

**Original article****Epidemiological Assessment of COVID-19 Clinical Symptoms and Its Associated Factors from Banten Districts: The Role of Gender Aspects**

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**Abstract**

**Objectives:** The symptoms of COVID-19 resemble those of a variety of mild to severe clinical conditions. Having epidemiological knowledge of the clinical symptoms of COVID-19 and associated factors may help health workers to diagnose and manage the disease. Assessment of COVID-19's clinical symptoms is therefore necessary to support health workers in Banten, Indonesia. **Materials and Methods:** In this descriptive cross-sectional study, we purposively analysed 1492 medical records from our online COVID-19 database. All data were analysed in a consecutive manner and were shown as percentages or significances. **Results:** Medical records revealed that 577 patients (39%) were male and 915 (61%) were female. Our sample contained 106 patients (7%) who tested positive for COVID-19. Among these 106 patients, 70 were asymptomatic (66%) while the rest (34%) had single or multiple clinical symptoms. The most common symptom was fever (16%), followed by cough (15%), fatigue (11%), headache (11%), dysphagia (10%), rhinorrhoea (8%), nausea (7%), dyspnoea (4%) and diarrhoea (2%). Subsequently, gender differences were found to be significantly associated with positive cases ( $p < 0.05$ ), the appearance of clinical symptoms ( $p < 0.05$ ), and decision whether to hospitalize or self-isolate ( $p < 0.05$ ). **Conclusion:** Fever, cough and fatigue predominated in the COVID-19 symptoms reported by our patients. Additionally, gender differences should be carefully considered in developing better management processes.

**Keyword:** COVID-19, sex characteristics, fever, cough, cross-sectional studies

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**Introduction:**

On March 11, 2020, the World Health Organization announced coronavirus disease (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as being a pandemic.<sup>1</sup> Since then,

the COVID-19 pandemic has become global, and its impacts have affected quality of life worldwide. Adding to the challenges for infection control and disease prevention, the symptoms of COVID-19 infection can vary from being entirely absent to

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being extremely serious.<sup>2-10</sup>

The symptoms also resemble many other disease symptoms, meaning that differentiating the clinical symptoms of COVID-19 from those of other respiratory diseases symptoms can be challenging. Fever, cough, and fatigue were the major complaints appearing in COVID-19 positive patients.<sup>11</sup> Though these symptoms were similar to those of other respiratory diseases, when these symptoms presented together, they had sensitivity of at least 50% as COVID-19 symptoms.<sup>12</sup> Therefore, fever, cough and fatigue were considered as 'red flags' for COVID-19, meaning the likelihood of a COVID-19 diagnosis increased when these symptoms were present.<sup>12</sup>

Furthermore, specific symptoms such as anosmia, as a pathognomonic symptom for COVID-19, was reported to have sensitivity of below 50% as a COVID-19 symptom.<sup>12</sup> Some symptoms were also claimed to be related to severity and mortality. In brief, gastrointestinal, and respiratory symptoms were closely related to severe COVID-19 outcomes, while pneumonia and end organ failure were significantly associated with higher mortality.<sup>11</sup> Additionally, recent evidence has reported that many factors, including older age, male gender, diabetes mellitus and hypertension comorbidity, play significant roles in COVID-19 mortality.<sup>11</sup>

Using our laboratory online database, this study aimed to gather the clinical symptoms that were reported by our COVID-19 positive patients and to analyse the associated factors involved in COVID-19 outcomes. Through this study we plan to develop a better approach to COVID-19 management.

## Methods and Materials:

### Design of study

A cross-sectional study of secondary data was carried out using the laboratory online database of our university's COVID-19 biomolecular laboratory (C.094 Laboratorium Terpadu Fakultas Kedokteran Universitas Islam Negeri Syarif Hidayatullah Jakarta). A cohort method was used over a three-month period. Positive COVID-19 patients in the database were confirmed by real-time PCR assay. All data from the laboratory online database were treated in accordance with the Helsinki Declaration and ethically approved by our Ethics Committee Faculty of Medicine Universitas Islam Negeri Syarif Hidayatullah with the registry number of B-005/F12/KEPK/TL.00/02/2021.

### Data sampling

All data in the laboratory online database of the COVID-19 biomolecular laboratory (C.094 Laboratorium Terpadu Fakultas Kedokteran Universitas Islam Negeri Syarif Hidayatullah Jakarta) were purposively included in this study (n=1492). Incomplete data were excluded.

### Statistical analysis

From the laboratory online database, epidemiological data were generated directly as descriptive data in number and percentage format. Further statistical analysis was performed using non-parametric chi-squared testing wherever applicable. Probability value of less than 0.05 ( $p < 0.05$ ) was considered as significant.

### Ethical Approval:

This research proposal was accepted by the Ethics Committee Faculty of Medicine Universitas Islam Negeri Syarif Hidayatullah with the registry number of B-005/F12/KEPK/TL.00/02/2021

### Results:

#### General characteristics of the data

As depicted in Table 1, 1492 data items were collected from our COVID-19 biomolecular laboratory online database over a three-month period. Most of the patients registered in the laboratory online database were female (61%), almost twice the proportion of male patients (39%). Positive cases were confirmed by RT-PCR assay in 106 patients (7%).

**Table 1.** General characteristics of patients' samples (n=1492)

Subjects	Number	Percentages
Gender		
Male	577	39
Female	915	61
RT-PCR Results		
Negative	1386	93
Positive	106	7

#### General characteristic of data from positive patients

The general characteristics of our positive patients are displayed in Table 2. Seventy-five percent of the positive samples came from government or private hospitals and the rest came from government laboratories (25%). Female patients predominated in the positive cases (72%) compared to the male

patients (28%). Most of the patients (65%) stated that they did not have any contact with positive patients prior to the COVID-19 diagnosis while the rest (35%) stated that they were infected from their close family environment.

**Table 2.** General characteristics of data from positive patients (n=106)

Positive patients	Number	Percentages
Sources of samples		
Hospitals	80	75
Government	26	25
Laboratory		
Gender		
Male	30	28
Female	76	72
Patient contact		
Yes	37	35
No	69	65
Comorbidity		
Cardiovascular	3	3
Diabetes mellitus	3	3
Asma	1	1
Clinical outcome		
Symptomatic	36	34
Asymptomatic	70	66
Clinical symptoms (n=36)		
Fever	17	47
Cough	16	44
Fatigue	12	33
Headache	12	33
Sore throat	11	31
Rhinorrhea	9	25
Nausea	7	19
Dyspnea	4	11
Diarrhea	2	6
Treatment		
Hospitalization	22	21
Self-isolation	84	79

Seven positive patients (7%) had histories of comorbidities including hypertension or cardiovascular disease (3%), diabetes mellitus (3%) and asthma (1%). Interestingly, 66% of the positive patients confirmed that they did not experience any symptoms, while the rest experienced various symptoms including fever (47%), cough (44%), fatigue (33%), headache (33%), sore throat (31%), rhinorrhoea (25%), nausea (19%), dyspnoea (11%) and diarrhoea (6%) (Table 2). Fever, cough, fatigue, and headache were the most common symptoms experienced by the positive patients. Reflecting the

predominance of asymptomatic patients and those with mild symptoms, only 21% of patients were referred for hospitalization, while 79% preferred to self-isolate in their own homes.

**Factors associated with positive patients**

As depicted in Table 3, positive patients were predominantly female (5% of the total sample), more than twice as many as their male counterparts (2%), with this difference reaching statistical significance.

**Table 3.** Factors associated with positive patients (n=106)

	Factors	Number (%)	Significances
Male	Positive	30 (2)	p=0.02
	Negative	547 (37)	
Female	Positive	76 (5)	p=0.03
	Negative	839 (56)	
Male	Symptomatic	15 (14)	p=0.50
	Asymptomatic	15 (14)	
Female	Symptomatic	21 (20)	p=0.07
	Asymptomatic	55 (52)	
Male	Contact	9 (8)	p=0.01
	Non-contact	21 (20)	
Female	Contact	28 (26)	p=0.01
	Non-contact	48 (46)	
Male	Comorbid	4 (4)	p=0.07
	Non-comorbid	26 (25)	
Female	Comorbid	3 (3)	p=0.01
	Non-comorbid	73 (69)	
Male	Hospitalization	11 (10)	p=0.01
	Self-isolation	19 (18)	
Female	Hospitalization	11 (10)	p=0.01
	Self-isolation	65 (62)	

Significant difference was also observed in the ratio between symptomatic and asymptomatic male and female patients. The ratio of male patients in these categories was 1:1, while in the female patients the ratio was 1:2.6. From these ratios it is evident that female patients tended more frequently to be asymptomatic than their male counterparts. Additionally, positive cases in the male and female patients were not related to prior contact or previous history of disease comorbidity (Table 3). For the treatment decision, the ratio of hospitalization to self-isolation in the male patients was 1:1.8 while in the female patients this ratio was 1:6.2, with the difference reaching statistical significance. Based on this result, it can be seen that male patients tended

to be more frequently hospitalized than their female counterparts regardless of the aetiology of the decision (Table 3).

### Discussion:

Significant findings of our results were as follows: (1) fever, cough, fatigue and headache predominated the clinical symptoms of COVID-19 positive cases from our laboratory online database; (2) female patients significantly predominated positive cases (72%) compared to male patients (28%); (3) of the COVID-19 positive patients, 66% did not experience any clinical symptoms with female patients more frequently being asymptomatic; and (4) more male patients tended to be hospitalized compared to female patients.

The clinical symptoms of COVID-19, both respiratory and non-respiratory, resemble those of other diseases, and so knowledge of COVID-19's clinical symptoms as related to specific areas or countries is essential for better management of COVID-19 cases. Our results show that most of the positive patients in our sample (66%) were asymptomatic and did not experience any symptoms during their positive phase. Consistent with these findings, 79% of these positive patients were recommended to self-isolate and only 21% were hospitalized as a result of serious disturbances in their respiratory function. Two studies from Japan recently reported that the proportions of asymptomatic COVID-19 patients in their study populations were 30.8% and 51.7%.<sup>13,14</sup> Asymptomatic COVID-19 patients play an important role in the rapid spreading of COVID-19, since asymptomatic patients can be carriers of the SARS-CoV-2 virus without knowing they have the disease. Management of asymptomatic COVID-19 patients has thus become an important challenge in the eradication of COVID-19; because they have no clinical symptoms and/or have poor prevention awareness, they rarely seek medical advice, even though they actively spread the infection.<sup>15</sup> Therefore, finding asymptomatic positive patients through regular tracing should be a key point for early prevention of COVID-19 cases in the community.<sup>15</sup> Our laboratory online database has shown that the most common symptoms in our symptomatic patients (34%) were fever, cough, fatigue and headache. Generally, these symptoms may resemble many other diseases, such as common cold, acute upper respiratory infection, ear, and nose infection and so on, making it difficult to rule in or out a diagnosis of COVID-19. However, cough has been reported as having 67.4% sensitivity as a

COVID-19 symptom and fever as having sensitivity of 53.8%.<sup>12</sup> Anosmia has sensitivity of less than 50%, however specificity raises this to more than 90%.<sup>11</sup> Collectively, fever, cough and anosmia may be useful as red flag symptoms of COVID-19 in regard to their sensitivities and specificities. These red flag symptoms may be useful in preliminary screening to identify people who need further testing for COVID-19.

Interestingly, we found that gender differences are significantly associated with positive cases in patients. Of the 7% of positive cases of COVID-19 in the sample, female patients significantly predominated (5% of the sample). Some reported evidence has shown that male patients predominate in positive cases; however, in some of the East Asia and European studies, females predominate in positive cases, especially in areas where they actively participate in the community.<sup>16-19</sup> Consistent with previous findings, our results show that females tend to be the more vulnerable subjects of the COVID-19 pandemic. One possible explanation is related to the female proportion of the population being greater than the male, thus translating into greater risk of COVID-19 exposure. Consequently, gender disparities significantly contribute to positive cases of COVID-19 and appear differentially among countries. Specific approaches based on gender data should be considered to improve management of COVID-19. Additionally, the ratio between asymptomatic and symptomatic presentation was 1:2.6 in the female patients compared to 1:1 in the male patients, with these differences reaching statistical significance. Taken together, positive cases were predominated by females who tended to be asymptomatic, suggesting that female positive patients could play a significant role as carriers in the rapid spreading of COVID-19. Therefore, COVID-19 management should give more attention to female patients in the tracing of COVID-19 cases.

From the aspect of treatment decision, gender differences also make significant contributions. The ratio between hospitalization and self-isolation was 1:1.8 in the male positive patients compared to 1:6.2 in the female positive patients. Therefore, the males tended to be more frequently hospitalized than the female patients. These findings are consistent with our previous findings that female positive patients tend to be asymptomatic and so do not need hospitalization. One recent meta-analysis reported that male COVID-19 patients tended to

have more severe symptoms compared to female patients.<sup>11</sup> Moreover, fatality rate was higher in male patients, hypothetically due to prior cardiovascular disease or smoking history<sup>20</sup> and the male patients' specific health behaviours.<sup>21</sup> COVID-19 with lung involvement was also prominent in male patients than in the female patients in one study at Dhaka City, Bangladesh.<sup>22</sup> Consistent with previous data, the male COVID-19 patients tended to stay longer in hospital, recovering more slowly than the female patients. Male COVID-19 patients were also twice as likely to die from COVID-19 as female patients.<sup>23,24</sup> Several possible explanations of this can be put forward based on the general protective mechanisms in female patients in facing COVID-19 infection. The first of these protective mechanisms derives from better female resistance to viral, bacterial, fungal, and parasitic infections reflecting higher innate immune response and higher expressions of inflammatory and cytotoxic proteins.<sup>16,25-27</sup> A second possible protective mechanism derives from the well-documented effect of estrogen as a stimulator for immune response through the proliferation of T-cells, increased toll-like receptor 4 (TRL4) expression and increased humoral responses from B lymphocytes and antibodies.<sup>16,25,28</sup> Taken together, our results show that the female patients have a greater opportunity to be infected by SARS-CoV-2 virus since their population is bigger than the male patients.

Moreover, female positive patients tend to be asymptomatic and so act as potent carriers of

COVID-19, spreading the virus to their families and communities. Fortunately, most of the female positive patients did not need hospitalization. Conversely, even though fewer positive cases were observed among male patients, male positive patients tended to be symptomatic, more severely affected and more frequently hospitalized.

### Conclusion

The present study indicates that greater attention should be given not only to the wide spectrum of COVID-19 clinical symptoms but also to the central role of gender differences in response to COVID-19.

**Conflict of interest:** None declared

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Data gathering: FRS, EAS, CA, AAH, ASS, DA, MS, SNAJ

Data analysis and consultation: FRS, EAS, CA, AAH, ASS, DA, MS, SNAJ

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