http://ijnms.net/index.php/ijnms
ORIGINAL RESEARCH

e- ISSN: 2686-2123
p- ISSN: 2686-0538

VACCINATION STATUS AND THE SEVERITY OF COVID-19 PATIENTS

Mugi Hartoyo, Budiyati, Riskiyana Sukandhi Putra, Tajudin Hudaiby Nizar
Poltekkes Kemenkes Semarang
E-mail: hartoyo.mugi@yahoo.com

ABSTRACT

Introduction: On January 30, 2020, the SARS-CoV-2 outbreak was a public health emergency of international concern. At the end of 2022 there was still the spread of COVID-19 even though the pandemic status had changed to endemic. One of the efforts to reduce the risk of being infected with COVID-19 is the provision of vaccines to the community. However, previous studies have shown that some people who have been vaccinated still have confirmed COVID-19 with varying severity and symptoms. The purpose of the study was to determine the relationship between vaccination status and the severity of COVID-19.
Method: This quantitative research with a retrospective cohort study was applied to 92 COVID-19 patients at a secondary hospital in Purbalingga, Central Java, Indonesia recruited by proportional simple random sampling technique. The data were collected from the medical records of COVID-19 patients from May to August 2021. The severity and symptoms of COVID-19 were determined based on the guidelines of the National Institutes of Health which include asymptomatic infection, mild symptoms, moderate symptoms, severe symptoms, and critical. The collected data were analyzed using the Fisher's Exact test.
Results: Of the 92 respondents, there were 49 (53.35%) male patients and the most comorbid was diabetes mellitus with a total of 28 (30.4%) patients. Respondents who have not been vaccinated are 64 (69.6%) patients. Patients with a high severity level of COVID-19 were more frequently found among respondents who had not been vaccinated, 54 (58.7%). There is a relationship between vaccination status and the severity of COVID-19 (p = 0.000). The public is advised to complete the vaccine status that has been facilitated by the government.
Conclusion: Vaccination potentially reduces the severity of COVID-19.

Keywords

COVID-19, Severity, Vaccination

INTRODUCTION

Coronavirus disease 2019 or Covid-19 is a new type of highly contagious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS–CoV-2) (Cascella et al., 2021). At the end of January 2020, the World Health Organization (2021) declared that the SARS-CoV-2 outbreak was a public health emergency of international concern. The COVID-19 pandemic has urged the international scientific community to find therapies and vaccines that can control SARS-CoV-2 (Kaur & Gupta, 2020).

The Ministry of Health of the Republic of Indonesia (2021) reports that on September 22, 2021, there have been 4,198,678 cases since Covid-19 entered Indonesia, and 140,954 cases have died. According to Worldometer data on July 5,

2022, there were 6,095,351 cases of Covid-19 in Indonesia, with 156,758 deaths. The Ministry of Health of the Republic of Indonesia (2021) reported that on September 22, 2021, Indonesia was ranked 19th with the most cases in the world. Central Java province occupies the 3rd most total cases in Indonesia, namely 456,579 cases, and the highest mortality prevalence with 32,401 cases (Ministry of Health of the Republic of Indonesia, 2021). In Purbalingga Regency on December 25, 2021, there were 20,673 Covid-19 cases and 1,213 deaths (Purbalingga District Health Office, 2021). The prevalence of death in Purbalingga is 6% which is almost double the national death rate (Purbalingga District Health Office, 2021).

If not treated properly, Covid-19 patients will experience acute respiratory distress syndrome and death (Fatoni, 2021). Based on government reports, the age group with the highest death rate is over 60 years old (Ministry of Health of the Republic of Indonesia, 2021). One of the causes of the high mortality of elderly people with Covid-19 is the low vaccination coverage among them (Ministry of Health of the Republic of Indonesia, 2021). Data to the Ministry of Health of the Republic of Indonesia as of November 8, 2021, dose 1 vaccine has only been given to 9,299,745 people, or 43% of the total target for the elderly (Ministry of Health of the Republic of Indonesia, 2021). Doubts about the effectiveness and safety of vaccines are one of the reasons for slow vaccination in the community (Putri et al., 2021). Acceleration of vaccination is very important to deal with wave 3 of Covid-19 in early 2022 (Ministry of Health of the Republic of Indonesia, 2021).

The right action to reduce mortality due to Covid-19 is mass vaccination (WHO, 2021). Vaccines are one of the most reliable and cost-effective public health interventions ever implemented that save millions of lives every year (El-Elimat et al., 2021). The initial focus of the SARS-CoV-2 vaccine was to prevent symptomatic and often severe diseases (WHO, 2021). The effectiveness of the Sinovac vaccine has been studied in Chile with an efficacy of 65.9% for the prevention of Covid-19 and 87.5 for the prevention of hospitalization (Jara et al., 2021). Research in the UK on the AstraZeneca vaccine with the results of being able to prevent symptomatic Covid-19 as much as 73-85% after the second dose (Pritchard et al., 2021). Research in Indonesia by the Health Research and Development Agency of the Ministry of Health of the Republic of Indonesia on 71,455 health workers in Jakarta shows that the length of treatment for health workers who have been vaccinated is relatively shorter (Ministry of Health of the Republic of Indonesia, 2021). Vaccination is recognized to be very effective, but vaccine effectiveness decreases after 200 days, especially for older patients or those with certain comorbidities, so additional protection in the form of a booster vaccination is needed (Wright et al., 2022).

Previous studies have proven that there is a relationship between vaccination status and severity in Covid-19 patients. These studies have been carried out in various countries and Jakarta, Indonesia, but have never been carried out in the Purbalingga Regency, Central Java. So, it is necessary to research "The relationship between vaccination status and the severity of Covid-19 in Purbalingga Regency". Another reason is the low number of third dose vaccination coverage as of April 5, 2022 (8.12%) in Purbalingga Regency, Central Java (Ministry of Health of the Republic of Indonesia, 2021). The purpose of this study was to determine the relationship between vaccine status and the severity of COVID-19 patients.

METHODS

The research design used is correlational analytic. The approach used is a retrospective cohort study, which looks at the vaccine status and severity of Covid-19 from the respondents' medical records from May to August 2021 at the Dr. R. Goeteng Taroenadibrata Purbalingga, Central Java.

The study population was Covid-19 patients who had been treated at the Dr. R. Goeteng Taroenadibrata Purbalingga a total of 884 patients with details in May 2021 54 patients were hospitalized, in June 2021 there were 130 patients, in July 2021 there were 425 patients, and August 2021 there were 275 patients. The sampling technique used is proportional simple random sampling. The research sample was calculated using the

Lemeshow formula with the results of 92 respondents (May = 6, June = 13, July = 44, August = 29).

The instrument used consists of a checklist to determine the vaccine status of respondents referring to the Centers for Disease Control and Prevention (CDC) which classifies vaccine status as follows: not vaccinated, the first dose vaccinated, and a complete dose of vaccine. The second checklist to find out the severity of Covid-19 refers to the National Institutes of Health (2021). The severity of Covid-19 is divided into 4 classifications: asymptomatic, mild symptoms, moderate symptoms, and severe/critical symptoms. The relationship between vaccine status and COVID-19 severity was tested using Fisher Exact non-parametric statistics.

RESULTS

Respondent characteristics

Table 1. Frequency distribution of respondent characteristics based on age, gender, occupation, education, and comorbidities (N = 92)

Characteristics	Distribution	
	Frequency	Percentage (%)
Age		
21-30 years	11	12
31- 40 years	12	13
41-50 years	15	16.3
51-60 years	28	30.4
61-70 years	21	22.8
71-80 years	5	5.4
Gender		
Male	49	53,3
Female	43	46,7
Educational background		
Elementary school	35	38
Junior high school	16	17.3
Senior high school	27	29,3
College	14	15,2
Occupation		
Health workers	3	3.3
Farmer	9	9.8
Self-employed	49	55.3
Housewife	21	22.8
Government employees	10	10.9
Comorbid		
DM	28	30.4
Cardiovascular disease	18	19.6
Hypertension	23	25
Respiratory disease	11	12
HIV/AIDs	1	1.1
Without comorbid	11	12

Commented [A1]: Bold

Table 1 shows that the majority of the age of Covid-19 patients are in the range of 50-60 years with a total of 28 (30.4%) respondents. There are 49 (53.3%) male patients with Covid-19, 35 (38%) respondents with an elementary school education level, and 49 (55.3%) respondents who are self-employed. Diabetes mellitus was the most comorbid,

with 28 (30.4%) respondents.

Vaccination status

Table 2. Distribution of the frequency of vaccination status of Covid-19 patients (N = 92)

Vaccination status	Frequency	Percentage (%)
Not vaccinated	64	69.6
The first dose of the vaccine	5	5.4
Second dose of vaccine	23	25
Total	92	100

Table 2 shows that of the 92 samples, 64 (69.6%) respondents had not been vaccinated, 5 (5.4%) had received the first dose of vaccine, and 23 (25%) respondents had received the second dose of vaccine.

The severity of the Covid-19 patient

Table 3. Frequency distribution of severity of Covid-19 patients (N = 92)

Vaccination status	The severity of the Covid-19 patient			
	Asymptomatic	Mild	Moderate	Severe/Critical
Not vaccinated	0 (0%)	3 (3.3%)	7 (7.6%)	54 (58.6%)
The first dose of the vaccine	0 (0%)	2 (2.2%)	0 (0%)	3 (3,3%)
Second dose of vaccine	0 (0%)	21 (22.8%)	0 (0%)	2 (2.2%)
Total	0 (0%)	26 (28.3%)	7 (7.6%)	59 (64.1%)

In table 3, it can be seen that from 92 respondents there were 59 (64.1%) patients with severe/critical symptoms, 26 (28.3%) patients with mild symptoms, and 7 (7.6%) patients with moderate symptoms. There were 54 (58.6%) respondents who had not been vaccinated and experienced severe symptoms. In respondents who had been vaccinated with the first dose, 3 people were experiencing severe symptoms. Of the respondents who had received the second dose of the vaccine, there were 2 people with severe symptoms, and 21 people experiencing mild symptoms.

Relationship between vaccination status and severity of Covid-19 patients

Table 4. Fisher Exact test results: Relationship between vaccine status and disease severity (N = 92).

Vaccination status	Severity				p-value	OR
	Asymptomatic - mild		Moderate - severe			
	N	%	N	%		
Not vaccinated	4	4.3	62	67.3	0.000	65.1
Vaccine doses 1 & 2	21	22.8	5	5.4		
Total	25	27.1	67	72		

Table 4 shows that 62 (67.3%) respondents who have not been vaccinated experienced moderate to severe Covid-19 symptoms. Meanwhile, only 5 (5.4%) respondents who had received doses 1 and 2 of the vaccine experienced severe symptoms. The results of the Fisher Exact test get a p-value of 0.000 (<0.05) and an OR value of 65.1 which means that there is a relationship between vaccination status and the severity of Covid-19, where individuals who are not vaccinated have a 65.1 times greater chance of experiencing moderate to severe symptoms than those who are vaccinated.

DISCUSSION

Respondent characteristics

Of the 92 respondents, there were 28 (30.4%) patients with an age range of 51-60 years and 21 (22.8%) patients with an age range of 61-70 years. Chen et al (2020) explained that most of the Covid-19 patients who were hospitalized were over 50 years old (67%). People aged over 50 years have an increased risk of being infected with Covid-19 or even dying from Covid-19 due to degeneration factors and comorbidities (Pastor-Barriuso et al., 2020; Israfil et al., 2021). One of the factors that contribute to the risk of being infected with Covid-19 and death in the

elderly is the presence of comorbidities because the average number of comorbidities grows gradually with age (Divo et al., 2014). The results of this study also showed that more men were hospitalized (53.3%, n = 92) than women. Chen et al (2020) in their research stated that more men with Covid-19 were hospitalized by 68%. Another study by Sadie et al (2021) showed that men received more intensive care in hospitals than women. Although epidemiological studies reveal differences in mortality rates between men and women among people diagnosed with Covid-19 and the reasons behind gender differences in mortality remain unknown (Wenham et al., 2020). There are several possible reasons explaining that females, who carry an X chromosome, have a high density of immune-related genes, resulting in biological differences that may contribute to faster pathogen clearance than males (Gompers et al., 2021). Women have higher innate and adaptive responses, resulting in a better immune response than men (Klein & Flanagan, 2016).

At the education level, it is known that there are 35 (38%) respondents who have an elementary school educational background. The causal relationship between lower education and the risk of COVID-19 severity is still not epidemiologically clear, as to whether people with lower educational backgrounds are more likely to develop severe COVID-19 symptoms (Yoshikawa & Asaba, 2021). However, people with low education may be more likely to be socio-economically disadvantaged and have an increased risk of SARS-CoV-2 transmission due to poor housing, overcrowding, and essential low-paying jobs that make social distancing all the more glaring (Yoshikawa & Asaba, 2021).

Most of the respondents' occupations were self-employed (55.3%, n = 92) and the least were health workers (3.3%, n = 92). Research conducted by Chen et al (2020) shows that self-employed rank first to be exposed to Covid-19. Employment can have a relationship with the incidence of Covid-19 (Selden & Berdahl, 2021). Some work that cannot be done at home has the potential to increase the incidence of Covid-19 numbers (Selden & Berdahl, 2021).

Diabetes mellitus was the most common comorbidity suffered by respondents (30.4%, n = 92), followed by hypertension (25%, n = 92), and cardiovascular disease (19.6%, n = 92). Older adult Covid-19 patients of all ages who have underlying medical conditions, such as diabetes and hypertension, have shown a poorer prognosis (Singh et al., 2020). Sanyaolu et al., (2020) also explained that Covid-19 patients who have co-morbidities with diabetes, hypertension, and cardiovascular disease have a risk of developing the severity of Covid-19 disease.

From the results of this study and previous studies, it can be concluded that over 50 years of age have a higher risk of being exposed to Covid-19, men are more at risk of infection than women, and education is not directly related to the risk of being infected with Covid-19. Work done outside the home, such as self-employment, has the potential to spread Covid-19. The most co-morbidities in Covid-19 patients are DM, hypertension, and cardiovascular disease.

Vaccination status of Covid-19 patients at RSUD Dr. R. Goeteng Taroenadibrata Purbalingga.

The results showed that 64 (69.6%) of Covid-19 patients who were hospitalized had not been vaccinated. A study by the Agency for Health Research and Development (LITBANGKES) in 2021 showed that the elderly was ranked first as 9308 (75%) patients who had not been vaccinated (Ministry of Health of the Republic of Indonesia, 2021). Zhang et al. (2022) stated that respondents who were not vaccinated were more likely to be hospitalized. Vaccination coverage in Indonesia as of June 30, 2021, is still very low, for the first dose, which is only 16% of the total target population, and the second dose of 12% of the target population (Ministry of Health of the Republic of Indonesia, 2021). The low vaccination rate may be due to doubts and hoax news circulating in the community, causing some people to be reluctant to vaccinate (Ministry of Health of the Republic of Indonesia, 2021).

The severity of Covid-19 patients

Of the 92 respondents, 54 (58%) patients had severe symptoms. Research by Zhang et al.

(2022) showed that patients who had a history of not being vaccinated had a moderate to severe risk of severity, even though none of the respondents who had not been vaccinated showed mild symptoms. Another study by Hu et al. (2022) showed that the non-vaccinated group had more severe symptoms than those who had been given the first or complete dose. The severity of symptoms in patients infected with Covid-19 varies greatly from asymptomatic to critical illness with deadly complications (Li et al., 2021). Several studies have suggested that several factors may be responsible for the severity of Covid-19, such as unvaccinated, hypertension, diabetes, and smoking (Rodriguez-Morales et al., 2020). Butt et al. (2022) conducted a cohort study of people with Covid-19 in Qatar concluding that infection with the Delta variant of SARS-CoV-2 was associated with more severe illness, and not being vaccinated was associated with a greater likelihood of critical illness.

Relationship between vaccination status and severity of Covid-19 patients

The results of this study indicate a relationship between vaccination status and the severity of Covid-19 (p = 0.000) with an OR value of 65.1 which means that individuals who are not vaccinated have a moderate to the severe chance of 65.1 times compared to those who have been vaccinated. Research conducted by Zhang et al (2022) showed that all unvaccinated patients had severe symptoms, and 17.8% of vaccinated patients had mild symptoms. Dyer (2021) argues that people who have not been vaccinated have an 11 times higher risk of being hospitalized than those who have received the first or second dose of the vaccine. Fisman et al (2022) also stated that the risk of infection was significantly higher among unvaccinated persons than among vaccinated persons. The contribution to infection among those vaccinated decreased from 15% to 10% and among those who were not vaccinated increased from 62% to 79% (Fisman et al., 2022). The body of a person who has been injected with the vaccine will stimulate antibodies to learn and recognize the weakened virus. Thus, the body will be exposed to the virus and reduce the risk of exposure (Ministry of Health of the Republic of Indonesia, 2021). With an immune condition that has recognized the virus, if a person's immune system is defeated and then exposed, the impact or symptoms of the virus will be weakened (Ministry of Health of the Republic of Indonesia, 2021).

A study conducted in Malaysia comparing the number of deaths of 20,823 cases with vaccination status showed that there was a significant difference between Covid-19 patients who died not being vaccinated as much as 43.2 times the age standard death rate per 100,000 population compared to those who were fully vaccinated with a p-value $\geq$ 0.05 (Abdul Taib et al., 2022). Research by Al Kaabi et al. (2021) conducted in the United Arab Emirates and Bahrain using the Sinopharm vaccine involving 40,382 participants randomized to receive at least 1 dose of 2 vaccines showed that there was effectiveness of 72.5% to 77.8 in individuals who had been completely vaccinated. Further Al Kaabi et al. (2021) concluded that the SARS-CoV-2 vaccine significantly reduced the risk of Covid-19 symptoms (95% CI = 90-97%; P <0.001).

Different research results are shown by research conducted by the Health Research and Development Agency (Badan LITBANGKES) involving 71,455 health worker respondents in the April-June 2021 period in DKI Jakarta which shows that health workers who are confirmed positive have almost no difference between those who have been vaccinated with dose 1 (4,02%) with 2 (5,03%). Likewise, the prevalence of the level of care in health workers who were vaccinated with the first dose and those not vaccinated there was no different, namely 0.31% and 0.35%, respectively. However, it is much lower for health workers who have been vaccinated at 0.17%. This also occurred in the mortality rate, there was no difference between unvaccinated and partially vaccinated (0.03%). However, health workers who are fully vaccinated have a very low mortality rate of 0.003%.

CONCLUSION

It can be concluded that:

1. Most of the respondents are men over 50 years old, work as self-employed, and the most comorbid is diabetes mellitus.
2. Respondents who have not been vaccinated are 64 (69.6%) patients.
3. Respondents with severe illness symptoms are patients who have not been vaccinated (54 people).
4. There is a relationship between vaccination status and the severity of Covid-19 (p = 0.000).

RECOMMENDATION

Based on the results of the study, it is recommended for people who have not been vaccinated to immediately vaccinate at the nearest vaccine service unit. Health service providers are expected to continue to provide education regarding invitations to participate in vaccines facilitated by the government.

REFERENCES

Abdul Taib, N. A., Baha Raja, D., Teo, A. K. J., Kamarulzaman, A., William, T., HS, A.-S., Mokhtar, S. A., Ting, C.-Y., Yap, W. A., Kim, M. C. Y., & Edwin Amir, L. (2022). Characterization of COVID-19 deaths by vaccination types and status in Malaysia between February and September 2021. The Lancet Regional Health - Western Pacific, 18, 100354. https://doi.org/10.1016/j.lanwpc.2021.100354

Al Kaabi, N., Zhang, Y., Xia, S., Yang, Y., Al Qahtani, M. M., Abdulrazzaq, N., Al Nusair, M., Hassany, M., Jawad, J. S., Abdalla, J., Hussein, S. E., Al Mazrouei, S. K., Al Karam, M., Li, X., Yang, X., Wang, W., Lai, B., Chen, W., Huang, S., Yang, X. (2021). Effect of 2 Inactivated SARS-CoV-2 Vaccines on Symptomatic COVID-19 Infection in Adults. JAMA, 326(1), 35. https://doi.org/10.1001/jama.2021.8565

Fatoni, A.Z. (2021). Acute Respiratory Distress Syndrome (ARDS) pada Pneumonia COVID-19. Journal of Anaesthesia and Pain, 2021, 2(1), 11–24.

Butt, A. A., Dargham, S. R., Chemaitelly, H., Al Khal, A., Tang, P., Hasan, M. R., Coyle, P. V, Thomas, A. G., Borham, A. M., Concepcion, E. G., Kaleeckal, A. H., Latif, A. N., Bertollini, R., Abou-Samra, A.-B., & Abu-Raddad, L. J. (2022). The severity of Illness in Persons Infected With the SARS-CoV-2 Delta Variant vs Beta Variant in Qatar. JAMA Internal Medicine, 182(2), 197–205. https://doi.org/10.1001/jamainternmed.2021.7949

Cascella, M., Rajnik, M., Aleem, A., Dulebohn, S. C., & Di Napoli, R. (2021). Features, Evaluation, and Treatment of Coronavirus (COVID-19). In StatPearls. http://www.ncbi.nlm.nih.gov/pubmed/32150360

Chen, N., Zhou, M., Dong, X., Qu, J., Gong, F., Han, Y., Qiu, Y., Wang, J., Liu, Y., Wei, Y., Xia, J., Yu, T., Zhang, X., & Zhang, L. (2020). Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. The Lancet, 395(10223), 507–513. https://doi.org/10.1016/S0140-6736(20)30211-7

Divo, M. J., Martinez, C. H., & Mannino, D. M. (2014). Aging and the epidemiology of multimorbidity. European Respiratory Journal, 44(4), 1055–1068. https://doi.org/10.1183/09031936.00059814

Dyer, O. (2021). Covid-19: Unvaccinated face 11 times the risk of death from delta variant, CDC data show. BMJ, n2282. https://doi.org/10.1136/bmj.n2282

El-Elimat, T., AbuAlSamen, M. M., Almomani, B. A., Al-Sawalha, N. A., & Alali, F. Q. (2021). Acceptance and attitudes toward COVID-19 vaccines: A cross-sectional study from Jordan. PLOS ONE, 16(4), e0250555. https://doi.org/10.1371/journal.pone.0250555

Fisman, D. N., Amoako, A., & Tuite, A. R. (2022). Impact of population mixing between vaccinated and unvaccinated subpopulations on infectious disease

dynamics: implications for SARS-CoV-2 transmission. Canadian Medical Association Journal, 194(16), E573–E580. https://doi.org/10.1503/cmaj.212105

Gompers, A., Bruch, J. D., & Richardson, S. S. (n.d.). (2021). Are COVID-19 Case Fatality Rates a Reliable Measure of Sex Disparities? Women's Health Issues : Official Publication of the Jacobs Institute of Women's Health, 32(2), 87–89. https://doi.org/10.1016/j.whi.2021.11.007

Hu, Z., Tao, B., Li, Z., Song, Y., Yi, C., Li, J., Zhu, M., Yi, Y., Huang, P., & Wang, J. (2022). Effectiveness of inactivated COVID-19 vaccines against severe illness in B.1.617.2 (Delta) variant–infected patients in Jiangsu, China. International Journal of Infectious Diseases, 116, 204–209. https://doi.org/10.1016/j.ijid.2022.01.030

Israfil, S. M. H., Sarker, M. M. R., Rashid, P. T., Talukder, A. A., Kawsar, K. A., Khan, F., Akhter, S., Poh, C. L., Mohamed, I. N., & Ming, L. C. (2021). Clinical Characteristics and Diagnostic Challenges of COVID−19: An Update From the Global Perspective. Frontiers in Public Health, 8. https://doi.org/10.3389/fpubh.2020.567395

Jara, A., Undurraga, E. A., González, C., Paredes, F., Fontecilla, T., Jara, G., Pizarro, A., Acevedo, J., Leo, K., Leon, F., Sans, C., Leighton, P., Suárez, P., García-Escorza, H., & Araos, R. (2021). Effectiveness of an Inactivated SARS-CoV-2 Vaccine in Chile. New England Journal of Medicine, 385(10), 875–884. https://doi.org/10.1056/NEJMoa2107715

Kaur, S. P., & Gupta, V. (2020). COVID-19 Vaccine: A comprehensive status report. Virus Research, 288, 198114. https://doi.org/10.1016/j.virusres.2020.198114

Ministry of Health of Indonesia Republic. (2021). *Tips Cegah Penularan Covid-19 : Hindari Kerumunan*. Kementrian Kesehatan Indonesia.

Klein, S. L., & Flanagan, K. L. (2016). Sex differences in immune responses. Nature Reviews Immunology, 16(10), 626–638. https://doi.org/10.1038/nri.2016.90

Li, X., Zhong, X., Wang, Y., Zeng, X., Luo, T., & Liu, Q. (2021). Clinical determinants of the severity of COVID-19: A systematic review and meta-analysis. PLOS ONE, 16(5), e0250602. https://doi.org/10.1371/journal.pone.0250602

Liu, Y., Ning, Z., Chen, Y., Guo, M., Liu, Y., Gali, N. K., Sun, L., Duan, Y., Cai, J., Westerdahl, D., Liu, X., Xu, K., Ho, K., Kan, H., Fu, Q., & Lan, K. (2020). Aerodynamic analysis of SARS-CoV-2 in two Wuhan hospitals. *Nature, 582*(7813), 557–560. https://doi.org/10.1038/s41586-020-2271-3

National Institutes of Health *(2021). Clinical Spectrum of SARS-CoV-2 Infection. https://www.covid19treatmentguidelines.nih.gov/overview/clinical-spectrum/*

P*astor-Barriuso, R., Pérez-Gómez, B., Hernán, M. A., Pérez-Olmeda, M., Yotti, R., Oteo-Iglesias, J., Sanmartín, J. L., León-Gómez, I., Fernández-García, A., Fernández-Navarro, P., Cruz, I., Martín, M., Delgado-Sanz, C., Fernández de Larrea, N., León Paniagua, J., Muñoz-Montalvo, J. F., Blanco, F., Larrauri, A., & Pollán, M. (2020). Infection fatality risk for SARS-CoV-2 in community dwelling population of Spain: nationwide seroepidemiological study. BMJ, m4509. https://doi.org/10.1136/bmj.m4509*

Pritchard, E., Matthews, P. C., Stoesser, N., Eyre, D. W., Gethings, O., Vista, K.-D., Jones, J., House, T., VanSteenHouse, H., Bell, I., Bell, J. I., Newton, J. N., Farrar, J., Diamond, I., Rourke, E., Studley, R., Crook, D., Peto, T. E. A., Walker, A. S.,

& Pouwels, K. B. (2021). Impact of vaccination on new SARS-CoV-2 infections in the United Kingdom. Nature Medicine, 27(8), 1370–1378. https://doi.org/10.1038/s41591-021-01410-w

Purbalingga District Health Office (2021). Monitoring data Covid-19 Kabupaten Purbalingga, Retrived September 22, 2021 from: http://corona.purbalinggakab.go.id/

Putri, K. E., Wiranti, K., Ziliwu, Y. S., Elvita, M., Y, F. D., S, P. R., & Niman, S. (2021). Kecemasan Masyarakat Akan Vaksinasi Covid-19. Jurnal Keperawatan, 9(3), 539–548. https://jurnal.unimus.ac.id/index.php/JKJ/article/view/7794

Rodriguez-Morales, A. J., Cardona-Ospina, J. A., Gutiérrez-Ocampo, E., Villamizar-Peña, R., Holguin-Rivera, Y., Escalera-Antezana, J. P., Alvarado-Arnez, L. E., Bonilla-Aldana, D. K., Franco-Paredes, C., Henao-Martinez, A. F., Paniz-Mondolfi, A., Lagos-Grisales, G. J., Ramírez-Vallejo, E., Suárez, J. A., Zambrano, L. I., Villamil-Gómez, W. E., Balbin-Ramon, G. J., Rabaan, A. A., Harapan, H., … Sah, R. (2020). Clinical, laboratory and imaging features of COVID-19: A systematic review and meta-analysis. Travel Medicine and Infectious Disease, 34, 101623. https://doi.org/10.1016/j.tmaid.2020.101623

Sadie, S., Sarah, H., Rahayma, S., Jennifer, L., Michael, P., & Anna, S. (2021). The Impact of Age, Sex, and Race on the Association of Risk Factors and Mortality in COVID-19 Patients. Journal of Infectious Diseases and Epidemiology, 7(6). https://doi.org/10.23937/2474-3658/1510215

Sanyaolu, A., Okorie, C., Marinkovic, A., Patidar, R., Younis, K., Desai, P., Hosein, Z., Padda, I., Mangat, J., & Altaf, M. (2020). Comorbidity and its Impact on Patients with COVID-19. SN Comprehensive Clinical Medicine, 2(8), 1069–1076. https://doi.org/10.1007/s42399-020-00363-4

Selden, T. M., & Berdahl, T. A. (2021). Risk of Severe COVID-19 Among Workers and Their Household Members. JAMA Internal Medicine, 181(1), 120. https://doi.org/10.1001/jamainternmed.2020.6249

Singh, A. K., Gupta, R., Ghosh, A., & Misra, A. (n.d.). Diabetes in COVID-19: Prevalence, pathophysiology, prognosis and practical considerations. Diabetes & Metabolic Syndrome, 14(4), 303–310. https://doi.org/10.1016/j.dsx.2020.04.004

Wenham, C., Smith, J., Morgan, R., & Gender and COVID-19 Working Group. (2020). COVID-19: the gendered impacts of the outbreak. Lancet (London, England), 395(10227), 846–848. https://doi.org/10.1016/S0140-6736(20)30526-2

WHO. (2021). Interim statement on booster doses for COVID-19 vaccination. https://www.who.int/news/item/22-12-2021-interim-statement-on-booster-doses-for-covid-19-vaccination---update-22-december-2021

WHO. (2021a). Transmission of SARS-CoV-2: implications for infection prevention precautions. World Health Organization. https://www.who.int/news-room/commentaries/detail/transmission-of-sars-cov-2-implications-for-infection-prevention-precautions

WHO. (2021b). WHO Regional Office for Europe: Nearly half a million lives saved by COVID-19 vaccination in less than a year.

Wright, B. J., Tideman, S., Diaz, G. A., French, T., Parsons, G. T., & Robicsek, A. (2022). Comparative vaccine effectiveness against severe COVID-19 over time in US hospital administrative data: a case-control study. The Lancet

Respiratory Medicine, 10(6), 557–565. https://doi.org/10.1016/S2213-2600(22)00042-X

Yoshikawa, M., & Asaba, K. (2021). Educational Attainment Decreases the Risk of COVID-19 Severity in the European Population: A Two-Sample Mendelian Randomization Study. Frontiers in Public Health, 9. https://doi.org/10.3389/fpubh.2021.673451

Zhang, X.-B., Yang, S.-J., Lin, Y., Chen, L.-L., Zhuang, Y.-L., & Zeng, H.-Q. (2022). Clinical Characteristics of COVID-19 Patients' Postvaccination. Viral Immunology, 35(3), 236–243. https://doi.org/10.1089/vim.2021.0204