

Gender Difference in Perceived Symptoms and Laboratory Investigations in Suspected and Confirmed COVID-19 Cases: A Retrospective Study

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Abstract

Background: Evaluating gender-specific effects of COVID-19 is important to develop effective therapeutic strategies. The aim of this study was to explore gender difference in perceived symptoms and laboratory investigations in suspected and confirmed cases. **Methods:** This is a retrospective study that included data from suspected COVID-19 patients during the first wave of the pandemic. Participants using the phone triaging system at Kasralainy outpatient clinics were included. The analyzed data included patient history and results of nasopharyngeal swab and laboratory data. **Results:** Out of 440 COVID-19 suspected cases, 56.36% were females. The perceived COVID-19 symptoms showed no significant gender difference in suspected cases while in confirmed cases females were 4 times more likely to complain of cough [OR (95% CI) 3.92 (1.316–11.68), *P*-value .014] and 5 times more likely to experience loss of smell or taste [OR (95% CI) 4.84 (1.62–14.43), *P*-value .005]. Laboratory markers revealed high levels of aspartate aminotransferase, alanine aminotransferase, blood urea, serum creatinine, creatine kinase, and serum ferritin in males and this was statistically significant (*P*-value <.001) in suspected and confirmed cases. Females confirmed with COVID-19 were 80%, 97%, and 97% less likely to have high levels of ALT, creatin kinase, and serum ferritin [OR (95% CI) 0.20 (0.07–0.54), 0.07 (0.01–0.38), and 0.07 (0.01–0.90), *P*-value .002, .002, and .041, respectively]. **Conclusion:** Gender differences were found in laboratory markers in COVID-19 suspected and confirmed cases and in perceived symptoms in confirmed cases.

Keywords

COVID-19 suspected cases, gender difference, phone triage

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Introduction

Coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 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.^{1,2}

Being a global health threat, researchers investigated the prognostic and risk factors associated with severity and

mortality. Researchers as well observed preexisting conditions that may be related to severe and fatal outcomes. Apart from chronic medical conditions and old age (>65 years),

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male gender was associated with more severe forms of the disease.^{3,4}

Although the number of recorded confirmed cases is similar in males and females, however the mortality rate tends to be higher in males. At the beginning of 2021, the number of COVID-19 deaths worldwide was approximately 777 000 men, 578 000 women, and the sex was unknown in 633 000 deaths. Since then, researchers started to investigate whether men are more susceptible to dying from COVID-19 than women.^{4,5}

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.⁶ Higher smoking rate in males may explain the cause of COVID-19 severity, especially with multiple researches highlighted the association of smoking with poor prognosis. Smoking negatively affects the lung, making the individual susceptible to multiple respiratory system-related diseases. Also, smoking reduces immunity against infectious pathogens, mainly viruses, causing increased risk of repeated respiratory infections.^{7,8} Smokers were seven times more prone to death risk by influenza. Similarly, during the Middle East respiratory syndrome coronavirus outbreak, higher mortality rates were reported among smokers.^{9,10}

Angiotensin-converting enzyme2 (ACE2) is a regulatory molecule of renin angiotensin system in the physiological function of the kidney, heart, gastrointestinal tract and recently analyzed to be expressed in the secretory cells of the respiratory tract. These organs happen to be target sites for SARS-CoV-2 infection. Expression of ACE2 was found to be higher in smokers compared with non-smokers.¹¹

Other factors that may explain the gender difference in COVID-19 prognosis are the immune suppressive effect of testosterone,¹² the immune enhancing effect of estrogen,¹³ localization of immune response genes on X Chromosome so higher female immunity may be because of the presence of double X chromosome,¹⁴ higher expression of pro-inflammatory cytokines in males in acute inflammation which may cause patient death because of cytokine storm¹⁵ and finally gender specific response to stress.¹⁶

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. Yet, no significant difference regarding disease duration between males and females was reported.¹⁷

Studies carried out on hospitalized patients reported significant gender difference in laboratory values, including complete blood count, lymphocytes, platelet count, liver enzymes, creatinine, D-Dimer, ferritin, C-Reactive Protein, and troponin.¹⁸

Gaining insights from patients presenting to primary care clinics about perceived symptoms of COVID-19 is crucial. Knowledge regarding gender difference can aid in adopting a quick response to prevent unpleasant disease outcome. To our knowledge, no sufficient data is available regarding gender difference in COVID-19 patients presenting to the outpatient clinics, as all available data are from hospitalized patients.

The aim of this study was to explore gender difference in perceived symptoms and laboratory investigations in COVID-19 suspected and confirmed cases calling COVID-19 phone triaging system. Understanding these differences is crucial for primary care physicians to guide the diagnosis and subsequent management decision.

Methods

This is a retrospective study that included data from suspected patients (over 16 years) during the first wave of the COVID-19 pandemic in Egypt. All participants using the phone triaging system at Kasralainy outpatient clinics and referred for confirmation of diagnosis in June and July 2020 were included in the study. Exclusion criteria included suspected patients with incomplete data.

The phone triaging system acted as the primary gate for all suspected patients at Kasralainy outpatient clinics. These outpatient clinics are the clinics for Cairo University hospitals which are considered the largest governmental hospitals in Egypt offering medical services for patients from all governorates as well as employees at Cairo University. Skilled family physicians responded to the patients' calls with a comprehensive phone consultation. Perceived symptoms and risk factors were assessed. Suspected patients were then referred for Real-Time Polymerase Chain Reaction (RT-PCR) assay of the nasopharyngeal swab and laboratory investigations.

The analyzed data included:

- Baseline characteristics, including age, sex, and marital status
- Comorbidities and risk factors of COVID-19 including contact with COVID-19 patients
- Results of real-time PCR
- Laboratory data including Complete blood count (CBC), C - reactive protein CRP, Lactate Dehydrogenase (LDH), and Ferritin

Ethical Approval

Approval was obtained from the ethical committee of the Faculty of Medicine, Cairo University.

Confidentiality of the data was ensured throughout the research.

Statistical Analysis

The variables were presented in numbers and percentages. Chi-square test was used to test for associations between gender and different variables in the suspected participants and the positive-PCR participants. Logistic regression analysis was done after adjustment for age, smoking, being healthcare worker, and having comorbidities or immunodeficiency. The regression model was tested for accuracy with area under the ROC curve of 0.85. The *P*-value is considered significant if $<.05$.

Results

The measured variables are COVID 19 related variables regarding symptoms and lab investigations. All the variables are represented in categorical (not numerical) manner for more clinical relevance.

Out of 440 COVID-19 suspected cases, 248 (56.36%) were females. Table 1 shows the suspected participants' characteristics in association with gender as 63.08% of them were in the 16 to 45 years age group and 51.25% were healthcare workers. Regarding the risk factors among the participants, only 12.44% were smokers, 34.77% have other comorbidities and 3.69% have immunodeficiency conditions or on medications. Nearly half of the participants (51.03%) visited a place where confirmed cases of COVID-19 were diagnosed and three-fourths (79.73%) were in contact with patients with respiratory symptoms.

Among all socio-demographic and risk factors, only being healthcare worker and smoker showed significant association with gender, as 142 (63.11%) of healthcare workers were females (*P*-value .004) and 48 (92.31%) of smokers were males (*P*-value $<.001$). Among all the suspected participants, the perceived COVID-19 symptoms showed no significant difference between males and females, although all the symptoms were slightly more prevalent in females.

As shown in Table 2, several laboratory markers revealed significant gender differences among the suspected COVID-19 participants. In CBC parameters, gender differences were significantly related to red blood cells (RBCs), platelets, and monocytes with *P*-values .001, .035, and .031, respectively. Regarding blood chemistry markers, high levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), blood urea, serum creatinine, creatine kinase (CK), and serum ferritin were more prevalent in males. While normal levels of these markers were more prevalent in females, with statistically significant difference. Among all the suspected COVID-19 patients, 213 (48.41%) were confirmed as COVID-19 cases by PCR, 117 (54.93%) of them were females and 96 (45.07%) were males.

Table 1. Characteristics of Participants Suspected for COVID-19 (n = 440).

	Total	Females	Males	<i>P</i> -value*
	n (%)			
Socio-demographic and risk factors				
Age group				
16-45	258 (63.08)	153 (59.30)	105 (40.70)	.324
46-85	151 (36.92)	82 (54.30)	69 (45.70)	
Healthcare worker				
No	214 (48.75)	106 (49.53)	108 (50.47)	.004
Yes	225 (51.25)	142 (63.11)	83 (36.89)	
Smoking				
No	366 (87.56)	233 (63.66)	133 (36.34)	$<.001$
Yes	52 (12.44)	4 (7.69)	48 (92.31)	
Previous visit of a place with confirmed COVID-19 cases				
No	213 (48.97)	113 (53.05)	100 (46.95)	.149
Yes	222 (51.03)	133 (59.91)	89 (40.09)	
Previous contact with respiratory symptoms cases				
No	89 (20.27)	47 (52.81)	42 (47.19)	0.462
Yes	350 (79.73)	200 (57.14)	150 (42.86)	
Presence of comorbidities				
No	287 (65.23)	159 (55.40)	128 (44.60)	.577
Yes	153 (34.77)	89 (58.17)	64 (41.83)	
Presence of immunodeficiency disorders or drugs				
No	418 (96.31)	233 (55.74)	185 (44.26)	.043
Yes	16 (3.69)	13 (81.25)	3 (18.75)	
Symptoms				
Fever				
No	105 (23.97)	65 (61.90)	40 (38.10)	.174
Yes	333 (76.03)	181 (54.35)	152 (45.65)	
Cough				
No	151 (34.47)	77 (50.99)	74 (49.01)	.114
Yes	287 (65.53)	169 (58.89)	118 (41.11)	
Sore throat				
No	166 (37.90)	90 (54.22)	76 (45.78)	.473
Yes	272 (62.10)	157 (57.72)	115 (42.28)	
Vomiting or diarrhoea				
No	249 (56.98)	138 (55.42)	111 (44.58)	.673
Yes	188 (43.02)	108 (57.45)	80 (42.55)	
Malaise				
No	70 (15.98)	36 (51.43)	34 (48.57)	.361
Yes	368 (84.02)	211 (57.34)	157 (42.66)	
Loss of smell or taste				
No	304 (69.09)	165 (54.28)	139 (45.72)	.187
Yes	136 (30.91)	83 (61.03)	53 (38.97)	

**P*-value was calculated using Chi-square test, and is considered significant if $<.05$.

Table 3 shows the gender differences in socio-demographic, risk factors and symptoms among COVID-19 confirmed cases only (213 participants). Being healthcare worker and smoker were also significantly associated with

Table 2. Laboratory Characteristics of Participants Suspected for COVID-19 (n = 440).

	Total	Females n (%)	Males	P-value*
Complete blood count (CBC)				
Red blood cells				
Erythrocytopenia	7 (1.64)	6 (85.71)	1 (14.29)	.001
Normal	79 (18.54)	58 (73.42)	21 (26.58)	
Erythrocytosis	340 (79.81)	175 (51.47)	165 (48.53)	
Platelets				
Thrombocytopenia	63 (14.79)	26 (41.27)	37 (58.73)	.035
Normal	347 (81.46)	203 (58.50)	144 (41.50)	
Thrombocytosis	16 (3.76)	10 (62.50)	6 (37.50)	
White blood cells				
Leucopenia				
Leucopenia	27 (6.34)	18 (66.67)	9 (33.33)	.512
Normal	337 (79.11)	186 (55.19)	151 (44.81)	
Leucocytosis				
Leucocytosis	62 (14.55)	35 (56.45)	27 (43.55)	
Neutrophils				
Neutropenia				
Neutropenia	58 (13.94)	31 (53.45)	27 (46.55)	.730
Normal	324 (77.88)	180 (55.56)	144 (44.44)	
Neutrophilia				
Neutrophilia	34 (8.17)	21 (61.76)	13 (38.24)	
Lymphocytes				
Lymphopenia				
Lymphopenia	13 (3.07)	5 (38.46)	8 (61.54)	.107
Normal	270 (63.68)	161 (59.63)	109 (40.37)	
Lymphocytosis				
Lymphocytosis	141 (33.25)	72 (51.06)	69 (48.94)	
Monocytes				
Monocytopenia				
Monocytopenia	18 (4.25)	15 (83.33)	3 (16.67)	.031
Normal	340 (80.19)	191 (56.18)	149 (43.82)	
Monocytosis				
Monocytosis	66 (15.57)	32 (48.48)	34 (51.52)	
Eosinophils				
Eosinocytopenia				
Eosinocytopenia	54 (12.74)	32 (59.26)	22 (40.74)	.062
Normal	360 (84.91)	204 (56.67)	156 (43.33)	
Eosinophilia				
Eosinophilia	10 (2.36)	2 (0.84)	8 (4.30)	
Basophils				
Normal	416 (100.00)	232 (55.77)	184 (44.23)	
Chemistry				
Aspartate aminotransferase (AST)				
Normal				
Normal	359 (81.78)	217 (60.45)	142 (39.55)	<.001
High				
High	80 (18.22)	30 (37.50)	50 (62.50)	
Alanine aminotransferase (ALT)				
Normal				
Normal	271 (61.73)	176 (64.94)	95 (35.06)	<.001
High				
High	168 (38.27)	71 (42.26)	97 (57.74)	
Blood urea				
Low				
Low	38 (8.66)	29 (76.32)	9 (23.68)	<.001
Normal				
Normal	167 (38.04)	107 (64.07)	60 (35.93)	
High				
High	234 (53.30)	111 (47.44)	123 (52.56)	
Serum creatinine				
Normal				
Normal	423 (96.36)	246 (58.16)	177 (41.84)	<.001
High				
High	16 (3.64)	1 (6.25)	15 (93.75)	
Lactate dehydrogenase (LDH)				
Normal				
Normal	47 (10.71)	26 (56.52)	21 (43.71)	.525
High				
High	392 (89.29)	221 (56.38)	171 (43.62)	
Creatine kinase (CK)				
Normal				
Normal	383 (87.24)	237 (61.88)	146 (38.12)	<.001
High				
High	56 (12.76)	10 (17.86)	46 (82.14)	

(continued)

Table 2. (continued)

	Total	Females	Males	P-value*
		n (%)		
C-reactive protein (CRP)				
Normal	264 (60.14)	148 (56.06)	116 (43.94)	.916
High	175 (39.86)	99 (56.57)	76 (43.43)	
Serum ferritin				
Low	27 (7.24)	24 (88.89)	3 (11.11)	<.001
Normal	232 (62.20)	153 (65.95)	79 (34.05)	
High	114 (30.56)	34 (29.82)	80 (70.18)	
PCR				
Negative	227 (51.59)	131 (57.71)	96 (42.29)	.557
Positive	213 (48.41)	117 (54.93)	96 (45.07)	

*P-value was calculated using Chi-square test, and is considered significant if $< .05$.

Table 3. Gender Differences in Socio-Demographic, Risk Factors, and Symptoms Among COVID-19 Confirmed Cases (n=213).

	Total	Females	Males	P-value*
		n (%)		
Socio-demographic and risk factors				
Age group				
16-45	124 (61.69)	72 (58.06)	52 (41.94)	.396
46-85	77 (38.31)	40 (51.95)	37 (48.05)	
Healthcare worker				
No	110 (51.89)	51 (46.36)	59 (53.64)	.007
Yes	102 (48.11)	66 (64.71)	36 (35.29)	
Smoking				
No	187 (91.67)	113 (60.43)	74 (39.57)	<.001
Yes	17 (8.33)	0 (0.00)	17 (100.00)	
Previous visit of a place with confirmed COVID-19 cases				
No	115 (54.76)	62 (53.91)	53 (46.09)	.671
Yes	95 (45.24)	54 (56.84)	41 (43.16)	
Previous contact with respiratory symptoms cases				
No	53 (24.88)	29 (54.72)	24 (45.28)	.971
Yes	160 (75.12)	88 (55.00)	72 (45.00)	
Presence of comorbidities				
No	133 (62.44)	74 (55.64)	59 (44.36)	.788
Yes	80 (37.56)	43 (53.75)	37 (46.25)	
Presence of immunodeficiency disorders or drugs				
No	201 (95.71)	211 (55.22)	90 (44.78)	.499
Yes	9 (4.29)	6 (66.67)	3 (33.33)	
Symptoms				
Fever				
No	48 (22.54)	27 (56.25)	21 (43.75)	.835
Yes	165 (77.46)	90 (54.55)	75 (45.45)	
Cough				
No	74 (34.91)	33 (44.59)	41 (55.41)	.030
Yes	138 (65.09)	83 (60.14)	55 (39.86)	
Sore throat				
No	93 (43.87)	48 (51.61)	45 (48.39)	.422
Yes	119 (56.13)	68 (57.14)	51 (42.86)	

(continued)

Table 3. (continued)

	Total	Females	Males	P-value*
		n (%)		
Vomiting or diarrhoea				
No	126 (60.00)	68 (53.97)	58 (46.03)	.777
Yes	84 (40.00)	47 (55.95)	37 (44.05)	
Malaise				
No	29 (13.74)	14 (48.28)	15 (51.72)	.435
Yes	182 (86.26)	102 (56.04)	80(43.96)	
Loss of smell or taste				
No	136 (63.85)	67 (49.26)	69 (50.74)	.027
Yes	77 (36.15)	50 (64.94)	27 (35.06)	

*P-value was calculated using Chi-square test, and is considered significant if $< .05$.

gender of the confirmed cases as 66 (64.71%) of healthcare workers were females (P -value .007) and 17 (100%) of smokers were males (P -value $< .001$). Nearly two-thirds of the confirmed cases complained of cough, and 60.14% of them were females (P -value 0.030). One-third of the confirmed cases complained of loss of smell or taste, and 50 (64.94%) of them were females (P -value 0.027).

Gender differences in laboratory investigations among confirmed cases were nearly similar to the differences revealed among the suspected cases, as shown in Table 4. All confirmed cases with erythrocytopenia and most cases with normal RBCs count were females (P -value .014). Monocytes also revealed significant difference between males and females (P -value .013). Nearly 60% of confirmed cases with high AST, ALT, and serum ferritin were males (P -value .023, $< .001$, and $< .001$, respectively). Also, 10 (90.91%) and 22 (84.62%) of confirmed cases with high serum creatinine and high creatine kinase were males (P -value .002 and $< .001$, respectively). Blood urea showed significant gender difference, while LDH and CRP were not significantly different among both genders.

The adjusted logistic regression was presented in Table 5. Confirmed COVID-19 cases aging 46 to 85 years were 4.5 times more likely to be females compared to males [OR (95% CI) 4.51 (1.28–15.93), P -value 0.019]. Confirmed COVID-19 female cases were 4 times more likely to complain of cough [OR (95% CI) 3.92 (1.316–11.68), P -value .014] and 5 times more likely to experience a loss of smell or taste [OR (95% CI) 4.84 (1.62–14.43), P -value .005]. Compared to males, females confirmed with COVID-19 were 80%, 97%, and 97% less likely to have high levels of ALT, creatin kinase, and serum ferritin [OR (95% CI) 0.20 (0.07–0.54), 0.07 (0.01–0.38), and 0.07 (0.01–0.90), P -value .002, .002, and .041, respectively].

Discussion

Evaluation of gender-specific effects of COVID-19 is of utmost importance to address the short and long-term disease

complications. The aim of this study was to explore gender difference in perceived symptoms and laboratory investigations among patients using COVID-19 phone triaging system. Gender-dependent differences were found in COVID-19 suspected and confirmed cases.

Various COVID-19 researches showed different gender prevalence depending on clinical setting.¹⁹ In our study, females represented 56.36% of COVID-19 suspected cases and 117 (54.93%) of confirmed cases.

Confirmed COVID-19 cases aging 46 to 85 years were 4.5 times more likely to be females compared to males. While other studies found that young adult females were significantly more likely to be COVID-19 positive.²⁰ Female sex hormones play an important role in different health aspects including inflammation and innate and adaptive immunity, therefore higher levels of pro-inflammatory cytokines are usually found in postmenopausal women. It also affects the expression and activity of ACE-2 receptors, which is thought to have an important role in the progression of COVID-19.²¹

In our study, the perceived COVID-19 symptoms showed no significant gender difference in suspected cases, although all the symptoms were slightly more prevalent in females. While in confirmed cases, cough and loss of smell or taste were significantly more common in female patients. Predominance of cough in confirmed COVID-19 females could be due to the fact that 100% of the smoking participants in the study were males and could be chronic cough complainers affecting their perception of COVID-19 related cough.

While in a study conducted on 4780 patients in 2020, headache and anosmia were significantly more frequent in females.²⁰ While another study found that gastrointestinal symptoms including nausea, vomiting and diarrhea, were significantly more frequent in women than men.²² This suggests greater ACE2 expression in females' alimentary tract. However, the gastrointestinal symptoms were not dominant during the first wave of COVID-19 that was the time of data collection of the study.

Table 4. Gender Difference in Laboratory Investigations Among COVID-19 Confirmed Cases (n=213).

	Total	Females n (%)	Males	P-value*
Complete blood count (CBC)				
Red blood cells				
Erythrocytopenia	5 (2.46)	5 (100.00)	0 (0.00)	.014
Normal	40 (19.70)	27 (67.50)	13 (32.50)	
Erythrocytosis	158 (77.83)	78 (49.37)	80 (50.63)	
Platelets				
Thrombocytopenia	33 (16.26)	13 (39.39)	20 (60.61)	.130
Normal	163 (80.30)	92 (56.44)	71 (43.56)	
Thrombocytosis	7 (3.45)	5 (71.43)	2 (28.57)	
White blood cells				
Leucopenia				
Leucopenia	21 (10.34)	13 (61.90)	8 (38.10)	.719
Normal	162 (79.80)	87 (53.70)	75 (46.30)	
Leucocytosis				
Leucocytosis	20 (9.85)	10 (50.00)	10 (50.00)	
Neutrophils				
Neutropenia				
Neutropenia	41 (20.60)	21 (51.22)	20 (48.78)	.883
Normal	146 (73.37)	80 (54.79)	66 (45.21)	
Neutrophilia				
Neutrophilia	12 (6.03)	7 (58.33)	5 (41.67)	
Lymphocytes				
Lymphopenia				
Lymphopenia	10 (4.95)	3 (30.00)	7 (70.00)	.154
Normal	143 (70.79)	83 (58.04)	60 (41.96)	
Lymphocytosis				
Lymphocytosis	49 (24.26)	24 (48.98)	25 (51.02)	
Monocytes				
Monocytopenia				
Monocytopenia	15 (7.43)	13 (86.67)	2 (13.33)	.013
Normal	151 (74.75)	82 (54.30)	69 (45.70)	
Monocytosis				
Monocytosis	36 (17.82)	15 (41.67)	21 (58.33)	
Eosinophils				
Eosinocytopenia				
Eosinocytopenia	38 (18.81)	23 (60.53)	15 (39.47)	.224
Normal	162 (80.20)	87 (53.70)	75 (46.30)	
Eosinophilia				
Eosinophilia	2 (0.99)	0 (0.00)	2 (100.00)	
Basophils				
Normal	199 (100.00)	108 (54.27)	91 (45.73)	
Chemistry				
Aspartate aminotransferase (AST)				
Normal				
Normal	168 (78.87)	99 (58.93)	69 (41.07)	.023
High				
High	45 (21.13)	18 (40.00)	27 (60.00)	
Alanine aminotransferase (ALT)				
Normal				
Normal	121 (56.81)	81 (66.94)	40 (33.06)	<.001
High				
High	92 (43.19)	36 (39.13)	56 (60.87)	
Blood urea				
Low				
Low	16 (7.51)	13 (81.25)	3 (18.75)	.023
Normal				
Normal	84 (39.44)	50 (59.52)	34 (40.48)	
High				
High	113 (53.05)	54 (47.79)	59 (52.21)	
Serum creatinine				
Normal				
Normal	202 (94.84)	116 (57.43)	86 (42.57)	.002
High				
High	11 (5.16)	1 (9.09)	10 (90.91)	
Lactate dehydrogenase (LDH)				
Normal				
Normal	19 (8.92)	13 (71.18)	6 (28.82)	.171
High				
High	194 (91.08)	104 (53.61)	90 (46.39)	
Creatine kinase (CK)				
Normal				
Normal	187 (87.79)	113 (60.43)	74 (39.57)	<.001
High				
High	26 (12.21)	4 (15.38)	22 (84.62)	

(continued)

Table 4. (continued)

	Total	Females	Males	P-value*
	n (%)			
C-reactive protein (CRP)				
Normal	129 (60.85)	72 (55.81)	57 (44.19)	.689
High	83 (39.15)	44 (53.01)	39 (46.99)	
Serum ferritin				
Low	12 (6.25)	11 (91.67)	1 (8.33)	<.001
Normal	103 (53.65)	68 (66.02)	35 (33.98)	
High	77 (40.10)	24 (31.17)	53 (68.83)	

*P-value was calculated using Chi-square test, and is considered significant if < .05.

Table 5. Logistic Regression for Prediction of Gender Difference in Symptoms and Labs.

	Adjusted logistic regression [^]		
	Odds ratio (OR)	95% Confidence interval (CI)	P-value*
Age group			
46-85	4.51	1.28-15.93	.019
Healthcare worker			
Yes	2.33	0.93-5.88	.072
Cough			
Yes	3.92	1.316-11.68	.014
Loss of smell or taste			
Yes	4.84	1.62-14.43	.005
Monocytes			
Monocytopenia	4.47	0.43-46.20	.208
Monocytosis	0.66	0.20-2.20	.505
Eosinophils			
Eosinocytopenia	2.40	0.67-8.56	.177
Blood urea			
Normal	0.16	0.02-1.28	.084
High	0.14	0.017-1.13	.065
Alanine aminotransferase			
High	0.20	0.07-0.54	.002
Aspartate aminotransferase			
High	0.70	0.20-2.49	.584
Creatine kinase			
High	0.07	0.01-0.38	.002
Serum ferritin			
Normal	0.13	0.01-1.44	.097
High	0.07	0.01-0.90	.041

[^]The regression model was adjusted for age, work, smoking, comorbidities, and immunodeficiency.

*P-value is considered significant if < .05.

Several laboratory markers revealed significant gender differences among the suspected and confirmed COVID-19 participants. Gender differences were significantly related to red blood cells (RBCs), platelets, and monocytes. Also, high levels of AST, ALT, blood urea, serum creatinine, creatine kinase, and serum ferritin were significantly higher in

males. These lab findings render males as the more susceptible party for organ impairment at the time of the presentation despite the health care equity. This was similar to a study conducted by Raimondi,²² where AST and ALT were significantly higher in males than in females and levels of urea and creatinine were significantly lower in female.

A recent study done by Vahidy et al,¹⁸ showed the following eminent laboratory values among hospitalized COVID-19 male patients; lymphocytopenia, thrombocytopenia and elevated levels of pro-calcitonin, aspartate and alanine transaminases, total bilirubin, creatinine, C-Reactive protein, serum ferritin, and venous lactate.

A study conducted by Ancochea et al,²⁰ found that male patients significantly suffered more from lymphopenia and worse renal function than female patients. But on the contrary to our study, they found no significant difference regarding liver function parameters.

These gender differences among the suspected and confirmed COVID-19 participants can be attributed to the higher levels of ACE2 and Trans-membrane Protease Serine 2 (TMPRSS2) in males, as well as suppressive hormonal influences on the immune response.²³

Larger sample population is needed to further investigate the gender difference among COVID-19 patients presenting to primary care or hospital outpatient settings. The several epidemiological studies discussing the gender difference aid in deeper comprehension of the disease course and impact the clinical judgment and case management. This study shed some light on the existent and reported gender differences in presentation of COVID-19 disease. Primary health care physicians should be aware of these differences to guide the diagnosis and subsequent management decisions. As example for this cough in adult females if a late symptom can be considered as alarming, normal lab results in suspected cases especially females should not prohibit further investigations, and males could have disturbed lab results early in disease presentation. These results would help in developing specific and effective therapeutic strategies.

Conclusion

In conclusion, gender-dependent differences were found in COVID-19 suspected and confirmed cases using COVID-19 phone triaging system. Gender is considered an important variable in future COVID-19 research. Confirmed COVID-19 cases aging 46 to 85 years were 4.5 times more likely to be females compared to males. Cough and loss of smell or taste were significantly more common in female patients. Several laboratory markers revealed significant gender differences among the suspected and confirmed COVID-19 participants. Understanding these differences is crucial for primary health care physicians to guide the diagnosis and subsequent management decisions.

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