Original Article

Clinico-epidemiological profile and outcomes of adults with COVID-19: A hospital-based retrospective study in Kerala, India

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Abstract

Introduction: The clinical and epidemiological presentations of patients with coronavirus disease 2019 (COVID-19) in India is still not well explored. We studied the epidemiological and clinical profile and outcomes of COVID-19 patients admitted to a tertiary care private hospital in Kerala, India. **Methods:** In this retrospective study, we analyzed data of 476 adult (≥18 years) COVID-19 patients admitted to a tertiary care hospital in Kerala from September 1, 2020 to March 31, 2021. The patients were categorized into mild, moderate, and severe cases and followed till discharge or death. Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 23.0 with a significance set at $P < 0.05$. **Results:** The median age was 57 years (56% men). Mild, moderate, and severe cases accounted for 17%, 65%, and 18%, respectively. Around 75% had at least one comorbidity, and 51% had multiple comorbidities. The most common comorbidities were diabetes (45%), hypertension (44%), dyslipidemia (15%), and cardiac problems (12%). The elevated D-dimer values among patients in different categories were significantly different, with 74% in severe, 46% in moderate, and 19% in mild category patients. Serum ferritin, C-reactive protein, lactic acid dehydrogenase, and neutrophil to lymphocyte ratio values were significantly higher for severely ill patients. Thirty deaths (67% men) occurred during the study period, with a case fatality rate of 6.3%. Mortality mainly happened in the older age group (80%) and those with multimorbidity (90%). **Conclusion:** Age and multimorbidity are the major contributing factors for death in hospitalized COVID-19 patients. Generalization of the findings necessitates well-designed large-scale studies.

Keywords: Clinical, coronavirus, COVID-19, epidemiological, hospitalized, India, Kerala, symptoms

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Introduction

The coronavirus disease 2019 (COVID-19) affects almost every country in the world and is one of the most challenging public health problems globally. As of January 31, 2022, there were more

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than 376.48 million confirmed cases and around 5.67 million COVID-19 deaths globally.[1] India reported the second-largest number of 41.47 million cases after the United States of America (USA) with 73.53 million cases and the third-largest number of 0.49 million deaths after the USA (0.87 million) and Brazil (0.62 million). India's national COVID-19 vaccination strategy covers more than 1672.94 million vaccine doses as of February 2, 2022.[2]

The first confirmed COVID-19 case in India was reported from Kerala state on January 30, 2020.[3] Despite having a large number of cases (6.07 million) in the second and third wave of COVID-19, the state of Kerala reported a case fatality rate (CFR) of 0.91%,[3] which is one of the lowest among the major states in the country.[2] Kerala is the most advanced state in India in terms of both epidemiological and demographic transition.[4] The state has the largest proportion of elderly (12.6%) compared with the national average (8.6%) of India.[5] Most of the noncommunicable diseases such as diabetes, cardiovascular diseases (CVD), chronic respiratory disease, and cancer are highly prevalent in Kerala.[4] The state also has the third-highest density of population (860/km^2) among the major states compared with the national average of 382/km^2.[5] All these factors are favorable for higher morbidity and mortality for COVID-19. However, due to the better health infrastructure, almost universal access to healthcare, very high literacy rates, strong decentralized and participatory governments, Kerala could reduce the COVID-19 mortality rates.[6,7] As per the latest national sample survey organization (NSSO) report, 58% of the in-patient services, excluding childbirth, are provided by private hospitals in Kerala.[8] During the COVID-19 pandemic, Kerala Government obtained strong support from the private hospitals in managing COVID-19 patients. Only a few studies were reported from Kerala on clinical characteristics and outcomes of COVID-19 patients. One such study based on 202 COVID-19-positive patients, during the initial stage of the pandemic (up to March 31, 2020),[9] reported only two deaths with a CFR of 0.99%. Another study from the state based on 32 patients reported a CFR of 3.1%.[10] However, there is no comprehensive hospital-based study on the epidemiological and clinical characteristics, comorbidities, and outcomes of COVID-19 patients from Kerala. The present study was therefore aimed at investigating the epidemiological and clinical profile, and outcomes of COVID-19 patients admitted in a tertiary care private hospital in Kerala.

Materials and Methods

This was a retrospective study performed among reverse transcriptase-polymerase chain reaction (RT-PCR)-confirmed COVID-19 patients admitted in a tertiary care hospital in Kerala. The hospital is a super specialty hospital with more than 350-bed strength in urban Thiruvananthapuram, the capital city of Kerala. There are a total of seven medical-surgical intensive care units (ICUs) and 24 ventilator beds. We included all adult (≥18 years) COVID-19 patients admitted to wards and ICUs of the hospital from September 1, 2020 to March 31, 2021.

We collected patients' epidemiological and clinical characteristics, comorbidity, and outcome data from the hospital medical records. A total of 507 COVID-19 RT-PCR-confirmed patients were admitted to the hospital during the study period. After excluding the patients below the age of 18 years (n = 28) and those with inadequate data (n = 3), the present study analyzed data from a sample of 476 adult patients. The data were reviewed by a team of physicians, epidemiologists, and a biostatistician.

Information on age, gender, place of residence, clinical data (symptoms), comorbidities and laboratory tests and outcomes (duration of hospitalization and mortality) were recorded. Demographic details, symptoms, and comorbidities were available for all patients. We analyzed the initial laboratory values (available for 75% of the patients) taken at the time of admission.

Deaths are defined based on Indian Council of Medical Research (ICMR) criteria for COVID-19 provided by the World Health Organization[11] as deaths resulting from clinically compatible illness in a probable or confirmed COVID-19 case unless there is a clear alternative cause of death that cannot be related to COVID-19 disease.[12] CFR was defined as the number of deaths per 100 COVID-19-positive cases. Discharge of patients from the hospital was done based on the Government of Kerala guidelines.[13]

We divided the patients into three categories based on the severity of the disease: mild, moderate, and severe cases as per the Kerala Government criteria.[14] The mild category includes category "A" patients with a mild sore throat, cough, or diarrhea; moderate category includes category "A" plus those with two or more diseases (including lung, heart, liver, kidney, neurological disease, hypertension, hematological disorders, uncontrolled diabetes, cancer, and the human immunodeficiency virus [HIV]-acquired immunodeficiency syndrome [AIDS]), or aged 60 years and above or "A" with cardiovascular diseases; severe category included those with breathlessness, chest pain, drowsiness, fall in blood pressure, hemoptysis, cyanosis, or worsening of an underlying condition. The symptoms such as fever, cough, dyspnea, loss of smell, tiredness, and headache and comorbidities such as hypertension, diabetes, dyslipidemia, coronary artery disease (CAD), heart failure (HF), chronic obstructive pulmonary disease (COPD), tuberculosis (TB), chronic kidney disease (CKD), atrial fibrillation (AF), cancer, asthma or respiratory disease, rheumatological conditions, and hypothyroidism were recorded. Data on comorbidities were obtained from their medical history or recorded by a physician at the time of admission. Other symptoms and comorbidities that were not highly prevalent were also noted and categorized under "others." We analyzed blood pressure values measured at the time of admission. We also recorded information on travel and contact history. Laboratory details such as elevated D-dimer (≥0.50 mg/L), serum ferritin, CRP (C-reactive protein), LDH (lactic acid dehydrogenase), and neutrophil to lymphocyte

ratio (NLR; the number of neutrophils divided by the number of lymphocytes), were taken for analysis

The data were entered in Excel and analyzed using Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA, version 23.0 for Windows). For continuous variables, mean (standard deviation, SD) or median (25^{th}–75^{th} centiles [range]) and for categorical variables, frequency and percentages were presented. The continuous variables were compared using Student's *t*-test or Kruskal–Wallis test and categorical variables with Chi-square or Fisher's exact test. The institute ethics committee (IEC) approved the study (AHRI/EC/31/2021 dated 29^{th} March 2021).

Results

The median age of the study patients was 57 years ranging from 19 to 91 years, and 56% were male patients. Baseline characteristics and clinical outcomes of patients are presented in Table 1. More than half of the patients were urban residents (58%). Seven percent reported travel history and 24.6% reported contact history. All patients, except three, were residents of Kerala. Mild, moderate, and severe patients accounted for 17.0% (n = 81), 64.7% (n = 308), and 18.3% (n = 87), respectively. A total of 64 (13.4%) patients required treatment in ICU.

The common symptoms reported were fever (53.8%), cough (41.4%), dyspnea (23.7%), and sore throat (14.1%), and there is no gender difference seen. Around 75% had at least one comorbidity, and 51.1% had multiple comorbidities. The most common comorbidities were diabetes (45.0%), hypertension (43.9%), dyslipidemia (15.1%), and cardiac problems (12.6%). There were nine cancer patients, and 30% reported other problems like arthritis, migraine, drug allergy, and gastric ulcer. Discharge characteristics of patients by age group are presented in Table 2. The mean duration of stay at the hospital was 11 days, with a significant difference between those who had not survived (14 days) and those who survived (10 days) at the time of discharge.

Thirty deaths (67% men) occurred during the study period, with a CFR of 6.3%. Of them, the mean age was 66.7 ± 12.2 years. All these patients were treated in ICU. Mortality mainly happened in the age group of 60 years and older (80%; 24/30). Deaths among patients below the age of 60 years (n = 6) were all men. All deaths (n = 10) among women were in the age group of 60–79 years. Around 70% of the deaths among men were among older adults (60 and above age). CFR and the proportion of severely ill patients by age groups are presented in Figure 1.

Among women patients, 10 deaths occurred (mean age at death: 70 years) with a CFR of 4.7%, and among men, 20 deaths occurred (mean age at death: 65 years) with a CFR of 7.5%. Of the patients, who died, all except one patient had at least one comorbidity, and 27 patients (90%) had multimorbidity (more than one comorbidity). Among them, 73.3% had diabetes, 73.3% hypertension, 30.0% had cardiac problems, 13.3% had dyslipidemia, and 13.3% had chronic kidney disease. Three of them were cancer patients, and four had hypothyroidism. CFR was high among CAD patients (11.7%), hypertensive (10.5%), and diabetes (10.3%). The CFR among patients without any comorbidity was 0.8%, among those with one comorbidity was 1.8% and among those with multimorbidity was 11.1%.

Table 1: Baseline characteristics and clinical outcome of patients hospitalized with COVID-19

Characteristics	*n* (%)
Age (in years)	
<60	258 (54.2)
≥60	218 (45.8)
Gender	
Men	265 (55.7)
Women	211 (44.3)
Place of residence	
Rural	202 (42.4)
Urban	274 (57.6)
Symptoms	
Fever	256 (53.8)
Cough	197 (41.4)
Dyspnea	113 (23.7)
Sore throat	67 (14.1)
Myalgia	49 (10.3)
Headache	44 (9.2)
Anosmia	27 (5.7)
Tiredness	28 (5.9)
Taste loss	25 (5.2)
Comorbidities	
No comorbidity	119 (25.0)
Hypertension	209 (43.9)
Diabetes	214 (45.0)
Dyslipidemia	72 (15.1)
CAD	60 (12.6)
HF	5 (1.1)
COPD	10 (2.1)
TB	6 (1.3)
CKD	17 (3.6)
AF	5 (1.1)
Cancer	9 (1.9)
Asthma/Respiratory	26 (5.5)
Rheumatology	6 (1.3)
Hypothyroidism	56 (11.8)
Others	143 (30.0)
Blood Pressure (Means±SD)	
SBP	134±18.1
DBP	83±9.9
Category of patients	
Mild	81 (17.0)
Moderate	308 (64.7)
Severe	87 (18.3)
Clinical Outcome	
Nonsurvivors	30 (6.3)
Survivors	446 (93.7)

CAD, coronary artery disease; HF, hear failure; COPD, chronic obstructive pulmonary disease; TB, tuberculosis; CKD, chronic kidney disease; AF, atrial fibrillation; SBP, systolic blood pressure; DBP, diastolic blood pressure

The details of laboratory results in different categories of patients are presented in Table 3. D-dimer elevation (≥0.50 mg/L)

was seen in 45.6% of the patients and was significantly increased with the severity of the disease. There was not much difference between the proportion of elevated D-dimer among men (47.4%) and women (43.5%). There was a significant difference in D-dimer elevation between younger (<60 years) and older patients (≥60 years) (34.4% vs. 58.8%). The median serum ferritin values, CRP, LDH, and NLR, were significantly increasing with the severity of COVID-19 patients.

Discussion

To our knowledge, this is the first comprehensive study to explore the patient characteristics of hospitalized COVID-19 patients from Kerala, India. The study patients are categorized based on the severity using the standard protocol. Our study patients were older compared with other Indian studies[15,16] and younger compared with patients reported from the USA[17] and Norway.[18] Most of the studies reported from India are based on a smaller sample size (SS) (SS: 114 adults,[15] SS: 224 adults,[16] SS: 50 children,[19] and SS: 197 adults).[20] The epidemiological characteristics of 1,632 hospitalized patients was reported from Rajasthan.[21] However, the clinical characteristics of the patients were not reported in the above study.

A study among hospitalized COVID-19-positive patients in the Maharashtra state of India reported a CFR of 29.4%.[20] A study from a Delhi hospital reported a CFR of 4.5%,[22] and another study among 224 COVID-19 patients in Rajasthan reported a CFR of 2.23%.[16]

Table 2: Discharge status by age group and sex of patients hospitalized with COVID-19

Discharge status	Age group		Total
	<60 years	≥60 years	
Nonsurvivors			
Men	6 (30.0)	14 (70.0)	20 (100.0)
Women	0 (0.0)	10 (100.0)	10 (100.0)
Total	6 (20.0)	24 (80.0)	30 (100.0)
Survivors			
Men	131 (53.5)	114 (46.5)	245 (100.0)
Women	121 (60.2)	80 (39.8)	201 (100.0)
Total	252 (56.5)	194 (43.5)	446 (100.0)

The higher proportion of men, older persons, and those with comorbidities are similar to that reported from China and New York.[17,23] The finding of a higher proportion of men being hospitalized for COVID-19 is consistent with earlier findings from many parts of the world.[24-27] A study among 1,632 COVID-19 patients in Rajasthan state reported higher mortality among older people with comorbidities.[21] A prospective observational study among hospitalized COVID-19 patients from the same state reported a higher proportion of men, urban residents, and those belonging to the middle socioeconomic class.[16] In the present study, 75% of patients had at least one comorbidity, which is higher than the earlier reports from Kerala[10,11] and also from other Indian states of Delhi (38.6%),[28] Maharashtra (47.2%),[20] and Chandigarh (29.8%).[15] However, higher comorbidity was reported among 93.9% of the hospitalized COVID-19 patients in the USA.[17] The higher comorbidity rate in our study might be a reflection of the higher overall morbidity rate of the state, which is three times that of the national average.[9] Diabetes and hypertension were the most common comorbidities, similar to studies reported elsewhere.[23,24,27,29] Fever was the most frequent symptom reported in this study, similar to that reported from other Indian studies.[15,21]

Our CFR of 6.3% was consistent with the 6.6% reported among hospitalized COVID-19 patients from Delhi, India.[28] This is in contrast to that reported among hospitalized patients from

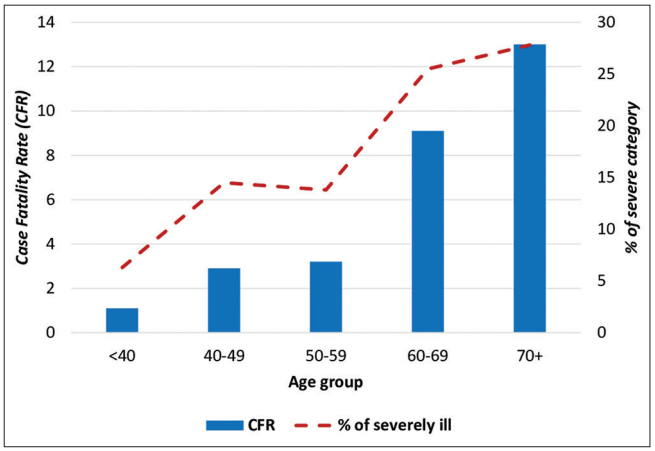

Figure 1: Case fatality rate (CFR) and proportion of severely ill patients in COVID-19 confirmed hospitalized patients

Table 3: Selected baseline laboratory results of patients hospitalized with COVID-19 in different categories

Vitals	Category (Median [IQR]/*n* [%])				Significance
	Mild	Moderate	Severe	Total	
Ferritin (ng/mL)					
Median (IQR) *n*=367	66 (25-173)	128 (51-242)	170 (96-384)	130 (51-243)	0.020
CRP (mg/dL)					
Median (IQR) *n*=364	5.0 (5.0-6.4)	5.5 (5.0-18.4)	32.4 (16.4-78.3)	5.9 (5.0-21.9)	<0.001
LDH (units/L)					
Median (IQR) *n*=365	198 (167-222)	203 (179-243)	265 (213-352)	207 (179-253)	<0.001
NLR					
Median (IQR) *n*=383	1.6 (1.1-2.2)	2.0 (1.3-3.1)	4.3 (2.3-8.3)	2.1 (1.3-3.3)	<0.001
Elevated D-dimer*(mg/L) *n*=360	18.8%	46.6%	73.7%	45.6%	<0.001

*D-dimer ≥0.50 mg/L, CRP, C-reactive protein; LDH, lactic acid dehydrogenase; NLR, neutrophil to lymphocyte ratio; IQR, interquartile range

Chandigarh (2.6%)[15] and Rajasthan (2.5%)[21] states of India and also from other countries like Iran (8.0%)[24] and the USA (21%).[17] Higher mortality among older people and those with comorbidity was similar to that reported earlier from Rajasthan.[21] Our findings can be generalized only to similar settings since there is a significant difference in population prevalence of comorbidity and demographics of Kerala compared with other Indian states. The study was done during the first COVID-19 surge, and the participants were not vaccinated at the time of the study.

The median CRP, LDH, and NLR values were significantly higher in severe category patients than in mild and moderate category patients. Our study reported that severity was significantly associated with D-dimer and serum ferritin values in COVID-19 patients similar to that reported earlier.[30] Our findings have important implications for the knowledge on the epidemiological and clinical profile of COVID-19 patients, which will help the healthcare professionals to improve their practices to reduce morbidity and mortality related to COVID-19.

Our study has some limitations. Since this is a retrospective study, there was some missing information in the hospital records. Secondly, the study included patients admitted to a single tertiary care hospital limiting generalizability. Thirdly, we relied on self-reports for some of the co-morbidities. Finally, the sample size was not predefined. Another limitation was that the clinical and laboratory values were available only for a subgroup of patients. During the initial period of the study, all category patients were admitted. Later, based on the Government guidelines, mild category patients were not admitted, which might alter the results of this study compared with other studies that have more moderate and severe category patients. The study center is a private hospital, and the hospitalization was not exclusively based on disease severity. In-hospital deaths alone were counted for "mortality" status.

Summary

In this single-center study of 476 COVID-19-positive patients in Kerala, we report an in-hospital CFR of 6.3%. There is evidence that the Asian population is more susceptible to COVID-19 compared with other races.[29,31] The findings of our study offer important information concerning the use of COVID-19 data from hospital records from an Indian state with the highest density of doctor and nurse workforce.[7] Age and multimorbidity might be contributing factors for death in hospitalized COVID-19 patients. Ninety percent of the patients who died had multimorbidity, and 80% of patients who died were elderly (age ≥60 years). A high CFR of 6.3% was reported even with unrestricted availability of all treatment options and ICU facility in a super specialty hospital. This needs to be further explored with well-designed large-scale studies. The epidemiological and clinical profiles of similar studies in the future may be different because of the impact of vaccination on death and serious complications.[32]

Key points

- Three-fourths of the study participants had at least one comorbidity, and half of them had multiple comorbidities.
- Higher age and multimorbidity were the major factors contributing to death in hospitalized COVID-19 patients
- Severity was significantly associated with elevation of D-dimer and serum ferritin values.

Ethical clearance

The study was duly approved by Institute Ethics Committee vide letter no. AHRI/EC/31/2021 (mentioned in material method section).

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Nil.

Conflicts of interest

There are no conflicts of interest.

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