Original Article

Gender Difference in Coronavirus Disease 2019 (COVID-19)

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Abstract

Introduction: In Bangladesh, males were more affected by Coronavirus Disease 2019 (COVID-19) than females. However, there is a paucity of data regarding gender-based differences in the outcomes of COVID-19 patients. Therefore, the objective of this study was to compare the demographic and clinical characteristics, as well as the in-hospital outcomes, of COVID-19–positive male and female patients.

Methods: This prospective observational study included all consecutive confirmed symptomatic and asymptomatic COVID-19 positive patients from March 8th, 2020, to July 7th, 2023, at the National Heart Foundation Hospital & Research Institute of Bangladesh. Baseline and clinical characteristics & in-hospital outcome of both genders were assessed for comparison.

Results: This study included a total of 2506 confirmed COVID-19 positive patients. Of them 1684 (67.2%) patients were male and 822 (32.8%) were female. Male were older (52.45 ±14.86 years vs 45.90 ± 17.33 years; p=0.001) than female and had more co-morbidities (p= 0.001) than female. Among healthcare personnel, 27.0% were female and 13.6% were male (p=0.001). Male had more risk factors and comorbidities than female: cardiovascular disease (81.1% vs 64.4%; p=0.001); hypertension (62.8% vs 50.0%; p=0.001); dyslipidemia (27.5% vs 20.9%; p=0.001) and obesity (35.0% vs 25.4%; p=0.001). Female were more symptomatic (73.7% vs 69.7%; p=0.03) than male. Cough, sore throat, abdominal symptoms, numbness and dizziness were significantly higher in female than male. Male had more severe form of COVID-19 disease {(moderate: 2.4% vs 1.9%; p=0.49), (severe: 6.8% vs 5.2%; p=0.13)}. Male were more hospitalized (44.4% vs 34.9%; p=0.009) than female and most of the female treated either in home isolation or in institutional isolation (65.1% vs 59.6%; p=0.008). Male had non-significantly higher mortality rate than female (4.2% vs 3.5%; p=0.4).

Conclusion: COVID-19 male was usually older, had more comorbidities, a higher probability of hospitalization, increased risk of moderate-severe COVID-19 and associated with non-significantly higher mortality rate as compared with female.

Key Ward: COVID-19, Gender, Demographics, Clinical features, In-hospital outcome

Introduction

During the 2003 Severe Acute Respiratory Syndrome (SARS) outbreak caused by the SARS-CoV-1 virus, studies found that women had a lower mortality risk compared to men [1]. Similarly, research on Middle East respiratory syndrome (MERS)-CoV showed that men were more frequently infected and had higher death rates than women [2]. Recent data on COVID-19 also indicate that males experience more severe disease outcomes and higher death rates than females [3–5]. In many Asian countries, men have been affected by COVID-19 more than women, with male-to-female infection ratios ranging from approximately 1.1 to 1.93:1 [6–9]. However, in European populations, the opposite trend has been observed, where females tend to be infected more, with a male-to-female ratio of about 0.47:1 [10,11]. While many developed nations report similar infection and death numbers across genders, several countries show a disproportionate burden among men [12]. For instance, men make up 88% of cases in Bahrain, 85% in Qatar, 75% in Saudi Arabia and South Sudan, 74% in Pakistan, and 71% in Bangladesh. Death rates in Chad, Bangladesh, Malawi, Qatar, and Pakistan also skew heavily male, with 74–80% of fatalities occurring in men. Conversely, countries such as Ukraine, Moldova, Poland, Latvia, Jamaica, Georgia, and Armenia report that females account for 55–60% of COVID-19 infections [12]. These gender differences in viral infection outcomes likely result from multiple factors, including variations in hormone

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levels, immune system responses, genes located on the X chromosome, genetic susceptibility, and societal influences related to gender roles [13–15]. Our study aimed to analyze the differences in demographic profiles, clinical features, and hospital outcomes between male and female patients diagnosed with COVID-19.

Materials and methods

This prospective observational study was carried out in the non-COVID tertiary cardiac care hospital (National Heart Foundation Hospital & Research Institute, Dhaka, Bangladesh) from March 08, 2020, to July 07, 2023. All admitted patients, who subsequently got diagnosed as COVID positive and health care personnel of this hospital, who become COVID positive were included in this study. Both symptomatic and asymptomatic patients were included in this study. The study was approved by the Ethics Review Committee of National Heart Foundation Hospital & Research Institute (N.H.F.H. & R.I./4-14/7/AD-1105) and written informed consent was obtained from all patients or patients' attendance.

Baseline variables, comorbidities, clinical presentation, treatment, and severity of COVID-19 were analysed. Baseline information included age, risk factors and co-morbidities (hypertension, diabetes mellitus, dyslipidemia, obesity, cardiovascular disease, chronic obstructive pulmonary disease /bronchial asthma (COPD/BA), chronic kidney disease). The degree of severity of COVID-19 was classified as mild, moderate, severe, and critical ill [16,17]. Participants were considered partially vaccinated (PV) if received one dose of vaccine, fully vaccinated (FV) if received two doses of vaccine and boosted if received three doses of vaccine.

Descriptive statistics were used to characterize the study population. Continuous variables are described using the mean and standard deviation (SD), and compared using unpaired student's 't' test. Discrete variables were expressed as frequency rates and percentage. Categorical variables between groups were compared using the chi-square test or Fisher's exact test. A p value <0.05 was considered statistically significant. All analyses were performed using SPSS statistical software version 16.0 (SPSS Inc., Chicago, IL, USA).

Results

During this period a total of 2506 patients were included. Of whom 1684 (67.2%) patients were male and 822 (32.8%) were female. Male were older (52.45 ±14.86years vs 45.90 ± 17.33 years; p=0.001) than female and had more co-morbidities (p= 0.001) than female. Among healthcare personnel, 27.0% were female and 13.6% were male (p=0.001). Male had more risk factors and comorbidities than female: cardiovascular disease (81.1% vs 64.4%; p=0.001); hypertension (62.8% vs 50.0%; p=0.001); dyslipidemia (27.5% vs 20.9%;p=0.001) and obesity

(35.0% vs 25.4%; p=0.001). Among male 29.2% were unvaccinated, 5.6% received PV, 24.2% FV, 13.1% booster dose. On the other hand, 30.0% female were unvaccinated, 11.2% received PV, 19.8% FV, 7.8% booster dose. Gender-specific baseline characteristics of COVID-19 patients are presented in Table 1. Most of the male had multiple comorbidities (Figure 1).

Table 1: Gender-specific baseline characteristics of COVID-19 patients (n-2506)

Variables	Male (n=1684)	Female (n=822)	p value
	Mean±SD/ f(%)	Mean±SD/f (%)	
Age (Mean±SD) year	52.45 ±14.86	45.90 ± 17.33	0.001#
Patient category			
HCP	229(13.6%)	222(27.0%)	0.001*
Non-HCP	1455(86.4%)	600(73.0%)	0.001*
Risk factors & comorbidities			
HTN	1057(62.8%)	411(50.0%)	0.001*
DM	690(41.0%)	313(38.1%)	0.16*
Dyslipidemia	463(27.5%)	172(20.9%)	0.001*
Cardiovascular disease	1366(81.1%)	529(64.4%)	0.001*
COPD/BA	93(5.5%)	46(5.6%)	0.94*
Obesity	590(35.0%)	209(25.4%)	0.001*
CKD	635(37.7%)	291(35.4%)	0.26*
Number of comorbidities			0.001*
<4	862(51.2%)	558(67.9%)	
≥4	822(48.8%)	264(32.1%)	
Diagnosis			0.001*
COVID-19 only	287(17.0%)	262(31.9%)	
COVID-19 with heart Disease	1397(83.0%)	560(68.1%)	

COVID-19: coronavirus disease 2019; DM: diabetes mellitus; HCP: healthcare personnel; non-HCP: non-healthcare personnel; SD: standard deviation; HTN: hypertension; COPD: chronic obstructive pulmonary disease; BA: Bronchial asthma; CKD: chronic kidney disease. *Chi square test was done to find out the significance; #Student's 't' test was done to find out the significance.
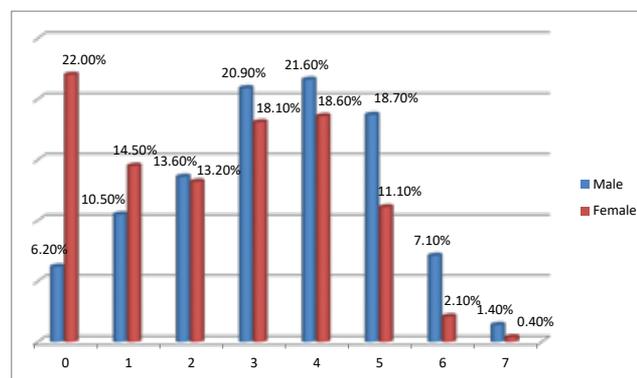

Figure 1: Bar diagram showing number of comorbidities among male and female with coronavirus disease 2019 (n=2506)

Female were more symptomatic (73.7% vs 69.7%; p=0.03) than male. Prolonged duration of symptoms was observed among female patients (3.6 ± 4.4 days vs 3.2 ± 3.6 days). Cough (38.3% vs 32.2%; p=0.003), sore throat (13.3% vs 5.9%; p=0.001), diarrhea (5.6% vs 2.8%; 0.001), anosmia (13.3% vs 5.3%; p=0.001), fatigue (33.5% vs 25.5%; p=0.001), headache (18.4% vs 11.0%; p=0.001), body-ache

(26.0% vs 17.3%; p=0.001), anorexia (16.1% vs 8.2%; p=0.001), nausea (7.2% vs 2.6%; p=0.001), vomiting (8.0% vs 2.2%; p=0.001), abdominal pain (3.5% vs 1.3%; p=0.001), numbness (3.5% vs 1.4%; p=0.001) and dizziness (13.5% vs 8.9%; p=0.001) were significantly higher in female than male. Gender-specific clinical presentations of COVID-19 patients are outlined further in Table 2.

Table 2: Gender-specific clinical presentation of coronavirus disease 2019 patients (n=2506)

Variables	Male (n=1684) f(%)	Female(n=822) f(%)	p value*
Clinical presentation			
Symptomatic	1174(69.7%)	606(73.7%)	0.03
Asymptomatic	510(30.3%)	216(26.3%)	
Duration of symptoms (Mean±SD) days	3.2±3.6	3.6±4.4	0.009
Fever	849(50.4%)	436(53.0%)	0.21
Cough	543(32.2%)	315(38.3%)	0.003
Sore throat	100(5.9%)	109(13.3%)	0.001
Shortness of breath	619(36.8%)	290(35.3%)	0.47
Diarrhea	47(2.8%)	46(5.6%)	0.001
Anosmia	89(5.3%)	109(13.3%)	0.001
Fatigue	430(25.5%)	275(33.5%)	0.001
Headache	185(11.0%)	151(18.4%)	0.001
Body-ache	292(17.3%)	214(26.0%)	0.001
Anorexia	138(8.2%)	132(16.1%)	0.001
Nausea	44(2.6%)	59(7.2%)	0.001
Vomiting	37(2.2%)	66(8.0%)	0.001
Abdominal pain	22(1.3%)	29(3.5%)	0.001
Numbness	23(1.4%)	29(3.5%)	0.001
Dizziness	150(8.9%)	111(13.5%)	0.001
Generalized itching	37(2.2%)	25(3.0%)	0.2

COVID-19: *Chi square test was done to find out the significance.

Patients were treated either in hospital or in isolation. Oxygen therapy (low flow, high flow) was given when required. Prone positioning was advised for all patients. Treatment outline is given in Table 3. Ivermectin received 35.2% male and 35.2% female. Three male (0.2%) and one female (0.1%) received hydroxy-chloroquine. Only 33 (2.0%) male& 12 (1.5%) female received favipiravir. Only few males and female required remdesivir (4.3% vs 4.7%; p=0.64).

Table 3: Gender-specific distribution of treatment of COVID-19 patients (n=2506)

Variables	Male (n=1684) f (%)	Female (n=822) f (%)	p value*
Antibiotics			
IV	499 (29.6%)	224 (27.3%)	0.001
Oral + IV	78 (4.6%)	29 (3.5%)	
Oral	480 (28.5%)	306 (37.2%)	
Not received	627 (37.2%)	263 (32.0%)	
Antibiotics			
Single	809 (48.0%)	449 (54.6%)	0.008
Double	248 (14.8%)	110 (13.4%)	
Not received	627(37.2%)	263 (32.0%)	
Steroids	90(5.3%)	47(5.7%)	0.7
Favipiravir	33(2.0%)	12 (1.5%)	0.37
Remdesivir	73(4.3%)	39(4.7%)	0.64
Ivermectin	593 (35.2%)	311(37.8%)	0.2
Hydroxy-chloroquine	3(0.2%)	1(0.1%)	0.73
Enoxaparine	1337 (79.4%)	503 (61.2%)	0.001
Rivaroxaban	1346 (79.9%)	507 (61.7%)	0.001

COVID-19: coronavirus disease 2019; IV: intravenous. *Chi square test was done to find out the significance.

Regarding antibiotic therapy, 809 (48.0%) male & 449 (54.6%) female were treated with a single antibiotic, and 248 (14.7%) male& 110 (13.4%) female were given double antibiotic therapy (p=0.008). The antibiotics used generally covered common pathogens. The antibiotics used were doxycycline, azythromycin, cephalosporins, fluoroquinolones, carbapenems and β-lactamase inhibitors. Intravenous (IV) antibiotic therapy (29.6% vs 27.3%) and double antibiotics (14.8% vs 13.4%) were given more in male patients. Most of the patients received either ivermectin plus azithromycin or ivermectin plus doxycycline combination. The duration of antibiotic treatment was 5–10 days. Steroid therapy with methylprednisolone and dexamethasone for 3–7 days was received only few males and female (5.7% vs 5.3%; p=0.7). Low molecular weight heparin was used more in male than female (79.4% vs 61.2%; p=0.001) followed by rivaroxaban (10 mg once daily for 1 month). We administered vitamin C, vitamin D3 and zinc to most of the patients.

Male were more hospitalized (44.4% vs 34.9%; p=0.009) than female and most of the female treated either in home isolation or in institutional isolation (65.1% vs 59.6%; p=0.008). In male patients- mild disease was 59.9% (1009), moderate disease was 2.4% (40); severe disease was 6.8% (114) and critical ill was 0.7% (11). In female patients-mild disease was 65.6% (539), moderate disease was 1.9% (16); severe disease was 5.2% (43) and critical ill was 1.0% (8) (Table 4). Male had non-significantly higher mortality rate than female (4.2% vs 3.5%; p=0.4).

Table 4: Gender-specific in-hospital outcome of COVID-19 patients (n=2506)

Variables	Male (n=1684) f (%)	Female (n=822) f (%)	p value*
Hospitalization	680 (44.4%)	287 (34.9%)	0.009
Home isolation	1004 (59.6%)	535 (65.1%)	0.008
Disease severity			
Asymptomatic	510(30.3%)	216(26.3%)	0.038
Mild	1009(59.9%)	539(65.6%)	0.006
Moderate	40(2.4%)	16(1.9%)	0.49
Severe	114(6.8%)	43(5.2%)	0.13
Critical ill	11(0.7%)	8(1.0%)	0.38
Mortality	71 (4.2%)	29 (3.5%)	0.4

COVID-19: coronavirus disease 2019. *Chi square test was done to find out the significance.

Discussion

Key findings from our study include: (1) Females were underrepresented among COVID-19 patients compared to males (2) Male patients were generally older and had a higher prevalence of comorbid conditions (3) Female patients exhibited a greater number of clinical symptoms than their male counterparts (4) Males experienced more severe disease and had higher hospitalization rates and (5) Although mortality was slightly higher among males, the difference was not statistically significant.

In our cohort, men accounted for 67.2% of cases. Early reports from China suggested a predominance of male COVID-19 patients, yet more recent data from other regions indicate that females may sometimes have higher infection rates. For example, the Korean Society of Infectious Diseases reported that among 4,212 confirmed cases, 37.7% were male and 62.3% female [18]. This contrasts with data from China, where males constituted approximately 51% of COVID-19 cases [18]. An Italian study with 783 patients found a male-to-female ratio of about 2.1:1, indicating greater male involvement [19]. Similarly, Sha et al. observed 72.4% male cases [20], and Raimondi et al. reported 55.7% males [21]. In contrast, Su et al. found a slight female predominance, with a male-to-female ratio of roughly 0.87:1 (53% males vs. 47% females) [22].

Our study revealed that males were significantly older, with a mean age of 52.45 ±14.86 years compared to 45.90 ±17.33 years in females and also had more comorbidities. However, other studies did not find significant gender differences in age or comorbidity burden [20-23]. For instance, one study reported a median age of 58 years with no difference between genders (56 years for males vs. 59 years for females) [20]. An Italian study noted an average age of 67.6 years and no significant difference between sexes (67.0 vs. 67.8 years) [21]. Su et al. [22] found the mean age to be 38.6 years without gender variation (39.3 vs. 37.9 years) and Taiwanese public surveillance data showed similar median ages for males and females (59 vs. 63 years) with comparable comorbidity rates [23].

In our study, female was more symptomatic and had prolonged duration of symptoms. Symptoms such as cough, sore throat, diarrhea, loss of smell, fatigue, headache, muscle aches, anorexia, nausea, vomiting, abdominal pain, numbness, and dizziness were more frequent among females. Conversely, Su et al. [22] found no significant gender difference in symptom presentation, including cough, fever, sore throat, malaise, and anosmia, a finding echoed by Jin et al. [23]. Sha et al. [20] reported a higher incidence of fever in males (90.4% vs. 82.0%), while Raimondi et al. observed more gastrointestinal symptoms in females (24.6% vs. 15.7%) [21]. One possible explanation for increased gastrointestinal symptoms in females is a higher expression of ACE2 receptors in the transverse colon [21].

Regarding disease severity, more males required hospitalization (44.4% vs. 34.9%; p=0.009), while a greater proportion of females had mild illness (65.6% vs. 59.9%; p=0.006). Males had a higher likelihood of developing moderate to severe COVID-19. This gender difference in disease severity may be influenced by factors such as viral entry mechanisms, immune and inflammatory responses, and endothelial or vascular function [21]. Although Sha et al. [20] did not find a statistically significant difference in severity, severe cases were more common in men (24.3% vs. 19.1%). Jin et al. [23] similarly reported males tending toward more severe disease presentations (p=0.035).

Mortality in our cohort was slightly higher among males (4.2% vs. 3.5%), but this difference lacked statistical significance (p=0.4). Other studies, however, have demonstrated a significant gender disparity in death rates [20-23]. For example, Sha et al. [20] reported a lower fatality rate in females compared to males (4.4% vs. 10.0%; p=0.031). Multivariate analysis linked increased mortality to age, male sex, and comorbidities [20]. An Italian study observed higher 28-day mortality in men (38.1% vs. 26.1%; p=0.018), though gender was not an independent predictor once disease severity was accounted for [21]. Taiwan's surveillance data revealed that male COVID-19 patients had a 6.4 times higher mortality rate than females (3.2% vs. 0.5%, p<0.05) and accounted for 2.4 times more deaths (70.3% vs. 29.7%, p=0.016) [23]. Despite similar infection rates, men face worse outcomes and higher mortality independent of age [23]. Underlying biological and genetic factors, including differences in immune response and hormonal influences, are believed to contribute to this gender disparity [24]. A meta-analysis of over three million cases globally further confirmed that, although infection rates are similar between sexes, men are nearly three times more likely to require intensive care and have increased odds of death compared to women [25].

Limitation
Our study has a few important limitations. First, it was carried out in a cardiac hospital that was not exclusively dedicated to COVID-19 care. Second, the study included asymptomatic patients, which might have influenced the findings. Third, a large proportion of the male participants had underlying coronary artery disease, potentially affecting outcomes. Finally, we did not assess biological factors such as hormonal status and immune function, nor did we evaluate gender-related influences like lifestyle habits and socioeconomic conditions.

Conclusion
Male COVID-19 patients were generally older, had a greater burden of comorbid conditions, faced a higher likelihood of hospitalization, and were at increased risk of developing moderate to severe disease. Although mortality rates were higher among males, the difference compared to females was not statistically significant.

Acknowledgement

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