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Editorial Team



Chatarina Umbul Wahjuni

Editor in Chief

Department of Epidemiology, Biostatistics, Population Studies, and Health Promotion, Faculty of Public Health, Universitas Airlangga, Indonesia

0000-0001-9518-5930

C U Wahyuni

Scopus' 22958724600

6055273



Kurnia Dwi Artanti

Managing Editor

Department of Epidemiology, Biostatistics, Population Studies, and Health Promotion, Faculty of Public Health, Universitas Airlangga, Indonesia

0000-0002-2372-666X

Kurnia Dwi Artanti

Scopus' 57208226137

5991894



Arief Hargono

Managing Editor

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0000-0001-8978-9877

Arief Hargono

Scopus' 57208225627

5975513



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Fariani Syahrul

Scopus' 57208227712

6069583



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0000-0002-2900-908X

Laura Navika Yamani

Scopus' 56185456000

6690253



Febri Dwirahmadi

International Editorial Board

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0000-0002-9367-3452

Febi Dwirahmadi, Ph.D.

Scopus[®]

55900228400



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0000-0003-0296-8843

-

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National Institute of Infectious Diseases (NIID) Tokyo, Japan

0000-0001-7543-3589

-

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54402515900



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0000-0002-0707-1093

-

Scopus[®]

7403092686



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Nomor : 3148/UN3.1.10/KP/2023

Yang bertandatangan di bawah ini :

Nama : Dr. Santi Martini, dr. M.Kes
NIP : 196609271997022001
Pangkat/Golongan : Pembina / Gol. (IV/a)
Jabatan : Dekan

Dengan ini menerangkan bahwa :

Nama : Dr. Hari Basuki Notobroto, dr., M.Kes
NIP : 196506251992031002
Pangkat/Golongan : Pembina (Gol. IV/a)
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Telah melaksanakan penelitian dengan judul sebagai berikut :

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Adapun penelitian tersebut layak dilakukan dan menghasilkan output yang sangat baik, meskipun belum ada *Uji Ethical Clearance* karena merupakan penelitian menggunakan metode **Systematic Review**.

Demikian surat keterangan ini kami buat untuk dapat dipergunakan sebagai persyaratan pengusulan Jabatan Fungsional Guru Besar.

Surabaya, 24 April 2023



Dr. Warti Martini, dr. M.Kes
NIP. 196609271997022001



SYSTEMATIC REVIEW

ASSOCIATED RISK OF DEATH FROM COVID-19 INFECTION IN PATIENTS WITH HYPERTENSIVE CO-MORBIDITIES

Keterkaitan risiko kematian infeksi COVID-19 pada pasien dengan kormobiditas hipertensi

Nina Widyasari^{1,3}, Hari Basuki², Chatarina Umbul Wahjuni^{2,3}

¹East Java Provincial Health Office, ninawidyasari79@yahoo.com

²Faculty of Public Health, Universitas Airlangga, haribasuki.n@fkm.unair.ac.id

³Departement of Epidemiology, Faculty of Public Health, Universitas Airlangga, chatrin03@yahoo.com

Corresponding Author: Chatarina Umbul Wahjuni, chatrin03@yahoo.com, Departement of Epidemiology, Faculty of Public Health, Universitas Airlangga, Mulyorejo, Surabaya, 60115, Indonesia

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ABSTRACT

Background: The COVID-19 pandemic caused by the SARS-CoV-2 virus has left infected patients with comorbidities in severe and deadly conditions. Hypertension is a non-communicable disease (NCD) and is one of the most common comorbidities observed in COVID-19 patients. **Purpose:** This study aims to understand the relationship between hypertension and the risk of death through COVID-19. **Method:** The study employed a systematic review of journals. Journals and articles related to hypertension and COVID-19 were collected and analyzed. The inclusion criteria was COVID-19 articles pertaining to hypertensive patients, and the exclusion criteria was articles that did not use English as well as those that did not display full text. **Result:** Hypertension is a multifactorial disease. The presence of hypertension is often not realized by the sufferer. A COVID-19 infection can worsen the condition of the person and can cause damage to vital organs. The use of antihypertensive drugs of the angiotensin-converting enzyme inhibitor (ACEI) and the angiotensin receptor blocker (ARB) groups can be continued to be administered to hypertensive patients. There should be no cause for concern for these patients to develop COVID-19 infections by taking these drugs. **Conclusion:** The risk of developing hypertension is that it can cause organ damage and lead to various complications. The SARS-CoV-2 infection in people with hypertension as a comorbidity, could worsen the condition of the individual until death occurs. Thus, hypertension management is necessary to properly minimize the severity.

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ABSTRAK

Pendahuluan: Pandemi COVID-19 disebabkan oleh virus SARS-CoV-

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2 membuat pasien yang terinfeksi dengan kormobiditas dalam kondisi parah dan mematikan. Hipertensi merupakan penyakit tidak menular (PTM) dan termasuk salah satu kormobid yang paling umum ditemukan pada pasien COVID-19. **Tujuan:** Kajian ini bertujuan untuk memahami keterkaitan hipertensi terhadap risiko keparahan infeksi COVID-19. **Metode:** Desain dalam artikel ini menggunakan sistematis review jurnal dengan mengumpulkan dan menganalisis jurnal yang terkait dengan hipertensi dan COVID-19 dengan kriteria inklusi artikel COVID-19 yang berkaitan dengan pasien hipertensi dan kriteria eksklusi adalah artikel yang tidak menggunakan bahasa inggris dan artikel yang ditampilkan tidak full text. **Hasil:** Hipertensi merupakan penyakit multifaktorial, keberadaan hipertensi sering kali tidak disadari oleh penderitanya sedangkan infeksi COVID-19 dapat memperparah kondisi orang tersebut dan dapat mengakibatkan kerusakan pada organ. Penggunaan obat anti hipertensi golongan Angiotensin-Converting Enzyme Inhibitor (ACEI) dan Angiotensin Receptor Blocker (ARB) dapat dilanjutkan tanpa ada kekhawatiran akan menyebabkan pasien hipertensi cenderung rentan terjadi infeksi COVID. **Kesimpulan:** Hipertensi berisiko menimbulkan kerusakan organ dan berbagai komplikasi sedangkan infeksi SARS-CoV-2 pada orang dengan kormobiditas hipertensi dapat berisiko memperparah kondisi hingga terjadi kematian, maka diperlukan pengelolaan hipertensi dengan baik untuk meminimalisir tingkat keparahan.

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INTRODUCTION

COVID-19 is a disease that has spread widely throughout the world and has caused a large number of deaths. COVID-19 is an animal disease (zoonosis) that is transmitted from animals to humans. A study revealed that SARS can be transmitted from civets to humans and that MERS can be transmitted from camels to humans. The first time COVID-19 was reported was in December 2019. To be precise, the first strain appeared in Wuhan, Hubei Province, China (Wang, Pan, & Cheng, 2020). Previously, the COVID-19 disease had never been identified in humans. A shrimp seller in Wuhan city was identified as the originating point of the coronavirus pandemic. On March 12, 2020, the World Health Organization (WHO) marked the outbreak as a pandemic. The total number of confirmed COVID-19 cases globally, as of 15 June, 2020, reached 7,823,289, with 431 deaths (case fatality rate=5.50%), with 195 out of the 215 countries locally transmitting the virus. In Indonesia, the number of positive cases reached 39,294 with 2,198 deaths (case fatality rate=5.60%) (Ministry of Health RI, 2020).

COVID-19 spreads faster than MERS and SARS. This could be due to its higher transmissibility compared to other viruses. There are several comorbidities, which when co-existing

with COVID-19, can cause an increased risk of infection, deteriorate an individual's health severely, and lead to death. The most commonly reported disease comorbidities are hypertension (30%), diabetes (19%), and coronary heart disease (8%) (P. Zhou et al., 2020). Basically, high blood pressure occurs when blood pressure rises to unhealthy levels, which is a common health problem. Hypertension is more often referred to as a silent killer because it often appears without showing any symptoms. In general, hypertension occurs in people who are at an old age (Kusumawaty, Hidayat, & Ginanjar, 2016).

The COVID-19 pandemic began with the emergence of a mysterious pneumonia case in Wuhan, China at the end of 2019. Data that has emerged from various countries affected by COVID-19 has indicated that hypertension is related to the adverse effects of COVID-19 exposure (Ruan, Yang, Wang, Jiang, & Song, 2020).

The results of the report by Guan et al (2020), who studied 1,099 patients that were confirmed positive for COVID-19, indicated that the highest infection factor was hypertension, affecting as many as 15% of the total number of patients. There were 173 patients with severe conditions. The most common comorbidity was hypertension

(23.75%), and as many as 35.50% of the patients required the treatment of triggers or ventilators. In research studies being conducted at present, the majority of patients who die also have hypertension. Another study conducted by Zhang, Penninger, Li, Zhong, & Slutsky (2020), with 140 patients having COVID-19, revealed that 37.90% of the patients who experienced severe conditions had hypertension. About 23.7%–30% of the patients treated for infection developed severe conditions.

Data from Italy indicated that 49% or 509 out of the 1,043 patients had hypertension. With the current situation, the results of this retrospective study still have its limitations with regard to the speed of data collection. At the time the data revealing the diagnosis of hypertension from Italy and China arrived, the use of antihypertensive drugs, adherence, patient control and heterogeneity of the patient population were still unknowns because the data in Italy was obtained from an ad hoc questionnaire, and the data from China was obtained based on electronic medical records. A meta-analysis of six studies with 1,527 patients revealed that 17.10% of the patients with COVID-19 had hypertension, and patients with severe conditions were twice as likely to develop hypertension compared to patients who showed mild symptoms (Huang et al., 2020).

Hypertension is a very serious NCD. WHO estimated that, in 2020, NCD would cause 73% of deaths and 60% of all illnesses in the world. Uncontrolled hypertension can lead to heart attacks, strokes, kidney disorders, and blindness. Many factors make hypertensive patients vulnerable to COVID-19. Various research studies have revealed that COVID-19 patients, who have hypertension as a comorbidity, face a high risk of severity (Ruan, Yang, Wang, Jiang, & Song, 2020). The purpose of writing this article is to examine the associated risk of death from COVID-19 infection in patients with hypertensive comorbidities.

METHOD

A systematic review method was employed, which examined the development of COVID-19 to determine the relationship of high risk of COVID-19 exposure in people with hypertension as a comorbidity. The inclusion criteria was COVID-19 articles related to hypertensive patients while the exclusion criteria was articles that did not use English and articles that did not display the full

text. Table 1 indicates the classification of hypertension employed in this research. Article searches were limited only to articles in English and were accessed over the internet from databases such as PubMed, ScienceDirect, and the National Center for Biotechnology Information (NCBI). Keywords used were hypertension and COVID-19.

Table 1.
Classification of Hypertension

Category	Systolic mmHg	Diastolic mmHg
Normal BP	<130	<85
High to Normal BP	130-139	85-89
Grade 1 Hypertension	140-159	90-99
Grade 2 Hypertension	≥ 160	≥ 100

Source: Unger et al (2020)

The literature search was carried out on July 16, 2020. The search was done by title and abstract. The researchers subsequently searched for complete and downloadable journals in order to locate valid sources. The journals obtained were then extracted by the researchers independently. Articles that met the inclusion criteria were collected and examined systematically. Based on the results from the search and analysis process, five articles that met the criteria were obtained (Figure 1).

The researchers conducted an initial search using the keyword COVID-19 with hypertension as a comorbidity. The search was carried out in PubMed (94 journals), ScienceDirect (79 journals), and NCBI (32 journals). After following the aforementioned criteria and carrying out the screening process, the researchers retrieved literature from five international journals (Figure 1).

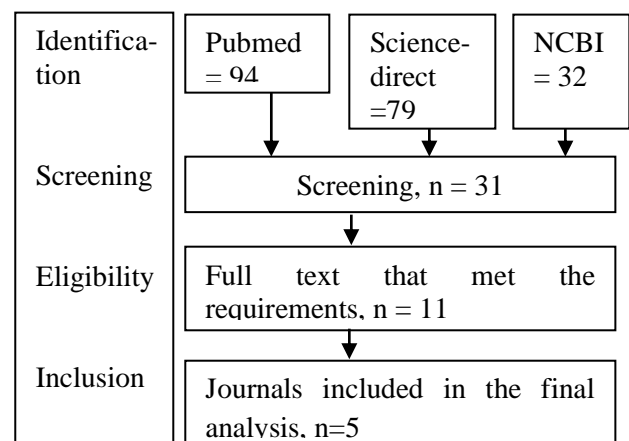


Figure 1. Flow chart of selected studies for systematic review and meta-analysis (PRISMA).

RESULTS

After the process of tracing articles using three databases and passing the screening process, 31 health journals mentioning COVID-19 with hypertension as a comorbidity were obtained. The journals were not only screened but underwent several stages to confirm the validity of the

journals analyzed. The aim was for the data used to produce accurate, clear, and reliable information. The article evaluation process, which was primarily based on the inclusion criteria set, produced thirteen articles. Based on eligibility, in accordance with the author's motive, data from five journals was retrieved (Table 2,3).

Table 2
Characteristics Research about COVID-19

Name/Year/Tittle	Sample Size	Method	Result
Wu et al (2020) Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China	201 patients with confirmed COVID-19 pneumonia admitted to Wuhan	Retrospective cohort study	The 201 patients (128 males and 73 females) were divided into two groups: 84 patients had Acute Respiratory Disease (ARDS) and 117 patients did not experience ARDS. It was revealed that the number of COVID-19 patients who experienced ARDS, with hypertension as a comorbidity, were 23 out of the 84 patients (27.40%), while the COVID-19 patients who did not experience ARDS, with hypertension as a comorbidity, were 16 out of the 117 patients (13.70%).
Yuan, Yin, Tao, Tan, & Hu (2020) Association of radiologic findings with mortality of patients infected with 2019 novel coronavirus in Wuhan, China	27 patients included 12 men and 15 women, with the median age of 60 years (Interquartile Rate (IQR) 47–69)	Retrospective study	The 27 patients were divided into two treatment groups: the surviving and the non-surviving groups. The number of patients in the group who were able to survive with hypertension as a comorbidity was zero, while the number of patients who could not survive with hypertension as a comorbidity was five (p-value=0.01).
F. Zhou et al (2020) Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study	191 patients (135 from Jinyintan Hospital and 56 from Wuhan Pulmonary Hospital)	Retrospective, multi-centered cohort study	The number of patients included in this study were 191 (135 from Jinyintan Hospital and 56 from Wuhan Pulmonary Hospital), out of which 137 were discharged and 54 died in hospital. The number of patients who had a comorbidity were 91 (48%), with hypertension being the most common in 58 (30%) patients.
Guan et al (2020) Clinical characteristics of coronavirus disease 2019 in China	1,099 patients with laboratory confirmed Covid-19 from 552 hospitals in 30 provinces, autonomous regions, and municipalities in mainland China on January 29, 2020	Study Oversight	The results of the analysis revealed that there were 1,099 positive COVID-19 patients, out of which 165 patients had hypertension as a comorbidity, however, these patients were again grouped based on the severity of the disease: the patient group with the most severe—41 patients (23.70%), and the patient group with a less severe disease were 124 patients (13.40%).
Huang et al (2020) Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China	All patients with suspected 2019-nCoV were admitted to a designated hospital in Wuhan	Prospectively collected and analyzed data on patients	A sample of 41 patients undergoing intensive care at the hospital were identified as having a laboratory-confirmed COVID-19 infection. As many as 30 (70%) patients were male, and out of these 30 patients, six (15%) patients had a history of suffering from hypertension.

Table 2.

General characteristics of the patients

Source	N	Mean Age (Years)	Males N (%)	HT N (%)	Diabetes N (%)	CVD N (%)	Note
Wu et al (2020)	201	51	128	39	22	8	Old age is associated with a higher risk of developing more severe ARDS and possible death due to a less restrictive immune response.
Yuan, Yin, Tao, Tan, & Hu (2020)	27	60	12	5	6	3	The number of comorbidities in the mortality group was significantly higher than in the survival group, especially comorbidities in hypertension, diabetes, and heart diseases.
F. Zhou et al (2020)	191	56	119	58	36	15	Out of the 191 patients, 137 patients were discharged and 54 died in hospital. 91 (48%) patients had comorbidities, with hypertension being the most common (30%), diabetes (19% of the patients), and coronary heart disease (15% of the patients).
Guan et al (2020)	1099	47	459	165	81	15	Out of the 67 patients (6.10%), including 5.00% of the patients who were admitted to the ICU, 2.30% used invasive mechanical ventilation, and 1.40% of the patients died.
Huang et al (2020)	41	49	11	6	8	6	41 hospitalized patients were identified as having the 2019-nCoV infection. Most of the infected patients were male 30 (73% of the 41 patients). Less than half of the patients (13 patients, 32%) had an underlying disease. The number of patients who had diabetes was 8 (20%); 6 (15%) patients had hypertension; and 6 (15%) patients had a cardiovascular disease.

The courting among excessive blood strains and the improved chances of developing pneumonia turned into a topic of examination, whereby an analysis of UK's Biobank facts of 107,310 high blood pressure sufferers was conducted. It was discovered that 3% of the sufferers developed pneumonia afterwards. Patients with high blood pressure had additionally been discovered to be more at risk of facing acute breathing sickness and 'persistent respiratory illnesses, regardless of age, sex, smoking status, and BMI. Generalizing these symptoms to be those caused by a COVID-19 infection was a reasonable one. This caused many researchers to target high blood pressure to be a robust indicator of the severity of a COVID-19 infection (Gupta, Ghosh, Kumar, & Misra, 2020).

According to Figure 2, out of the five publications used in this study, the results of the

meta-analysis conducted to test the magnitude of variation in observed correlations were most likely caused by a sampling error, $df=4$ ($p<0.01$). From these results, a statistical test was then carried out. The I^2 statistic indicated the proportion of variance in the observed effects caused by the sampling error. In this case, the proportion of variance in the observed effect due to the sampling error was $I^2=97\%$.

From the results of the analysis carried out, it was revealed that COVID-19 patients, with hypertension as a comorbidity, face significantly high risks of death, which indicated that there was a relationship between hypertension and COVID-19 patients. A cohort analysis was then carried out to validate the results that had been obtained from previous research studies. The results of the analysis revealed that there was a difference in the prevalence of hypertension, according to region and race. Early identification

of the phenotype of patients who are at a higher risk of dying due to COVID-19 infection is important. The initial knowledge obtained about comorbidities that can increase the risk of death of COVID-19 patients is fundamental for both outpatients and inpatients to maintain and increase surveillance until the disease is cured because COVID-19 infection can quickly turn acute and turn ARDS into Multi Organ Failure (MOF). From the results of this analysis, the inclusion variable of the study was only grouping patients who recovered and those who died, however, the facts that are coming out from other investigations conducted are that many researchers are still uncertain about the results due to the severity of the disease and because of researchers using different criteria (Wu et al., 2020).

There are several studies that discuss COVID-19. In one of the studies, the authors mentioned that among the 3,017 hospitalized COVID-19 sufferers, 53% were recognized to have high blood pressure. Furthermore, the mortality cost in patients with Angiotensin-Converting Enzyme Inhibitor (ACEI) for the treatment of high blood pressure was 27% (p value=0.01); the mortality cost in patients with the Angiotensin Receptor Blocker (ARBs) was 33% (p =0.12); and the mortality cost in patients when anti-hypertensive agents were used was 39%. Therefore, treatment using ACEI and ARB can be administered to people with COVID-19 who have hypertension as a comorbidity. This finding was supported by other examinations. One such examination was conducted with 126 COVID-19 sufferers, who had hypertension as a comorbidity. They were grouped into two categories, with 43 patients being treated with ARBs/ACEIs and 83 patients being treated with non-ARBs/non-ACEIs, according to the patients' conditions. Then a random selection was done based on age and sex. The results of this analysis revealed that ARB/ACEI decreased the number of crucial cases: as much as 9.30% vs 22.90% (p value=0.06), and a decrease in mortality was observed by 4.70% vs 13.30% (p value=0.22) (Yang et al., 2020).

Basically, when a structural examination was conducted, it was revealed that SARS-CoV-2 used Angiotensin - Converting Enzyme 2 (ACE2) as a receptor. In addition, it was also revealed that calcium channel blocker (CCB) treatment for people with high blood pressure does not lead to an increase in ACE2 regulation, which is basically used as a safe drug for high

blood pressure in COVID-19 patients. However, this finding is not always supported because it refers to a retrospective research that was conducted previously using samples of COVID-19 sufferers who consumed ACEI and ARBs. The COVID-19 pandemic has turned out into what it is today because of SARS-CoV-2. Transmission takes place through splashes of fluid that come out while sneezing or coughing. The Wuhan coronavirus shared 80% of its genome with the coronavirus responsible for the SARS outbreak, whose viral genome was shaped like a bat, so the speculation emerged that SARS-CoV-2 originated from bats, which then mutated and infected people (P. Zhou et al., 2020). Mammals and birds are ideal viral reservoirs (Rothan & Byrareddy, 2020). Nevertheless, the type of animals that can transmit COVID-19 are still unknown. It has become even more important to find out the cause for COVID-19's origin because people can easily transmit this virus to others. The majority of loss-of-life instances due to COVID-19 have been observed in humans having high blood pressure as a comorbidity (Guan et al., 2020).

Hypertension can be defined as a state of systolic blood pressure (>140 mmHg) and/or diastolic blood pressure (>90 mmHg). Hypertension, also known as high blood pressure, can be classified as primary (essential) hypertension or secondary hypertension. When the cause of hypertension is unknown (idiopathy), it is called essential or primary hypertension. When a cause can be found, it is called secondary or non-vital hypertension. Primary hypertension can be caused by changes in lifestyle or the type of lifestyle followed. Secondary hypertension can be caused because of kidney disorders, endocrine disorders, coronary heart disease, and kidney disorders. In most cases, people who have high blood pressure do not realize that they have it. At the same time, too much blood pushing against the artery wall continuously over a period of time can result in complications. Hypertension is one of the reasons for causing harm to numerous organs, either affecting the organs directly or indirect. Organ harm, in hypertensive sufferers, is usually determined by a left ventricular hypertrophy, angina or a myocardial infarction, coronary heart failure, stroke, continual kidney disorder, peripheral arterial disorder, and retinopathy. For this purpose, it is crucial to perform an early diagnosis to suitably reduce morbidity and mortality and save ourselves from befalling harm. Hypertension can be interpreted as persistent blood

pressure, wherein the blood pressure is constantly above 140/90 mmHg. From this description, it can be concluded that high blood pressure is a chronic growth in systolic blood pressure, above 140 mmHg, due to different complicated and interconnected conditions (Bjertness et al., 2016).

Factors Affecting Hypertension

Hypertension, in general, has no specific causes. This disease occurs in response to an increase in the peripheral pressure. There are several other factors that influence hypertension: genetic, sex, obesity, stress, physical activity, nutrition intake, and smoking (Gunawan & Adriani, 2020).

Genetic

Genetic factors in certain families can play a role in causing hypertension. Individuals who have parents with hypertension are twice at risk of developing hypertension (Arum, 2019).

Sex

Men and women have the same prevalence of hypertension. In general, women go through a premenopausal period, between 45 and 55 years of age. However, during this period of time, women are protected by the estrogen hormone, which is useful in increasing High-Density Lipoprotein (HDL) levels. This increases immunity in women and can reduce the risk of other diseases that can

trigger the development of the COVID-19 virus (Kusumawaty, Hidayat, & Ginanjar, 2016).

Obesity

Being overweight is a determining factor of high blood pressure in the majority of ethnicities of various ages (Supriyono, 2019). Obesity can cause heart failure because body fat causes blood volume to rise higher and makes the heart work harder to pump blood all throughout the body (Arum, 2019).

Stress

Stress can trigger an increase in blood pressure. The hormone adrenaline increases when under stress and can cause blood pumping from the heart to pump faster. Thus, the blood pressure increases (Gunawan & Adriani, 2020).

Physical activity

Playing a sport can prevent the onset of a non-communicable disease, because regular exercise can reduce peripheral resistance, which can reduce blood pressure in hypertension and train the heart muscles to get accustomed to performing heavier work in certain conditions. Low physical activity tends to be associated with obesity. People with low physical activity tend to have a faster heart rate, so the heart muscles must work harder during contractions. The harder and more often the heart pumps, the greater will be the effort exerted by the arteries (Supriyono, 2019).

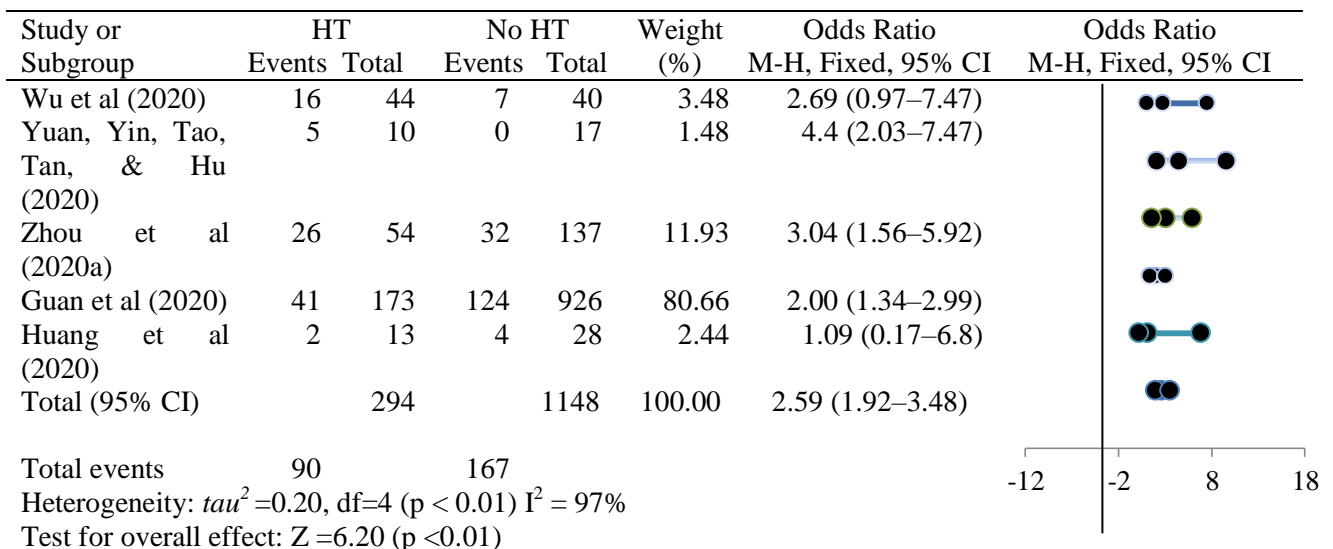


Figure 2. Forest plots of primary outcome caused mortality among covid-19 with hypertension

Nutrition intake

The WHO suggests restricting the amount of salt intake to reduce the risk of hypertension. The recommended amount of sodium should not be more than 100 mmol (about 2.40 grams of sodium or 6 grams of salt) per day. Excessive sodium consumption can cause the concentration of sodium in the extracellular fluid to increase, resulting in an increase in blood volume that can influence hypertension (Arum, 2019).

Cigarette smoking

Smoking can increase blood pressure. Heavy smoking is associated with an increase in the incidence of malignant hypertension and the risk of renal artery stenosis with arteriosclerosis. A prospective cohort study with 28,236 subjects who had no history of hypertension. In the study group, 51% of the participants did not smoke; 36% of the smokers were beginners; 5% of the subjects smoked about 1–14 cigarettes per day; and 8% of subjects smoked more than 15 cigarettes per day. The time period for the research was 9.80 years. It was concluded that the majority of hypertension events occurred in subjects who were part of the group that smoked more than 15 cigarettes per day (Bowman, Gaziano, Buring, & Sesso, 2007).

DISCUSSION

COVID-19 is an autoimmune disease that easily infects a person when their immune system is compromised. Precautionary measures for people who have hypertension triggers need to be increased because the presence of hypertension is often not realized by a patient. Hypertension is associated with pumping blood throughout the body. Problems related to abnormal blood pressure can cause various changes in the cardiovascular system. Most of the hypertension cases are closely linked to age: the elderly are more at risk because there is a gradual decline in organ function during old age. The risk of organ damage or the risk of complications makes a hypertensive patient vulnerable to SARS-CoV-2 infection (Ruan, Yang, Wang, Jiang, & Song, 2020).

Hypertension is a major risk factor for heart diseases, congestive heart failure, congestive, stroke, vision problems, and kidney diseases. High blood pressure generally increases the risk of complications. Untreated hypertension will affect the performance of all organ systems and ultimately shorten life expectancy by 10 to 20 years. Mortality in hypertensive patients is faster if

the disease is not controlled and has caused complications to several vital organs. The most common cause of death is a heart disease, with or without stroke and kidney failure (Xu et al., 2020).

The American College of Cardiology (2020), highlighted some more complications related to the heart that COVID-19 patients with acute heart complications could face, including heart failure, infarction, myocarditis, etc. A retrospective study conducted by Wang, Pan, & Zheng (2020), who reviewed and treated 138 patients who were tested positive for COVID-19, revealed that 16.70% of the patients had dysrhythmia, and 7.20% of the patients had an acute heart injury. Ruan, Yang, Wang, Jiang, & Song (2020) in China also obtained a similar finding based on a study conducted with 150 patients in Jin Yin-tan Hospital and Tongji Hospital. There were 68 deaths (7%) due to heart damage and respiratory failure, so it was concluded that COVID-19 could cause damage to the heart. These findings also received support from a study conducted by Huang et al (2020) with 41 patients who were tested positive for COVID-19. 12% of the patients suffered acute heart damage with elevated levels of troponin.

In early 2020, a report based on the complete RNA sequence of the SARS-CoV-2 virus contained information that was found to be similar to the SARS outbreak caused by the SARS-CoV virus, which became a global outbreak and killed 774 people in 2003 (Xiantian et al., 2020; F. Zhou et al., 2020). The process through which SARS-CoV infects the lung cells has been identified in the mechanism of the infection process. SARS-CoV-2 was found to be similar to SARS-CoV. ACE2 when administered as a receptor was found to infect cells (Bobeck, Holtzclaw, Brown, & Clark, 2020; Zhang, Penninger, Li, Zhong, & Slutsky, 2020). After publishing these findings, there was a controversy in therapy related to the continuation or cessation of ACEI and ARB in COVID-19 patients with hypertension as a comorbidity (Yang et al., 2020).

The European Society of Cardiology (ESC), the American College of Cardiology (ACC), and the Canadian Cardiovascular Society (CCS) publish the latest treatment guidelines for hypertensive patients associated with the COVID-19 outbreak. The results of the publication were also adopted by the Indonesian Cardiovascular Specialist Association (PERKI), which was released on March 26, 2020 (Liberale et al., 2020). These three institutions state that, in humans, there has not been any link found between the use of ACEI or

ARB with the increasing severity that occurs in COVID-19 patients. The following recommendation can be provided to COVID-19 patients, who have hypertension as a comorbidity: Patients who have been previously suffering from hypertension can be administered with ACEI or ARB drugs. The consumption of these drugs can continue with medical supervision, and the patient need not feel anxious or worried about feeling more vulnerable to being infected with COVID-19 as long as they continue to adopt a healthy lifestyle, eat a balanced diet, perform some exercise, and take precautions against COVID-19 according to established government protocols (Guan et al., 2020). In protection against pneumonia, it is suspected that the use of ACEI or ARB will increase the amount of angiotensin that protects the lungs (Caldeira, Alarcão, Vaz-Carneiro, & Costa, 2012).

CONCLUSION

Hypertension is a multifactorial disease. Blood pressure in humans increases with age. Regular blood pressure monitoring and sticking to a healthy lifestyle are needed to minimize the risk of severity. The use of anti-hypertensive drugs, ACEI or ARB, can be continued to be administered to control blood pressure because uncontrolled high blood pressure can cause various complications and increase susceptibility to SARS-CoV-2 infection. Hypertension, when not treated for a long time in a patient without COVID-19 infection, can impact organ damage. The presence of COVID-19 infection in people with hypertension can worsen a person's condition and result in death.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTIONS

HB and CUW contributed greatly to the design and conceptualization. NW contributed to the process of analyzing and interpreting the data. In addition, the three authors collaborated with each other to compile the article and critically revised it. They also provided the approval for the final drafting of the article.

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