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

Marwa Mostafa Ahmed1, Amal M. Sayed2, Dina El Abd2, Samar Fares1, Marwa Sayed Mohamed Said1, and Eman Elsayed Sedik Ebrahim1

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

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),
male gender was associated with more severe forms of the disease.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{11}

Other factors that may explain the gender difference in COVID-19 prognosis are the immune suppressive effect of testosterone,\textsuperscript{12} the immune enhancing effect of estrogen,\textsuperscript{13} localization of immune response genes on X Chromosome so higher female immunity may be because of the presence of double X chromosome,\textsuperscript{14} higher expression of pro-inflammatory cytokines in males in acute inflammation which may cause patient death because of cytokine storm\textsuperscript{15} and finally gender specific response to stress.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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 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 1. Characteristics of Participants Suspected for COVID-19 (n = 440). |
|-----------------------------|-------------|------|------|
|                             | Total       | Females | Males | $P$-value* |
| 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) | .799 |
| Healthcare worker           |             |       |       |            |
| No                          | 214 (48.75) | 106 (49.53) | 108 (50.47) | .004 |
| Yes                         | 225 (51.25) | 142 (63.11) | 83 (36.89) | .004 |
| Smoking                     |             |       |       |            |
| No                          | 366 (87.56) | 233 (63.66) | 133 (36.34) | .001 |
| Yes                         | 52 (12.44)  | 4 (7.69) | 48 (92.31) | .001 |
| Presence of comorbidities   |             |       |       |            |
| No                          | 287 (65.23) | 159 (55.40) | 128 (44.60) | .577 |
| Yes                         | 153 (34.77) | 89 (58.17) | 64 (41.83) | .043 |
| Presence of immunodeficiency disorders or drugs |
| No                          | 418 (96.31) | 233 (57.74) | 185 (42.26) | .043 |
| Yes                         | 16 (3.69)   | 13 (81.25) | 3 (18.75) | .043 |
| Symptoms                    |             |       |       |            |
| Fever                       |             |       |       |            |
| No                          | 105 (23.97) | 65 (61.90) | 40 (38.10) | .174 |
| Yes                         | 333 (76.03) | 181 (54.35) | 152 (45.65) | .174 |
| Cough                       |             |       |       |            |
| No                          | 151 (34.47) | 77 (50.99) | 74 (49.01) | .114 |
| Yes                         | 287 (65.53) | 169 (58.89) | 118 (41.11) | .114 |
| Sore throat                 |             |       |       |            |
| No                          | 166 (37.90) | 90 (54.22) | 76 (45.78) | .473 |
| Yes                         | 272 (62.10) | 157 (57.72) | 115 (42.28) | .473 |
| Vomiting or diarrhoea       |             |       |       |            |
| No                          | 249 (56.98) | 138 (55.42) | 111 (44.58) | .673 |
| Yes                         | 188 (43.02) | 108 (57.45) | 80 (42.55) | .673 |
| Malaise                     |             |       |       |            |
| No                          | 70 (15.98)  | 36 (51.43) | 34 (48.57) | .361 |
| Yes                         | 368 (84.02) | 211 (57.34) | 157 (42.66) | .361 |
| 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) | .187 |

*P-value was calculated using Chi-square test, and is considered significant if $<.05$. 
Table 2. Laboratory Characteristics of Participants Suspected for COVID-19 (n = 440).

|                         | Total       | Females     | Males       | P-value*  |
|-------------------------|-------------|-------------|-------------|-----------|
|                         | n (%        |            |             |           |
| **Complete blood count (CBC)** |             |             |             |           |
| **Red blood cells**     |             |             |             |           |
| Erythrocypenia          | 7 (1.64)    | 6 (85.71)   | 1 (14.29)   | .001      |
| Normal                  | 79 (18.54)  | 58 (73.42)  | 21 (26.58)  |           |
| Erythroctysis           | 340 (79.81)| 175 (51.47) | 165 (48.53) |           |
| **Platelets**           |             |             |             |           |
| Thrombocypenia          | 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              | 27 (6.34)   | 18 (66.67)  | 9 (33.33)   | .512      |
| Normal                  | 337 (79.11)| 186 (55.19)| 151 (44.81)|           |
| Leucocytosis            | 62 (14.55)  | 35 (56.45)  | 27 (43.55)  |           |
| **Neutrophils**         |             |             |             |           |
| Neutropenia             | 58 (13.94)  | 31 (53.45)  | 27 (46.55)  | .730      |
| Normal                  | 324 (77.88)| 180 (55.56)| 144 (44.44)|           |
| Neutrophilia            | 34 (8.17)   | 21 (61.76)  | 13 (38.24)  |           |
| **Lymphocytes**         |             |             |             |           |
| Lymphopenia             | 13 (3.07)   | 5 (38.46)   | 8 (61.54)   | .107      |
| Normal                  | 270 (63.68)| 161 (59.63)| 109 (40.37)|           |
| Lymphocytosis           | 141 (33.25)| 72 (51.06)  | 69 (48.94)  |           |
| **Monocytes**           |             |             |             |           |
| Monocytopenia           | 18 (4.25)   | 15 (83.33)  | 3 (16.67)   | .031      |
| Normal                  | 340 (80.19)| 191 (56.18)| 149 (43.82)|           |
| Monocytosis             | 66 (15.57)  | 32 (48.48)  | 34 (51.52)  |           |
| **Eosinophils**         |             |             |             |           |
| Eosinocypenia           | 54 (12.74)  | 32 (59.26)  | 22 (40.74)  | .062      |
| Normal                  | 360 (84.91)| 204 (56.67)| 156 (43.33)|           |
| 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                  | 359 (81.78)| 217 (60.45)| 142 (39.55)| <.001     |
| High                    | 80 (18.22) | 30 (37.50)  | 50 (62.50)  |           |
| Alanine aminotransferase (ALT) |       |             |             |           |
| Normal                  | 271 (61.73)| 176 (64.94)| 95 (35.06)  | <.001     |
| High                    | 168 (38.27)| 71 (42.26)  | 97 (57.74)  |           |
| Blood urea              |             |             |             |           |
| Low                     | 38 (8.66)   | 29 (76.32)  | 9 (23.68)   | <.001     |
| Normal                  | 167 (38.04)| 107 (64.07)| 60 (35.93)  |           |
| High                    | 234 (53.30)| 111 (47.44)| 123 (52.56)|           |
| Serum creatinine        |             |             |             |           |
| Normal                  | 423 (96.36)| 246 (58.16)| 177 (41.84)| <.001     |
| High                    | 16 (3.64)   | 1 (6.25)    | 15 (93.75)  |           |
| Lactate dehydrogenase (LDH) |       |             |             |           |
| Normal                  | 47 (10.71) | 26 (56.52)  | 21 (43.71)  | .525      |
| High                    | 392 (89.29)| 221 (56.38)| 171 (43.62)|           |
| Creatine kinase (CK)    |             |             |             |           |
| Normal                  | 383 (87.24)| 237 (61.88)| 146 (38.12)| <.001     |
| 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 (45.00) | 72 (55.00)|           |
| 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)
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 (1.31–11.68), 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. 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. 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.  

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. While another study found that gastrointestinal symptoms including nausea, vomiting and diarrhea, were significantly more frequent in women than men. 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 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.
| Table 4. Gender Difference in Laboratory Investigations Among COVID-19 Confirmed Cases (n=213). |
|-------------------------------------------------|
| **Total** | **Females** | **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 | 21 (10.34) | 13 (61.90) | 8 (38.10) | .719 |
| Normal | 162 (79.80) | 87 (53.70) | 75 (46.30) |
| Leucocytosis | 20 (9.85) | 10 (50.00) | 10 (50.00) |
| **Neutrophils** | | | |
| Neutropenia | 41 (20.60) | 21 (51.22) | 20 (48.78) | .883 |
| Normal | 146 (73.37) | 80 (54.79) | 66 (45.21) |
| Neutrophilia | 12 (6.03) | 7 (58.33) | 5 (41.67) |
| **Lymphocytes** | | | |
| Lymphopenia | 10 (4.95) | 3 (30.00) | 7 (70.00) | .154 |
| Normal | 143 (70.79) | 83 (58.04) | 60 (41.96) |
| Lymphocytosis | 49 (24.26) | 24 (48.98) | 25 (51.02) |
| **Monocytes** | | | |
| Monocytopenia | 15 (7.43) | 13 (86.67) | 2 (13.33) | .013 |
| Normal | 151 (74.75) | 82 (54.30) | 69 (45.70) |
| Monocytosis | 36 (17.82) | 15 (41.67) | 21 (58.33) |
| **Eosinophils** | | | |
| Eosinocytopenia | 38 (18.81) | 23 (60.53) | 15 (39.47) | .224 |
| Normal | 162 (80.20) | 87 (53.70) | 75 (46.30) |
| 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 | 168 (78.87) | 99 (58.93) | 69 (41.07) | .023 |
| High | 45 (21.13) | 18 (40.00) | 27 (60.00) |
| Alanine aminotransferase (ALT) | | | |
| Normal | 121 (56.81) | 81 (66.94) | 40 (33.06) | <.001 |
| High | 92 (43.19) | 36 (39.13) | 56 (60.87) |
| Blood urea | | | |
| Low | 16 (7.51) | 13 (81.25) | 3 (18.75) | .023 |
| Normal | 84 (39.44) | 50 (59.52) | 34 (40.48) |
| High | 113 (53.05) | 54 (47.79) | 59 (52.21) |
| Serum creatinine | | | |
| Normal | 202 (94.84) | 116 (57.43) | 86 (42.57) | .002 |
| High | 11 (5.16) | 1 (9.09) | 10 (90.91) |
| Lactate dehydrogenase (LDH) | | | |
| Normal | 19 (8.92) | 13 (71.18) | 6 (28.82) | .171 |
| High | 194 (91.08) | 104 (53.61) | 90 (46.39) |
| Creatine kinase (CK) | | | |
| Normal | 187 (87.79) | 113 (60.43) | 74 (39.57) | <.001 |
| 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 COVID-19 participants. Understanding these differences is crucial for primary health care physicians to guide the diagnosis and subsequent management decisions.

Authors’ Note

The work was conducted at Family Medicine Department at Faculty of Medicine- Cairo University- Egypt

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID IDs

Marwa Mostafa Ahmed https://orcid.org/0000-0002-5461-7861
Samar Fares https://orcid.org/0000-0002-3438-1329
Eman Elsayed Sedik Ebrahim https://orcid.org/0000-0003-0267-2129

References

1. World Health Organization. WHO coronavirus disease (COVID-19) pandemic. Accessed May 10, 2021. www.who.int/emergencies/diseases/novel-coronavirus-2019
2. World Health Organization. WHO coronavirus disease (COVID-19) dashboard. 2021. Accessed May 30, 2021. https://covid19.who.int/
3. Hu J, Wang Y. The clinical characteristics and risk factors of severe COVID-19. Gerontology. 2021;67:255-266. doi:10.1159/000513400
4. Klein SL, Morgan R. The impact of sex and gender on immunotherapy outcomes. Biol Sex Differ. 2020;11(1):24.
5. Global Health 50/50. The Sex, Gender and COVID-19 project. University College of London. 2017-2020. Accessed May 15, 2021. https://globalhealth5050.org/covid19/
6. 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.
7. Gao K, Shi X, Wang W. The life-course impact of smoking on hypertension, myocardial infarction and respiratory diseases. Sci Rep. 2017;7(1):4330-4336.
8. Qiu F, Liang CL, Liu H, et al. Impacts of cigarette smoking on immune responsiveness: Up and down or upside down? Oncotarget. 2017;8(1):268-284.
9. Çörtük M, Acat M, Yazici O, et al. Retrospective review of epidemic viral pneumonia cases in Turkey: a multicenter study. Exp Ther Med. 2017;13(4):1431-1437.
10. Bleibtreu A, Bertine M, Bertin C, Houhou-Fidouh N, Visseaux B. Focus on Middle East respiratory syndrome coronavirus (MERS-CoV). Med Mal Infect. 2020;50(3):243-251.
11. Smith JC, Sausville EL, Girish V, et al. Cigarette smoke exposure and inflammatory signaling increase the expression of the SARS-CoV-2 receptor ACE2 in the respiratory tract. Dev Cell. 2020;53(5):514-529.e3.
12. Furman D, Hejblum BP, Simon N, 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):869-874.
13. Taneja V. Sex hormones determine immune response. Front Immunol. 2018;9:1931.
14. Quakkelaar ED, Melief CJ. Experience with synthetic vaccines for cancer and persistent virus infections in nonhuman primates and patients. *Adv Immunol*. 2012;114:77-106.

15. Seki M, Kohno S, Newstead MW, et al. Critical role of IL-1 receptor-associated kinase-M in regulating chemokine-dependent deleterious inflammation in murine influenza pneumonia. *J Immunol*. 2010;184(3):1410-1418.

16. Kvetnanský R, Pacák K, Fukuhara K, et al. Sympathoadrenal system in stress. Interaction with the hypothalamic-pituitary-adrenocortical system. *Ann N Y Acad Sci*. 1995;771:131-158.

17. Lechien JR, Chiesa-Estomba CM, Place S, 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.

18. Vahidy FS, Pan AP, Ahnstedt H, 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.

19. Abate BB, Kassie AM, Kassaw MW, Aragie TG, Masresha SA. Sex difference in coronavirus disease (COVID-19): a systematic review and meta-analysis. *BMJ Open*. 2020;10:e040129. doi:10.1136/bmjopen-2020-040129

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. Al-Lami RA, Urban RJ, Volpi E, Algburi AMA, Baillargeon J. Sex hormones and novel corona virus infectious disease (COVID-19). *Mayo Clin Proc*. 2020;95:1710-1714.

22. Raimondi F, Novelli L, Ghirardi A, 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. doi:10.1186/s12890-021-01455-0

23. Mukherjee S, Pahan K. Is COVID-19 gender-sensitive? *J Neuroimmune Pharmacol*. 2021;16:38-47. doi:10.1007/s11481-020-09974-z