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Association of underlying comorbidities and progression of COVID-19 infection amongst 2586 patients hospitalised in the National Capital Region of India: a retrospective cohort study

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Abstract

This study is conducted to observe the association of diabetes (DM), hypertension (HTN) and chronic kidney disease (CKD) on the prognosis and mortality of COVID-19 infection in hospital admitted patients with above mentioned comorbidities. This is a single centre, observational, retrospective study carried out at Sir Ganga Ram Hospital, Delhi, India. The burden of comorbidities on the prognosis and clinical outcome of COVID-19 patients admitted patients from April 8, 2020, to October 4, 2020. Chi-square and relative risk test were used to observe the association of comorbidities and disease prognosis. A total of 2586 patients were included in the study consisting of 69.6% of male patients. All the comorbidities were significantly associated with ICU admission and mortality. The relative risk showed that CKD is most prone to severity as well as mortality of the COVID-19 infection followed by HTN and DM. Further with the increase in number of underlying comorbidities, the risk of ICU admission and mortality also increases. Relative risk of the severity of COVID-19 infection in younger patients with underlying comorbidities are relatively at higher risk of severity of disease as well as to mortality compared to the elderly patients with similar underlying condition. Similarly, it is found that females are relatively at higher risk of mortality as compared to the males having same comorbid conditions except for the hypertensive patients. Diabetes, hypertension and CKD, all are associated with progression of COVID-19 disease to severity and higher mortality risk. The number of underlying comorbid condition is directly proportional to the progression of disease severity and mortality.

Keywords Coronavirus disease 2019 (COVID-19) · Diabetes · Hypertension · Chronic kidney disease · Severity · Mortality

Introduction

Coronavirus disease 2019 (COVID-19) emerged from Wuhan, China in December 2019 is one of the biggest threats that the entire humankind is facing today [1, 2]. The COVID-19 infection is rapidly spreading and there is a limited knowledge on what would impact the virus critically. Previous studies have reported association of blood groups with susceptibility and mortality of COVID-19 infection [3–5]. Old age and comorbidities have been reported to have poor prognosis of COVID-19 infection. Various studies reported the impact of underlying comorbid conditions of the patients such as DM, HTN, chronic kidney disease (CKD), chronic liver disease (CLD), chronic obstructive pulmonary disease (COPD), cancer, dementia and lung diseases as the major risk factors for COVID-19 disease severity and mortality [6–12].

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The risk factors associated with COVID-19 mortality have still not been adequately known. Diabetes is posed to increased risk of hospitalisation and intensive care unit (ICU) admission [13, 14]. Diabetes is also common amongst the patients with fatal outcomes of COVID-19 disease [15–18]. Patients with underlying hypertension are also reported to be associated with poor disease prognosis, longer duration of recovery and mortality [7, 19, 20]. CKD another one of the most common comorbidities around the globe is reported to be significantly associated with mortality in COVID-19 patients [21, 22]. The clinical outcomes and length of stay are directly related with the underlying comorbid condition of patients [23] Liu et al. found that elderly COVID-19 patients are more susceptible to ICU admission along with higher risk of mortality [24]. Yet the clinical data to guide policy makers and healthcare professional is still insufficient.

Therefore, it is very crucial to assess any association of comorbidity to establish risk stratification of COVID-19 patient for a better management disease and prevent severe outcomes to decrease the burden on national healthcare systems. The research question of the study is to observe the association of DM, HTN and CKD on the prognosis of COVID-19 infection. Additionally, we investigated the association with age and sex which allows us to identify specific conditions that affects the prognosis of COVID-19 infection.

Methods

Study design

This is a single centre, retrospective study which was carried out at Sir Ganga Ram Hospital, Delhi, India. The study has been reviewed and approved by Ethics Committee of Sir Ganga Ram Hospital.

We investigated the burden of comorbidities on the prognosis and clinical outcome of COVID-19 patients admitted to Sir Ganga Ram Hospital, New Delhi. The impact of COVID-19 and comorbidity was analysed based on the susceptibility to severity of disease (ICU admission), recovery or length of stay at hospital and lastly the mortality. Association was analysed with DM, HTN and CKD. Patients were selected strictly either having underlying condition of DM, HTN and CKD, either alone or in groups of these three conditions. The patients included in this study are RT-PCR confirmed COVID-19 patients admitted from April 8, 2020, to October 4, 2020. The patients were followed up till the time of discharge or decease. Patients with other comorbidities than the above-mentioned three were not included in the study.

Data analysis

Statistical Package for Social Sciences (SPSS) Version 18 and MedCalc (statistical software) was used for the analysis. Chi-square test was used to analyse the distribution of different comorbidities. Relative Risk (RR) test was applied to study the risk of underlying comorbidities of the COVID-19 infected patients. Relative risk is reported with 95% confidence intervals (CIs). Mann–Whitney test is used to explore the relationship between recovery period (length of stay at hospital) and comorbidities.

The association of COVID-19 disease with severity, length of stay and mortality. First, the data are analysed on the basis of comorbidities, i.e. diabetic patients are compared to non-comorbid patients, hypertensive patients to non-hypertensive patients and lastly CKD patients to non-CKD patients. Further, the analysis of multiple comorbid conditions was analysed on comparing any one underlying comorbid condition out of the three mentioned with no comorbid patients. Similarly, any two comorbidities and all the three comorbidities were compared with patients having no comorbidities. Here the association of sex and age groups are not considered, and the association was tested based on the underlying comorbid condition and COVID-19 disease prognosis.

For the analysis of impact of different sex and age group of the COVID-19 patients, the underlying comorbidities are segregated as DM, HTN, CKD, DM + HTN, DM + CKD, HTN + CKD and DM + HTN + CKD, which are compared with non-comorbid COVID-19 patients to understand the precise association of the combination underlying conditions and COVID-19 disease prognosis. These combinations of underlying comorbid conditions are analysed whilst testing the association based on sex and age.

Continuous variables are present as median (IQR) or mean ± standard deviation. The categorical variables are presented as frequencies (percentages). For analysis 2-tailed test with p value < 0.05 is considered as statistically significant. Here, we have used chi-square test, Mann–Whitney U test and Relative Risk to analyse the association of underlying comorbidities with severity, recovery duration and mortality of the COVID-19 infected patients.

Results

Records of COVID-19 infected patients admitted in the hospital were extracted out based on the inclusion and exclusion criteria. A total of 2586 patients were included

Table 1 Demographic profile of study population ($n = 2586$)

Characteristics	Frequency (%)
Age	
18–59 (< 60)	1682 (65.0%)
≥ 60	904 (35%)
Sex	
Males	1800 (69.6%)
Females	786 (30.4%)
ICU admission	
Yes	779 (30.1%)
No	1807 (69.9%)
Outcomes	
Recovered	2269 (87.7%)
Deceased	317 (12.3%)

in the study. Out of 2586, 69.6% of the patients were male. 35% of the patients were of age greater than equal to 60 years (Table 1). 48.7% of the COVID-19 infected patients had no underlying comorbidity. Whereas 15% of the patients had DM, followed by HTN in 10.4% and CKD in 0.8% of the patients. The underlying comorbid condition of the patients were further classified on the basis of combination of underlying conditions, i.e. DM + HTN, DM + CKD, HTN + CKD and DM + HTN + CKD in 19.3%, 0.6%, 1.4% and 3.8%, respectively (Fig. 1).

Association of comorbidity with the severity of COVID-19 infection

The severity of COVID-19 is measured on the basis of admission to ICU. The association of DM, HTN and CKD with susceptibility to severity of COVID-19 infection was analysed with distribution of comorbidity amongst the COVID-19 infected patients who required ICU admission (COVID + ICU +) and those who do not required ICU admission (COVID + ICU-). The patients having diabetic condition was compared to non-diabetic patients irrespective of presence of any other conditions ($p \leq 0.001$; RR: 1.28, 95% CI 1.14–1.44). Similarly, hypertensive to non-hypertensive ($p \leq 0.001$; RR: 1.39, 95% CI 1.24–1.56) and CKD patients were compared to non-CKD patients ($p \leq 0.001$; RR: 1.65, 95% CI 1.39–1.95). All the three comorbidities, i.e. DM, HTN and CKD showed significant impact with p value < 0.001 of the underlying comorbid condition in prognosis of COVID-19 disease severity (Table 2). The relative risk of these comorbidities showed that CKD is most prone to severity of the COVID-19 infection followed by HTN and DM.

On comparing the impact of multiple comorbidities with the severity of COVID-19 infection it is found that presence of comorbidity poses greater risk of ICU admission when compared to the patient with no underlying comorbidity. As the number of comorbidities in patients are increased, the risk of severity of COVID-19 infection also increases significantly as observed through the relative risk analyses (Table 2).

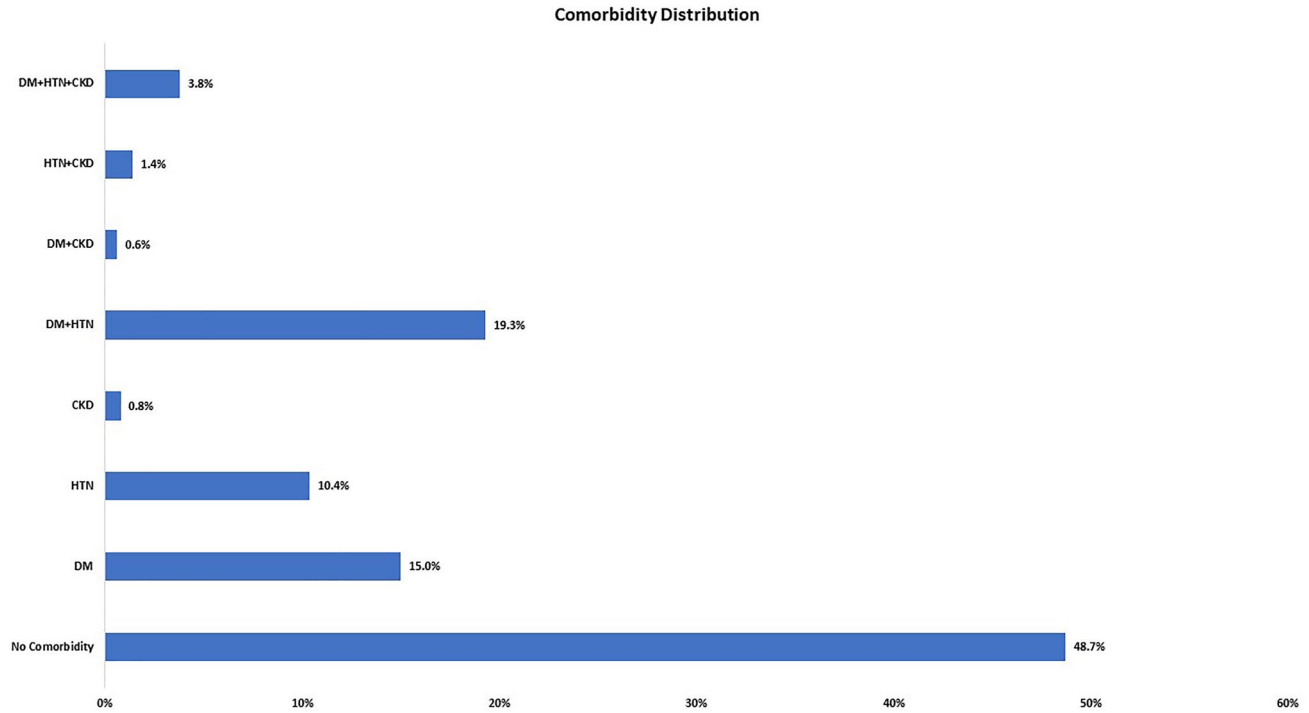

Fig. 1 Distribution of underlying comorbid conditions of the study population

Table 2 Distribution of comorbidities between COVID + ICU + and COVID + ICU-

Comorbidity	Total ($n=2586$)	COVID + ICU + ($n=779$)	COVID + ICU- ($n=1807$)	p value	RR (95% CI)
Diabetes				< 0.001	1.28 (1.14–
Yes	1002	348 (34.7%)	654 (65.3%)		1.44)
No	(38.7%) 1584 (61.3%)	431 (27.2%)	1153 (72.8%)		
Hypertension				< 0.001	1.39 (1.24–
Yes	903 (34.9%)	333 (36.9%)	570 (63.1%)		1.56)
No	1683 (65.1%)	446 (26.5%)	1237 (73.5%)		
CKD				< 0.001	1.65 (1.39–
Yes	170 (6.6%)	81 (47.6%)	89 (52.4%)		1.95)
No	2416 (93.4%)	698 (28.9%)	1718 (71.1%)		
Multiple comorbidities					
1. Comorbidity	677 (26.2%)	206 (30.4%)	471 (69.6%)	< 0.001	1.20 (1.03–
No comorbidity	1259 (48.7%)	320 (25.4%)	939 (74.6%)		1.39)
2 comorbidities	552 (21.3%)	203 (36.8%)	349 (63.2%)	< 0.001	1.45 (1.25–
No comorbidity	1259 (48.7%)	320 (25.4%)	939 (74.6%)		1.67)
3 comorbidities	98 (3.8%)	50 (51.0%)	48 (49.0%)	< 0.001	2.01 (1.62–
No comorbidity	1259 (48.7%)	320 (25.4%)	939 (74.6%)		2.49)

Under the multiple comorbidity section, 1 comorbidity refers to any single underlying condition of the patient, it can be DM or HTN or CKD. 2 comorbidity refers to the combination of any two underlying comorbid condition out of the above mentioned three comorbidities. Lastly 3 comorbidity means the patients have all the three, i.e. DM, HTN and CKD condition

Association of comorbidity with the recovery duration of COVID-19 infection

The median (IQR) recovery duration or the length of stay at the hospital was found to be significantly greater amongst the patients with comorbidity on applying Mann–Whitney test. Diabetes as well as hypertension found to be significantly associated with greater recovery duration. Whereas no association is found for patients with CKD to non-CKD. Multiple number of comorbidities in patient are also found to be associated with the length of recovery (Table 3).

Association of comorbidity with mortality of COVID-19 infection

To test the association of comorbidity with COVID-19 mortality, comorbidity distribution was compared amongst deceased and recovered COVID-19 infected patients. Significant difference was found for underlying comorbid condition of the patients. DM ($p \leq 0.001$; RR: 2.02, 95% CI 1.65–2.49), HTN ($p \leq 0.001$; RR: 2.33, 95% CI 1.89–2.86) and CKD ($p \leq 0.001$; RR: 3.18, 95% CI 2.51–4.04) all are significantly associated with mortality amongst COVID-19 patients. Comparison of multiple underlying comorbid conditions in COVID-19 patients, showed that number of comorbidities are also significantly associated with outcome of the patients. With the increase of underlying comorbid condition of the COVID-19 infected patients, the risk of

Table 3 Comparison of comorbid groups distribution and recovery duration (LOS) of patients with COVID-19

Comorbidity	Total ($n=2586$)	Median LOS	IQR	p value
Diabetes				< 0.001
Yes	1002 (38.7%)	10	7–15	
No	1584 (61.3%)	9	6–12	
Hypertension Yes	903 (34.9%)	10	7–15	< 0.001
No	1683 (65.1%)	9	6–12	
CKD				0.660
Yes	170 (93.4%)	9.5	6–17	
No	2416 (6.6%)	9	7–13	
Multiple comorbidities				
1 Comorbidity	677 (26.2%)	10	7–14	< 0.001
No Comorbidity	1259 (48.7%)	9	6–12	
2 comorbidities	552 (21.3%)	10	7–15	< 0.001
No Comorbidity	1259 (48.7%)	9	6–12	
3 comorbidities	98 (3.8%)	10.5	6–19	< 0.001
No Comorbidity	1259 (48.7%)	9	6–12	

Under the multiple comorbidity section, 1 comorbidity refers to any single underlying condition of the patient, it can be DM or HTN or CKD. 2 comorbidity refers to the combination of any two underlying comorbid condition out of the above mentioned three comorbidities. Lastly 3 comorbidity means the patients have all the three, i.e. DM, HTN and CKD condition

mortality also increases. CKD is found to be most susceptible to death outcome in the COVID-19 infected patients followed by HTN and lastly DM as shown in Table 4.

Stratified analysis by age groups

The COVID-19 infected patients were divided into groups of age < 60 years and ≥ 60 years. Chi-square test is applied to compare the association of underlying comorbid conditions with the susceptibility of severity (ICU admission). The association of underlying comorbidities and severity are analysed based on the segregated groups of comorbidities with patients having no comorbidities. The groups are divided as DM, HTN, CKD, DM + HTN, DM + CKD, HTN + CKD and DM + HTN + CKD. As the name suggests the group DM, HTN and CKD comprise of patients with only single comorbidity and rest all the comorbid groups have patients having combination of comorbid conditions.

COVID-19 infected patients having DM, HTN or CKD have no association with the severity of disease irrespective of the age of the patients. On analysing the multiple or combination of these comorbidities with severity it was found that amongst the COVID-19 infected patients of age less than 60 years, DM + HTN and DM + HTN + CKD are significantly associated with risk to ICU admission. Whereas underlying DM + CKD amongst < 60 years patients is almost significantly associated ($p = 0.051$) with higher risk of ICU admission or severity of disease. Amongst elderly patients of age greater than equal to sixty years, it was found that underlying comorbid conditions does not have any impact in severity of disease except for the patients with all the three comorbidities, i.e. DM + HTN + CKD (refer to Fig. 2 and *Supplementary* Table 1).

The analysis of relative risk of the of severity of COVID-19 shows that younger patients with underlying comorbidities are relatively at higher risk of severity of COVID-19 infection compared to the elderly patients with similar underlying condition except for DM (< 60 years = RR: 0.98, 95% CI 0.76–1.26; ≥ 60 years = RR: 1.09, 95% CI 0.82–1.43) where the relative risk of ICU admission amongst patients with age less than < 60 years is comparatively lower but almost similar to the patients with age ≥ 60 years (Fig. 3).

On comparing the association of mortality with underlying comorbid conditions in COVID-19 patients, it is found that CKD is significantly associated with mortality of the patients regardless of the age of the patients. Amongst the patients of age < 60 years, combination of DM + HTN, HTN + CKD and DM + HTN + CKD are at significantly higher risk to mortality on comparing with the non-comorbid COVID-19 patients. Whereas amongst the patients of age ≥ 60 years it is found that patients having all the three comorbidities are associated with mortality due to COVID-19 infection (Supplementary table 2). The relative risk analysis found that patients belonging to younger age group (< 60 years) are relatively at higher risk of mortality as compared to older patients (≥ 60 years) with same underlying conditions.

Table 4 Distribution of comorbidities amongst deceased and recovered COVID-19 infected patients

Comorbidity	Total	Deceased	Recovered	*p* value	RR (95% CI)
Diabetes				< 0.001	2.02 (1.65–2.49)
Yes	1002 (38.7%)	178 (17.8%)	824 (82.2%)		
No	1584 (61.3%)	139 (8.8%)	1445 (91.2%)		
Hypertension				< 0.001	2.33 (1.89–2.86)
Yes	903 (34.9%)	176 (19.5%)	727 (80.5%)		
No	1683 (65.1%)	141 (8.4%)	1542 (91.6%)		
CKD				< 0.001	3.18 (2.51–4.04)
Yes	170 (93.4%)	58 (34.1%)	112 (65.9%)		
No	2416 (6.6%)	259 (10.7%)	2157 (89.3%)		
Multiple comorbidities					
1 Comorbidity	677 (26.2%)	73 (10.6%)	603 (89.4%)	< 0.001	1.46 (1.09–1.96)
No comorbidity	1259 (48.7%)	93 (7.4%)	1166 (92.6%)		
2 Comorbidities	552 (21.3%)	116 (21.0%)	436 (79.0%)	< 0.001	2.85 (2.21–3.67)
No comorbidity	1259 (48.7%)	93 (7.4%)	1166 (92.6%)		
3 Comorbidities	98 (3.8%)	36 (36.7%)	62 (63.3%)	< 0.001	4.97 (3.59–6.88)
No comorbidity	1259 (48.7%)	93 (7.4%)	1166 (92.6%)		

Under the multiple comorbidity section, 1 comorbidity refers to any single underlying condition of the patient, it can be DM or HTN or CKD. 2 comorbidity refers to the combination of any two underlying comorbid condition out of the above mentioned three comorbidities. Lastly 3 comorbidity means the patients have all the three, i.e. DM, HTN and CKD condition

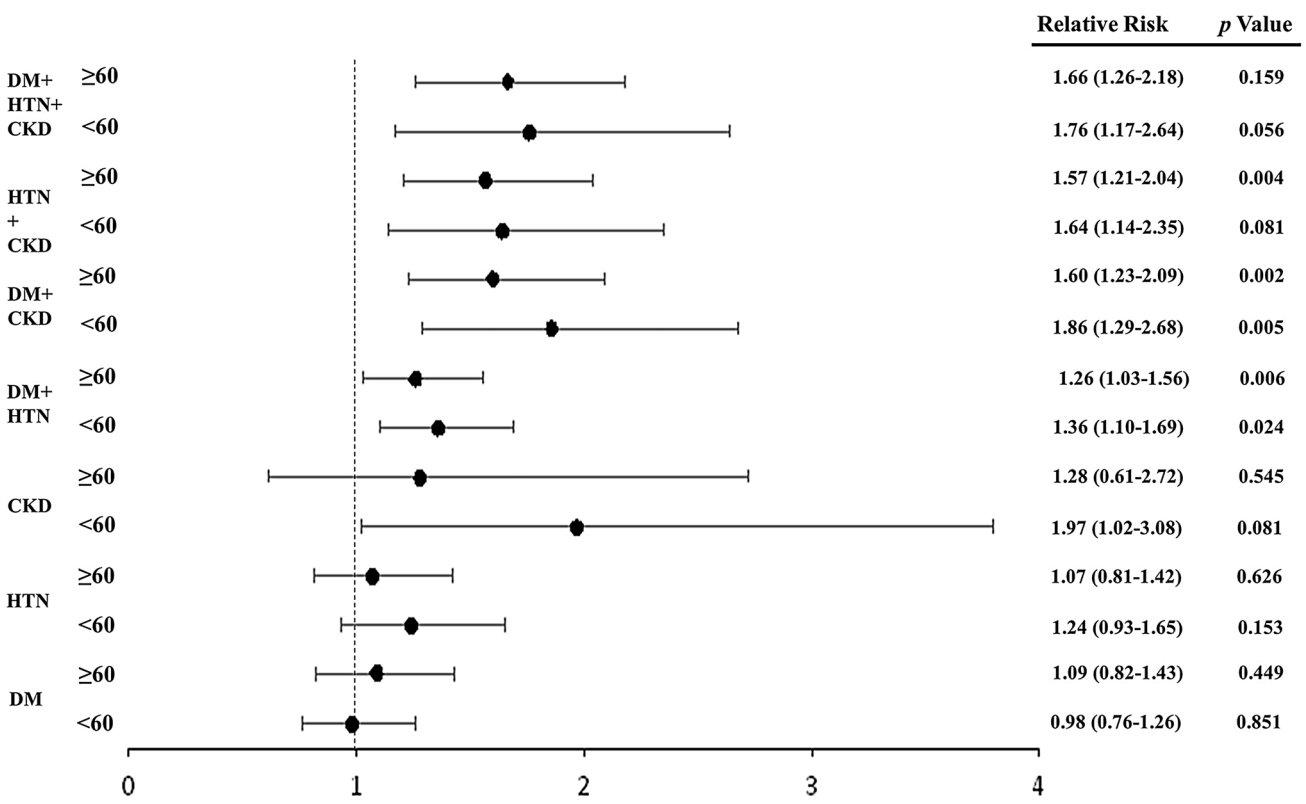

Fig. 2 Relative risk distribution of underlying comorbid conditions with severity of COVID-19 infection based on the basis of age

Stratified analysis by sex

COVID-19 infected males and females were analysed to observe the association of underlying comorbidities and susceptibility of COVID-19 infection to severity of disease and mortality due to infection. COVID-19 infected male patients having HTN, DM + HTN, DM + CKD and DM + HTN + CKD groups are found to be significantly associated to higher risk of disease severity or ICU admission. Whereas amongst females DM + HTN and DM + HTN + CKD underlying comorbidities poses a higher risk of severity of disease (*Supplementary Table 3*). On comparing the relative risk of ICU admission in COVID-19 patients it was observed that females with DM, HTN, DM + HTN, HTN + CKD are more prone to severity of disease and ICU admission as compared to the males with same underlying conditions (Fig. 4).

For association of comorbidity with mortality in COVID-19 patients it was found that amongst females, each comorbid groups are significantly associated with mortality in COVID-19 patients except for hypertensive condition. In males no association of comorbidities with mortality was found in DM, HTN and HTN + CKD patients (Fig. 3b and *Supplementary Table 4*). The relative risk analysis showed that females are at greater risk of mortality as compared to the males having same comorbid conditions except for the hypertensive patients where the relative risk of mortality in females is less than the males (Fig. 5).

Discussion

The current study was undertaken to evaluate the association of comorbidities with prognosis of COVID-19 infection. For this study we have considered three most common comorbidities throughout the world, i.e. diabetes, hypertension and chronic kidney disease. Further we have analysed the impact of multiple underlying comorbid conditions on the prognosis of COVID-19 infection. The prognosis of COVID-19 infection is varying, and it suggests that the patients who develop severe illness and severe inflammatory response might experience longer exposure to virus and thereby longer recovery period [25].

The Angiotensin-Converting Enzyme 2 (ACE2) pathway have a major role in the prognosis of COVID-19 disease [26]. The SARS-CoV-2 spike glycoprotein can be used to develop drugs and vaccines. It can also enter lung cells through the ACE2 receptor. ACE2 was first discovered in 2000 as a homolog of the ACE receptor, with 40 percent identity and 60 percent similarity [27, 28]. Researchers have

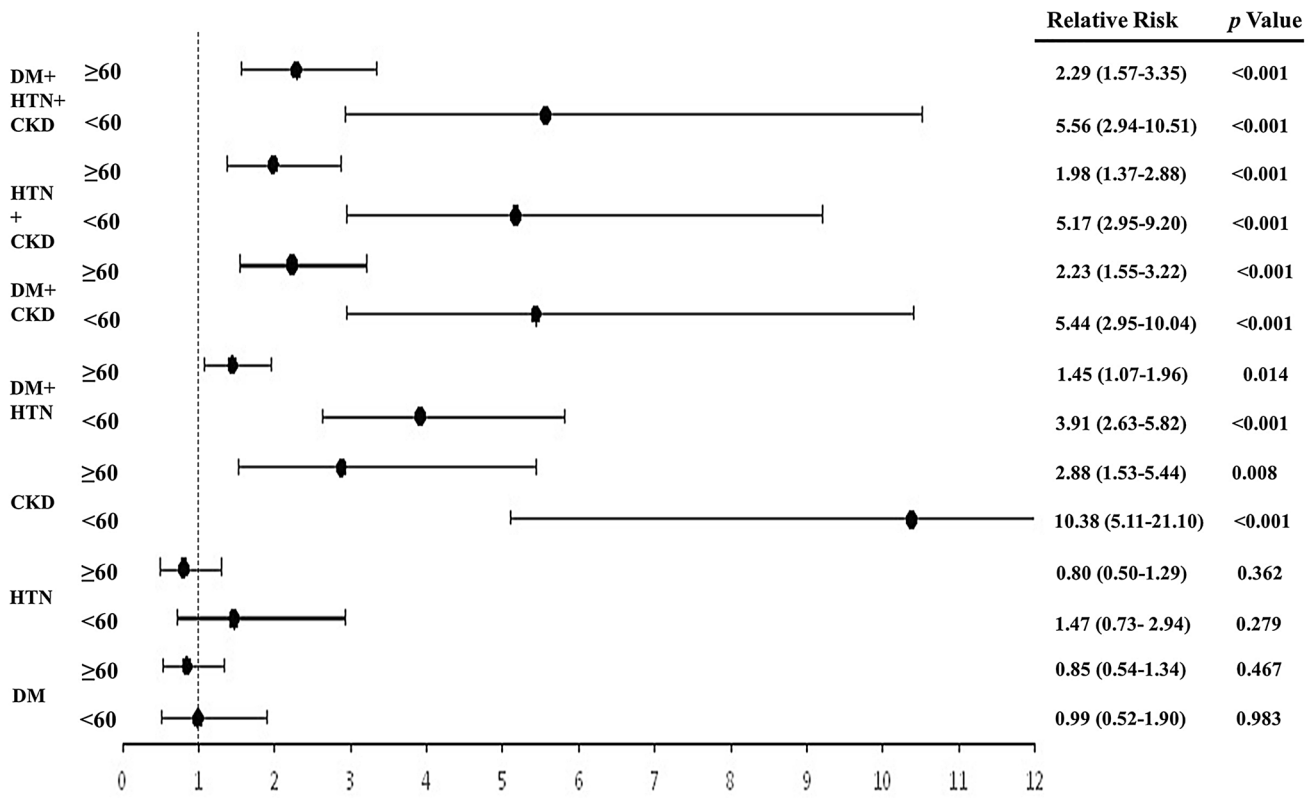

Fig. 3 Relative risk distribution of underlying comorbid conditions with mortality due to COVI-19 infection based on age groups

been examining ACE2 tissue expression at both the mRNA and protein levels in the hopes of uncovering organs that are more prone to infection due to the wide spectrum of symptoms experienced by people infected with COVID-19. Surprisingly, ACE2 expression in experimental models and in the human transcriptome was revealed to be exceedingly low in the lung, largely limited to a small number of type II alveolar epithelial cells utilising various databases [29, 30]. The significance of ACE2 shedding has yet to be fully understood, but in the context of the COVID-19 pandemic, understanding the mechanism that leads to ACE2 shedding, sACE2 function, and its plasma level could lead to the development of better therapies and diagnostic tools to track disease progression and severity. It has been demonstrated, for example, that SARS-CoV-2 binding to ACE2 causes ADAM17-dependent shedding, boosting SARS-CoV-2 absorption into cells [31]. Figure 6 depicts the entry of SARS-CoV-2 virus in the cell via ACE2 receptors and the pathways that are involved in the process of prognosis of COVID-19 infection.

Our analysis of COVID-19 infected patients in Delhi, India shows that the underlying comorbid conditions are significantly associated with ICU admission, duration of recovery and mortality. CKD is associated with the highest risk of mortality in COVID-19 infected patients out of the three studied comorbidities, followed by HTN and the least for DM. On analysing the association of multiple comorbidities, it is found that with the increase in number of comorbidities, the risk of severity of disease as well as the risk of mortality also increases indicating a directly proportional relation with the number of comorbidities.

All the patients of the study population received treatment based on their presenting signs and symptoms as per the attending physician's discretion along with the hospital/institutions protocol based on the national guidelines for the management of COVID-19 of government of India which were changing from time to time. Several different medicines are used for the treatment of these patients which includes anticoagulants, antibiotics, hydroxychloroquine (HCQ), azithromycin, doxycycline, ivermectin, remdesivir, steroids (dexamethasone or methylprednisolone), tocilizumab and oxygen support or ventilators as per the requirement and need of the patient.

The rate of ICU admission amongst the COVID-19 infected patients is reported to be lower in other countries such as Republic of Korea [32], Mexico [33], America [34, 35], United Arab Emirates [36] and Iran [37] than the present study. Similarly, the mortality rate reported in our study was lower than that reported in other studies from different countries like the United States of America [35, 38],

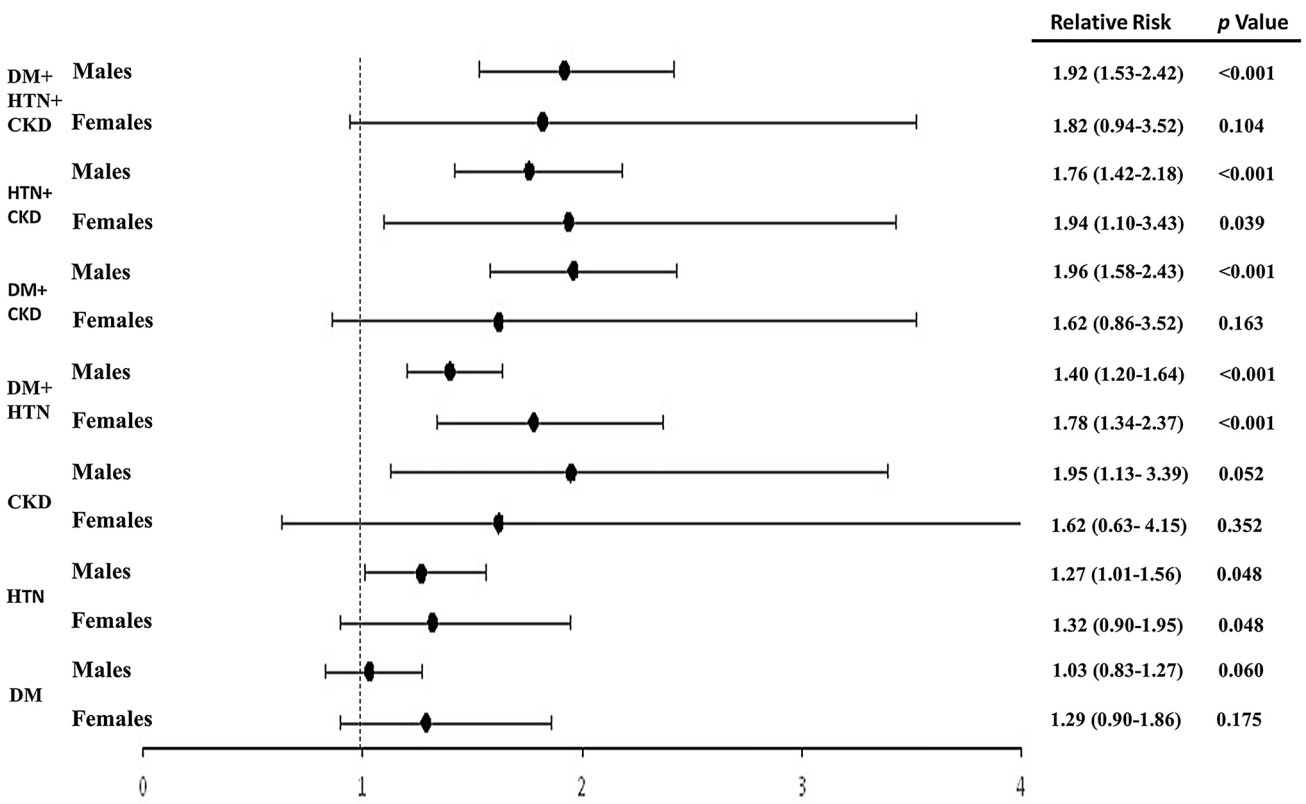

Fig. 4 Relative risk distribution of underlying comorbid conditions with severity of COVID-19 infection based on sex

the United Arab Emirates [39]. Whereas other countries like Mexico [33] and Republic of Korea [7, 32] seem to have lower mortality rate than the present study on Indian population.

Cegan et al. performed a cross national study to assess the role of comorbidities and age in progression of COVID-19 infection. It was found that with the increase in number of comorbidities the rate of ICU admission as well as mortality increases [34]. The result from this study is similar to the result of our study which also reported increased percentage of patients admitted to ICU and mortality with increased number of underlying comorbid conditions in COVD-19 patients. Our study moves a step further and also calculates the relative risk of ICU admission and mortality with the number of comorbid conditions which also found a higher relative risk with increased number of comorbidities. Another study from UAE observed similar results as of this study and found that comorbidities are associated with higher risk of mortality and observed diabetes, hypertension as well as CKD, all are significantly at higher risk of mortality [40] Diabetes is one of the most reported comorbidities associated with disease progression and mortality of COVID-19 [41–43]. Cho et al., reports DM, HTN and CKD to be significantly associated with mortality of the patients [7]. This study resembles with the results of these mentioned study studies with comorbidities being significantly impacting the disease outcome and mortality due to COVID-19.

In the present study we found that diabetes and hypertension are related to longer recovery period and CKD have no association with the recovery duration in COVID-19 infected patients. In a study from USA by Aldhaeefi et al., it was found that hypertension as well as CKD are associated with longer duration of COVID-19 negativity in patients, whereas no association of diabetes with recovery time in COVID-19 patients was reported [20]. On observing multiple underlying comorbidities in COVID-19 infected patients with patients having no comorbidity, the recovery duration was found to be significant in all the three categories. Further a clarity is missing on the persistent positivity of PCR test for SARS-CoV-2 virus may be due to a live virus or it might be reflecting residual viral RNA from the dead virus.

Sex of the COVID-19 infected patients have been previous reported to affect the disease progression and outcome of COVID-19 infection. Males are reported to be at higher risk of infection than females [44]. This can be further observed in many studies where the number of COVID-19 infected males are as much as twice the number of COVID-19 infected female [18, 39, 45, 46]. In our study we found that even though the number of COVID-19 admitted male patients are more than the twice of females. But on

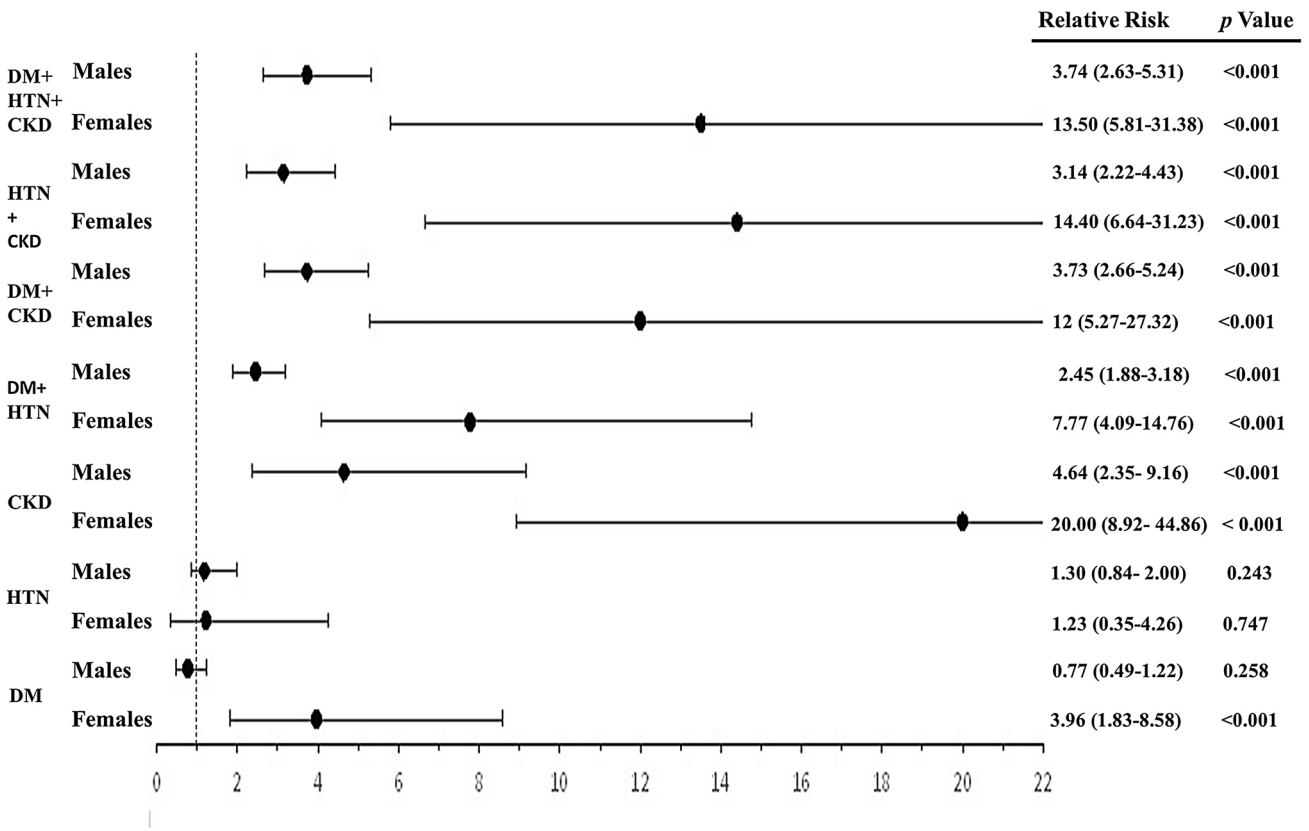

Fig. 5 Relative risk distribution of underlying comorbid conditions with mortality due to COVID-19 infection based on sex

calculating the risk ratio of males and females with same underlying comorbid conditions it was observed that the risk of severity of infection and mortality is higher amongst the females.

Delayed clearance of SARS-CoV-2 or longer duration of recovery is associated with higher mortality rate [40]. Delayed clearance is also found amongst the elderly patients [46, 47]. In another study by Wang et al. it was found that amongst the non-survivor ICU patients, nearly 76% of the patients were of age greater than 60 years. Our study contradicts these results and finds that patients of age less than sixty years are at higher risk of ICU admission as well as mortality compared to the patients of age group ≥ 60 years with same underlying comorbid conditions [23]. We analysed the association of each comorbidity segregated into each possible different groups that can be categorised amongst the three comorbidities. The strength of association of these comorbidities decreased with age. The relative risk for mortality was greater for patients with age < 60 years in contrast to patients with age ≥ 60 years for all the three comorbidities. The results are similar to that of a retrospective study from Mexico involving COVID-19 patients who had diabetes also showed that the older patients have lower hazard ratio then the patients of young age group [27].

Limitations

The major limitation of the study is the non-availability of patient's presenting symptoms and the treatment offered to the patient. Further the duration of the study was wide, the treatment guidelines were dynamic which was changing continuously based on the national guidelines for management of COVID-19 which might have affected the progression of disease.

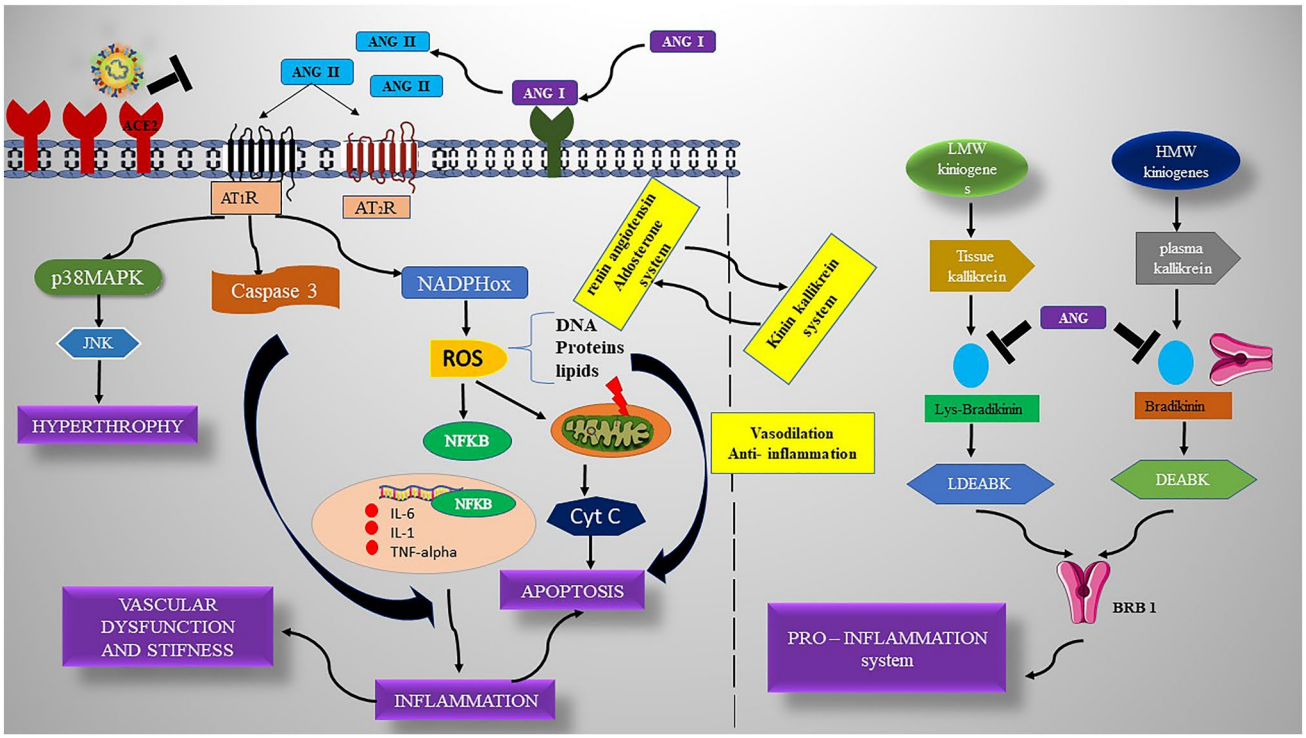

Fig. 6 Dysregulation of the RAAS and KKS in SARS-CoV-2 infection: SARS-CoV-2 interaction to the ACE2 receptor can result in its interaction to RAAS and KKS dysregulation. Indeed, AngII is not converted in to Ang1–7 and over activate its receptor AT1R, causing vasoconstriction, production of proinflammatory cytokines such as TNFα, IL6, IL1 and ROS formation through NADPH oxidase. ACE2 also vital role in the regulation of KKS by inactivating both LDEABK and DEABK making them unable to interact to the receptor BRB1, respectively. The excessive triggering of BRB1 receptor has been shown to enhance inflammation and coagulation

Conclusion

Diabetes mellitus, hypertension and chronic kidney disease, all are associated with progression of COVID-19 disease to severity and higher mortality risk. The number of underlying comorbid condition is directly proportional to the progression of disease severity and mortality. In Indian population, adults with age less than 60 years are susceptible to severe disease progression than the older individuals with same underlying comorbid conditions. Lastly, females are at higher risk of disease severity than males of same underlying comorbid conditions.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s11010-022-04485-2.

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