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Gender Specific Difference and Clinical Spectrum of COVID-19 Patients Admitted in Tertiary Care Hospital of Northern India

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ABSTRACT

Objectives: In a tertiary care hospital in Northern India, we examined the demographic, biochemical, and clinical risk factors related to gender differences in COVID-19 patients who were hospitalized.

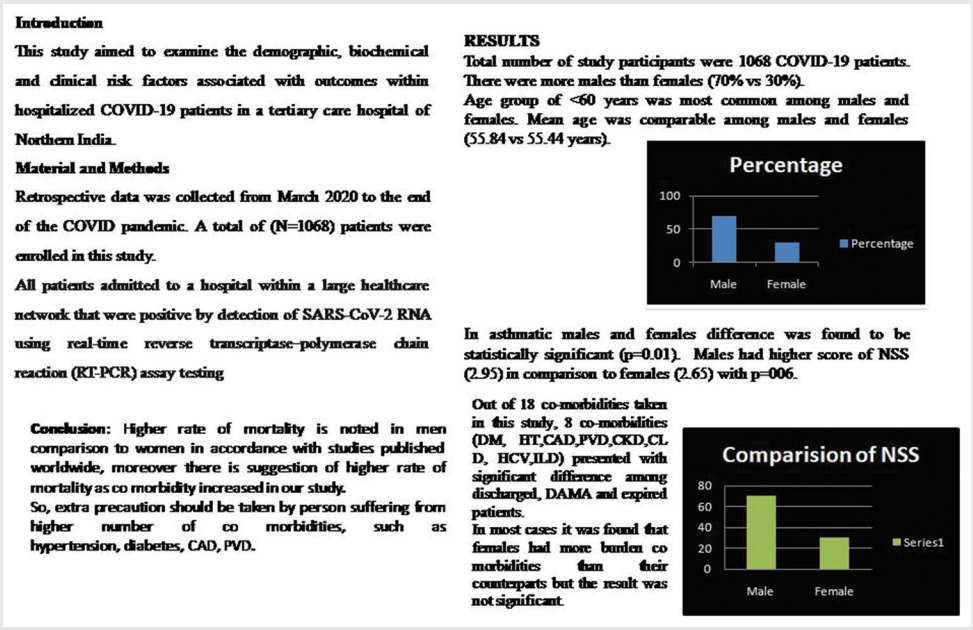
Materials and Methods: The study was carried out in a hospital with tertiary care. In this retrospective comparative observational study the data was collected from march 2020 to end of COVID pandemic. Analyses were done on the $n = 1068$ individuals who were hospitalized during the study period.

Results: There were 1068 individuals evaluated in the trial, with a male-to-female ratio of 2.3:1. Males and females had similar mean ages (55.84 vs. 55.44 years). Difference was found to be statistically significant in asthmatic boys and females ($P = 0.01$). In our study, a novel severity score (NSS) was utilized to forecast inpatient mortality in COVID-19 patients. NSS scores were higher for men (2.95) than for women (2.65), with $P = 006$. Under the categories "Expired," "discharged against medical advice (DAMA)," and "Discharged," all the criteria that have been previously analyzed were compared. Based on the number of comorbidities, there was a clear, significant difference between patients who were discharged, expired, and under DAMA, with a $P = 0.001$. Majority of patients with comorbidities that most frequently impacted the cardiovascular and respiratory outcomes.

Conclusion: Studies conducted globally found that men experienced a higher rate of mortality. Our study also indicates that when the number of comorbidities rises, the death rate rises. Therefore, individuals with a larger number of comorbidities, such as hypertension, diabetes, coronary artery disease, and peripheral vascular disease, should exercise particular vigilance.

Keywords: Coronavirus disease-19, Outpatients, Hospital

ABSTRACT IMAGE



INTRODUCTION

Since the start of the global coronavirus disease (COVID-19) pandemic in December 2019, every aspect of people's existence has been impacted. The World Health Organization designated the current coronavirus disease (Severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2] infection) a global pandemic on March 11, 2020. The first verified COVID-19 case and death occurred in India on January 27, 2020, and March 12, 2020, respectively. For health-care professionals looking to better patient outcomes, it is critical to comprehend how COVID-19 evolves among hospitalized patients. Estimates of the mortality rates among COVID-19 patients are especially crucial for monitoring the caliber and efficacy of hospital care. Men with the 2019 novel COVID-19 have a more severe illness and a greater mortality rate than women.

According to reports from China, males made up 60% of COVID-19 patients, and men died from the disease at a rate of 2.8% compared to 1.7% for women. In Italy, males accounted for 70% of the fatalities. These findings suggest that COVID-19 may have a gender component, with older males dying at higher rates and men more likely to be severely affected.[1-4] To comprehend the effects of this public health emergency on various people, families, and communities and to develop equitable and sustainable interventions, we also need to identify the phenotypical differences in severe case manifestations of COVID-19 in males and women. This study aimed to examine the demographic, biochemical, and clinical risk factors associated with outcomes within hospitalized COVID-19 patients in a tertiary care hospital of Northern India.

MATERIALS AND METHODS

The study was carried out in a specialized care facility. Retrospective comparative observational research the (retrospective data March 2020 to the end of the COVID pandemic). Analyses were done on the $n = 1068$ patients who were hospitalized during the study time. The information was divided into categories A (females) and B (males) (males). With a male-to-female ratio of 2.3:1, $n = 320$ of these belonged to Group A (females), and $n = 748$ to Group B (males). All patients admitted to a hospital in a large healthcare network who tested positive for SARS-CoV-2 RNA using real-time reverse transcriptase-polymerase chain reaction (RT-PCR) assay testing, either carried out inside the hospital system or documented at an outside system before transfer, were considered to meet the inclusion criteria. The research excluded patients who were hospitalized but later found to be RT-PCR negative and RT-PCR positive patients treated as outpatients (home isolation).

Age, sex, and length of hospital stay were among the data examined. Comorbidities of all kinds, including diabetes, hypertension (HT), coronary artery disease (CAD), heart failure (HF), peripheral vascular disease (PVD), prosthetic valves, chronic kidney disease (CKD), renal disease, chronic

liver disease (CLD), hepatitis C virus (HCV), HIV, drug addiction, obesity, asthma, chronic obstructive pulmonary disease, interstitial lung disease (ILD), cancer, and hepatitis B surface antigen, were observed. Clinical parameters such as respiratory rate, sulfur dioxide (SO_2), mean blood pressure, systolic blood pressure, and diastolic blood pressure were recorded.

There were records of hematological variables such as international normalized ratio (INR), C-reactive protein (CRP), D-dimer, and blood urea nitrogen (BUN). In addition, the ultimate result for each patient – discharge or mortality – was established. The aforementioned factors were combined to create a COVID-19 severity value, which ranges from 0 to 10. The in-hospital mortality index was created using these inputs. The patient was discharged, expired, and discharged against medical advise as a result of his or her final hospital outcome (discharged against medical advice [DAMA]).

Range, mean, standard deviation (SD), frequencies (number of cases), and relative frequencies (percentages), as applicable, were used to characterize the data. Kolmogorov–Smirnov test was used to assess whether the data were normally distributed.

Using independent samples for parametric and non-parametric data, respectively, the Student *t*-test and Mann–Whitney U-test were used to compare quantitative variables between the research groups. Analysis of variance was used to compare quantitative variables between the research groups. Chi-square[2] and exact tests were used to compare categorical data when the anticipated frequency was <5. Statistical significance was defined as a chance value $P < 0.05$. The statistical program for Microsoft Windows (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) was used for all statistical computations.

RESULTS

Total number of study participants was 1068 COVID-19 patients. All of them were treated at DMC&H, Ludhiana, that is, tertiary level hospital, from which $n = 320$ belong to Group A (Female patients) and $n = 748$ were Group B (Males) with a male: female = 2.3:1. Among cohort of 1068 study subjects, 723 were discharged, 246 were deceased, and 78 were DAMA. In the present study, there were more males than females (70% vs. 30%). Age group of <60 years was most common among males and females. Mean age was comparable among males and females (55.84 ± years vs. 55.44 ± years). In asthmatic males and females, difference was found to be statistically significant ($P = 0.01$). A novel severity score (NSS) to predict inpatient mortality in COVID-19 patients was used in this study [Table 1].

NSS was graded into low-risk patients (0–3 points), moderate-risk patients (4–7 points), and high-risk patients (>7 points). Total six parameters were used to calculate NSS which include age group, BUN, CRP, INR, mean arterial pressure, and SO_2. Out of which INR, CRP, and BUN showed significant difference between males and females, INR ($P = 0.00$), CRP, and BUN ($P = 0.001$). Males had higher score of NSS (2.95) in comparison to females (2.65) with $P = 006$. Among deceased study, subjects mostly were males (72%).

All the parameters studied so far were compared under three headings, expired, DAMA, and discharged. There was no significant difference among discharged, expired, and DAMA patients on basis of gender. There was marked significant difference between discharged, expired, and DAMA patients on basis of no of comorbidities with $P = 0.001$, as shown in [Table 2].

Out of 18 comorbidities taken in this study, eight comorbidities (diabetes mellitus, HT, CAD, PVD, CKD, CLD, HCV, and ILD) presented with significant difference among discharged, DAMA, and expired patients, as given in [Table 3].

In most cases, it was found that females had more burden comorbidities than their counterparts, but the result was not significant.

DISCUSSION

A wide range of viruses known as the coronavirus family can cause illnesses such as the common cold, serious pneumonia, SARS,[2] and Middle east respiratory syndrome. Clinical and epidemiological characteristics of COVID-19 patients have recently been described. At our tertiary care facility, a retrospective comparative analysis of COVID-19 patients was

Table 1: Score factor of patients.

Scoring factors	Score assigned
Age	
≥60 years	1
≥70 years	2
≥80 years	3
Oxygen saturation	
≤94%	1
MAP	
≤80 mmHg	1
≤70 mmHg	2
≤60 mmHg	3
BUN	
>30 mg/dL	1
CRP	
>10 mg/dL	
INR	
>1.2	1
Total score	10

MAP: Mean arterial pressure, BUN: Blood urea nitrogen, CRP: C-reactive protein, INR: International normalized ratio

Table 2: Number of comorbidities.

Number of comorbidities	Discharge (*n*=723) (%)	Expired (*n*=246) (%)	DAMA (*n*=78) (%)	Total	*P*-value
0	292 (40)	64 (26)	24 (31)	380	0.0001
1	180 (25)	58 (24)	16 (21)	254	
2	198 (27)	64 (26)	27 (35)	289	
3	45 (6)	45 (18)	8 (10)	98	
4	8 (1)	12 (5)	3 (4)	23	
5	0 (0)	3 (1)	0 (0)	3	

DAMA: Discharged against medical advice

Table 3: Comparison of comorbidity.

Comorbidity	*P*-value
DM	0.001
HT	0.003
CAD	0.0001
HF	0.205
PVD	0.038
Prosthetic valve	0.653
CKD	0.0001
Renal Tx	0.051
CLD	0.0001
HCV	0.042
HBsAg	0.196
HIV	0.196
Drug addict	0.205
Obesity	0.272
COAD	0.099
Asthma	0.538
ILD	0.038

DM: Diabetes mellitus, HT: Hypertension, CAD: Coronary artery disease, HF: Heart failure, PVD: Peripheral vascular disease, CKD: Chronic kidney disease, CLD: Chronic liver disease, HCV: Hepatitis C virus, HBsAg: Hepatitis B surface antigen, HIV: Human immunodeficiency virus, COAD: Chronic obstructive pulmonary disease, ILD: Interstitial lung disease

conducted. Different variables for mortality and morbidity were compared between both genders. In addition, clinical parameters for DAMA, expired, and discharged patients were examined. To forecast inpatient mortality for patients who presented with SARS-Co-V-2 infection to hospital emergency rooms, we used a novel severity scoring method. In our research, a NSS with a ratio of 2.3:1 was used on 1068 subjects, 320 of whom were female and 748 of whom were male.

Patients from Groups A and B presented with comparable severity, we discovered. However, mortality rates were higher among men than women, which was consistent with numerous studies conducted around the globe. When comparing the numbers of comorbidities under discharged, expired, and DAMA, the study showed a huge disparity.

One of the first studies to look into how gender affects the morbidity and mortality of SARS-COV-2 transmission was conducted by Jin *et al*.[5] Men with COVID-19 are more likely to experience worse outcomes and pass away, regardless of age, according to this research, which compared the severity and mortality of male and female patients with COVID-19.

While there is no difference in the proportion of male and female patients with confirmed COVID-19, Gruijter *et al*.'s[6] meta-analysis of 3,111,714 COVID-19 patients found that male patients have nearly 3 times the odds of needing intensive treatment unit (ITU) admission (odds ratio [OR] = 2.84; 95% confidence interval [CI] = 2.06, 3.92) and higher odds of dying (OR = 1.39; 95% CI = 1.31, 1.47) compared to female patients. About 72% of the deceased study subjects in our study were discovered to be men.

Males, when compared to a matched cohort of females of a similar age, have a greater risk of mortality, hospitalization, and mechanical ventilation, according to Singh *et al*.[7]

This gender-based risk of poor outcomes is more evident in older patients with COVID-19. Men with COVID-19 infection have a >50% higher chance of all-cause death, severe COVID-19 infection, or ICU admission than women, according to Kragholm *et al*.[8] Age-adjusted relative mortality risk ratio for men in the Hong Kong SARS-CoV-1 epidemic was 1.62 (95% CI = 1.21, 2.16) [Table 1]. Male sex was linked to an odds ratio of 3.10 (95% CI = 1.64, 5.87; *P* = 0.001) for ITU admission or mortality during the same outbreak in Singapore.[9]

According to these findings, the substantial sex bias seen in the COVID-19 pandemic is likely caused by fundamental differences in the immune response between males and females, even though socioeconomic factors may be influencing some aspects of the pandemic.[5] There are differences in the expression of angiotensin-converting enzyme 2 (ACE2) receptors between the sexes, which promote the entry of the SARS-CoV-2 virus and human-to-human transmission. Because the ACE2 gene is situated on the X-chromosome and may be affected by estradiol, it may be able to avoid X-inactivation in females.[5] High protein expression of the ACE2 receptor in particular organs has previously been linked to specific organ failures, as shown by matching clinical parameters in SARS patients.

It has been demonstrated that patients with diabetes or cardiovascular diseases as well as males as compared to

women have higher levels of circulating ACE2.[10] The advantage of females in COVID-19 may be explained by sex variations in the innate and adaptive immune systems. Comparatively to men, females have more CD4+ T-cells, stronger CD8+ T-cell cytotoxic activity, and higher B-cell immunoglobulin production within the adaptive immune system. In a research by Elezkurtaj *et al*.,[10] clinical records revealed that respiratory insufficiency predominated in the majority of cases, but that sepsis, an infection-related condition, was the most common clinical cause of death.

In their research, the majority of patients who passed away had been identified with comorbidities that most frequently impacted the cardiovascular and respiratory systems: arterial HT, chronic kidney or heart disease, and chronic pulmonary disease.

In the current research, we used patient characteristics and clinical parameters gathered on the first day of hospital presentation to compute a preexisting novel scoring system that could aid in predicting the severity of COVID-19 infection.

The fact that our research was conducted in a tertiary hospital means that its findings cannot be generalized to the general population. The findings may be skewed toward higher mortality because the data were collected at the peak of the pandemic, when hospitals were under a lot of strain.

CONCLUSION

Our study, men presented with higher rate of mortality, according to studies compared worldwide. Our study also suggests, there is higher rate of mortality as number of comorbidities increase. Hence, extraprecaution should be taken by person suffering from higher number of comorbidities, such as HT, diabetes, CAD, and PVD.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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