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ORIGINAL ARTICLE

The Relation of Sex Difference with COVID-19 Outcomes: A Cross-sectional Study

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ABSTRACT

Key words:
Coronavirus disease, Sex Difference, COVID-19 Outcomes

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***Background**: A virus known as SARS-CoV-2 is the cause of coronavirus disease 2019 (COVID-19). A novel coronavirus is causing the epidemic, which has given rise to millions of infections and deaths globally. SARS-CoV-2 infections can range in clinical presentation from asymptomatic to severe or critical. The disease is revealing profound differences between males and females in disease outcomes worldwide. Sex has been identified as additional risk factor that cause a varied COVID-19 outcomes. **Objective**: The present cross-sectional study aimed to make a comparison between males and females COVID-19 patients which focused on demographic, clinical and biomarkers of the two groups. **Methodology:** One hundred COVID-19 patients (48 males and 52 females) were participated in the study. Every patient underwent thorough laboratory evaluation, and the physicians diagnosed each one based on their complete medical history. **Results:** The findings showed that all of the biomarkers studied were elevated in both males and females, and some of these parameters showed a significant difference between males and females, others did not. Additionally, a significant correlation was found between the parameters that were analyzed within the same sex. **Conclusion**: According to the study's findings, both males and females are at risk and have higher levels of clinical and biochemical indicators; however, males are marginally more likely than females to get COVID-19, exhibit more severe symptoms and have a poorer prognosis.*

INTRODUCTION

The World Health Organization (WHO) has designated COVID-19 as an international public health emergency from 2020[1]. Serious public health concerns have been raised by the COVID-19 pandemic, which has spread quickly over the world and is mostly causing respiratory illnesses with high fatality rates, especially among the elderly[2]. Numerous factors have been associated with severity, mortality, and poor outcomes in hospitalized patients with the infection, including age, sex, employment in the healthcare industry, hypertension, diabetes, asthma, and chronic obstructive pulmonary disease (COPD)[3].

Millions of infections and fatalities have been reported as a result of the global pandemic caused by SARS-CoV-2[4]. The size of the inoculum, the age of the patient, the existence of comorbidities, obesity, and other factors have all been shown to raise the risk of death[5, 6]. Sex differences is the predictive role of several biomarkers that have been found to predict the outcome of COVID-19 severity. Sex-disaggregated statistics are crucial for comprehending the population's risk, infection, and disease distribution as well as the degree to which sex influences clinical outcomes[7]. Some studies have reported that male patients had higher rates of severe sickness, death from COVID-19 and acute care admission compared to female patients[8]. In contrast, the long lasting COVID syndrome trend showed that females are more likely to be afflicted[9], however, it is unclear what the differences are between male and female COVID-19 patients and what could be the reason for this observation[10, 11]. Recognizing the extent to which disease epidemics impact males and females differently is crucial for understanding the primary and secondary effects of a health emergency on diverse individuals and communities, as well as for creating equitable, effective policies and interventions. Therefore, the current study aims to find differences in COVID-19 patients' sex-specific biomarkers.

METHODOLOGY

Participants:

The study comprised one hundred COVID-19 participants with age matching (37–61 years), 48 of them were male and 52 were females. Based on a positive reverse transcription real-time polymerase chain reaction (rRTPCR) test for COVID-19, positive IgM, and additional symptoms (fever, coughing, and loss of taste and smell), the physician's determined that every patient had SARS-CoV-2 sickness. Patients with hepatic and renal problems, as well as pre-diagnostic conditions such type 1 diabetes, were excluded from the study.

Every case was given a questionnaire that asked about their name, age, gender, height, weight, marital status, duration of illness, previous medical history, blood pressure, body temperature, oxygen saturation (SpO2), plasma use, and O2 aspiration use, among other details, and the treatment mode.

Statistical Analysis:

SPSS software (version 25) was used to analyze the data and determine how the results were distributed. The mean, standard deviation, and percentage of the results were displayed. The subdivided groups were compared using the chi-squared and t-tests. To evaluate the correlation between the parameters, Pearson's correlation coefficients (r) were employed. P-values below 0.05 were considered statistically significant.

RESULTS

Demographic characteristics of males and females COVID-19 patients

The demographic characteristics of the studied groups were illustrated in table1.

Table 1: Demographic characteristics of males and females COVID-19 patients

Variables	Males (N=48)	Females (N=52)	P value
Age (yr)	49.67±12.27	45.37±13.97	0.105*
BMI (Kg/m^2)	25.47±3.8	28.56±4.37	0.013*
Marital status (Married) N (%)	46 (95.8%)	37 (71.2%)	0.001**
Heart Disease N (%)	0 (0%)	4 (7.7%)	0.119**
Respiratory Disease N (%)	3 (6.3%)	1 (1.9%)	0.384**
T2DM N (%)	9 (18.8%)	17 (32.7%)	0.17**

Results expressed as mean±SD and as percentage.
P-values were calculated using the pooled T-test (*) and Chi-square test (**).

The results indicates that the two groups were matched in the age and differs in BMI and marital status. The table also showed the percentage of the clinical data (heart disease, respiratory disease, T2DM).

Clinical and biomarker data in males and females COVID-19 patients

The clinical and biomarker data for COVID-19 patients for both males and females, are shown in Table 2.

Table 2: Clinical and biomarker information for COVID-19 patients, both male and female

Parameters		Males (N=48)	Females (N=52)	P value
IgG	(negative/Positive) (%)	35/13 (72.9%/ 27.1%)	30/22 (57.7%/ 42.3%)	0.143**
IgM		19/29 (39.6%/ 60.4%)	11/41 (21.2%/ 78.8%)	0.05**
S.Ferritin (ng/ml)	(mean ±SD)	315.58±135.96	264.26±134.82	0.03*
CRP mg/l (<10)		64.18±20.051	45.53±22.611	0.05*
WBC(*10^9)/L		7.54±3.108	7.50±3.200	0.95*
D-Dimer (µg/ml)		1.06±0.833	1.13±0.97	0.72*
SPO2		88.35±7.18	88.67±5.02	0.79*
DBP(mm/Hg)		81.77±11.22	84.37±17.28	0.37*
SBP(mm/Hg)		123.96±15.94	128.37±18.223	0.20*

Results expressed as mean±SD and as percentage.
P-values were calculated using the pooled T-test (*) and Chi-square test (**).
Abbreviations: CRP: C-Reactive Protein; IgG: Immunoglobulin G; IgM: Immunoglobulin M , WBC: White blood cells, SPO2: oxygen saturation, DBP: Diastolic blood pressure, SBP: Systolic blood pressure.

According to the data, Only IgM, S.ferritin, and CRP revealed a significant difference between males and females; no significant difference was seen in the remaining parameters.

Table 3: Correlation between several characteristics in the female patients

		IgG	IgM	BMI	SBP	DBP	SPO2	D-Dimer	S.Ferritin	CRP	WBC
IgG	r	1	0.444**	0.166	-0.030	-.036	-0.303*	0.212	0.290*	0.123	-0.034
	p		0.001	0.241	0.831	0.797	0.029	0.131	0.037	0.386	0.813
IgM	r	0.444**	1	0.393**	0.084	0.237	-0.374**	0.259	0.186	0.204	0.057
	p	0.001		.004	0.556	0.091	0.006	0.064	0.187	0.148	0.689
BMI	r	0.166	0.393**	1	0.257	0.081	-0.282*	0.083	0.309*	0.229	-0.064
	p	0.241	0.004		0.066	0.569	0.043	0.560	0.026	0.103	0.653
SBP	r	-0.030	0.084	.257	1	0.663**	-0.247	0.129	0.246	0.140	-0.077
	p	0.831	0.556	.066		0.000	0.078	0.362	0.078	0.322	0.589
DBP	r	-0.036	0.237	0.081	0.663**	1	-0.298*	0.113	.263	0.263	-0.084
	p	0.797	0.091	0.569	0.000		0.032	0.427	0.060	0.060	0.553
SPO2	r	-0.303*	-0.38**	-0.282*	-0.247	-0.298*	1	-0.431**	-0.644**	-0.640**	-0.141
	p	0.029	0.006	0.043	0.078	0.032		0.001	0.000	0.000	0.319
D-Dimer	r	0.212	0.259	0.083	0.129	0.113	-0.431**	1	0.417**	0.421**	-0.103
	p	0.131	0.064	0.560	0.362	0.427	0.001		0.002	0.002	0.469
S.Ferritin	r	0.290*	0.186	0.309*	0.246	0.263	-0.644**	0.417**	1	0.386**	-0.067
	p	0.037	0.187	0.026	0.078	0.060	0.000	0.002		0.005	0.636
CRP	r	0.123	0.204	0.229	0.140	0.263	-0.640**	0.421**	0.386**	1	-0.069
	p	0.386	0.148	0.103	0.322	0.060	0.000	0.002	0.005		0.626
WBC	r	-0.034	0.057	-0.064	-0.077	-0.084	-0.141	-0.103	-0.067	-0.069	1
	p	0.813	0.689	0.653	0.589	0.553	0.319	0.469	0.636	0.626	

**Correlation is significant at the 0.01 level.
*Correlation is significant at the 0.05 level.

Table 3 displayed the findings of the correlation analysis of various characteristics among the females. Two levels of significant correlation are shown by these results: (**) denotes a high correlation when p<0.01, and a correlation at p<0.05 is indicated by (*).

Table 4: Correlation of different variables within the male patients.

		IgG	IgM	BMI	SBP	DBP	SPO2	D-Dimer	S.Ferritin	CRP	WBC
IgG	r	1	0.493**	-0.180	0.025	0.029	-0.235	0.175	0 .158	0.050	0.142
	p		0.000	0.221	0.864	0.842	0.108	0.235	0.285	0.737	0.336
IgM	r	0.493**	1	0.003	0.473**	0.474**	-0.373**	0.143	0.213	-0.018	0.105
	p	0.000		0.985	0.001	0.001	0.009	0.331	0.146	0.905	0.476
BMI	r	-0.180	0.003	1	0.162	-0.012	-0.338*	0.017	-0.067	0.136	-0.253
	p	0.221	0.985		0.272	0.937	0.019	0.909	0.653	0.358	0.083
SBP	r	0.025	0.473**	0.162	1	0.661**	-0.107	-0.019	-0.008	-0.079	-0.062
	p	0.864	0.001	0.272		0.000	0.468	0.897	0.956	0.591	0.674
DBP	r	0.029	0.474**	-0.012	0.661**	1	-0.061	-0.016	0.077	-0.053	0.025
	p	0.842	0.001	0.937	0.000		0.682	0.915	0.603	0.718	0.865
SPO2	r	-0.235	-0.37**	-0.338*	-0.107	-0.061	1	-0.295*	-0.603**	-0.561**	0.092
	p	0.108	0.009	0.019	0.468	0.682		0.042	0.000	0.000	0.535
D-Dimer	r	0.175	0.143	0.017	-0.019	-0.016	-0.295*	1	0.558**	0.304*	0.119
	p	0.235	0.331	0.909	0.897	0.915	0.042		0.000	0.035	0.422
S.Ferritin	r	0.158	.213	-.067	-.008	.077	-0.603**	0.558**	1	0.384**	-0.001
	p	.285	.146	.653	.956	.603	0.000	0.000		0.007	0.993
CRP	r	0.050	-0.018	0.136	-0.079	-0.053	-0.561**	0.304*	0.384**	1	-0.167
	p	0.737	0.905	0.358	0.591	0.718	0.000	0.035	0.007		0.256
WBC	r	0.142	0.105	-0.253	-0.062	0.025	0.092	0.119	-0.001	-0.167	1
	p	0.336	0.476	0.083	0.674	0.865	0.535	0.422	0.993	0.256	

**Correlation is significant at the 0.01 level.
*Correlation is significant at the 0.05 level.

Table 4 displayed the findings of the correlation analysis of various variables among the male patients. Two levels of significant correlation are also shown by these results: (**) at p<0.01 and (*) at p<0.05.

DISCUSSION

Both males and females show high severity, according to the comparison statistics between the sexes (tables 1 and 2), however males differ significantly from females in a few of the parameters that were examined. Furthermore, tables 3 and 4 showed a significant correlation between the parameters within the same sex. Numerous studies and works have examined the role of sex on the epidemic outcomes. According to the clinical results, males are more likely than females to have a severe and fatal COVID-19 infection[12, 13]. Several investigations revealed similar findings[14, 15] and in Ontario, Canada[16], while males accounted for almost 72% of cases with COVID-19 in Pakistan[17]. Based on data from Global Health, males in various nations have a high proportion of COVID-19-related deaths and confirmed cases[18]. These findings might be the result of behavioral differences and roles that raise the possibility of getting COVID-19, which are more common in males. For example, participating in important activities during funeral ceremonies and working in basic vocations and industries that demand that they stay active, even throughout the containment period, they engage with others and work outside of their homes.. Males typically don't stay at home because of this; instead, they sit with other people and take off their masks to smoke and drink. Males are more prone to get COVID-19 as a result of this elevated exposure level[19].

However, the transmembrane protease serine 2 (TMPRSS2) and the receptor for angiotensin-converting enzyme 2 (ACE2) are necessary for SARS-CoV-2 to successfully enter the body[20]. Therefore, variations in COVID-19 severity and mortality may be explained by sex-based variations in ACE2 receptor and TMPRSS2 expression[21]. Sex-based differences in immune responses could possibly be the cause of these discrepancies. Generally speaking, females can mount a stronger immune response to immunizations and illnesses[22]. According to certain earlier research on coronaviruses in mice, estrogen might offer some protection. The immune response's escalation phase, which results in a greater production of cytokines, is suppressed by estrogens[23]. Knowledge of the sex sensitivities of COVID-19 infection is essential to developing efficient COVID-19 treatment options and medications[24]. The severity of COVID-19 disease development is linked to other comorbidities. Cardiovascular concomitant diseases have been linked to many of the worse outcomes associated with COVID-19. However, this could be due to various comorbidities in addition to a cardiovascular condition, or it could result directly from the cardiovascular disease[25]. Additionally, more severe cases of COVID-19 were more common in people with type 2 diabetes[26]. Type 2 diabetic individuals needed more interventions during their hospital stay than non-diabetic patients, according to a cohort study of 7337 COVID-19 patients with and without the disease. In addition to the considerable difference between male and female patients with type 2 diabetes, the overall mortality rate was found to be higher for those with poorer blood glucose control than for those with better glucose control[27].

Along with other comorbidities, poor disease progression has been associated with chronic obstructive pulmonary disease (COPD). A meta-analysis of numerous Chinese research found that patients with preexisting COPD who were identified with COVID-19 had a four-fold greater mortality rate[28].

According to an Italian research on 3,200 fatalities from COVID-19, males were more likely than girls to die across all age categories, with almost 70% of deaths occurring in this demographic[29]. Males were older and more likely to be hospitalized among 14,712 male and female patients with confirmed COVID-19, according to an international health research database employing the TriNetX Network , and more likely to have heart failure, Nicotine use, diabetes, hypertension, coronary heart disease, and obstructive pulmonary disease. Additionally, males were more likely than females to die from all causes. Additionally, males died at a higher rate than females from any reason[30]. Furthermore, even after adjusting for comorbidities, age, and the use of angiotensin receptor blockers (ARBs) or angiotensin-converting enzyme inhibitors (ACEIs), the cumulative likelihood of survival was considerably lower among males[31]. It has been established that sex disparities in incidence and disease severity are caused by differences in the susceptibility and reaction of males and females to viral infections[32]. Sex hormones, which are crucial for both innate and adaptive immunity, may be the cause of females' decreased vulnerability to viral infections[33].

CONCLUSION

Males are somewhat more vulnerable to COVID-19 infection than females, present with a more severe disease, and have a worse prognosis, according to the current study's findings. Both sexes are at risk and have higher clinical and biochemical markers.

Limitations of the study:

First, the sample size is relatively small. The vigorous criteria used to choose the study's subjects constitute the second constraint.

Ethical approval:

The study was approved by the Ethics Committee of the Faculty of pharmacy, Kufa University and accomplished as per the Iraqi institutional audit board (IRB) (711/2021), authorized the protocol.

Author's contributions

Each contributing author participated in the preparation of the manuscript.

A conflict of interest

According to the authors, there is no conflict of interest.

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