Journal of Epidemiology and Public Health (2021), 06(03): 268-280
Masters Program in Public Health, Universitas Sebelas Maret

Meta-Analysis

Risk of Death in COVID-19 Patients with Comorbidity of Chronic Kidney Disease: Meta Analysis

Isna Nur Rohmah[1)], Didik Gunawan Tamtomo[2)], Bhisma Murti[1)]

[1)]Masters Program in Public Health, Universitas Sebelas Maret
[2)]Faculty of Medicine, Universitas Sebelas Maret

ABSTRACT

Background: Coronavirus disease 2019 or known as COVID-19 was a disease caused by severe acute respiratory coronavirus 2 (SARS-CoV-2). There are seven comorbidities that experience the most severity and death when infected with COVID-19, namely hypertension, diabetes mellitus, cardiovascular disease, chronic obstructive pulmonary disease, chronic kidney disease, cerebrovascular disease, and cancer. This study aimed to estimate the magnitude of the risk of death in COVID-19 patients with comorbid chronic kidney disease, with a meta-analysis of primary studies conducted by previous authors.
Subjects and Method: This study was a systematic review and meta-analysis with the following PICO, population: COVID-19 patients. Intervention: comorbid chronic kidney disease. Comparison: no comorbid chronic kidney disease. Outcome: death. The articles used in this study were obtained from three databases, namely Google Scholar, Pubmed, and Science Direct. Keywords to search for articles "Chronic Renal Disease" OR "Chronic Kidney Disease" AND COVID-19 OR SARS-CoV-2 AND Mortality OR Death. The articles included are full-text English with a cohort study design from 2020 to 2021 and report on adjusted Odds Ratio (aOR) in multivariate analysis. Article selection is done by using PRISMA flow diagram. Articles were analyzed using the Review Manager 5.3 application.
Results: A total of 12 cohort studies involving 234,124 COVID-19 patients from America, Europe and Indonesia were selected for a systematic review and meta-analysis. The data collected showed that COVID-19 patients with comorbid chronic kidney disease had a 4.61 times risk of death compared to COVID-19 patients without comorbid chronic kidney disease (aOR= 4.61; 95% CI= 3.30 to 6.45; p<0.001)
Conclusion: Chronic kidney disease increases risk of death in COVID-19 patients.

Keywords: chronic kidney disease, COVID-19, SARS-CoV-2, mortality

Correspondence:
Isna Nur Rohmah. Masters Program in Public Health, Universitas Sebelas Maret. Jl. Ir. Sutami 36A, Surakarta 57126, Central Java, Indonesia. Email: isnanr28@gmail.com. Mobile: 081327215685.

Cite this as:
Rohmah IN, Tamtomo DG, Murti B (2021). Risk of Death in COVID-19 Patients with Combidity of Chronic Kidney Disease: Meta Analysis. J Epidemiol and Public Health. 06(03): 268-280. https://doi.org/10.26911/-jepublichealth.2021.06.03.01.

BACKGROUND

Coronavirus disease 2019 or known as COVID-19 was a disease that first appeared in Wuhan, China in December 2019. The World Health Organization (WHO) confirmed that COVID-19 was caused by severe acute respiratory coronavirus 2 (SARS-CoV-2). Based on global data reported on October 8, 2021, the number of confirmed cases of COVID-19 by WHO region is 91,014,944 in the Americas, 71,486,376 in Europe, 43,300,384 in Southeast Asia,

15,934,629 in the Eastern Mediterranean, 8,787,304 in the Western Pacific, and 6,074,624 in Africa. The most deaths from COVID-19 occurred in America (2,235,162), followed by Europe (1,355,383), Southeast Asia (680,736), Eastern Mediterranean (292,739), Africa (147,777), and the Western Pacific (119,676) (WHO, 2021).

Common symptoms when infected with the SARS-CoV-2 virus are fever (98%), cough (76%), and myalgia or fatigue (44%) (Huang et al., 2020). Some patients experience sputum production, rhinorrhea, chest tightness, sore throat, nausea, vomiting, diarrhea, headache, ageusia, and anosmia several days before the onset of fever, suggesting that fever is very important but not the only initial symptom of infection. Some patients have only a mild fever, mild fatigue, or even no symptoms (Guan et al., 2020; (Chen et al., 2020).

The study of Wu and McGoogan (2020) stated that in 44,415 patients with confirmed COVID-19, 81% had mild respiratory problems, 14% had moderate pneumonia, and 5% had critical illness. Some patients with dyspnea and hypoxemia can rapidly progress to acute respiratory distress syndrome (ARDS), septic shock, blood clotting dysfunction, and even organ failure leading to death (Tsai et al., 2021). Some of the diseases that cause death are chronic kidney disease, chronic obstructive pulmonary disease (COPD), cerebrovascular disease for acute respiratory distress syndrome (ARDS), coronary heart disease for heart disorders (Fang et al., 2020).

Chronic kidney disease is a condition in which the kidneys are damaged so they cannot filter blood. Chronic kidney disease affects 8% to 16% of the population worldwide and is a leading cause of death (NIH, 2017; Gansevoort et al., 2013; Matsushita et al., 2020; Etgen et al., 2012; Chin et al., 2008; O'Callaghan et al., 2011; Chen et al., 2019).

Based on this background, a comprehensive study is needed from various primary studies on the risk of death of COVID-19 patients with comorbid chronic kidney disease. This study aims to estimate the magnitude of the risk of death in COVID-19 patients with comorbid chronic kidney disease, with a meta-analysis of the primary study conducted by the previous authors.

SUBJECTS AND METHOD

1. Study Design

This research was a systematic review and meta-analysis. The articles used in this study were obtained from several databases, namely Google Scholar, Pubmed, and Science Direct between 2020 and 2021. The selection of articles was carried out using PRISMA flow diagrams. The keywords to search for articles are as follows "Chronic Renal Disease" OR "Chronic Kidney Disease" AND COVID-19 OR SARS-CoV-2 AND Mortality OR Death.

2. Inclusion Criteria

The inclusion criteria in this research article are: full-text articles using a cohort study design, research subjects are COVID-19 patients, research outcomes are death, multivariate analysis with adjusted Odds Ratio (aOR) to measure the estimated effect.

3. Exclusion Criteria

The exclusion criteria in this research article are: articles published in languages other than English, statistical results reported in the form of bivariate analysis, articles before 2020.

4. Operational Definition of Variable

The search for articles was carried out by considering the eligibility criteria determined using the PICO model. Population: COVID-19 patients. Intervention: comorbid chronic kidney disease. Comparison: no

comorbid chronic kidney disease. Outcome: death.

Chronic kidney disease comorbidity is defined as a condition that shows a decrease in kidney function within three months or more, with the categorization of chronic kidney disease comorbid or without chronic kidney disease comorbidity. The instruments used are health records/medical records and officer data collection records related to the diagnosis of chronic kidney disease. The measurement scale is categorical.

Death in COVID-19 patients was defined as the death status of patients diagnosed with COVID-19, categorized as dead or alive. The instrument used is a death certificate document with a COVID-19 diagnosis. The measurement scale is categorical.

5. Instrument Study

Research is guided by the PRISMA flow diagram and quality assessment using the Critical Appraisal Skills Program (CASP, 2018).

6. Data Analysis

The data in the study were analyzed using the Review Manager application (RevMan 5.3). Forest plots and funnel plots were used to determine the size of the relationship and heterogeneity of the data. The fixed effect model is used for homogeneous data, while the random effect model is used for heterogeneous data across studies.

RESULTS

The article search process was carried out through several journal databases including Google Scholar, Pubmed, and Science Direct. The review process for related articles can be seen in the PRISMA flow diagram in figure 1. Research related to the risk of death of COVID-19 patients with comorbid chronic kidney disease consists of 12 articles from the initial search process yielding 1,297 articles, after the deletion process of published articles with 47 of which meet the requirements for further full-text review. A total of 12 articles that met the quality assessment were included in the quantitative synthesis using a meta-analysis.

It can be seen in Figure 2 that the research articles come from three continents, namely America (New York, United States, Michigan, Brazil), Europe (Ireland, Sweden, Georgia, France), and Asia (Indonesia). Table 1, the researchers conducted an assessment of the quality of the study. Table 2 shows that 12 articles from a cohort study provide evidence of the association of the effect of comorbid chronic kidney disease on the risk of death of COVID-19 patients.

Based on the results of the forest plot, the cohort study showed that COVID-19 patients with comorbid chronic kidney disease had a 4.61 times risk of death compared to COVID-19 patients without comorbid chronic kidney disease (aOR = 4.61; 95% CI = 3.30 to 6.45), and the results was statistically significant ($p < 0.001$). The heterogeneity of the research data showed $I2 = 86\%$ so that the distribution of the data was declared heterogeneous (random effect model).

The funnel plot results show a publication bias with an overestimated effect which is characterized by an asymmetric distribution between the right and left plots. There are seven plots on the right, four plots on the left, and one plot touching the vertical line. The plot on the right side of the graph has a standard error (SE) between 0 and 0.8. The plot on the left side of the graph has a standard error (SE) between 0 and 0.4.

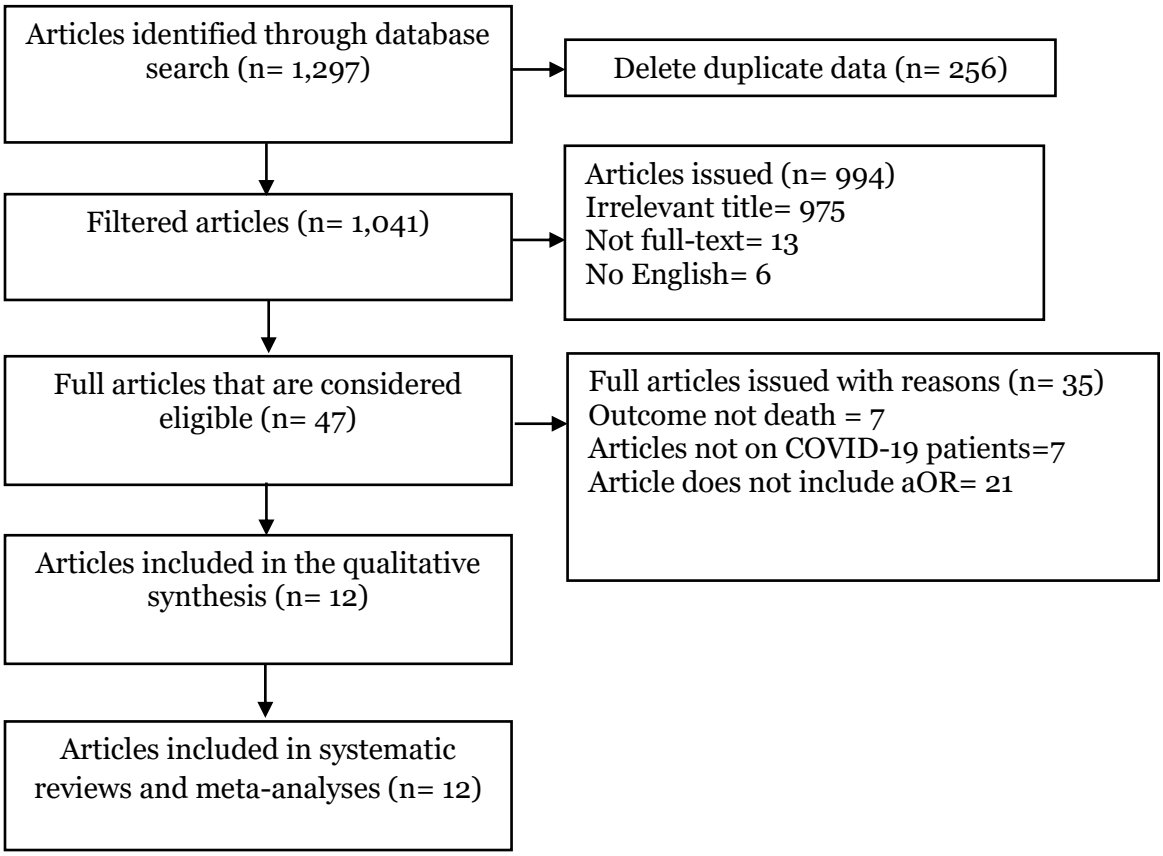

Figure 1. PRISMA flow diagram

Figure 2. Map of the study area of patient mortality risk COVID-19 with comorbid chronic kidney disease

Table 1. Assessment of study quality published by the Critical Appraisal Skills Program (CASP)

No	Indicators	Publication (Author and Year)					
		Chilimuri et al. (2020)	Fried et al. (2021)	Klang et al. (2020)	Muhammad et al. (2021)	Mulhem et al. (2021)	Pietre et al. (2021)
1	Does this research address a clearly focused problem?	2	2	2	2	2	2
2	Was the group recruited in an acceptable way?	2	2	2	2	2	2
3	Is chronic kidney disease exposure accurately measured to minimize bias?	2	2	2	2	2	2
4	Was the outcome (death status) accurately measured to minimize bias?	2	2	2	2	2	2
5	Did the author identify all the important confounding factors? Has the author taken into account confounding factors in the design and/or analysis?	2	2	2	2	2	2
6	Was the follow-up subject complete enough? Was the follow-up of the subject long enough?	2	2	2	2	2	2
7	Are the results of this study reported in aOR?	2	2	2	2	2	2
8	How precise is the result?	2	2	2	2	2	2
9	Do you believe the results?	2	2	2	2	2	2
10	Can the results be applied to the local population?	2	2	2	2	2	2
11	Are the results of this study consistent with other available evidence?	2	2	2	2	2	2
12	What are the implications of this research for practice?	2	2	2	2	2	2
	Total	24	24	24	24	24	24

Note:

2: Yes; 1: Can't tell; 0: No

Table 1. Next

No	Indicators	Publications (Author and Year)					
		Rustgi et al. (2020)	Bennett et al. (2021)	Chew et al. (2020)	Chishinga et al. (2020)	Kaeuffer et al. (2020)	Surendra et al. (2021)
1	Does this research address a clearly focused problem?	2	2	2	2	2	2
2	Was the group recruited in an acceptable way?	2	2	2	2	2	2
3	Is chronic kidney disease exposure accurately measured to minimize bias?	2	2	2	2	2	2
4	Was the outcome (death status) accurately measured to minimize bias?	2	2	2	2	2	2
5	Did the author identify all the important confounding factors? Has the author taken into account confounding factors in the design and/or analysis?	2	2	2	2	2	2
6	Was the follow-up subject complete enough? Was the follow-up of the subject long enough?	2	2	2	2	2	2
7	Are the results of this study reported in aOR?	2	2	2	2	2	2
8	How precise is the result?	1	2	2	2	1	1
9	Do you believe the results?	2	2	2	2	2	2
10	Can the results be applied to the local population?	2	2	2	2	2	2
11	Are the results of this study consistent with other available evidence?	2	2	2	2	2	2
12	What are the implications of this research for practice?	2	2	2	2	2	2
	Total	23	24	24	24	23	23

Note:

2: Yes; 1: Can't tell; 0: No

Table 2. Description of the primary studies included in the meta-analysis primary studies

No	Author (year)	Country	Study Design	Sample		P (Population)	I (Intervention)	C (Comparisons)	O (Outcome)	aOR (CI 95%)
				COVID-19	PGK					
1	Chilimuri *et al.* (2020)	New York	Retrospective Cohort	375	51	Male and female COVID-19 patients aged 48-75 years	Chronic kidney disease comorbidities	No comorbid chronic kidney disease	Death	1.33 (0.63 to 2.77)
2	Fried *et al.* (2021)	The USA	Retrospective Cohort	11,721	1,427	Male and female COVID-19 patients over 18 years old	Chronic kidney disease comorbidities	No comorbid chronic kidney disease	Death, Requires mechani-cal ventilation	1.66 (1.45 to 1.91)
3	Klang *et al.* (2020)	New York	Retrospective Cohort	6,760	342	COVID-19 patients mean age 72.4 years and women mean age 77.4 years	Chronic kidney disease comorbidities	No comorbid chronic kidney disease	Death	0.70 (0.50 to 0.90)
4	Muhammad *et al.* (2021)	The USA	Retrospective Cohort	200	60	Male and female COVID-19 patients mean age 58.9 years	Chronic kidney disease comorbidities	No comorbid chronic kidney disease	Death	1.25 (0.56 to 3.01)
5	Mulhem *et al.* (2021)	Michigan	Retrospective Cohort	3,219	1,299	Male and female COVID-19 patients mean 65.2 years old	Chronic kidney disease comorbidities	No comorbid chronic kidney disease	Death	1.73 (1.40 to 2.15)
6	Pietre *et al.* (2021)	Brazil	Retrospective Cohort	181,964	9,820	Male and female COVID-19 patients mean age 59.44 years	Chronic kidney disease comorbidities	No comorbid chronic kidney disease	Death	1.49 (1.19 to 1.86)

Table 2. Next

No	Author (Year)	Country	Study Design	Sample		P (Population)	I (Intervention)	C (Comparisons)	O (Outcome)	aOR (CI 95%)
				COVID-19	PGK					
7	Rustgi et al. (2020)	The USA	Retrospective Cohort	403	289	Male and female COVID-19 patients aged >18 years	Chronic kidney disease comorbidities	No comorbid chronic kidney disease	Death	2.40 (1.14 to 5.04)
8	Bennett et al. (2021)	Ireland	Retrospective Cohort	19,789	558	Male and female COVID-19 patients	Chronic kidney disease comorbidities	No comorbid chronic kidney disease	Death, enter the ICU	1.75 (1.29 to 2.38)
9	Chew et al. (2020)	Swedia	Retrospective Cohort	1,563	64	Male and female COVID-19 patients	Chronic kidney disease comorbidities	No comorbid chronic kidney disease	Death	0.70 (0.30 to 1.40)
10	Chishinga et al. (2020)	Georgia	Retrospective Cohort	2,820	260	Male and female COVID-19 patients	Chronic kidney disease comorbidities	No comorbid chronic kidney disease	Death, hospitali-zation and ICU admission	1.70 (0.90 to 3.10)
11	Kaeuffer et al. (2020)	France	Retrospective Cohort	1,045	172	Male and female COVID-19 patients between the ages of 20 and 100	Chronic kidney disease comorbidities	No comorbid chronic kidney disease	Death, admitted to ICU	2.30 (1.30 to 3.90)
12	Surendra et al. (2021)	Indonesia	Retrospective Cohort	4,265	108	Male and female COVID-19 patients aged 0 to 70 years	Chronic kidney disease comorbidities	No comorbid chronic kidney disease	Death	2.60 (1.64 to 4.13)

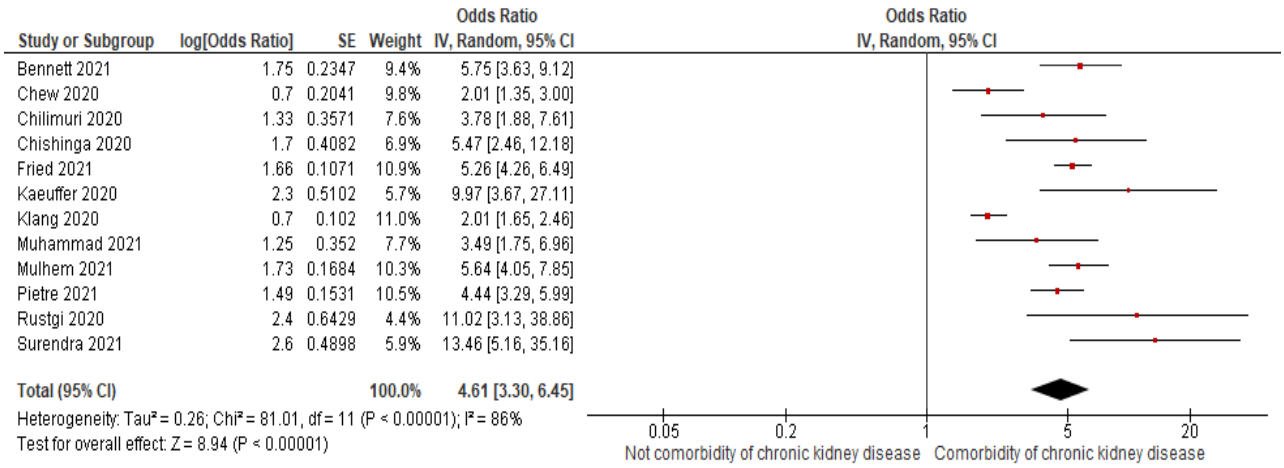

Figure 3. Forest Plot of Death Risk in COVID-19 Patients with Comorbid Chronic Kidney Disease

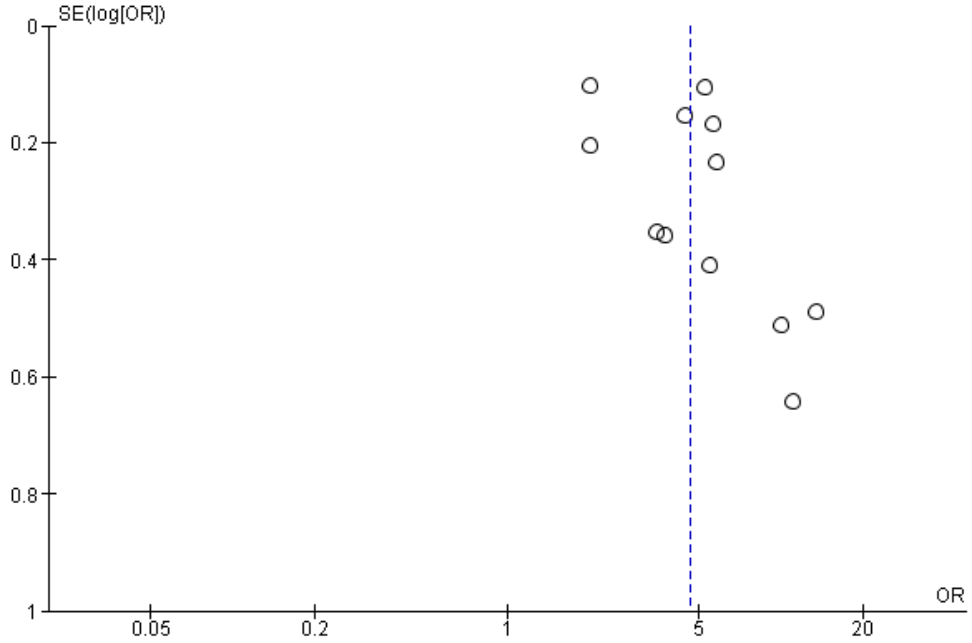

Figure 4. Funnel Plot of Death Risk in COVID-19 Patients with Comorbid Chronic Kidney Disease

DISCUSSION

This systematic study and meta-analysis of research raised the risk of death in COVID-19 patients with comorbid chronic kidney disease. This study discusses chronic kidney disease which is considered important because it is one of the risk factors that can aggravate and cause death in COVID-19 patients.

Comorbid chronic kidney disease may increase the risk of death in COVID-19 patients. This is in line with the research of Almazeedi et al. (2020) revealed the effect of co-morbid chronic kidney disease on the likelihood of being admitted to the Intensive Care Unit (ICU) or an increased risk of death for COVID-19 patients (aOR = 2.19; 95% CI = 0.27 to 16.08). Another finding from a retrospective cohort study of the

Wuhan region, China which included 3,309 COVID-19 patients and 57 individuals with comorbid chronic kidney disease, also revealed an influence between chronic kidney disease comorbidity on the risk of death of COVID-19 patients. Among COVID-19 patients who had comorbid chronic kidney disease had an increased risk of death (aOR= 2.85; 95% CI= 1.42 to 5.73) (Chen et al., 2020).

Several studies have stated that age, secondary infection, the presence of previous comorbidities, and the presence of inflammatory indicators that have increased in the blood are fatal predictors of the condition of COVID-19 patients. There were significant differences in the number of white blood cells, absolute values of lymphocytes, platelets, albumin, total bilirubin, blood urea nitrogen, blood creatinine, myoglobin, cardiac troponin, C-reactive in the group of patients who survived. protein (CRP) and interleukin-6 (IL-6) (Ruan et al., 2020).

Kidneys are one of the organs that have ACE2 receptors. Angiotensin-converting enzyme (ACE) 2 is a common binding site (receptor) for SARS-CoV and SARS-CoV-2. When a person has chronic kidney disease, there will be an increase in ACE2 receptor expression (Ding et al., 2004; Zou et al., 2020). When SARS-CoV-2 binds to the ACE2 receptor, it will inhibit the normal function of ACE so that tissue damage can occur (Bourgonje et al., 2020; Hoffmann et al., 2020).

Inflammation is a very important factor associated with malnutrition in patients with chronic kidney disease. Various cytokines associated with inflammatory events, especially IL-1, IL-6 and TNF-α are proinflammatory cytokines that are directly involved in chronic kidney disease patients. The inflammatory process is associated with an increase in the burden of oxidative stress which causes the formation of advanced glycosylation end-products (AGEs), AGEs and their receptors cause an increase in the production of interleukin-6 (IL-6) by monocytes and indirectly to excess CRP formation in the liver, causing inflammation. Chronic inflammation characterized by an increase in pro-inflammatory cytokines such as TNF- and IL-6 has been increasingly recognized as one of the important factors for the aggravation of chronic kidney disease.

Patients with chronic kidney disease have high levels of interleukin-6 (IL-6). C-reactive protein (CRP), growth differentiation factor 15 (GDF15), pentraxin 3 (PTX3), and interleukin (IL-6) are inflammatory mediators whose circulating levels are elevated in chronic kidney disease patients. Accumulation of uremic toxins, fluid overload, development of oxidative stress, among other chronic kidney disease disorders contribute to an increase in IL-6; Decreased renal function by reducing IL-6 clearance also contributes to its elevated levels. Likewise, the dialysis procedure contributes to stimulating the inflammatory response which can further increase the production of IL-6. (Rocha et al., 2021; Li et al., 2020).

Patients with COVID-19 also experience increased levels of interleukin-6 (IL-6) which is the main trigger for cytokine storms. Cytokine storm will trigger a severe inflammatory immune response that contributes to the incidence of ARDS, multi-organ failure, and ultimately can cause death in COVID-19 patients (Li et al., 2020).

Furthermore, hyperfiltration occurs in the kidney, this process occurs due to vasoconstriction in the efferent arteriole in the kidney which causes intra-glomelural

hypertension. This increased pressure can damage endothelial cells. Endothelial cell damage can be exacerbated in conditions infected with SARS-CoV-2, namely the direct invasion mechanism of SARS-CoV-2 into vascular endothelial cells, excess systemic inflammatory response, and hypoxic conditions.

Ultimately, in patients with COVID-19, an exaggerated immune response occurs and causes a systemic cytokine storm that triggers the systemic inflammatory response syndrome (SIRS) which can cause systemic endothelial damage and a hypercoagulable state that increases the risk of systemic macrothrombosis and microthrombosis. Macrothrombosis manifestations can be in the form of venous thromboembolism or arterial thromboembolism, while microthrombotic manifestations can play a role in the ARDS process and multiorgan failure to death (Cuker and Flora, 2021; Willim et al., 2020).

As a result, the above-mentioned mechanisms can contribute to the worsening of the patient's condition due to SARS-CoV-2 infection, even leading to death. The limitations of this study are that there is a language bias because it only uses English articles, a publication bias shown in the funnel plot results, and a search bias because it only uses three databases.

AUTHOR CONTRIBUTION

Isna Nur Rohmah is the main researcher who selects topics, searches for and collects research data. Didik Gunawan Tamtomo and Bhisma Murti analyzed data and reviewed research documents.

FUNDING AND SPONSORSHIP

This study is self-funded.

CONFLICT OF INTEREST

There is no conflict of interest in this study.

ACKNOWLEDGMENT

We thank the database providers Google Scholar, Pubmed, and Science Direct.

REFERENCES

Almazeedi S, Al-Youha S, Jamal MH, Al-Haddad M, Al-Muhaini A, Al-Ghimlas, Al-Sabbah S (2020). Characteristics, risk factors and outcomes among the first consecutive 1096 patients diagnosed with COVID-19 in Kuwait. EClinicalMedicine. 24 (100448) 1-9. doi: 10.1016/j.eclinm.-2020.100448.

Bourgonje AR, Abdulle AE, Timens W, Hillebrands J, Navis GJ, Gordijn SJ, Bolling MC (2020). Angiotensin-converting enzyme-2 (ACE2), SARS-CoV-2 and pathophysiology of coronavirus disease 2019 (COVID-19). J. Pathol. 251(3):228-248. doi: 10.100-2/path.5471.

CASP (2018). Critical appraisal skills programme cohort study checklist. Retrieved from https://casp-uk.net/-wpcontent/uploads/2018/01/CASP-Cohort-Study-Checklist_2018.pdf.

Chen TK, Knicely DH, Grams ME (2019). Chronic kidney disease diagnosis and management. JAMA. 322 (13): 1294-1304. doi: 10.1001/jama.2019.14745.

Chen Y, Guo Y, Pan Y, Zhao ZJ (2020). Structure analysis of the receptor binding of 2019-nCoV. Biochem Biophys Res Commun. 525(1): 135-140. doi: 10.1016/j.bbrc.2020.02.071.

Chin HJ, Song YR, Lee JJ, Lee SB, Kim KW, Na KY, Kim S et al. (2008). Moderately decreased renal function negatively affects the health-related quality of life among the elderly Korean population: a population-based study. Nephrol Dial Transplant. 23(9): 2810-2817. doi: 10.10-93/ndt/gfn132.

Cuker A, Flora P (2021). COVID-19: Hypercoagulability. Retrieved from https://www.uptodate.com/contents/covid-19-hypercoagulability.

Ding Y, He L, Zhang Q, Huang Z, Che X, Hou J, Wang H et al. (2004). Organ distribution of severe acute respiretory syndrome (SARS) associated coronavirus (SARS-CoV) in SARS patients: implications for pathogenesis and virus transmission pathways. J Pathol. 203 (2): 622-630. doi: 10.1002/-path.1560.

Etgen T, Chonchol M, Förstl H, Sander D (2012). Chronic kidney disease and cognitive impairment: a systematic review and meta-analysis. Am J Nephrol. 35 (5): 474-482. doi: 10.1159/000338135.

Fang X, Li S, Yu H, Wang P, Zhang Y, Chen Z, Li Y, et al. (2020). Epidemiological, comorbidity factors with severity and prognosis of COVID-19: A systematic review and meta-analysis. Aging. 12 (13): 12493-12503. doi: 10.18632/aging.103579.

Gansevoort RT, Correa-Rotter R, Hemmelgarn BR, Jafar TH, Heerspink HJL, Mann JF, Matsushita K et al. (2013). Chronic kidney disease and cardiovascular risk: epidemiology, mechanisms, and prevention. Lancet. 382 (9889): 339-352. doi: 10.1016/S0140-6736(13)-60595-4.

Guan W, Ni Z, Hu Y, Liang W, Ou C, He J, Liu L et al. (2020). Clinical characteristics of coronavirus disease 2019 in china. New Eng J Med. 382 (18): 1708-1720. doi: 10.1056/NEJMoa2002032.

Li X, Geng M, Peng Y, Meng L, Lu S (2020). Molecular immune pathogenesis and diagnosis of COVID-19. J Pharm Anal. 10 (2): 102-108. doi: 10.1016/j.jpha.2020.03.001.

Matsushita K, Velde MVD, Astor BC, Woodward M, Levey AS, Jong PED, Coresh J et al. (2010). Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality: a collaborative meta-analysis of general population cohorts. Lancet. 375(9731): 2073-2081. doi: 10.1016/S0140 6736-(10)60674-5.

NIH (2017). Chronic kidney disease (CKD). National institutes of health. Retrieved from https://www.niddk.nih.gov-/health-information/kidney-disease-/chronic-kidneydisease-ckd/what-is-chronic-kidney-disease.

O'Callaghan CA, Shine B, Lasserson DS (2011). Chronic kidney disease: a large-scale population- based study of the effects of introducing the CKD-EPI formula for eGFR reporting. BMJ Open. 1 (2): 1-10. doi: 10.1136/bmjopen-2011-000308.

Rocha S, Valente MJ, Coimbra S, Catarino C, Rocha-Pereira P, Oliveira JG, Madureira J et al. (2021). Interleukin 6 (rs1800795) and pentraxin 3 (rs-2305619) polymorphisms-association with inflammation and all-cause mortality in end-stage-renal disease patients on dialysis. Sci Rep. 11: 14768. doi: 10.1038/s41598-021-940-75-x.

Ruan Q, Yang K, Wang W, Jiang L, Song J (2020). Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med. 46: 846-848. DOI: 10.1007-/s00134-020-05991-x.

Tsai PH, Lai W, Lin Y, Luo Y, Lin Y, Chen H, Chen Y et al. (2021). Clinical manifestation and disease progresssion in COVID-19 infection. J Chin

Med Assoc. 84(1): 3-8. doi: 10.1097-/JCMA.0000000000000463.

WHO (2021). WHO coronavirus (COVID-19) Dashboard. World Health Organization. Retrieved from https://covid-19.who.int/.

Willim HA, Hardigaloeh AT, Supit AI, Handriyani (2020). Koagulopati pada Coronavirus Disease-2019 (COVID-19) (Coagulopathy in Coronavirus Disease-2019 (COVID-19): Tinjauan Pustaka. Intisari Sains Medis. 11 (3): 749-756.doi: 10.15562/ism.v11i3.766.

Wu Z, McGoogan JM (2020). Characteristics of and Important Lessons from the Coronavirus Disease 2019 (COVID-19) Outbreak in China. JAMA. 323(13): 1239 1242. doi: 10.1-001/jam-a.2020.2648.

Zou X, Chen K, Zou J, Han P, Hao J, Han Z (2020). Single-cell RNA-seq data analysis on the receptor ACE2 expression reveals the potential risk of different human organs vulnerable to 2019-nCoV infection. Front Med. 12: 1-8. doi: 10.1007/s11684-020-07-54-0.