Original Article

JHSMR Journal of Health Science and Medical Research

Clinical and Epidemiological Characteristics of Elderly Patients with Coronavirus Disease-19 at a Tertiary Care Center in South India

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Received 1 December 2022 ● Revised 13 April 2023 ● Accepted 19 April 2023 ● Published online 22 June 2023

Abstract:

Objective: To evaluate the clinical features and laboratory profile of elderly patients with Coronavirus Disease-19 (COVID-19) at a tertiary care centre in South India.

Material and Methods: A hospital-based retrospective study was conducted in 1,744 elderly patients by collecting the clinical and laboratory data from COVID-19 confirmed patients from May 2020 to June 2021 in a tertiary care hospital in Bangalore, India. The clinical features, comorbidities, serum biochemical parameters and inflammatory markers were recorded and collated with disease outcomes. The clinical presentation, inflammatory markers were studied and compared between survivors and non-survivors. P-value less than 0.05 set as statistical significance.

Results: The mean age of the patients was 69.7±7.4 years and the male: female ratio was 1.65:1. The most common comorbidity reported in elderly patients with COVID-19 was type 2 diabetes mellitus (46.8%), followed by hypertension (35.7%), chronic kidney disease (10.7%), and ischemic heart disease (6.47%). 41.9% of the patients did not have any co-morbidities. Out of the 1,744 elderly patients, 164 (9.4%) died and mortality was highest in the COVID-19 patients with severe disease (103 patients, 62.8%). Inflammatory markers of neutrophil/lymphocyte ratio (N/L ratio), lactate dehydrogenase (LDH), ferritin, C-reactive protein (CRP), D-Dimers and interleukin-6 were significantly elevated among the patients who did not survive.

Conclusion: Mortality was highest in elderly COVID-19 patients with severe disease and most of the patients who died had one or more comorbidities. Neutrophilia, lymphopenia, eosinopenia along with elevated N/L ratio, LDH, ferritin, D-dimer, IL-6 and CRP were significantly associated with adverse disease outcomes.

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J Health Sci Med Res .....
doi: 10.31584/jhsmr.2023963
www.jhsmr.org

Keywords: COVID-19 in Geriatrics, elderly, inflammation

Introduction

Coronavirus disease-2019 (COVID-19) disease was declared a global pandemic on March 11, 2020 following its appearance in 2019[1]. As of July 13, 2022, there were 43,669,850 and 525,519 fatalities from COVID-19 in India[2]. COVID-19 evolved rapidly and unpredictably as it spread world-wide, and affected frontline healthcare workers as well as the general population[3]. A COVID-19 infection usually begins with flu-like symptoms[4]. The clinical presentation of COVID-19 is varied, ranging from asymptomatic infection to mild symptoms such as dry cough to severe symptoms such as fever and dyspnoea due to acute respiratory distress syndrome (ARDS) that can lead to death. Asymptomatic transmission has also been observed in a huge number of cases that makes infection control difficult[5,6].

A COVID-19 infection is characterized by elevated inflammatory markers and can have "cytokine storm". Hemogram parameters, especially NLR, are elevated in the inflammatory conditions such as inflammatory bowel disease, diabetes mellitus[7,8], thyroiditis[9], irritable bowel disease[10], myocardial infarction[11] and also in COVID-19 infection[12,13] . C-reactive protein (CRP) and CRP derived markers have recently been recommended as predictors of inflammation in diabetic nephropathy[14], thyroiditis, hepatitis[15] and Covid-19 infection[16]. Advanced age is one of the foremost risk factors for a poor prognosis of COVID-19 infections[17,18]. Recent studies on COVID-19 have observed that elderly COVID-19 patients with two or more comorbidities such as cardiovascular disease, diabetes mellitus, hypertension, chronic obstructive pulmonary disease, malignancies, and chronic kidney diseases have high fatality rates[19].

A predictive study on COVID-19 in elderly patients is required to comprehend its characteristics among aging patients to reduce the mortality rate and improve the disease outcomes. The geriatric population represents a specific group of high-risk patients for developing COVID-19 with rapidly progressive clinical deterioration[5]. This study aimed to evaluate the comorbidities and clinical parameters in relation to the COVID-19 outcomes in older patients.

Material and Methods

A hospital-based retrospective study was carried out in elderly COVID-19 patients aged ≥60 years hospitalized in a tertiary care hospital in Bengaluru, India, between June 2020 and May 2021 by collecting the medical data from 1,744 laboratory-confirmed cases. The investigation was conducted following approval from the Ethics Committee of the Institute (MSRMC/EC/AP-04/05-2021).

The study included 1,744 elderly subjects aged ≥60 years and diagnosed with mild, moderate or severe COVID-19 based on the WHO guidelines[21]. Oro-nasopharyngeal swab-based testing using Reverse Transcription-Polymerase Chain Reaction (RT-PCR) was employed for laboratory confirmation of COVID-19. A case was labelled as confirmed positive if RT-PCR testing showed a positive result, irrespective of clinical signs or symptoms[20].

Sample size- The sample size was calculated using the following formula:

$$\text{Sample size} = \left[\frac{p\ (1-p)\ z^2}{d^2}\right]$$

Where, "p" is the percentage incidence of a state or condition (proportion or prevalence), "d" is the percentage maximum error, and "z" is the value corresponding to the level of confidence required. The prevalence of non-survivors in COVID-19 patients was assumed to be 30%

with a 95% confidence level and 5% error. As per the calculation, the minimum sample size required was 323 subjects.

Information pertaining to the patient's demographic details, clinical symptoms/signs, clinical progression/outcomes, and comorbidities were obtained from hospital records without disclosing patient identity. COVID-19 symptoms and laboratory profiles were noted for each patient. The study subjects were grouped based upon the outcomes (survivor or died). The severity of COVID-19 was principally grouped as mild, moderate, or severe based on clinical severity and assessment parameters, i.e.:[21].

Mild: Patients with uncomplicated upper respiratory tract infection, with or without mild symptoms such as fever, cough, sore throat, nasal congestion, malaise, headache, and without evidence of breathlessness or hypoxia i.e., normal oxy-hemoglobin saturation (SpO2>94%).

Moderate: Clinical features of dyspnoea and/or hypoxia, fever, cough, SpO2<94% (range 90-94%) at room air, or a respiratory rate of 24 per min or higher.

Severe: Clinical signs of pneumonia plus one of the following: respiratory rate>30 breaths/min, severe respiratory distress, SpO2<90% at room air.

The laboratory parameters including serum biochemical parameters were recorded and correlated with the disease outcomes. The levels of inflammatory markers of neutrophil/lymphocyte ratio (N/L ratio), lactate dehydrogenase (LDH), ferritin, D-dimer, interleukin-6 (IL-6) and C-reactive protein (CRP) were recorded. As per the national policy for older persons of the Ministry of Social Justice & Empowerment, Government of India, the patients were classified into three categories: Young old (60-69 years), Old (70-79 years) and Older Old (≥80 years)[22]. The severity and outcomes of COVID-19 illness among the different age groups of the study geriatric patients were studied.

Statistical analysis of the clinical data was performed using the R program v4.0.3. The data were compared as means and percentages of distribution among the three groups. Continuous variables were analyzed using mean ±standard deviation (S.D.) and categorical variables by a frequency table. A quantile plot/Kolmogoro-Smirnov test was performed to check the normality of the variables. The independent sample t-test or Mann Whitney U-test was performed to compare the three groups. The chi-square test was used to find the relation between categorical variables. A p-value≤0.05 was deemed to indicate statistical significance.

Results

The study enrolled 1,744 elderly patients who were admitted with COVID-19 illness. COVID-19 severity, outcome, symptoms, and comorbidities are described in the Table 1. The mean age of the patients was 69.71±7.42 years. 970 (55.9%) patients were in the 60-69 years age group, 560 (32.1%) were in 70-79 years age group and 208 (11.9%) were more than 80 years old.

More males were infected (n=1,087, 62.3%) than females (n=657, 37.7%) with a ratio of 1.65:1. The mortality in our study patients was 9.4% (n=164).

Among all the patients, 1,034 (59.3%) had mild infection, 428 (24.5%) had moderate infection and 282 (16.2%) had severe disease (Table 1). The major disease symptoms were fever (n=1214, 69.6%), cough (n=650, 37.3%), myalgia (n=556, 31.9%), sore throat (n=486, 27.9%) and breathlessness (n=405, 23.2%). 334 subjects (19.2%) did not show any disease symptoms. Loss of smell and taste, headache, vomiting and rhinitis were the minor symptoms noted.

Table 1 Demographic and clinical characteristics and laboratory findings of the study patients with Coronavirus disease

	Variable	Number (%)
Sex	Male	1,087 (62.3)
	Female	657 (37.7)
Severity of	Mild	1,034 (59.3)
COVID-19	Moderate	428 (24.5)
	Severe	282 (16.2)
Outcome	Survived	1,580 (90.6)
	Died	164 (9.4)
Symptoms	None	334 (19.2)
	Fever	1214 (69.6)
	Cough	650 (37.3)
	Myalgia	556 (31.9)
	Sore throat	486 (27.9)
	Dyspnoea	405 (23.2)
	Loss of smell and taste	260 (14.9)
	Headache	178 (10.2)
	Nausea and vomiting	90 (5.1)
	Rhinitis	73 (4.1)
Co-morbidities	None	730 (41.9)
	Type 2 diabetes mellitus	816 (46.8)
	Hypertension	622 (35.7)
	Chronic kidney disease	187 (10.7)
	Ischaemic heart disease	113 (6.4)
	Chronic obstructive pulmonary disease	88 (5.0)
	Hypothyroidism	67 (3.8)
	Chronic liver disease	46 (2.6)
	Bronchial asthma	38 (2.1)
	Seizure disorder	21 (1.2)

The most common comorbidity in the study of COVID-19 patients was T2DM (n=816, 46.8%) followed by HTN (n=622, 35.7%), chronic kidney disease (CKD) (n=187, 10.7%), ischemic heart disease (IHD) (n=113, 6.4%), COPD (n=88, 5.0%). 730 (41.9%) patients did not have any comorbid conditions.

There was a significant correlation between gender and outcome. 118 (10.8%) of the males succumbed to the COVID-19 infection, 46 (7%) of the females succumbed to COVID-19 infection. This difference was statistically significant. Mortality was highest in patients with severe disease (n=103, 5.9%). In patients with moderate disease, mortality was 2.06% (n=36). Mortality was least in mild disease (n=25, 1.43%). (Table 2).

Table 2 Comparison of clinical variables with outcome in study patients with Coronavirus disease-19

Variable		Death [n (%)]	Survival [n (%)]	p-value
Sex	Male	118 (10.8)	969 (89.2)	<0.001*
	Female	46 (7)	611 (93)	
COVID-19	Mild	25 (15.2)	1,009 (63.8)	<0.001*
severity	Moderate	36 (21.9)	392 (24.8)	
	Severe	103 (62.8)	179 (11.3)	

Chi-square test was used for all the variables. *significant association between variables with outcome (p-value<0.05). COVID-19, Coronavirus disease 2019

When the laboratory data were compared with outcomes (Tables 3 and 4), it was observed that elevated white blood cells (WBCs) (p-value=0.002), neutrophil count (p-value<0.001), lymphopenia (p-value<0.001), low eosinophil count (p-value<0.001), monocyte count (p-value<0.001), prothrombin time (PT) (p-value<0.01), international normalized ratio (INR) (p-value<0.007), aspartate aminotransferase (AST) (p-value<0.001), alanine transaminase (ALT) (p-value<0.001), serum albumin (p-value<0.001), serum creatinine (p-value<0.007) and blood urea nitrogen (BUN) (p-value<0.001) were significantly associated with disease outcomes in the study subjects. However, platelet count, activated partial thromboplastin time (aPTT) and serum uric acid were not significantly associated with disease outcome.

Table 3 Laboratory parameters in the study of COVID-19 patients

Variable	Mean (S.D.)	Median
Haemoglobin (gm%)	12.5±2.5	12.8
WBCs ($\times10^7$/L)	8,425.7±5,240.6	7,100
Neutrophil count ($\times10^7$/L)	73.7±123.6	72
Lymphocyte count ($\times10^9$/L)	19.8±11.9	18
Eosinophil count ($\times10^9$/L)	1.0±1.7	0.4
Monocyte count ($\times10^9$/L)	8.1±5.2	7.8
Platelet count ($\times10^9$/L)	2.7±4.2	2.0
Serum creatinine (mg/dL)	1.1±1.4	0.8
Serum uric acid (mg/dL)	4.6±2.0	4.2
BUN (mg/dL)	14.9±13.3	11
AST (units/L)	38.6±25.6	32
ALT (units/L)	34.6±35.9	27
Serum albumin (g/dL)	3.7±0.9	3.7
APTT (seconds)	30.6±11.1	29.7
PT (seconds)	14.6±8.7	13.6
INR (ratio)	1.4±4.2	1.0
N/L (neutrophils/lymphocytes) (ratio)	6.9±9.0	4.0
D-dimers (mg/L FEU) (n=1,130)	6.1±51.4	0.76
LDH (units/L)	333.2±204.3	279
Ferritin (ng/mL)	313.1±311.1	207
IL-6 (pg/mL) (n=488)	201.6±684.0	34.4
CRP (mg/L)	6.7±9.5	3.2
Random blood sugar (mg/dl)	171.5±107.9	127
Sodium (meq/l)	134.6±10.7	136
Potassium (meq/l)	5.3±13.6	4.5
Chloride (meq/l)	99.8±8.5	101

ALT=alanine transaminase, APTT=activated partial thromboplastin time, AST=aspartate aminotransferase, BUN=blood urea nitrogen, CRP=C-reactive protein, COVID-19=corona virus disease 2019, FEU=fibrinogen-equivalent units, IL-6=interleukin-6, INR=international normalized ratio, LDH=lactate dehydrogenase, N/L ratio, PT=prothrombin time, S.D.=standard deviation, WBC=white blood cells

Table 4 Comparison of laboratory parameters of study patients with outcomes

Variables	Death		Survival		p-value
	Mean (S.D.)	Median	Mean (S.D.)	Median	
WBCs ($\times 10^7$/L)	10,265±7,242.1	8,550	8,234.6±4,950.8	7,000	0.002*
Neutrophil count ($\times 10^7$/L)	81.5±9.8	83	72.9±129.7	70.3	<0.001*
Lymphocyte count ($\times 10^9$/L)	11.9±7.9	10.9	20.6±11.9	18.7	<0.001*
Eosinophil count ($\times 10^9$/L)	0.7±1.4	0.1	1.1±1.7	0.4	<0.001*
Monocyte count ($\times 10^9$/L)	5.3±3.0	4.7	8.4±5.3	8	<0.001*
Platelet count ($\times 10^9$/L)	2.6±4.0	2.0	2.7±4.2	2.0	0.098
APTT (seconds)	33.3±14.3	30.6	30.3±10.6	29.6	0.100
PT (seconds)	15.5±6.8	14.1	14.5±8.8	13.6	0.01*
INR (ratio)	1.4±1.0	1.1	1.3±4.4	1.0	<0.007*
AST (units/L)	51.4±41.4	41	37.3±22.9	31	<0.001*
ALT (units/L)	46.5±72.7	30	33.3±29.2	26.5	<0.001*
Serum albumin (g/dL)	3.6±2.5	3.5	3.7±0.5	3.8	0.001*
Serum creatinine (mg/dL)	1.1±1.2	0.8	1.1±1.4	0.8	0.007*
Serum uric acid (mg/dL)	4.6±2.3	4.1	4.6±2.0	4.3	0.200
BUN (mg/dL)	17.70±15.96	12	14.71±13.01	10.7	<0.001*

Mann Whitney U test was used for all the variables. *statistically significant (p-value<0.05), ALT=alanine transaminase, APTT=activated partial thromboplastin time, AST=aspartate aminotransferase, BUN=blood urea nitrogen, INR=international normalized ratio, PT=prothrombin time, S.D.=standard deviation, WBC=white blood cells

Table 5 Comparison of different inflammatory markers with outcome in study patients

Variable	Death		Survival		p-value
	Mean (S.D.)	Median	Mean (S.D.)	Median	
N/L (ratio)	13.2±14.2	7.9	6.2±8.1	3.77	<0.001*
D-dimers (mg/L FEU)	21.6±133.8	1.0	4.6±34.3	0.74	<0.001*
LDH (units/L)	452.6±237.5	394	321.5±197.1	273	<0.001*
Ferritin (ng/mL)	508.5±415.7	378.5	292.9±290.9	195	<0.001*
IL-6 (pg/mL)	272.7±458.3	75.4	195.3±700.7	32.0	<0.001*
CRP (mg/L)	13.6±11.5	9.6	6.0±9.0	2.87	<0.001*

Mann Whitney U test was used for all the variables. *statistically significant (p-value<0.05); CRP=C-reactive protein, FEU=fibrinogen-equivalent units, IL-6=interleukin-6, LDH=lactate dehydrogenase, N/L ratio=neutrophil/lymphocyte ratio

Table 6 Severity and outcomes of COVID-19 illness among the different age groups the study patients

Age category	Number N=1,744 (%)	Mild illness (%)	Moderate illness (%)	Severe illness (%)	Death (%)
60-69	976 (55.9)	592 (60.6)	243 (24.8)	141 (14.4)	77 (7.8)
70-79	560 (32.1)	310 (35.3)	139 (24.8)	111 (19.8)	63 (11.2)
>80	208 (11.9)	132 (63.4)	46 (22.1)	30 (14.4)	24 (11.5)

Among the different inflamatory markers studied, N/L ratio, LDH, ferritin, CRP, D-dimer and IL-6 were significantly (p-value<0.001) associated with outcome (Table 5).

The majority of patients, i.e. 55.9%, were young old (60-69 years). 32.1% were old (70-79 years) and the least number of patients, i.e. 11.9%, were in the older old (≥80 years) category. The severity and outcomes of COVID-19 illness among the different age groups of the study patients has been summarized in Table 6. It was observed that among all age groups of geriatrics patients, mild COVID-19 illness was most common. However, mortality was highest among the patients who were more than 80 years (11.5 %).

Discussion

COVID-19 poses significant risks to aged patients, especially those with comorbidities. This study evaluated the clinical and epidemiological features of aged COVID-19 patients. In India, elderly men, and women both have high mortality risk and thus require special care when infected[23]. In this study, COVID-19 infection was nearly 1.5 times more common in males than females. This finding is similar to previous reports in aged patients from India[24,25]. Previous studies proposed that susceptibility to viral infections may be linked to gender[26]. In the case of gender as a factor, oestrogen confers women an increased resistance by enhancing an adaptive immune response against viral infections, while testosterone contributes to the repression of the innate immune response, which makes men more vulnerable to virus-related infections.

The major disease symptoms found in our study were fever, dry cough, breathlessness, and fatigue/myalgia. The findings of our study are similar to the many other studies done in COVID-19 infections in elderly people[24,25]. Krishnasamy et al. from India reported that 66.3% of their study subjects with COVID-19 infections were male, and the most common presenting indications were fever (69.9%), cough (29.6%), generalized body pain (10.4%), difficulty in breathing (10.1%) and fatigue (10.1%)[24].

Among the comorbidities observed with COVID-19 infections in our study, hypertension and T2DM were found as major comorbidities in more than 50% of the patients. Many previous studies have reported that diabetes and hypertension were the most common underlying diseases associated with COVID-19 patients[18,19,27]. The high rate of associated comorbidities in severe COVID-19 may be ascribed to the angiotensin-converting enzyme (ACE2), which is widely distributed in the heart, kidneys and lungs, and acts as an adverse regulator of the renin-angiotensin system[28]. Further, SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) uses ACE2 receptors that increase host susceptibility to viral entry, which partially explains the high occurrence of hypertension in COVID-19 patients with acute conditions.

In the assessment of the laboratory parameters with outcome, WBCs, neutrophil count, lymphocyte count, eosinophil count, monocyte count, PT, APTT, AST, ALT, BUN, and serum albumin were significantly associated with disease outcomes. In an earlier study by Jing-Liang et al. on COVID-19, the levels of lymphocytes, uric acid, and globulin in T2DM patients were significantly higher than in other patients. In contrast, C-reactive protein (CRP), creatinine and lactic dehydration (LDH) levels in our patients were lower than those in the COVID-19 alone (p-value<0.05) & COVID-19+T2DM groups (p-value<0.05). No considerable differences were observed between the 3 age groups regarding the levels of alanine aminotransferase (ALT), white blood cells (WBCs), aspartate aminotransferase (AST), globulin, and blood urea nitrogen (BUN) (p-value>0.05)[29]. Nor were important differences seen in the ALT, WBC, AST, globulin, and BUN levels in any of the study groups. In another study, subjects with COVID-19 had lower counts

of leucocytes, lymphocytes, eosinophils, platelets, and haemoglobin, but higher neutrophil-lymphocyte ratios (NLR) and monocyte-lymphocyte ratios (MLR) than the controls[18]. These findings indicate that assessment of haematological and other biochemical parameters can be useful in the forecast of severe COVID-19 cases.

In accordance with the existing evidence, the association of COVID-19 with the elevated inflammatory markers N/L ratio, CRP, LDH and ferritin were found significantly related to disease outcome. Ferritin and LDH were estimated in 1,744 aged patients, with fatality in 164 subjects, while 1,580 subjects survived. Previous investigations on elevated inflammatory markers reported the relation of WBC, CRP, serum ferritin and IL-6 with severe COVID-19[31,32]. In this study, IL-6 showed significant correlation with outcome. Inflammatory markers are related to the severe conditions of COVID-19, so the assessment of inflammatory indicators may help clinicians to screen and estimate the intensity and forecast of COVID-19.

Previous studies on comparisons between various age groups found that severe/critical type, hypertension, and diabetes mellitus were more common in the elderly group comparedwith those ≤60 years[33], which is in accordance with our study results.

There was an indirect relationship between age and oxygen saturation (p-value<0.001) found in a previous study[34], which was similar to our study showing that the mean SPO2% levels in our elderly COVID-19 population were lower (92.9±8.5).

This study has made an addition to valuable insights in comprehending the disease depiction of COVID-19 patients, inclusive of its behaviour and severity scale, which is critical to determine the appropriateness and adequacy of mitigation strategies and to enable planning and designing healthcare needs. Factors contributing to the advancement of COVID-19, such as host comorbidities, specific inflammatory markers and drug resistance or side-effects, require to be appraised and should form the epicentre of focus, especially in aging patients with risk factors. The findings of the study demonstrate that elderly people are susceptible to severe COVID-19 infection. Most of the elderly people in the study with severe COVID-19 infection had elevated NLR, LDH, and D-Dimers. These parameters in elderly patients can help clinicians to identify patients at risk of developing severe infection and begin timely intensified monitoring and treatment of these patients. The limitations of the study were that it was a single-centre study and long-term follow-ups of the patients were not carried out.

Conclusion

In this study, an attempt was made to study the clinical features, laboratory parameters and inflammatory markers of aged COVID-19 patients. Mortality was highest in COVID-19 patients with severe disease and most of the patients who died had one or more comorbidities. Abnormal laboratory parameters like elevated neutrophil count, low eosinophil count, raised liver enzymes and elevated inflammatory markers of N/L ratio, LDH, ferritin, D-dimer, IL-6 and CRP were significantly associated with adverse disease outcomes.

Funding sources

This research received no specific grants from any funding agencies in the public, commercial, or non-profit sectors.

Conflict of interest

There are no conflicts of interest to declare.

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