Scientific Foundation SPIROSKI, Skopje, Republic of Macedonia
Open Access Macedonian Journal of Medical Sciences. 2022 Apr 16; 10(E):643-646.
https://doi.org/10.3889/oamjms.2022.8709
eISSN: 1857-9655
Category: *E - Public Health*
Section: *Public Health Epidemiology*

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

Liganda Endo Mahata[1,2]*, Mutia Lailani[3], SM Rezvi[1], Syandrez Prima Putra[1,4]*, Andani Eka Putra[1,4]

[1]Center for Diagnostic and Research on Infectious Disease (PDRPI), Faculty of Medicine, Universitas Andalas, Padang, Indonesia; [2]Department of Pharmacology and Therapeutics, Faculty of Medicine, Universitas Andalas, Padang, Indonesia; [3]Department of Physiology, Faculty of Medicine, Universitas Andalas, Padang, Indonesia; [4]Department of Microbiology, Faculty of Medicine, Universitas Andalas, Padang, Indonesia

Edited by: Slavica Hristomanova-Mitkovska
Citation: Mahata LE, Lailani M, Rezvi SM, Putra SP, Putra AE. Age and Sex Differences in COVID-19 Clinical Symptom: Analysis of 19,588 Indonesian Cases. Open Access Maced J Med Sci. 2022 Apr 16; 10(E):643-646. https://doi.org/10.3889/oamjms.2022.8709
Keywords: COVID-19; Age; Sex; Symptom; Asymptomatic
***Correspondence:** Liganda Endo Mahata, Department of Pharmacology and Therapeutics, Faculty of Medicine, Universitas Andalas, Padang, Indonesia. E-mail: ligandaendomahata@med.unand.ac.id
Received: 22-Jan-2022
Revised: 04-Mar-2022
Accepted: 06-Apr-2022

Funding: The funding was received from Faculty of Medicine, Universitas Andalas, with grant number 678/UN16.02.D/PP/2021.
Competing Interests: The authors have declared that no competing interests exist

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 ± 3.65 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) 41.26 ± 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 1.766, 95% CI 1.594–1.957; and elderly OR 1.981, 95% CI 1.412–2.780; $P < 0.001$). Females were more likely than males to be asymptomatic (OR 1.105, 95% CI 1.042–1.172).

Conclusions: The younger age and the female sex are associated with asymptomatic COVID-19 cases in the earliest molecular diagnosis.

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, 2021a) [16]. At the same time, 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 Elkbuli, 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

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.

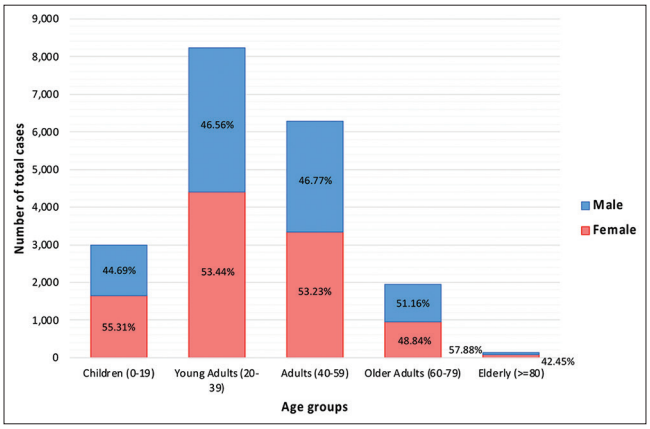

Figure 1: Characteristic of age groups

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

Table 1: Characteristic of the study samples

Variable	Group	N	%	Age (year)				Sex				p-value***
				Median	Mean	SD	p-value**	Female (n)	%	Male (n)	%	
Age (year)		19,588	100.00	36	37.12	17.22						
Sex	Female	10,427	53.23	35	36.75	17.10	<.001*					
	Male	9,161	46.77	36	37.55	17.35						
Age Group (year)	Children (0–19)	2,996	15.30	13	11.82	5.70	<.001*	1,657	55.31	1,339	44.69	<0.001*
	Young Adults (20–39)	8,228	42.01	29	29.51	5.52		4,397	53.44	3,831	46.56	
	Adults (40–59)	6,286	32.09	49	49.29	5.63		3,346	53.23	2,940	46.77	
	Older Adults (60–79)	1,939	9.90	65	65.76	4.86		947	48.84	992	51.16	
	Elderly (>=80)	139	0.71	82	83.31	3.65		80	57.55	59	42.45	
Clinical symptoms Groups	Asymptomatic	12,790	65.30	33	34.92	16.57	<.001*	6,919	54.10	5,871	45.90	0.001
	Symptomatic	6,798	34.70	41	41.26	17.65		3,508	51.60	3,290	48.40	

*P <.05=significant difference; **Mann-Whitney/Kruskal–Wallis test; ***Chi-squared/Chi-squared for trends test.

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

Variable	Group	Asymptomatic Group versus Symptomatic Group				
		Odds	OR	95% CI		p-value**
Age Group (year)	Children (0–19)	3.292	0.471	0.426	0.519	<0.001*
	Young Adults (20–39)	2.261	0.685	0.639	0.734	
	Adults (40–59)	1.549	reff	reff	reff	
	Older Adults (60–79)	0.877	1.766	1.594	1.957	
	Elderly (≥ 80)	0.782	1.981	1.412	2.780	
Sex	Female	1.972	1.105	1.042	1.172	0.001*
	Male	1.784				

*p-value < 0.05=Significant difference; **Chi-squared/Chi-squared for trends test; OR: Odd ratio; CI: Confidence interval; Reff: Reference.

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 tend to have symptomatic cases ($p < 0.001$). Moreover, in sex group, we found that female group is more prevalent to have asymptomatic cases compared to male (OR (95% CI): 1.105 (1.042–1.172), $p < 0.001$).

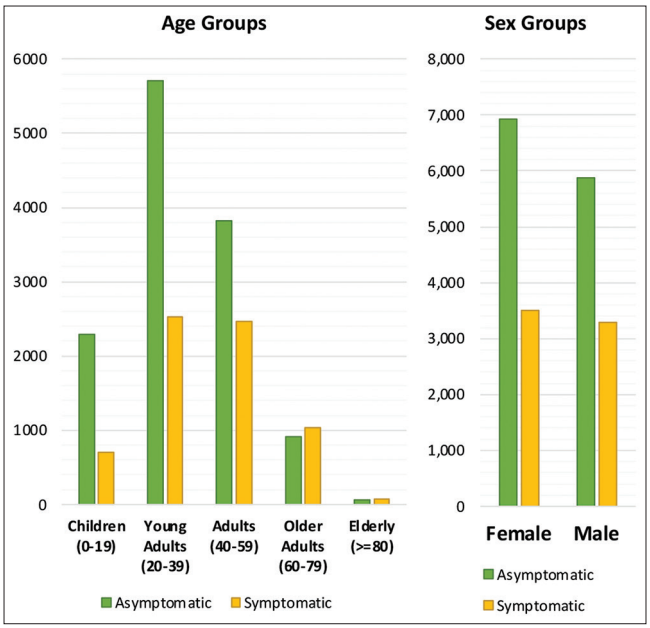

Figure 2: The number of asymptomatic and symptomatic case in age groups and sex groups

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.

Acknowledgment

We would sincerely appreciate all the PDRPI staff for their contribution in providing the data, especially the managerial boards: Linosefa, Gestina Aliska, Nita Afriani, Desmawati, Dessy Arisanty, Ikhwan Resmala Sudji, and Syafrizayanti. We also thank the Medical Faculty of Universitas Andalas which provide the funding of this project.

References

1. Asfahan S, Deokar K, Dutt N, Niwas R, Jain P, Agarwal M. Extrapolation of mortality in COVID-19: Exploring the role of age, sex, co-morbidities and health-care related occupation. Monaldi Arch Chest Dis. 2020;90(2):313-7. https://doi.org/10.4081/monaldi.2020.1325
2. Banko A, Petrovic G, Miljanovic D, Loncar A, Vukcevic M, Despot D, *et al*. Comparison and sensitivity evaluation of three different commercial real-time quantitative PCR kits for SARS-CoV-2 detection. Viruses. 2021;13(7):1321. https://doi.org/10.3390/v13071321
   PMid:34372527
3. Chen Z, Wang B, Mao S, Ye Q. Assessment of global asymptomatic sars-cov-2 infection and management practices from China. Int J Biol Sci. 2021;17:1119-24. https://doi.org/10.7150/ijbs.59374
   PMid:33867834
4. Gao Z, Xu Y, Sun C, Wang X, Guo Y, Qiu S, *et al*. A systematic review of asymptomatic infections with COVID-19. J Microbiol Immunol Infect. 2021;54(1):12-6. https://doi.org/10.1016/j.jmii.2020.05.001
   PMid:32425996
5. Ghisolfi S, Almås I, Sandefur JC, von Carnap T, Heitner J, Bold T. Predicted COVID-19 fatality rates based on age, sex, comorbidities and health system capacity. BMJ Glob Health. 2020;5(9):e003094. https://doi.org/10.1136/bmjgh-2020-003094
   PMid:3291285
6. Jain V, Yuan JM. Predictive symptoms and comorbidities for severe COVID-19 and Intensive Care Unit admission: A systematic review and meta-analysis. Int J Public Health. 2020;65:533-46. https://doi.org/10.1007/s00038-020-01390-7
7. Johansson MA, Quandelacy TM, Kada S, Prasad PV, Steele M, Brooks JT, *et al*. SARS-CoV-2 transmission from people without COVID-19 symptoms. JAMA Network Open. 2021;4(1):e2035057. https://doi.org/10.1001/jamanetworkopen.2020.35057
   PMid:33410879
8. Mesas AE, Cavero-Redondo I, Álvarez-Bueno C, Cabrera MA, de Andrade SM, Sequí-Dominguez I, *et al*. Predictors of in-hospital COVID-19 mortality: A comprehensive systematic review and meta-analysis exploring differences by age, sex and health conditions. PLoS One. 2020;15:e0241742. https://doi.org/10.1371/journal.pone.0241742
   PMid:33141836
9. O'Brien J, Du KY, Peng C. Incidence, clinical features, and outcomes of COVID-19 in Canada: Impact of sex and age. J Ovarian Res. 2020;13(1):134. https://doi.org/10.1186/s13048-020-00734-4
   PMid:33234144
10. Ralli M, Morrone A, Arcangeli A, Ercoli L. Asymptomatic patients as a source of transmission of COVID-19 in homeless shelters. Int J Infect Dis. 2021;103:243-5. https://doi.org/10.1016/j.ijid.2020.12.031
    PMid:33321208
11. Sen-Crowe B, McKenney M, Elkbuli A. COVID-19 laboratory testing issues and capacities as we transition to surveillance testing and contact tracing. Am J Emerg Med. 2021;40:217-9. https://doi.org/10.1016/j.ajem.2020.05.071
    PMid:32513451
12. Stadler RN, Maurer L, Aguilar-Bultet L, Franzeck F, Ruchti C, Kühl R, *et al*. Systematic screening on admission for SARS-CoV-2 to detect asymptomatic infections. Antimicrob Resist Infect Control. 2021;10:2-5. https://doi.org/10.1186/s13756-021-00912-z
    PMid:33640031
13. Teherán AA, Camero Ramos G, Prado de la Guardia R, Hernández C, Herrera G, Pombo LM, *et al*. Epidemiological characterisation of asymptomatic carriers of COVID-19 in Colombia: A cross-sectional study. BMJ Open. 2020;10(12):e042122. https://doi.org/10.1136/bmjopen-2020-042122
    PMid:33293326
14. Voinsky I, Baristaite G, Gurwitz D. Effects of age and sex on recovery from COVID-19: Analysis of 5769 Israeli patients. J Infect. 2020;81(2):e102-3. https://doi.org/10.1016/j.jinf.2020.05.026
    PMid:32425274
15. World Health Organization. Coronavirus Disease 2019 (COVID-19) Situation Report –89. Geneva: World Health Organization; 2020. Available from: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200418-sitrep-89-covid-19.pdf [Last accessed on 2020 Apr 18].
16. World Health Organization. COVID-19 Weekly Epidemiological Edition 51. Geneva: World Health Organization; 2021. https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19-3-august-2021 [Last accessed on 2021 Aug 03].
17. World Health Organization. Weekly Operational Update on COVID-19. Vol. 67. Geneva: World Health Organization; 2021. p. 1-14.