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Gender differences among hospitalized COVID-19 patients

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ABSTRACT

Background: A growing body of evidence indicates gender difference in the severity of COVID-19.
Objectives: The aim of the present study is to highlight gender difference regarding symptoms, laboratory investigations, complications, and outcome parameters of COVID-19 in admitted cases during the first wave of the disease.
Methods: A cross sectional retrospective descriptive epidemiological approach was carried out using electronic patients' records review.
Results: One thousand and one hundred fifty males (77.6%) and 332 females (22.4%) cases for COVOD-19 were subjected to the final analysis. The proportions of general body ache, loss of smell and sore throat were significantly higher among females (13.9%, 2.7% and 15.7%) than males (9.9%, 0.3% and 11.0%), whereas shortness of breath was significantly higher in males than females. A significantly higher proportion of women were more likely to suffer from low ferritin level than men, whereas men were more likely to suffer from a low lymphocytic count. Also, a higher proportion of males suffered from high levels of creatinine than females. No significant difference between males and females regarding COVID-19 complications except for respiratory complications that were more significantly encountered among males than females. Not only more males (11.9%) tended to use oxygen therapy than females (7.2%) but they used it through nasal masks (54% compared with 29.2%) and at a higher flow rate (26.3% compared with 8.3% at a flow rate more than 10 L/min). A higher percentage of male cases then females required to be admitted to the ICU significantly ($p < 0.001$) as 9.7% of males needed care in the intensive care units (ICU) compared with only 3.3% of females.
Conclusions: There is a difference of COVID-19 presentation, severity, and hospitalization, between men and women. Overall, this renders males to be at a higher risk for severe forms of the COVID-19 disease especially with regard to respiratory complications.

INTRODUCTION:

Coronavirus disease (COVID-19) was first described in China in December 2019 as a severe form of acute respiratory syndrome, and since then has spread worldwide to be announced by the World Health Organization (WHO) in July 2020 as an out-of-control global pandemic. By May 2021, the number of confirmed infections reached over 169 million with more than 3.5 million deaths reported to the WHO.(1) COVID-19 virus is one of the seven coronaviruses that cause infections in humans, it became an epidemic in a brief period and had a considerable impact on a global scale.(2) Whenever a new infectious disease emerges, knowledge regarding clinical features, diagnostic tools and treatment options is critical.(3) A growing body of evidence indicates gender difference in the clinical outcomes of COVID-19.(4, 5)

Men are consistently over-represented in COVID-19 severe outcomes, including higher fatality rates. There is a difference in the perceived symptoms between males and females where evidence suggested that female patients significantly experienced fatigue, anosmia, headache, sore throat, and nasal obstruction more than male patients. However, male patients significantly experienced other symptoms as cough and fever. (6) Apart from chronic medical conditions and old age (>65years), male gender was associated with more severe forms of the disease. Although the number of recorded confirmed cases is similar in males and females, however the mortality rate tends to be higher in males. (7) The severity of COVID-19, as measured by hospitalisation, admission to intensive care units, intubation for mechanical ventilation, and death, has consistently been 1.5 to 2 times greater for men than for women around the world.(8-10)

These differences are likely due to gender-specific behaviors, genetic and hormonal factors, and sex differences in biological pathways related to COVID-19 infection. Several social, behavioral, and comorbid factors are implicated in the generally worse outcomes in men compared with women. (11)

Essential for the success of clinical care is awareness by clinicians that the diseases they are treating, are characterised by differences between women and men in epidemiology, pathophysiology, clinical manifestations, psychological effects, progression, and response to treatment. (12) It is

important to identify the degree to which COVID-19 affects males and females differently to understand the disease consequences and explore the prognostic factors for individualized assessment. (11)

This study aimed at exploring gender difference perceived symptoms, laboratory investigations, complications, and outcome parameters of COVID-19 in admitted cases during the first wave of the disease.

SUBJECTS AND METHODS

Setting:

This study was conducted in Jaber Al-Ahmed hospital. The time interval of the study was set as four months from April to July 2021.

Study design:

A cross sectional retrospective descriptive epidemiological approach was carried out using electronic patients' records review, aiming at highlighting gender difference among hospitalized COVID-19 patients in Jaber hospital in Kuwait regarding personal characteristics, presenting manifestations, investigations, vital signs on admission, associated chronic diseases, COVID-19 complications, and outcome parameters.

Sampling:

A time sample (four months) was set for this study starting from February to May 2019. All admitted cases during this period were included in the study. This period was chosen as during that time all positive cases for COVID-19 (both Kuwaiti and non-Kuwaiti) across all health governorates were referred to this hospital. After this period, only Kuwaiti patients were admitted to this hospital.

Research tools:

A pre-designed structured questionnaire was designated for data collections. It included the following domains:

- Personal characteristics as age, gender, nationality, Smoking, weight, and height.
- Associated co-morbid conditions mainly hypertension, cardiovascular and respiratory diseases, diabetes, dyslipidemia, and endocrine insufficiency.
- Presenting symptoms mainly general, respiratory and gastrointestinal symptoms.
- Investigations and vital signs on admission as systolic blood pressure (SBP) (mmHg), diastolic blood pressure (DBP) (mmHg), heart rate (PPM), respiratory rate (BPM), blood oxygen saturation (SpO2) (%), D-Dimer (ng/mL), CRP (mg/L), LDH (IU/L), troponin (ng/L), ferritin (ng/mL), lymphocytic count, serum creatinine (µmol/L), blood sugar (mmol/L), glycated Hb (HbA1c) (mmol/mol).
- COVID-19 complications as respiratory, infection, and others complications
- Outcome parameters as oxygen therapy, duration of hospital stay, admission to the ICU, need of intensive ventilation and outcome on discharge

Normal blood oxygen level is defined as 95-100% when measured with a pulse oximeter. (13) Normal level of serum ferritin is considered as 20 to 250 ng/mL for adult males, and 10 to 120 ng/mL for adult females 18 to 39 years and 12 to 263 ng/mL for females 40 years and older. (14, 15) A normal level of serum creatinine is defined as 61.9 to 114.9 µmol/L for men and 53 to 97.2 µmol/L for women. (16)

All the necessary approvals for carrying out the research were obtained. The Ethical Committee of the Kuwaiti Ministry of Health approved the research. The permission of the Deputy Ministry of Health in Kuwait as well as head of Jaber hospital were obtained. The researchers were trained on skills required to carry this research efficiently in terms of how to review patient's medical record for abstracting the rquired data and to enter these data into the pre designed file. A pilot study was carried out on 20 cases.

Data management:

The data collected was logged in the google form directly. Daily revision of the completed data was routinely carried out. After completing data collection through google forms, this data was red on an Excel sheet that was in turn changed into an SPSS file (Statistical Package for Social Science, version 22) for the analysis.

Data cleaning was performed through checking possible mistakes by a serried range, minimum and maximum values as well as frequency distribution and cross tabulations to ensure that all questions had valid codes and values.

Categorical variables are presented as frequencies (number and percentages) and continuous variables as means (with SDs) or medians (with interquartile ranges [IQRs]). Simple descriptive statistics were used. Comparison between groups were performed using Chi square or Fisher' Exact tests for categorical data and student *t*-test or Wilcoxon rank sum test for qualitative variables.

RESULTS

Reviewing the medical records of the cases admitted to the selected hospital during the defined period resulted in inclusion of 1482 positive cases for COVID-19. One thousand and one hundred fifty males (77.6%) and 332 females (22.4%) were subjected to the final analysis.

Table 1 describes the gender differences regarding personal characteristics of the included

patients. The mean age of females (44.1±14.6) was insignificantly higher than that of males (43.0±14.6) (t = 1.82, P=0.07). Cases in the age group ≥ 60 years represented 18.7% of females and 11.6% of males. There was a significant difference between male and female cases regarding nationality (χ^2 = 194.0, P<0.001). Just less than half of male cases were Indian (46.0%) while 48.5% of female cases were Kuwaiti, whereas the least proportion were noticed in Bengali both in males (10.1%) and females (3.3%). The least governorates that presented in both males and females were Al-Jahra and Mubarak Al-Kabeer, while 31.6% of male cases were residents of Farwaniya and 27.1% of female cases were from Hawalli (χ^2 = 25.76, P<0.001). The BMI was significantly higher in females (29±6.3) than males (27.0±4.8), (t = 3.81, P<0.001). Smoking was rarely reported in both males and females, in spite being significantly more presented in males than females.

Table (1): Personal characteristics of male and female hospitalized COVID-19 patients

Variable	Males (n=1150)		Females (n=332)		Test of significance (p)
	No.	%	No.	%	
Age (years)					
<30	165	14.3	51	15.4	
30-39	351	30.5	96	28.9	
40-49	299	26.0	65	19.6	
50-59	202	17.6	58	17.5	
≥60	133	11.6	62	18.7	
Mean ± SD	43.0 ± 12.7		44.5±14.6		t = 1.82
Min - Max	19 – 94		19 – 85		P = 0.07
Nationality:					
Kuwaiti	197	17.1	161	48.5	χ^2=193.99
Indian	529	46.0	60	18.1	p<0.001
Egyptian	133	11.6	17	5.1	
Bengali	116	10.1	11	3.3	
Others	175	15.2	83	25.0	
Governorate					
Capital	283	25.1	74	22.5	χ^2=25.76
Hawalli	205	18.2	89	27.1	p<0.001
Farwaniyah	356	31.6	84	25.5	
Ahmadi	187	16.6	47	14.3	
Jahra	50	4.4	8	2.4	
Mubarak Alkabeer	46	4.1	27	8.2	
BMI:*					
Under-weight	4	1.0	2	1.5	
Normal	143	34.8	32	24.6	
Over-weight	183	44.5	44	33.8	
Obese	56	13.6	32	24.6	
Severe obese	25	6.1	20	15.4	
Mean ± SD	27.00 ± 4.78		29.00 ± 6.32		t = 3.81
Min - Max	16.18 – 59.86		18.42 – 52.62		p < 0.001
Smoking:**					
No	300	83.8	131	95.6	χ^2=12.30
Yes	58	16.2	6	4.4	p<0.001

*: missing 739 males and 202 females

**: missing 792 males and 195 females

Table 2 shows the frequency of chronic diseases among the studied patients. The proportions of diabetes mellitus, respiratory diseases and hypothyroidism were significantly higher in female than male cases (χ^2 = 10.01, P=0.002), (χ^2 = 24.19, P<0.001) and (χ^2 = 28.80, P<0.001) respectively. As shown in table 3, higher proportion of females (13.9%) complained from general body ache than males (9.9%) significantly (χ^2 = 4.16, P=0.04). Also, the proportions of loss of smell and sore throat were higher among females (2.7% and 15.7%) than males (0.3% and 11.0%) significantly (P< 0.001 and P = 0.02 respectively). Shortness of breath was significantly higher in males than females (11.3% versus 7.2%, P = 0.03).

Table (2): Frequency of chronic diseases among male and female hospitalized COVID-19 patients

Chronic diseases	Males (n=1150)		Females (n=332)		Test of significance (p)
	No.	%	No.	%	
Hypertension:	204	17.7	71	21.4	X^2=2.27 (P=0.15)
Cardiovascular	59	5.1	14	4.2	X^2=0.46 (P=0.57)
Dyslipidemia	25	2.2	7	2.1	X^2=0.01 (P=0.94)
Diabetes mellitus	172	15.0	74	22.3	X^2=10.01 (p=0.002)
Respiratory diseases	31	2.7	29	8.7	X^2=24.19 (p<0.001)
Renal diseases	22	1.9	10	3.0	X^2=1.47 (P=0.23)
Hypothyroidism	10	0.9	18	5.4	X^2=28.80 (p<0.001)
Immune suppression	2	0.2	2	0.6	Fisher's Exact (P=0.22)
Organ transplant	2	0.2	2	0.6	Fisher's Exact (P=0.22)
Others:	43	3.7	34	10.2	X^2=22.11 (p<0.001)

Table (3): Frequency of presenting manifestations of male and female hospitalized COVID-19 patients

Manifestations	Males (n=1150)		Females (n=332)		Test of significance (p)
	No.	%	No.	%	
General					
Fever	324	28.2	80	24.1	X^2=2.16 (P=0.14)
Headache	43	3.7	16	4.8	X^2=0.79 (P=0.28)
Body aches	114	9.9	4.6	13.9	X^2=4.16 (p=0.04)
Fatigue	16	1.4	7	2.1	X^2=0.87 (p=0.35)
Respiratory					
Cough	372	32.3	122	36.7	X^2=2.24 (p=0.13)
Blocked nose	9	0.8	2	0.6	Fisher's Exact (P=1.00)
Loss of smell	4	0.3	9	2.7	Fisher's Exact (P<0.001)
Sore throat	127	11.0	52	15.7	X^2=5.18 (p=0.02)
Chest pain	9	0.8	0	0.0	Fisher's Exact (P=0.22)
Shortness of breath	130	11.3	24	7.2	X^2=4.60 (p=0.03)
Gastrointestinal					
Loss of taste	8	0.7	7	2.1	Fisher's Exact (P=0.02)
Nausea	13	1.1	7	2.1	Fisher's Exact (P=0.18)
Vomiting	16	1.4	6	1.8	Fisher's Exact (P=0.61)
Diarrhea	34	3.0	15	4.5	X^2=1.97 (p=0.16)
Abdominal pain	4	0.3	3	0.9	Fisher's Exact (P=0.19)
Others	14	1.2	2	0.6	Fisher's Exact (P=0.55)

Table 4 presents the investigations and vital signs on admission among the studied case. The mean systolic blood pressure was significantly higher in males (127.8±15.9) than in females (124.1±17.2), (p < 0.001). Diastolic blood pressure showed the same pattern. However, no significant difference between both sexes regarding hypertension. Blood oxygen concentration was significantly lower in males than females. The median value of LDH was significantly higher in males than females (243 versus 217, P =0.04). The median level of ferritin in blood was higher in males than females significantly, p <0.001. However, the median

value of lymphocytic level was significantly higher in females than males (2.0 versus 1.7, p < 0.001). Significant higher percentage of males presented with high level of blood creatinine (7%) then females (3.9%), p = 0.04.

Table (4): Investigations and vital signs on admission among male and female hospitalized COVID-19 patients

Investigations and vital signs	Male		Female		Test of significance (p)
SBP (mmHg)					
Number	1150		332		*t* = 3.60
Min - Max	72 – 230		90 - 190		P < 0.001
Mean ± SD	127.8±15.9		124.1±17.2		
DBP (mmHg)					
Number	1150		332		*t* = 3.20
Min - Max	38 – 120		52 – 115		P =0.001
Mean ± SD	79.3±9.2		77.5±8.5		
Measuring blood pressure:					
Normal	950	826	280	84.3	χ^2=0.55
Hypertension	200	17.4	55	15.7	P=0.46
Heart rate (BPM)					
Number	1150		332		*t* = 0.99
Min - Max	47 – 140		58 – 128		P = 0.33
Mean ± SD	85.4±12.7		86.2±12.1		
Respiratory rate (BPM)					
Number	1150		332		*t* = 1.04
Min - Max	12 – 44		18 – 32		P = 0.30
Mean ± SD	21.1±2.4		20.9±1.7		
SpO2 (%)					
Number	1150		332		*t* = 2.32
Min - Max	71 – 100		92 – 100		P = 0.02
Mean ± SD	97.4±2.4		97.7±1.4		
SpO2 (%) level:					
<90	19	1.7	0	0.0	χ^2=7.18
90 -	4	4.2	9	2.7	P=0.03
≥95	1083	94.2	323	97.3	
D Dimer (ng/mL)					
Number	216		46		Mann-Whitney U
Median	274		255		P = 0.67
IQR	270		411		
CRP (mg/L)					
Number	843		162		Mann-Whitney U
Median	8		7		P = 10
IQR	37		15.3		
LDH (IU/L)					
Number	191		42		Mann-Whitney U
Median	243		217		P = 0.04
IQR	185.6		124.2		
Troponin (ng/L)					
Number	76		23		Mann-Whitney U
Median	8		6		P = 0.59
IQR	9.8		12.5		
Ferritin (ng/mL)					
Number	144		49		Mann-Whitney U
Median	561		79.8		P < 0.001
IQR	773.0		334.2		
Ferritin level:					
Normal	142	98.6	32	65.3	Fisher's Exact
Low	2	1.4	17	34.7	P<0.001

Table 4: continues

Lymphocytic count					
Number	1150		332		Mann-Whitney U
Median	1.70		2.00		P < 0.001
IQR	1.20		1.28		
Creatinine (µmol/L)					
Number	1150		332		Mann-Whitney U
Median	79.00		58.16		P < 0.001
IQR	19.00		14.00		
Creatinine level:					
Normal	1070	93.0	319	96.1	X^2=4.05
High	80	7.0	13	3.9	P=0.04
Blood sugar (mmol/L)					
Number	1150		332		Mann-Whitney U
Median	5.80		5.60		P = 0.07
IQR	2.29		1.85		
HbA1c (mmol/mol)					
Number	76		16		Mann-Whitney U
Median	9.35		8.45		P = 0.31
IQR	4.40		3.77		

As shown in table 5, no significant difference between male and females cases regarding COVID-19 complications except for respiratory complications that were more significantly encountered among males than females as acute respiratory failure (p = 0.01), pneumonia (p = 0.03) and ARDS (p 0.03).

Table (5): Frequency of complications among male and female hospitalized COVID-19 patients

Complications	Males (n=1150)		Females (n=332)		Test of significance (p)
	No.	%	No.	%	
Respiratory					
Acute respiratory failure	172	15.0	32	9.6	X^2=6.14 (P=0.01)
Pneumonia	52	4.5	6	1.8	X^2=5.05 (P=0.03)
ARDS	52	4.5	6	1.8	X^2=5.042 (P=0.03)
Infection					
Secondary infection	45	3.9	9	2.7	X^2=1.06 (P=0.30)
Sepsis	29	2.5	7	2.1	X^2=0.19 (P=0.67)
Septic shock	19	1.6	3	0.9	Fisher's Exact (P=0.60)
Others					
Acute kidney injury	44	3.8	7	2.1	X^2=2.29 (P=0.13)
Cardiac	33	2.9	7	2.1	X^2=0.57 (P=0.45)
Neurological	9	0.8	2	0.6	Fisher's Exact (P=1.00)
DIVC	7	0.6	1	0.3	Fisher's Exact (P=0.69)
Acute liver injury	7	0.6	1	0.3	Fisher's Exact (P=0.69)
MSIS	6	0.5	1	0.3	Fisher's Exact (P=1.00)
Rhabdomyolysis	6	0.5	2	0.6	Fisher's Exact (P=1.00)
Miscellaneous	20	1.7	3	0.9	X^2=1.18 (P=0.28))

The outcome parameters of admitted cases were presented in table 6. The proportion of cases who were subjected to oxygen therapy was significantly higher in males than females (11.9% versus 7.2%, p = 0.02). Meanwhile, higher proportion of males (26.3%) than females (8.3%) required O2 flow higher than 10L/min, p <0.001. just above one third of male cases stayed in the hospital for less than 5 days, and only 17.8% stayed ≥ 20 days. Contrary, 21.2% of female cases stayed in the hospital for less than 5 days whereas 27.4% stayed for ≥ 20 days. A difference that was statistically significant (p< 0.001) A higher percentage of male cases (9.7%) than females (3.3%) required to be admitted to the ICU significantly, p < 0.001.

Table (6): Outcome parameters of male and female hospitalized COVID-19 patients

Outcome	Male		Female		Test of significance (p)
	No.	%	No.	%	
Oxygen therapy					
No	1013	88.1	308	92.8	$\chi^2 = 5.84$
Yes	137	11.9	24	7.2	P = 0.02
Type of oxygen therapy					
Mask	74	54.0	7	29.2	$\chi^2 = 5.05$
Nasal	63	46.0	17	70.8	P = 0.03
O2 (L/min)					
1 – 5	75	54.7	20	83.3	$\chi^2 = 6.95$
6 – 10	26	19.0	2	8.3	P = 0.03
> 10	36	26.3	2	8.3	
Median (IQR)	5 (9)		2 (3)		Mann-Whitney U P = 0.001
Duration of Hospital stay (days)					
< 5	434	37.7	70	21.2	$\chi^2 = 36.45$
5 – 9	190	16.5	68	20.5	P < 0.001
10 – 14	154	13.4	53	16.0	
15 – 19	167	14.5	50	15.1	
≥ 20	205	17.8	91	27.4	
Median (IQR)	4 (14)		13 (17)		
ICU admission					
No	1038	90.3	321	96.7	$\chi^2 = 13.98$
Yes	112	9.7	11	3.3	P < 0.001
Duration of ICU stay (days)					
1 – 10	50	44.6	5	45.5	Fisher's Exact
> 10	62	55.4	6	54.5	P = 1.00
Median (IQR)	12 (15)		12 (14)		Mann-Whitney U P =0.10
Intensive ventilation					
No	35	31.5	4	36.4	Fisher's Exact
Yes	76	68.5	7	63.6	P = 0.743
Outcome at discharge					
Recovery	1101	95.7	324	97.6	$\chi^2 = 2.39$
Death	49	4.3	8	2.4	P = 0.12

DISCUSSION

It is important to reveal the extent to which COVID-19 affects both sexes to elucidate the disease outcome and investigate the prognostic factors for individualized assessment. (11) The available literature dealing with the impact of sex on the outcome and severity of COVID-19 have rarely linked this relationship with the preventive and clinical settings. The current study included 1482 hospitalized COVID-19 patients to study clinical, laboratory and outcome differences between males and females. The overall male/female ratio was 3.46 (1150 males/332 females). This high male/female ratio may have multiple explanations. This may reflect the nature of Kuwait as an attracting country of immigrant workers with a higher proportion of males in the middle age groups. Also, several hospital-based studies revealed an androgen-mediated condition that may have a role in the progression of COVID-19 disease. (17, 18)

The most common perceived manifestations by both males and females were cough (33.3%), fever (27.3%), sore throat (12.1%), body aches (10.8%) and shortness of breath (10.4%). Loss of both smell and taste were significantly more commonly prevalent among females (2.7% and 2.1%) than males (0.3% and 0.7%), while shortness of breath was significantly more common among males (11.3%) than females (7.2%). Also, a significantly higher proportion of females (15.7%) suffered from sore throat than males (11.3%). A retrospective study revealed similar results to the current one regarding loss of taste, smell and sore throat. (19) However, other main manifestations such as cough and fever were more common among males while they did not show any significant difference in the current study. Another study conducted in 2020 revealed that loss of smell and headache were more frequent in female (20) while another study revealed that gastrointestinal manifestations including nausea, vomiting and diarrhea were significantly more frequent

in women than men. (21) The differences between these studies might be attributed to both the design and setting of the studies as well as the sex ratio where males were more common in the current study. Also, the dominance of gastrointestinal manifestations differed from one wave of the disease to another. (19)

Laboratory investigations provide valuable information about both the clinical status and severity of hospitalized COVID-19 patients. Consistent with other studies, the current research revealed significant differences among multiple laboratory investigations between males and females. (21, 22) A significantly higher proportion of women (34.77%) were more likely to suffer from low ferritin level than men (1.47%). However, men were more likely to suffer from a low lymphocytic count with a median of 1.7 compared with a median of 2.0 for women. Also, a higher proportion of males (7.0%) suffered from high levels of creatinine than females (3.9%). Lymphopenia and low ferritin levels were also demonstrated among males in other studies. (21, 22) Other laboratory findings such as thrombocytopenia, elevated levels of calcitonin, aspartate and alanine transferase, total bilirubin, C-reactive protein and venous lactate were demonstrated among male hospitalized COVID-19 cases. (22) These findings, on hospital admission, may render males more susceptible for a worse outcome than females.

Results from observational studies revealed that COVID-19 males tended to have a higher risk of both morbidity and mortality impacts. (8, 23, 24) Participants of the current study suffered from multiple complications. The most common ones were the respiratory complications mainly acute respiratory failure (ARF), pneumonia and acute respiratory distress syndrome (ARDS) which all were significantly more frequently encountered among males (15.0%, 4.5%, 4.5% respectively) than females (9.6%, 1.8%, 1.8% respectively). This might be attributed to the higher proportion of smoking among men revealed in this study. Higher smoking rate in males may explain the cause of COVID-19 severity Smoking negatively affects the lung, making the individual susceptible to multiple respiratory system related diseases. Also, smoking was revealed to reduce immunity against viruses causing a high risk of repeated multiple respiratory diseases especially repeated respiratory infections. (25, 26)

This high rate of respiratory complications among males was reflected upon the need to use oxygen therapy as well as its pattern and flow rate. Not only more males (11.9%) tended to use oxygen therapy than females (7.2%) but they used it through nasal masks (54% compared with 29.2%) and at a higher flow rate (26.3% compared with 8.3% at a flow rate more than 10 L/min).

Several studies revealed that more male COVID-19 patients needed admission to the intensive care units. (8, 9, 27, 28) Data from five European countries (France, Italy, Spain, Switzerland, and Germany) highlight this difference, with men 50% more likely to be admitted to ICU than women. (11) The findings of the current study are consistent with these studies, as 9.7% of males needed care in the intensive care units (ICU) compared with only 3.3% of females however. The duration of admission was more or less similar for both sexes. The higher respiratory complications might be behind the high rate of ICU admission among males while the similar duration of care may be attributed to both the pattern and quality of care inside these units. Another factor to be considered is the ratio of males/females of this study (3.46) which reflects a high rate of hospitalization of men than women.

International data from several countries showed a male/female case fatality ratio ranging from 1.6 to 2.8. (29) Data from China, South Korea, Italy, and autopsy findings from Germany have illustrated that males formed 59–75% of COVID-19 deaths. (5, 30 – 32) A large study from the United Kingdom, dealt with more than 17 million COVID-19 patients, identified that males have a 59% increase in risk of death in comparison to females. (31) The current study also revealed a ratio of hospitalized male/female mortality of 1.79 (4.3% compared with 2.4%). However, this difference is not statistically significant. The higher mortality among males of the current study can be attributed to the significantly higher respiratory complications among males. Again, respiratory failure was stated as the main cause of mortality among COVID-19 patients. (33)

In general, sex disparity of COVID-19 mortality can be explained by a both biological (chromosomes, reproductive organs, and related sex hormones) and gender factors (social and cultural behaviors and activities). (11)

Men have higher age-adjusted rates of pre-existing co-morbidities associated with poor COVID-19 prognosis, including hypertension, cardiovascular disease (CVD), and chronic obstructive pulmonary disease (COPD). (9, 24, 28, 34) Even after adjustment for age, the effect of co-morbidities on COVID-19 mortality was greater for men than women. (5) Klein in 2012 reported that after virus infection, females have been observed to mount more robust humoral and adaptive immune responses than males. As a result of heightened immunity to viruses, both the intensity and prevalence of viral infections are often lower for females than males. (7) Other factors that may explain the gender difference in COVID-19 prognosis are the immune suppressive effect of testosterone, the immune enhancing effect of estrogen, (35, 36)

The main limitation of the current study is being hospital based and depending mainly on secondary data (records of hospitalized patients). However, the large number of recruited cases and a selection of the only specialized hospital to deal with COVID-19 cases from all districts of Kuwait can provide both power and advantage for carrying out this study.

CONCLUSIONS

This study demonstrates a difference of COVID-19 presentation, severity, and hospitalization, between men and women. Overall, this renders males to be at a higher risk for severe forms of the COVID-19 disease especially with regard to respiratory complications. Hospital physicians should be aware of these differences to guide the diagnosis and subsequent management decisions. These results would help in developing specific and effective management strategies.

REFERENCES

1. World Health Organization. WHO coronavirus disease (COVID-19) pandemic. Accessed May 10, 2021. www.who. int/emergencies/diseases/novel-coronavirus-2019
2. Lake MA. What we know so far: COVID-19 current clinical knowledge and research. Clin Med (Lond) (2020);20 (2): 124–7.
3. Siddamreddy S, Thotakura R, Dandu V, Kanuru S, Meegada S. Corona virus disease 2019 (COVID-19) presenting as acute ST elevation myocardial infarction. Cureus 2020; 12 (4): e7782. doi: 10.7759/cureus.7782
4. Sun Y, Dong L. Wang L, Xie H, Li B, et al. Characteristics and prognostic factors of disease severity in patients with COVID-19: The Beijing experience, J. Autoimmun 2020; 112: 102473. doi: 10.1016/j.jaut.2020.102473
5. Jin J-M, Bai P, He W, Wu F, Liu X-F, st al. Gender differences in patients with COVID-19: focus on severity and mortality. Front Public Health 2020;8:152. doi: 10.3389/fpubh.2020.00152.
6. Lechien JR, Chiesa-Estomba CM, Place S, Laethem YV, Cabaraux P, et al. Clinical and epidemiological characteristics of 1420 European patients with mild-to-moderate coronavirus disease 2019. J Intern Med 2020; 288(3):335-344.
7. Klein SL, Morgan R. The impact of sex and gender on immunotherapy outcomes. Biol Sex Differ 2020;11(1):24.
8. Guan WJ, Ni ZY, Hu Y, Liang W, Ou C, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020; 382: 1708–20.
9. Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, et al. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy Region, Italy. JAMA 2020; 323: 1574–81
10. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized With COVID-19 in the New York City Area. JAMA 2020; 323(20):2052-9.
11. Gebhard C, Regitz-Zagrosek V, Neuhauser HK, Morgan R, Klein SL. Impact of sex and gender on COVID-19 outcomes in Europe. Biol Sex Differ 2020;11:29.
12. Mauvais-Jarvis F, Merz N2, Barnes PJ, Brinton RD, Carrero J, et al. Sex and gender: modifiers of health, disease, and medicine. Lancet 2020; 396(10250): 565-82.
13. Silverston P, Ferrari M, Quaresima V. Pulse oximetry in primary care: factors affecting accuracy and interpretation. British Journal of General Practice 2022; 72 (716): 132-133.
14. Brittenham GM. Disorders of iron homeostasis: iron deficiency and overload. In: Hoffman R, Benz EJ, Silberstein LE, et al, (eds) *Hematology: Basic Principles and Practice 2018*. 7th ed. Philadelphia, PA: Elsevier; chap 36.
15. University of Rochester. Normal level of serum Ferritine. Medical Center Rochester, NY(2022). https://www.urmc.rochester.edu/encyclopedia/content.aspx?contenttypeid=167&contentid=ferritin_blood#:~:text=The%20normal%20range%20for%20ferritin,females%2C%2040%20years%20and%20older
16. Mount Sibai. Normal adult level of serum creatinine. Icahn School of Medicine at Mount Sinai 2020. https://www.mountsinai.org/health-library/tests/creatinine-blood-test
17. Goren A, Vaño-Galván S, Wambier CG, McCoy J, Gomez-Zubiaur A, et al. A preliminary observation: Male pattern hair loss among hospitalized COVID-19 patients in Spain – A potential clue to the role of androgens in COVID-19 severity. J Cosmet Dermatol 2020;19(7):1545-7.
18. Wambier CG, Vaño-Galván S, McCoy J, Gomez-Zubiaur A, Herrera S, et al. Androgenetic alopecia present in the majority of patients hospitalized with COVID-19: The “Gabrin sign.”. J Am Acad Dermatol 2020; 83(2):680-2.
19. Ahmed M, Sayed A, El-Abd D, Fares S, Said MS, et al. Gender difference in perceived symptoms and laboratory investigations in suspected and confirmed COVID-19 cases: A retrospective study. J Prim Care Community Health 2021; 21:1-10.
20. Ancochea J, Izquierdo JL, Soriano JB. Evidence of gender differences in the diagnosis and management of coronavirus disease 2019 patients: an analysis of electronic health records using natural language processing and machine learning. J Womens Health. 2021;30(3):393-404.
21. Raimondi F, Novelli L, Ghirardi A, Russo FM, Pellegrini D, et al. Covid-19 and gender: lower rate but same mortality of severe disease in women: an observational study. BMC Pulm Med. 2021; 21(1):96-106.
22. Vahidy FS, Pan AP, Ahnstedt H, Munshi Y, Choi HA et al. Sex differences in susceptibility, severity, and outcomes of coronavirus disease 2019: cross-sectional analysis from a diverse US metropolitan area. PLoS One. 2021;16(1):e0245556.
23. Wang X, Fang J, Zhu Y, Chen L, Ding F, et al. Clinical characteristics of noncritically ill patients with novel coronavirus infection (COVID-19) in a

Fangcang Hospital. Clin Microbiol Infect. 2020;26(8):1063-8.
24. Petrilli CM, Jones SA, Yang J, Rajagopalan H, O'Donnell L, et al. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. BMJ 2020; 369:m1966.
25. Gao K, Shi X, Wang W. The life-course impact of smoking on hypertension, myocardial infarction and respiratory diseases. Sci Rep 2017;7(1):4330-6.
26. Qiu F, Liang CL, Liu H, Zeng YQ, Hou S, et al. Impacts of cigarette smoking on immune responsiveness: Up and down or upside down? Oncotarget. 2017;8(1):268-84.
27. Simonnet A, Chetboun M, Poissy J, Raverdy V, Noulette J, et al. High prevalence of obesity in severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) requiring invasive mechanical ventilation. Obesity (Silver Spring) 2020;28(7):1195-9.
28. Yang J, Zheng Y, Gou X, Pu K, Chen Z, et al. Prevalence of comorbidities and its effects in coronavirus disease 2019 patients: a systematic review and meta-analysis. Int J Infect Dis. 2020;94:91-5
29. Global Health 50/50. The Sex, Gender and COVID-19 Project. Tracking differences in COVID-19 infection, illness and death among women and men and producing the world's largest analysis of sex and gender in national COVID-19 health policies. https://globalhealth5050.org/the-sex-gender-and-covid-19-project/Accesswed 2022
30. Chen T, Wu D, Chen H, Yan W, Yang D, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. BMJ 2020;368:m1091.
31. Williamson EJ, Walker AJ, Bhaskaran K, Bacon S, Bates C, et al. Factors associated with COVID-19 death using OpenSAFELY. Nature 2020; 584:430–6.
32. Wichmann D, Sperhake J-P, Lu¨tgehetmann M, Steurer S, Edler C, et al.. Autopsy findings and venous thromboembolism in patients with COVID-19. Ann Intern Med 2020; doi:10.7326/M20-2003.
33. Guzik TJ, Mohiddin SA, Dimarco A, Patel V, Savvatis K, et al. COVID-19 and the cardiovascular system: implications for risk assessment, diagnosis, and treatment options. Cardiovasc Res 2020;116:1666–87.
34. Mehra MR, Desai SS, Kuy S, Henry TD, Patel AN. Cardiovascular disease, drug therapy, and mortality in Covid-19. N Engl J Med. 2020;01:01.
35. Taneja V. Sex hormones determine immune response. Front Immunol. 2018; 9:1931.
36. Furman D, Hejblum BP, Simon N, Jojic V, Dekker CL, et al. Systems analysis of sex differences reveals an immunosuppressive role for testosterone in the response to influenza vaccination. Proc Natl Acad Sci USA. 2014;111(2):869-74.

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