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Research Article

The Analysis of Medicine-taking Compliance Towards Therapy Outcome in Hypertension Patients at Community Health Centers in Yogyakarta Municipality

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ABSTRACT

Compliance to medication has a significant role in regulating the blood pressure and the risk for Atherosclerosis Vascular Disease (ASCVD) in Diabetes Mellitus Type 2 (DMT2) patients with hypertension as comorbidity. This study (n=523) aimed to analyzed this relationship at community health centers Yogyakarta municipality. We conducted an observational study with a cross-sectional design to analyze the medical record data collected during January-December 2023 among patients categorized under the inclusion criteria. Compliance was measured using the Medication Possession Ratio (MPR) then descriptively and correlatively with Chi-square analyses. No significant relationship is showed between the compliance of antihypertensive therapy to blood pressure (p=0.867>0.05) and ASCVD risk (p=0.080>0.05; OR=0.662; 95%CI:0.416-1.052). Age (p=<0.001), gender (p=<0.001) and BMI (p=0.0014) had a highly significant relationship with ASCVD risk, but only BMI (p=0.007<0.005; OR 1.812) showed significant relationship with controlled blood pressure. The research findings reveal that compliance to antihypertensive therapy does not have a significant relationship with blood pressure control or ASCVD risk in patients with DMT2 and hypertension as comorbidities in Yogyakarta municipality. Highlighting the need for further investigation, it is vital to include other factors into blood pressure management.

INTRODUCTION

High blood pressure, often known as hypertension, is a major risk factor for a cardiovascular disease and is frequently associated with diabetes mellitus (DM). Both can raise the risk of coronary heart disease, stroke, and death by up to 60% (Sihombing, 2017). Patient adherence to treatment influences therapy success. The research on the adherence of patients with DM type-2 (DMT2) shows a relatively low percentage of 39.6%, (Srikartika *et al*., 2016)(Rasdianah *et al*., 2016). Aronow and Shamliyan (2018) reported the decline of coronary heart disease, stroke and diabetic kidney in line with the decrease of blood pressures that reaches <140/90 mmHg on patients with DM. The study in 2021-2022 which analyzed the relationship between the degree of adherence towards the clinic outcomes shows that patients had a low adherence (57%) due to lapses in treatment obedience, with a low clinic outcome achievement (Christiyani *et al*., 2023).

There are many factors that can influence therapy adherence, including education level, social support, drug side effects, and the complexity of drug regimens. Previous research employed Medication Possession Ratio (MPR) to assess medication compliance in individuals with metabolic syndrome and hypertension as comorbidities. This study emphasized the significance of monitoring and increasing treatment compliance in order to obtain optimal therapy outcomes (Setiawan *et al*., 2022). The MPR technique collects data on patient's drug

ownership, and it is done by studying records of medication re-taken by patients, in order to determine to what extent patients still have their medications.

The research was conducted at Yogyakarta Municipality Health Clinics, where they serve as a model of the primary health facility. According to 2018 Riskesdas data, the average prevalence of DM in this city was 4.79%, which was greater than the average national prevalence of 2%. According to Yogyakarta Municipality Health Service (2022), there were 13,676 people with diabetes and 28,420 people with hypertension who received standard health services in Yogyakarta Municipality. These numbers indicated an increase from the 2021 data when 12,554 people with diabetes and 26,720 people with hypertension received the same services (Dinas Kesehatan Kota Yogyakarta, 2023).

The prevention of Atherosclerosis Vascular Disease (ASCVD) today can be predicted by using the risk calculation of cardiovascular disease in the next 10 years (Soelistijo *et al*., 2021). One research using MPR method in 2022 in Pontianak mentions that there is a relation between the blood pressures among patients with hypertension towards the adherence for drug-taking (Asseggaf and Ulfah, 2022). A 2018 study in Sleman that compared five methods for ASCVD risk estimation stated that the PCE and FRS BMI methods were not significantly different in predicting ASCVD risk (p=0.11) (Dwivani *et al*., 2018). ASCVD risk assessment using FRS BMI is very useful and practical, making it easier to detect early disease signs and to control cardiovascular risk factors, including systolic blood pressure, smoking habits and body mass index (BMI) (Calisanie *et al*., 2020). Knowing the relationship between the compliance of DM comorbid hypertension patients in taking antihypertensive drugs and the handling of blood pressure and the risk of ASCVD is important for developing interventions for patients to improve hypertension management in the municipality of Yogyakarta.

METHODS

This research used an observational analytic approach with a cross-sectional research design. The research permit was issued by the Ethics Commission of Respati University Yogyakarta number 0244.3/FIKES/PI/XII/2023. The respondent data were obtained from the Community Health Center Information System (SIMPUS). Respondents' data were taken from the medical records of all patients with a diagnosis of DMT2 comorbid hypertension who were with a referral and/or regular patients at Yogyakarta Municipality Health Center with the following criteria: 40-70 years of age, receiving or taking routine medication at least 3 times in a 1 year period (January 1–December 31 2023), having the information of the dates of visits, weight, height, last blood pressure records, as well as having complete data on DM and hypertension medication names. The exclusion criteria from the data collection covered the incomplete data and patients with advanced diagnoses for coronary heart disease and stroke.

The 2019 Hypertension Management Consensus (Lukito *et al*., 2019) categorizes guarded blood pressure if persons who are <65 years of age have the systole and diastole at ≤130/79 mmHg and uncontrolled at >130/79 mmHg. The age category of > 65 years, the blood pressure is well-restrained if the systole/diastole is at 130-139/79 mmHg, and uncontrolled at > 130-139/79 mmHg. BMI is categorized as underweight, normal, overweight and obese (Kemenkes, 2019; https://p2ptm.kemkes.go.id/infographicp2ptm/obesitas/tabel-batas-ambang-indeks-massa-tubuh-imt). However, for the purpose of comparison in data analysis in this study, BMI was categorized into normal and overweight.

The patient compliance was measured using the Medication Possession Ratio (MPR) in percentages, which is the ratio of the real number of days a patient has a supply of medication during a certain period divided by the number of days they should have received the medication plus the number of days they received the medication at the last prescription (Suhadi *et al*., 2016). It is categorized as compliant if the average MPR value is ≥80% and non-compliant if <80%. The ASCVD risk score was calculated using the FRS BMI calculator available in Excel spreadsheets on the following website: https://www.framinghamheartstudy.org/fhs-risk-functions/cardiovascular-disease-10-year-risk/ (Framingham Heart Study, n.d.).

A quantitative analysis was conducted using IBM SPSS version 29 for Windows (IBM Corp., Chicago) to achieve the research objectives. A univariate analysis was employed to see the distribution of respondents, normality test using Kolmogorov-Smirnov, then bivariate analysis correlation test to assess the relationship between variables using Chi-square test (Vusvitasari *et al*., 2015).

RESULTS AND DISCUSSION

Of the 548 patient medical records incorporated in this study, the total samples that met the inclusion and exclusion criteria were 523 patients who had the characteristics pinpointed in Table 1. A total of 355 (67.9%) were women and 168 (32.1%) were men. Age was grouped into two age ranges - between 40-59 years (37.5%) and 60-70 years (62.5%). Most respondents (51.4%) fell into the obese category with a body mass index > 25. The types of antihypertensive drugs given in this population were quite diverse. Single therapies were most widely used, accounted for 90.2% (472 patients) with the greatest variation being the CCB group at 86% and the rest being the ACEI, ARB and Diuretic groups (Table 2). In this population, Amlodipine still appeared to be the drug of choice for the treatment of hypertension. A combination therapy where 2 hypertension drugs were prescribed comprised the 9% (47 patients) and the remaining 0.8% (4 patients) used a combination of 3-4 drugs. A combination of medications may be necessary in hopes of achieving optimal blood pressure control.

Table 1. Baseline Characteristics of DMT2 Patients with Comorbid Hypertension During January-December 2023

Characteristics	Patients (N= 523)	
	N	%
Gender		
Male	168	32.1
Female	355	67.9
Age (years)		
40-59	196	37.5
60-70	327	62.5
Body Mass Index		
Underweight (<18,5)	14	2.7
Normal (18,5-22,9)	132	25.1
Overweight (23-24,9)	108	20.7
Obesity (>25)	269	51.4
Hypertension Therapy		
Mono therapy	472	90.2
Combination of 2 agents	47	9
Combination of 3 agents	4	0.8
Average MPR Value (Compliance)		
Compliance (≥80%)	306	58.5
Not Compliance (<80%)	217	41.5
Controlled Blood Pressure		
Yes	121	23.1
No	402	76.9
ASCVD Classification		
Low (<10%)	0	0
Moderate (10-20%)	86	16.4
High (>20%)	437	83.6
Number of Diagnoses		
2 (DMT2 and HT)	468	89.5
>2	55	10.5
Polypharmacy		
Yes (> 5 drugs)	20	3.8
No (< 5 drugs)	503	96.2
Aspirin Therapy		
Yes	16	3.1
No	507	96.9
Statin Therapy		
Yes	37	7.1
No	486	92.9

Table 2. Characteristics of Therapy

Hypertensive Agent	**N =523**	**%**
CCB (Amlodipine)	449	86
ACEI	13	2.5
ARB	5	1
Diuretic	2	0.4
ACEI and CCB	4	0.8
ACEI and Diuretic	1	0.2
Beta Blocker and ACEI	1	0.2
Beta Blocker and CCB	1	0.2
Beta Blocker and Diuretic	3	0.6
CCB and ARB	6	1.1
CCB and ACEI	9	1.7
CCB and Beta Blocker	2	0.4
CCB and Diuretic	20	3.8
CCB, Diuretic and ACEI	2	0.4
ACEI, Beta Blocker and CCB	1	0.2
ARB, Beta Blocker and CCB	3	0.6

A continuous low compliance to treatment dosage among hypertensive patients can reduce their optimal therapeutic outcomes, increase the risk of complications, decrease quality of life, and increase health care costs (Azmi *et al*., 2021). The result shows that 306 patients (58.5%) belong to the compliance category and the remaining 41.5% are disobedient. The MPR calculations were performed when the medication claim data showed a minimum of three medication takings.

The data for blood pressure were taken from the community health clinics which patients visited during the medication treatment, both for routine check-ups and on sick visits. Blood pressure control categories were differentiated based on the patient's age. Most patients (76.9%) had uncontrolled blood pressures and only 23.1% were well-monitored. The major population (86%) received CCB monotherapy. Uncontrolled blood pressure is influenced by many factors other than patient compliance. Studies have shown that optimal dose titration and the use of combination therapy when needed are crucial for having controlled blood pressure (Egan *et al*., 2018). Patients with uncontrolled hypertension may require an evaluation of antihypertensive combinations to reach the goal therapy. A study in the United States of America (USA) reported that the trend of using dual or triple agents can improve blood pressure trends in patients (Derington *et al*., 2020). The INASH consensus states that the recommended treatment strategy in current hypertension management guidelines is use of a combination therapy to achieve blood pressure targets. When widely available and feasible, it can be administered in a single combination form to improve medication compliance. Drug doses may not be optimal, as most of the population receives monotherapy, while a combination of hypertension medications and lifestyle changes may be deemed necessary (Lukito *et al*., 2019).

The risk for ASCVD was predicted using the FRS BMI formula calculator with some indicators of gender, age, systole, hypertension status, smoking status, diabetes status and BMI. The results, then, were categorized as low, medium and high risk. Smoking and alcohol

consumption are associated with the health mechanisms that narrow blood vessels and stimulate the sympathetic nervous system, thereby, speeding up the heart rate (Nagao *et al*., 2021). Passive smokers also have an equally high risk for developing hypertension, where after smoking one cigarette for 15 minutes, there is a stimulation in the sympathetic nerves and an increase in catecholamine and damage to the baroreflex so that pressure will increase (Suhadi *et al*., 2016). From the data source, the smoking status of the population is non-informative, so, in this study it is ignored or the population was assumed as non-smokers. Results showed no patients experienced low ASCVD risk in this population. The moderate category was only 16.4% and the remaining 83.6% were at high risk of experiencing ASCVD regardless of their smoking status. It is evident that age, gender and BMI play a significant role in the increased risk of ASCVD in this population.

The research population was patients who had two diagnoses (hypertension and DMT2). There are 10.5% had additional diagnoses such as hypercholesterolemia, arthritis, hyperuricemia and tuberculosis. Only 7.1% of them received statin therapy and 3.1% aspirin. The polypharmacy category is more salient when the patients received more than five types of medication in the last prescriptions. There were only 3.8% of the patients who underwent polypharmacy. Additional medications were given when the patients experienced other complaints such as influenza or skin disease.

The normality test for all variables showed that the results of the research data were abnormally distributed (sig.<0.05]. Bivariate analysis was employed to see the relationship between variables, namely patient compliance in antihypertensive therapy to blood pressure and ASCVD risk, which are presented in Table 3. The research results showed compliance to antihypertensive therapy did not have a significant impact on controlled blood pressure (p 0.867>0.05). Compliance or not to antihypertensive therapy had the same likelihood of having controlled blood pressure. The Odds Ratio (OR) of 0.965 indicates that patient compliance had a slightly lower chance of having controlled blood pressure then non-compliance, although this was not statistically significant. In accordance with the research in 2020 at Jetis Health Center in Yogyakarta (Husna *et al*., 2023), there was no significant relationship between compliance and achieving blood pressure targets. The same results were also revealed from another research on the elderly hypertensive population at RSCM Jakarta (Khomaini *et al*., 2017) and a study on antihypertensive therapy in Samarinda geriatrics (Azmi *et al*., 2021). Different from the previous research, the study in Pontianak stated that there was a significant relationship between the degree of hypertension and patient medication adherence (Asseggaf and Ulfah, 2022).

The OR of 0.662 from the correlation test between compliance to antihypertensive therapy and ASCVD risk meant that compliance patients had 0.662 times (66.2%) lower chance of having a high ASCVD risk than non-compliant patients. In other words, adherence patients with compliance had 33.8% lower chance of having high ASCVD risk. However, this finding cannot be completely concluded because the p-value=0.080>0.05, indicating there was no significant relationship statistically. Others factors such as age, gender, BMI and other comorbidities may play a role in determining ASCVD risk.

A correlation test was then also conducted to determine whether the effect of compliance with antihypertensive therapy on clinical outcome namely controlled blood pressure and ASCVD risk, differed among patient groups with characteristics such as age, gender and BMI (Table 4). BMI was categorized statistically with normal and obese references.

The result showed that there was no significant relationship between age and controlled blood pressure between the 40 - 59 and 60 - 70 years age groups (p 0.773>0.005). Meanwhile, there was a very significant relationship between age and ASCVD risk between the age groups, with <0.001 which is much smaller than 0.05 with a 95% CI (5.606-17.509) indicating that this difference is statistically highly significant. The OR of 9.907 indicates that patients aged 40-59 had an almost 10 times greater chance of having a high ASCVD risk compared with other age groups. A study in Malang showed that high cardiovascular risk is common among Indonesian adults aged ≥ 40 years and the level of preventive treatment is low (Maharani *et al*., 2019).

Table 3. The Correlation Between Compliance to Antihypertensive Therapy to Controlled Blood Pressure and ASCVD Risk in Patients with DM2 Comorbid Hypertension

Variable	Blood Pressure (N)		p-value	OR (95% CI)	ASCVD Risk		p-value	OR (95% CI)
	Controlled	Un-controlled			Moderate	High		
Compliance	70	236	0.867	0.965 (0.64-1.457)	43	263	0.080	0.662 (0.416-1.052)
Not Compliance	51	166			43	174		

*p-value <0.05 = significant difference.

Table 4. The Correlation Between Age, Gender and Body Mass Index to Controlled Blood Pressure and ASCVD Risk in Patients with DMT2 Comorbid Hypertension

Variable	Blood Pressure (N)		p-value	OR (95% CI)	ASCVD Risk		p-value	OR (95% CI)
	Controlled	Un-controlled			Moderate	High		
Age (years)								
40-59	44	152	0.773	0.940 (0.616-1.433)	69	127	<0.001*	9.907 (5.606-17.509)
60-70	77	250			17	310		
Gender								
Male	36	132	0.524	0.866 (0.557-1.348)	10	158	<0.001*	0.232 (0.117-0.462)
Female	85	270			76	279		
BMI								
Normal	45	99	0.007	1.812 (1.175-2.794)	33	111	0.014	1.829 (1.126-2.970)
Overweight	76	303			53	326		

*p-value <0.05 = significant difference.

Gender is one important risk factor ASCVD. Although its specific risk is not yet revealed, a literature review (Appelman *et al*., 2014) indicated that the prevalence was higher in women. There has been some recent evidence that cardiovascular risk factors specific to women such as pregnancy complications, polycystic ovary syndrome (PCOS) and menopause hormones increase the ASCVD risks (Appelman *et al*., 2014; Rajendran *et al*., 2023). In line with this finding, the result showed that there is a significant relationship with ASCVD risk, as indicated by p-value <0.001. The OR 0.232 shows that men have an almost 4 times lower chance of having a higher ASCVD risk than women. Conversely, there was no significant relationship between gender and controlled blood pressure (p 0.524>0.05). Gender differences in antihypertension treatment have shown no significant differences between men and women in a European study (Muiesan *et al*., 2016). Similarly, there was no significant influence of gender, despite the impact of a brief counseling intervention and motivational SMS, in a study conducted at the outpatient clinic of hospital in Bantul, Yogyakarta (Saputri *et al*., 2016).

A significant relationship was found between normal BMI and obesity with controlled blood pressure (p 0.007<0.05) as well as ASCVD risk (p 0.014<0.05). The patients with obesity have an almost 2 times greater chance of having uncontrolled blood pressure (OR 1.812) and high ASCVD risk (OR 1.829) compared to those with normal BMI. This indicates that generally, the higher the BMI, the higher the ASCVD risk will be. In accordance with the theory that modifiable cardiovascular risk factors such as lipid profile, lifestyle and obesity disorders (Hendra *et al*., 2022) and obesity are determining factors in blood pressure in most ethnic groups of all ages (Natekar *et al*., 2014). The findings of this study are in line with a study conducted at a Community Health Center in East Java which found that BMI significantly correlates with blood pressure (Kurniawan *et al*., 2021). Another

study on workers at PT. X in 2021 also mentioned a significant correlation using the FRS method (p=0.004) (Anharudin and Tejamaya, 2022).

The significant relationship between compliance to antihypertensive therapy, age, gender and BMI with controlled blood pressure was not found. The medication compliance alone is not sufficient to achieve an optimal blood pressure control in this population. Developing a prospective cohort research or identifying other factors that may affect blood pressure control among patients with DMT2 who have comorbid hypertension, such as lifestyle (diet and physical activity), history of illnesses, duration of hypertension or DM, smoking status or alcohol consumption and possibly socio-economic factors, is necessarily to be carried out. By comprehensively knowing the proven factors that might have some influence, it is hoped that there will be some innovative interventions developed by Pharmacists to improve curbing patient blood pressure, such as education management and counseling on the lifestyle modification, physical exercise and optimal medicine therapy management.

Measuring ASCVD risk requires information on the patient's smoking status. However, because the data collection used the electronic medical records, the researchers assumed that the entire population did not smoke. This approach is one of the limitations of this study. Further analysis using questionnaires, observations or interviews can be done to determine the causes of the unchecked blood pressure among the majority of the population, that might have stemmed from other factors such as the patient's lifestyle or the frequency of blood pressure measuring and type of recording mechanism for patients at the respective health facilities' information system.

CONCLUSIONS

Based on the research results, there is no significant relationship between the compliance to antihypertensive therapy with either blood pressure control or ASCVD risk in patients with DMT2 and hypertension as a comorbidity at Community Health Centers in Yogyakarta Municipality.

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CONFLICT OF INTEREST

The authors declare there's no conflict of interest.

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