

Original Research Article

A study of COVID-19 infection, severity and associated factors among the patients admitted at a tertiary care center in southern Rajasthan

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ABSTRACT

Background: Since December 2019, there has been various outbreaks of corona virus disease 2019 (COVID-19) disease. Whole world is combating this virus, but its reported clinical characteristics as well as outcomes vary greatly amongst studies. This study was conducted to study the clinical features, laboratory findings, comorbidities and severity of the disease among the patients admitted in tertiary care centre in Rajasthan.

Methods: It was a hospital-based cross-sectional study conducted from 1st January 2021 to 30th June 2022 in a tertiary care hospital in Udaipur, Rajasthan. All the patients diagnosed with the help of reverse transcription polymerase chain reaction (RT-PCR) for COVID-19, during the study period were included in the study. After taking consent, pre designed questionnaire was used to collect the personal, demographic and clinical information. Radiological, laboratory and mortality data were collected from hospital record.

Results: A total of 400 patients were included in the study. Mean age of the patients was 46.83 ± 17.09 years. Fever (88%) and cough (80%) were the most common symptoms followed by breathlessness (65.8%). About 31.8% (127) patients were found to have severe covid. Severity was found to be significantly associated with increasing age, urban area, breathlessness, co morbidities and D dimer, CRP and IL-6 levels (p value <0.05).

Conclusions: India being a diverse country with a range of sociodemographic characteristics existing within the population, needs a robust approach to control the COVID 19 pandemic. This study presents the factors associated with severe disease and can help to formulate preventive and control strategies.

Keywords: COVID-19, India, Infection, Severity

INTRODUCTION

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), the virus responsible for causing coronavirus disease 2019 (COVID-19) pandemic, has involved millions of cases worldwide.¹ It is a rapidly progressing global disease that may present with a variety of clinical manifestations with every new wave, and symptoms are not limited to just respiratory system. In adults, although COVID-19 presents typically as pneumonia and acute respiratory distress syndrome (ARDS), however it is now being recognized to be a multisystem disease. In contrast, most children with COVID-19 are either asymptomatic or have mild to moderate illness. Severe or critical illness is

found to be rare. Literature shows that SARS-CoV-2 infection triggers innate as well as adaptive immune response.² Tissue damage can result due to excessive pro-inflammatory response or dysregulated host response. The subsequent widespread immune dysregulation causes the release of massive amounts of cytokines and chemokines (cytokine storm). This cytokine storm, the attribute of SARS CoV-2 infection, evolves through many pathways, like the macrophage activation pathway, which leads to the release of interleukin-6 (IL-6) and other biomarkers. This activates several cell types and forms a positive feedback loop. Due to unregulated release of interleukins, particularly IL-6, several downstream pathways are stimulated, and further

increases the production of acute-phase reactants like C-reactive protein (CRP).² Studies have demonstrated that higher levels of IL-6 are correlated with severity and bilateral interstitial lung involvement. Many acute inflammatory markers have been identified as significant markers of severity and mortality in several meta-analyses and systematic reviews.³ With every new wave of this pandemic the clinical presentation has been found to be overlapping with other typical COVID-19 symptoms like fever, breathlessness and cough. The diagnosis and control strategies need to be made through a combined diagnostic approach. Data from various Indian states have provided a detailed view into severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission pathways and mortality. Reported cases and deaths have been concentrated in high incidence settings.⁴

With this study we aimed to provide clinic epidemiological profile of COVID-19 patients admitted in a tertiary care center of Udaipur in the state of Rajasthan. We also studied the demographic characteristics and relevant laboratory findings of the patients and evaluated their association with severity of disease.

METHODS

It was a hospital-based cross-sectional study conducted from 1st January 2021 to 30th June 2022 in a tertiary care hospital in Udaipur, Rajasthan. All the patients diagnosed with the help of reverse transcription polymerase chain reaction (RTPCR) for COVID-19, during the study period were included in the study. Purposive, consecutive sampling was used to include the patients. The purpose of study was explained to patient's attendants/relatives and after the written consent, the pre-structured and pre designed questionnaire was filled according to the information given by patient's attendants/relatives and radiological, laboratory and mortality data was collected from hospital record during their stay at hospital. Severity of the disease was classified according to radiological high-resolution computed tomography (HRCT) chest score. The patients with HRCT score of 1 to 8 were classified as mild covid, score of 9 to 15 were termed as moderate and the patients with HRCT score of more than 15 were classified as severe COVID disease.⁵

Data confidentiality and privacy was maintained at all stages of the study. Option to exit the study was kept open to participants at all times. Sample size was calculated using following formula,

$$N = \left[\frac{(Z_{\alpha})^2 P(100 - P)}{(E)^2} \right]$$

Z_{α} is 95% confidence level =1.96.

P is prevalence of COVID-19, diagnosed as positive with RTPCR as 9.4%, taken from a study done by Rajni et al in Rajasthan.⁶

E is margin of error =3%.

The sample size was calculated as 364. After taking 10% non-response rate, total sample size of 400 study subjects was considered.

Statistical analysis

Data entry was done in MS Excel and statistical analysis was done using SPSS IBM version 21. Descriptive analysis was done using mean and SD, ratio, proportion and percentage.

Inferential analysis was done using test of significance using Student t test (unpaired) and Chi square test. $P < 0.05$ was considered as level of statistical significance.

Ethical considerations

Before commencing the study, clearance was obtained from the Institutional ethics committee. Data confidentiality and privacy was maintained at all stages of the study. Option to exit the study was kept open to participants at all times.

RESULTS

Mean age of the patients was 46.83 years (SD=17.09). Majority (42.75%) were in the age group of 18-40 years followed by 41-60 years of age (30%). Out of the total patients, 67.8% were females and 32.2% were males. Most (85.3%) of the patients were from urban area. Sociodemographic variables are shown in Table 1.

Table 1: Sociodemographic variables of the study participants.

Variables	Number	Percentage
Age in years (mean±SD)	46.83±17.09	
Gender	Male	129
	Female	271
Marital status	Married	85
	Unmarried	47
Residence	Urban	341
	Rural	59
Caste	General	314
	OBC	63
	SC	18
	ST	5
Religion	Hindu	367
	Muslim	25
	Christian	8

Table 2 shows the clinical characteristics of the patients. Regarding the symptoms, fever was the most common symptom observed in 352 (88%) followed by cough in 320 (80%), breathlessness in 263 (65.8%), myalgia in 120 (30%), anosmia in 16 (4%), rhinorrhea in 14 (3.5%),

vomiting in 7 (1.8%) and diarrhea in 5 (1.3%) patients. Out of 400 covid patients, 151 (37.85%) had contact history and 39 (9.8%) had travel history. Regarding the comorbidities, hypertension was most common and was seen in 209 (52.3%), diabetes mellitus in 155 (38.8%), cardiac disease in 52 (14.2%), tuberculosis or respiratory disease in 33 (8.3%), renal disease in 22 (5.5%), neurological disease in 17 (4.3%), thyroid in 17 (4.3%) and mental illness, anemia and some other co morbidities was seen in few covid patients. Out of total patients, 244 (61.0%) were admitted in ward and 156 (39%) were admitted in ICU. Majority of person who died were admitted in ICU. Out of total patients, 309 (77.3%) were cured and 91 (22.8%) died.

With the increase in age proportion of patients with mild severity decreased and proportion of moderate and severe case were increased with the increase in age. Regarding

the association of age and severity of disease, it was found that there was significant association of age and severity ($p < 0.001$). Out of 271 female patients, 113 (41.7%) had mild HRCT score, 83 (30.63%) had severe and 75 (28.68%) had moderate severity HRCT score and in 129 male patients, 53 (41.09%) had mild HRCT score, 44 (34.11%) had severe and 22 (17.05%) had moderate severity HRCT score. There was insignificant association of gender and severity of disease ($p > 0.05$). Among patients with symptom and complaint of breathlessness, 124 (47.15%) had severe HRCT score, 85 (32.32%) had mild and 54 (20.53%) had moderate HRCT score ($p < 0.001$). The severity score was significantly associated with the symptom of breathlessness, vomiting and diarrhea ($p < 0.05$). There was significant difference in IL-6, D-Dimer and CRP values between patients with mild, moderate and severe HRCT thorax score ($p < 0.05$).

Table 2: Clinical characteristics of the study participants.

Variables	Number	Percentage
Symptoms	Fever	352
	Cough	320
	Breathlessness	263
	Myalgia	120
	Anosmia	16
	Rhinorrhoea	14
	Vomiting	7
	Diarrhoea	5
Source of contact	Contact history	151
	Travel history	39
Co morbidities	Hypertension	209
	Diabetes mellitus	155
	Cardiac disease	52
	Respiratory disease	33
	Renal disease	22
	Neurological disease	17
	Thyroid	17
	Mental illness	3
	Anaemia	2
	Others	6
Place of admission	Ward	244
	ICU	156
Biochemical markers (Mean±SD)	D-Dimer (normal value <500 ng/ml)	2100.28 (5529.84)
	CRP (normal value <5 mg/l)	67.62 (106.16)
	IL-6 (normal value <7.0 pg/ml)	69.63 (100.79)
Outcome	Cured	309
	Deceased	91

Table 3: Association of various variables with severity of disease.

Variables	Categories		Severity (HRCT score)			P value
			Mild (N=166)	Moderate (N=107)	Severe (N=127)	
			N ()	N (%)	N (%)	
Age (in years)	18-40	171	88 (51.46)	25 (14.62)	58 (33.92)	<0.001
	41-60	120	56 (46.67)	32 (26.67)	33 (27.5)	
	61-80	105	23 (21.90)	49 (46.67)	33 (31.43)	

Continued.

Variables	Categories		Severity (HRCT score)			P value
Gender	Female	271	113 (41.7)	75 (28.68)	83 (30.63)	0.737
	Male	129	53 (41.09)	22 (17.05)	44 (34.11)	
Residence	Rural	59	13 (22.03)	17 (28.81)	29 (49.15)	0.001
	Urban	341	153 (44.87)	90 (26.39)	98 (28.74)	
Symptoms	Fever	352	150 (42.61)	97 (27.56)	105 (29.83)	0.082
	Cough	320	138 (43.13)	87 (27.19)	95 (29.69)	0.194
	Breathlessness	263	85 (32.32)	54 (20.53)	124 (47.15)	<0.001
	Myalgia	120	44 (36.67)	36 (30.00)	40 (33.33)	0.411
	Anosmia	16	10 (62.50)	3 (18.75)	3 (18.75)	0.22
	Rhinorrhoea	14	4 (28.57)	4 (28.57)	6 (42.86)	0.56
	Vomiting	7	7 (100)	0	0	0.007
	Diarrhoea	5	5 (100)	0	0	0.03
Comorbidities	Hypertension	209	71 (33.97)	54 (25.84)	84 (40.19)	<0.001
	Diabetes mellitus	155	57 (36.77)	37 (23.87)	61 (39.35)	0.034
	Cardiac disease	57	19 (33.33)	10 (17.54)	28 (49.12)	0.009
	Respiratory disease	33	8 (24.24)	5 (15.15)	20 (60.61)	0.001
	Renal disease	22	5 (22.73)	3 (13.64)	14 (63.64)	0.004
	Neurological disease	17	1 (5.88)	4 (23.53)	12 (70.59)	0.001
	Thyroid	17	7 (41.18)	1 (5.88)	9 (52.94)	0.067
	Mental illness	2	1 (50.00)	0	1 (50.00)	0.475
	Anaemia	1	0	1 (100)	0	0.293
	Others	6	1 (16.67)	4 (66.67)	1 (16.67)	0.148
		Normal value	Mild (166) Mean±SD	Moderate (107) Mean±SD	Severe (127) Mean±SD	
Biochemical markers	D-Dimer	<500 ng/ml	614.78 (667.68)	1082.21 (1943.84)	4899 (14661.24)	<0.001*
	CRP	<5 mg/l	30.49 (94.81)	63.86 (68.60)	118.99 (124.14)	<0.001*
	IL-6	<7.0 pg/ml	21.96 (23.31)	61.36 (82.19)	140.58 (133.99)	<0.001*

DISCUSSION

In our study, the mean age of patients was 46.83±17.09 years, which is comparable to other studies done in Rajasthan and other parts of the country.⁷⁻¹⁰ Most (85.3%) of the patients were from urban area. This finding is similar to other studies done in India.^{7,9} Verma et al revealed that more than half (54.6%) of patients were from urban area.⁷ It is believed that COVID-19 being highly transmissible disease, spreads easily in densely populated urban areas as compared to rural areas. A study done by Bhadra et al revealed that the moderate association between COVID-19 spread and population density were higher for larger population density.⁸ In our study, increased age was found to be significantly associated with more severe disease (p value <0.001). This finding is similar to the results shown by other studies, where age was found to be significantly associated with the severity of disease as well as mortality.⁹⁻¹¹ In our study, fever was the most common symptom (88%) followed by cough (80%), breathlessness (65.8%), myalgia (30%), anosmia (4%), rhinorrhoea (3.5%), vomiting (1.8%) and diarrhoea (1.3%). Out of all the patients with history of breathlessness, about 47.15% had severe HRCT score, 20.53% had moderate and 32.32% had mild HRCT score. The severity of the diseases was found to be significantly associated with presence of breathlessness among patients (p<0.001). All

the patients with complaint of vomiting and/ diarrhoea had only mild covid. Studies have demonstrated that breathlessness is significantly associated with a higher mortality among COVID-19 patients.^{7,12} However, it was not always correlated with the severity of the disease. A retrospective study done by Guan et al found that out of 1,099 patients, 86% had abnormal CT scans and low PaO₂/FiO₂ ratios, however out of total only 18.6% of patients had breathlessness.¹³ This difference could be attributed the fact that breathlessness is subjective, and physical or clinical characteristics may under or, overestimate patients' discomfort. Literature shows that studies have reported a wide range of prevalence of breathlessness as presenting symptom. Some of this variability can be explained by the different tools used for evaluation of breathlessness, as they were not specified in the majority of studies.¹⁴ Moreover, breathlessness is a common symptom in the general population, and patients may contract COVID-19 already suffering from breathlessness. This could lead to an overestimation of the number of patients experiencing breathlessness related to COVID-19. Therefore, variation in breathlessness could be a better measure of breathlessness caused by COVID-19.¹⁵

In our study, the patients suffering from comorbidities such as hypertension, diabetes mellitus, cardiac disease, respiratory disease, renal disease and neurological disease

were found to have significantly higher severity score. This finding is comparable to the results shown by a systematic review done by Radwan et al, which revealed that presence of comorbidities among COVID-19 patients, increases the probability of having severe COVID-19 by approximately three times (OR=2.85, 95% CI=2.1-3.9) among the patients.¹⁶ This finding is consistent with the results shown by Liu et al, Zhang et al, and Guan et al, which revealed the presence of comorbidities among severe cases of COVID-19 as 25.6%, 79.3%, and 23.7% respectively.^{13,17,18} The findings of Huang et al and Zhang et al reported these comorbidities as mainly hypertension, diabetes, and cardiovascular diseases (CVD).^{18,19} The systematic review done by Radwan et al showed that hypertension was significantly associated with a two times increased risk of severe COVID (OR=2.05, 95% CI=1.56-2.70). Similar results were shown by Lippi et al, according to which, hypertensive patients had about 2.5 times risk of severe COVID-19 (OR: 2.49, 95%CI 1.98 -3.12).²⁰ In our study, the biochemical markers such as IL-6, D-Dimer and CRP were found to be significantly associated with severity of the disease. This finding is similar to many other studies done about COVID-19 and biomarkers, which showed them to be significantly associated with severe disease.²¹⁻²³

CONCLUSION

The COVID-19 pandemic has displayed the considerable variations in patients' demographics, access to healthcare, health system infrastructure, access to health care and preparedness among various regions, which significantly impacts the outcomes of this disease. This study aims to elucidate the socio demographic, clinical characteristics, co morbidities, laboratory changes and other significant factors associated with the severity of COVID-19 disease. These factors are crucial for developing the preventive strategies and health policy changes required to combat this disease.

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