Original Research Article

Comorbidities Associated with Mortality in COVID-19 Patients: A Retrospective Study at a Tertiary Health Care Hospital

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Abstract

Introduction: Due to unprecedented outbreak of COVID-19 worldwide since December 2019, the knowledge about which health conditions may impact the likelihood of a person getting infected and dying with COVID-19 is limited. It is observed that the mortality rate varies from one region to another region across globally. It remains unclear how the pre-existing health conditions affect the risk of infection and severity of COVID-19. The present study was undertaken to describe the presence of associated comorbidities in the adult patients who died of COVID-19 at a tertiary care hospital in this part of India.**Methods:** The present study is a hospital based retrospective study, done at Yenepoya Medical College and Hospital which is a tertiary health care hospital. Data was collected from the medical records of patients above 16 years of age who died due to COVID-19 illness and details of the age, gender distribution, associated co morbidities, and laboratory investigation reports of the patients at the time of admission were obtained. Data was analyzed and compared as mean and percentage of distribution among different groups.**Results:** Out of 110 deaths due to COVID-19, 76 (69.09%) were males and 34 (30.9%) were females. The average age of the patients died due to COVID-19 is 57.44±13.01years. The overall COVID-19 mortality above the age of 60 years is 49.09% (54). The mortality was lowest in the age group of 16-30 years (4, 3.63%). The most prevalent comorbidity associated with COVID-19 mortality observed in the study is diabetes mellitus (73, 66.3%) followed by systemic hypertension (57, 51.81%). The other comorbidities observed in the present study are: cardiovascular diseases (21, 19.09%), chronic kidney diseases (10, 9.09%), malignancies (11, 10%), chronic respiratory diseases (9, 8.1%), cerebrovascular diseases (8, 7.2%) and chronic liver diseases (7, 6.3%). Overall, 8 (7.27%) patients among 110 patients had no prior comorbidities.**Conclusions:** In this study we found a significant effect of age, gender and other comorbidities on risk of mortality among patients with COVID-19. In our study mortality in COVID-19 patients with age ≥60 years were at a significantly high compared to those aged <60 years. Male patients with COVID-19 were associated with significantly increased risk of mortality compared to females. Mortality was significantly higher in those patients with diabetes, hypertension, cardiovascular disease, cerebrovascular disease, respiratory disease, chronic kidney disease, chronic liver disease and malignancy. Adequate protection and interventions in COVID-19 patients, particularly in male patients with age ≥60 years may significantly reduce the risk of mortality.

Keywords: Outbreak; Comorbidities; Mortality; COVID-19.

Introduction

Since first reported in Wuhan, China, in December 2019, the Novel Corona virus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), has rapidly spread, and led to public health emergency internationally. As of 31st August 2021, a total of 216867420 confirmed cases, including 4507837 deaths globally and 34000000 infections including 435000 deaths in India, have been reported[1]. The clinical presentation of COVID-19 is varies from mild to moderate symptoms of cough, sore throat, headache, rhinorrhoea, vomiting and diarrhoea, fever and shortness of breath to complex disease of severe pneumonia, acute respiratory distress syndrome, septic shock and multiple organ failure. Use of facial masks, social distancing and lockdowns has been introduced to slow the spread of infection in many countries. Despite these measures the outbreak of COVID-19 has overwhelmed healthcare systems in several countries. Inadequate medical resources have warranted the identification of risk factors for the diagnosis and severity of COVID-19. Due to unprecedented outbreak of COVID-19

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worldwide, the knowledge about which health conditions may impact the likelihood of a person getting infected and dying with COVID-19 is limited.Some previous studies have shown that older age and pre-existing chronic health conditions such as hypertension, diabetes, obesity, cardiac disease, chronic kidney disease and liver disease may increase the risk of corona virus infection and also mortality with COVID-19[2-8]. It is also observed that the mortality rate varies from one region to other region across globally. It remains unclear how comorbidities affect the risk of infection and severity of COVID-19.More studies are needed to know the effect of comorbidities on the risk of death in patients infected by COVID-19. The present study was undertaken to describe the presence of associated comorbidities in the adult patients who died of COVID-19 at a tertiary care hospital in this part of India. This will help showing which comorbidities might pose the patients at risk of more severe illness and death. Such information may be useful for health authorities in the decision-making process for interventions during the epidemic.

Materials and Methods

The present study is a hospital-based retrospective, cross sectional study done at Yenepoya Medical College and Hospital which is a tertiary health care hospital and a designated COVID treatment centre that shares high number of COVID patients.

All the adult patients above the age of 16 years, who were RT-PCR (reverse – transcription polymerase chain reaction) positive for SARS-CoV-2 and died due to COVID-19 illness between the months of 1st March 2020 to 31st August 2020, were included in this study. Data was collected and analyzed from the medical records of patients who died due to COVID-19 illness during this period. Details of the age, gender distribution, associated comorbidities, and laboratory investigation reports of the patients at the time of admission were obtained.

These COVID-19 patients were categorized based upon the different underlying comorbidities to evaluate their relationship with COVID-19 related mortalities. Data was analyzed and compared as mean and percentage of distribution among different groups. We determined the associations between age, sex, comorbidities, and death with COVID-19 during the study period.

Results

A total of 110 deaths reported due to COVID-19 from 1st April 2020 to 30th September 2020. Out of these deaths 76 (69.09%) were males and 34 (30.9%) were females. The average age of the patients died due to COVID-19 is 57.44±13.01 years. The average age of males is 58.26±12.9 years and the average age of females is 55.61± 13.14 years.The highest mortality (44, 40%) was seen in the age group of 61-75 years which is closely followed by 45-60 years age group (42, 38.18%). The overall COVID-19 mortality above the age of 60 years is 54 (49.09%). The mortality was lowest in the age group of 16-30 years (4, 3.63%).

Majority of the patients 48(43.64%) patients survived more than 7 days. About 25(22.73%) patients succumbed within 3 days of admission. 32(29.09%) patients survived between 3 to 6 days. 5(4.54%) patients died on the day of admission. The mean duration of time between hospitalization to death is about 9.22 days.

The most prevalent comorbidity associated with COVID-19 mortality observed in the study is diabetes mellitus (73, 66.63%) followed by systemic hypertension (57, 51.81%). The other comorbidities observed in the present study are – cardiovascular diseases (21, 19.09%), chronic kidney diseases (10, 9.09%), malignancies (11, 10%), chronic respiratory diseases (9, 8.1%), cerebrovascular diseases (8, 7.2%) and chronic liver diseases (7, 6.36%).Overall, 8(7.27%) patients among 110 deaths had no prior comorbidities. About 33(30%) patients had only one comorbidity, 30(27.27%) patients had two comorbidities and about 35(35.45%) patients had three comorbidities in this study.

Table 1: Comorbidities and distribution of patients with COVID-19 mortality

Comorbidities	Number	Percentage
Diabetes mellitus	73	66.63%
Systemic hypertension	57	51.81%
Old age (>60 years)	54	49.09%
Cardiovascular disease	21	19.09%
Malignancies	11	10%
Chronic kidney disease	10	9.09%
Chronic respiratory diseases	9	8.1%
Cerebrovascular disease	8	7.2%
Chronic liver disease	7	6.36%

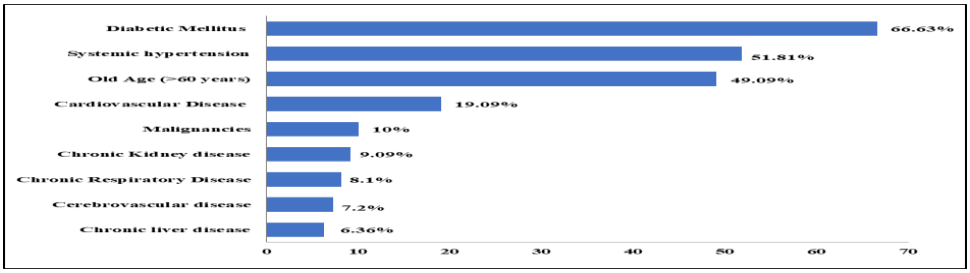

Fig 1: Comorbidities and distribution of patients with COVID-19 mortality

Table 2: Age group and mortality of COVID-19 patients

Age group (years)	Number	Percentage
16-30	4	3.63%
31-45	10	9.09%
46-60	42	38.18%
61-75	44	40%
76-100	10	9.09%

Table 3: Number of comorbidities and mortality of COVID-19 patients

Number of comorbidities	Number	Percentage
0	8	7.27%
1	33	30%
2	30	27.27%
3	39	35.45%

Table 4: Mean and Standard deviation of continuous laboratory data along with the confidence interval

Laboratory data	N	Mean	Standard Deviation	95% Confidence Interval	
				Lower	Upper
Differential counts–Neutrophils	105	80.3891	17.55904	76.9910	83.7872
Lymphocytes	105	11.0454	10.51395	9.0107	13.0801
ESR	61	49.413	35.4958	40.322	58.504
Creatinine (mg/dl)	99	2.179	2.8673	1.607	2.751
Blood urea	104	73.681	54.1807	63.144	84.218
LFT-Total bilirubin	100	1.359	1.7964	1.003	1.715
Serum Albumin	91	3.6134	.79176	3.4485	3.7783
SGOT	98	163.000	673.0001	28.072	297.928
SGPT	97	89.268	256.8122	37.509	141.027
Sr. LDH	75	672.933	474.7117	563.712	782.155
Sr. Ferritin	93	635.944	330.7234	567.832	704.056
D-dimer	80	4043.8622	3687.55529	3223.2370	4864.4875
C-Reactive Protein	95	73.932	23.7371	69.096	78.767

Discussion

Although most people infected with severe acute respiratory syndrome corona virus-2 (SARS CoV-2) that causes corona virus disease-2019 (COVID-19) have mild symptoms, some people may develop life threatening complications like ARDS, septic shock, myocarditis, arrhythmia, renal failure and DIC, which may lead to death. Older people and those with comorbidities are at higher risk of severe disease and death[8,13,15].India has a population with high prevalence of chronic comorbidities, which may increase the risk of fatal complications due to COVID-19. The identification of these comorbidities will help in the management of COVID-19. This study attempts to describe the comorbidities present in the patients who died of COVID-19 in Yenepoya Medical College and Hospital, Mangalore, a tertiary health care hospital.The average age of the patient at the time of death in our study is 57.44 ±13.01 years. The highest mortality 40% (44) was seen in the age group of 60-74 years and the overall COVID mortality in patients with >60 years of age is 49.09% (54). Similarly in a study done at Rajasthan by Bhandari S et al mean age during death due to COVID-19 is 53.41±18.42 years and the mortality in patients with >60 years was reported as 41.18%. A study done at China by Qiu P et al reported the mean age at the time of death as 69.9 years. Surendra H et al in a study done at Jakarta (Indonesia) reported the mortality is about 65% in patients with >60 years of age[9-12].Many other studies also shown that advanced age is closely related to the severely poor prognosis of COVID-19[17]. The changes in the pulmonary physiology, pathology and function in older population leads to altered response and susceptibility to lung infections[18].The older people generally have other comorbidities which can contribute to the severity of illness.Of the total deaths due to COVID-19, 69.09% are males and 30.9% are females in this study. The male to female ratio of death is 2.38:1. Study by Bhandari S et al reported 62.74% of deaths due to COVID are males and ratio of male to female deaths is 1.68:1[9].In a study at China Qiu.P et al observed that 66.6% of patients are males and 33.4% are females who died of COVID-19[10]. Surendra H et al in his study at Jakarta reported that among the patients died due COVID, 61% are males and 39% are females[12]. Similar observations are made in other studies where male sex is more susceptible to COVID-19 infection and mortality[2,3,6,7,13-19]The most common comorbidity found in COVID-19 related mortality in this study is diabetes mellitus (66.63%) which is followed by systemic hypertension (51.81%). In most of the other studies systemic hypertension has emerged as most common comorbidity followed by diabetes mellitus in COVID associated mortality[8-10,12,14,16].In patients suffering from hypertension, ACE-2 inhibitors and ARBs are frequently used. These inhibitors upregulate expression of ACE-2 receptors, thereby leading to increased susceptibility to SARS-CoV-2 infection. Higher expression of receptor cells in the lungs makes infection more vulnerable and chances of severe lung injury and increased chances of respiratory failure. In diabetics a dysregulated immune response with increased ACE-2 receptors and furin expression may lead to a higher lung inflammation rate and lower insulin levels. The convenient entry of virus along with impaired function of T cells and elevated levels of IL-6 plays a life-threatening situation for diabetic patients infected with SARS CoV-2 virus, leading to severe COVID-19 disease and mortality.About 19.09% of the total patients who died with COVID-19 had cardiovascular diseases (CVD) as the comorbidity in this study. Many previous studies also shown CVD is one of the common associated comorbidities in COVID-19 with mortality ranging from 12.4% to 22% of the total deaths[9,10-14]. The mechanism behind the association between CVD and COVID-19 is not precise. High risk of COVID-19 in pre-existing CVD patients might be due to presence of ACE receptors on cardiac muscles suggesting potential involvement of CVS system in SARS-CoV-2 infection. Patients with CVD have a higher risk of developing acute coronary syndrome in acute infections. An increased rate of inflammatory cytokines in COVID-19 cases mediate atherosclerosis, procoagulant activation, and hemodynamic instability leading to ischemia and thrombosis [15].7.2% of patients with COVID mortality in this study had history of cerebrovascular disease. In meta-analysis, by Patel U et al, it is observed that COVID-19 patient with pre-existing cerebrovascular disease had 2.67-fold high risk of poor outcomes[19]. The exact pathophysiology behind role of pre-existing cerebrovascular disease and poor outcome is still to be determined but such patients are at high risk due to underlying concurrent conditions such as old age, hypertension, cardiovascular disorders like arrhythmia, diabetes, low immunity-related COVID-19 severity, etc. Such patients are also at risk of developing cardio-embolic events secondary to viral and bacterial infection or new cerebrovascular events secondary to thrombotic microangiopathy, hypercoagulability leading to macro-

and micro-thrombi formation in the vessels, hypoxic injury, disruption of the blood and blood brain barrier[19].In our study among the patients who died of COVID-19, 9.09% had chronic kidney disease (CKD), 8.1% had respiratory diseases (COPD, ILD) and 6.36% had chronic liver disease (CLD). Other authors also described presence of varying degrees of CKDs, CLDs and respiratory diseases in patients who died of COVID-19[9-14]. ACE-2 receptors present on liver cells mediate the entry of SARS-CoV-2 inside the liver cells leading to liver injury and abnormal elevation of liver enzymes. The expression of ACE-2 receptors is increased in COPD, contributing to the establishment of severe symptoms among COVID-19 individuals, including structural damage to lungs, weak immunity, and hyper mucous production. Patients with renal diseases are more likely to suffer from COVID-19 infection due to an increase in ACE-2 expression. SARS-CoV-2 affects the kidneys by direct cellular injury or sepsis, leading to a cytokine storm[15].About 10% of the patients who died due to COVID-19 had malignancy in this study. Studies by Surendra H et al, Qiu P et al and Sanyaolu A et al had reported that 0.4%, 4.28% and 8.1% of patients had malignancy respectively, who died due to COVID-19[10,12,14]. Patients suffering from any malignancy are at a higher risk of developing COVID-19 infection due to the weak immune response. SARS-CoV-2 gets an efficient replication environment in these individuals to initiate infection.In this study 8(7.27%) patients who died due to COVID-19 had no prior comorbidities.

Conclusions

In this study we found a significant effect of age, gender and other comorbidities on risk of mortality among patients with COVID-19. In our study mortality in COVID-19 patients with age ≥60 years were at a significantly high compared to those aged <60 years. Infection with COVID-19 is associated with substantial mortality mainly in older patients (≥60 years) with comorbidities. Male patients with COVID-19 were associated with significantly increased risk of mortality compared to females. Mortality was significantly higher in those patients with diabetes, hypertension, cardiovascular disease, cerebrovascular disease, chronic respiratory disease, chronic kidney disease, chronic liver disease and malignancy. The conditions associated with high mortality can help recognizing patients with COVID-19 who are at higher risk of a poor prognosis. Adequate protection and interventions in these COVID-19 patients and particularly in male patients with age ≥60 years may significantly reduce the risk of mortality. Patients with comorbidities should take necessary precautions to avoid getting infected with SARS CoV-2, as they are prone for severe disease. These precautions include regular hand washing with soap and water or use of alcohol-based hand sanitizer, practicing social distancing, wearing a face mask in public places, and avoiding going to public places unless it is necessary.

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