A study clinical profile and factors associated with death in the COVID patients at dedicated covid hospital

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Abstract

Background: The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a global public health concern because of its higher transmission around the world. Increasing age, male gender, patients presenting with symptoms of fever, cough, breathlessness, smoking, alcohol consumption, comorbidities were significantly associated with mortality among COVID-19 patients. Present study was conducted to study the risk factors associated with mortality among COVID-19 patients in a tertiary care hospital. **Material and Methods:** Present study was single-center, prospective, observational case record based study, conducted in patients of age ≥18yrs, with COVID RT-PCR positive (oropharyngeal or nasopharyngeal swab) or HRCT-CHEST suggestive of COVID 19. **Results:** Mortality rate was 10.6 %. In non survivors, patients with age > 60 years were 70.71 %. Higher mortality was noted in male gender (survivors 59.58 % vs non-survivors 70.58 %) and difference was statistically significant (p=0.034). Major symptoms such as Fever and Breathlessness had statistically significant difference between survivors and non-survivors group (p=0.001). Pre-existing morbidity such as Diabetes, Cardiovascular disease/ Hypertension, Chronic lung disease, Severe kidney impairment, Tuberculosis and Severe liver disease were significant among non-survivor group as compared to survivor group, difference was statistically significant (p<0.001). Addictions such as smoking, alcohol consumption and tobacco chewing were significant among non-survivor group as compared to survivor group, difference was statistically significant (p < 0.001). **Conclusion:** In present study age > 60 years, male gender, combination of fever, breathlessness, severe disease as ICMR grading, pre-existing morbidity such as diabetes, cardiovascular disease/ hypertension, and addictions such as smoking, alcohol consumption and tobacco chewing were important factors associated with death in the COVID patients.
Keywords: ICMR grading, pre-existing morbidity diabetes, cardiovascular disease, smoking, COVID 19

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Access this article online	
Quick Response Code:	Website: www.medpulse.in
	Accessed Date: 14 November 2021

INTRODUCTION

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a global public health concern because of its higher transmission around the world. Approximately 80% of the COVID-19 patients present with mild to moderate disease with symptoms such as mild upper respiratory tract illness fever, cough, myalgia, fatigue, anosmia, breathlessness and pneumonia. Around 20% of the COVID-19 patients present with severe acute respiratory illness and most of these severe patients succumb to death.[1] In patients with critical disease, complications such as respiratory failure, acute respiratory

distress syndrome (ARDS), sepsis and septic shock, thromboembolism, and/or multiorgan failure, including acute kidney injury and cardiac injury are noted.[2] Drugs like steroids, hydroxychloroquine, protease inhibitors like lopinavir and ritonavir, favipiravir, remdesivir, and immunosuppressants are being used to manage the symptoms of COVID-19. Nevertheless, there is still no established treatment option for SARS-CoV-2.[3] Increasing age, male gender, patients presenting with symptoms of fever, cough, breathlessness, smoking, alcohol consumption, comorbidities were significantly associated with mortality among COVID-19 patients.[4] Present study was conducted to study the risk factors associated with mortality among COVID-19 patients in a tertiary care hospital.

MATERIAL AND METHODS

Present study was single-center, prospective, observational case record based study, conducted at Department of General Medicine, Viswanbharathi Medical College And Hospital, Kurnool, India working as a dedicated tertiary level COVID facility. Study duration was of 6 months. Study was approved by institutional ethical committee. Patients of age ≥18yrs, with COVID RT-PCR positive (oropharyngeal or nasopharyngeal swab) or HRCT-CHEST suggestive of COVID 19 were considered for study. Patients taken discharge against medical advice, lost to follow up were excluded from study. Patients demographic details, clinical history, significant medical history, physical examination findings, laboratory investigations (CBC, plasma glucose, LFT, KFT, serum electrolytes, serum ferritin, LDH, D-dimers and CRP levels), radiological investigations (X ray chest, HRCT) were noted at baseline. Patients were managed as per current Guidelines and Protocol issued by government of India. At discharge/death clinical course, follow-up investigations, treatment details were noted in case record form. Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Frequency, percentage, means and standard deviations (SD) was calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. Difference of proportions between qualitative variables were tested using chi-square test or Fisher exact test as applicable. P value less than 0.5 was considered as statistically significant.

RESULTS

During study period 321 patients satisfying study criteria were evaluated. Mortality rate was 10.6 %. Among survivors, majority of patients admitted were from 46-60 years age group (36.24 %) followed by 31-45 years age group (30.31 %). In non survivors, patients with age > 60 years were 70.71 %. Mean age was 47.11 ± 13.2 years in survivor group while the same was 61.02 ± 14.3 years in non-survivor group, and difference was statistically significant (p=0.018). Higher mortality was noted in male gender (survivors 59.58 % vs non-survivors 70.58 %) and difference was statistically significant (p=0.034). Major symptoms such as Fever and Breathlessness had statistically significant difference between survivors and non-survivors group (p=0.001). As per ICMR grading Disease severity among nonsurvivors was 2.94 %, 14.71 % and 82.35 % in Asymptomatic + mild, Moderate and Severe groups respectively. While in survivors group, disease severity was 44.25 %, 31.01 % and 24.74% in Asymptomatic + mild, Moderate andSevere groups respectively and difference was statistically significant (p < 0.001). Pre-existing morbidity such as Diabetes, Cardiovascular disease/ Hypertension, Chronic lung disease , Severe kidney impairment, Tuberculosis and Severe liver disease were significant among non-survivor group as compared to survivor group, difference was statistically significant (p<0.001). Addictions such as smoking, alcohol consumption and tobacco chewing were significant among non-survivor group as compared to survivor group, difference was statistically significant (p < 0.001).

Table 1: Baseline characteristics of patients

Variable	Survivors (n=287)		Non Survivors (n=34)		P value
	N	%	N	%	
Age (in years)					
19-30	32	11.15	1	2.94	
31-45	87	30.31	3	8.82	
46-60	104	36.24	6	17.65	
61 – 75	43	14.98	17	50	
>75	21	7.32	7	20.59	
Mean age	47.11 ± 13.2		61.02 ± 14.3		0.018
Sex					0.034
Male	171	59.58	24	70.59	
Female	116	40.42	10	29.41	

Major symptoms					
Fever	211	73.52	31	91.18	0.001
Cough	231	80.49	30	88.24	0.053
Breathlessness	187	65.16	33	97.06	0.001
Disease severity		0		0	< 0.001
Asymptomatic + mild	127	44.25	1	2.94	
Moderate	89	31.01	5	14.71	
Severe	71	24.74	28	82.35	
Pre-existing morbidity					< 0.001
Diabetes	11	3.83	14	41.18	
Cardiovascular disease/ Hypertension	45	15.68	19	55.88	
Chronic lung disease	2	0.7	5	14.71	
Severe kidney impairment	4	1.39	8	23.53	
Tuberculosis	1	0.35	1	2.94	
Severe liver disease	3	1.05	2	5.88	
Addictions					< 0.001
Smoking	21	7.32	16	47.06	
Active	8	2.79	11	32.35	
Previous (less than 5 years ago)	13	4.53	5	14.71	
Alcohol consumption	121	42.16	18	52.94	
Tobacco chewing	56	19.51	14	41.18	

A statistically significant difference found between survivors and non survivors with respect to Heart Rate, Respiratory Rate, Systolic blood pressure, serum ferritin, D-dimer and LDH on admission.

Table 2: Comparison of various parameters on admission

Variable	Survivors (Mean ± SD)	Non Survivors (Mean ± SD)	P value
Heart Rate	89.21 ± 12.35	100.32 ± 16.86	<0.001
Respiratory Rate	21.89 ± 6.27	28.42 ± 8.93	0.006
SBP	115.56 ± 12.43	128.63 ± 18.26	<0.001
S. FERRITIN	257.26 ± 139.16	643.86 ± 275.35	<0.001
LDH	214.43 ± 105.38	647.52 ± 418.61	<0.001
D-dimer	411.92 ± 215.38	1073.25 ± 752.11	<0.001

Complications such as Acute Respiratory Distress Syndrome, Septic shock, Disseminated Intravascular Coagulation, Acute Kidney Injury, Myocardial infarction and Liver failure were significant among survivor group as compared to non-survivor group, difference was statistically significant (p<0.001). Majority of deaths were noted in within 10 days of admission (67,64 %), Hospital stay was more in survivor group (15.21 ± 8.2 days) as compared to non-survivor group (11.56 ± 9.3 days) and, difference was statistically significant (p<0.001). While ICU stay was more in non-survivor group (10.02 ± 6.3 days) as compared to survivor group (5.34 ± 3.2 days) and, difference was statistically significant (p<0.001). Respiratory support (Oxygen by nasal prongs/ non-rebreathing mask, Non-invasive ventilation, Invasive mechanical ventilation) requirement was more in non-survivor group as compared to survivor group, difference was statistically significant (p<0.001). Also, duration of mechanical ventilation was more in non-survivor group (8.3 ± 6.5 days) as compared to survivor group (5.9 ± 4.5 days) and, difference was statistically significant (p<0.001)

Table 3: Outcome measures

Variable	Survivors (n=287)		Non Survivors (n=34)		P value
	N	%	N	%	
Complications					<0.001
Acute Respiratory Distress Syndrome	21	7.32	22	64.71	
Septic shock	10	3.48	12	35.29	
Disseminated Intravascular Coagulation	36	12.54	19	55.88	
Acute Kidney Injury	13	4.53	8	23.53	
Myocardial infarction	3	1.05	5	14.71	
Liver failure	2	0.7	2	5.88	
Other characteristics		0		0	
Hospital stay (in days)	15.21 ± 8.2		11.56 ± 9.3		<0.001
ICU stay (in days)	5.34 ± 3.2		10.02 ± 6.3		<0.001

Mortality (days since primary admission)					
< 5			11	32.35	
5-10			12	35.29	
11-15			5	14.71	
>15			6	17.65	
Respiratory support received					<0.001
Oxygen by nasal prongs/ non-rebreathing mask	65	22.65	34	100	
Non-invasive ventilation	41	14.29	4	11.76	
Invasive mechanical ventilation	32	11.15	30	88.24	
Duration of mechanical ventilation (in days)	5.9 ± 4.5		8.3 ± 6.5		
Time (in days) from treatment initiation to death.			8.6 ± 5.7		

DISCUSSION

The adaptive immune response to infection is multi-faceted and complex, and it involves a variety of cell types and factors such as chemokines, cytokines, enzymes, and hormones.[5] In majority of Coronavirus disease 2019 (COVID-19) patients, symptoms at onset are relatively mild and a significant proportion of patients do not show apparent symptoms prior to the development of respiratory failure.[6] Clinically, this makes it difficult to predict the progression of severity in patients until respiratory failure develops. Early risk prediction and effective treatment can reduce mortality and morbidity as well as relieve resource shortages. Older age, smoking and underlying noncommunicable diseases (NCDs), such as diabetes, hypertension, cardiac disease, chronic lung disease and cancer, have been reported as risk factors for severe disease and death.[6] In a retrospective cohort study, Zhou *et al.* demonstrated that COVID-19 positive patients with pre-existing diabetes had 2.85 times the risk of mortality due to COVID-19 compared to patients without pre-existing diabetes, and those with comorbid hypertension had thrice the odds of mortality compared to non-hypertensive patients.[7] In the study by Kumar *et al.*,[8] the risk of mortality in patients positive for COVID-19 and pre-existing diabetes was shown to be twice than that observed in non-diabetic patients. A meta-analysis predicted that the likelihood of death was higher in patients with hypertension, diabetes, and cardiovascular disease. COVID-19 positive patients with comorbid cardiovascular disease had 3.32 times the risk of mortality than those without cardiovascular disease.[9] Increased COVID-19 mortality among smokers might be due to the detrimental action of tobacco smoke on the immune system, direct lung injury, up-regulation of SARS-CoV-2 receptor, Angiotensin-converting enzyme 2 (ACE2) in human cells due to smoking.[10,11] In a study from AIIMS, New Delhi, Amandeep Singh *et al.*,[12] noted that mortality was higher in elderly age group and was statistically significant (p<0.05). Among patients who presented with all three symptoms at presentation (fever, cough and dyspnea), 43% succumbed to disease. Looking at severity, 38% were mild, 42% were moderate and 20% were severe cases at admission. The mortality was highest in severe group (90%). Prior co morbidities were seen in 60% cases. Hypertension (24%) was the commonest followed by diabetes (18%) and CKD (6%). 66.7 % of patients with CKD died. Among non-survivors, 37.5% were anaemic and 72.7% had leucocytosis (p<0.05). 53.8% patients with raised urea and 36.3% patients with raised creatinine also died. Anudeep A *et al.*,[13] noted that Diabetes Mellitus was the most common comorbidity. The most common complication observed was ARDS(94%). History of smoking, hypertensives and those treated with tocilizumab had significantly higher mortality (p<0.05). Patients treated with antivirals has significantly better outcome. The mean duration of ICU stay was 9.2±3.7 days mortality rate was 38%. Pan F *et al.*,[14] studied 124 patients with severe COVID-19 on admission, divided into discharge group (n=35) and death event group (n=89). Persistently lower lymphocyte with higher levels of CRP, PCT, IL-6, neutrophil, LDH, D-dimer, cardiac troponin I (cTnI), brain natriuretic peptide (BNP), and increased CD4+/CD8+ T-lymphocyte ratio and were observed in death events group, while these parameters stayed stable or improved in discharge group. On admission, the levels of SpO2, lymphocyte, CRP, PCT, and LDH could predict the prognosis of severe COVID-19 patients. Systematic inflammation with induced cardiac dysfunction was likely a primary reason for death events in severe COVID-19 except for acute respiratory distress syndrome. Patients with severe illness usually developed acute respiratory distress syndrome (ARDS) that requires invasive mechanical ventilation therapy in the intensive care unit (ICU), and the mortality rate was reported around 50-60%.[15] In meta-analysis by Noor FM,[16] a total of 58 studies with 122,191 patients were analyzed. The pooled prevalence rate of mortality among the hospitalized COVID-19 patients was 18.88%. An significant association were found between mortality among COVID-19 infected patients and older age (> 65 years vs. < 65 years) (p < 0.001), gender (male vs. female) (p < 0.001), ICU admitted patients (p < 0.001), obesity (p < 0.05), hypertension (p < 0.001), diabetes (p < 0.001), cardiovascular disease (p < 0.05), and cancer (p < 0.001).

In addition, significant association for high risk of mortality were also found for cerebrovascular disease, COPD, coronary heart disease, chronic renal disease, chronic liver disease, chronic lung disease and chronic kidney disease. Chidambaram V et al.,[17] conducted a meta-analysis of 109 articles, risk of mortality was higher in patients with increasing age, male gender, dyspnea, diabetes, hypertension. Congestive heart failure, hilar lymphadenopathy, bilateral lung involvement and reticular pattern were associated with severe disease. Clinically relevant cut-offs for leukocytosis (>10.0 x10^9/L), lymphopenia (< 1.1 x10^9/L), elevated C-reactive protein (>100mg/L), LDH(>250U/L) and D dimer (> 1mg/L) had higher odds of severe disease and greater risk of mortality. The identification of COVID-19-related symptoms associated with mortality and severe disease is especially important since this is among the most readily accessible information during the initial evaluation of patients. Still aggressive implementation of prevention strategies, including social distancing and rigorous hand hygiene, may benefit the population as a whole, as well as those at highest risk for COVID-19–related complications

CONCLUSION

In present study age > 60 years, male gender, combination of fever, breathlessness, severe disease as ICMR grading, pre-existing morbidity such as diabetes, cardiovascular disease/ hypertension, chronic lung disease, severe kidney impairment, and addictions such as smoking, alcohol consumption and tobacco chewing were important factors associated with death in the COVID patients.

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