Introduction

By the beginning of August 2021, the SARS-CoV-2 that led to the coronavirus disease 2019 (COVID-19) had infected 202 million people and killed 4 million (the World Health Organization, 2021b) [17]. As of the latest data, Indonesia was heavily affected by the virus, with 12,444 new deaths (the World Health Organization, 2021b) [17].

Early detection of an infected individual is the main challenge to control the disease and cut off the viral transmission (Gao et al., 2021) [4]. To date, COVID-19 is best diagnosed with SARS-CoV-2 nucleic acid detection by quantitative reverse transcription-polymerase chain reaction (q-RT-PCR) (Banko et al., 2021) [2]. Targeted q-RT-PCR test in a community should increase the probability of COVID-19 case finding, especially in a prevalent population (Sen-Crowe, Mckenney and Elkbull, 2021) [11].

The COVID-19 clinical manifestations are highly variable from mild to critical. The most predictive symptoms were dyspnea, cough, and fever (Jain and Yuan, 2020) [6]. However, some patients with positive q-RT-PCR confirmation have no typical clinical symptoms or signs. These asymptomatic cases mostly have the potential to be a source of new outbreaks (Teherán et al., 2020; and Ralli et al., 2021) [13]. Therefore, it is essential to find other predictive factors that contribute to targeting the asymptomatic COVID-19 cases. The finding should help the health workers and policymakers to control viral transmission efficiently, especially in limited resources.

Several studies have reported age and sex as the predictive factors for incidence, clinical manifestation, and fatality rates of COVID-19 (Ghisolfi et al., 2020; Mesas et al., 2020; and O’Brien, Du, and Peng, 2020) [5], [8], [9]. Meanwhile, none of these findings adequately evaluate the age and sex differences in

Age and Sex Differences in COVID-19 Clinical Symptom: Analysis of 19,588 Indonesian Cases

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Abstract

BACKGROUND: Asymptomatic COVID-19 cases are potential for SARS-CoV-2 outbreaks source, yet the feasible predictive factors are unclear.

AIM: Our study aimed to determine the age and sex differences in the presence of COVID-19 clinical symptoms at the initial diagnosis.

METHODS: We examined the results of individual first-time quantitative reverse transcription-polymerase chain reaction (q-RT-PCR) of 19,588 COVID-19 positive cases registered at the Center for Diagnostic and Research on Infectious Disease Laboratory (PDRPI Lab), Faculty of Medicine, Universitas Andalas, Padang, Indonesia, from April 2020 to December 2020. Asymptomatic cases were those who had no symptoms at the initial confirmation while symptomatic had. The differences of age (classified into five age groups) and sex (female or male) were evaluated in both cases to see their significance.

RESULTS: A total of 12,790 (65.30%) of COVID-19 cases were asymptomatic. The COVID-19 patients had average age (mean ± SD) of 37.12 ± 17.22 years old (y.o.). Younger adults (20–39 y.o.; 42.01%; average age (mean ± SD) 29.51 ± 5.52 y.o.) were the most affected, followed by adults (40–59 y.o.; 32.09%, average age (mean ± SD) 49.29 ± 5.63 y.o.), children (≤19 years; 15.30%; average age (mean ± SD) 11.82 ± 5.70 y.o.), older adults (60–79 years; 9.90%; average age (mean ± SD) 65.76 ± 4.86 y.o.), and elderly (≥80 years; 0.71%; average age (mean ± SD) 83.31 ± 5.65 y.o.). Female cases (53.23%; average age (mean ± SD) 34.92 ± 16.57 y.o.) were more prevalent than males (46.77%; average age (mean ± SD) 31.26 ± 17.65 y.o.), with a significant mean age difference (P < 0.001). The odds of being asymptomatic were increased in the younger age group (adults OR as the reference; children OR 0.471, 95% CI 0.426–0.519; younger adults OR 0.68, 95% CI 0.639–0.734; older adults OR 0.678, 95% CI 0.624–0.739; elderly OR 0.71, 95% CI 0.654–0.777). Females were more likely than males to be asymptomatic (OR 2.19, 95% CI 1.96–2.45).

Conclusions: The younger age and the female sex are associated with asymptomatic COVID-19 cases in the earliest molecular diagnosis.
asymptomatic and symptomatic cases at the first-time q-RT-PCR diagnosis. To the best of our knowledge, a similar study also still does not exist in Indonesia. To fill the gap, we analyzed large retrospective COVID-19 recorded cases in West Sumatra, Indonesia. This study aimed to determine the differences of age and sex in the appearance of COVID-19 clinical symptoms.

### Methods

**Study design and data collection**

This project was a cross-sectional study using a retrospective q-RT-PCR COVID-19 confirmed cases recorded in the laboratory of the Center for Diagnostic and Research on Infectious Disease (PDRPI laboratory) Padang, Indonesia. The population was individuals who tested COVID-19 positive with the q-RT-PCR test. The study samples were obtained from medical records in the PDRPI laboratory from April to December 2020, as many as 19,588 cases. All data variables were recorded from each specimen during the first-time q-RT-PCR positive result, including age in years, sex, and clinical symptom. This research has been ethically approved by the Ethics Committee of the Faculty of Medicine, Universitas Andalas (grant number 463/UN.16.2/KEP-FK/2021). Informed consent has been received from the PDRPI laboratory to use the secondary data.

**Definition and statistical analysis**

The term age was the biological age recorded within specimen data (in years). According to the WHO, the age was classified into five groups: (1) children (0–19 years), (2) younger adults (20–39 years), (3) adults (40–59 years), (4) older adults (60–79 years), and (5) elderly (80 years or older) (the World Health Organization, 2020). The term sex was female or male. Asymptomatic and symptomatic terms defined clinical symptoms. Asymptomatic cases were those who registered no symptoms, close contact, or for screening purposes only. The symptomatic cases included all patients that were hospitalized, suspected, or has been deceased. Data analysis including Mann-Whitney, Kruskal–Wallis, Chi-squared, or Chi-squared for trends test was used when appropriate. p-value <0.05 was statistically significant.

### Results

In this study, we found that asymptomatic cases were more prevalent than symptomatic (65.30%). The positively tested individuals were aged 37 years on average. The younger adults (aged 20–39 years) were more frequent than other age groups. Female sex was more prevalent than males in both asymptomatic and symptomatic cases. Figure 1 demonstrated the number of cases and sex differences that we found in each age groups. Furthermore, Table 1 describes the characteristic of the research samples in detail.

![Figure 1: Characteristic of age groups](https://oamjms.eu/index.php/mjms/index)

In general, the figure showed the number of cases in each group of age. The figure also demonstrated the differences of sex percentage in those groups. Overall, the male sex had higher percentages compared to female in all age groups, except in older adults.

The table describes the median and mean (± SD) age of all samples, as well as in different sex. The median and mean (± SD) age and percentage of male and female in each age groups as well as symptom groups are also presented. Furthermore, the table presents the age trends and sex differences in age groups (year) and clinical symptom groups. Overall, statistical analysis showed significant differences in percentage of total male cases and female cases, as well as in comparison of cases numbers in age groups and clinical symptoms groups. In addition, in further analysis to compare the number of males and females in all those groups, the results showed significant differences as well.

To determine the differences in age and sex distribution in both asymptomatic and symptomatic cases, we compared the two variables, as shown in Figure 2 and Table 2. Our findings revealed a higher odd of being asymptomatic in younger age groups. The children had 2 times the probability than adults of being asymptomatic. In contrast, the elderly had a 2 times higher chance than adults of being symptomatic. In this case, there was a relationship between age group and clinical symptoms. A similar association was also observed in sex, where the females had slightly higher odds than males of being asymptomatic. Finally, the differences in age and sex were significant in both clinical cases.

Overall, asymptomatic cases are more prevalent in children, young adult, and adults, while in older adults and elderly, asymptomatic cases are...
less common. On the other hand, both in female and male groups, asymptomatic cases are higher than symptomatic cases; thus, further statistical analysis was performed to compare those groups.

**Table 2: Differences of age and sex in clinical symptoms**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Asymptomatic Group</th>
<th>Symptomatic Group</th>
<th>p-value**</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age Group (year)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Children (0–19)</td>
<td>3.292</td>
<td>0.471</td>
<td>0.426</td>
</tr>
<tr>
<td>Young Adults (20–39)</td>
<td>2.261</td>
<td>0.685</td>
<td>0.639</td>
</tr>
<tr>
<td>Adults (40–59)</td>
<td>1.549</td>
<td>ref</td>
<td>ref</td>
</tr>
<tr>
<td>Older Adults (60–79)</td>
<td>0.677</td>
<td>1.766</td>
<td>1.594</td>
</tr>
<tr>
<td>Elderly (&gt;=80)</td>
<td>0.782</td>
<td>1.981</td>
<td>1.412</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1.972</td>
<td>1.105</td>
<td>1.042</td>
</tr>
</tbody>
</table>

In this table, we compared the number of cases with symptoms and without symptoms of COVID-19 in different group of age and sex. Overall, statistical analysis showed trends in age groups, which the children, young adults and adults tend to have asymptomatic cases; meanwhile, the older adults and elderly tends to have symptomatic cases (p < 0.001). Moreover, in sex group, we found that female group is more prevalent to have asymptomatic cases with symptoms and without symptoms of COVID-19. The clinical symptoms were unexposed, some were pre-symptomatic, so q-RT-PCR is the gold standard to confirm (Chen et al., 2021) [3]. Despite the urgent need to detect asymptomatic infections in a population to reduce viral transmission, it is better to focus on universal infection control in targeted settings (Stadler et al., 2021) [12]. Since the screening in our population study primarily targeted asymptomatic individuals in the first-confirmed test, analysis of their age and sex characteristics should be important in determining a better health protocol policy.

**Discussion**

The investigation of age and sex as feasible and potential predictors of the presence of COVID-19 symptoms should lead to a better understanding of viral infection control. Although age and sex are associated with clinical outcomes and mortality (Asfahan et al., 2020; and Voinsky, Baristaite, and Gurwitz, 2020), [1], [14] their effects on the development of symptoms are unclear. Here, we found that the younger age and the female sex increase the probability of being asymptomatic. This finding should also predict the risks of the primary viral transmission source.

Here, we evaluated a large scale of positive COVID-19 patients in the Indonesian population, particularly examined from a central laboratory of West Sumatra province. We found that the majority of cases were asymptomatic at the earliest diagnosis (Table 1). It is similar to the results of a meta-analysis study, which estimated that more than half of confirmed cases were asymptomatic at the first positive test and were primarily transmitting the virus (Johansson et al., 2021) [7]. However, the incidence of asymptomatic SARS-CoV-2 infections highly varied in different regions with an approximately maximum range of 70%. The clinical symptoms were unexposed, some were pre-symptomatic, so q-RT-PCR is the gold standard to confirm (Chen et al., 2021) [3]. Despite the urgent need to detect asymptomatic infections in a population to reduce viral transmission, it is better to focus on universal infection control in targeted settings (Stadler et al., 2021) [12]. Since the screening in our population study primarily targeted asymptomatic individuals in the first-confirmed test, analysis of their age and sex characteristics should be important in determining a better health protocol policy.

We have presented large data of cases, but, nevertheless, our study did not show specific symptoms in group with COVID-19 symptoms due to the lack of information. However, to the best of knowledge, this is a descriptive study with the largest data in Indonesia in terms of COVID-19 epidemiology. We also could not perform linear regression analysis due to the weakness. Thus, we recommended future study to do more analysis in sex and age effects on COVID-19.
Conclusions

Our study result illustrates that the younger age and the female sex are associated with asymptomatic COVID-19 cases in the earliest molecular diagnosis.

Ethical Review

This research has been ethically approved by the ethics committee of the Faculty of Medicine, Universitas Andalas with registration number 463/UN.16.2/KEP-FK/2021. Consent to use secondary data are received from PDRPI Laboratory.

Authors’ Contributions

All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

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References