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Comorbidities And Their Impact On Covid 19 Outcome

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Abstract:

Introduction: Since November 2019, the rapid outbreak of coronavirus disease 2019 (COVID-19) has resulted in considerable morbidity and mortality all over the world and has become a public health emergency of international concern. The most common comorbidities reported with COVID-19 are hypertension, diabetes and cardiovascular diseases. A high proportion of COVID-19 patients admitted in ICU have multiple comorbidities.
Methods: This single-center observational retrospective study conducted with aim to assess the impact of comorbidities on the severity of COVID- 19 and to study the clinical outcome of patients with COVID-19 infection with comorbidities. The study population consisted patients with moderate to severe COVID-19 symptoms, aged >18 years. Comorbidity is defined as having at least one of the following before diagnosis of COVID-19: hypertension, diabetes mellitus, coronary heart disease, stroke, chronic lung disease, chronic kidney disease, chronic liver disease, hematologic disease, autoimmune disease and malignancy.
Results: Diabetes Mellitus was found to be the commonest comorbidity in 56.5% patients followed by hypertension in 28.7% patients and COPD was found in 16.7% patients either alone or in combination with other diseases. The other noted diseases were renal disease and malignancy. There was remarkable declination in the clinical outcome of patients with comorbidities and COVID-19 infection. The mortality rate within our study is about 23.2%. The incidence of breakthrough infection was 2.7%.
Conclusion: The individuals with the comorbidities should be vaccinated on a first priority subject to the availability of SARS-CoV-2 vaccine. Maximizing vaccine uptake should be the top priority.

Keywords: Comorbidities, COVID-19, Vaccine, Breakthrough infection, Mortality.

Introduction:

Since November 2019, the rapid outbreak of coronavirus disease 2019 (COVID-19) has resulted in considerable morbidity and mortality all over the world and has become a public health emergency of international concern[1]. The most common comorbidities reported with COVID-19 are hypertension, diabetes and cardiovascular diseases[2] . Older adults and people of any age who have underlying medical conditions such as hypertension and diabetes, have shown worse prognosis[3]. People with chronic obstructive pulmonary disease (COPD) or any respiratory illnesses are also at higher risk for severe illness from COVID-19[4].

Analyzing the clinical and epidemiological data of COVID-19 suggest that specific comorbidities increase the risk of infection with worse lung injury and death. Also, a high proportion of COVID-19

patients admitted in ICU have multiple comorbidities[5]. Studies have found that having one or more comorbidity significantly increases the severity of the COVID-19, mostly in aged patients, and is associated with increased need for Intensive Care Unit (ICU) support in high-risk patients[6].

In this study, we have highlighted the impact of various comorbidities on the severity of COVID19 disease.

Objectives:

The current study aimed

1. To assess the impact of comorbidities on the severity of COVID- 19
2. To study the clinical outcome of patients with COVID-19 infection with comorbidities.
3. To assess the breakthrough infection after vaccination.

Methods:

Study Design

This single-center observational retrospective study was conducted in Dr.Yaswant Singh Parmar Government Medical College, Nahan(H.P.) which is a tertiary level hospital in Himachal Pradesh (India) from 1 May 2021 to 15 June 2021. The study population consisted patients with moderate to severe COVID-19 symptoms, aged >18 years who were admitted in either the COVID ward or the ICU of the "COVID-19 unit" of the hospital.

On admission, all patients were tested for COVID-19 using RT-PCR (real-time reverse-transcriptase polymerase chain reaction) for human corona virus (SARS-CoV-2) and diagnosis was confirmed. The hospital has a triage system in the emergency department for all admitted patients at the time of hospital-entry. The categorisation and clinical management for patients with COVID-19 were followed as per ICMR guidelines.

All necessary laboratory tests were performed during hospitalization. History of chronic diseases, diagnostic and therapeutic interventions, survival/mortality records were assessed accurately to estimate the impact of comorbidities on disease severity and to know clinical outcome of patients. The discharge from COVID-19 ward or COVID-19 ICU (with or without need for mechanical ventilation support) and discharge to general ward/home had been recorded.

Comorbidities were determined on patient's self-report on admission. Comorbidities were initially treated as a categorical variable (yes versus no). Furthermore, comorbidities were sorted according to the organ systems (i.e. respiratory, cardiovascular, endocrine). Comorbidities that were classified into the same organ system (i.e. coronary heart disease, hypertension) would be merged into a single category.

Comorbidity is defined as having at least one of the following before diagnosis of COVID-19: hypertension, diabetes mellitus, coronary heart disease, stroke, chronic lung disease, chronic kidney disease, chronic liver disease, hematologic disease, autoimmune disease and malignancy.

The primary end-point of our study was a composite measure which consisted of discharge, referral or death. These composite measures were adopted because of serious outcomes of infections.

Inclusion and Exclusion Criteria

The participants were evaluated against the following inclusion criteria:

1) Age > 18 years

2) No history of hospitalization within the last 4-weeks of admission;

3) Positive RTPCR for COVID-19 with moderate-to-severe category as per ICMR guidelines.

4) No current pregnancy;

The exclusion criterias were as follows:

1) Patient with newly diagnosed comorbidity (i.e. after hospital admission);

2) Any history of trauma or surgical procedure within the last 3 months of admission; History of receiving immunosuppressants.

3) Patients with asymptomatic (no significant symptoms of COVID-19) and mild COVID-19 (may have fever, loss of sense of smell, extreme tiredness, sore throat, etc.) were not hospitalized and excluded from the study.

Data collection

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Demographic, comorbidities, clinical, laboratory, imaging examination, treatment, and outcome data were collected using a standardized case-report form. All clinical outcomes were recorded for patients who completed their hospital course at study end (discharged, referred or dead).

Results:

In total 156 COVID-19 patients with moderate-to-critical category were admitted in the "COVID-19 unit". Among them, 108 patients were finally included in the present study after evaluating against inclusion and exclusion criteria. All patients were followed until discharge or death or referral. So no case was censored once enrolled in the study. The number of male patients (61) was more than of female patients (47) as seen in Table1.

Data was analysed. Chi-square test was used to compare categorical variables, p-value <0.05 was considered significant.

Table 1: Sex Distribution among Covid positive patients

Male Patients	61
Female Patients	47

The maximum number of patients were in the age group of 61-70 years (30) followed by 51-60 years (22). The mean age of participants was 55.5 years as shown in Figure 1.

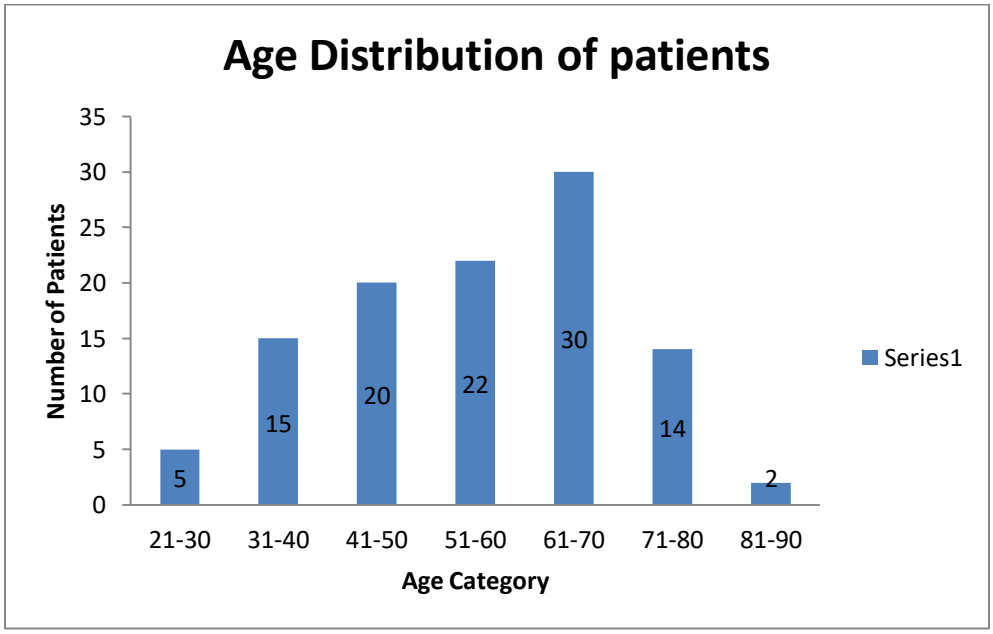

Figure 1: Age Distribution among Covid positive patients

Of 108 patients, 80 (74.1%) patients presented with one or more comorbidities. 51(47.2%) patients had single comorbidity and rest 29 (26.9%)t had two or more than two comorbidities. Only 28 patients did not had any previously diagnosed comorbidity as shown in Figure 2.

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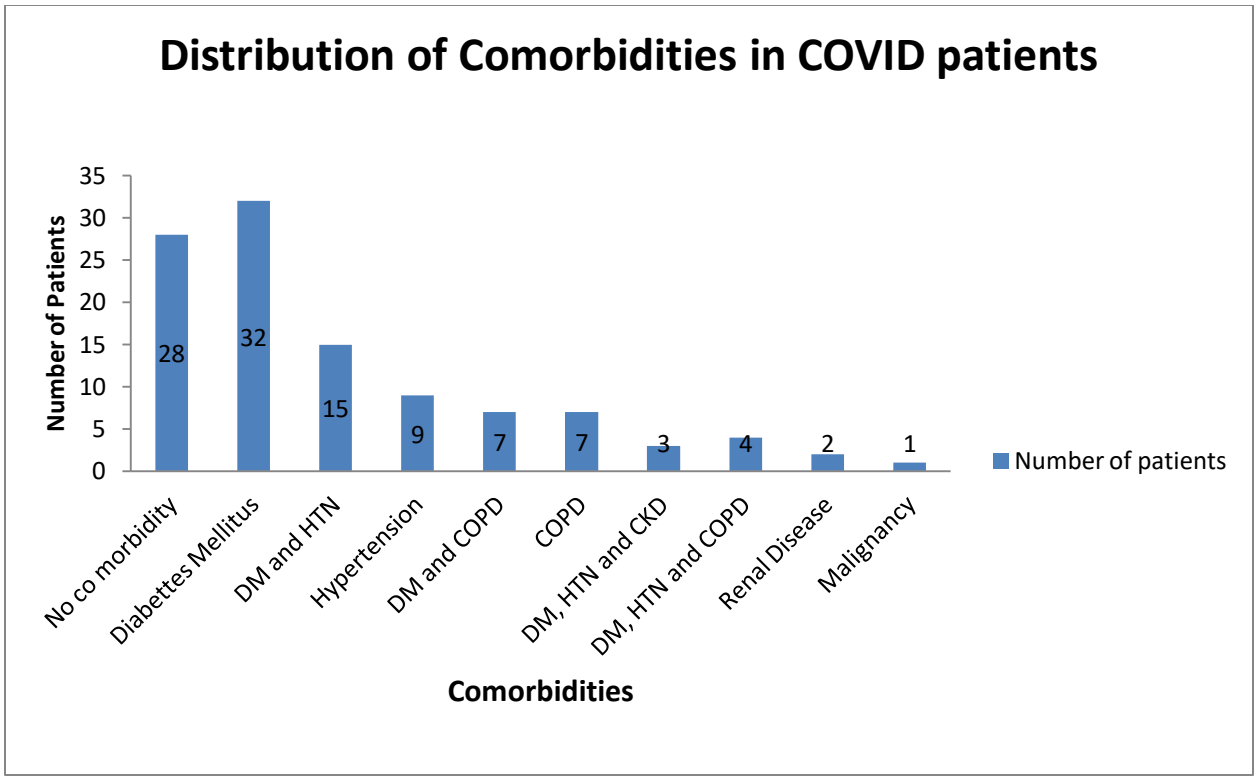

Figure 2: Distribution of Comorbidities among Covid positive patients

Diabetes Mellitus was found to be the commonest comorbidity in 61(56.5%) patients followed by hypertension in 31(28.7%) patients and COPD was found in 18 (16.7%) patients either alone or in combination with other diseases. The other noted diseases were renal disease and malignancy.

The result also included 25 deaths (men were 64% and women were 36%). Regarding the age group, maximum deaths were reported in the age group of 61-70 years followed by 71-80 and 51-60 years as shown in Table 2 & Figure 3.

Table 2: Sex Distribution in Deceased patients

Male Patients	16 (64%)
Female Patients	9 (36%)

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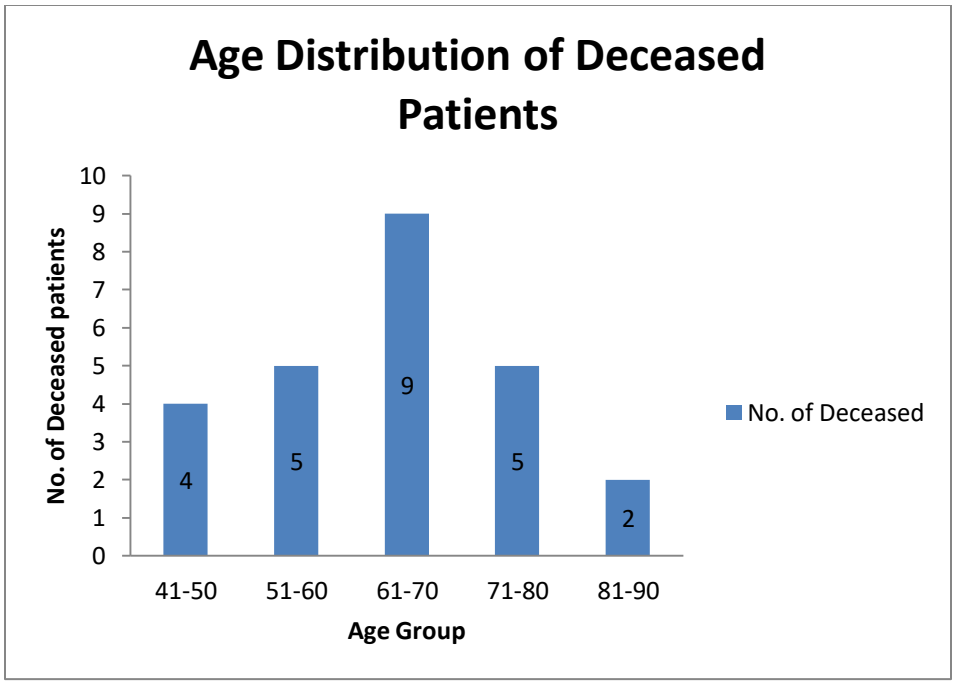

Figure 3: Age Distribution among Deceased patients

In deceased patients, chronic conditions such as Diabetes, Hypertension and COPD were observed to be the risk factors as compared to other underlying disease states as shown in (Figure 4). Diabetes was seen in 72% of deceased patients.

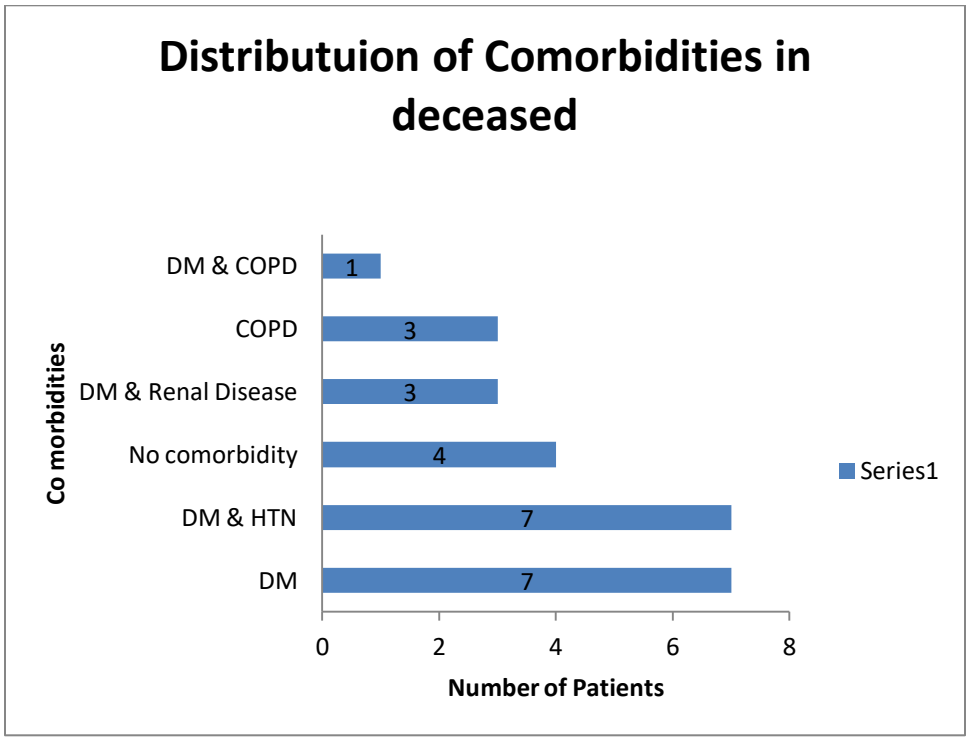

Figure 4: Distribution of Comorbidities among Deceased patients

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Table 3: Distribution of Patients according to co morbidity and its association with outcome

Co morbidity	No. of patients (n=108) No. (%)	Outcome		p value[1]
		Expired	Survived	
		No. (%)	No. (%)	
Diabetes Mellitus				
Present	61(56.48%)	18 (29.5%)	43 (70.5%)	0.074218
Absent	47(43.51)	7 (14.9%)	40 (85.1%)	
Hypertension				
Present	31(28.7%)	7 (22.5%)	24 (77.5%)	0.929303
Absent	77(71.3%)	18 (23.37%)	59 (76.63%)	
COPD				
Present	18 (16.67%)	3 (16.67%)	15 (83.33%)	0.475108
Absent	90 (83.33%)	22 (24.44%)	68 (75.56%)	
Renal Disease				
Present	5 (4.7%)	3 (60%)	2 (40%)	0.045439*
Absent	103 (95.3%)	22 (21.35%)	81 (78.65%)	
Malignancy				
Present	1(0.92%)	0	1(100%)	0.581373
Absent	107 (99.08%)	25 (23.36%)	82 (76.64%)	

[1] Chi square test, *Significant

Diabetes was the most common comorbidity present with an overall prevalence of 56.5% with mortality was 29.5% among diabetics. However, the association of outcome with Diabetes was insignificant (p> 0.05).

Similarly the association of mortality in hypertension, COPD and malignancy was also insignificant.

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Chronic renal disease was present in 4.7%. The mortality was significantly higher among whom renal disease was present (60%) than absent (21.35%). The association of outcome with renal disease was statistically significant (p= 0.04)

Status of Vaccination:

While recording the vaccination status it was found that out of 108 patients enrolled in the study only 3 patients were fully vaccinated while 21 patients had received first dose of vaccination. Rest 84 of them were not vaccinated at the time of presentation. The similar trend of vaccination was also found in deceased patients. Total 25 deaths were recorded in the study. It was found that 19 deceased were not vaccinated, 5 were partially vaccinated and only one patient was fully vaccinated as shown in Table 4.

Table 4: Vaccination Status among Covid patients and Deceased

Vaccination Status	In Covid Patients	In Deceased
Nil	84 (77.77%)	19 (76%)
Partial	21 (19.4%)	5 (20%)
Full	3 (2.7%)	1 (4%)
Total	108	25

Discussion:

COVID-19 outbreak have caused significant global morbidity and mortality, in addition to undermining the economic and social well-being of individuals and communities. Across the world, people with comorbidities have been identified as a high-risk group wherein the persons infected with SARS-CoV-2 virus has a greater chance of becoming critically ill and even dying. The risk is higher in older people with comorbidities. In this study, the presence of one or more comorbidities in patients was associated with an increased risk of developing severe illness. In our study, Diabetes is commonest comorbidity in moderate to severe patients of Covid 19 (56.5%). People with diabetes are inclined to get infections due to impaired phagocytic cell capabilities. An elevated level of ACE-2 receptors which are known to facilitate entry of SARS-COV-2 inside human body have been found to be causally related to diabetes and might prejudice them to infections[7].

Study by Yang J et al [6] suggests that 11-58% of all Covid patients have diabetes and risk of ICU admissions in Covid 19 individuals with diabetes is 14.2% higher than non diabetics. In our study we found that overall diabetes was in 61 (56.5%) patients out of which 18(72%) belonged to non survivor group.

In other studies[7,8,9] approximately 23% of hypertensive Covid patients were reported and in our study 31(28.7%) were found hypertensive. In patients of COPD, the expression of ACE-2 receptors is increased contributing to the establishment of severe symptoms among Covid 19 individuals. In our study 18 (16.7%) of patients were having COPD. We found 5(4.7%) of patients of renal disease including CKD in our study.

Huang et al [8] firstly reported that confirmed COVID-19 cases had common comorbidities, including HTN, DM, cardiac diseases, and COPD. Similarly other studies have also reported, HTN, CHD, and DM as the most common comorbidities in COVID-19

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patients[9,10,11]. So patients with underlying chronic diseases, including DM and HTN are at increased risk of severe COVID-19 infections.

There was remarkable declination in the clinical outcome of patients with comorbidities and COVID-19 infection. In our study we found that 21 deceased out of 25 deceased (84%) were having one or more comorbidities. The subjects with comorbidities were linked to a more severe disease outcome when infected with the novel corona virus as compared with patients with no underlying disease[12]. The SARS-CoV-2 infection becomes detrimental when it confronts a person with comorbidity, and the management of these patients with appropriate medical care is an imperative step towards their survival. The mortality rate within our study is about 23.2% which is much higher than the national rate 1.37% [13] probably because our study included only hospital admissions.

In our study the association of common comorbidities like Diabetes, hypertension and COPD as not statistically significant as compared to Covid 19 patients without these co morbidities, except for renal disease where association was found to be significant.

Vaccine Breakthrough:

A vaccine breakthrough occurs when an immunized individual contracts that disease they are vaccinated against. In case of Covid 19, vaccine breakthroughs are defined as individuals who test positive for SARS-CoV-2 after 14 days of complete vaccinationOur study suggested that almost 78% of admitted patients and 76% of deceased were not vaccinated. The infection after first dose of vaccine was 19.4% and after second dose of vaccine was 2.7%. So the incidence of breakthrough infection was 2.7%. The breakthrough infection reported by Rana et al after second dose of vaccination in Health care workers is 1.6% [14] which is lesser than our study as we are dealing with comorbid patients.

The majority of people admitted to the hospital are unvaccinated. So the vaccination is effective in reducing incidence, hospitalization, and deaths, especially among vulnerable individuals with comorbidities and risk factors. So vaccine administration should been a high priority especially among comorbid patients to prevent this devastating toll. The similar results were reported by Moghadas et al [15] in the study that showed that vaccination can have a substantial impact on mitigating COVID-19 outbreaks, even with limited protection against infection. Vaccine cannot stop the transmission of disease. So compliance with non-pharmaceutical interventions such as hand washing, social distancing, wearing mask and use of hand sanitizer are essential to achieve this impact.

Limitations:

Our study has several limitations. First, our study was limited by the observational nature, included the small sample size, single center data and short duration of the study.

Second, the past history was provided by the patients or their relatives. Some patients might have unknown comorbidities due to the lack of previous basic medical data.

Another limitation is possible information bias because data extracted from clinical histories were used. These data were collected to guarantee the clinical care of the patients and not for the purpose of this research. However, given that the majority of variables recorded are routinely used in clinical practice and are recorded reliably, for the best care of patients, we assume that if there was information bias, this was limited or of little impact on the analyses.

Randomized controlled trials are highly required to analyze the impact of individual comorbidity in worsening the COVID-19 outcome.

Conclusion:

SARS-CoV-2 is affecting globally a large population with pneumonia-like symptoms, and the patients with comorbidities are at utmost risk of infection. Covid 19 patients with comorbidities are at increased risk of severe illness and require meticulous care as compared to patients without comorbidities The meticulous management of COVID-19 patients with comorbidities in contrast to patients without comorbidities is emphasized to control the jeopardy of life. The comorbid individuals must undertake vigilant preventive measures to protect themselves during the pandemic. Although having one or more comorbidity is linked to increased disease severity but no clear association was foung between having

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thse risk factors and increase risk of fatality compared to those without co morbid illnesses.

The individuals with the comorbidities should be vaccinated on a first priority subject to the availability of SARS-CoV-2 vaccine. Maximizing vaccine uptake should be the top priority for policy makers across the world in order to end this pandemic.

Community awareness programs and patient education activities need to be stronger in the communities to enhance patients' awareness regarding the exacerbating-risk of COVID-19 infection with multiple chronic diseases, mostly in the elderly population.

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