Interrelation between Handwashing and the Severity of COVID-19: A non-representative cross-sectional study

Nabila Putri Firdalina[1], Riry Ambarsarie[2]*, Utari Hartati Suryani[3], Dessy Triana[4], Nikki Aldi Massardi[5]

[1] Medical Program, Faculty of Medicine and Health Sciences, Universitas Bengkulu, Kandang Limun, Muara Bangka Hulu, Bengkulu, Indonesia

[2] Department of Medical Education, Faculty of Medicine and Health Sciences, Universitas Bengkulu, Kandang Limun, Muara Bangka Hulu, Bengkulu, Indonesia

[3] Department of Microbiology Faculty of Medicine and Health Sciences, Universitas Bengkulu, Kandang Limun, Muara Bangka Hulu, Bengkulu, Indonesia

[4] Department of Parasitology, Faculty of Medicine and Health Sciences, Universitas Bengkulu, Kandang Limun, Muara Bangka Hulu, Bengkulu, Indonesia

[5] Department of Pathology Anatomy, Faculty of Medicine and Health Sciences, Universitas Bengkulu, Kandang Limun, Muara Bangka Hulu, Bengkulu, Indonesia

Abstract: Corona Virus Disease 2019 (COVID-19) pandemic remains a global issue, including in Indonesia. Handwashing using soap can reduce the viral load of the SARS-CoV-2 virus and prevent coinfection, which can worsen symptoms in COVID-19 patients. This study aims to determine the relationship between knowledge, attitudes, and handwashing behavior to the severity of COVID-19. Research using a cross-sectional and retrospective approach was conducted from July to December 2020 in Bengkulu Province. About 107 respondents had been confirmed positive for Covid-19 with the rt-PCR test, aged 17-60 years, and were willing to participate. Knowledge, attitudes, and behaviors were assessed using validated questionnaires and data on the severity of disease obtained from epidemiological forms. The collected data were then analyzed using chi-square statistical tests. 107 respondents had already filled in the questionnaires. The Chi-square test showed no significant association between knowledge (p 0.081), attitude (p 0.216), and behavior (p 0.136) of handwashing to the severity of COVID-19. A good level of knowledge, attitudes and behaviors about handwashing using soap did not adequately affect the severity of covid-19 patients. The good level of knowledge, attitude, and practice of HWUS were not significant enough to affect the severity of the COVID-19 disease.

Keywords: knowledge; attitude; behavior; HWUS; severity of COVID-19

INTRODUCTION

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) caused by Coronavirus 2019 (COVID-19) was first identified in China as a new type of coronavirus. The virus spreads massively from human to human in a short and sustained time. Due to the rapid spread around the world, on March 11, 2020 the World Health Organization (WHO) designated COVID-19 as a pandemic.[1] The number of cases reported in Indonesia cumulatively as of October 17, 2021, amounted to 4.23 million cases with 142,952 deaths. The percentage of deaths in Indonesia (3.38%) is still high compared to the world average (2.04%). The death rate also ranked Indonesia the second highest in Asia.[2]

Death of COVID-19 patients usually occurs in patients with severe disease severity. COVID-19 patients are declared seriously ill if they have clinical manifestations of severe Acute Respiratory Tract Infection and are said to be critically ill if there is clinical Acute Respiratory Distress Syndrome (ARDS).[3] The incidence of co-infection due to viruses, bacteria, or fungi is often associated with worsening conditions of COVID-19 patients and increased mortality incidence. Coinfection is also associated with a higher frequency of patients entering

the Intensive Care Unit (ICU) room. The most common causes of coinfection in bacteria are pneumonia-causing bacteria such as *Klebsiella pneumoniae* (9.9%), *Streptococcus pneumoniae* (8.2%), and *Staphylococcus aureus* (7.7%). The most coinfection-causing viruses are influenza type A (22.3%), influenza type B (3.8%), and respiratory syncytial virus (3.8%), while the most coinfection-causing mushrooms are Aspergillus.[4]

Common symptoms of COVID-19 patients are fever, fatigue, and dry cough. Some patients may experience aches and pains, loss of smell, missing tasting, conjunctivitis, headache, stuffy nose, runny nose, diarrhea, sore throat, and skin rash.[3] The overall percentage of cases with mild to critical symptoms is divided into 40% of patients experiencing mild pain, 40% of patients experiencing moderate pain, including pneumonia, 15% of patients experiencing severe pain, and 5% of others in critically ill. The criteria for clinical symptoms in COVID-19 patients are divided into asymptomatic (asymptomatic), mild pain, moderate pain, severe pain and critical illness.[5]

Prevention of the occurrence of coinfection can be done by washing hands with soap. When a person washes his hands using soap, the content of surfactants that are hydrophilic/lipophilic can facilitate the flushing of microorganisms in hand.[6] The active content of soap can also damage lipid membranes or viral capsules so that it can inactivate the virus.[7] Hand washing using soap can reduce the incidence of Acute Respiratory Tract Infection by 20% and diarrhea by 30%, which means washing hands with soap can prevent the incidence of infection.[8]

Hand washing using soap can be done in several conditions such as after contact with a sick person, before preparing food, before and after eating, before and after handling wounds, after using a toilet, after coughing or sneezing using the hands, and after throwing and or tackling garbage.[9] During the COVID-19 pandemic, hand washing was also done before and after holding the eyes, nose, mouth, holding a mask, venturing from crowded places, and holding surfaces that are often touched by others, for example, door handles, tables, supermarket baskets, screens / ATM buttons.[10]

Hand washing using soap behavior in the community in Bengkulu Province is still relatively low, as evidenced by data from basic health research in 2018 as the province with the highest incidence of diarrhea in Indonesia.[11] The knowledge, attitudes, and behavior of hand washing using soap in the community need to be measured, especially in the COVID-19 pandemic, to at least give an idea of the extent of clean and healthy living behaviors of the people in Bengkulu Province.

Based on the description above, research linking knowledge, attitudes, and behaviors of hand washing using soap to the severity of COVID-19 patients' disease is still uncertain. In Indonesia, researchers have not found similar studies, so more research on this issue needs to be conducted. This study aims to determine the relationship between knowledge, attitudes, and behavior of hand washing using soap to the severity of COVID-19 patients' disease.

MATERIAL AND METHOD

Participation and procedure

A cross-sectional and retrospective study approach was conducted among individuals aged 17-60 years. The surveys were conducted from July to December 2020, immediately after Indonesia's government's implementation of large-scale social distancing, including Bengkulu province. A semi-structured questionnaire was designed for the Google survey tool (Google Forms). The generated link was shared personally with respondents who had been confirmed positive for Covid-19 with a positive RT-PCR test result and were willing to participate in this study. The investigators' decision to collect the data using online approaches was predicated on maintaining large-scale social distance in Bengkulu. Initially, 112 potential respondents provided written informed consent online. 107 respondents completed the entire survey, generating a response rate of 95.5%. The inclusion criteria to participate in the study were those confirmed positive for Covid-19 with a positive RT-PCR test result, aged 17-60 years, and voluntary participation.

Measures

Semi-structured and self-reported questionnaires contained informed consent and questions regarding knowledge, attitude, practice and severity of the disease.

Knowledge, attitude and practice

To assess the respondents' level of knowledge, attitude and practice, 30 questions (including 10 for knowledge, 10 for attitude and 10 for practice) were included. The survey questions were adapted from World Health Organization (WHO) tools for hand hygiene surveys[7]. After completing the initial draft of the survey, the questionnaire was validated and adopted as follows; firstly, the questionnaire was sent to three academic experts knowledgeable in the area. After coordination and consensus of all experts' opinions, the final questionnaire was drafted and underwent pilot testing in 30 individuals to confirm the reliability of the

questionnaire. The data from the pilot study were loaded into SPSS version 25 and subjected to reliability coefficient analysis. Regarding the pilot data, Cronbach's alpha coefficient of the knowledge, attitude, and practice were 0.60, 0.43, and 0.74, respectively, and overall, Cronbach's alpha of KAP questions was 0.73, indicating acceptable internal consistency. In terms of field data, Cronbach's alpha coefficient of the knowledge, attitude, and practice were 0.60, 0.20, and 0.63, respectively, and overall, Cronbach's alpha of KAP questions was 0.60.

The knowledge section consisted of 10 items, and each question had a possible response of "Yes", "No," and "Do not know" (e.g., Is handwashing using soap and running water effective in preventing the transmission of Covid-19?). The correct answer (Yes) was coded as 1, while the wrong answer (No/Do not know) was coded as 0. The total score ranged from 0–10, with an overall greater score indicating more accurate knowledge. A cut-off level of ≥ 6 was set for more accurate knowledge.

The attitude section consisted of 10 items, and the response of each item was indicated on a 4-point Likert scale as follows 1 ("Strongly Disagree"), 2 ("Disagree"), 3 ("Agree"), and 4 ("Strongly Agree") (e.g., After covering the mouth and nose when coughing or sneezing, a person needs to wash hands immediately). The total score was calculated by summating the raw scores of the ten questions ranging from 0 to 20, with an overall greater score indicating more positive attitudes towards handwashing using soap. A cut-off level of ≥ 26 was set for more positive attitudes toward handwashing using soap.

The practice section included 10 items of practice measures responding to the handwashing using soap in the Covid-19 era, and each item was responded as "Yes", "No", and "Sometimes" (e.g., Do you wash your hands before entering a store or public place?). Practice items' total scores ranged from 0–20, with an overall greater score indicating more frequent practices towards handwashing using soap. A cut-off level of ≥ 11 was set for more frequent practices.

The severity of COVID-19 patients in Bengkulu Province was recorded from July to December 2020. Classification severity of COVID-19 was based on the clinical massiveness of patients, namely: asymptomatic (asymptomatic patients), mildly ill (patients did not show specific symptoms such as flu), moderate pain (mild pneumonia), severe pain (severe pneumonia / severe ARI), and critically ill (ARDS). The data included primary data collected directly through questionnaires disseminated online and secondary data obtained from Bengkulu Provincial Health Office documents in the form of epidemiological investigation forms.

Statistical analysis

The data analysis was performed using Microsoft Excel 2019 and SPSS version 23.0. Microsoft Excel was used for editing, sorting, and coding. The excel file was then imported into SPSS software. Descriptive statistics (frequencies, percentages, means, standard deviations) and first-order analyses (i.e., chi-square tests) were performed.

Ethical considerations

The study was conducted based on the Institutional Research Ethics and the declaration of Helsinki. Formal ethical approval was granted by the Health Research Ethics Committee of the Faculty of Medicine and Health Sciences, University of Bengkulu, number: 266/UN30.14.9/LT/2020. The consent form documented the study's aims, nature, and procedure. Anonymity and confidentially were strictly maintained.

RESULT

This study showed the frequency distribution of knowledge levels, attitudes, and behaviors of HWUS and the characteristics of 107 respondents. Respondents consisted of 51 (47.7%) females and 56 (52.3%) males. On average, respondents were 46-40 years (34.6%). The majority of respondents had good levels of knowledge (71%), attitudes (80.4%), and behavior (92.5%) of HWUS. It found that the degree of severity of the most diseases was asymptomatic at 63 (58.9%) respondents and the degree of severity of the least severe disease was 5 (4.7%) respondents. In addition, there were also 34 (31.8%) respondents with comorbidities. The characteristics of respondents in this study are displayed in Table 1.

Table 1. Overview of hand washing knowledge level, attitudes, behaviors and characteristics of respondents

Category	Frequency	Percentage (%)
Knowledge level of HWUS		
Good	76	71.0
Poor	31	29.0
Attitude level of HWUS		
Positive	86	80.4
Negative	21	19.6
Behavior level of HWUS		
Active	99	92.5
Passive	8	7.5
Age distribution		
17-25 years	22	20.6
26-35 years	15	14
36-45 years	33	30.8
46-60 years	37	34.6
Severity of disease		
Asymptomatic	63	58.9
Mild	26	24.3
Moderate	13	12.1
Severe	5	4.7
Critically ill	0	0
Comorbidity		
With	34	31,8
Without	73	68,2

Table 2. The relationship between Handwashing knowledge and the severity of COVID-19

Knowledge of HWUS	The severity of COVID-19 patients								Total	p
	Asymptomatic		Mild		Moderate		Severe			
	N	%	N	%	N	%	N	%		
Good	50	79.37	17	65.38	7	53.85	2	40.00	76	
Poor	13	20.63	9	34.62	6	46.15	3	60.00	31	0.081
Total	63	100.00	26	100.00	13	100.00	5	100.00	107	

Based on Table 2, there is no significant association between HWUS knowledge levels and the severity of COVID-19 patients' disease. The study results from the Chi-square test obtained a P-value of 0.081, indicating that a person's knowledge of HWUS did not affect the severity of the disease in COVID-19 patients.

Table 3. The relationship between handwashing attitude and the severity of COVID-19 Patients

Attitudes of HWUS	The severity of COVID-19 patients' disease								Total	p
	Asymptomatic		Mild		Moderate		Severe			
	N	%	N	%	N	%	N	%		
Positive	51	80.95	17	80.95	13	72.22	5	100.00	86	
Negative	12	19.05	4	19.05	5	27.78	0	0.00	21	**0.216**
Total	63	100.00	21	100.00	18	100.00	5	100.00	107	

Based on table 3, a p-value of 0.216 indicates that the level of a person's attitude regarding HWUS does not affect the severity of the disease in COVID-19 patients. Moreover, most respondents had a positive attitude related to HWUS, but among them were respondents with severe disease.
Based on table 4, a p-value of 0.136 indicates that the level of a person's behavior regarding HWUS does not affect the severity of the disease in COVID-19 patients.

Table 4. The relationship between handwashing behavior and the severity of COVID-19

Practice of HWUS	The severity of COVID-19 patients' disease								Total	p
	Asymptomatic		Mild		Moderate		Severe			
	N	%	N	%	N	%	N	%		
Positive	59	93.65	25	96.15	10	76.92	4	80.00	98	
Negative	4	6.35	1	3.85	3	23.08	1	20.00	9	0.136
Total	63	100.00	26	100.00	13	100.00	5	100.00	107	

DISCUSSION

This study selected respondents at the productive age of 17-60 years. The results of this study showed that the age group of respondents was in the age range of 36-45 years, as many as 33 people and the age range of 46-60 years, as many as 37 people. It is in line with the data released by the COVID-19 Task Force (2021) that the age group of the majority of COVID-19 positive cases in Indonesia is the productive age consisting of the age group of 31-45 years, with a total of 29%, 19-30 years with a total of 25%, and 46-59 years with a total of 22%.[12]

The severity of the disease due to SARS-CoV-2 infection in the respondents was asymptomatic for 58.9% (63 people), mildly ill for 24.3% (26 people), moderately ill for 12.1% (13 people), and severely ill for 4.7% (5 people), and severe pain for 4.7% (5 people). Based on the Ministry of Health (2020), the severity of patients will be more severe if they show clinical symptoms of pneumonia, such as tightness to ARDS. Washing hands with soap can prevent respiratory tract infections such as pneumonia.[8]

Most respondents had a good level of knowledge (71%), attitude (80.4%), and behavior (92.5%) of HWUS. Knowledge is important in shaping health behaviors, especially hand washing. Knowledge-based behavior will last longer than behavior that is not based on knowledge[13]. Most of the respondents in this study supported health attitudes and behaviors and were already aware that HWUS attitudes and behaviors are important in lowering the incidence of infectious diseases.

Subsequent data on the study showed that 80.4% (86%) of respondents had a positive attitude, and 92.5% (99 people) behaved actively. It indicated that most of the respondents in this study supported health attitudes and behaviors and were already aware that HWUS attitudes and behaviors are important in lowering the incidence of infectious diseases. However, an attitude cannot be easily realized since it requires factors such as the availability of hand washing facilities, reinforcing factors in the form of invitations to others or health rules, as well as knowledge influenced by experience, mass media, and educational institutions, emotions, and many more.[10]

Level of knowledge, attitudes, and behaviors are often associated with the incidence of an infection[14]. A proper handwashing activity using soap can significantly decrease exposure to infectious disease-causing organisms[15]. The results of this study showed that a person with a good level of knowledge, attitude, and behavior of HWUS was not effective enough in preventing severe disease severity in COVID-19 patients if infected in the future. A person with good HWUS knowledge, such as knowing how to wash hands properly and how long it takes, accompanied by a good HWUS attitude such as diligently using a hand sanitizer, routine hand washing with soap before eating, always washing hands after getting out of the crowd, and others do not guarantee that they can turn their illness level into mild when infected with severe SARS-CoV-2.

Hand washing using soap activities may affect the severity of COVID-19 disease, as previous theories were linked to virulence and coinfection factors. However, the effect is not statistically significant due to the multifactorial degree of severity of COVID-19 disease. In addition, retrospective research designs with cross-sectional studies may affect the answers from respondent questionnaires, where after exposure to COVID-19, respondents will become more careful and diligent in washing their hands.

It also explains that when the health protocol campaign during the COVID-19 pandemic is not enough only by inviting people to wash hands with soap[16], it is also necessary to implement other health protocols consisting of 5M, namely wearing masks, washing hands with soap and running water, maintaining distance, staying away from crowds, and limiting mobilization and interaction and 3T, namely testing, tracing, and treatment. In addition, the community needs to vaccinate against COVID-19.[17]

In addition to vaccines, many other factors, such as age, can affect the severity of COVID-19 patients' disease. Perrotta et al. (2020) stated that the old age group is a cluster of high risk of severe symptoms.[18] It is because there has been an aging process in the elderly. Aging causes a decrease in the number of cilia in the respiratory tract, a decrease in the size of the airway/collapse, and an increase in the nasal cavity volume.

Therefore, it can lower respiratory resistance in the nasal cavity, which affects the pathophysiology of COVID-19 disease. In addition, aging can lead to immunosenescence or decreased immune system.

Older patients with a good state of immunity may experience mild asymptomatic-pain symptoms, as found in this study. It occurred because the response of individual immunity to disease can vary in addition to age factors. The immune response is influenced by genetic factors, nutritional factors before and during illness, certain drugs such as immunosuppressants, comorbid factors, stress factors, lifestyles, etc. In patients with certain immune system conditions, such as having low antibody levels due to failure to produce a productive anti-viral immune response or an excessive (uncontrolled) immune response will lead to worsening of symptoms of COVID-19.[19] Excessive immune responses such as cytokine storm states are known to play a role in the occurrence of respiratory distress of COVID-19 patients who experience respiratory distress and ARDS including to the degree of severe pain and pain critical.[20]

Hand washing using soap is only one aspect assessed in this study, especially from the generator factor. In terms of generator, agent, and environment, many aspects cannot be controlled only by washing hands with soap. Furthermore, there is also still a lot more to note. Hand washing with soap should be done with other behavior modifications. Washing hands will not benefit us if it is the only thing carried out. Thus, it is necessary to modify other behaviors that have been campaigned by the government, namely 5M, which consists of washing hands with soap, maintaining distance, avoiding crowds, wearing masks, and reducing mobility. In addition, the public also needs to vaccinate, participate in screening for the diagnosis of COVID-19, not delay if sick, and participate in quarantine if infected so as not to harm others.

By seeing the fact that Indonesia is a multi-ethnic country with vastly different economic income, education levels and traditions, it is expected that the levels of knowledge, attitude, and prevention will also markedly differ in the population. Although good KAP was present in a sizeable proportion of the sample, likely, population sectors that have no access to the internet or live in regions with a less likely fast escalation of transmission may also display reduced KAP when standard education and dissemination initiatives are promulgated and implemented. Furthermore, it is highly probable that large clusters of people will become less informed and adoptive of prevention practices on COVID-19. It can be seen from most of the respondents with a good level of knowledge, attitude and practices, but at the same time, they also have a history of the severity of COVID-19.

CONCLUSION

A good level of knowledge, attitudes and behaviors toward handwashing using soap did not adequately affect the severity of covid-19 patients. The good level of knowledge, attitude, and practice of HWUS was not significant enough to affect the severity of COVID-19 disease, so it was necessary to tighten other health protocols such as maintaining immunity, vaccination, and the application of 5M and 3T.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. World Health Organization. Weekly epidemiological update. 2020 [cited 2020 Nov 19]. Available from: https://www.who.int/publications/m/item/weekly-epidemiological-update---10-november-2020.
2. Zheng, Z., Peng, F., Xu, B., Zhao, J., Liu, H., Peng, J., et al. Risk factors of critical & mortal COVID-19 cases: A systematic literature review and meta-analysis. The Journal of infection. 2020. 81(2): e16–e25. https://doi.org/10.1016/j.jinf.2020.04.021
3. WHO. WHO Director-General's remarks at the Media Briefing on 2019-nCoV on 11 February 2020. https://www.who.int/dg/speeches/detail/who-director-general-s-remarks-at-the-media-briefing-on-2019-ncov-on-11-february-2020. Accessed 20 May 2020
4. Langford BJ, So M, Raybardhan S, Leung V, Westwood D, MacFadden DR, Soucy JPR. Bacterial co-infection and secondary infection in patients with COVID-19: a living rapid review and meta-analysis. Clinical microbiology and infection: the official publication of the European Society of Clinical Microbiology and Infectious Diseases, 2020; 26(12): 1622–1629. https://doi.org/10.1016/j.cmi.2020.07.016.
5. Htun, Y. M., Win, T. T., Aung, A., Latt, T. Z., Phyo, Y. N., Tun, T. M., Htun, N. S., Tun, K. M., & Htun, K. A. Initial presenting symptoms, comorbidities and severity of COVID-19 patients during the second wave of the epidemic in Myanmar. Tropical Medicine and Health, 2021; 49(1). https://doi.org/10.1186/s41182-021-00353-9

6. COVID-19. Infection Prevention and Control During Health Care When Coronavirus Disease (COVID-19) is Suspected or Confirmed. https://www.who.int/publications/i/item/WHO-2019-nCoV-IPC-2020.4. Accessed 3 Jul 2020.

7. WHO., 2009. WHO Guidelines on Hand Hygiene in Health Care: First Global Patient Safety Challenge Clean Care Is Safer Care. Geneva: World Health Organization. Retrieved from https://www.ncbi.nlm.nih.gov/books/NBK144046/

8. Rabie, T., Curtis, V. Handwashing and risk of respiratory infections: a quantitative systematic review. *Tropical Medicine & International Health : TM & IH*, 2006a; 11(3): 258–267. https://doi.org/10.1111/j.1365-3156.2006.01568.x

9. UNICEF. Everything You Need to Know About Washing your Hands to Protect Against Coronavirus (COVID-19)|UNICEF. https://www.unicef.org/coronavirus/everything-you-need-know-about-washing-your-hands-protect-against-coronavirus-covid-19. Accessed 28 May 2020.

10. Alzyood M, Jackson D, Aveyard H, Brooke J. COVID-19 reinforces the importance of handwashing. *Journal of clinical nursing*, 2020; 29(15-16): 2760–2761. https://doi.org/10.1111/jocn.15313.

11. Dinas Kesehatan Provinsi Bengkulu, 2018. Perkembangan Kasus Diare Provinsi Bengkulu. https://covid19.bengkuluprov.go.id/Databengkulu/filepdf/234

12. Satgas COVID-19. Analisis Data COVID-19 Indonesia 17 October 2021. 2021.

13. Hand Hygiene and Infection Control Survey Pre- And peri-H1N1-2009. Pandemic: Knowledge and Perceptions of Final Year Medical Students in Singapore: PubMed. https://pubmed.ncbi.nlm.nih.gov/21808958/. Accessed 2 Jul 2020.

14. Lau LL, Hung N, Go DJ, Ferma J, Choi M, Dodd W, Wei X. Knowledge, attitudes and practices of COVID-19 among income-poor households in the Philippines: A cross-sectional study. *J. Glob. Health* 2020; 10, 011007. https://doi.org/10.7189/jogh.10.011007

15. World Health Organization (WHO). Guide to Local Production: WHO-Recommended Handrub Formulations (WHO, 2010).

16. Wong, J. S. W. & Lee, J. K. F. The common missed handwashing instances and areas after 15 years of hand-hygiene education. *J. Environ. Public Health* 2019, 5928924. https://doi.org/10.1155/2019/5928924

17. Kemenkes RI. Pedoman Pencegahan dan Pengendalian Covid-19. Vol. 20, Kementrian Kesehatan RI. 2020. 1–214 p.

18. Perrotta F, Corbi G, Mazzeo G, Boccia M, Aronne L, D'Agnano V, et al. COVID-19 and the elderly: insights into pathogenesis and clinical decision-making. *Aging Clin Exp Res*. 2020;32(8):1599–608. https://doi.org/10.1007/s40520-020-01631-y

19. Brodin P. Immune determinants of COVID-19 disease presentation and severity. Nat Med [Internet]. 2021;27(1):28–33. Available from: https://doi.org/10.1038/s41591-020-01202-8

20. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Yi, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020. 395: 497-506 https://doi.org/10.1016/S0140-6736(20)30183-5