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**Research Article** 

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# Effect of Antihypertensive Therapy Compliance Using Medication Possession Ratio Method on Blood Pressure in Patients with Hypertension

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Article Info	ABSTRACT
Received: 11-09-2021	Hypertension is a circulatory system disorder that causes an increase
Revised: 01-02-2022	in blood pressure, specifically systolic blood pressure ≥140 mmHg or
Accepted: 23-03-2022	diastolic blood pressure ≥90 mmHg. Hypertension can cause serious
	medical conditions such as damage to various organs. The
*Corresponding author:	complications caused by hypertension can be prevented with
Christianus Heru Setiawan	treatment regularly to achieve controlled blood pressure. This study
email: chs_heru@usd.ac.id	determines the relationship between antihypertensive therapy
	compliance to blood pressure in hypertensive patients. This type of
Keywords:	research is analytical observational with retrospective cohort design
Antihypertensive;	and purposive sampling techniques. The data were obtained from
compliance; hypertension;	patients' medical records, including demographic data, blood pressure,
medication possession	and prescribed drugs. The subject's compliance was measured using
ratio; primary health care	the Medication Possession Ratio (MPR). A total of 124 subjects met the
	inclusion criteria. The data were analyzed using a chi-square test with
	Yates correction. Most patients had uncontrolled blood pressure as
	much as 101 patients. The statistical analyses show that
	antihypertensive therapy compliance affects controlled blood pressure
	in patients with hypertension (p= 0.00). More efforts to support
	adherence to hypertensive treatment should be initiated to have
	greater effect on therapy compliance.

## INTRODUCTION

Hypertension is diagnosed when a patient's systolic blood pressure (SBP) in the office or clinic is ≥140 mm Hg and/or their diastolic blood pressure (DBP) is ≥90 mm Hg following repeated examinations (Unger et al., 2020). Hypertension has become a significant problem in public health in both developed and developing countries. An estimated 1.13 billion people worldwide suffer from hypertension. Most (two-thirds) live in low- and middle-income countries (Kemkes RI, 2019; Muhadi, 2016). Hypertension is one of the most common diseases that cause a serious medical condition. It can significantly cause complications that hit various target organs, such as the heart, brain, kidneys, eyes, and peripheral arteries. Damage to the organs depends on how high the blood pressure is and how long it is controlled or left untreated (Muhadi, 2016).

In most cases, hypertension is often called a "silent killer" because it usually occurs without complaints, so sufferers do not know if they have hypertension. Then unwittingly, sufferers experience complications in vital organs such as the heart, brain, or kidneys (Sulistvarini, 2013). The prevalence of hypertension will continue to increase sharply. The prediction is that in 2025, as many as 29% of adults worldwide will be affected hv hypertension. Hypertension has resulted in approximately 8 million deaths each year, of which 1.5 million deaths occur in Southeast Asia. The increasing number of patients with hypertension can lead to an increased burden on health costs. The prevalence of hypertension in Yogyakarta based on the Basic Health Research in 2018 was 11.01% or higher when compared to the national total (8.8%). This prevalence places Yogyakarta in 4th place as a province with

increased cases of hypertension (Dinas Kesehatan DIY, 2018).

Therapeutic compliance is essential in achieving a therapeutic goal (Karuniawati and Supadmi, 2016). Adherence is defined as the extent to which a patient's behaviors, such as taking a medication, following a diet, or executing lifestyle changes, correspond with the agreed recommendations from a healthcare provider. Nonadherence to antihypertensive treatment affects 10-80% of patients with hypertension and is one of the key drivers of suboptimal BP control. Insufficient compliance to antihypertensive treatment correlates with the magnitude of BP elevation and indicates poor prognosis in patients with hypertension (Unger et al., 2020). Medication Possession Ratio (MPR) is one of the valid methods used to measure patient obedience due to its reliable nature. The MPR value is calculated by comparing the number of days a patient gets the drug by the number of days from initial prescribing to final prescribing (Kozma et al., 2013).

This research was conducted at the Primary Health Care (PHC) because Primary health care is the first-line health facility to maintain primary health (Bappenas, 2018). The strengthening of primary health services will show a suitable patient outcome. Researchers can provide information on how much compliance the patient takes the drug measured using the MPR method in PHC. In addition, an assessment of patient compliance taking medication is one way that can be done to prevent or delay disease progression, lower the frequency of hospitalization, while reducing the burden of health costs, and presenting another way of assessing therapeutic adherence.

#### METHODS

This type of research is an analytic observational study with a retrospective cohort design and purposive sampling method. This retrospective cohort study was conducted by taking secondary data from the medical records of outpatients from the PHC diagnosed with hypertension in January-December 2019. The inclusion criteria were: patients who were taking antihypertensive drugs, having BP control at least three times for one year, and having complete medical records, including patient personal data and drug use data. The exclusion criteria were: hypertensive patients with heart complications, stroke, and kidney disease. The Medical and Health Research Ethics Committee of the Faculty of Medicine, Universitas Gadjah Mada Yogyakarta (KE/FK/0358/EC/2020) has approved the procedure used in this study.

We found 174 patients with hypertension who met medical records' inclusion criteria (Figure 1). There were 50 subjects excluded, consisting of 15 subjects diagnosed with heart disease. 13 subjects diagnosed with a stroke, and 22 subjects diagnosed with kidney disease. Based on for the Prevention, Detection, Guideline Evaluation, and Management of High Blood Pressure in Adults (2017), the subject's BP was categorized as controlled (BP<130/80 mmHg) and uncontrolled (systolic BP≥130 or diastolic BP  $\geq$ 80 mmHg). The patient therapy compliance was assessed based on the MPR score. Subjects with good compliance have a MPR value >0.8 and subjects with less insufficient compliance have a MPR value of  $\leq 0.8$  (Kozma *et al.*, 2013). The following is the formula for calculating MPR: Days of getting the drug

 $R = \frac{1}{\text{days should get the drug} + \text{last prescribing drug day}}$ 





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<b>Table 1.</b> Characteristics of patients in the period January-December 2019				
Characteristics of Patients	Patients (n= 124)			
	n	%		
Gender				
Male	52	41.94		
Female	72	58.06		
Hypertensive therapy				
Mono therapy	107	86.29		
>1 therapy	17	13.71		
Mean blood pressure (mmHg)*				
Systolic blood pressure (mmHg)	$136.33 \pm 14.26$			
Diastolic blood pressure (mmHg)	84.04 ± 8.35			
Mean age (years)*	55.92 ± 11.88			
Mean duration of the disease (years)*	6.10 ± 2.71			
Mean MPR value*	$0.59 \pm 0.31$			

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\*numeric data presented as mean±SD, standard deviation

Table 2. The correlation between patient characteristics and treatment compliance based on Medication
Possession Ratio (MPR)

Variable		Treatment Compliance			
		Good Compliance (n = 56)	Insufficient Compliance (n = 68)	<i>p</i> -value	RR
Gender	Male	23	29	1.00*	0.97
	Female	33	39		
Age	< 60 year	41	38	0.07*	1.56
	≥60 year	15	30		
Duration of	< 10 year	47	60	0.67*	0.83
hypertension	≥ 10 year	9	8		
Total of therapy	Monotherapy	48	59	1.0.0*	0.05
	>1 therapy	8	9	1.00*	0.95

\*Yates chi-square correction test; p>0.05 = not significantly correlated.

The data were processed using statistical programs with computerized software at the Center for Clinical Epidemiology and Biostatistics Unit (CE&BU) Study of the Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada Yogyakarta using SPSS 22 (IBM Corp., Armonk, NY) program. Systolic and diastolic BP data were analyzed using chi-square tests with Yates correction. The interpretations of the analysis results were obtained from comparative tests and relative risk values (RR) with a significant *p*-value of <0.05.

#### RESULTS AND DISCUSSION

Table I shows the distribution of patient characteristics in the January-December 2019 period. In this study, the characteristics of patients with hypertension were primarily female patients (58.06%). The percentage of monotherapy in patients was more significant (86.29%). The mean BP of the patients indicated most of the patients had uncontrolled blood

pressure, with the average BP of patients at 136.33/83.04 mmHg. The patient's average age indicated that most patients are not elderly, with an average age of 55.92 years. The data showed most of the patients have been suffering from hypertension for a long time, with the average duration of the disease being 6.1 years. Most of the patients in this study had a low level of treatment compliance with an average MPR score of 0.59.

Based on a World Health Organization (WHO, 2021) summary, in 2015, 1 in 4 men and 1 in 5 women suffered from hypertension. Furthermore, data obtained from the Health Profiles in 2019 Yogyakarta city showed that in 2018 more cases of hypertension were found in women (63%) than males (37%) (Dinas Kesehatan Kota Yogyakarta, 2019). Women tend to take more BP measurements compared to men (women 76% and men 71% *p*<0.001), and women tend to have a good level of awareness about high BP compared to men (women 55% and men 43%, *p*<0.001) (Rahman *et al.*, 2017). In a study conducted by Everett and Zajacova (2015), men were less likely than women to report their hypertensive status. Early detection and treatment of hypertension can prevent or slow down organ damage in the reversible stage. Many factors play a role when choosing the best treatment option. Healthy lifestyle changes, such as diet, physical activity, quitting smoking, and managing stress are first-line choices. If BP control is not achieved, medical management and increased obedience are the next options (Singh *et al.*, 2020).

According to Unger et al. (2020), therapy treatment in patients with hypertension can be done with two types of treatment, namely essential and optimal. Essential is the primary treatment that needs or must be done to treat hypertension, while optimal is the type of treatment to get better results. For essential treatment, treatment should be evidence-based, using a once-a-day therapeutic regimen that provides 24-hour BP control. The treatment should be affordable and cost-effective compared to other agents. Importantly, the treatment should be tolerated well by patients. A study conducted by Jankowska-Polańska et al. (2017), obtained a smaller percentage of mono-therapy patients at 24.2% compared to patients who used poly-therapy at 75.8%. The administration of hypertensive therapy aims to achieve controlled BP treatment by increasing the dose of monotherapy or using a combination of drugs (Guerrero-García and Rubio-Guerra, 2018). In a study conducted by Nagappa et al. (2018), many patients with hypertension fail to achieve BP goals treated at primary health centers in South India. As many as sixty-three patients (a quarter of patients) from 259 patients with hypertension could not achieve controlled BP. This could be due to non-compliance with treatment and/or

insufficient drug therapy. Uncontrolled BP is a cardiovascular risk factor that can cause organ damage (Yaxley and Thambar, 2015).

Table II shows that the number of patients with good compliance was slightly smaller, amounting to 56 patients compared with those with insufficient compliance, which were 68 patients. The results showed that more than half of the patients did not regularly redeem their drugs at the PHC. Statistical analysis showed that gender, age, duration of hypertension, and total therapy had no significant relationship to adherence (p>0.05). Most of the test subjects in this study had a low level of obedience with an average MPR score of 0.59. The female patients had higher levels of adherence than male patients, whereas women's behavior in search of health was higher than that of men (Wiarsih et al., 2020). Another study conducted by Teshome et al. (2017) by administering a questionnaire to 337 patients with hypertension who participated in the study found that patients aged >60 years were 67% less likely to comply with antihypertensive treatment compared to vounger patients (OR=0.33, 95% CI: 0.11, 0.98). Age influences the health practices of everyday individuals through changes in mindset and behavior (Nurhidayati et al., 2018). Elderly patients' adherence to treatment tends to decline for various reasons, one of which is a decline in cognitive function that can lead to depression with age (Burnier et al., 2020). Negative thoughts, behaviors, and uncomfortable feelings can lead individuals to more serious psychological problems, such as depression, trauma, and anxiety disorders. Dysfunctional thoughts and behaviors create uncomfortable or negative feelings. Therefore, a healthy mindset must be reconstructed so that the person can return to functioning normally (Manuntung, 2018).

		Blood pressure			
Variable		Controlled (n = 23)	Uncontrolled (n = 101)	<i>p</i> -value	RR
Gender	Male	11	41	0.69*	1.27
	Female	12	60		
Age	< 60 year	15	64	1.00*	1.07
	≥60 year	8	37		
Duration of the	< 10 year	18	89	0.31+	0.57
disease	≥ 10 year	5	12		
Hypertensive	Monotherapy	19	88	0.52+	0.76
therapy	>1 therapy	4	13		
Treatment	Good Compliance	22	34	0.00*	26.71
Compliance	Insufficient Compliance	1	67	0.00	

 Table 3. The correlation between patient characteristics and blood pressure

\*Yates chi-square correction test; +Fisher Test; p>0.05 = not significantly correlated

Table III showed that most patients had uncontrolled BP ( $\geq 130/80$  mmHg) with as much 101 patients, compared to those who had controlled BP (<130/80 mmHg) with as much 23 patients. Statistical analysis showed that gender, age, duration of disease, and hypertensive therapy had no significant correlation on the patient's BP (p>0.05). However, treatment compliance was significantly associated with the patient's BP (p=0.00). The results also show an RR value of 26.71 (95% CI: 3.716, 192.050), which means patients with good treatment compliance have a 27 times probability of experiencing controlled BP than patients with insufficient treatment compliance. The results of this study are similar to previous research conducted by Jankowska-Polańska et al. (2017), which examined the same aspects. The results found that there was no relationship between the period of the disease and the patient's compliance status (p = 0.113). Another study noted that the results of patients with a more extended period of more than ten years have a higher level of compliance compared to patients with a shorter period. The patients tended to have more information about the hypertensive disease than patients who have a shorter history of hypertension (Abbas et al., 2017). Another factor that affects compliance is the number of therapies. There is a correlation between the number of therapies and compliance (p = 0.041). Simplifying antihypertensive therapy may increase the patient's motivation to adhere to a medical regimen strictly. The number of tablets minimized and the administration schedule of antihypertensive drugs simplified may affect the effectiveness of therapy (Uchmanowicz et al., 2018b).

The study by Choi, Kim, and Kang (2017) examined the same aspects, namely looking at the relationship between gender and BP control. The results also stated that the number of female respondents had more data on BP control than male respondents, but gender had no significant effect on BP control (p = 0.477). Also, they found that premenopausal women have a lower risk and incidence of hypertension compared to men. In premenopausal times women have progesterone and estrogen hormones to protect blood vessels from oxidative and inflammatory stress. Estrogen increases angiotensinogen and decreases Angiotensin-Converting Enzvme (ACE) activity, aldosterone production, and renin production. However, in menopause, endothelial levels and oxidative stress are increased, affecting blood pressure through increased reabsorption of sodium and vasoconstriction of blood vessels (Gudmundsdottir et al., 2012).

The research conducted by Mitra and Wulandari (2019) investigated the relationship between the age factor and its effect on BP control. The results say that the age factor significantly affects BP control (p = 0.005). The aging process results from decreased or disappearing ability to maintain the balance and regulation of the body systems. The ability of various organs and cells to maintain their form and function gradually disappears (Widodo and Physiological Sumardino. 2016). changes associated with aging lead to an increase in SBP. an increase in average arterial pressure, an increase in pulse pressure, and a decrease in the ability to respond to sudden hemodynamic changes. In older people, the central artery system is stiffer than peripheral arteries. reactive oxygen, inflammatorv Increased cytokines, and endothelial dysfunction are some causes that cause structural changes and arterial dysfunctions seen along with aging. High elastin degradation and collagen deposition are two characteristic changes seen with age. The ratio of collagen to elastin increases with age which causes increased arterial stiffness; this change can also occur in ventricular smooth muscle cells (Singh et al., 2020). Patients with hypertension who suffered for <5 years tended to have controlled BP compared to patients  $\geq$ 5 years, but these factors had no significant effect (p=0.48) on BP control (Asgedom et al., 2016). Longsuffering from hypertension can cause heart physiology in the aging process and hypertrophy or heart enlargement. At the same time, other organs experience shrinkage or shrinking as well as stenosis in blood vessels that are getting smaller due to the aging process. In the process of the heart wall thickening, the heart valves also begin to thicken and stiffen (Nurhidayati et al., 2018).

There was a significant association between the increase in the number of drugs used against controlled BP (Wachholz *et al.*, 2016). The same results were also found in Egan *et al.* (2012) study, which indicated that the number of therapies has a significant relationship (p=0.001) to controlled blood pressure. The study found that patients who received a combination of therapies gave better hypertension control in the first year than patients receiving monotherapy. The research results concluded that using more combination therapy as initial therapy could improve hypertension control and cardiovascular disease in the first year of treatment (Egan *et al.*, 2012).

The patients with hypertension who

reach BP control targets tend to adhere to treatment. Patients with a history of high compliance tend to have controlled BP compared to patients with low compliance (Liberty et al., 2017). The results from another study said that about 73.91% of patients who received antihypertensive treatment were unable to reach the blood pressure target <130/80 mmHg (Jesus et al., 2016). Low regulation in the administration of therapy in patients may result from several factors, such as; socioeconomic (income, culture, economic and geographical conditions), patient characterization (health beliefs, discipline, and awareness), psycho-social (psychiatric/depressive conditions. low personality, and pessimistic attitude (narrow insight and lazy), disease characteristics (chronic abuser), aspects of facilities and health workers (ease of accessing health services, staff's responding, empathy attitude, and ability of health workers to respect patient), communication, and social (social support, education provision, counseling program) (Edi, 2015). The lack of cooperation and adherence to accepted therapeutic regimens is one of the most challenging factors contributing to the low therapeutic success in many chronic diseases (Uchmanowicz et al., 2018a). The condition for achieving the desired therapeutic effect is to take the drug as prescribed, comply with medical recommendations, and cooperate during each stage of treatment.

This research has some limitations in the methods. The MPR method only assesses the adherence of prescription-refill without actually determining whether the patient consumes the medicine prescribed by the doctor. The researchers also did not conduct a direct interview with the patient, so they do not know the co-morbid condition of the study subjects (patients with hypertensive) when undergoing therapy.

## CONCLUSIONS

The patient's compliance in taking antihypertensive drugs significantly affect controlling blood pressure statistically. Characteristics of patients with hypertensive based on the highest percentage results are female gender (58.06%), antihypertensive monotherapy (86.29%), an average systolic blood pressure (136.33 mmHg), an average diastolic pressure (84.04 mmHg), an average age (55.92 years), an average duration of the disease (6.1 years), and an average MPR (0.59). More efforts to support adherence to hypertensive treatment should be initiated to have greater effect on therapy compliance.

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