

Gender-based differences in COVID-19

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Abstract

The coronavirus disease (COVID-19) is a novel emerging infectious disease spreading worldwide. To further understand the disease, we compared its clinical characteristics, symptoms and outcomes by gender. In an analysis of public surveillance data of Taiwan from January 21 to April 18, 2020, a total of 398 patients were diagnosed with COVID-19 by the detection of severe acute respiratory syndrome coronavirus 2 in pharynx swabs. We divided the patients into two groups: men and women. The associated data were collected, and multivariate comparisons of radiographic infiltration were conducted to analyse the gender-based differences. The mean incubation period was 5.4 ± 5 days, and the incubation period in men was 3.2 days longer than that in women (8 ± 8.1 vs. 4.8 ± 3 , $p = 0.05$). The male patients with COVID-19 with infiltration in chest X-rays (CXR) were 12 years older than their female counterparts. The mortality rate in the male patients with COVID-19 was 6.4-fold higher than that in the female patients (3.2% vs. 0.5%, $p < 0.05$). The patients with comorbidities of diabetes mellitus and hypertension were vulnerable to infiltration in CXR and the patients with COVID-19 who had infiltration in CXR easily ended up with intubation, intensive care unit admission and mortality. Moreover, female patients with COVID-19 who had fever, cough and dyspnoea were susceptible to infiltration in CXR. Irrespective of whether the cases were imported female from Europe, America or Asia, indigenous male, the factors associated with death in patients with severe COVID-19 were male sex, elderly, female with fever, cough, dyspnoea and DM.

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Introduction

On December 31, 2019, the World Health Organization (WHO) country office in China was informed of the detection of atypical pneumonia in Wuhan, a city in the Hubei province. The initial name given to the disease was 2019-nCoV which was then revised to coronavirus disease (COVID-19) on February 11, 2020. The COVID-19 outbreak is a worldwide concern as the

novel coronavirus has already spread in 188 countries/regions and can cause atypical pneumonia, respiratory failure and death. The Global Initiative on Sharing Avian Influenza Data is modeled on guidelines for sharing data of large-scale biological research [1]. According to the Global Initiative on Sharing Avian Influenza Data, until May 27, 2020, there were 5,626,047 confirmed COVID-19 cases and 351,815 deceased cases worldwide.

Taiwan had abundant experience of a successful fight against severe acute respiratory syndrome (SARS) in 2003. On January 21, 2020, the first case of COVID-19 imported by airplane was found in Taiwan, and on the same day, the government appealed

to the public to stop traveling to Wuhan. Subsequently, on January 23, 2020, fever patients must be arranged to go to an outdoor fever screening station for screening examination when febrile patients visiting our emergency department to prevent in-hospital contamination. If the patients had a history of flying from Wuhan and China, we performed COVID-19 viral testing and treated them in accordance with the patient's condition immediately in a negative pressure isolation room if the test result was positive. The setting up of our outdoor fever screening station was eight days before the WHO declaring that COVID-19 met the criteria for a "Public Health Emergency of International Concern" on January 31, 2020.

On February 2, 2020, the Taiwan Ministry of Education postponed the new semester until February 25, 2020. On February 10, 2020, all the passengers who had traveled to China, Hong Kong and Macau or transited these countries and entered Taiwan were quarantined for 14 days. During these 14 days, strict enforcement of home quarantine and home isolation were performed by the people themselves and laws of fines for non-compliance were announced by the government. If the people had fever, they could dial the special line of 1922 after which emergency medical technicians wearing personal protection equipment drove them to an emergency department for professional fever screening. Thus, the control of the epidemic was gradually processed to make it drip-proof. In the past, several studies have implied that male sex, old age and the presence of comorbidities were risk factors for mortality [2–5]. We further examined the patients with COVID-19 with an aim to understand the differences between men and women in terms of clinical characteristics, symptoms and outcomes.

Materials and methods

An analysis of the public surveillance data in Taiwan from January 21 to April 18, 2020, revealed that 398 patients were diagnosed with COVID-19 by the detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) via real-time reverse transcription polymerase chain reaction (real-time RT-PCR) test using pharynx swabs.

We divided the patients into two groups: men and women. The associated objective data collected for statistical analysis included importation and travel history, days until symptom occurrence, days between symptom occurrence and confirmation of the diagnosis, lung infiltration on chest radiographs (CXR) or computed tomographs, intensive care unit (ICU) admission, mortality and symptoms including fever and lung infiltration. Subjective data included shortness of breath, rhinorrhea, cough, nasal stuffiness, headache, sore throat, anosmia, dysgeusia, muscle pain, general malaise and chest pain described by the patients.

We also performed multivariate comparisons of radiographic infiltration by gender. The age, origin of transmission, symptoms, comorbidities and outcomes were also compared with determine the gender-based differences.

For statistical analyses, continuous data are expressed as mean \pm standard deviation (SD) and compared using Student's *t*-test. On the other hand, categorical data are described as a percentage (followed by the number of patients represented). Furthermore, the χ^2 test was used to analyse categorical data. All the statistical tests were two-tailed, and statistical significance was defined as $P < 0.05$. All the statistical analyses were conducted using IBM SPSS Statistics for Windows, Version 25.0, IBM Corp., Armonk, NY, USA.

Results

In total, the data of 398 patients with COVID-19, from January 21 to April 18, 2020, were collected. The mean age was 38.6 ± 16.8 years (mean \pm SD), and the male:female ratio was approximately 0.87:1 (men, $n = 187$; women, $n = 211$). The mean incubation period (IP) was 5.4 ± 5 days, and the IP in men was 3.2 days greater than that in women (8 ± 8.1 vs. 4.8 ± 3 , $p = 0.05$) (Table 1).

In the indigenous cases and those imported from Europe, America, Asia, Africa and Oceania, the number of cases were equal in both genders and there was no obvious difference in the case numbers indigenous or imported anywhere ($p = 0.439$ and 0.913). The incidence of CXR infiltration in COVID-19 patients ranged from 7.6% to 9.6% in females and males, respectively, with a mean of 8.5% and there was no statistical difference between the two sexes.

In the multivariate comparisons of X-ray infiltration by gender, we observed that the male patients with COVID-19 having CXR infiltration were 12 years older than the female patients with COVID-19. The patients with comorbidities of diabetes mellitus (DM) and hypertension were vulnerable to CXR infiltration, and the patients with COVID-19 who had CXR infiltration eventually ended up with intubation, ICU admission and mortality. Moreover, female patients with COVID-19 who had fever, cough and dyspnoea were susceptible to CXR infiltration (Table 2). The mortality rate in the male patients with COVID-19 was 6.4-fold higher than that in the female patients (3.2% vs. 0.5%, $p < 0.05$).

There was no gender-based differences in the presentation of symptoms such as cough, fever, sore throat, rhinorrhea, malaise, nasal stuffiness, muscle pain, anosmia, headache, diarrhea, dysgeusia, chest pain, dyspnoea and also the asymptomatic state ($p = 0.568, 0.726, 0.399, 0.083, 0.226, 0.234, 0.170, 0.204, 0.148, 0.832, 0.882, 0.937, 0.581, 0.318$, respectively) [Fig. 1].

TABLE 1. Comparisons of COVID-19-infected patients by gender

COVID-19 patients	Male 187 (47)	Female 211 (53)	Total (398)	p-Value
Age (years)	39.3 ± 17.0	37.9 ± 16.6	38.6 ± 16.8	0.711
Day to symptom (days)	8 ± 8.1	4.8 ± 3.0	5.4 ± 5.0 (101)	0.05
Symptom to diagnosis (days.)	7.4 ± 5.6	7.5 ± 5.6	7.5 ± 5.6 (374)	0.193
Indigenous n (%)	25 (13.4)	29 (13.7)	54 (13.6)	0.913
Imported: Europe	78 (41.7)	88 (41.7)	166 (41.7)	0.439
Imported: America	41 (21.9)	54 (25.6)	95 (23.9)	
Imported: Asia	32 (17.1)	36 (17.1)	68 (17)	
Imported: Africa	9 (4.8)	3 (1.4)	12 (3)	
Imported: Oceania	2 (1.1)	1 (0.5)	3 (0.8)	
Test at airport	49 (26.2)	58 (27.5)	107	0.773
Mortality (%)	6 (3.2)	1 (0.5)	7 (1.8)	0.038*
ICU admission (%)	3 (1.6)	0 (0)	3 (0.8)	0.065
Other diseases				
DM (%)	2 (1.1)	0 (0)	2 (0.5)	0.132
HTN (%)	3 (1.6)	1 (0.5)	4 (1.0)	0.259
Uremia (%)	1 (0.5)	0 (0)	1 (0.3)	0.288
Lung infiltration (%)	18 (9.6)	16 (7.6)	34 (8.5)	0.467
Symptoms				
Cough (%)	80 (42.8)	90 (42.3)	170 (42.7)	0.568
Fever (%)	73 (39.0)	86 (40.8)	159 (39.9)	0.726
Sore throat (%)	54 (28.9)	53 (25.1)	107 (26.9)	0.399
Rhinorrhoea (%)	39 (20.1)	60 (28.4)	99 (24.9)	0.083
Malaise (%)	30 (16.0)	25 (11.8)	55 (13.8)	0.226
Nasal stuffiness (%)	20 (10.7)	31 (14.7)	51 (12.8)	0.234
Muscle pain (%)	27 (14.4)	21 (10.0)	48 (12.1)	0.170
Anosmia (%)	18 (9.6)	29 (13.7)	47 (11.8)	0.204
Headache (%)	20 (10.7)	14 (6.6)	34 (8.5)	0.148
Diarrhoea (%)	14 (7.5)	17 (8.1)	31 (7.8)	0.832
Dysgeusia (%)	10 (5.3)	12 (5.7)	22 (5.5)	0.882
Chest pain (%)	9 (4.8)	10 (4.7)	19 (4.8)	0.937
SOB (%)	6 (3.2)	9 (4.3)	15 (3.8)	0.581
Asymptomatic (%)	10 (5.3)	7 (3.3)	17 (4.3)	0.318

All data are in form of n (%).
DM, diabetes mellitus; SOB, shortness of breath.

TABLE 2. Multivariate comparisons in X-ray infiltration by gender

X-ray infiltration	Male (n = 18) (9.6)	Female (n = 16) (7.6)	All 34 (8.5)	P value
Age (years)	57.8 ± 17.1	45.9 ± 19.2	52.2 ± 18.8	0.001 ^a
Imported	11 (61.1)	13 (81.3)	24 (70.6)	0.002 ^a
Indigenous	7 (38.9)	3 (18.8)	10 (29.4)	0.009 ^a
Incubation period	4.0 ± 2.9	5.0 ± 5.3	4.3 ± 3.5	0.095
Symptoms to diagnosis	9.9 ± 8.9	9.7 ± 9.3	9.8 ± 9.0	0.002 ^a
Diabetes mellitus	2 (11.1)	0 (0)	2 (5.9)	0.007 ^a
Hypertension	2 (11.1)	0 (0)	2 (5.9)	0.038 ^a
Uremia	1 (5.6)	0 (0)	1 (2.9)	0.085
Fever	12 (66.7)	11 (68.8)	23 (67.6)	0.001 ^a
Cough	9 (50)	11 (68.8)	20 (58.8)	0.027 ^a
Headache	3 (16.7)	3 (18.8)	6 (17.6)	0.057
Muscle pain	5 (27.8)	2 (12.5)	7 (20.6)	0.098
Throat pain	2 (11.1)	6 (37.5)	8 (23.5)	0.408
Rhinorrhoea	7 (38.9)	4 (25)	11 (32.4)	0.196
Chest pain	1 (5.6)	1 (6.3)	2 (5.9)	0.496
Diarrhoea	2 (11.1)	0 (0)	2 (5.9)	0.493
Dyspnoea	3 (16.7)	4 (25)	7 (20.6)	<0.001 ^a
Anosmia	1 (5.6)	2 (12.5)	3 (8.8)	0.410
Malaise	4 (22.2)	3 (18.8)	7 (20.6)	0.172
Intubated	2 (11.1)	0 (0)	2 (5.9)	0.020 ^a
ICU admission	2 (11.1)	0 (0)	2 (5.9)	0.020 ^a
Mortality	4 (22.2)	1 (6.3)	5 (14.7)	<0.001 ^a
Asymptomatic	0 (0)	0 (0)	0 (0)	0.212

ICU, intensive care unit.
^aStatistical significance.

Discussion

Gender distribution and ages of patients with COVID-19

The COVID-19 outbreak involved various races worldwide and presented different clinical pictures. In accordance with the majority of reports from Asia, COVID-19-affected males more

than females with a male:female ratio of 1.1—1.93:1 [5–8]. Contrastingly, in Europe, COVID-19-affected females more with a male:female ratio of 0.47:1 [9,10]. In an Italian study (n = 783), the male:female ratio of patients with COVID-19 was 2.1:1; therefore, it affected more men than women [11]. In early February 2020, we knew that COVID-19-affected males more commonly, unlike SARS that was female predominant, and the preferred age was estimated to be approximately 20 years

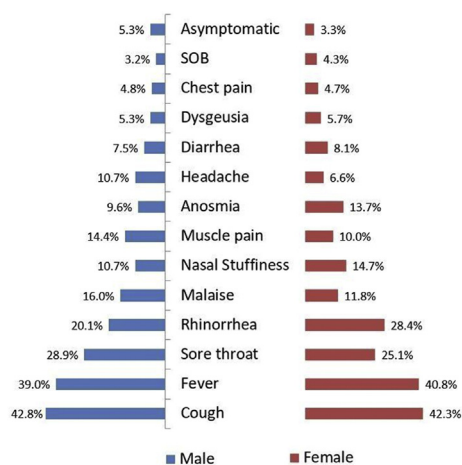


FIG. 1. List of symptoms in patients with COVID-19 classified by gender.

greater than that of SARS [6]. Furthermore, more overseas students who traveled from Europe and America lowered the mean age of COVID-19 cases owing to their young age.

In our study, the mean age of the 398 patients with COVID-19 was 38.6 ± 16.8 years, and there was no significant difference between male and female patients with respect to age (39.3 vs. 37.9, $p = 0.711$). This result corresponded with a report from Europe ($n = 1420$) where it was observed that the mean age of patients with COVID-19 was 39.2 ± 12.1 years [9]. Age is the strongest risk factor for hospital admission in accordance with a report from the United States ($n = 5279$). Other risks factors include male sex, a body mass index >40 kg/m², chronic kidney disease and heart failure [12].

On May 26, 2020, 7 patients died of COVID-19 in Taiwan, and the mean age of expired patients was 62.1 ± 15 years, which was 23.5 years greater than the mean age of all patients with COVID-19 (38.6 years). This result corresponded to that of a report from Wuhan, China, where the median age of deceased patients was 68 years [2]. Another report published on May 7, 2020, reported a total of 50 death cases with a median age of 70 years [13]. Therefore, the elderly is at risk for COVID-19 mortality. This result is comparable with those of the majority of studies that reported that male sex, old age and comorbidities are risk factors for mortality in patients with COVID-19 [2,5].

Longer incubation period of COVID-19 in men

The majorly reported IP in the previous report of COVID-19 was approximately 6 days. In a report from Qingdao City on March 31, 2020, the mean IP was 6.28 days [10]. Another report from Wuhan ($n = 104$) reported the median IP to be 6 days [14]. On April 29, 2020, in a report from Shanghai ($n = 333$), the median IP was found to be longer at 7.2 days [15]. In our study, the mean IP of COVID-19 was 5.4 ± 5 days (range,

1—27) and the IP in the male patients with COVID-19 was 3.2 days greater than that in the female patients (8 vs. 4.8, $p = 0.05$).

Risk factors for CXR infiltration in patients with COVID-19

Approximately half of the patients with COVID-19 (46.4%) revealed infiltration in their CXR [8]. In the past, no reports have mentioned the risk factors for CXR infiltration in patients with COVID-19. In Taiwan, more indigenous male and imported female COVID-19 patients had lung infiltrations. We found that male patients with COVID-19 with CXR infiltration were 12 years older than their female counterparts (57.8 vs. 45.9). The patients with comorbidities of DM and hypertension were vulnerable to CXR infiltration, and the patients with COVID-19 who had infiltrated CXRs easily ended up with intubation, ICU admission and mortality in our study. Moreover, female patients with COVID-19 who had fever, cough and dyspnoea were susceptible to CXR infiltration.

Symptoms of COVID-19 by gender

In our study, the most common symptoms of COVID-19 were cough (42.7%), fever (39.9%), pain in the throat (26.9%) and rhinorrhea (24.9%), without statistical gender-based differences. This result is comparable with that of a report from Korea on April 6, 2020, that reported cough, throat pain and fever to be the most common symptoms in patients with COVID-19 [8].

In a report from Europe published on April 30, 2020, the most common symptoms were headache (70.3%), anosmia (70.2%), nasal stuffiness (67.8%), cough (63.2%), fatigue (63.3%), muscle pain (62.5%), rhinorrhea (60.1%), gustatory dysfunction (54.2%), sore throat (52.9%) and fever (45.4%) [9]. In Taiwan, COVID-19 cases were imported from Europe (41.7%), America (23.9%), Asia (17%), Oceania (0.8%) and some were indigenous cases (13.6%). Therefore, the presented symptoms vary in reports based on only Europe.

In Europe, young patients more frequently had ear, nose and throat complaints, whereas elderly patients often presented with fever, fatigue and loss of appetite. Loss of smell, headache, nasal stuffiness and fatigue were more prevalent in female patients [9].

In our study, asymptomatic patients with COVID-19 accounted for 4.3%, which corresponds with a report from Wuhan (4.8%) [14].

Outcomes and prognosis of COVID-19 by gender

The patients with COVID-19 having DM showed a higher rate of receiving mechanical ventilator support, intensive care admission (2.3-fold) and higher mortality (2-fold). Eight-day-longer hospital stays were noted in patients with DM and COVID-19 than in those without DM [16,17].

Numerous studies have reported that male sex, old age, lymphopenia, high lactate dehydrogenase levels, myo-cardiac injury, hypoalbuminemia and hyperglycemia were associated with death in patients with severe COVID-19 [2–5,7,17–19]. On May 16, 2020, severe obesity, old age and male sex were found to be independently associated with higher in-hospital mortality, and worse in-hospital outcomes were concluded from a study in New York [20].

The mean duration of COVID-19 symptoms in mild to moderate cured patients was 11.5 ± 5.7 days [9]. The median duration between the first symptoms and death was 12.5 days, whereas the median duration between admission and death was 8.50 days [21]. In the clinical course of COVID-19, 7 to 13 days after illness onset is the critical stage [19].

On May 26, 2020, 7 patients died of COVID-19 in Taiwan, showing a mortality rate of 1.6% (7/441). This result corresponds to a report from Wuhan on April 12, 2020 (1.1%) [3]. Of the seven deceased patients with COVID-19, 85.7% (6/7) were men and only one was a woman. The mortality rate from the report of Wuhan ($n = 104$) was lower (0.96%) [14].

Limitations

This was a retrospective study and data were gathered from public surveillance information disclosed by the Taiwan Centers for Diseases Control. Some parameters are lacking, and some data were missing. We have endeavored to describe the whole view of cases with the limited data.

Conclusions

The male patients with COVID-19 with infiltration in CXR were older than female patients. The patients with comorbidities of DM and hypertension were vulnerable to CXR infiltration, and the patients with COVID-19 who had infiltrated CXR easily ended up with intubation, ICU admission, and mortality in our study. Moreover, female patients with COVID-19 who had fever, cough and dyspnoea were more susceptible to infiltration in CXR than those without these symptoms. Irrespective of whether the cases were imported female from Europe, America or Asia, indigenous male, the factors associated with death in patients with severe COVID-19 were male sex, elderly, female with fever, cough, dyspnoea and DM.

Ethical approval committee

This study that does not require ethical approval and the analysis of data sets, either open source or obtained from other researchers, where the data are properly anonymised and informed consent was obtained at the time of original data collection.

Transparency declaration

We declare there is no conflict of interest statement.

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None.

Author contributions

Y-J Su designed study, gathered data, wrote the draft, revised and corresponded.

K-C Kuo and

T-W Wang gathered data.

C-W Chang contributed to statistical analysis and figures presentation.

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