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Clinico-demographic Features in Middle- and Older-Aged COVID-19 Deceased Patients: A Comparative Study in India

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Abstract

Introduction: The novel coronavirus pandemic has ravaged the word since late 2019 and caused many deaths among populations. Our aim was to study clinico-demographic features in middle- and older-aged coronavirus disease 2019 (COVID-19) deceased patients.

Methods: The present cross-sectional study was done in the Department of Biochemistry, in collaboration with the Department of Medicine, in a tertiary care hospital in Mumbai, India. The clinico-demographic data of COVID-19 positive deceased patients who died at our centre during the period of April 1, 2020 to April 30, 2020 were procured. The diagnosis of COVID-19 was based on reverse transcriptase–polymerase chain reaction (RT-PCR) test results. A total of 110 patients were included in the study and categorized according to their age into three groups: (1) young adults (aged 18-35 years), (2) middle-aged adults (aged 36-55 years), and (3) older adults (aged>55 years), and various clinico-demographic features were evaluated. The Mann-Whitney U test for non-parametric data and unpaired t-test for the parametric data were used for comparisons.

Results: The incidence of COVID-19 was found to be significantly higher in the older age group ($P=0.0001$). Diabetes (43.6%) and hypertension (40.9%) were the most common comorbidities present in nearly half of the study population**.** The median age of the patients died due to COVID-19 was 57.0 years, and there was a higher percentage of men (67.3%) compared to women (32.7%) among the deceased. Clinical and biochemical parameters were compared between middle-aged and older-aged groups. Hypertension and diabetes were significantly higher in the older-aged group compared to the middle-aged group ($P<0.001$). No significant difference could be observed in the sign and symptoms and biochemical parameters between these groups.

Conclusion: The clinico-demographic features and mortality in middle-aged and older-aged deceased COVID-19 patients were similar. Close monitoring and early therapeutic interventions in both age groups will help to diminish mortality.

Keywords: COVID-19, Clinical factors, Demographic features, Mortality, Coronavirus, Pandemic

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Introduction

The novel coronavirus pandemic, known as coronavirus disease 2019 (COVID-19), instigated by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2), has freshly become a community health emergency of worldwide concern. The SARS-CoV-2 created havoc across the world, with 204 644 849 confirmed cases and 4 323 139 deaths until August 12, 2021.[1]

The clinical indices of COVID-19 in different age groups are heterogeneous; few are asymptomatic while most present with mild to moderate ailment with respiratory or flu-like sign and symptoms.[2]

Highly severe cases of COVID-19 disease with higher mortality have been described in elderly population and in those with chronic co-morbidities, such as hypertension, cardiac disease, diabetes and they are considerably susceptible to critical to fatal outcomes. At admission, 20%–51% of patients were stated as having at least any one comorbidity, with hypertension (10%–15%) and diabetes (10%–20%).[3] An aging population is most vulnerable to the infection and least able to recover compared to younger population.

Most of the previous studies have been done on total populations and limited data is available about clinical and demographic features in different age groups.[4] Therefore,

the current study aimed to determine the association of clinico-demographic features of COVID-19 deceased patients with age.

Material and Methods

Study Design, Setting, and Participants

This was a cross-sectional study done by the Department of Biochemistry, in collaboration with Department of Medicine, in a tertiary care hospital of Mumbai, India. Consecutive sampling strategy was used for data collection. Clinico-demographic data of COVID-19 positive deceased patients who died at our centre during the period of April 1, 2020 to April 30, 2020 was abstracted by one of the authors from clinical record under the supervision of an experienced physician. The diagnosis of COVID-19 was confirmed by positive reverse transcriptase–polymerase chain reaction (RT-PCR) test results performed at our centre. Information about onset of illness to first hospital admission, hospital stay duration, age, gender, co-morbid conditions, signs and symptoms, complete blood count, SpO_2, pCO_2 pO_2 cause of death were noted and used for data analysis. Study subjects pool was comprised of total 110 patients. The patients were further categorized according to their age into three groups: (1) young adults (aged 18-35 years), (2) middle-aged adults (aged 36-55 years), and (3) older adults (aged > 55 years).[5]

Definitions

Hypertension: Standard adult blood pressure is defined as a blood pressure of 120 mm Hg when the heart beats (systolic) and a blood pressure of 80 mm Hg when the heart relaxes (diastolic). When systolic blood pressure is ≥ 140 mm Hg and/or a diastolic blood pressure ≥ 90 mm Hg, the blood pressure is considered to be elevated or high.[6]

Type 1 (hypoxemic) respiratory failure has a PaO_2 less than 60 mm Hg with normal or subnormal $PaCO_2$. In this type, the gas exchange is impaired at alveolo-capillary membrane level.[7]

Statistical Analysis

Kolmogorov-Smirnov test was used to check normality of continuous data. Continuous variables were expressed as Mean (standard error of the mean, SEM) or median (interquartile range, IQR) for normal and skewed data respectively. Non-parametric data was compared with the Mann-Whitney U test, and parametric data was compared with unpaired *t* test. Categorical variables were stated as number (%) and compared by Fisher's exact test/χ^2 test between middle age and older age COVID-19 patient groups. A *P* value of < 0.05 was considered statistically significant. Statistical analysis was done using the SAS software, version 9.4.

Results

Clinical and Biochemical Characteristics of Study Population

A total of 110 confirmed COVID-19 patients were hospitalized and died at our centre during April 2020. The study population was further divided according to the age into (1) young adult (18-35 years), (2) middle age adults (36-55 years), and (3) older age adults (> 55 years). Age and gender distribution of the study population has been presented in Figure 1 (age and gender distribution of the participants).

Out of 110 participants, 5 (4.5%) were in the young adult group, 44 (40%) were in the middle-aged group, and 61 (55.5%) were in older aged group. No children or adolescents were present in our study. We further compared clinical features and biochemical parameters between the middle age and older age groups. The young age group comprised of a very low number (n = 5) of patients and could not be analysed for clinical and biochemical parameters.

The median age of the patients who died due to COVID-19 infection was 57.0 years, including a higher percentage of men (67.3%) compared to women (32.7%). Diabetes (43.6%) and hypertension (40.9%) were the most common comorbidities present in nearly half of the study population. Details of demographic characteristic, comorbidities and sign and symptoms in patients are presented in Table 1. The most common symptoms observed at the time of admission were breathlessness (93 [84.5%] of 110 patients), fever (75 [68.1%]), and cough (65 [59%]). Less common symptoms were altered sensorium (13 [11.8%]), chest pain (8 [7.3%]), diarrhoea (8 [7.3%]), and vomiting (5 (4.5%]). Type 1 respiratory failure was the cause of death in (100 [90.9%]) of the patients.

The median time from the onset of illness to first hospital admission was 3.0 (IQR: 2.0-5.0) days. The median time from first hospital admission to death

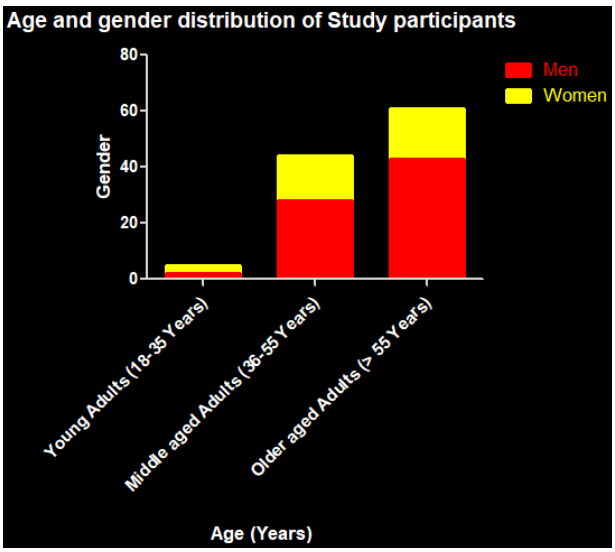

Figure 1. Age and Gender Distribution of the Participants.

Table 1. Baseline Demographic and Clinical Characteristics of Study Population

Characteristics	Total Patients (N = 110)	Middle Age Adults (36-55 years) (n = 44)	Older Adults (>55 years) (n = 61)	*P* Value of gender
Age (y), Median (IQR)	57.0 (48.7-65.0)	49.0 (45.0-51.7)	64.0 (60.0-71.0)	<0.0001[a]
Gender, No. (%)				
Men	74 (67.3)	28 (63.6)	43 (70.5)	
Women	36 (32.7)	16 (36.4)	18 (29.5)	
Any comorbidity, No. (%)				
Hypertension	48 (43.6)	14 (31.8)	34 (55.7)	0.01[b]
Diabetes mellitus	45 (40.9)	15 (34.0)	30 (49.2)	0.12 [ns]
DM and HTN both	26 (23.6)	5 (11.3)	22 (36.0)	0.004[a]
Chronic kidney disease	8 (7.3)	6 (13.6)	2 (3.3)	0.06 [ns]
Tuberculosis	3 (2.7)	2 (4.5)	1 (1.6)	0.57 [ns]
IHD	10 (9.0)	2 (4.5)	8 (13.1)	0.18 [ns]
CVD	2 (1.8)	0 (0.0)	2 (3.3)	0.50 [ns]
Hypothyroidism	3 (2.7)	2 (4.5)	1 (1.6)	0.57 [ns]
Liver diseases (Jaundice/alcoholic liver disease/ hepatic encephalopathy)	3 (2.7)	1 (2.3)	1 (1.6)	1.0 [ns]
No comorbidity	29 (26.3)	10 (22.7)	17 (27.8)	0.65 [ns]
Signs and symptoms, No. (%)				
Breathlessness	93 (84.5)	38 (86.3)	50 (81.9)	0.60 [ns]
Fever	75 (68.1)	33 (75.0)	38 (62.2)	0.10 [ns]
Cough	65 (59.0)	28 (63.6)	33 54.0)	0.42 [ns]
Altered sensorium	13 (11.8)	5 (11.3)	8 (13.1)	1.0 [ns]
Chest pain	8 (7.3)	2 (4.5)	6 (9.8)	0.46 [ns]
Diarrhoea	8 (7.3)	3 (6.8)	5 (8.1)	1.0 [ns]
Vomiting	5 (4.5)	0 (0.0)	1 (1.6)	1.0 [ns]
Respiratory failure (type-1) as a cause of death	100 (90.9)	41 (93.1)	56 (91.8)	1.0 [ns]

Abbreviations: NS, not significant; IHD, Ischemic heart disease; CVD, cardiovascular disease; DM, diabetes mellitus; IQR, interquartile range.
[a] $P<0.001$; [b] $P<0.01$.

was also 3·0 days (IQR: 2.0-5.0). The blood counts of 49 (44.5%) patients showed leucocytosis, and 6 (5.4%) patients had leukopenia (white blood cell count less than 4 × 10^9/L) while 32 (29.0%) patients had thrombocytopenia (platelet count < 150 × 10^9/L). Low Hb levels (< 12.0 g/dL) were observed in 50% of patients.

At the time of admission, 63 (57.3%) of 110 patients were severely hypoxic (O_2 saturation < 85%), and 43 (39.1%) were hypoxic (O_2 saturation 85%-94%). Acid-base imbalance was also present in patients as pCO_2 (30.1 [IQR 24.0-36.6]) and pO_2 (55.3 [IQR 4.8-77.9]) levels were lower compared to the normal ranges (Table 2).

Comparison of Clinical and Biochemical Characteristics Between Middle-Aged and Older-Aged Groups

Clinical and biochemical variables were compared between the middle-aged and older-aged groups. Hypertension was significantly prevalent in older-aged group compared to the middle-aged group ($P<0.01$). Patients with both diabetes and hypertension were significantly higher in older-aged group compared to the middle-aged group (($P<0.001$). No significant difference could be observed in signs and symptoms and any biochemical parameters between these groups (Tables 1 and 2).

Median time from the illness onset to the first hospital admission was 4.0 days in the middle-aged group and 3.0 days in the older-aged group. Median time from the first hospital admission to death was also 3.0 days in middle-aged and older-aged patients. Duration from the onset of illness to the first hospital admission and to death in middle-aged and older-aged groups is presented in Figure 2 (Days from the onset of illness to the first hospital admission and from hospitalization to death in middle-aged and older-aged patients with COVID-19 disease).

Discussion

The outcome and sternness of COVID-19 primarily depends on the patient's age and comorbidities. COVID-19 is most expected to be fatal to elders with pre-existing health related disorders. In our study we reported the features of confirmed COVID-19 positive patients who died at our centre. We also explored middle-

Table 2. Laboratory Findings of COVID-19 Positive Patients on Admission to Hospital

Characteristics	Total Patients (N = 110) Median (IQR)	Middle Age Adults (36-5.5 Years) (n = 44) Median (IQR)	Older Adults (>55 Years) (n = 61) Median (IQR)	*P* Value
White blood cell count, × 10^9/L (normal range- 4.0-10.0 × 10^9/L), No. (%)	9.4 (7.0-13.8)	9.7 (7.1-13.6)	9.3 (7.0-13.6)	0.81^{ns}
<4 Leucopenia	6 (5.4%)	3 (6.8%)	3 (4.9%)	-
4-10 Normal	55 (50%)	21 (47.7%)	32 (52.4%)	-
>10 Leukocytosis	49 (44.5%)	20 (45.4%)	26 (42.6%)	-
Hemoglobin,[a] (g/L)	11.6±2.3	11.43±0.36	11.92±0.27	0.27^{ns}
<12.0 (g/L), No. (%)	55 (50%)	25 (56.8%)	27 (44.3%)	-
Platelet count × 10^9/L (Normal range- 150-400 10^9/L)	190 (140-240)	180 (125-220)	200 (140-260)	0.32^{ns}
<150 × 10^9/L Thrombocytopenia	32 (29.0%)	13 (29.5%)	16 (26.2%)	-
Oxygen saturation (%)	78.5 (63.5-91.0)	77.5 (63.0-90.0)	77.0 (60.0-91.0)	0.98 ^{ns}
Normal≥95%	1 (0.9%)	1 (2.2%)	0 (0.0%)	-
Hypoxic 85%-94%	43 (39.1%)	17 (38.6%)	24 (39.3%)	-
Severely hypoxic<85%	63 (57.3%)	26 (59.0)	37 (60.6%)	-
pCO2 mm Hg, Normal range (35-45 mm Hg)	30.1 (24.0-36.6)	32.0 (26.0-37.5)	29.5 (24.0-36.6)	0.40^{ns}
pO2 mm Hg, Normal range (70-100 mm Hg)	55.3 (40.8-77.9)	55.0 (42.0-72.0)	55.8 (38.7-77.9)	0.87^{ns}
pH Normal range (7.35-7.45)	7.35 (7.30-7.42)	7.35 (7.26-7.42)	7.35 (7.30-7.42)	0.16^{ns}
Days from illness onset to hospital admission	3 (2-5)	4 (2-7)	3 (2-5)	0.28^{ns}
Days from first hospital admission to death	3 (2-5)	3 (2-4)	3 (1-5)	0.93^{ns}

Abbreviations: NS, not significant; IQR, interquartile range.
[a]For Hemoglobin, data is presented as mean and SEM.

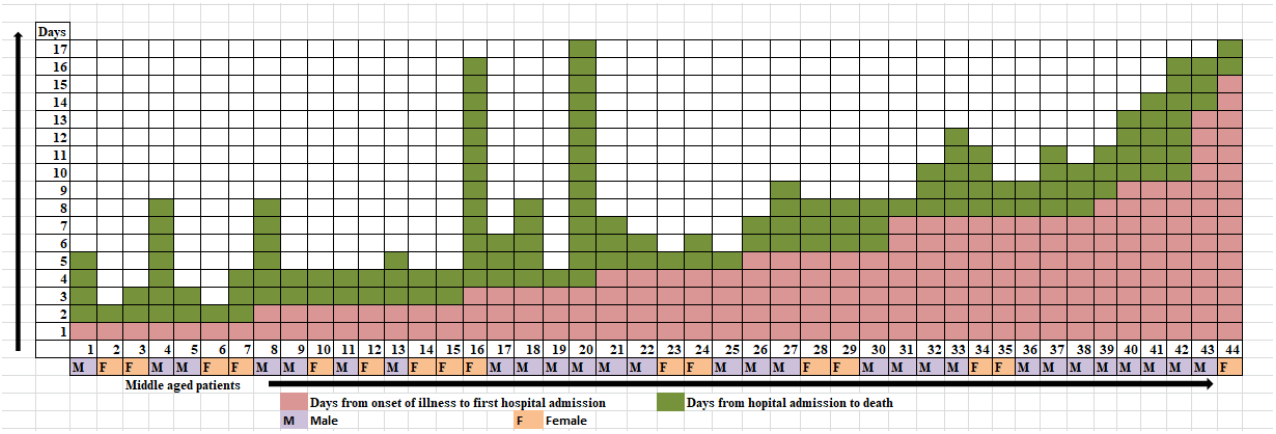

Figure 2. Days From the Onset of Illness to the First Hospital Admission and From Hospitalization to Death in Middle-Aged and Older-Aged Patients With COVID-19 Disease.

aged and older-aged patients' vulnerability to COVID-19 associated complications in terms of different clinical and demographic features.

In our study, it was observed that out of 110 deceased COVID-19 positive patients, 55% were of older age, and 40% were middle-aged, showing that older patients were highly prone to the COVID-19 infection and mortality than younger and middle-aged patients. Young patients' low mortality rate (4.5%) can be elucidated by strong viral alter signals in young individuals. Immune system is activated by binding of the SARS-CoV-2 virus to ACE2 enzymes of upper respiratory epithelial cells. The virus entry into alveolar pneumocytes stimulates alveolar macrophages to release cytokines, T cells activation, and lymphocytes' activation to prevent the infection.

The exact cause for more fatal SARS-CoV-2 infections in the elderly is not identified, but various theories are suggested that comprise alterations to the NAD+ levels, immune cell repertoire, the epigenome, inflammatory activity and progressive age.[8] Slow initial viral alert signals

with faulty macrophages and T cells function causes spread of infection. This specifies towards cytokine storm (increased inflammatory cytokine signalling) which causes hypoxia, coagulopathy, and microvasculature clotting and organ failure.[8] Age related changes in lung anatomy and muscle atrophy in older individuals may also lead to altered respiratory system function. Similarities had been noted in age groups affected by COVID-19 and earlier beta coronavirus infections. Liu et al observed that aged patients were more diseased by earlier MERS-CoV and SARS-CoV.[9]

In our study 67.3% were men and 32.7% were women. In both middle aged and older aged groups, percent of men were higher compared to women. It shows that mortality rate was higher in male.[10] According to Zirui et al on the location of *ACE2* on X-chromosome, there may be alleles that provide resistance to COVID-19 which explains the lesser mortality among females. Additionally, estrogen increases the immunity while testosterone has an immunosuppressive effect. So, the disease severity may differ due to the hormonal immune regulation effect.[11,12]

Common co-morbidities present in our study were diabetes mellitus and hypertension. Elder patients had higher rate of hypertension compared to middle aged patients. Huang et al also reported hypertension as the commonest co-morbidity present in COVID-19.[13] It might be due to SARS-CoV infection mediated inflammation and immune dysregulation that could help to explain the increased risk of cardiovascular diseases.[14] Garbati et al stated that apart from circulatory diseases, diabetes was the other common comorbidity in patients with COVID-19.[15] There are certain co-morbidities which often coexist like diabetes and hypertension. In this study, coexisting co-morbidities diabetes and hypertension were significantly higher in the group with elderly individuals than middle aged group. In these patients with two or more comorbidities, the risk of poor prognosis was higher compared with patients who had no or any one comorbidity.[3]

Breathlessness, fever and dry cough were the most common symptoms of COVID-19 in our study. Total 57.3% patients were severely hypoxic and 39.1% were hypoxic at the time of admission. There was no significant difference between middle aged and older aged group in term of frequency of symptoms. Type 1 respiratory failure was the most common cause of death in both the groups. Chopra et al found shortness in breath, fever and cough as the common symptoms in COVID-19 elder patients.[11] Reuters in his report has explained that the damage triggered by the corona virus to the red blood cells membranes that transport oxygen is the reason why many COVID-19 patients have drastically low oxygen levels by Hospimedica International staff writers posted on July 8 2020.[16] Low median levels of pCO_2 and pO_2 in both groups indicates towards hypocapnia and hypoxia. Our findings were similar to the findings by Wang et al who on clinical examination of severe cases of COVID-19 observed a decreased arterial oxygen partial pressure to fractional inspired oxygen ratio with associated tachypnea and hypoxia and low CO2 (34 mm Hg) levels in COVID-19.

In this study 50% patients had anemia and 44.5% patients were having leucocytosis. Thrombocytopenia was present in 29.0% patients at the time of admission which indicates towards the disease severity at the time of admission. No significant difference between older and middle-aged group for these parameters shows that hemocytometric parameters were equally altered in both groups. Some studies reported lower concentrations of Hb of elderly patients in 41%–50% of cases upon admission. In another study, Zheng et al found that Hb level decreased with disease progression.[17,18] Khartabil et al observed lymphopenia as a consistent finding, and neutrophils had the tendency to rise with disease progression; and their surge might be provoked by bacterial co-infections and medications like corticosteroids.[16] Low platelet count was identified as a prognostic factor in several smaller studies on adults and the aged. Xu et al observed that in older patients (>60 years) who had lymphopenia, thrombocytopenia, and more systemic symptoms, these factors were linked with disease severity and mortality.[19]

The median duration from illness onset to first hospital admission and from first hospital admission to death was 3 days. Similar trend was observed in both the groups which indicate towards poor prognosis. Feng et al found that mean interval between hospitalization and death was 17.5 days (range: 4–21 days).[20]

Limitations

This study could not compare clinico-demographic features of young adults with middle aged or older aged group because of low count of patients in young adult group. We used clinical and biochemical data procured at the time of admission, detailed day wise data from hospital admission till death of patients may give more detailed insight about patient's clinical condition.

Conclusion

The clinico-demographic features and prognosis of the disease vary among patients of different ages. In our study both the middle age and older age deceased patients showed similar clinical manifestations. A meticulous assessment of age may help physicians worldwide to establish risk stratification for all COVID-19 patients. Considering the contagious nature of COVID-19 disease, there is an urgent need to identify and monitor the high-risk populations. Unlike many other studies our study found that along with elderly patients the middle-aged patients are also at high risk hence close monitoring and early therapeutic intervention in both the age groups may contribute in better prognosis.

Authors' Contribution

AC, SK, SM and MB formulated the hypothesis. SK and MB collected data. SM analysed the data. SM and SK prepared manuscript. MB and AC reviewed the manuscript.

Competing Interests

None.

Ethical Approval

The study was approved by Institutional Ethics Committee (IEC-II/OUT/459/2020).

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