Journal of Acute Disease

Original Article

doi: 10.4103/2221-6189.312154 jadweb.org

Clinical, laboratory and radiological features and outcomes of moderate to severe COVID−19 patients: A descriptive retrospective study

Hardeva Ram Nehara[1], Sahaj Agrawal[1], Atma Ram Chhimpa[2], Sunil IH[1], Avadusidda Arakeri[1], Pramendra Sirohi[1]✉

Department of [1]Medicine, [2]Geriatric Medicine, SP Medical College, Bikaner, Rajasthan, India

ABSTRACT

Objective: To describe the clinical, laboratory and radiological characteristics and outcomes of moderate-to-severe coronvirus disease 2019 (COVID-19) patients.

Methods: We retrospectively analyzed 43 RT-PCR confirmed moderate-to-severe COVID-19 patients who were admitted to a tertiary care center. The primary composite outcomes were admission to intensive care unit, requirement of mechanical ventilation, and death.

Results: The median age of the patients was 50 years, and 62.8% of the patients were male. Out of 43 patients, 15 (34.88%) were categorized as severe. A total of 26 (60.47%) patients had 1 or more comorbidities [diabetes (34.88%) and hypertension (30.23%)]. The median duration from the onset of symptoms to admission was 3 days, and the most common symptoms were dyspnoea (90.7%), cough (79.07%), fever (69.77%), and body ache (46.51%). Leucopenia was presented in 14 (32.56%) patients, lymphopenia in 26 (60.47%) patients, and monocytosis in 7 (16.28%) patients. Besides, 40 (93.02%) patients had bilateral patchy nodular or interstitial infiltration on chest X-ray. The primary outcomes occurred in 20 patients (46.5%), among whom 8 required mechanical ventilation. The patients who had met the primary outcomes were older. They were prone to have at least 1 comorbidity (P=0.004), diabetes (P=0.01), hypertension, higher sequential organ failure assessment score, more tachycardia, lower SpO_2, lower PaO_2/FiO_2, more thrombocytopenia, and more pancytopenia.

Conclusions: This retrospective study identified several risk factors for poor outcomes in adults with COVID-19. In particular, older age, tachycardia, high SOFA score, low SpO_2, low PaO_2/FiO_2, presence of comorbidities in form of diabetes and hypertension, thrombocytopenia, and pancytopenia at admission were associated with higher odds of ICU admission, a requirement of mechanical ventilation and in-hospital death.

KEYWORDS: SARS-CoV-2; COVID-19; Moderate to severe; Outcome

1. Introduction

Severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) is the causative agent of the corona virus disease 2019 (COVID-19) that was declared as a global pandemic by World Health Organization on 11 March 2020. COVID-19 has an enormous effect on the health care system throughout the world and led to a huge mortality worldwide[1]. COVID-19 infection encompasses asymptomatic infection, mild upper respiratory tract illness, fever, cough, shortness of breath, fatigue, pneumonia, and other respiratory tract symptoms and in many cases, it progressed to respiratory failure and death. Patients who have any underlying comorbidities are more prone to serious illness after the infection[2,3]. The pathogenesis of COVID-19 is not understood yet but extensive damage of the lung is seen, which is associated with high initial viral load, neutrophil infiltration in the lung, and explosive elevated levels of proinflammatory cytokines and chemokines, and rapid decrease in peripheral T lymphocytes[4].

The majority of patients with COVID-19 infection had only mild symptoms, but around 15% of patients developed moderate-to-

✉To whom correspondence may be addressed. E-mail: drpsirohi@gmail.com

How to cite this article: Nehara HR, Agrawal S, Chhimpa AR, IH S, Arakeri A, Sirohi P. Clinical, laboratory, radiological features and outcome of moderate to severe COVID-19 patients: A descriptive retrospective study. J Acute Dis 2021; 10(2): 62-70.

Article history: Received 26 September 2020; Revision 4 March 2021; Accepted 10 March 2021; Available online 29 March 2021

severe disease that requires hospital admission and oxygen support, and approximately 5% required admission to an intensive care unit (ICU)[5]. At present, no effective therapy has been approved for COVID-19. Many drugs are being tried under the compassionate medication principle including remdesivir, tocilizumab, a monoclonal antibody against interleukin-6 (IL-6), and convalescent plasma with variable results[6-8].

The objective of this study is to describe the clinical, laboratory, radiological characteristics, and outcomes in moderate-to-severe COVID-19 patients who were successively hospitalized from 26th July 2020 to 10th August 2020.

2. Patients and methods

2.1. Study design and study population

This descriptive retrospective study included moderate-to-severe COVID-19 adult patients (>18 years of age) admitted in a dedicated COVID hospital, SP Medical College, Bikaner, a tertiary care center in Rajasthan. The study included all the adult patients with moderate-to-severe COVID-19 confirmed by RT-PCR admitted between 26th July 2020 and 10th August 2020. Diagnosis, classification of severity, and management were done as per protocol suggested by the Indian Ministry of Health and Family Welfare (MoHFW)[9].

2.2. Ethical approval

The study is approved by the Institutional Ethics and Research Board of SP Medical College, Bikaner (Rajasthan) India. Approval No. F. 29 (Acad) SPMC/2020/3327, dated 24/09/2020.

2.3. Data collection

Demographic, clinical, laboratory, radiological, course of management and outcomes were analyzed from all COVID-19 patients admitted in the hospital and categorized as moderate-to-severe disease as per MoHFW guideline. All clinical data regarding the history and clinical examination including heart rate, blood pressure, respiratory rate, SpO_2, Glasgow coma scale (GCS), and sequential organ failure assessment (SOFA) score, management, and outcomes were analyzed.

2.4. Primary outcomes

The primary composite outcomes were admission to ICU, requirement of mechanical ventilation and death.

2.5. Laboratory procedures

The nasal and nasopharyngeal swabs were taken for confirmation of COVID-19 using RT-PCR. All patients underwent blood investigations including complete blood count, plasma glucose, renal function, liver function, creatine kinase-MB (CK-MB), electrolytes, C-reactive protein, and arterial blood gases. Chest radiographs were also done for all patients and 6 patients underwent chest high-resolution computed tomography (HRCT). All demographical, clinical, and laboratory data were prospectively recorded.

2.6. Definitions

COVID-19 patients were categorized as moderate and severe as per the MoHFW guideline. Patients with clinical signs of pneumonia plus one of the following: respiratory rate>30 breaths/min, SpO_2<90% on room air were classified as severe. Patients with SpO_2<94% (90%-93%) on room air or respiratory rate of 24-30 per minute were classified as moderate[9]. Tachycardia was defined as heart rate more than 100 per minute; tachypnea was defined as respiratory rate more than 30 per minute; hypotension was defined as systolic BP less than 90 mmHg; leucopenia was defined by a total leucocyte count of less than 4 000 mm^3; lymphopenia was defined as an absolute lymphocyte count of less than 1 500 mm^3; monocytosis was defined as an absolute monocyte count of more than 950 mm^3; anemia was defined as hemoglobin less than 12 for females and less than 13 for males; thrombocytopenia was defined as a platelet count of less than 150 000 mm^3. Acute kidney injury (AKI) was diagnosed according to the KDIGO clinical practice guidelines[10]. Hypoalbuminemia was diagnosed when serum albumin was<3.5 g/dL.

2.7. Statistical analysis

All statistical analyses were performed using SPSS version 16.0 software. Continuous variables were represented using mean, median and interquartile range (IQR), and categorical variables were represented as frequency and percentage. Means for continuous variables were compared using independent *t*-tests if the data were normally distributed, otherwise, the Mann-Whitney test was used. *Chi*-square test was used to check proportions for categorical variables. The co-relation of clinical profile, presence of co-morbidities, and laboratory parameters with primary outcomes were analyzed by using the Pearson correlation coefficient. The significance level of the study was set at α=0.05.

3. Results

3.1. Demographic and clinical characteristics

The demographic characteristics, comorbidities, and symptoms of the patients are as shown in Table 1. The study population included 43 patients, out of which 28 (65.12%) patients were categorized as moderate, and 15 (34.88%) were categorized as severe COVID-19. The median age was 50 years (IQR: 44-62), and 27 (62.8%) patients were males. Out of the 43 patients, 19 (44.2%) patients did not report any history of contact with a COVID-19 patient or any travel history. Out of 43 patients, 20 patients (15

Table 1. Demographic characteristics, comorbidities and symptoms of the patients.

Baseline characteristics	Total (*n*=43)	Clinical category				Presence of primary composite outcomes			
		Moderate (*n*= 28)	Severe (*n*=15)	χ^2	*P*-value	Yes (*n*=20)	No (*n*=23)	χ^2	*P*-value
Sex									
Male	27 (62.79%)	18 (64.29%)	9 (60.00%)	0.07	0.43#	13 (65.00%)	14 (60.87%)	2.69	0.290#
Female	16 (37.21%)	10 (35.71%)	6 (40.00%)			7 (35.00%)	9 (39.13%)		
Co-morbidities									
Co-morbidities (at least 1)	26 (60.47%)	16 (57.14%)	10 (66.67%)	0.37	0.74	17 (85.00%)	9 (39.13%)	6.42	0.004*
Co-morbidities (at least 2)	11 (25.58%)	6 (21.43%)	5 (33.33%)	0.72	0.47	8 (40.00%)	3 (13.04%)	7.03	0.070
Diabetes mellitus	15 (34.88%)	8 (28.57%)	7 (46.67%)	1.40	0.31	11 (55.55%)	4 (17.39%)	6.96	0.010*
Hypertension	13 (30.23%)	7 (25.00%)	6 (40.00%)	1.04	0.32	9 (45.00%)	4 (17.39%)	4.85	0.090
CAD	3 (6.98%)	2 (7.14%)	1 (6.67%)	0.03	0.99	3 (15.00%)	0 (00.00%)	14.10	0.090
CKD	1 (2.33%)	0 (0.00%)	1 (6.67%)	1.91	0.34	1 (5.00%)	0 (00.00%)	4.48	0.460
COPD	2 (4.65%)	2 (7.14%)	0 (0.00%)	1.12	0.53	1 (5.00%)	1 (4.35%)	0.48	0.990
Bronchial asthma	4 (9.30%)	3 (10.71%)	1 (6.67%)	0.19	0.99	2 (10.00%)	2 (8.70%)	1.00	0.990
Hypothyroidism	2 (4.65%)	2 (7.14%)	0 (0.00%)	1.12	0.53	1 (5.00%)	1 (4.35%)	1.36	0.990
Symptoms									
Fever	30 (69.77%)	18 (64.29%)	12 (80.00%)	1.14	0.48	15 (75.00%)	15 (65.22%)	1.47	0.520
Headache	9 (20.93%)	4 (14.29%)	5 (33.33%)	2.14	0.23	8 (40.00%)	1 (4.35%)	37.13	0.006*
Body ache	20 (46.51%)	11 (39.29%)	9 (60.00%)	1.68	0.21	12 (60.00%)	8 (34.78%)	3.21	0.130
Fatigue	18 (41.86%)	10 (35.71%)	8 (53.33%)	1.25	0.33	10 (50.00%)	8 (34.78%)	1.72	0.360
Anosmia	4 (9.30%)	2 (7.14%)	2 (13.33%)	0.44	0.60	3 (15.00%)	1 (4.35%)	1.00	0.320
Ageusia	3 (6.98%)	2 (7.14%)	1 (6.67%)	0.01	0.99	2 (10.00%)	1 (4.35%)	0.46	0.580
Cough	34 (79.07%)	20 (71.43%)	14 (93.33%)	2.83	0.12	17 (85.00%)	17 (73.91%)	0.42	0.460
Sore throat	12 (27.91%)	8 (28.57%)	4 (26.67%)	0.01	0.99	6 (30.00%)	6 (26.09%)	0.04	0.990
Nasal discharge	5 (11.63%)	2 (7.14%)	3 (20.00%)	1.57	0.32	1 (5.00%)	4 (17.39%)	1.29	0.350
Hemoptysis	1 (2.23%)	0 (0.00%)	1 (6.67%)	1.91	0.34	1 (5.00%)	0 (0.00%)	4.48	0.460
Dyspnea	39 (90.70%)	24 (85.71%)	15 (100.00%)	2.36	0.28	19 (95.00%)	20 (86.96%)	1.00	0.610
Chest pain	11 (25.58%)	4 (14.29%)	7 (46.67%)	5.38	0.03*	8 (40.00%)	3 (13.04%)	3.08	0.070
Vomiting	11 (25.58%)	4 (14.29%)	7 (46.67%)	5.38	0.03*	8 (40.00%)	3 (13.04%)	3.08	0.070
Loose stools	1 (2.23%)	1 (3.57%)	0 (0.00%)	0.44	0.99	1 (5.00%)	0 (0.00%)	0.11	0.460
Altered sensorium	1 (2.23%)	0 (0.00%)	1 (6.67%)	1.91	0.34	0 (0.00%)	1 (4.35%)	0.23	0.990

IQR: Interquartile range; CAD: Coronary artery disease; CKD: Chronic kidney disease; COPD: Chronic obstructive pulmonary disease; #: comparison between different gender; *: statistically significant.

severe and 5 moderate) were shifted to ICU and among these, 8 (18.6%) patients required mechanical ventilation and subsequently expired, and the rest 12 (27.9%) patients recovered and were subsequently shifted to a non-COVID-19 ward after 2 consecutive negative RT-PCR 24 hours apart. Patients with severe COVID-19 were older than moderate COVID-19 by a median of 7 years. The patients who had met the primary outcomes were older with a median of 17 years (*P*=0.001). The median duration from the onset of the first symptom to hospital admission was 3 d (IQR: 2-5). The most common symptom was dyspnoea (90.7%) followed by cough (79.07%), fever (69.77%), and body ache (46.51%). Less common symptoms were fatigue, sore throat, chest pain, vomiting, headache, nasal discharge, anosmia, ageusia, loose stools, hemoptysis, and altered sensorium in decreasing order. Out of 43 patients, 26 (60.47%) had 1 or more co-morbidities. Diabetes mellitus (34.88%), hypertension (30.23%), and obstructive airway disease that include COPD and bronchial asthma (13.95%) were the three commonest comorbidities. Patients who met the primary outcomes (*n*=20) were more likely to be having at least one underlying comorbidity [17 (85.00%) *vs.* 9 (39.13%)], diabetic [11 (55.55%) *vs.* 4 (17.39%)] and headache [8 (40.00%) *vs.* 1 (4.35%)] compared with patients who did not meet the primary outcomes (*n*=23). There was a significant positive correlation between age (*r*=0.58; *P*<0.001), presence of at least 1 comorbidity (*r*=0.47; *P*=0.002), presence of diabetes (*r*=0.39; *P*=0.009), presence of hypertension (*r*=0.32; *P*=0.03) and composite outcomes (Table 2).

3.2. Laboratory and radiological findings

The laboratory parameters and radiological findings of the patients on admission are shown in Table 3. On admission, raised CK-MB was presented in 28 (65.12%) patients and was the most common laboratory finding, followed by anemia 27 (62.79%). Leucopenia was presented in 14 (32.56%) of the patients, with more than half of the patients have lymphopenia 26 (60.47%) and 7 (16.28%) patients have monocytosis. Neutrophil lymphocyte ratio (NLR) was 3.20 (IQR: 2.04-5.90) and was significantly higher in patients with severe disease [3.67 (2.50-5.90) *vs.* 2.97 (2.08-4.03); *P*=0.002) (Table 4). Thrombocytopenia was seen in 11 (25.58%) patients and pancytopenia in 6 (13.95%). Pancytopenia, and thrombocytopenia were found to be significantly more in patients who met the primary outcomes.

All the patients had abnormal chest X-rays at the time of admission. Out of 43 patients with moderate-to-severe COVID-19, 40 (93.02%) patients had bilateral patchy nodular or interstitial shadows in the peripheral and basal region. Three (6.98%) patients had unilateral patchy nodular infiltrates. Significant improvement in X-ray findings was seen after treatment in those patients who

Table 2. Correlation of clinical parameters, presence of co-morbidities, and laboratory parameters with the composite outcome.

Clinical parameters	*R*	95%*CI*	*P*-value
Age	0.58	44.31-76.39	<0.001*
HR	0.52	0.20-0.61	<0.001*
RR	0.29	21.32-40.87	0.050
SOFA	0.63	3.50-5.69	<0.001*
GCS	−0.24	9.68-19.71	0.130
SpO_2	−0.45	57.35-118.25	0.002*
PaO_2/FiO_2	−0.31	176.00-205.10	0.040*
Co-morbidities			
Co-morbidities (at least 1)	0.47	0.19-0.76	0.002*
Co-morbidities (at least 2)	0.31	0.01-0.69	0.041*
Diabetes mellitus	0.39	0.11-0.71	0.009*
Hypertension	0.32	0.02-0.67	0.030*
CAD	0.29	0.02-1.16	0.060
CKD	0.16	−0.48-1.57	0.290
COPD	0.02	−0.71-0.78	0.920
Hypothyroidism	0.02	−0.71-0.78	0.920
Laboratory parameters			
Leucopenia	0.05	−0.28-0.38	0.760
Lymphopenia	0.01	−0.33-0.31	0.950
Monocytosis	0.22	−0.12-0.71	0.160
Thrombocytopenia	0.31	0.05-0.72	0.040*
Anaemia	0.24	−0.07-0.56	0.130
Pancytopenia	0.43	0.23-0.53	0.004*
Deranged LFT	0.25	−0.06-0.62	0.100
AKI	0.24	0.23-1.67	0.110
Hypoalbuminemia	0.30	0.17-0.54	0.050
Raised CK-MB	0.29	0.01-0.63	0.050
Bilateral chest infiltrates	0.26	0.09-1.83	0.090

HR: heart rate; RR: respiratory rate; GCS: Glasgow coma scale; SOFA: sequential organ failure assessment; SpO_2: oxygen saturation; PaO_2: partial pressure of oxygen in arterial blood; FiO_2: fraction of inspired oxygen; CAD: coronary artery disease; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; LFT: liver function test; AKI: acute kidney injury; CK-MB: creatine kinase; *: statistically significant.

Table 3. Laboratory and radiological findings of the study patients.

Baseline characteristics	Total (*n*=43)	Clinical category				Presence of primary composite outcome			
		Moderate (*n*=28)	Severe (*n*=15)	χ^2	*P*-value	Yes (*n*=20)	No (*n*=23)	χ^2	*P*-value
Leucopenia	14 (32.56%)	9 (32.14%)	5 (33.33%)	0.006	0.930	7 (35.00%)	7 (30.43%)	0.100	0.750
Lymphopenia	26 (60.47%)	14 (50.00%)	12 (80.00%)	3.670	0.060	12 (60.00%)	14 (60.87%)	0.003	0.950
Monocytosis	7 (16.28%)	5 (17.86%)	2 (13.33%)	0.140	0.700	5 (25.00%)	2 (8.70%)	2.080	0.140
Thrombocytopenia	11 (25.58%)	7 (25.00%)	4 (26.67%)	0.010	0.900	8 (40.00%)	3 (13.04%)	4.080	0.040*
Anaemia	27 (62.79%)	16 (57.14%)	11 (73.33%)	1.090	0.290	15 (75.00%)	12 (52.17%)	2.380	0.120
Pancytopenia	6 (13.95%)	3 (10.71%)	3 (20.00%)	0.700	0.400	6 (30.00%)	0 (0.00%)	8.010	0.005*
Hepatic dysfunction	12 (27.91%)	3 (10.71%)	9 (60.00%)	11.790	0.001*	8 (40.00%)	4 (17.39%)	2.710	0.090
AKI	14 (32.56%)	6 (21.43%)	8 (53.33%)	4.520	0.030*	9 (45.00%)	5 (21.74%)	2.630	0.100
Hypoalbuminemia	15 (34.88%)	5 (17.86%)	10 (66.67%)	10.240	0.001*	10 (50.00%)	5 (21.74%)	3.760	0.050
Raised CK-MB	28 (65.12%)	13 (46.43%)	15 (100.00%)	12.340	<0.001*	17 (85.00%)	11 (47.83%)	3.760	0.050
B/L chest infiltrates	40 (93.02%)	25 (89.29%)	15 (100.00%)	0.720	0.180	20 (100.00%)	20 (86.96%)	2.800	0.090

AKI: acute kidney injury; Raised CK-MB >25 IU/L; CK-MB: Creatine kinase; B/L: Bilateral; *: Statistically significant.

recovered (Figure 1A and 1B). Six patients underwent chest HRCT, out of which, 2 patients had 25% lung field involvement, 2 patients had 25%-50% lung field involvement, and 1 patient had 50%-75% lung field involvement. On HRCT most common findings were the patchy area of ground-glass opacity predominantly subpleural in location (Figure 2A and 2B). There was a significant positive correlation between thrombocytopenia (r=0.31; P=0.04), pancytopenia (r=0.43; P=0.004), and composite outcomes (Table 2).

3.3. Vital signs and organ dysfunction

The clinical characteristics and vital signs of the patients are represented in Table 5. These parameters were recorded on the day of admission. Patients with a severe category had more tachycardia, tachypnea, and reduced levels of SpO_2 and PaO_2/FiO_2 as expected. The patients who met the primary composite outcomes had significantly more tachycardia [13 (65.0%)] and hypotension [6 (30%)]. Patients who met the primary composite outcomes also had higher SOFA scores. The median SpO_2 was 89.5%, PaO_2/FiO_2 was

Table 4. Quantitative laboratory parameters of the study patients.

Baseline clinical characteristics	Total (n=43)	Clinical category				Presence of primary composite outcomes			
		Moderate (n=28)	Severe (n=15)	t/U	P-value	Yes (n=20)	No (n=23)	t/U	P-value
Hb (g/dL) [median (IQR)]	12.28 (6.10-16.80)	12.70 (6.10-16.80)	11.90 (9.80-13.60)	0.87	0.380	11.65 (6.10-15.70)	12.60 (9.80-16.80)	2.13	0.030*
WBC counts (cells×10^3/μL) [median (IQR)]	5.26 (3.10-31.50)	6.28 (3.26-31.50)	4.80 (3.10-11.70)	1.52	0.130	4.62 (3.24-31.50)	5.66 (3.10-13.20)	1.02	0.310
Neutrophil count (cells×10^3/μL) [median (IQR)]	67.00 (55.80-77.00)	66.10 (55.80-74.20)	68.20 (64.70-77.00)	1.33	0.190	68.40 (63.50-73.10)	66.20 (55.80-77.00)	1.20	0.230
Lymphocyte count (cells×10^3/μL) [median (IQR)]	21.20 (11.70-28.50)	22.80 (18.30-28.50)	19.20 (11.70-25.90)	1.99	0.050	21.15 (11.70-27.00)	21.20 (16.60-28.50)	0.67	0.500
NLR [median (IQR)]	3.20 (2.04-5.90)	2.97 (2.08-4.03)	3.67 (2.50-5.90)	3.30	0.002*	3.35 (2.35-5.90)	3.13 (2.07-4.23)	1.61	0.110
Monocyte count (cells×10^3/μL) [median (IQR)]	8.20 (4.20-18.10)	7.35 (4.20-15.00)	9.20 (7.60-18.10)	0.53	0.590	9.45 (5.20-18.10)	7.10 (4.20-11.20)	2.13	0.030*
Platelets (cells×10^3/μL) [median (IQR)]	1.64 (1.34-4.20)	1.60 (1.35-4.20)	1.86 (1.34-3.21)	0.06	0.950	1.57 (1.34-3.21)	1.76 (1.45-4.20)	1.35	0.180
CK-MB (U/L) [median (IQR)]	33.00 (15.00-62.00)	25.00 (15.00-52.00)	52.00 (33.00-62.00)	7.23	<0.001*	30.50 (15.00-62.00)	33.00 (18.00-58.00)	0.62	0.530
AST (U/L) [median (IQR)]	34.00 (18.00-107.00)	31.50 (18.00-90.00)	44.00 (24.00-107.00)	3.40	0.001*	39.50 (24.00-107.00)	32.00 (18.00-104.00)	1.86	0.060
ALT (U/L) [median (IQR)]	34.00 (13.00-102.00)	32.00 (13.00-51.00)	46.00 (18.00-102.00)	3.12	0.003*	35.00 (13.00-96.00)	32.00 (18.00-102.00)	0.83	0.400
Creatinine (mg/dL) [median (IQR)]	0.84 (0.48-2.60)	0.80 (0.48-2.60)	1.10 (0.80-1.64)	0.91	0.360	0.95 (0.50-2.60)	0.76 (0.68-1.20)	2.81	0.007*
Albumin (g/dL) [median (IQR)]	3.65 (2.80-4.80)	3.79 (2.90-4.80)	3.40 (2.80-4.04)	3.11	0.003*	3.49 (2.80-4.03)	3.84 (3.30-4.80)	3.93	0.001*

Hb: hemoglobin; WBC: white blood cell counts; NLR: neutrophil to lymphocyte ratio; CK-MB: creatine kinase; AST: aspartate transaminase; ALT: alanine transaminase; *: statistically significant.

Table 5. Baseline clinical characteristics and vital signs of the study patients.

Baseline clinical characteristics	Total (n=43)	Clinical severity				Presence of primary composite outcomes			
		Moderate (n=28)	Severe (n=15)	$\chi^2/t/U$	P-value	Yes (n=20)	No (n=23)	$\chi^2/t/U$	P-value
GCS [median (IQR)]	15.00 (12.00-15.00)	15.00 (12.00-15.00)	15.00 (15.00-15.00)	1.04	0.310	15.00 (12.00-15.00)	15.00 (12.00-15.00)	1.56	0.120
GCS<15 [n (%)]	2 (4.65%)	2 (7.14%)	0 (0.00%)	1.12	0.280	2 (10.00%)	0 (0.00%)	2.41	0.100
HR [median (IQR)]	99.00 (84.00-136.00)	96.50 (84.00-126.00)	122.00 (108.00-136.00)	7.69	0.001*	115.00 (96.00-136.00)	96.00 (84.00-128.00)	3.35	0.002*
HR > 100/min [n (%)]	20 (46.51%)	5 (25.00%)	15 (100.00%)	26.49	<0.001*	13 (65.00%)	7 (30.43%)	5.13	0.020*
RR [median (IQR)]	29.00 (25.00-40.00)	28.00 (25.00-30.00)	33.00 (31.00-40.00)	9.52	0.001*	30.50 (25.00-40.00)	28.00 (25.00-36.00)	1.93	0.060
RR>30/min [n (%)]	15 (34.68%)	0 (0.00%)	15 (100.00%)	43.00	<0.001*	10 (50.00%)	5 (21.74%)	3.76	0.050
Systolic BP (mmHg) [median (IQR)]	124 (80.00-168.00)	125.00 (80.00-168.00)	124.00 (84.00-168.00)	0.05	0.950	111.00 (80.00-168.00)	126.00 (96.00-156.00)	1.05	0.290
Systolic BP <90 mmHg [n (%)]	6 (13.95%)	4 (14.29%)	2 (13.13%)	0.01	0.930	6 (30.00%)	0 (0.00%)	8.01	0.005*
SpO_2 (%) [median (IQR)]	90.00 (80.00-94.00)	91.50 (90.00-94.00)	86.00 (80.00-89.00)	9.15	0.001*	89.50 (80.00-92.00)	92 (84.00-94.00)	3.58	0.001*
SpO_2 < 94% [n (%)]	15 (34.88%)	0 (0.00%)	15 (100.00%)	43.00	<0.001*	10 (50.00%)	5 (21.74%)	3.76	0.050
PaO_2/FiO_2 (mm hg) [median (IQR)]	177.00 (124.00-198.00)	178.50 (163.50-192.00)	169.00 (104.00-214.00)	8.72	0.001*	104.00 (120.00-185.00)	189.00 (174.00-204.00)	4.25	<0.001*
SOFA score [median (IQR)]	3.72 (2.00-7.00)	3.00 (2.00-6.00)	3.00 (2.00-6.00)	0.04	0.960	4.00 (2.00-7.00)	3 (2.00-5.00)	5.08	<0.001*

HR: heart rate; RR: respiratory rate; GCS: Glasgow coma scale; SOFA: sequential organ failure assessment; SpO_2: oxygen saturation; PaO_2: partial pressure of oxygen in arterial blood; FiO_2: fraction of inspired oxygen; CAD: coronary artery disease; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; LFT: liver function test; AKI: acute kidney injury; CK-MB: creatine kinase; *: statistically significant.

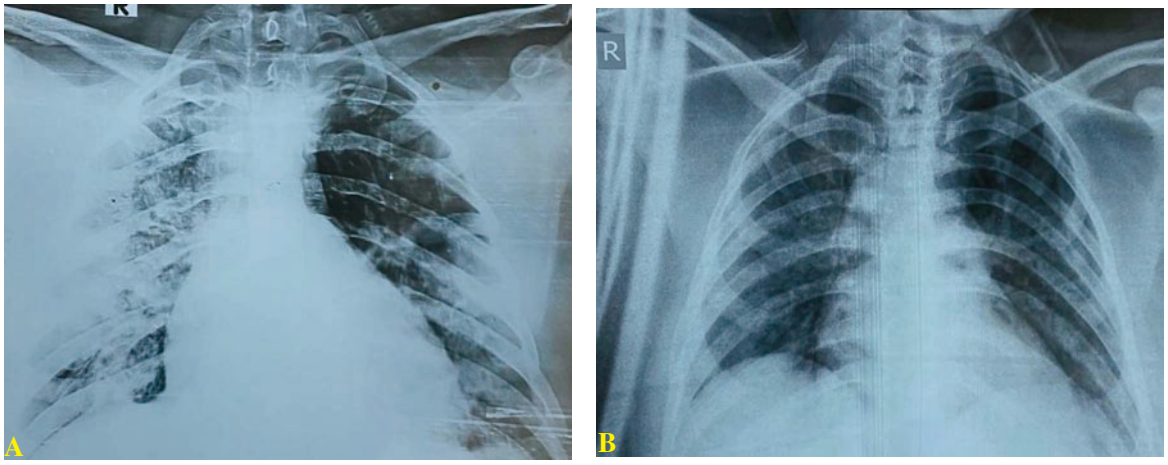

Figure 1. A: X-Ray chest posteroanterior view of a 28-year-old male with moderate COVID-19, showing bilateral basal and subpleural raticulonodular opacity. B: Significant improvement in X-Ray findings after remdesivir and convalescent plasma therapy.

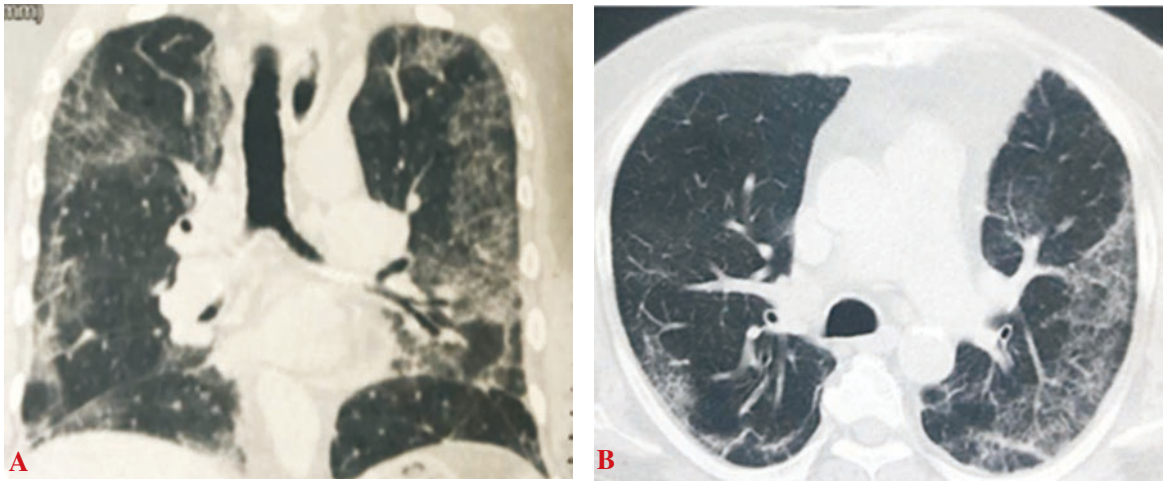

Figure 2. CT scan of a 67-year-old moderate COVID-19 patient showing multifocal ground-glass opacity, crazy paving, and subpleural reticular opacities in bilateral lung fields, involving all lobes, predominantly peripheral subpleural region. A: Coronal section; B: Axial section.

104, and the SOFA score was 4 (2.00-7.00) in the patients who met the primary composite outcomes (Table 5). There was a significant positive correlation between heart rate (r=0.52; P<0.001), SOFA score (r=0.63; P<0.001) and composite outcomes, and significant negative correlation between SpO_2 (r=0.45; P=0.002), PaO_2/FiO_2 (r=0.31; P=0.04) and composite outcome (Table 2).

3.4. Course of management and interventions

All the moderate-to-severe COVID-19 patients received tab azithromycin (500 mg once daily for 5 d), tab hydroxychloroquine (400 mg twice daily on day 1 followed by 200 mg twice daily for 4 d), tab vitamin C (500 mg twice a day), tab zinc (50 mg twice a day), injectable antibiotics, dexamethasone (6 mg once a day), low molecular weight heparin (except in 2 patients who had contraindication) and symptomatic treatment and supplemental oxygen therapy as per MoHFW guideline[9]. Out of the 43 patients, 13 (30.23%) received remdesivir, 2 (4.65%) patient received tocilizumab, 6 (13.95%) received remdesivir and convalescent plasma, 1 (2.33%) patient received remdesivir and tocilizumab, 1 (2.33%) patient received convalescent plasma and tocilizumab, and 2 (4.65%) patients received remdesivir, convalescent plasma, and tocilizumab as per institutional protocol. Out of 43 patients, 20 (46.5%) patients were shifted to ICU, 6 (13.95%) patients required vasopressors support, and 8 (18.60%) patients required mechanical ventilation and subsequently expired with a case fatality rate of 18.60%. Out of the 15 patients with severe category, 8 patients expired, and 7 recovered, and all 28 patients with moderate category recovered. Out of 13 patients who received remdesivir, 4 patients (30.76%) expired; out of 2 patients received tocilizumab, 1 (50%) expired; Out of 6 patients received remdesivir and convalescent plasma, 1 (16.67%) expired. All 2 (100%) patients who received remdesivir, convalescent plasma and tocilizumab expired. Besides, one patient who received remdesivir and tocilizumab recovered and 1 patient who received convalescent plasma and tocilizumab recovered (Figure 3).

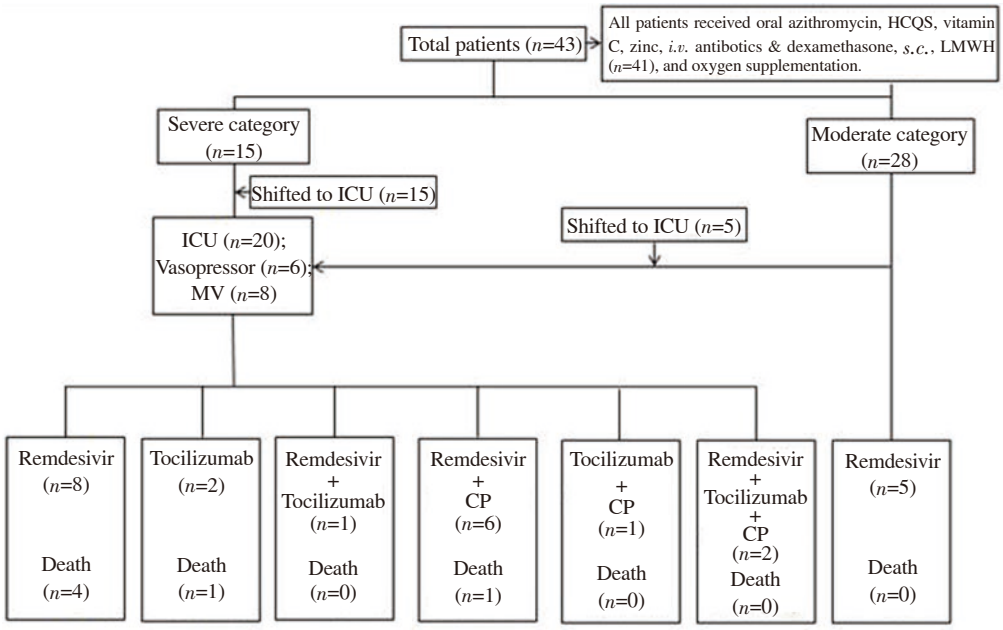

Figure 3. Flowchart showing course of management and outcome of COVID-19 patients. HCQS: hydroxychloroquine; *i.v.*: intravenous; *s.c.*: subcutaneous; LMWH: low molecular weight heparin; ICU: intensive care unit; MV: mechanical ventilation; CP: convalescent plasma.

4. Discussion

The median age of this study patient was 50 years (IQR: 44-62) and 27 (62.8%) patients were male, which was similar to earlier studies done in the Indian subcontinent[11-14]. The higher male predominance found in previous studies[3] may be due to more outdoor exposure by the male and possibly by the higher concentration of angiotensin-converting enzyme-2 (ACE-2) in males in comparison to females, as ACE-2 is proposed as a binding receptor for SARS-CoV-2[11]. Out of 43 patients, 19 (44.2%) patients did not report any history of contact with COVID-19 patient or any travel history, possibly due to community transmission of the disease as reported by previous studies[11]. Out of the 43 patients, 15 (34.88 %) were categorized as severe COVID-19. This number is similar to the studies of Wang *et al.* and Dosi *et al.*[3,13], but higher than the number of the study of Guan *et al.*[15], and lower than the number of study by Aggarwal *et al.*[11]. This may be due to the different patient populations in these studies.

The median duration from onset of symptoms to hospital admission was 3 d, which was similar to Aggarwal *et al.* study[11] but less than the Zhou *et al.* study[16]. This is explained by more severe cases in Zhou's study. The most common symptom was dyspnea (90.7%) followed by cough (79.07%), fever (69.77%), and body ache (46.51%). Less common symptoms were fatigue, sore throat, chest pain, vomiting, headache, nasal discharge, anosmia, ageusia, loose stools, hemoptysis, and altered sensorium in decreasing order. These findings are concordant to other previous studies[2,3,11,13,15-16]. Yan *et al.* reported that anosmia and ageusia are independently and strongly associated with COVID-19[17]. The high frequency of dyspnea and cough is due to the moderate-to-severe patients in this study.

Out of 43 patients, 26 (60.47%) had 1 or more co-morbidities. Diabetes mellitus (34.88%), hypertension (30.23%), and obstructive airway disease that include COPD and bronchial asthma (13.95%) were the three commonest comorbidities. These findings are in line with Aggarwal *et al.* study[11], whereas the percentages of co-morbidities were much lower in other previous studies[2,3,13,15-16]. This may be due to moderate-to-severe patients in this study, as severe disease was associated with more co-morbidities in earlier studies[3,15]. Patients who met the primary composite outcomes were more likely to have at least 1 co-existing comorbidity (P=0.002) and diabetes (P=0.009) compared with patients who did not meet the primary composite outcomes, which is similar to previous studies[3,11,15,18].

Leucopenia was presented in 14 (32.56%) patients, with the majority of patients have lymphopenia 26 (60.47%) and 7 (16.28%) patients have monocytosis. Plausible mechanisms of lymphopenia include (1) The virus might directly infect lymphocytes and destroy them, as lymphocytes have ACE2 receptor; (2) Inflammatory cytokines such as TNF alpha, IL-6 are released, leading to lymphocyte apoptosis[19]. Monocytosis was also reported by previous studies[11], and functional abnormalities of monocyte and their correlation with patient outcomes were reported by Zhang *et al.*[20]. In the current study, NLR was 3.2 (2.04-5.90) and was significantly higher in patients with severe disease compared to moderate disease [3.67 (2.50-5.90) *vs.* 2.97 (2.08-4.03)). Yang *et al.* reported that NLR more than 3.3 showed a superior prognostic

possibility of change of symptoms from mild to severe[21].

Thrombocytopenia was seen in 11 (25.98%) and pancytopenia in 6 (13.95%) of the patients possibly due to the similar pathophysiology. Pancytopenia was more common in patients who met the primary outcomes. These hematological findings are concordant to previous studies[3,11,15,19]. Anemia was seen in 27 (62.79%) patients, similar to Aggarwal *et al.* study[11], and this can be explained by a high prevalence of anemia in the Indian subcontinent.

Hypoalbuminemia was observed in 15 (34.88%) patients, and, hypoalbuminemia was found to be significantly more in patients who had severe disease compared to patients who had moderate disease, similar to previous studies[11,22]. There was no association of hypoalbuminemia with primary composite outcomes. Contrary to this, Hedlund *et al.* reported increased mortality and morbidity of hypoalbuminemia patients hospitalized with community-acquired pneumonia[23]. Raised CK-MB was observed in (65.12%) patients without any significant ECG changes and was found to be significantly increased in the patients with severe disease [15 (100.00%) *vs.* 13 (46.4%)], but no association of CK-MB with primary outcome was found. Contrary to this, raised CK-MB level was associated with higher in-hospital mortality in patients with COVID-19 in previous studies[11,24]. Hepatic dysfunction was seen in 12 (27.91%) patients in this study and was found to be significantly more in patients with severe disease, and this finding is in line with previous studies[3,15].

AKI was found in 14 (32.56%) patients and was found to be significantly more in patients with severe disease. Wang *et al.* found no association of AKI with the severity of disease and primary outcomes[3]. While other studies reported the association of AKI with the severity of disease and mortality in COVID-19 patients[11,15]. Proposed pathogenic mechanisms of AKI in COVID-19 are the direct effect of the virus on the nephrons, hypoxic injury due to respiratory failure, and circulatory shock.

The SOFA score is a diagnostic marker for sepsis and septic shock, and it can reflect the extent of multi-organ dysfunction[16]. Patients who met the primary outcomes had higher SOFA scores compared to the patients who did not meet [4 (2.00-7.00) *vs.* 3 (2.00-5.00)] in this study. Also, patients who met the primary outcome had more tachycardia, hypotension, and lower SpO_2 and PaO_2/FiO_2 at admission. These findings are concordant with previous studies[11]. These parameters are good prognostic predictors and should be considered to reduce mortality by providing early intensive care. In this study, the fatality was 18.6% because of the relatively severe patient cohort.

The delay in presentation to the hospital in this study was of a median of 3 d. Early recognition and contact tracing of COVID-19 positive individuals and awareness of the symptoms in the general population may help reduce delayed presentation in a state of severe disease to the hospital and possibly may prevent significant morbidity and mortality. To date, other than supportive care no specific treatment has been recommended for COVID-19. The treatment is symptomatic with antibiotics, steroids, anticoagulation, and oxygen therapy represents the major treatment intervention for patients with severe disease. Mechanical ventilation is required in cases of respiratory failure despite oxygen therapy although it has a poor outcomes.

Limitations of this study need to be mentioned, including the retrospective study design, small sample size, and all laboratory tests that were not done in all patients, including lactate dehydrogenase, d-dimer, IL-6, ferritin, pro-calcitonin, coagulation profile due to resource-limited settings.

To conclude, this retrospective study identified several risk factors for poor outcomes in adults with COVID-19. In particular, older age, tachycardia, high SOFA score, low SpO_2, low PaO_2/FiO_2, presence of comorbidities in form of diabetes and hypertension, thrombocytopenia, and pancytopenia at admission were associated with higher odds of ICU admission, a requirement of mechanical ventilation and in-hospital death. It is paramount to identify the high-risk population which includes the elderly and people with comorbidities, and early recognize high-risk symptoms and provide appropriate care.

Conflict of interest statement

The authors report no conflict of interest.

Acknowledgment

We are grateful to Dr. Ratiram Meena, Department of Community Medicine for helping in statistical analysis.

Authors' contributions

H.R.N. contributed to the project design, data interpretation, drafting the article, revising it critically; and final approval of the version to be published; P.S. and A.R.C. contributed by project design, data interpretation, statistical analysis, article preparing and submission; S.A., S.I.H., A.A. contributed by the collection of data, statistical analysis, and data interpretation. All authors contributed equally to the final version of the manuscript.

References

[1] Cucinotta D, Vanelli M. WHO declares COVID-19 a pandemic. *Acta Biomed* 2020; **91**(1): 157-160.

[2] Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020; **395**(10223): 507-513.

[3] Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected

pneumonia in Wuhan, China. *JAMA* 2020; **323**(11): 1061-1069.

[4] Li G, Fan Y, Lai Y, Han T, Li Z, Zhou P, et al. Coronavirus infections and immune responses. *J Med Virol* 2020; **92**(4): 424-432.

[5] WHO. Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected, 2020. [Online] Avaliable from: https://www.euro.who.int/en/health-topics/health-emergencies/coronavirus-covid-19/publications-and-technical-guidance/2020 /clinical-management-of-severe-acute-respiratory-infection-sari-when-covid-19-disease-is-suspected-interim-guidance,-13-march-2020. [Accessed on 25 August 2020].

[6] Liang CY, Tian L, Liu YZ, Hui N, Qiao GP, Li H, et al. A promising antiviral candidate drug for the COVID-19 pandemic: A mini-review of remdesivir. *Eur J Med Chem* 2020; **201**: 112527.

[7] Kewan T, Covut F, Al-Jaghbeer MJ, Rose L, Gopalakrishna KV, Akbik B. Tocilizumab for treatment of patients with severe COVID-19: A retrospective cohort study. *E Clinical Medicine* 2020; **24**: 100418.

[8] Chen L, Xiong J, Bao L, Shi Y. Convalescent plasma as a potential therapy for COVID-19. *Lancet Infect Dis* 2020; **20**(4): 398-400.

[9] Government of India Ministry of Health and Family Welfare Directorate General of Health Services. Clinical Management Protocol: COVID-19 Government of India Ministry of Health and Family Welfare Directorate General of Health Services (EMR Division) Version 4. [Online] Available from: https://www.mohfw.gov.in/pdf/ClinicalManagementProtocol forCOVID19dated27062020.pdf. [Accessed on 8 July 2020].

[10]Kellum JA, Lameire N, Aspelin P, Barsoum RS, Burdmann EA, Goldstein SL, et al. Kidney Disease Improving Global Outcomes (KDIGO) Clinical Practice Guideline for Acute Kidney Injury. *Kidney Inter Suppl* 2012; **2**(1): 1-138.

[11]Aggarwal A, Shrivastava A, Kumar A, Ali A. Clinical and epidemiological features of SARS-CoV-2 Patients in SARI Ward of a tertiary care centre in New Delhi. *J Assoc Phys India* 2020; **68**: 19-26.

[12]Bhandari S, Bhargava A, Sharma S, Keshwani P, Sharma R. Clinical profile of Covid-19 infected patients admitted in a tertiary care hospital in North India. *J Assoc Phys India* 2020; **68**: 13-17.

[13]Dosi R, Jain G, Mehta A. Patients of Coronavirus Disease 2019 at a tertiary care centre in central India. *J Assoc Phys India* 2020; **68**: 20-23.

[14]Bhadade R, Harde M, Kasbe A, Deshpande C, Dave S, Joshi M, et al. Appraisal of critically Ill COVID-19 patients at a dedicated COVID hospital. *J Assoc Phys India* 2020; **68**: 14-19.

[15]Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of Coronavirus Disease 2019 in China. *N Engl J Med* 2020; **382**(18): 1708-1720.

[16]Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020; **395**(10229): 1054-1062.

[17]Yan CH, Faraji F, Prajapati DP, Boone CE, DeConde AS. Association of chemosensory dysfunction and COVID-19 in patients presenting with influenza-like symptoms. *Int Forum Allergy Rhinol* 2020; **10**(7): 806-813.

[18]Guan WJ, Liang WH, Zhao Y, Liang HR, Chen ZS, Li YM, et al. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. *Eur Respir J* 2020; **55**(5): 2000547.

[19]Sharma D, Dayama A, Banerjee S, Bhandhari S, Chatterjee A, Chatterjee D. To study the role of absolute lymphocyte count and RDW in COVID 19 patients and their association with appearance of symptoms and severity. *J Assoc Phys India* 2020; **68**: 39-42.

[20]Zhang D, Guo R, Lei L, Liu H, Wang Y, Wang Y, et al. Frontline Science: COVID-19 infection induces readily detectable morphological and inflammation-related phenotypic changes in peripheral blood monocytes, the severity of which correlate with patient outcome. *J Leukoc Biol* 2021; **109**(1): 13-22.

[21]Yang AP, Liu JP, Tao WQ, Li HM. The diagnostic and predictive role of NLR, d-NLR and PLR in COVID-19 patients. *Int Immunopharmacol* 2020; **84**: 106504.

[22]Huang Y, Yang R, Xu Y, Gong P. Clinical characteristics of 36 non-survivors with COVID-19 in Wuhan, China. *medRxiv* 2020; doi:https://doi.org/10.1101/2020.03.24. 20042655.

[23]Hedlund JU, Hansson LO, Örtqvist ÅB. Hypoalbuminemia in hospitalized patients with community-acquired pneumonia. *Arch Intern Med* 1995; **155**(13): 1438-1442.

[24]Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. *JAMA Cardiol* 2020; **5**(7): 802-810.