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Original Article

Clinical characteristics and clinical predictors of mortality in hospitalised patients of COVID 19 : An Indian study

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ABSTRACT

Background: The rapid spread of the coronavirus disease 2019 (COVID-19) with high mortality rate necessitates disease characterization and accurate prognostication for prompt clinical decision-making. The aim of this study is to study clinical characteristics and predictors of mortality in hospitalized patients with COVID-19 in India.

Methods: Retrospective cohort study was conducted in a tertiary care hospital in northern India. All consecutive confirmed hospitalized COVID-19 cases aged 15 years and older from 13 Apr till 31 Aug 2020 are included. Primary end point was 30-day mortality.

Results: Of 1622 patients ,1536 cases were valid. Median age was 36 years, 88.3% were men and 58.1% were symptomatic. Fever (37.6%) was commonest presenting symptom. Dyspnea was reported by 15.4%. Primary hypertension (8.5%) was commonest comorbidity, followed by diabetes mellitus (6.7%). Mild, moderate, and severe hypoxemia were seen in 3.4%, 4.3%, and 0.8% respectively. Logistic regression showed greater odds of moderate/severe disease in patients with dyspnea, hypertension, Chronic Kidney Disease (CKD), and malignancy. Seventy six patients died (4.9%). In adjusted Cox proportional hazards model for mortality, patients with dyspnea (hazard ratio [HR]: 14.449 [5.043-41.402]), altered sensorium (HR: 2.762 [1.142-6.683]), Diabetes Mellitus (HR: 1.734 [1.001-3.009]), malignancy (HR:10.443 [4.396-24.805]) and Chronic Liver Disease (CLD) (HR: 14.432 [2.321-89.715]) had

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higher risk. Rising respiratory rate (HR: 1.098 [1.048-1.150]), falling oxygen saturation (HR: 1.057 per unit change 95% CI: 1.028-1.085) were significant predictors.

Conclusion: Analysis suggests that age, dyspnea, and malignancy were associated with both severe disease and mortality. Diabetes Mellitus and Chronic Liver Disease were associated with increased the risk of fatal outcome. Simple clinical parameters such as respiratory rate and oxygen saturation are strong predictors and with other risk factors at admission can be effectively used to triage patients.

Introduction

Coronavirus Disease 2019 (COVID-19) is a rapidly spreading pandemic characterized by respiratory disorder due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1] The virus is an enveloped RNA virus, which enter the cells by ACE II receptor. COVID-19 spreads by aerosols, droplets and by direct or indirect contact with an infected person. Although majority of patients are asymptomatic or minimally symptomatic, the disease, due its enormous numbers and its requirement of expensive intensive care, is putting a strain on healthcare services.

Given the rapid spread of COVID-19 and a steep rise in associated morbidity and mortality, the World Health Organization (WHO) declared it as a pandemic on 11 Mar 2020. Cases have, henceforth, grown exponentially with more than four crore affected worldwide and an excess of 11 lakh deaths till 24 Oct 2020. Ever since India announced its first case on 30 Jan 2020, it is reporting an increasing number of cases. COVID-19 cases in India crossed 78 lakhs as on 24 Oct 2020 with 1,17,992 deaths in India alone.

The management COVID-19 is peculiar and hurdled by numerous hindrances to routine diagnostic testing and evaluation. In our country, where healthcare infrastructure is often basic and lacking in specialised diagnostic facilities, triage and risk assessment based on clinical parameters can help in a big way in channelising healthcare efforts and resources. However, no reliable clinical models currently exist to predict outcomes or which enable to make well-informed decisions regarding hospital admission for patients with COVID-19. There is a felt need to delineate the disease characteristics in India and to determine the predictors of adverse outcomes in COVID-19. Initial studies in India describing the disease characteristics are limited with small numbers. This may be due to the vast number of the cases overwhelming the already perplexed healthcare infrastructure of the country, posing problems such lack of adequate documentation. In the given premise, the present study was planned to ascertain the clinical characteristics of the disease as well as the predictors of disease severity and mortality in our clientele who hail from various parts of the country and hence constitute a representative population. This study was carried out in a tertiary care centre at northern India.

Materials and methods

This is a retrospective cohort study carried out in a tertiary care hospital in northern India. All consecutive confirmed hospitalised COVID-19 cases from the first case, which was admitted on 13 Apr till 31 Aug 2020 were included. Clearance from the institute ethical committee was obtained.

The inclusion criteria included

1. Confirmed cases of SARS COVID-19 by RT PCR from posterior pharyngeal and nasal swabs
2. Age – 15 years and above

Exclusion

1. Age less than 15 years
2. All suspected cases or cases with positive rapid antigen test where COVID 19 RT PCR was negative
3. Associated confounding infectious diseases such as dengue, malaria, Urinary Tract Infection (UTI) at admission
4. Cases with missing variables

Primary end point

In-hospital all-cause mortality data collection.

A retrospective analysis of data of admitted patients was done, wherein the data recorded were inclusive of demographic profile, clinical profile, comorbidities and vital parameters at admission. The demographic profile included age and gender. Presenting symptoms were objectively recorded and included fever, sore throat, cough, nasal discharge, expectoration, myalgia, fatigue, diarrhoea, dyspnoea, vomiting, chest pain, headache, dysgeusia, anosmia, anorexia and altered sensorium. Comorbid conditions comprised of diabetes mellitus, hypertension, cardiac disease, chronic obstructive lung disease or airway diseases including asthma and bronchitis, renal disease, liver disease, malignancy and other diseases such as endocrine disorders. Vital parameters were recorded at the time admission and were inclusive of temperature, pulse rate, blood pressure, respiratory rate and the oxygen saturation (SpO2) by pulse oximetry.

Definitions

A confirmed case of COVID-19 was defined as a positive result by real-time reverse transcriptase– polymerase chain reaction (RT-PCR) assay of nasal and pharyngeal swab specimens.[2] Based on national guidelines, the patients were categorised into mild, moderate and severe disease using clinical parameters. Mild disease included patients with uncomplicated upper respiratory tract symptoms such as fever, sore throat, cough, malaise and headache without evidence of breathlessness or hypoxia. Patients with an oxygen-saturation of 90–94% or respiratory rate more than or equal to 24 breaths per minute were comprised of moderate disease and those who had an oxygen saturation of less than 90% or a respiratory rate of more than 30 breaths per minute with clinical signs of pneumonia constituted severe disease.[3] For purpose of descriptive analysis, standard definitions were used to dichotomise the vital parameters. Tachycardia was defined as a resting heart rate of more than 90 beats per minute, tachypnea as a resting breathing rate of greater than 20 and hypotension as a systolic blood pressure of less than 90 mm Hg. Hypoxemia was further categorised as mild (SpO2 90–94%), moderate (SpO2 75–89%) and severe (SpO2 <75%).

Statistical analysis

Demographic, clinical parameters and outcomes were initially analysed using descriptive statistics. Continuous variables were presented as median and interquartile range (IQR) and were compared by means of t-test or one-way analysis of variances (ANOVA) if normally distributed. Mann–Whitney U test and Kruskal–Wallis test were appropriately used for comparison of non-normally distributed data. Categorical variables were presented as percentages and as frequency distribution and compared by Chi-square tests. For continuous variables, receptor operation curves (ROCs) were plotted for sensitivity–specificity analysis and optimal cut-offs were decided for the predictor variables. Multiple logistic regression analysis for disease severity at admission was used to determine the predictive effect of various demographic and clinical parameters as well as that of underlying comorbidities with odds ratio (OR) and 95% confidence intervals being reported. Survival analysis was done using Cox-proportional hazards regression. Univariable models were adopted to evaluate individual risk factors pertaining to mortality. Multivariable analysis was done adjusting for potential confounding effects of other parameters. A two-sided alpha value of less than 0.05 was considered to be significant for 95% confidence interval and beta of 0.2. MS Excel 2016 was used for data handling and SPSS 23 and PASS 15.0.5 for data analysis.

Results

Demographic profile and symptoms at admission

The study was conducted in a tertiary care hospital in northern India. In all, 1654 patients diagnosed with COVID-19 by RT-PCR of posterior pharyngeal, and nasal swabs were admitted from 13 April till 31 Aug 2020. Out of these, 1622 hospitalised patients met the inclusion criteria for the study. Eighty-six patients were excluded due to missing variables; the resultant 1536 valid patients being selected for analysis. The median age of patients was 36 years; IQR was 20 with a range of 15–94 years. The age-wise distribution of cases is given in Table 1. It is evident that the highest proportion of cases were observed in the 30–45 years age group, which accounted for 39.3% of all cases. Males represented 1357 (88.3%) of the total cases while 179 (11.7%) were females. The mean duration of admission was 13 days with a maximum of 76 days.

A total of 893 (58.1%) patients were symptomatic, whereas 643 (41.9%) patients reported no symptoms at admission. The frequency distribution of presenting symptoms is given in Table 1. Fever was the most common presenting symptom but was seen only in 557 (37.6%) of patients. Cough was next common symptom and was present in 401 (26.1%) patients. Dyspnea was the third commonest symptom and was reported by 237 (15.4%) patients. Sore throat was seen only in 222 (14.5%) patients. Other less common symptoms included

Table 1 – Age-wise distribution of cases and mortality (n = 1536).

Table no. 1
A. Age-wise distribution of cases and deaths

Age in years	Numbers N-1536	Percentage of cases	No. of deaths(%) Total 76(4.9%)	Percentage of deaths
15–30	473	30.8	1	1.3%
31–45	603	39.3	11	14.5%
46–60	286	18.6	21	27.6%
61–80	152	9.9	34	77.8%
>80	22	1.4	9	11.8%

B- Frequency of symptoms at admission (n = 1536)

S. No.	Symptom	Total number: 1536 (%)
	Symptomatic	893 (58.1)
	Asymptomatic	643 (41.9)
1	Fever	558 (37.6%)
2	Cough	401(26.1%)
3	Dyspnea	237 (15.4%)
4	Sore throat	222 (14.5%)
5	Fatigue	95 (6.2%)
6	Coryza	32 (2.1%)
7	Anosmia	27 (1.8%)
8	Dysguesia	25 (1.4%)
9	Diarrhea	25 (1.6%)
10	Headache	73 (4.8%)
11	Vomiting	17 (1.1%)
12	Myalgia	153(10%)
13	Anorexia	24 (1.6%)
14	Altered sensorium	12 (0.8%)
15	Chest pain	13 (0.8%)
16.	Pain abdomen	5 (0.3%)
17	Dyspepsia	3(0.20%)
18	Odynophagia	1 (0.07%)
19.	Dysuria	1(0.07%)
20	Ischemic stroke	2(0.13%)
21	Seizure	3(0.20%)

Table 2 – Number of comorbidities and comorbidities.

A. Number of comorbidities	Frequency (N: 1536)	Percentage
1	196	12.8
2	76	4.9
3–4	40	2.6
>4	2	0.1
At least 1 comorbidity	314	20.44
No comorbidity	1222	79.56
B. Comorbidity conditions		**Number (%)**
Diabetes mellitus		103 (6.7%)
Hypertension		130 (8.5%)
Coronary artery disease		49 (3.2%)
Chronic obstructive pulmonary disease and bronchial asthma		8 (0.5%)
Chronic kidney disease		15 (1%)
Chronic liver disease		3 (0.2%)
Malignancy		45 (2.9%)
Cerebrovascular accident		11 (0.7%)
Other chronic conditions: Hypothyroidism, Hyperthyroidism, benign prostatic hypertrophy etc.		114 (7.4%)
Antenatal		9 (0.6%)

myalgia in 153 (10%) patients and fatigue in 95 (6.2%) patients. Headache, coryza, anosmia and dysgeusia were rather rare symptoms and were seen in 73 (4.8%), 32 (2.1%), 27 (1.8%) and 21 (1.4%) patients, respectively.

Comorbidities

Out of the 1536 cases, 196 (12.8%) of patients had had one comorbidity, 76 (4.9%) had two comorbidities and 42 (2.6%) had three or more comorbidities. A total of 1222 (79.6%) patients had no underlying comorbid conditions (Table 2). The relative frequencies of specific comorbidities have been shown in Table 2. Primary hypertension was the commonest comorbidity, seen in 130 (8.5%) patients, followed by diabetes mellitus in 103 (6.7%) patients. Coronary artery disease was present in 49 (3.2%) patients. Forty-five (2.9%) patients had underlying malignancy. Other less common comorbidities included Chronic Kidney Disease (CKD) in 15 (1%), chronic obstructive pulmonary disease and bronchial asthma in 8 (0.5%), cerebrovascular accident in 11 (0.7%) and CKD in 3 (0.2%) patients. There were nine cases with pregnancy. Other medical and surgical conditions were grouped together and were seen in 114 (7.4%) patients.

Clinical parameters at admission

Fever at admission was recorded in only 15 (1%) patients; whereas 86 (5.6%) patients had resting tachycardia and 7 (0.5%) patients were hypotensive at admission. Tachypnea at rest was observed in 172 (11.2%) patients. Majority of patients (n = 1404 [91.4%]) maintained a normal oxygen saturation at admission, while, mild, moderate and severe hypoxemia at

Table 3 – Predictors of moderate to severe disease (n = 1536).

Predictors	Predictor variables	Mild disease (n = 1361)	Moderate to severe disease (n = 175)	P value
	Median age	57 years	35 years	**<0.001**
Gender	Male	1216	141	0.002
	Female	145	34	
Symptomatic	Asymptomatic	640	2	<0.001
	Symptomatic	721	173	
Symptoms	Fever	444	134	<0.001
	Cough	290	111	<0.001
	Dyspnea	105	132	<0.001
	Sore throat	196	26	0.909
	Fatigue	62	33	<0.001
	Coryza	30	2	0.571
	Anosmia	26	1	0.354
	Dysgeusia	20	1	0.500
	Diarrhea	18	7	0.018
	Headache	69	4	0.129
	Vomiting	14	3	0.431
	Myalgia	125	28	0.007
	Altered sensorium	3	9	<0.001
	Chest pain	11	2	0.652
	Pain abdomen	3	2	0.103
	Anorexia	17	7	0.014
Comorbidities	Diabetes mellitus	62	41	<0.001
	Hypertension	71	59	<0.001
	Coronary artery disease	28	21	<0.001
	Chronic obstructive pulmonary disease and bronchial asthma	2	6	<0.001
	Chronic kidney disease	7	8	<0.001
	Chronic liver disease	3	0	1.000
	Malignancy	34	11	0.014
	Other comorbidities	82	32	<0.001
	Cerebrovascular accident	11	0	0.625

Table 4 – Predictors of moderate to severe disease – multiple logistic regression for adjusted and unadjusted odds ratio.

Predictors	Predictor variables	Crude odds ratio (OR) (95% CI)	P value	Adjusted odds ratio (OR) (95% CI)	P value
General	Age	1.087 (1.075–1.099)	<0.001	1.044 (1.027–1.061)	<0.001
	Gender (male vs female)	2.022 (1.339–3.054)	0.001	0.508 (0.279–0.927)	0.025
Symptoms	Symptomatic	37.563 (13.870–101.727)	<0.001	5.178 (1.626–16.492)	0.005
	Fever	6.289 (4.385–9.020)	<0.001	1.352 (0.787–2.322)	0.275
	Cough	6.501 (4.649–9.090)	<0.001	1.706 (1.066–2.731)	0.026
	Dyspnea	36.720 (24.674–54.649)	<0.001	12.075 (7.525–19.377)	<0.001
	Sore throat	1.037 (0.666–1.616)	0.872	–	–
	Fatigue	4.869 (3.085–7.686)	<0.001	2.490 (1.301–4.764)	0.006
	Coryza	0.513 (0.122–2.165)	0.364	–	–
	Anosmia	0.295 (0.040–2.188)	0.233	–	–
	Dysgeusia	0.385 (0.051–2.889)	0.354	–	–
	Diarrhea	3.109 (1.280–7.553)	0.012	3.198 (1.069–9.563)	0.038
	Headache	0.438 (0.158–1.215)	0.113	–	–
	Vomiting	1.678 (0.477–5.899)	0.011	–	–
	Myalgia	1.883 (1.208–2.936)	0.005	–	–
	Altered sensorium	24.542 (6.579–91.555)	<0.001	4.664 (0.486–44.748)	0.182
	Chest pain	1.419 (0.312–6.454)	0.651	–	–
	Pain abdomen	5.229 (0.868–31.515)	0.071	–	–
	Anorexia	3.294 (1.346–8.059)	0.009	1.172 (0.362–3.789)	0.791
Comorbidities	Diabetes mellitus	6.411 (4.159–9.882)	<0.001	0.796 (0.407–1.558)	0.506
	Hypertension	9.241 (6.231–13.705)	<0.001	1.961 (1.054–3.649)	0.033
	Coronary artery disease	6.492 (3.599–11.710)	<0.001	1.642 (0.679–3.970)	0.271
	Chronic obstructive pulmonary disease and bronchial asthma	24.124 (4.830–120.480)	<0.001	2.370 (0.390–14.403)	0.349
	Chronic kidney disease	9.266 (3.318–25.878)	0.002	6.917(1.576–30.364)	0.010
	Chronic liver disease	0.000	0.999	–	–
	Malignancy	2.618 (1.301–5.266)	<0.001	10.651 (3.652–31.062)	<0.001
	Other comorbidities	3.490 (2.240–5.439)	<0.001	1.264 (0.639–2.502)	0.501
	Cerebrovascular accident	0.000	0.999	–	–

Table 5 – Predictors of mortality (n = 1536).

Predictors	Predictor variables	Died (n = 76)	Survived (n = 1460)	P value
	Median age	63.5 years	35 years	<0.001
Gender	Male	59	1298	0.005
	Female	17	162	
Symptomatic	Asymptomatic	0	642	<0.001
	Symptomatic	76	818	
Symptoms	Fever	50	527	<0.001
	Cough	42	359	<0.001
	Dyspnea	68	169	<0.001
	Sore throat	10	212	0.868
	Fatigue	13	82	0.001
	Coryza	1	31	1.000
	Anosmia	0	27	0.641
	Dysgeusia	0	21	0.621
	Diarrhea	1	24	0.335
	Headache	0	73	0.046
	Vomiting	3	14	0.048
	Myalgia	4	149	0.235
	Altered sensorium	11	1	<0.001
	Chest pain	2	11	0.133
	Pain abdomen	0	5	1.000
	Anorexia	2	22	0.441
Vitals	Tachycardia	30	56	<0.001
	Tachypnea	64	108	<0.001
	Fever at admission	5	10	<0.001
	Shock	4	3	<0.001
	Mild hypoxemia (SpO2: 90–94%)	9	43	<0.001
	Moderate hypoxemia (75–90%)	38	28	
	Severe hypoxemia (<75%)	11	2	
Comorbidities	Diabetes mellitus	23	80	<0.001
	Hypertension	28	102	<0.001
	Coronary artery disease	11	38	<0.001
	Chronic obstructive pulmonary disease and bronchial asthma	2	6	<0.001
	Chronic kidney disease	4	11	<0.001
	Chronic liver disease	2	1	0.007
	Malignancy	11	34	<0.001
	Other comorbidities	19	95	<0.001
	Cerebrovascular accident	0	11	1.000

admission were seen in 52 (3.4%), 66 (4.3%) and 13 (0.8%) patients, respectively.

Demographic profile, symptoms and comorbidities as predictors of disease severity

Out of the total 1536 patients included in the study, 1361 (88.6%) patients had mild disease at admission. Moderate to severe disease at admission was observed in 175 (11.4%) patients. The association of disease severity at admission with the demographic and clinical profile and comorbidities is presented in Table 3. Patients with moderate to severe disease at admission had a median age of 57 years (IQR 23), which was significantly higher than patients with mild disease at admission (median 35, IQR 17). Patients with moderate to severe disease, compared with those with mild disease were more likely to be symptomatic (98.9% versus 52.9%). They had significantly high prevalence of fever at admission (76.6% versus 32.5%), cough (63.8% versus 21.3%) and dyspnea (75.4% versus 7.7%). Less common symptoms such as fatigue, diarrhea, myalgia, altered sensorium and anorexia were also significantly more prevalent in patients with moderate to severe disease than those with mild disease. Almost all comorbidities including diabetes mellitus, hypertension, coronary artery disease, COPD and bronchial asthma, chronic kidney disease, chronic liver disease, malignancy and other medical and surgical conditions such as hyperthyroidism or hypothyroidism or BPH were commoner in patients with severe disease. Chronic liver disease and cerebrovascular disease showed no significant association. The results of the multiple logistic regression for disease severity at admission is given in Table 4. It is evident from this analysis that, a rising age (OR 1.044, per year increase in age 95% CI 1.027-1.061) the male gender (OR 0.508 95% CI 0.279-0.927) positively correlated with the odds of moderate to severe disease. Symptomatic patients were associated with greater odds (OR 5.178 95% CI 1.626-16.492) of moderate to severe disease. Presenting complaints of cough (OR 1.706 95% CI 1.066-2.731), dyspnea (OR 12.075 95% CI 7.525-19.377), fatigue (OR 2.490 95% CI 1.301-4.764), underlying comorbidities including hypertension (OR 1.961 95% CI 1.054-3.649), CKD (OR 6.917 95% CI 1.576 -30.364) and malignancy (OR 10.6511 95% CI 3.352-31.062) significantly increased the odds of moderate to severe disease.

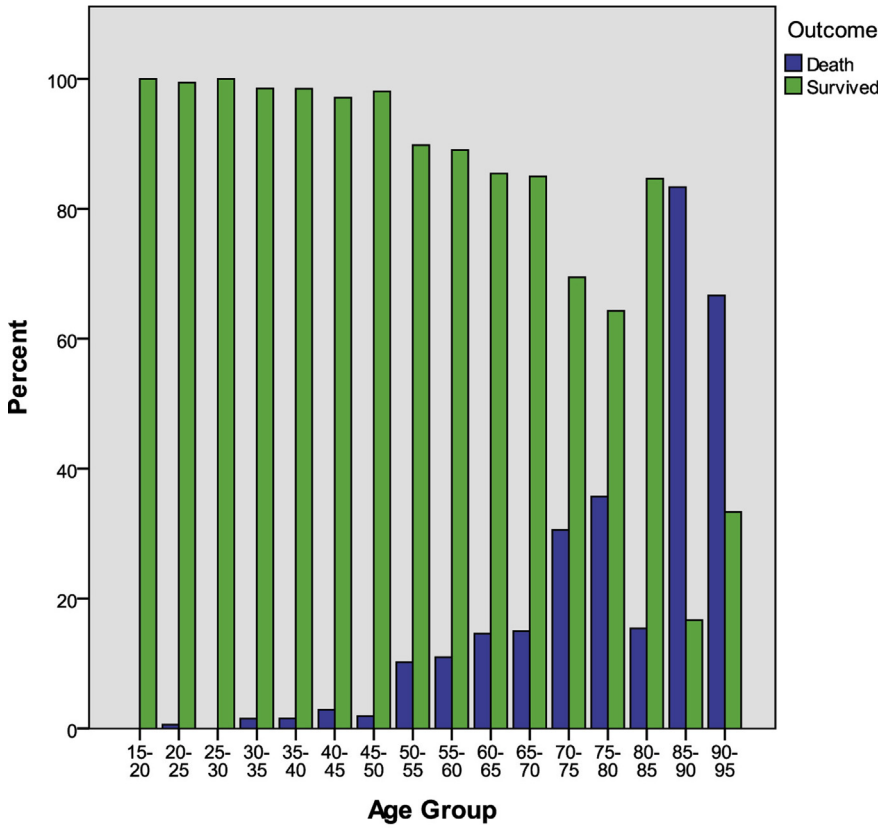

Fig. 1 – Age-wise distribution of cases and mortality.

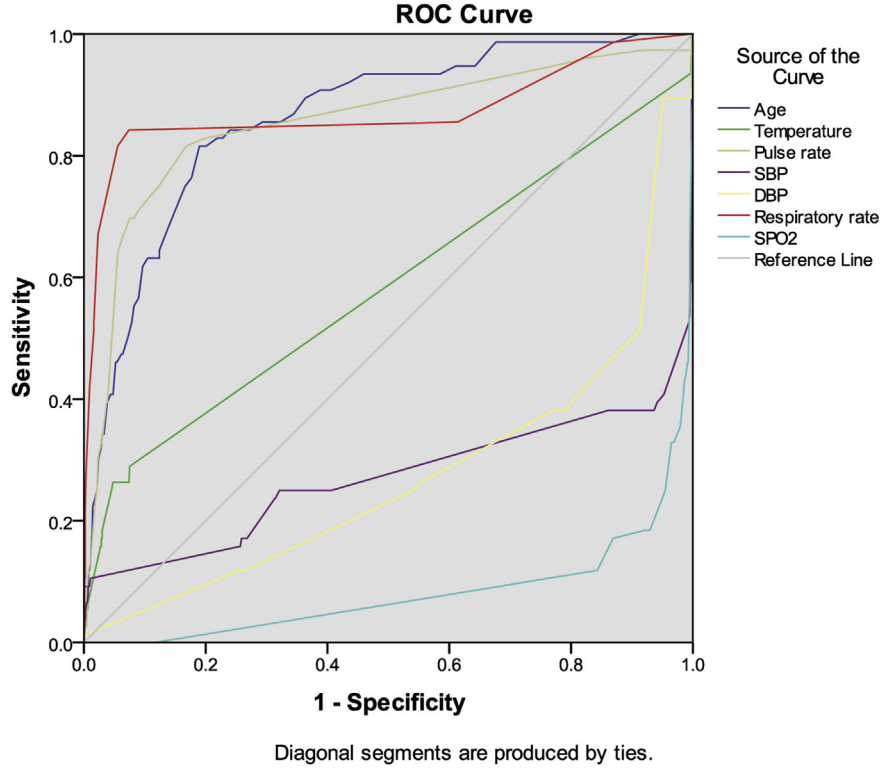

Fig. 2 – Sensitivity and specificity analysis for continuous predictors of mortality.

Table 6 – Predictors of mortality – Cox regression for unadjusted and adjusted hazards ratio (HR).

Predictors	Predictor variables	Crude HR (95% CI)	P value	Adjusted HR (95%CI)	P value
General	Age	1.081 (1.068–1.094)	<0.001	1.017 (1.000–1.035)	0.055
	Gender	2.690 (1.565–4.622)	<0.001	0.678 (0.328–1.398)	0.292
Symptoms	Symptomatic	14.762 (7.945–27.427)	<0.001	7.880 (1.938–32.036)	0.004
	Fever	3.058 (2.053–4.556)	<0.001	0.864 (0.455–1.643)	0.656
	Cough	3.774 (2.401–5.934)	<0.001	0.593 (0.321–1.095)	0.095
	Dyspnea	70.773 (32.449–154.361)	<0.001	14.449 (5.043–41.402)	<0.001
	Sore throat	0.909 (0.467–1.768)	0.778	–	Na
	Fatigue	3.560 (1.956–6.477)	<0.001	1.699 (0.080–3.602)	0.167
	Coryza	0.612 (0.085–4.403)	0.626	–	Na
	Anosmia	0.048 (0.000–81.766)	0.048	–	Na
	Dysgeusia	0.049 (0.000–208.914)	0.479	–	Na
	Diarrhea	0.937 (0.130–6.746)	0.949	–	Na
	Headache	0.041 (0.001–2.939)	0.143	–	Na
	Vomiting	4.460 (1.404–14.163)	0.011	0.355 (0.801–3.602)	0.172
	Myalgia	0.486 (0.178–1.332)	0.161	–	Na
	Altered sensorium	33.383 (17.493–63.706)	<0.001	2.762 (1.142–6.683)	0.024
	Chest pain	3.420 (0.839–13.938)	0.086	1.937 (0.441–8.502)	0.381
	Pain abdomen	0.050 (0.000–18197995.67)	0.765	–	Na
	Anorexia	1.726 (0.423–7.037)	0.446	–	Na
Vitals	Temperature	2.082 (1.664–2.605)	<0.001	–	Na
	Pulse rate	1.101 (1.086–1.116)	<0.001	–	Na
	Systolic BP	0.960 (0.952–0.968)	<0.001	0.981 (0.960–1.002)	0.072
	Diastolic BP	0.937 (0.925–0.950)	<0.001	1.014 (0.976–1.053)	0.476
	Respiratory rate	1.086 (1.074–1.098)	<0.001	1.098 (1.048–1.150)	<0.001
	SpO2	0.857 (0.863–0.887)	<0.001	0.943 (0.915–0.972)	<0.001
Comorbidities	Diabetes mellitus	8.158 (4.974–13.383)	<0.001	1.734 (1.001–3.009)	0.049
	Hypertension	8.010 (5.007–12.814)	<0.001	1.577 (0.890–2.792)	0.119
	Coronary artery disease	6.029 (3.117–11.438)	<0.001	1.280 (0.600–2.732)	0.523
	Chronic obstructive pulmonary disease and bronchial asthma	8.259 (3.325–20.515)	<0.001	0.733 (0.155–3.466)	0.695
	Chronic kidney disease	5.083 (1.804–14.326)	0.002	1.824 (0.560–5.936)	0.318
	Chronic liver disease	12.697 (3.112–51.797)	<0.001	14.432 (2.321–89.715)	0.004
	Malignancy	5.906 (3.112–1.207)	<0.001	10.443 (4.396–24.805)	<0.001
	Other comorbidities	4.168 (2.365–7.344)	<0.001	0.485 (0.236–0.996)	0.049
	Cerebrovascular accident	0.049 (0.000–141609.798)	0.692	–	Na

Outcome and predictors of bad outcome

A total of 76 patients succumbed to the illness bringing forth the case fatality rate to 4.9%. The frequency distribution of deaths with respect to age group is given in Table 1 and graphically shown in Fig. 1. The age-specific mortality rate (ASMR) was observed to be highest in the above 80 years age (group. 40.9%). The ASMR was 0.21% for 15–30, 1.82% for 30–45 years age group, 7.34% for 45–60 years age group and 22.36% for 60–80 years age group. It was observed that the mortality rate took a steep rise after 50 years of age as shown in Fig. 2. The median age of patients who died was 63.5 years (IQR 23), which was significantly higher than those who survived (median 35.0 years, IQR 19) (Table 6). ROCs for mortality showed that age >51 years predicted mortality with highest sensitivity (Sn 81.6%) and specificity (Sp 81%) (Fig. 2).

The association of demographic and clinical profile, vital parameters at admission and underlying comorbidities with mortality is shown in Table 5. The mortality rate among males was 4.34% and among females was 9.49%. All 76 (100%) of the patients who died were symptomatic, compared with 817 (56.0%) living patients who were symptomatic. It was observed that patients who died had a significantly greater prevalence of fever (65.8% versus 36.1%), cough (55.3% versus 24.6%) dyspnea (89.5% versus 11.6%), fatigue (17.1% versus 5.6%) and altered sensorium (14.5% versus 0.1%) at admission compared with those who survived. Patients who died were more likely to have tachycardia (39.5% versus 3.8%), tachypnea (84.2% versus 7.4%) and hypotension (5.3% versus 0.2%) at admission compared with those who survived ($p = 0.05$). ROCs for significant predictors of mortality included resting pulse rate >89 (Sn 81.6%, Sp 83.2%), respiratory rate at rest >21 (84.2% Sp 92.6%) and SpO2 <94% (Sn 81.6% Sp 92.9%) (Fig. 2). The mortality rate in patients with mild, moderate and severe hypoxemia was 17%, 57.6% and 84.6%, respectively. Comorbid conditions such as diabetes mellitus, hypertension, coronary artery disease, chronic kidney disease, COPD, chronic liver disease and malignancy were significantly associated with mortality (Table 5).

Outcome predictors-cox regression

The in-hospital all-cause mortality was analysed using cox-proportional hazards regression analysis. Univariate analysis revealed that an increasing age, male gender, fever, cough, dyspnea at admission, fatigue and altered sensorium were significantly associated with fatal outcome. However, in the multivariable analysis, only the presenting complaint of dyspnea (HR14.449 95%CI 5.043–41.402) and altered sensorium at admission (HR2.762 95%CI 1.142–6.683) were observed to be significant. Clinical parameters that significantly predicted poor outcome after adjustment included a rising respiratory rate (HR1.098 per unit change 95%CI 1.048–1.150) and falling oxygen-saturation (HR1.057 per unit change 95%CI 1.028–1.085). Among comorbidities only diabetes mellitus (HR1.734 95%CI 1.001–3.009), malignancy (10.443 95%CI 4.396–24.805) and chronic liver disease (HR14.432 95%CI 2.321–89.715) were significantly associated with mortality (Table 6). Survival curve for overall survival, hypoxemia, diabetes and malignancy are given in Figs. 3–6. The 30 days' survival for severely hypoxemic patients is only about 15%.

Discussion

This study is one of the largest studies addressing the clinical characteristics and mortality in hospitalised patients with COVID-19 in India. This study systematically evaluates the impact of demographic profile and clinical characteristics and that of comorbid conditions on the severity and mortality of COVID-19 patients at admission and analyses their prognostic role.

The median age of 36 years, as observed in the present study differed from that reported in an initial study from Wuhan where the median age was 64 years,[4] while another study from Wuhan reported a median age of 49 years.[2] A study from the United States showed mean age to be 55 years.[5] A recent global report by the World Health Organisation (WHO) established the median age as 51 years.[6] An Indian study reported the mean age of admitted patients to be 40.1 years,[7] whereas another Indian study observed a median age of 49 years.[7] It is evident that Indian patients hospitalized were younger compared with other parts of the world.

The median age of patients with moderate to severe disease compared with those with mild disease was significantly higher. The same applied to patients who died as against those who survived. Further, an increasing age was associated with a significantly greater odds of having a moderate to severe disease and showed a marginally significant association with the risk of death. Overall, age appears to have an effect on disease severity as well as mortality. A steep rise in the mortality rate was observed in patients above 50 years of age. This corresponded with the cut-off of 51 years, which predicted mortality with considerable sensitivity and specificity (Fig. 2). In the present study, the ASMR in patients above 80 was 40.9%, which was considerably higher compared with that observed in a study in southern India, which reported a mortality rate of 22.72% in patients above 75 years of age.[8] The original Wuhan study showed median age of patients at 51 years, and mean age of deceased persons was 68 years. In comparison, the median age of the deceased in our study was 63.5 years.[9] In the present study, 88.2% of the hospitalised patients were males. This distribution is similar to an Italian study where 72.9% of all patients were males[10] and a Wuhan study wherein 73% of admitted patients were males.[2] A WHO report specifies a sex ratio (male to female) among the confirmed cases to be 1.03:1.[6] An Indian study reported 71.4% males and 28.6% females.[8] This shows a male preponderance among admitted patients in general.

The mean duration of hospitalization was 13 days, which is consistent with a previous Indian study in which it was 11.54 days.[11] The case fatality rate in our study was 4.5%. A recent Indian study showed mortality to be 9.42%.[12]

A significant proportion of patients had no symptoms at admission (41.8%), which was comparable with an Indian study that reported 44.4% of patients to be asymptomatic.[7] In comparison, a recent analysis of hospitalised patients from China showed only 7.9% patients to be asymptomatic.[13] Only 37.6% patients in the present study presented with history of

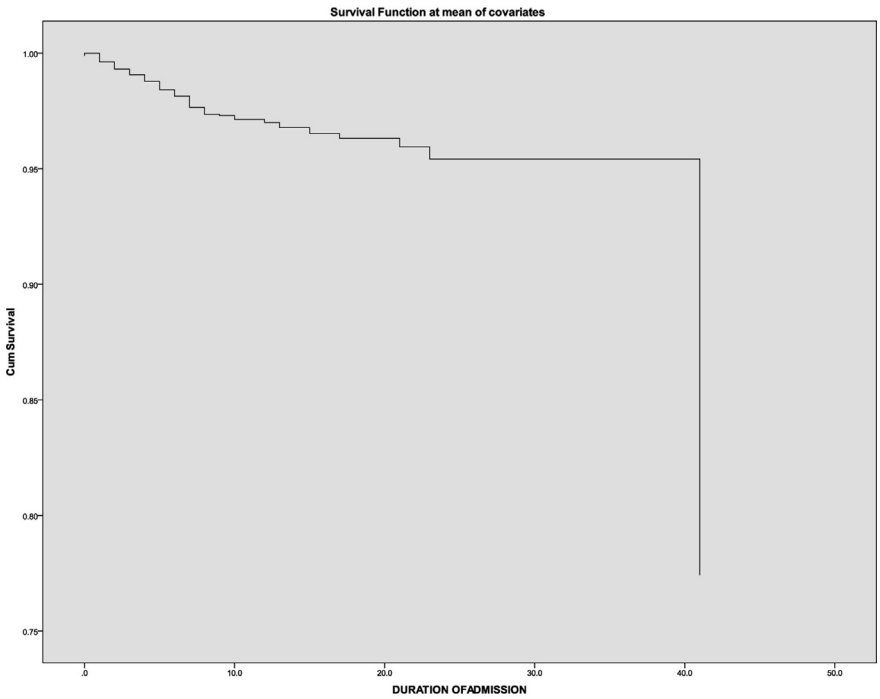

Fig. 3 – Overall survival function.

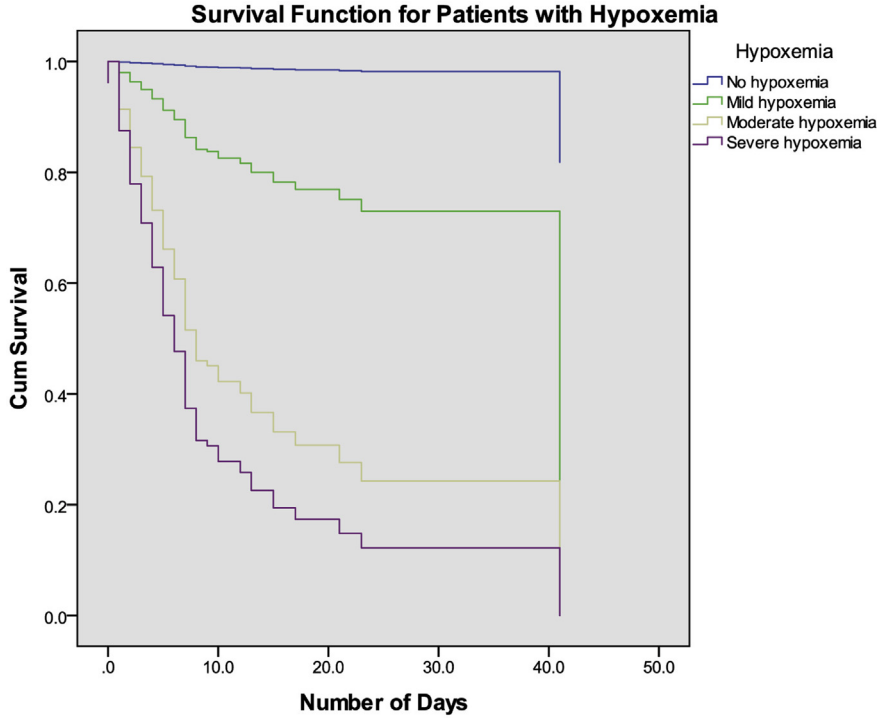

Fig. 4 – Survival function for hypoxemia at admission.

fever, whereas a Chinese study showed fever as the presenting complaint in 84.1%.[14] However, among symptomatic patients, 62.37% of our patients had history of fever. Cough was present in 26.1% of total patients and in 44.90% of symptomatic patients, which is consistent with other studies.[14,15] Dyspnea at admission was seen in 15.4% of total and 26.5% of symptomatic patients. An original Chinese study showed 6.9% patients presenting with dyspnea,[15] whereas a

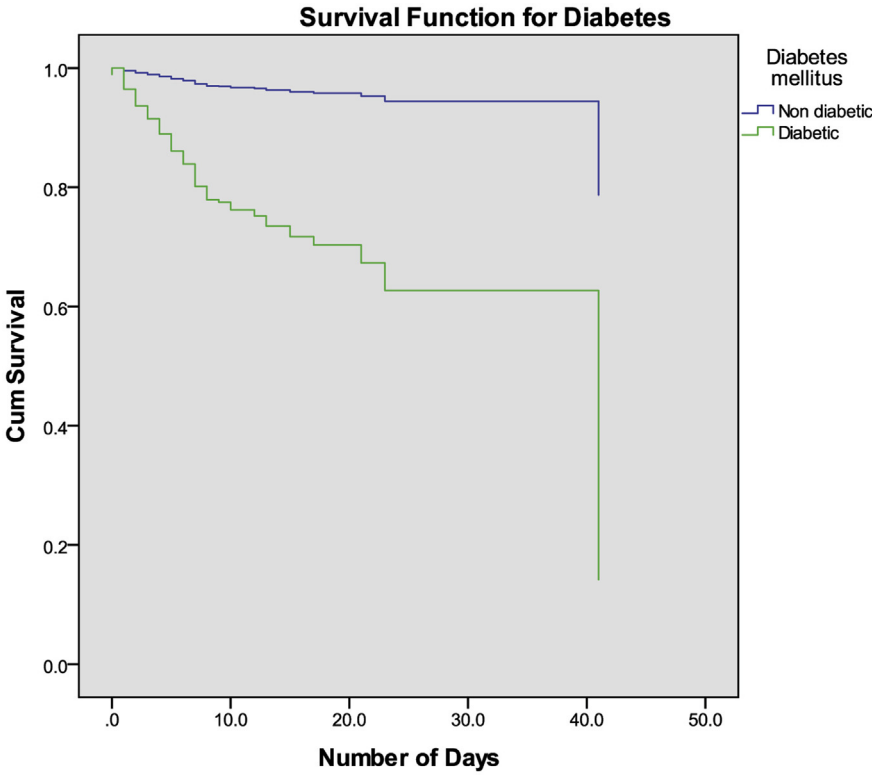

Fig. 5 – Survival function for diabetes mellitus.

recent Indian study observed that 25.83% of patients had dyspnea at presentation.[12] Another Indian study reported the prevalence of dyspnea as 71.9%.[16] These indicate that the prevalence of dyspnea at admission was more common in India. The prevalence of other symptoms, such as myalgia, dysgeusia, anosmia, headache as observed in the present study, were similar to a recent Indian study.[12]

In the present study, symptomatic patients had a significantly greater odds of having a moderate to severe disease. Furthermore, symptomatic patients were significantly associated with greater risk of mortality. Among all symptoms, dyspnea at admission was significantly associated with both the odds of having a moderate to severe disease as well as with the risk of mortality. The positive association of dyspnea with mortality has also been brought out by a recent meta-analysis involving a total of 2851 patients.[17] A less common symptom was altered sensorium, seen in less than 1% of admitted patients. It was observed that altered sensorium was though not associated with the odds of having a moderate to severe disease but predicted the risk of mortality with considerable significance. A recent analysis of 71 deaths due to COVID-19 concluded that altered mental status was very common in COVID-19 patients, being observed in 66% of the patients who had died and correlated significantly with a high risk of mortality.[18] In our study, even though altered sensorium was observed in only 11% of deceased patients, but still a significant association with the risk of mortality existed. This implies that patients with altered sensorium at admission may not have a more severe disease but are more likely to succumb to the illness.

It was observed that 11.2% of our patients had tachypnea at admission and 8.5% had hypoxemia (SpO2 < 95%). The presence of tachycardia, tachypnea, all degrees of hypoxemia and hypotension at admission were significantly more common in patients who had a fatal outcome. Furthermore, a resting pulse rate >89, respiratory rate at rest >21 and SpO2 <94% at admission predicted mortality with good sensitivity and specificity (Fig. 2). Among all vital parameters, a falling oxygen saturation and an increasing respiratory rate at admission were significantly associated with a greater risk of mortality in the present study. These findings corroborate with those from other studies.[19–21]

The prevalence of comorbidities in our study was 12.8%. Nearly 5% of patients had two or more comorbidities. This in sharp contrast to original study from Wuhan where 37.3% of patients had at least one comorbidity.[9] An Indian study showed 47.11% patients having at least one comorbidity,[12] while another Indian study reported 68.8% patients having at least one comorbidity and 40.6% patients with two or more comorbidities.[19] This shows a lower prevalence of comorbidities in patients included in the present study. This may be attributed to the fact that a greater proportion of our patients largely included healthy serving personnel.

In our study, primary hypertension was the commonest comorbidity (8.5%) followed by diabetes mellitus (6.7%) and coronary artery disease (3.2%). In a meta-analysis including 1576 COVID-19 patients, it was observed that hypertension (21.1%) was the most common condition followed by diabetes (9.7%), cardiovascular disease (8.4%) and chronic respiratory disease (1.5%).[22] In contrast, an Indian study reported diabetes

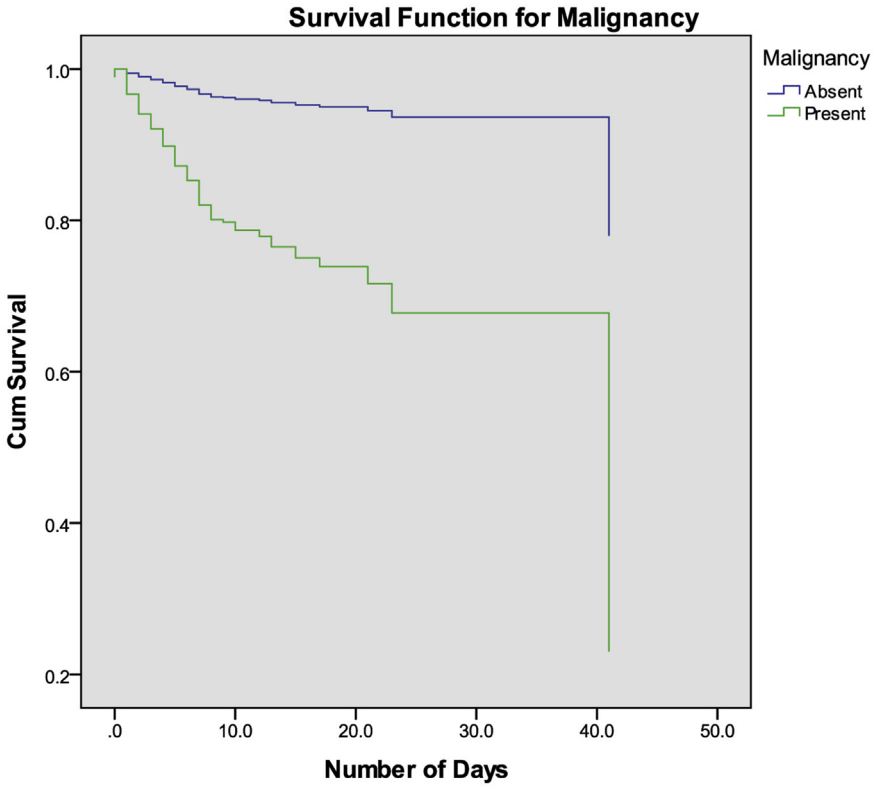

Fig. 6 – Survival function for patients with malignancy.

mellitus to be the commonest comorbidity (50%) followed by hypertension (34.4%), chronic chest conditions (28.1%) and heart disease (12.5%).[19] In our study, respiratory conditions including COPD and bronchial asthma was observed in only 0.5% of patients. Another Indian study reported diabetes mellitus in 11.1% patients,[23] comparable with that observed in our study.

All comorbid conditions including hypertension, diabetes mellitus, coronary artery disease, chronic kidney disease, chronic liver disease, COPD and malignancy were significantly more common in patients with moderate to severe disease compared with those with mild disease as well as in patients who suffered fatal outcome. In the multiple logistic regression analysis of disease severity, only hypertension, chronic kidney disease and malignancy were significantly associated with the odds of having moderate to severe disease. However, on multivariable Cox regression analysis for mortality, only diabetes mellitus, chronic liver disease and malignancy were significantly associated with greater risk of mortality. The case fatality rate among diabetic patients was as high as 22.3%. The risk of death in diabetic patients was 1.73 times that in the non-diabetics. A meta-analysis of 6452 patients from 30 different studies showed that diabetes was associated with composite poor outcomes in COVID-19 patients with a risk ratio (RR) of 2.38 ($p < 0.001$), and the RR for death was 2.12, which was comparable with that observed in our study.[24] Hypertension and chronic kidney disease, although associated with greater odds of a more severe disease, were not significantly associated with mortality. This suggests that patients with hypertension or chronic kidney disease have a greater likelihood of having a severe form of disease, but fare well and are less likely to succumb to the illness. An opposite is the case with patients having diabetes mellitus or chronic liver disease.

Cancer carried a high risk of death. Nearly 3% of our patients had malignancy, which was significantly associated with poor survival. A study of 105 cancer patients of COVID-19 in Wuhan had shown that cancer patients had higher risk of death.[25] The adjusted HR for death in cancer patients in our study was 10.44. Various studies have shown cancer to be high risk for mortality in COVID-19. Poor performance status, immunosuppression and poor nutrition in cancer patients may further enhance the risk of death. The mortality of cancer patients with COVID-19 was 24.4%. A US study of 1035 cancer patients with COVID-19 showed 13% mortality among cancer patients.[26] Another meta-analysis reported a 21.1% mortality rate among COVID-19 patients with underlying malignancy.[27]

Past cerebrovascular accident did not carry significant association with mortality. It is apparent that it is the functional status that contributes to mortality than mere history of past stroke with complete or partial recovery. It is also evident from the observations in the present study that patients with a poor neurological status, such as patients in altered sensorium at admission, were at a greater risk of a fatal outcome. Other comorbidities such as hypertension, coronary artery disease, chronic kidney disease and COPD, although significantly associated with mortality only in univariate analysis.

The predictors of disease severity and mortality in COVID-19 patients vary considerably among populations. This is a largest study in Indian subcontinent addressing the clinical characteristics and clinical predictors. Given that no reliable clinical models currently exist to predict outcomes for patients with COVID-19, the present study identifies clinical predictors of severe disease and that of poor outcomes in an Indian population. However, the present study has certain limitations. Due to the retrospective nature of the study, other predictors that have a significant effect could not be studied. The outcomes were evaluated at the end of follow-up period and not at fixed intervals during the course of the disease. Further large-scale and multicentric studies need to be planned to address these limitations.

Conclusion

This study highlights the importance of easily recordable basic clinical parameters which can predict the outcomes in COVID 19. Disease severity and risk of mortality increase with age. Mortality increases with age after 50 years. The risk of mortality is similar in both sexes. Patients with dyspnea at admission were found to have greater odds of having a more severe disease as well as were at a greater risk of mortality. Patients presenting with altered sensorium have high risk of mortality and are to be managed aggressively, with focus on improving the neurological status. Clinical parameters at admission such as tachypnea and even mild hypoxemia. Hypertension and chronic kidney disease showed greater odds of having a more severe disease but were not significantly associated with the risk of mortality. On the other hand, diabetes mellitus and chronic liver disease are main comorbid conditions, which portend bad prognosis in Indian population. Underlying malignancy is both a risk factor for severe disease and mortality. These parameters can be used to triage the patients at admission and may help in planning the management effectively in countries like India.

Disclosure of competing interest

The authors have none to declare.

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