Jurnal Berkala Epidemiologi
Volume 11 No 3. September 2023. 240-248
p-ISSN: 2301-7171; e-ISSN: 2541-092X

DOI: 10.20473/jbe.v11i32023.240-248
https://e-journal.unair.ac.id/JBE/
Email: jbe@fkm.unair.ac.id / jbepid@gmail.com

JBE Jurnal Berkala EPIDEMIOLOGI

Jurnal Berkala
EPIDEMIOLOGI
PERIODIC EPIDEMIOLOGY JOURNAL

ORIGINAL ARTICLE

THE EFFECT OF COMORBIDITIES ON MORTALITY IN COVID-19 PATIENTS IN dr RADEN SOEDARSONO HOSPITAL PASURUAN

Pengaruh Komorbid Terhadap Mortalitas Pada Pasien COVID-19 yang di RSUD dr. Raden Soedarsono Kota Pasuruan

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ARTICLE INFO

Article History:
Received, November, 21th, 2022
Revised form, March, 30th, 2023
Accepted, July, 3rd, 2023
Published online, September, 15th, 2023

Keywords:
comorbid;
mortality;
COVID-19;
Infectious disease
diabetes mellitus;
geriatric

Kata Kunci:
komorbid;
kematian;
COVID-19;
Penyakit infeksi
diabetes mellitus;
geriatri

ABSTRACT

Background: COVID-19 patients with comorbidities have the highest mortality risk in Indonesia during the pandemic. **Purpose**: This study purposed to determine the prevalence of comorbidities on mortality of COVID-19 patients at RSUD dr. Raden Soedarsono, Pasuruan. **Methods**: This study used a case-control design with 560 samples collected from January until December 2021. The samples consisted of 140 COVID-19 patients who were treated at RSUD dr. Raden Soedarsono, Pasuruan, in 2021 and declared dead as a case group, as well as 420 COVID-19 patients treated at RSUD dr. Raden Soedarsono, Pasuruan, in 2021 but did not die as a control group. The data were then analyzed using a logistic regression test with SPSS 22.0. **Results**: The results show that almost all COVID-19 patients did not have comorbidities of diabetes mellitus (85.50%), autoimmune (98.60%), kidney disease (98.20%), gastrointestinal diseases (92.10%), thrombosis and coagulation disorders (93.60%), myocardial injury (99.30%), heart failure (94.30%), hypertension (95.20%), and tuberculosis (5.70%). Also, almost all COVID-19 patients did not have comorbidities of geriatrics (71.60%), COPD (64.10%), and mortality status (25.00%). The results of the logistic regression test show that comorbidities of diabetes mellitus (P-value 0.01; OR 1.99) and geriatrics (P-value 0.00; OR 2.82) affect mortality in COVID-19 patients. Whereas comorbidities of autoimmune (P-value 0.84), kidney disease (P-value 0.37), gastrointestinal diseases (P-value 0.73), thrombosis and coagulation disorders (P-value 0.24), myocardial injury (P-value 0.84), heart failure (P-value 0.43), hypertension (P-value 0.93), COPD (P-value 0.86), and tuberculosis (P-value 0.15) do not affect mortality inCOVID-19 patients. **Conclusion**: Diabetes Mellitus and geriatrics are the most significant comorbidities in causing the death of COVID-19 patients at RSUD dr. Raden Soedarsono, Pasuruan.

How to Cite: Kencana, L. P., Kartiningrum, E. D., & Mafticha, E. (2023). The effect of comorbidities on mortality in COVID-19 patients in dr Raden Soedarsono Hospital Pasuruan. *Jurnal Berkala Epidemiologi, 11*(3), 240-248. https://dx.doi.org/10.20473/jbe.v11i32023.240-248

ABSTRAK

Latar Belakang: *Pasien COVID-19 dengan komorbid menempati urutan tertinggi penyebab mortalitas di Indonesia selama masa pandemi.* ***Tujuan:****.Tujuan penelitian untuk mengetahui pengaruh komorbid terhadap mortalitas pasien COVID-19 di RSUD dr. Raden Soedarsono Kota Pasuruan.* ***Metode:*** *Desain penelitian yang digunakan adalah case control dengan sampel berjumlah 560 yang dikumpulkan mulai bulan Januari - Desember 2021. Sampel terdiri atas 140 sampel kelompok kasus dan 420 sampel kelompok kontrol. Data yang terkumpul kemudian dianalisis menggunakan uji regresi logistik.* ***Hasil:*** *Hasil penelitian menunjukkan hamper seluruh pasien COVID-19 tidak memiliki komorbid diabetes mellitus (85,50%), autoimun (98,60%), penyakit ginjal (98,20%), gastrointestinal (92,10%), thrombosis dan gangguan koagulasi (93,60%), cedera miokardium (99,30%), gagal jantung (94,30%), hipertensi (95,20%), tuberkulosis (5,70%) dan sebagian besar pasien COVID-19 tidak memiliki geriatri (71,60%), PPOK (64,10%) dan berstatus meninggal (25,00%). Hasil uji statistic regresi logistic menunjukkan bahwa komorbid diabetes mellitus (P-value 0,01; OR 1,99) dan geriatri (P-value 0,00; OR 2,82) berpengaruh terhadap mortalitas pasien COVID-19. Sedangkan komorbid autoimun (P-value 0,84), penyakit ginjal (P-value 0,37), gastrointestinal (P-value 0,73), thrombosis dan gangguan koagulasi (P-value 0,24), cedera miokardium (P-value 0,84), gagal jantung (P-value 0,43), hipertensi (P-value 0,93), PPOK (P-value 0,86) dan tuberkulosis (P-value 0,15) tidak berpengaruh terhadap mortalitas pasien COVID-19.* ***Simpulan:*** *Diabetes Mellitus dan geriatric adalah komorbid yang paling signifikan dalam menyebabkan kematian akibat Covid 19 di rumah sakit*

INTRODUCTION

Coronavirus Disease 2019, most popular with the term COVID-19 is the latest variation of coronavirus that causes respiratory tract infections in humans. COVID-19 is named Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Cases of mortality due to COVID-19 are the main focus, especially in patients who are positively confirmed with COVID-19 and have comorbidities. In the United States, 94 % of cases of death are experienced by patients who are positively confirmed with COVID-19 and have comorbidities, and patients experience 6 % of cases of death due to COVID-19 (1). Cases of mortality due to COVID-19 with comorbidities occur in the United States and many countries, including Indonesia (2).

Comorbidities tend to increase health risks in patients because of a history of illness that can slow down the healing process. Patients with comorbidities are most at risk when infected with COVID-19. This happens because the patient's immune system is weakened due to the history of the disease. Also, patients with comorbidities may have an increased risk of poorer clinical outcomes and conditions (3). In East Java, 95% of patients positively confirmed with COVID-19 died because they have congenital (comorbid) diseases, namely heart and lung disease. COVID-19 patients with comorbidities of diabetes and hypertension are closely related to the severity of and mortality due to COVID-19 (4).

The prevalence of COVID-19 worldwide on March 28, 2022, reached 481 million positive cases and 6.12 million deaths. From all over the world, Indonesia is ranked 18th for COVID-19 cases (5). On March 28, 2022, based on a report from the COVID-19 Response Acceleration Task Force in Indonesia, the prevalence of COVID-19 reached 6,001,751 positive cases and 154,774 deaths. Comorbidities are the most common cause of death in patients positively confirmed with COVID-19 in several provinces, including East Java, Central Java, and South Sulawesi. East Java

Province is the province most at risk among the three regions.

The report of the East Java Provincial Health Office (2020) concerning COVID-19 cases on December 31, 2020, shows that there were a total of 84,152 positive cases with a Case Fertility Rate (CFR) of 6.92%. The East Java Provincial Health Office also states that the Pasuruan area has the highest Case Fertility Rate (CFR), 10.98%. The delay in hospital admission caused the death of COVID-19 patients in Pasuruan. Hence, patients only went to the hospital when their conditions were critical, with low oxygen saturation (less than 93). Most patients had a history of comorbidities, where diabetes was the most common, followed by hypertension and pulmonary disease (6). The high cases of COVID-19 in the Pasuruan area have resulted in the Indonesian government providing referral hospitals to handle COVID-19 disease, one of the hospitals is RSUD dr. Raden Soedarsono, Pasuruan.

A preliminary study conducted by researchers at RSUD dr. Raden Soedarsono, Pasuruan in the Pinere Room on February 14, 2022, obtained case data of patients who were positively confirmed with COVID-19 of 65 people, patients who recovered from COVID-19 of 49 people, patients who died due to COVID-19 of 16 people, COVID-19 patients with comorbidities of 40 people, and COVID-19 patients with comorbidities who died of 12 people. The comorbidities suffered by the patients included diabetes mellitus at 13.85%, hypertension at 7.69%, heart failure at 6.15%, and kidney failure at 4.61%. To reduce mortality in COVID-19 patients with comorbidities, conduct research to find out which comorbidities can exacerbate the symptoms of COVID-19. Therefore the researchers aimed to determine the prevalence of comorbidities on mortality in COVID-19 patients at RSUD dr. Raden Soedarsono, Pasuruan.

METHODS

This descriptive quantitative study uses an analytic observation method with a case-control design. The population of this study was all COVID-19 patients at RSUD dr. Raden Soedarsono, Pasuruan, from January to December 2021, namely 560 patients. The sampling technique used was total sampling. The case sample consisted of 140 COVID-19 patients who died, and the control sample consisted of 420 COVID-19 patients who are alive (survive COVID-19) with the inclusion criteria of patients diagnosed positive COVID-19 or reactive by RT-PCR test (nasopharyngeal swab or oropharyngeal swab and serum) who were treated at RSUD dr. Raden Soedarsono, Pasuruan, in 2021, and the exclusion criteria of pregnant women. The independent variables of this study were comorbidities of diabetes mellitus, geriatrics, autoimmune, kidney disease, gastrointestinal diseases, thrombosis and coagulation disorders, myocardial injury, heart failure, hypertension, Chronic Obstructive Pulmonary Disease (COPD), and tuberculosis. Meanwhile, the dependent variable of this study was the mortality status of COVID-19 patients. This study has passed an ethical review by the Health Research Ethics Committee (KEPK) of Stikes Majapahit Mojokerto with certificate No. 084/KEPK-SM/2022.

The instrument used was an observation sheet because the data used in the study were secondary data from the medical records of RSUD dr. Raden Soedarsono Pasuruan. Data analysis used a logistic regression test by SPSS.

RESULTS

Table 1 shows that the majority of COVID-19 patients at RSUD dr. Raden Soedarsono, Pasuruan, in this study, are 56-65 years old (19.70%) and females, with a total of 284 people (50.70%). Based on the case-control design of this study, there were two groups, namely the case group and the control group. The case group consisted of patients who died, while the control group consisted of patients who were alive (survived COVID-19).

It also shows that the majority of patients COVID-19 patients at RSUD dr. Raden Soedarsono, Pasuruan, in this study, do not have comorbidities of diabetes mellitus, with a total of 479 people (85.50%), geriatric, with a total of 401 people (71.60%), and autoimmune, with a total of 552 people (98.60%). In addition, it also shows that the majority of patients COVID-19 patients at RSUD dr. Raden Soedarsono, Pasuruan, in this study, do not have comorbidities of kidney disease, with a total of 550 people (98.20%); gastrointestinal diseases, with a total of 516 people (92.10%); thrombosis and coagulation disorders, with a total of 524 people (93.60%); myocardial injury, with a total of 556 people (99.30%); heart failure, with a total of 528 people (94.30%), hypertension, with a total of 533 people (95.20%), Chronic Obstructive Pulmonary Disease (COPD),

with a total of 359 people (64.10%), and tuberculosis, with a total of 528 people (94.30%).

Table 1
Characteristics of COVID-19 Patients at RSUD dr. Raden Soedarsono, Pasuruan

Variable	Mortality			
	Frequency		Percentage	
	Case	Control	Case	Control
Age (years old)				
0-5	1	79	1.25	98.75
6-11	2	35	5.41	94.59
12-16	6	12	33.33	66.67
17-25	8	14	36.36	63.64
26-35	8	51	13.56	86.44
36-45	19	63	23.17	76.83
46-55	28	68	29.17	70.83
56-65	39	71	35.45	64.55
>65	29	27	51.79	48.21
Gender				
Male	69	207	25.00	75.00
Female	71	213	25.00	75.00
Type of Comorbidities				
Diabetes Mellitus				
Yes	33	48	40.74	59.26
No	107	372	22.34	77.66
Geriatrics				
Yes	65	94	40.88	59.12
No	75	326	16.70	81.30
Autoimmune				
Yes	33	48	40.74	59.26
No	107	372	22.34	77.66
Kidney Disease				
Yes	2	8	20.00	80.00
No	138	142	25.09	74.91
Gastrointestinal disease				
Yes	11	33	25.00	75.00
No	129	387	25.00	75.00
Thrombosis and Coagulation Disease				
Yes	11	25	30.56	69.44
No	129	395	24.62	75.38
Myocardial Injury				
Yes	1	3	25.00	75.00
No	139	417	25.00	75.00
Heart failure				
Yes	6	26	18.75	81.25
No	134	394	25.40	74.60
Hypertension				
Yes	8	19	29.63	70.37
No	132	401	24.77	75.23
COPD				
Yes	48	153	23.88	76.12
No	92	267	25.63	74.37
Tuberculosis				
Yes	5	27	15.63	84.37
No	135	393	25.57	74.43

Source: RSUD dr. Raden Soedarsono, Pasuruan

Table 2 shows comorbidities that affect the mortality status of COVID-19 patients at RSUD dr. Raden Soedarsono, Pasuruan, namely diabetes mellitus (p-value: 0.01 OR: 1.99, CI (95%): 1.19-3.35 and geriatrician (p-value: 0.00 OR: 2.82 CI (95%): 1.86-4.29. Patients with diabetes mellitus are at almost a 2-fold risk of death compared to COVID-19 patients without diabetes mellitus, and the per cent likelihood of comorbidity of diabetes mellitus on the mortality status of COVID-19 patients ranges from 1.19 to 3.35. Patients with geriatrics are at almost a 3-fold risk of death compared to COVID-19 patients without geriatrics, with a 95% chance of comorbidities of geriatrics on the mortality status of COVID-19 patients ranges from 1.86 to 4.29.

DISCUSSION

Many factors influenced COVID-19 mortality. Gender, age, intra and extra-respiratory symptoms, hypertension, and chronic kidney disease increase the risk of mortality in COVID-19 patients (7). Diabetes mellitus is a chronic metabolic disease or disorder with multiple etiologies characterized by high blood sugar levels and disturbances in carbohydrate, lipid, and protein metabolism due to insufficiency (lack of potency) of insulin function. Insufficiency of insulin function can be caused by disruption or deficiency of insulin production by Langerhans beta cells of the pancreatic gland or caused by a lack of responsiveness of the body's cells to insulin (8). In 2020 diabetes mellitus occupies the second most common comorbidity case of COVID-19 in Indonesia and other countries (9). Patients with diabetes mellitus have elevated levels of purines in their blood. Purines can stimulate the entry of viruses that cause infection in the host cell. This causes patients with diabetes mellitus to be more at risk of being infected with COVID-19 (10). The relationship

between diabetes mellitus and COVID-19 is based on various pathophysiology, namely the mechanism of immunity and Angiotensin-Converting Enzyme 2 (ACE2). Patients with diabetes mellitus experience impaired immune response and viral clearance, making them more susceptible to infection. Inflammatory conditions in patients with diabetes mellitus can increase the risk of a cytokine storm, leading to shock, Acute Respiratory Distress Syndrome (ARDS), and worsening of COVID-19 symptoms and death. This is indicated by higher D-dimer levels in COVID-19 patients with diabetes mellitus compared to COVID-19 patients without diabetes mellitus (11).

Table 2
The Effect of Comorbidities on Mortality in COVID-19 Patients at RSUD dr. Raden Soedarsono, Pasuruan

Comorbidities	Mortality Status				*p -value*	OR (95% CI)
	Yes		No			
	n	%	n	%		
Diabetes Mellitus						
Yes	33	40.74	48	59.26	0.01	1.99
No	107	22.34	372	77.66		(1.19-3.35)
Geriatrics						
Yes	65	40.88	94	59.12	0.00	2.82
No	75	18.70	326	81.30		(1.86-4.29)
Autoimmune						
Yes	33	40.74	48	59.26	0.84	-
No	107	22.34	372	77.66		
Kidney Disease						
Yes	2	20.00	8	80.00	0.37	-
No	138	25.09	412	74.91		
Gastrointestinal diseases						
Yes	11	25.00	33	75.00	0,73	-
No	129	25.00	387	75.00		
Trombosis and coagulation disorders						
Yes	11	30.56	25	69.44	0.24	-
No	129	24.62	395	75.38		
Myocardial Injury						
Yes	1	25.00	3	75.00	0.84	-
No	139	25.00	417	75.00		
Heart failure						
Yes	6	18.75	26	81.25	0.43	-
No	134	25.4	394	74.6		
Hypertension						
Yes	8	29.63	19	70.37	0.93	-
No	132	24.77	401	75.23		
COPD						
Yes	48	23.88	153	76.12	0.86	-
No	92	25.63	267	74.37		
Tuberculosis						
Yes	5	15.63	27	84.37	5.00	-
No	135	25.57	393	74.43		

Source: RSUD dr Raden Soedarsono, Pasuruan, 2021

Patients with geriatrics usually are elderly patients with various diseases and disorders due to decreased organ function and physiology with social, economic, and environmental conditions requiring integrated health services (12). The elderly are more susceptible to various diseases due to the aging process. Aging is the process of gradually losing the ability of tissues to repair the damage they have suffered. The aging process is a continuous process naturally (13). Until now, compared to other age groups, detecting COVID-19 caused by a coronavirus in the elderly can cause more severe infection and death. This is due to the physical and psychological respiratory, gastrointestinal, and immune systems changes experienced by the elderly (14).

The changes experienced by the elderly and their relationship with COVID-19 infection in several systems include autoimmune disease, a disease of the immune system caused by an overreaction. Hence, self-antigens work abnormally and attack themselves. Those classified as autoimmune diseases include Juvenile Idiopathic Arthritis (JIA), multiple sclerosis, Systemic Lupus Erythematous (SLE), type 1 diabetes mellitus, Graves' syndrome, and scleroderma (15). It is generally known that patients with autoimmune diseases or inflammatory arthritis with high disease activity are more at risk of experiencing COVID-19 infection due to an immune deregulation condition. This study's results differ from those of a study by Aisyah et al (16) using a logistic regression method carried out based on data from the website of the COVID-19 Response Acceleration Task Force in Indonesia that patients with autoimmune diseases with COVID-19 infection have a 6-fold higher risk of death significantly compared to patients without autoimmune diseases (OR: 6.00: 95%CI: 2.41 – 14.94).

The kidney is the main target organ for SARS-CoV-2, and kidney failure is high in people with COVID-19. Impaired kidney function exacerbates damage to other organs. Older age, severe pneumonia, and pre-existing cardiovascular and kidney disease are potential risk factors for kidney failure in COVID-19 patients (17). This study is in line with a study by Satria et al (18) using an observational method in a retrospective study at Bhakti Dharma Husada Hospital Surabaya with a P-value of 0.44 more significant than the α value, so there is no effect between kidney disease on the risk of death of COVID-19 patients. However, the results of this study are not in line with the results of another study that has been carried out using an observational method in a retrospective study which shows that chronic kidney disease (OR 1.74; 95% CI: 1.35, 2.24) poses a significantly higher risk of death in COVID-19 patients (19). Patients with kidney disease are at higher risk of experiencing severity and even death when infected with COVID-19 and need hospital treatment because the coronavirus targets kidney cells. Lack of oxygen in the body can cause the kidneys to malfunction, cytokine storm (the immune system's response to the corona) can damage kidney tissue, and blood clots occur due to COVID-19 can block the kidney passages (17).

Gastrointestinal diseases are diseases that attack the digestive tract. Pathophysiology of COVID-19 disease, the coronavirus can affect various organs containing Angiotensin Converting Enzyme 2 (ACE-2) receptors. The virus will enter the organ through this receptor. Another mechanism that can occur is the systemic inflammatory response that occurs in COVID-19 patients. COVID-19 can develop into a Systemic Inflammatory Response Syndrome (SIRS) condition where a cytokine storm can directly cause damage to the intestinal epithelium. Damage to the intestinal epithelium causes malabsorption resulting in manifestations of nausea, vomiting, and diarrhea (20,21).

Thromboembolic disease or coagulation disorders in the blood vessels include pulmonary thromboembolism, deep vein thromboembolism (DVT), or other venous thrombosis (Venous Thromboembolism/VTE). The presence of COVID-19 disease plays a role in causing blood coagulation. This is because the blood vessels leading to the lungs are blocked, which interferes with transporting oxygen to the lungs and causes pulmonary embolism (22).

Myocardial injury may occur, especially in patients who already have cardiovascular disease. Systemic inflammation and pressure from increased coronary blood flow cause plaque rupture resulting in myocardial infarction. Acute cardiac injury is characterized by a significant increase in troponin I and an increase in ST. COVID-19 patients have a higher prevalence of myocardial injury, especially in patients treated in intensive care units with a poor prognostic factor and critical condition (23).

Heart failure is a disease caused by disturbances in the function of the heart and blood vessels. Patients with heart failure infected with

COVID-19 have a greater risk of worsening (even death) because the pathophysiological process of ACE-2 receptors in the cardiovascular system is the entry point for the COVID-19 virus and increases the risk of heart failure in COVID-19 patients, especially in a diseased heart that works harder to get blood and transports oxygen throughout the body. A diseased heart has problems pumping efficiently and burdens the entire body system. Patients with cardiovascular disease have an immune system that tends to be weak in responding to viruses (24).

Comorbidity of hypertension has no effect on the mortality of COVID-19 patients at RSUD dr. Raden Soedarsono, Pasuruan. This is because COVID-19 patients with hypertension do not experience complications and severe worsening of symptoms when patients receive treatment at the hospital. This study's results align with a study by Nadzifah & Hidajah (10) that hypertension is not significant in mortality in COVID-19 patients. COVID-19 patients with hypertension have the same clinical symptoms as patients without hypertension such as fever, nausea, and joint pain. However, 13 COVID-19 patients with hypertension died due to complications from other comorbidity factors. Medical record data show that COVID-19 patients who died had additional comorbidities of diabetes mellitus in 3 patients, geriatrics in 4 patients, thrombosis and coagulation disorders in 2 patients, and Chronic Obstructive Pulmonary Disease in 4 patients. The existence of additional comorbidities besides hypertension resulted in complications that worsened the condition of COVID-19 patients. For COVID-19 patients who only have hypertension, the clinical symptoms arising can still be handled by medical staff at RSUD dr. Raden Soedarsono, Pasuruan. Thus, COVID-19 patients who only have a comorbidity of hypertension can extend their life span.

Comorbidity COPD is at risk for COVID-19 infection, especially in severe COPD with a predicted VEP1 of less than 50%, a history of exacerbations with hospitalization, long-term oxygen requirements, shortness of breath symptoms, and other comorbidities. The systemic involvement that occurs in COVID-19 patients is thought to be due to ACE2, which is the receptor for virus entry into cells, is present in various cells in various organs, not just limited to the respiratory tract (25).

Comorbidity of tuberculosis has no effect on the mortality of COVID-19 patients at RSUD dr. Raden Soedarsono, Pasuruan. This is because COVID-19 patients at RSUD dr. Raden Soedarsono, Pasuruan, with tuberculosis, has the same clinical symptoms as patients without tuberculosis, such as fever, nausea, and joint pain. However, 6 COVID-19 patients with tuberculosis died due to complications from other comorbidity factors. Medical record data show that COVID-19 patients who died had additional comorbidities of diabetes mellitus in 5 patients and geriatrics in 1 patient. Additional comorbidities besides tuberculosis resulted in complications that worsened the condition of COVID-19 patients. For COVID-19 patients who only have tuberculosis, the clinical symptoms arising can still be handled by medical staff at RSUD dr. Raden Soedarsono, Pasuruan. Thus, COVID-19 patients who only have a comorbidity of hypertension can extend their life span.

CONCLUSION

The study results suggest that diabetes mellitus and geriatrics are the main comorbidities causing deaths in COVID-19 patients. Patients with diabetes mellitus have almost twice the risk of dying, while patients with geriatrics have almost three times the risk of dying compared to other comorbidities. Comorbidities of autoimmune kidney disease, gastrointestinal diseases, thrombosis and coagulation disorders, myocardial injury, heart failure, hypertension, COPD, and tuberculosis do not affect mortality in COVID-19 patients.

ACKNOWLEDGMENTS

We would like to deliver our gratitude to the head of STIKES Majapahit and the head National Seminar on big data and health development in Indonesia for the support and opportunities that have been given.

CONFLICT OF INTEREST

There are no financial, professional, or personal conflicts of interest affecting the writing or research of this research team.

AUTHOR CONTRIBUTIONS

LPK collected the data and got references for the article, EDK analized the data and wrote the article and EM wrote the results and discussion of the article and prepared the list of references.

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