disease state. This short single-center, observational study solely focused on the clinical profile, assessing NEWS-2, qSOFA, and CTSS scores on admission to predict progression to severe disease among moderate category COVID-19 patients at a dedicated COVID-19 hospital in Delhi during the second wave of COVID-19 in India. Moreover, the association of these scores with the inflammatory markers was also assessed in the study.

Materials and Methodology

Study design and criteria

This single-center, observational study was conducted over seven months from February to September 2021, in the Department of Medicine, Lok Nayak Hospital, New Delhi, where consecutive 100 laboratory-confirmed (Real-Time Polymerase Chain Reaction) or Rapid Antigen Test) COVID-19 patients belonging to the moderate category of clinical severity as per MoHFW criteria. As per the criteria, patients with pneumonia with clinical features of dyspnea and/or hypoxia, fever, cough, with a respiratory rate more or equal to 24 per minute or with SpO_2 < 94% (range 90%-93%) on room air with no sign of severe disease belong to the moderate category.[2,17] The study began after getting approval from the Institutional Ethical Committee of Maulana Azad Medical College and obtaining a written informed consent from each patient fulfilling the exclusion and inclusion criteria for participation in the study.

Inclusion and exclusion criteria

Laboratory-confirmed (Real-Time Polymerase Chain Reaction or Rapid Antigen Test) moderate category COVID-19 patients of age ≥18 years of either sex were recruited in the study. Females with pregnancy were excluded from the study.

Study size and sample size estimation

In a study among the 456 enrolled patients with moderate COVID-19, 55.0% had a poor prognosis. Poor prognosis referred to progression from moderate to severe, critical grade or death. Briefly, 33.99% of individuals worsened to a severe condition, 10.96% became critical cases, and 9.8% died.[18] Furthermore, due to the paucity of literature specifically on COVID-19 patients of the moderate category worldwide and in India, the sample size was calculated using the latest World Health Organization data which stated that 40% of COVID-19 patients developed disease of moderate clinical severity.[19]

The sample size was calculated with the following formula:

$N = Z^2(p)(1-p)/d^2$

Where, N = sample size

Z = 1.96 (confidence level of 95%)

p = population proportion (40%)

d = Precision required on either side of the proportion (10%)

The calculated sample size was found to be 92. The present study recruited about 100 laboratory-confirmed COVID-19 cases of the moderate category.

Outcome variables

Primary outcomes

1. To compare and correlate clinical, laboratory, and radiological characteristics of the moderate category COVID-19 patients based on the clinical end point in terms of progression to severe disease or not.

Secondary outcomes

1. To study the predictors of progression to severe disease among moderate COVID-19 patients during hospitalization and the correlation among qSOFA, NEWS-2, and CTSS scores and with inflammatory markers used in the study.

Methodology

In this study, 100 consecutive moderate-category COVID-19 patients, as per MoHFW criteria, were recruited based on inclusion and exclusion criteria after obtaining approval from the Institutional Ethical Committee and informed consent from each patient before participation. Patients underwent detailed clinical history, including demographic details, chief complaints, co-existing comorbidities, and relevant examination. Upon admission, routine vitals, including blood pressure (BP), respiratory rate, pulse rate, random blood sugar, and oxygen saturation via pulse oximeter, were measured along with calculating the NEWS-2 and qSOFA scores of every patient.

NEWS-2 score was calculated using respiratory rate, oxygen saturation, systolic BP, heart rate, level of consciousness, and temperature. The score was then calculated, and 2 points were added in case of supplemental oxygen need.[6] The qSOFA score included systolic blood pressure ≤ 100 mmHg, respiratory rate ≥22 breaths/min, and altered mental status. Each parameter was assigned 1 point, and the score was calculated by adding all points.[7]

Patients underwent a series of tests and evaluations to assess their condition. Upon admission, they underwent a bedside chest radiograph, blood parameters like complete blood counts, kidney function tests, liver function tests, serum electrolytes, inflammatory markers such as IL-6, ferritin, LDH, hs-CRP, D-dimer, INR, Procalcitonin, and BNP. Additionally, an arterial blood gas evaluation was also done. On the second or third day of admission, a computed tomography (CT) scan of the chest (HRCT, NCCT, or CECT) was performed for all the patients. The CTSS was calculated based on predefined radiological criteria.[8] During hospitalization, serum parameters and vitals were checked regularly to monitor the progression to severe disease. Severe disease was defined according to MoHFW criteria which states that patients with pneumonia and clinical features of dyspnea and or hypoxia, fever, and cough along with any one of the following: respiratory rate >30 breaths/min, severe respiratory distress, SpO_2 <90% on room air, or acute respiratory distress syndrome or sepsis/septic shock.[2] A proforma was used to collect relevant data, which included clinical history, symptomatology, vital profile, relevant examination findings, serum parameters, NEWS-2 score, and q-SOFA score on the admission day. Radiological assessments with chest CT were conducted on the second or third day. The collected data were tabulated and analyzed using appropriate statistical methods. During that period, patients were discharged after 10 days of symptom onset if symptoms resolved within three days and saturation more than 95% was maintained for the next four days without oxygen support.[20]

Statistical analysis

The data were compiled and analyzed using MS Excel (R) office 365, GraphPad prism 8.4.2 and SPSS version 25. Categorical variables were expressed in the form of proportions/percentages and compared using the Fisher's exact test/Chi-square test. Continuous variables were expressed as mean and standard deviation and analyzed using the Mann-Whitney test/Student's *t*-test (for independent group/unpaired data). A multivariate logistic regression analysis was done to assess the predictors of mortality with the risk assessment done in terms of Adjusted Odds-ratios (exp(B)) with 95% confidence interval (CI).

Results

Demographic and clinical profile

This study evaluated 100 consecutive moderate COVID-19 patients, 11 (11%) progressed to severe disease. Of those 11, eight died while three were discharged. The remaining 89 patients (89%) improved and were discharged without progressing to severe disease. The average age of patients was 55.6 ± 15.3 years (range 19-90) and most were male (n = 59). Those who progressed to severe disease tended to be older and of male gender. A comparative clinical profile of the study subjects is shown in Table 1a. The most common comorbidities were hypertension, followed by diabetes, while the most common complaints were dyspnea (95%), dry cough (88%), and fever (86%). Patients who progressed to severe disease were more likely to have chronic kidney disease (CKD), a longer duration of cough with expectoration, and a shorter duration of sore throat and vomiting. Statistical differences in respiratory rate and BP (systolic and diastolic) were seen; however, both systolic and diastolic BP were within the normal range.

Furthermore, patients who progressed to severe disease had a significantly higher average NEWS-2 score, with 72.73% (n = 8) scoring ≥7 and 45.45% (n = 5) having a qSOFA score of ≥2. In contrast, patients who did not progress to severe disease had a higher average glassgow coma scale (GCS) score and shorter hospital stay, Table 1a. Oxygen support was given to every patient; however, patients who progressed to severe disease needed high-flow nasal cannula (HFNC) (45.45%, n = 5) as a mode of oxygen supplementation. Among the patients who did not progress to severe disease, 28% (n = 25) were given supplemental oxygen via Venturi-Mask (VM) without further support for oxygenation. Patients with severe disease also had additional complications like acute kidney injury (n = 6) and fresh cerebral infarcts (n = 4).

Table 1a: Showing the clinical profiles of moderate category patients who progressed and who did not progress to severe disease during the hospital stay

Parameters	No progression to severe disease (*n*=89)	Progressed to severe Disease (*n*=11)	Overall (*n*=100)	*P* (<0.05=significant)
Demographic Profile				
Age [Mean±SD, years]	54.8±14.6	62.2±19.5	55.6±15.3	0.1297
Male [*n*, %]	51 (57.30)	8 (72.73)	59 (59)	0.3287
Comorbidity Profile (*n*, %)				
Hypertension	65 (73.03)	8 (72.73)	73 (73)	0.9118
Diabetes Mellitus	51 (57.30)	6 (54.55)	57 (57)	0.9317
Coronary Artery Disease	19 (21.35)	2 (18.18)	21 (21)	0.7365
Chronic Kidney Disease	6 (6.74)	4 (36.36)	10 (10)	0.0021
Chronic Obstructive Pulmonary Disease	3 (3.37)	1 (9.09)	4 (4)	0.3634
Chronic Liver Disease	3 (3.37)	0 (0.00)	3 (3)	0.5385
Symptom Profile (Mean±SD, days)				
Fever	4.08±1.52	3.71±1.12	4.05±2.38	0.6184
Dry Cough	4.44±2.52	4.13±2.48	4.41±2.24	0.2671
Cough with Expectoration	2.50±1.68	4.33±1.49	3.60±1.14	<0.0001
Vomiting	2.71±0.91	2.00±0.62	2.56±0.73	0.0137
Sore Throat	3.11±1.67	2.00±1.50	2.95±1.68	0.0383
Bodyache	4.06±1.59	3.83±1.79	4.03±1.67	0.6110
Loss of taste	3.88±2.15	4.00±2.16	3.89±1.76	0.6144
Loss of smell	4.00±1.49	5.00±2.64	4.14±2.27	0.3208
On Examination				
Glasgow Coma Scale (Mean±SD)	14.97±0.02	12.45±2.64	14.70±1.18	<0.0001
Systolic Blood Pressure (mm of Hg) (Mean±SD)	133.64±36.59	119.27±10.37	132.06±25.06	<0.0001
Diastolic Blood Pressure (mm of Hg) (Mean±SD)	83.08±15.49	76.91±19.64	82.40±12.17	<0.0001
Pulse Rate (beats/minute) (Mean±SD)	95.08±21.94	91.18±18.45	94.65±12.60	0.5736
Respiratory rate (breaths/minute (Mean±SD)	20.35±5.31	21.91±3.91	20.52±1.88	0.4633
Mode of Oxygen Support (*n*, %)				
Bilevel Positive Airway Pressure	34 (38.20)	3 (27.27)	37 (37)	0.4809
High-Flow Nasal Cannula	11 (12.36)	5 (45.45)	16 (16)	0.0050
Non-Rebreather Mask	19 (21.35)	3 (27.27)	22 (22)	0.6564
Venturi-Mask	25 (28.09)	0 (0.00)	25 (25)	0.0434
qSOFA Score				
0 (*n*, %)	41 (46.07)	0 (0.00)	41 (41)	0.0035
1 (*n*, %)	44 (49.44)	6 (54.55)	50 (50)	0.7504
2 (*n*, %)	4 (4.49)	5 (45.45)	9 (9)	<0.0001
NEWS2 Score				
Mean±SD	4.67±1.98	7.45±1.63	4.98±2.13	<0.0001
≥7 [High] (*n*, %)	17 (19.10)	8 (72.73)	25 (25)	0.0001
5 or 6 [Medium [(*n*, %)	30 (33.71)	3 (27.27)	33 (33)	0.6698
0-4 [low] (*n*, %)	42 (47.19)	0 (0.00)	42 (42)	0.0029
Complications (*n*, %)				
Acute Kidney Injury	17 (19.10)	6 (54.55)	23 (23)	0.0087
Diabetic Ketoacidosis	14 (15.73)	2 (18.18)	16 (16)	0.7169
Metabolic Acidosis	16 (17.98)	5 (45.45)	21 (21)	0.0358
Fresh cerebral infarcts	1 (1.12)	4 (36.36)	5 (5)	<0.0001
Mucormycosis	0 (0.00)	1 (9.09)	1 (1)	0.0045
Anemia	9 (10.11)	4 (36.36)	13 (13)	0.0151
Meningitis	0 (0.00)	2 (18.18)	2 (2)	0.0001
Duration of hospital stay [Mean±SD, days]	14.73±4.11	7.82±1.98	13.97±4.07	<0.0001

SD, Standard Deviation

Laboratory profile

Serum levels of LDH were raised in all the patients (n = 100), as shown in Table 1b. Moreover, patients who progressed to severe disease had significantly higher levels of serum Total Leukocyte Count (TLC), TLC of >11,000 cells/mm^3, Polymorphocytes/Lymphocytes ratio (P/L), AST, ALT, urea, creatinine, and all the

Table 1b: Comparing complete blood counts, biochemical profile, ABG analysis, and inflammatory markers between the groups

Parameters	No progression to severe disease (*n*=89)	Progressed to severe Disease (*n*=11)	Overall (*n*=100)	*P* (<0.05=significant)
Laboratory Profile (Mean±SD)				
Hb (12-15.5 g/dL)	11.67±3.29	10.73±3.15	11.565±2.31	0.3271
Hb <12 g/dL [*n*, %]	17 (19.10)	4 (36.36)	21 (21)	0.1871
TLC (cells/mm)	9,650.45±1,526.34	14,414.55±3,229.48	10,174.5±5,035.28	<0.0001
TLC >11,000 cell/mm^3 [*n*, %]	28 (31.46)	9 (81.82)	37 (37)	0.0012
P/L ratio	6.22±2.11	12.56±4.99	6.92±6.53	<0.0001
Platelet counts (1.50-4 lakhs/mm^3	1.98±0.49	1.60±0.35	1.9395±0.83	0.0145
Platelet counts <1.5 Lakhs/mm^3 [*n*, %]	28 (31.46)	9 (81.82)	27 (27)	0.4607
Total Bilirubin (0.2-1.3 mg/dL)	0.65±0.34	0.85±0.49	0.67±0.75	0.0838
Direct Bilirubin (mg/dL)	0.37±0.18	0.59±0.19	0.40±0.39	0.0002
AST (15-45 U/L)	59.33±31.02	144.45±45.51	68.69±96.30	<0.0001
ALT (5-50 U/L)	51.20±25.41	69.36±23.64	53.20±47.41	<0.0001
ALP (38-125 U/L)	105.70±30.97	122.91±40.88	107.59±56.80	0.0968
Blood Urea (19-43 mg/dL)	42.73±12.56	89.82±23.64	47.91±35.82	<0.0001
Serum creatinine (0.66-1.26 mg/dL)	1.19±0.51	2.68±1.24	1.35±1.67	<0.0001
Creatinine Phosphokinase-Total (55-170 U/L)	174.88±56.48	108.27±31.54	167.55±755.74	<0.0001
CPK-MB (0-25 U/L)	19.81±7.12	21.09±9.61	19.95±80.84	0.5902
Inflammatory Markers (Mean±SD)				
LDH (120-146 U/L)	351.31±90.37	441.18±162.35	361.20±109.63	0.0060
D-Dimer (<500 ng/ml)	836.36±255.84	1017.40±302.95	854.65±770.20	<0.0001
INR (<1.1)	1.00±0.33	1.03±0.46	1.00±0.23	0.6194
INR >1.2 [*n*, %]	6 (6.74)	4 (36.36)	10 (10)	0.0021
IL-6 (<7 pg/mL)	29.38±10.64	64.26±24.20	33.22±55.35	<0.0001
Hs-CRP (0.0-5.0 mg/L)	44.51±19.65	90.45±31.18	49.56±53.58	<0.0001
Ferritin Males=30-400 ng/ml Females=13-150 ng/ml	475.75±92.34	797.36±150.64	Males - 561.86±368.77 Females - 438.11±332.5	<0.0001
Procalcitonin (ng/mL)	1.27±0.61	11.49±3.84	2.40±9.27	<0.0001
Procalcitonin >2 [*n*, %]	11 (12.36)	6 (54.55)	17 (17)	0.0005
BNP (<125 pg/mL)	346.80±102.54	700.27±210.62	385.68±915.44	<0.0001
Arterial Blood Gas Analysis (ABG)				
pH <7.35 [*n*, %]	21 (23.60)	7 (63.64)	28 (28)	0.0055
PCO2 (35-45 mm Hg)	38.47±6.31	40.18±5.11	38.654±4.57	<0.0001
HCO3 <18 (mmol/L)	16 (17.98)	5 (45.45)	21 (21)	0.0055
Lactate (0.5-1.5 mmol/L)	1.02±0.618	2.31±2.11	1.1635±0.84	<0.0001
Lactate >1. 5 mmol/L [*n*, %]	23 (25.84)	10 (90.91)	33 (33)	<0.0001

Hb, Hemoglobin; TLC, Total Lymphocyte Count; hs-CRP, High-Sensitivity C-Reactive Protein; IL-6, Interleukin-6; INR, International Normalized Ratio; LDH, Lactate Dehydrogenase; P/L, Polymorphocytes/lymphocyte; ALP, Alkaline Phosphatase; ALT, Alanine Aminotransferase; AST, Aspartate Aminotransferase; BNP, Brain Natriuretic Peptide; pCO2, partial pressure of carbon dioxide

inflammatory markers, as well as INR of >1.2, procalcitonin of >2, pCO2, and lactate. They also had significantly lower platelet counts. However, the type of respiratory failure did not differ significantly, with most patients experiencing hypoxemic failure. Furthermore, patients with the severe disease also had significantly higher rates of deranged ABG profiles, including pH <7.35, HCO3 <18, and lactate >1.5.

Radiological profile

Chest radiograph showed consolidation in 98, followed by nodules and prominent broncho vascular markings in 50 and 29 patients. NCCT, CECT, and HRCT were performed in 72, 17, and 11 patients, respectively, which showed ground glass opacities and consolidation as the most common finding in 98 (98%) and 97 (97%) patients, respectively. Furthermore, the two groups had no significant differences regarding CT-based and chest radiograph findings except for intralobular septal thickening ($P = .0170$). However, the average CT severity score was 12.36 ± 4.12 (range: 23-2), and a higher score was seen in patients with progression to severe disease.

Predictors of severe disease among moderate COVID-19 patients

A multivariate analysis using logistic regression modelling was performed for the predictors of severe disease during the ward stay. The model had a predicted accuracy of 93.90%. The Hosmer and Lemeshow test were not significant (0.612), highlighting goodness of fit for the model [-2 Log likelihood: 38.119, Cox and Snell R Square: 0.268, Nagelkerke R Square: 0.535, Hosmer and Lemeshow Test: 6.311 (df = 8) ($P = .612$), and Predicted accuracy: 93.90].

The analysis revealed patients with male sex (1.25 times), CKD (2.86 times), leukocytosis (6.10 times), thrombocytopenia (1.04 times), anemia (9.3 times), higher qSOFA score (3.6 times), and higher NEWS-2 score on admission (1.56 times) had higher odds of progression to severe disease, as shown in Table 2.

ROC analysis for predictors of severe disease

An area under the curve (AUC) analysis based on the ROC curve was performed for various scores used in the study and their utility in predicting adverse outcomes. Based on the AUC analysis, it was seen that the qSOFA score and NEWS-2 score were the best modalities for progression to severe disease. NEWS-2 score, with an AUC of 85.8%, was slightly better than the qSOFA score, which had an AUC of 83.2%. The results for both these scores were significant statistically, as shown in Figure 1.

Correlation among qSOFA, NEWS-2 and CTSS scores and with inflammatory markers

Correlation among qSOFA, NEWS-2, and CTSS scores have been summarized in Table 3. A much stronger and significant correlation of qSOFA was seen with serum LDH, ferritin and hs-CRP, CTSS with the serum ferritin, IL-6 and LDH, and the NEWS-2 score with serum LDH, hs-CRP, and ferritin levels in the study. Furthermore, qSOFA and NEWS-2 scores were more positively correlated (Pearson r = 0.85, $P < .0001$), as shown in Figure 2a and b.

Discussion

This observational study recruited 100 consecutive moderate-category COVID-19 patients according to MoHFW criteria.[2] Due to a paucity of studies on the clinical profile of hospitalized moderate COVID-19, this study aimed to provide insights into it. The study's primary outcome was favourable, as only 11 patients (11%) of 100 progressed to severe disease, of which eight patients died and three patients were discharged, while the remaining 89 patients (89%) improved and were discharged. Thus, assessing the risk of progression to severe disease among moderate COVID-19 patients is crucial. Assessing these clinical characteristics on patient arrival could help physicians to plan further actions.

Demographic and clinical profile

The patients in our study had an average age of 55.6 ± 15.3 years (range: 90-19), with hypertension followed by diabetes being the most common comorbidities. Increasing age and multiple comorbidities are known risk factors for severe disease and unfavourable outcomes.[2,21-23] We found that patients who progressed to severe disease were older, male, and more likely to have CKD ($P = .0021$) as a comorbidity. Similarly, another study found that increased age, male gender, and CKD had a prognostic value for mortality and/or severe disease in COVID-19 patients.[5] Dyspnea, dry cough, and fever in order were the most common complaints, but those with severe disease had a longer duration of cough with expectoration, sore throat, and vomiting. Another study showed dyspnea as the only symptom predictive of severe disease and intensive care unit admission.[24]

Area Under the Curve

Test Result Variable(s)	Area	Std. Error	Asymptotic Sig	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
qSOFA score	.832	.057	.000	.721	.943
NEWS 2 SCORE (on admission)	.858	.050	.000	.761	.955
CT SEVERITY SCORE (OUT OF 25)	.637	.106	.140	.428	.846

b. Null hypothesis: true area = 0.5

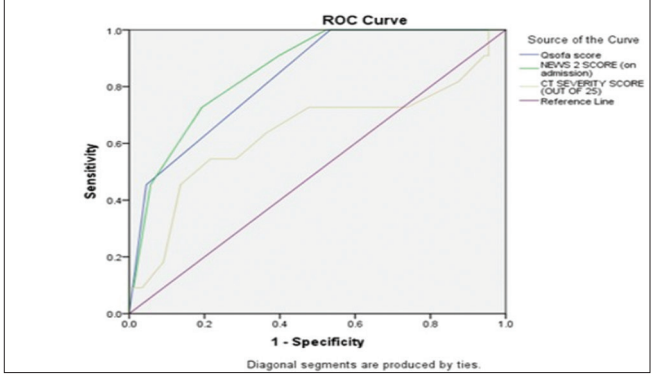

Figure 1: Based on the AUC analysis of the ROC curve, it was seen that the NEWS-2 score with an AUC of 85.8% was slightly better than the qSOFA score, which had an AUC of 0.832 or 83.2%. The results for both these scores were significant statistically. The qSOFA score and NEWS-2 score were the best modalities for predicting the progression to severe disease

Table 2: Variables with higher odds of progressing to severe disease using Multivariate Analysis logistic regression model

STEP 1a	B	S.E	Wald	df	Sig.	Exp (B)	95% CI for Exp (B) Lower	95% CI for Exp (B) Upper
Age in years	0.024	0.034	0.503	1	0.478	1.025	0.958	1.095
Sex	0.224	1.033	0.047	1	0.828	1.251	0.165	9.468
CKD	1.053	1.433	0.541	1	0.462	2.867	0.173	47.511
PClt1.5L	0.041	1.036	0.002	1	0.969	1.042	0.137	7.930
Hblt12	2.240	1.327	2.851	1	0.091	9.392	0.698	126.446
QSOFA score	1.303	1.405	0.860	1	0.354	0.3681	0.235	57.790
NEWS2 score	0.449	0.467	0.923	1	0.337	1.566	0.627	3.910
CT severity	0.145	0.164	0.781	1	0.377	0.865	0.626	1.194
Constant	-12.773	5.040	6.423	1	0.011	0.000		

Table 3: Showing the correlation of qSOFA, CTSS and NEWS 2 scores with inflammatory markers used in the study

Parameters	Pearson r	95% confidence interval	*R* squared	*P* (two-tailed)
qSOFA and Inflammatory markers				
LDH	0.58	0.44 to 0.70	0.34	<0.0001
CPK Total	-0.031	-0.23 to 0.17	0.00095	0.7611
D-DIMER	0.27	0.075 to 0.44	0.072	0.0073
INR	0.058	-0.14 to 0.25	0.0034	0.5657
IL-6	0.25	0.061 to 0.43	0.065	0.0106
hs-CRP	0.33	0.14 to 0.49	0.11	0.0009
Ferritin	0.38	0.19 to 0.53	0.14	0.0001
Procalcitonin	0.18	-0.012 to 0.37	0.034	0.0656
BNP	0.16	-0.036 to 0.35	0.026	0.1074
CTSS and inflammatory markers				
LDH	0.36	0.18 to 0.52	0.13	0.0002
CPK Total	0.14	-0.051 to 0.33	0.021	0.1465
D-DIMER	0.12	-0.080 to 0.30	0.014	0.243
INR	0.26	0.066 to 0.43	0.066	0.0089
IL6	0.38	0.20 to 0.53	0.14	<0.0001
HS-CRP	0.21	0.021 to 0.39	0.046	0.0301
FERRITIN	0.43	0.26 to 0.57	0.18	<0.0001
Procalcitonin	0.21	0.020 to 0.39	0.045	0.031
BNP	0.27	0.082 to 0.44	0.073	0.0057
NEWS 2 score and Inflammatory markers				
LDH	0.69	0.58 to 0.78	0.48	<0.0001
CPK Total	0.13	-0.060 to 0.32	0.018	0.1746
D-DIMER	0.33	0.15 to 0.49	0.11	0.0006
INR	0.28	0.088 to 0.44	0.076	0.0047
IL6	0.35	0.17 to 0.51	0.12	0.0003
HS-CRP	0.49	0.33 to 0.62	0.24	<0.0001
FERRITIN	0.45	0.28 to 0.59	0.2	<0.0001
Procalcitonin	0.35	0.16 to 0.50	0.12	0.0003
BNP	0.31	0.12 to 0.47	0.095	0.0014

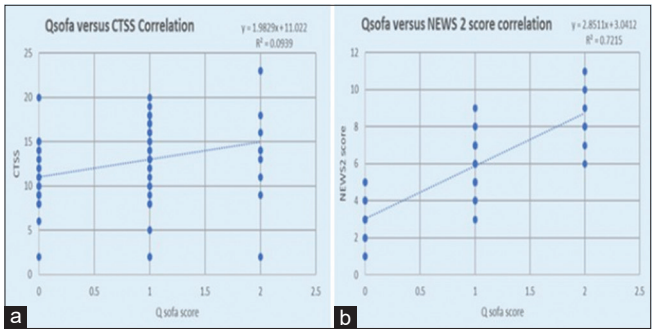

Figure 2: Scatter Diagram (a) qSOFA score and CTSS were positively and significantly correlated with each other (Pearson r - 0.31, 95% confidence interval - 0.12 to 0.48, R squared - 0.094, *P* (two-tailed) - 0.0020, *P* and lt; 0.05). (b) Similarly, qSOFA and NEWS-2 scores were positively and significantly correlated with each other (Pearson r - 0.85, 95% confidence interval - 0.78 to 0.90, R squared - 0.72, *P* (two-tailed) and lt; 0.0001, *P* and lt; 0.05)

Vitals assessment, calculation of qSOFA, and NEWS-2 score

In the severe group, there were significantly lower level of consciousness, GCS score, and BP (systolic and diastolic); however, both systolic and diastolic readings were within normal range. In a study, altered consciousness was directly linked to mortality, and a lower GCS score had increased mortality risk.[25] Similarly, increased mortality was seen in our study among severe COVID-19 patients. Patients in the severe group had a higher respiratory rate, a qSOFA score of 2 or more, and a higher NEWS-2 (score ≥7). Previous studies have shown that a NEWS-2 score of ≥6 at admission predicted severe disease and was superior to a qSOFA score of ≥2.[9] In another study, a NEWS-2 score of ≥5 at admission predicted mortality and the need for mechanical ventilation.[16] In our study, patients who progressed to severe disease had a higher respiratory rate and required HFNC as a mode of oxygen supplementation. Similarly, a Calligaro GL *et al.*[26] study found that HFNO for severe COVID-19 was feasible and helped to wean without mechanical ventilation. Hence, a higher respiratory rate, NEWS-2 score ≥7, and a qSOFA score of ≥2 could help identify at-risk individuals who need priority medical care.

Laboratory assessment

Patients who progressed to severe disease had significantly elevated levels of average serum TLC, TLC of >11,000 cells/mm^3, a higher P/L (Polymorphocytes/Lymphocytes) ratio, AST, ALT, urea, and serum creatinine. Additionally, they exhibited significantly elevated inflammatory markers (LDH, D-dimer,

IL-6, hs-CRP, ferritin, procalcitonin, BNP) as well as deranged ABG profile (pH <7.35, HCO3 <18, lactate >1.5) and lower platelet count. These laboratory findings are consistent with previous studies.[21,27-29] Studies have shown that raised NLR, CRP, and serum ferritin levels at admission could predict severity.[18,19] Furthermore, elevated NLR ratio and CRP on admission have been associated with progression to critical condition and death among moderate COVID-19 patients.[18] Raised levels of inflammatory markers, CRP, procalcitonin, IL-6, and D-dimer levels have been liked to mortality and unfavourable outcomes.[12,20] A progressive decline in the lymphocyte count and a rise in the D-dimer were seen in nonsurvivors compared to survivors.[27] Other studies have shown similar results using inflammatory markers in predicting outcomes among COVID-19 patients.[5,30-32] Moreover, our study found no difference in respiratory failure distribution between the two groups. However, acute respiratory distress syndrome was identified as the significant cause of mortality in patients who deteriorated. Overall, the laboratory findings are consistent with previous studies, highlighting the importance of monitoring inflammatory markers and laboratory parameters to predict disease severity and outcomes.

Radiological assesemnt

The baseline CT severity score was higher in patients who progressed to severe disease (14.27 vs. 12.13, P = .1038). Similarly, a study showed a higher CTSS score was associated with the severity of COVID-19, oxygen requirement, and length of hospital stay.[12] Another retrospective study found A CT score of ≥18 predictive of death and associated with increased mortality risk, especially in severe and critical patients.[8] Likewise, our study also showed that a higher baseline CTSS could help predict severe disease.

NEWS-2, qSOFA, and CTSS scores and their correlation with inflammatory markers

Our study found stronger correlation between the qSOFA score and serum levels of LDH, ferritin and hs-CRP, CTSS with the serum ferritin, IL-6 and LDH levels, and NEWS-2 score with serum LDH, hs-CRP, and ferritin levels. According to ROC curve analysis, the qSOFA (AUC of 0.832 or 83.2%) and NEWS-2 (AUC of 0.858 or 85.8%) scores were significant predictors of severe disease, with NEWS-2 being slightly better.

Another study found NEWS-2 score was superior to CRB-65 and SIRS criteria and predicted severe disease and in-hospital mortality better than qSOFA on admission.[9] A Chinese study also showed that the baseline NEWS-2 score was superior to qSOFA in predicting mortality among hospitalized COVID-19 patients.[10] CT severity score positively correlated with lymphopenia, increased serum CRP, d-dimer, ferritin levels, and COVID-19 severity in terms of oxygen requirement and hospital stay.[12] Similarly, raised CRP levels have been proposed as a predictor of COVID-19 severity, with a positive correlation with abnormal CT findings.[32] In our study, higher chest CTSS was significantly correlated with the serum ferritin, IL-6, and LDH levels and could aid in predicting severe disease in hospitalized moderate COVID-19 patients.

Numerous previous studies have shown similar correlation findings.[18,33-40] A systematic review showed variables like male sex, chronic kidney disease, high blood procalcitonin, high WBC count, high blood lactate, low blood platelet count, high blood D-dimer, high LDH, high CRP, high IL-6, high blood neutrophil count, and high BNP had prognostic value for mortality and/or severe disease in COVID-19 patients, similar to our study.[5] However, in our study, CPK-total was significantly elevated among nonsevere disease patients, while the MB fraction was comparable. This could be due to a small sample size in the severe group. Therefore, assessing the clinical scores like NEWS-2 and qSOFA, along with the inflammatory markers, could help in early triaging, predicting the risk of progression, and guiding treatment decisions.

We found a dearth of literature on studies solely focussed on the clinical profile of the hospitalized moderate-category of COVID-19 patients as per MoHFW criteria in India or worldwide. Thus, we conducted a brief study on such patients' clinical, laboratory, and radiological profiles and explored predictors of progression to severe disease by using scores like qSOFA, NEWS-2, and CTSS and their correlation. Therefore, our study brings out vital considerations to be kept while dealing with moderate COVID-19 patients, like clinical profile and using scores like NEWS-2 or qSOFA, especially for primary care physicians and family physicians, to plan timely referrals and medical care.

Limitation of Study

The study had limited statistical power due to a smaller sample size, being single-centered toward the end of the second wave of COVID-19 in India. A follow-up and including additional risk prediction scores like SOFA could have made the results more meaningful. Large-scale studies with extensive sample sizes are necessary to explore further and validate our findings.

Conclusion

Moderate COVID-19 patients can progress to severe disease and further complications. Our study found patients of the male gender, CKD as comorbidity, a TLC of >11,000/mm^3, platelet count of <1.5 lakhs/mm^3, Hb of <10 g/dL, higher qSOFA score (≥2), and higher NEWS-2 score on admission had higher odds of progression to severe disease. qSOFA, CTSS, and NEWS-2 scores significantly correlated with inflammatory markers. NEWS-2 score (AUC 85.8%) slightly better predicted progression to severe disease than the qSOFA score (AUC 83.2%). These findings can help in the clinical management and monitoring of moderate COVID-19 patients.

Recommendations and future prospects

Through our study, we would like other studies to validate our findings, especially in the Indian settings and assess the

manifestations of long COVID-19 syndrome in moderate COVID-19 and further follow-up.

Key take-home message

Physicians should be well worse with clinical profile and predictors of severe disease among moderate COVID-19 patients. These found in our study are as follows:

Clinical Profile: Elderly, Male gender, CKD comorbidity, altered sensorium, low GCS score, and a higher NEWS-2 (score ≥7) better than a qSOFA score of ≥2.

Laboratory Profile: Elevated levels of serum TLC, TLC of >11,000 cells/mm^3, a higher P/L (Polymorphocytes/Lymphocytes) ratio, AST, ALT, urea, serum creatinine, inflammatory markers (LDH, D-dimer, IL-6, hs-CRP, ferritin, procalcitonin, BNP), as well as deranged ABG profile (pH <7.35, HCO3 <18, lactate >1.5), and lower platelet count.

Radiological Profile: Higher baseline CT severity score.

Hence, correlating clinical assessment with risk prediction scores like NEWS-2 score and qSOFA and inflammatory markers could aid in better patient triaging and management.

Declaration of patient consent

All authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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