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RESEARCH ARTICLE

ASSOCIATION BETWEEN ORAL CONTRACEPTIVES USE AND HYPERTENSION AMONG WOMEN OF REPRODUCTIVE AGE AT PUSKESMAS KALUMATA

(HUBUNGAN ANTARA PENGGUNAAN KONTRASEPSI ORAL DENGAN KEJADIAN HIPERTENSI PADA WANITA USIA SUBUR DI PUSKESMAS KALUMATA)

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ABSRACT

Hypertension is defined as a medical condition in which blood pressure persistently exceeds the normal limit of ≥140/90 mmHg. In 2018, the prevalence of hypertension in Indonesia reached 34.11%. One significant contributor factor to the development of hypertension is the use of oral contraceptives, which can influence the renin-angiotensin-aldosterone (RAA) system and promote atherosclerosis, leading to elevated blood pressure. This quantitative study aimed to investigate the association between oral contraceptive use and hypertension among women of reproductive age. An observational cross-sectional design was employed. A total of 44 respondents were selected using incidental sampling, and data were analyzed using the Chi-square test. The results showed that 56.8%of respondents were non-hypertensive , 61.4% used combined oral contraceptives, 61.4% were aged >35 years old , 54.5% had used contraception for ≥ 2years , and were overweight (59.1%). Bivariate analysis demonstrated a significant association between oral contraceptive use and hypertension (p = 0.03), as well as between body mass index and hypertension (p = 0.02).to Specifically, women using combined oral contraceptives were found to have a 4.063 times higher risk of developing hypertension compared to those using oral progestins. This increased risk may be attributed to the estrogen components, which can affect the RAA system and contribute to elevated blood pressure through angiotensin II-mediated mechanism. In contrast, no significant association was observed between age and the incidence of hypertension in this population (p = 0.143). Similarly, the duration of oral contraceptive use was not significantly associated with hypertension, (0.107), a finding that may be influenced by the relatively small sample size.

Keywords : body mass index, duration, hypertension, oral contraceptive

ABSTRAK

Hipertensi merupakan suatu kondisi medis yang terjadi ketika tekanan darah seseorang melebihi batas normal, yaitu ≥140/90 mmHg. Prevalensi hipertensi di Indonesia pada tahun 2018 sebesar 34,11 persen. Salah satu penyebab utama hipertensi adalah penggunaan kontrasepsi oral. Kontrasepsi oral dapat mempengaruhi sistem renin angiotensin aldosteron dan menyebabkan terjadinya aterosklerosis yang memicu peningkatan tekanan darah. Tujuan penelitian untuk mengetahui hubungan antara penggunaan kontrasepsi oral dengan hipertensi pada wanita usia subur. Penelitian ini adalah penelitian kuantitatif dengan desain observasional menggunakan pendekatan cross-sectional dan uji Chi-square. Teknik pengambilan sampel menggunakan sampling insidental, jumlah sampel sebanyak 44 orang. Penelitian ini menemukan proporsi responden lebih banyak yang tidak mengalami hipertensi (56,8%), menggunakan kontrasepsi oral kombinasi (61,4%), berusia di atas 35 tahun (61,4%), telah menggunakan kontrasepsi setidaknya selama dua tahun (54,5%), dan indeks tubuh gemuk (59,1%). Analisis bivariat mengungkapkan hubungan antara penggunaan kontrasepsi oral dan hipertensi (nilai p = 0,03), serta hubungan antara indeks massa tubuh dan hipertensi pada wanita subur yang menggunakan kontrasepsi oral (nilai p = 0,02). Jika dibandingkan dengan mereka yang menggunakan progestin oral, mereka yang menggunakan pil kombinasi oral memiliki risiko 4,063 kali lebih besar untuk mengalami hipertensi, karena terdapat hormon estrogen yang mampu mempengaruhi RAA system dan memicu peningkatan tekanan darah melalui hormon ang iotens in 2. Tidak ada hubungan antara usia dengan kejadian hipertensi pada wanita pengguna kontrasepsi oral (nilai-p = 0,143). Durasi penggunaan kontrasepsi oral juga tidak berhubungan dengan kejadian hipertensi, dengan nilai-p 0,107 (> 0,05). Hal tersebut dipengaruhi oleh jumlah sampel yang cenderung kecil.

Kata kunci: hipertensi, indeks massa tubuh, kontrasepsi oral, lama penggunaan

INTRODUCTION

Hypertension is a medical condition characterized by blood pressure exceeding normal value.[1] It is clinically defined as a sustained elevation in systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg.[2] Hypertension is often referred to as the "silent killer", because hypertensive patients often don't experience symptoms until they suffer complications resulting from hypertension, making it a leading cause of morbidity and mortality.[3] According to the World Health Organization (WHO), the global number of individuals with hypertension increased from 594 million in 1975 to 1.13 billion in 2015.[4] By 2019, this number had reached 513,337 reported cases , with South Asia having the highest burden at 138,236 cases.[5] In Indonesia, the prevalence of hypertension was recorded at 34.11% in 2018. Provincial data show notable variation, with North Maluku reporting a prevalence of 24.65%. Similarly, Ternate City recorded a hypertension prevalence of 22.43%.[6] In response to this growing burden, the WHO has set a target to reduce the global prevalence of hypertension by 33% between 2010 and 2030.[4]

Hypertension is caused by several factors, one of which is the use of

medications including oral contraceptives.[1] Users of combined oral contraceptives are 1.44 times more likely to experience hypertension.[7] The use of oral contraceptives, especially in combined forms containing estrogen and progesterone, can contriute to the development hypertension. High-dose estrogen (estrogen >50 mcg and progesterone 1-4 mcg) can increase blood pressure by 6/3 mmHg.[8]

In an observational study of 16 individuals who developed hypertension while using combined oral contraceptives, increased blood pressure (BP) was observed 3 to 36 months after initial use, with an average BP of 170/100 mmHg. BP decreased significantly in all users within 2 to 6 months after discontinuing contraception. Among 68,297 individuals aged 25-42 years in the United States, systolic blood pressure was 0.7 mmHg higher and diastolic was 0.4 mmHg higher in oral contraceptive users compared to non-users. Most participants used combined oral contraceptives.[9]

The estrogen contained in birth control pills can influence the renin-angiotensin-aldosterone (RAA) system by stimulating hepatic synthesis , a renin substrate. Meanwhile, the progesterone content in both combined pills and progestin-only contraceptives can cause atherosclerosis by increasing levels of low-density lipoprotein cholesterol and decreasing levels of high-density lipoprotein cholesterol levels, which narrows blood vessels and triggers an increase in peripheral blood pressure, ultimately contributing to the development of increased blood pressure or hypertension.[10–12] However, according to a study by Syandravhirana, Susanti and Nurmeliani (2021) reported no significant association between oral contraceptive use and the incidence of hypertension.[13]

In Indonesia, contraceptive pills rank as the second most widely used contraceptive method, following injectable contraceptives, accounting for 12.1% of overall use.[14] Data from the Ternate City Health Office show that the number of active oral contraceptive users in Ternate City during the period of January to June 2023 was 744 individuals, with the highest number in the working area of Puskesmas Kalumata.[15] Based on these observations, it is important to know about the association between the use of oral contraceptives and the incidence of hypertension, particularly at Puskesmas Kalumata where the prevalence of birth control pill users in notably high in Ternate City.

METHODS

This study employed a quantitative, analytical observational design using a cross-sectional approach. The research was

conducted in the working area of the Kalumata Public Health Center (Puskesmas), Ternate City, North Maluku, from December 2023 to January 2024. The population in the study consisted of women of reproductive age using oral contraceptives (both combined and progestin-only preparations) within the working area of the Puskesmas Kalumata, totaling 50 individuals. The final sample comprised 44 subjects who met the inclusion criteria and were enrolled in the study. Participants were eligible for inclusion if they were: women aged 15-49 years; current users of oral contraceptives (birth control pills); attending Puskesmas Kalumata and/or residing within the working area of the Puskesmas Kalumata, and willing to participate in the study. Respondents were excluded from the study if they met any of the following criteria: a history of or currently use of anti-hypertensive medication; smoking; the presence of heart or kidney disease; or pregnancy.. The sampling technique employed used was incidental sampling. Primary data were obtained directly from study subjects through questionnaires, blood pressure measurements, using an automatic blood pressure monitorBody weight was assessed with a digital scale, and height was measured using a stature meter. The hypertension criteria was determined following the guidelines from the European Society of Cardiology (ESC) and the European Society of Hypertension (ESH) 2018. The body mass index (BMI) was classified into two categories: overweight (BMI >25 kg/m²) and normal (BMI 18.5 – 25 kg/m²), based on the 2014 guidelines from the Indonesian Ministry of Health. In accordance with Sari (2019), women aged ≥35 years were considered to have a higher risk of increased blood pressure compared to those aged <35 years.[16] The obtained data was then collected using the Microsoft Excel and subsequently analyzed using the Statistical Package for Social Science (SPSS). Univariate analysis was conducted to determine the frequency distribution of each study variable . Bivariate analysis was performed to examine the association between independent variables and the dependent variable using the Chi-square test. The research received ethical approval from the Health Research Ethics Commission of the Faculty of Medicine, University of Mataram, as indicated in ethical approval letter number: 535/UN18.F8/ETIK/2023.

RESULTS AND DISCUSSION

Respondent Characteristics

Table 1 presents the distribution of respondent characteristics. Regarding clinical condition, the majority of women of reproductive age using oral contraceptives

were non-hypertension (56.8%). Combined oral contraceptives containing both estrogen and progestin were the most widely used formulation , accounting for 61.4% of respondents.

In terms of age distribution, respondents aged ≥35 years was the predominant age group among oral contraceptives users in the working area of the Puskesmas Kalumata. The distribution of respondents based on the duration of oral contraceptive use was mostly ≥2 years of use with a total of 24 patient (54.5%). Based on body mass index (BMI), it was dominated by respondents who were classified as overweight (BMI >25 kg/m²), with a total of 26 patients (59.1%).

Table 1 Respondent characteristics

Variable	Number	Percentage (%)
Hypertension		
Yes	19	43,2
No	25	56,8
Oral Contraceptive		
Combined	27	61,4
Progestin	17	38,6
Age		
<35 years	17	38,6
≥35 years	27	61,4
Duration of Use		
<2 years	20	45,5
≥2 years	24	54,5
Body Mass Index		
Overweight	26	59,1
Normal	18	40,9

Body Mass Index and Hypertension

Table 2 shows a statistically significant association between body mass index (BMI) and the incidence of hypertension among women of reproductive age using oral contraceptives at Puskesmas Kalumata (p = 0.02 (<0.05)). Research by Muna and Helda (2020) showed consistent results reporting that obesity and the use of oral contraceptives were associated with the incidence of hypertension in Indonesia (p = 0.0001), and obesity significantly increased the risk of hypertension among women using oral contraceptives, by 1.11 -fold increased risk (PR 2.11, 95% CI : 1.83-2.43).[17] According to Shariq and McKenzie (2020), the mechanism of hypertension due to obesity is very complex and includes excessive activation of the sympathetic nervous system, stimulation of renin angiotensin aldosterone system (RAAS), changes in

adipose tissue-derived cytokines such as leptin, insulin resistance, and structural and functional changes in the kidneys. Excessive sympathetic nervous system activation contributes to increased angiotensin II formation and enhanced renin release from the kidneys. The formation of angiotensin 2 stimulates the adrenal glands to secrete aldosterone, which plays a role in increasing cardiac output and reabsorption of sodium and water by the renal tubules. Several factors are implicated in the overactivation of the sympathetic nervous system , including abnormal adipokine secretion from adipose tissue, insulin resistance, baroreceptor dysfunction, and stimulation via the RAAS. Furthermore, individuals with obesity frequently presents with obstructive sleep apnea (OSA), which induces chronic intermittent hypoxia and causing activation of carotid chemoreceptors, which increases sympathetic nervous system activity.[18,19]

Age and Hypertension

Based on the results of the statistical test in Table 2, age was not significantly associated with the incidence of hypertension among women of reproductive age using oral contraceptives, ($p = 0.143$ (>0.05)). These results are in line with the research by Apriani, Nurmainah, and Susanti (2022) at Puskesmas Pal III Pontianak, which also reported no significant association between age and hypertension incidence ($p=1.000$).[20] However, these results contrast with those of Rahmi (2018), which showed a significant association between age and hypertension among birth control pill users (p-value = 0.000).[21]

Age is recognized as a nonmodifiable risk factor for hypertension. As a person ages, the risk of hypertension also increases due to physiological changes in the heart, blood vessels, and hormones. As age advances, the elasticity (flexibility) of the arteries also decreases, resulting in hampered blood circulation and increased heart workload. The consequent elevation in cardiac pumping pressure ultimately leading to high blood pressure. Additionally, aging is associated with a disruption or decrease in the body's ability to metabolize fat, promoting lipid accumulation within blood vessels, known as atherosclerosis. Atherosclerotic plaque will impede blood flow, so when the artery loses elasticity coupled with the presence of plaque, the artery hardens, and simultaneously, there is blood forcing its way through the narrowed artery, thereby resulting in increased blood pressure.[22]

Although the majority of hypertension cases in the present study occurred among respondents aged ≥35 years, the statistical analysis did not show a significant association. This discrepancy

may be attributable to the relatively small sample size and the limited number of hypertension cases identified.

Relationship Between Duration of Oral Contraceptive Use and Hypertension Incidence

As presented in Table 2, no statistically association was observed between the duration of oral contraceptive use and the incidence of hypertension among women of reproductive age using oral contraceptives at Kalumata Community Health Center (p = 0.107). This finding is consistent with the research conducted by Alfan, Nurmainah, and Wahdaningsih (2019) at Puskesmas Perumnas II Pontianak, which also reported no significant relationship between duration of oral contraceptive use and the hypertension incidence .[23]

In contrast, a meta-analysis by Liu et al. (2017) demonstrated a positive association between duration of oral contraceptive use and the risk of hypertension. Their findings indicated that the risk of hypertension increased with prolonged use, with a 13% increase in risk for every 5 years of contraceptive use.[24]Other evidence suggests that oral contraceptives use exceeding 24 months is associated with blood pressure increase of 5.8/3.6 mmHg.[25]

Although the majority of hypertension cases in the present study occurred among respondents with a duration of use ≥2 years, this difference did not reach statistical significance. This may be attributable to the relatively small sample size and the difference between the two durations of use variable groups (<2 years and ≥2 years) was not too far apart.

Association Between Duration of Oral Contraceptive Use and Hypertension Incidence

The analysis revealed a statistically significant association between oral contraceptive use and the incidence of hypertension among women of reproductive age at Puskesmas Kalumata (p = 0.03 (<0.05)),. Research conducted by Afshari, Alizadeh-Navaei, and Moosazadeh in 2021 obtained similar results, which demonstrated that a higher frequency of hypertension among women using oral contraceptives compared to non-users, with a statistically significant difference (p = <0.001) and odd ration (OR) of 1.38. [26]

Similarly, a meta-analysis by Zuhaira, Pamungkasari, and Widyaningsih Vitri (2022), using 7 case-control articles from China, Ethiopia, and the United States, found that oral contraceptive use significantly influenced the risk of hypertension risk (p = 0.004) with an odds ratio (OR) of 1.44.[7]

In contrast, a study by M. Thaha, Angraeni A, and Sidik A (2016) at Puskesmas Segeri found no significant association between oral contraception use and the incidence of hypertension (p = 0.680).[27]

The estrogen hormone present in combined oral contraceptives affects the renin-angiotensin-aldosterone system by stimulating the synthesis of renin substrate (angiotensinogen) in the liver, thereby increasing angiotensinogen production. Angiotensinogen is subsequently converted to angiotensin 1 by reninm an enzyme produced in the kidneys. Angiotensin 1 is then converted to angiotensin 2 in the lungs via angiotensin-converting enzyme (ACE). Angiotensin 2 plays an important role in increasing blood pressure; angiotensin 2 is a vasoconstrictor that causes vasoconstriction of arterioles, and leads to an increase in total peripheral resistance, and thereby elevating blood pressure. Furthermore, angiotensin 2 stimulates aldosterone production, a hormone that plays a role in promoting sodium and extracellular fluid retention. This increases blood volume and cardiac output, further contributing to blood pressure elevation.[10,11]

This mechanism has also been proven by experimental research conducted by Byrne et al. (1994), who showed that administration of estrogen (ethinyl estradiol) and levonorgestrel, both singly and in combination, cinduced hypertension in a rat model. Specifically, ethinyl estradiol administration was associated with increased levels of renin substrate (angiotensinogen) and angiotensin II.[28]

In addition to estrogen, combined oral contraceptives contain a progestin, which increases LDL (low-density lipoprotein) levels and decreases HDL (high-density lipoprotein) levels by inhibiting HDL production. This can lead to atherosclerosis, which narrows blood vessels and triggers an increase in peripheral blood pressure, thus affecting elevated blood pressure and the development of hypertension.[10–12]

Table 2 Bivariate analysis

Variable	Category	Hypertension				Total		*P-Value*
		Yes		No				
		N	%	N	%	N	%	
Body Mass Index	Overweight	15	57,7	11	42,3	26	100	**0,02**
	Normal	4	22,2	14	77,8	18	100	
Oral Contraceptive	Combined	15	55,6	12	44,4	27	100	**0,03**
	Progestin	4	23,5	13	76,5	17	100	
Age	<35 years	5	29,4	12	70,6	17	100	**0,143**
	≥35 years	14	51,9	13	48,1	27	100	
Duration of Use	<2 years	6	30	14	70	20	100	**0,107**
	≥2 years	13	54,2	11	45,8	24	100	

CONCLUSION

This study demonstrates a significantly association between oral contraceptive use and the incidence of hypertension among women of reproductive age at Puskesmas Kalumata. Additionally, body mass index was also found to be significantly associated with the incidence of hypertension in this population of oral contraceptive users. Meanwhile, no significant associations were observed between either age or duration of oral contraceptive use and the incidence of hypertension among women of reproductive age at Puskesmas Kalumata.

CONFLICT OF INTEREST

The authors declare no conflicts of interest in the preparation and publication of this scientific article.

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