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Research Article

The Association Between Medication Adherence and Blood Pressure Control in End-Stage Renal Disease Patients with Hemodialysis

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ABSTRACT

End-Stage Renal Disease (ESRD) is a severe kidney disorder that contributes to an increased risk of mortality in the world. This condition is often related with hypertension. Low medication adherence was affecting uncontrolled blood pressure in ESRD. The research aimed to analyze the association between medication adherence and blood pressure control in ESRD patients. This cross-sectional study with 77 respondents was conducted in September 2020 at the Dialysis Unit of the Private Hospital "X" Buleleng Bali by purposive sampling technique. The respondents must be ≥18 years, diagnosed with ESRD and hypertension, underwent hemodialysis (HD) twice a week, received the same antihypertensive for 3 months, have complete medical record data, and signed the informed consent form. Patients with cognitive impairment, unable to communicate, pregnant or breastfeeding, and received the Erythropoiesis Stimulating Agent (ESA) treatment were excluded. Kruskal-Wallis test was used in data analysis. Most of the patients were <65 years (80.52%), male (70.13%), primary education (57.14%), without complications (57.1%), and duration of illness <5 years (89.61%). Patients were in the high adherence (61.04%) and 66.23% of patients had uncontrolled blood pressure. The association between medication adherence and blood pressure control was not significant (p=0.478). However, these results show that high medication adherence could impact on good blood pressure control.

INTRODUCTION

End-Stage Renal Disease (ESRD) is a condition of permanent loss of kidney function with a glomerular filtration rate (GFR) <15 mL/minute/1.73m^2 for >3 months (Farida *et al.,* 2018). Therefore, patients with ESRD must undergo hemodialysis (HD) as lifelong renal replacement therapy (Bindroo, 2018). In 2017, ESRD became the 12th leading cause of death globally (Bikbov *et al.,* 2020). Based on data from the Indonesian Renal Registry (IRR), there was an increase in the number of patients with ESRD in Indonesia from 1,885 people in 2007 to 132,142 people in 2018 (IRR, 2018). DKI Jakarta and Bali occupy the top two positions as provinces with the highest incidence of ESRD in Indonesia (Riskesdas, 2018).

More than 50% of ESRD patients have hypertension (Ku *et al.,* 2019; Sinha *et al.*, 2019). Hypertension occurs due to loss of kidney function which causes impaired sodium secretion thereby increasing extracellular volume which has an impact on increasing blood pressure (Ku *et al.*, 2019). Hypertension in patients with ESRD will increase the deterioration of kidney conditions (Chang *et al.*, 2010). Accordingly, the 2020 International Society of Hypertension (ISH) and Kidney

Disease Improving Global Outcomes (KDIGO) or Kidney Disease Outcome Quality Initiative (KDOQI) explained that antihypertensive therapy is needed to control patients' blood pressure.

Even though antihypertensives have been prescribed, there are still 72-80% of ESRD patients who had uncontrolled blood pressure (>140 mmHg) (Gallacher *et al.,* 2020; Sinha *et al.*, 2019). This is due to the low level of medication adherence. Medication adherence is defined as the conformity of the patient's behavior to the recommendations for drug use from health workers (Nielsen *et al.,* 2018). The research of Tangkiatkumjai *et al.* (2020) and Tesfaye *et al.* (2020), found that 21-74% of ESRD patients with poor adherence had blood pressure >150/90 mmHg (p<0.05).

Table 1. Sociodemographic Features of Patients

Sociodemographic features	N (%)
Age	
<65 years	62 (80.52%)
≥65 years	15 (19.48%)
Gender	
Female	23 (29.87%)
Male	54 (70.13%)
Level of Education	
Illıterate	7 (9.09%)
Primary Education	44 (57.14%)
High School	16 (20.78%)
Higher Education	10 (12.99%)
Complications	
With complications	34 (43.58%)
Hyperuricemia	13 (16.66%)
Digestive disorders	9 (11.55%)
Cardiovascular disorders	8 (10.25%)
Respiratory disorders	2 (2.56%)
Anemia	2 (2.56%)
Without complications	44 (56.41%)
Duration of illness	
< 5 years	69 (89.61%)
5-10 years	7 (9.09%)
> 10 years	1 (1.30%)

Uncontrolled blood pressure in patients with ESRD will have a negative impact on increasing the risk of mortality (Ku *et al.,* 2019; Tangkiatkumjai *et al.,* 2017). Therefore, it is important to conduct this study to determine the association between medication adherence and blood pressure control of ESRD patients undergoing HD.

METHODS

This research was an observational study with a cross-sectional design conducted at the Dialysis Unit of the Hospital "X" Buleleng Bali in September 2020. The direct population was used as the research sample through the purposive sampling technique, which consisted of 77 patients. The study sample had met the inclusion criteria, namely aged ≥18 years, suffered from ESRD with hypertension, received the same antihypertensive for 3 months, HD twice a week, and signed the informed consent. Exclusion criteria were patients with cognitive impairment, unable to communicate, pregnant and lactating, and receiving Erythropoiesis Stimulating Agent (ESA) therapy. The data collection technique was through direct interviews accompanied by the provision of a Probabilistic Medication Adherence Scale (ProMAS) adherence questionnaire and based on the patient's medical records.

The ProMAS questionnaire in the Indonesian version has been declared valid and reliable with a Cronbach's alpha value of 0.81 and a reliability value of 0.72 (Kleppe *et al.,* 2015). The results of the measurement of adherence were categorized into four groups based on the scores, namely low adherence (0-4), medium-low (5-9), medium-high (10-14), and high adherence (15-18). Meanwhile, blood pressure control refers to the 2020 ISH guidelines. It is categorized as controlled if blood pressure <130/80 mmHg at age <65 years and blood pressure <140/80 mmHg at age ≥65 years. Conversely, if the blood pressure is > 130/80 mmHg (age <65 years) and > 140/80 mmHg (age ≥65 years) it is included in the uncontrolled category (Unger *et al.,* 2020). The research data were then analyzed using the Kruskal-Wallis test if not meeting the requirements with the Chi-square test to see the correlation between variables in the categorical data. This research had obtained a research permit and ethical license numbered (009/EA/KEPK-BUB-2021).

RESULTS AND DISCUSSION

Patient Sociodemographics

Most of the patients with ESRD in this study were male (70.13%), aged <65 years (80.52%), primary education (57.14%), without complications (57.1%), and 89.61% of them suffered from ESRD for <5 years (Table 1). Men are more at risk of experiencing ESRD because they have a heavier kidney work in secreting waste as a result of more daily intake than women, besides that it is also exacerbated by unhealthy lifestyles such as smoking and alcohol consumption (Goldberg *et al.*, 2016; Gonzales *et al.,* 2017). Patients with age >40 years are more at risk of developing ESRD, since the kidneys begin to atrophy, causing decreased blood flow, and decreased GFR around 0.75 mL/minute/1.73m^2 (Anita *et al.*, 2017; Arifa *et al.,* 2017). Patients with primary education levels are more at risk of experiencing ESRD due to low knowledge of the disease and healthy behavior (Saputra *et al.,* 2020). Meanwhile, the duration of patients suffering from ESRD is related to the patient's endurance to dialysis therapy while complications are related to the number of drugs received and the risk of mortality in patients with ESRD (Ariyani, 2017; Parker *et al.,* 2019).

Overview of Medication Adherence Rate

The description of medication adherence was obtained based on the results of the questionnaire scoring listed in Table 2. It can be seen that the percentage of answers that lead to non-adherence of several statements in the questionnaire still reached 35% (questions number 2, 4, and 6). This indicates that some patients with ESRD have not yet received antihypertensive therapy in accordance with the instructions of health workers. However, Table 3 shows the majority of patients had high adherence to treatment (61.04%). Similar results were found in the study of Naalweh *et al.* (2017) and Ohya *et al.* (2019), that found the number of ESRD patients with high adherence reached 93% to antihypertensive treatment. Treatment adherence has been widely studied and associated with various aspects that can affect the changes in patients' health status, and one of the aspects studied in this study is the patient's characteristics.

Table 2. Probabilistic Medication Adherence Scale (ProMAS) Answer

Item	Questions	Yes n (%)	No n (%)
1	It has happened at least once that I forgot to take (one of) my medicines.	23 (30%)	54 (70%)
2	It happens occasionally that I take (one of) my medicines at a later moment than usual.	27 (35%)	50 (65%)
3	I have never (temporarily) stopped taking (one of my) medicines.	58 (75%)	19 (25%)
4	It has happened at least once that I did not take (one of) my medicines for a day.	27 (35%)	50 (65%)
5	I am positive that I have taken all the medication that I should have taken in the previous year.	51 (66%)	26 (34%)
6	I take my medicines exactly at the same time every day.	50 (65%)	27 (35%)
7	I have never changed my medicine use myself.	70 (91%)	7 (9%)
8	In the past month, I forgot to take my medicine at least once.	22 (29%)	55 (71%)
9	I faithfully follow my doctor's prescription concerning the moment of taking my medicines.	54 (70%)	23 (30%)
10	I sometimes take (one of) my medicines at a different moment than prescribed (e.g., with breakfast or in the evening).	22 (29%)	55 (71%)
11	In the past, I once stopped taking (one of) my medicines completely.	7 (9%)	70 (91%)
12	When I am away from home, I occasionally do not take (one of) my medicines.	12 (16%)	65 (84%)
13	I sometimes take less medicine than prescribed by my doctor.	14 (18%)	63 (82%)
14	It has happened (at least once) that I changed the dose of (one of) my medicines without discussing this with my doctor.	9 (12%)	68(88%)
15	It has happened (at least) once that I was too late with filling a prescription at the pharmacy.	17 (22%)	60 (78%)
16	I take my medicines every day.	64 (83%)	13 (17%)
17	It has happened (at least once) that I did not start taking a medicine that was prescribed by my doctor.	9 (12%)	68 (88%)
18	I sometimes take more medicines than prescribed by my doctor.	11 (14%)	66 (86%)

Table 3. Level of Adherence

Adherence level	N (%)
Low (0-4)	5 (6.49%)
Medium-low (5-9)	11 (14.29%)
Medium-high (10-14)	14 (18.18%)
High (15-18)	47 (61.04%)
Total	77 (100%)

Table 4. Blood Pressure Control

Blood pressure control	N (%)
Controlled (<130/80 mmHg or <140/80 mmHg)	26 (33.77%)
Uncontrolled (>130/80 mmHg or >140/80 mmHg)	51 (66.23%)
Total	77 (100%)

Judging by age, generally the memory capacity of patients <65 years old is better able to remember the schedule and treatment regimens compared to those aged ≥65 years (Kushariyadi, 2013). In terms of gender differences, men pay more attention to instructions and advice from prescribers in undergoing treatment that is triggered by family support and motivation (Mahmoodi *et al.,* 2019; Yap *et al.,* 2016). Furthermore, in terms of education level, patients with primary education can be more adherent because they are more willing to comply with treatment instructions from health workers (Jain *et al.,* 2018). The absence of complications in patients has an impact on increasing adherence as a result of the number of drugs consumed is less than patients with complications (Dawood *et al.,* 2018). Furthermore, regarding the duration of suffering from the disease, patients with ESRD <5 years tend to be more worried about their condition, causing greater motivation or awareness to control blood pressure (Anwar *et al.*, 2019).

Blood Pressure Control in ESRD Patients

Table 4 shows that 66.23% of patients had uncontrolled blood pressure. This finding is in line with the research results of Altun *et al.* (2012), Cai *et al.* (2013), and Stern *et al.* (2014), that more than 70% of ESRD patients with hypertension have uncontrolled blood pressure despite taking antihypertensives. Uncontrolled blood pressure in this study can be influenced by various aspects of triggers, including sociodemographic characteristics and the use of antihypertensives (Ferdianam *et al.,* 2019; Nilrohit *et al.,* 2017).

In this study, most of the patients were <65 years old, male, and had a history of primary education. Age and gender differences can affect blood pressure control in ESRD patients. This is confirmed in the research of Nilrohit *et al.* (2017), that found patients aged <65 years and male are generally more active and have a poorer lifestyle such as smoking or alcohol consumption which has an impact on poor blood pressure control. Lower levels of education can reduce the patient's ability to maintain health, especially in controlling blood pressure (Ozen *et al.,* 2019; Trianni e*t al.,* 2012). In addition to patient sociodemographic characteristics, inappropriate use of antihypertensives is also associated with blood pressure control. The ESRD patients who take antihypertensives not according to instructions or drinking rules from health workers can cause blood pressure to become uncontrolled (Abegaz *et al.,* 2016).

Table 5. Association Between Medication Adherence and Blood Pressure Control

Adherence Level	Blood pressure			*p*-value*
	Controlled	Uncontrolled	Total	
Low (0-4)	1 (1.3%)	4 (5.2%)	5 (6.5%)	
Medium-low (5-9)	3 (3.9%)	8 (10.4%)	11 (14.3%)	
Medium-high (10-14)	5 (6.5%)	9 (11.7%)	14 (18.2%)	0.478
High (15-18)	17 (22.1%)	30 (39.0%)	47 (61.0%)	
Total	26 (33.8%)	51 (66.2%)	77 (100%)	

Note: *significant at $p<0.05$.

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The Association Between Medication Adherence and Blood Pressure Control

The results showed there was no significant association between medication adherence and blood pressure control (p=0.478) (Table 5). Similar results were found by Kumboyono (2012) and Schmieder *et al.* (2016), that indicated medication adherence has no effect on blood pressure control in patients with ESRD (p>0.05). In this study, the highest percentage of controlled (22.1%) and uncontrolled (39%) blood pressure were both indicated by patients with high adherence. Therefore, although the results were not significant, medication adherence still had a positive impact on improving the patient's blood pressure control.

Other aspects can affect the results that are not significant. First, based on the description of the patient's medication adherence (Table 3), most of the patients had high adherence (61.04%) so that the highest percentage of uncontrolled blood pressure was also likely to happen in patients with high adherence. Second, in terms of patient characteristics (Table 1), it has been previously explained that differences in sociodemographic characteristics in ESRD patients can affect blood pressure control (Nilrohit *et al.,* 2017; Ozen *et al.,* 2019). The third is the difference in the patient's physiological condition and lifestyle. In general, ESRD patients find it difficult to achieve controlled blood pressure even though the patient has adhered to treatment (Gallacher *et al.,* 2020). This can be caused by differences in physiological conditions such as sympathetic nerve overactivity, volume overload and endothelial dysfunction, and an unhealthy lifestyle. Sympathetic overactivity in ESRD patients can be caused by stress and anxiety experienced during therapy. Sympathetic activity will trigger the activation of the renin-angiotensin-aldosterone system (RAAS) which causes vasoconstriction and increased fluid retention resulting in an increase in blood pressure (Ku *et al.,* 2019; Stern *et al.,* 2014). Volume overload or excess extracellular volume will increase peripheral tissue perfusion and then stimulate peripheral vascular resistance, while endothelial dysfunction occurs due to impaired nitric oxide (NO) production, oxidative stress, and increased endothelin levels which cause an increase in peripheral vasoconstriction, thus triggering an increase in blood pressure in patients with ESRD (Ku *et al.,* 2019).

An unhealthy lifestyle, especially those related to limiting sodium intake, can affect changes in blood pressure (Thalib, 2019). A study found that the average community in Bali has a habit of eating foods high in sodium and has become a culture that is difficult to change, so that blood pressure is more difficult to control even after routine use of antihypertensives (Dharmapatni *et al*., 2020). Sodium has the ability to bind fluid which causes blood volume to increase and triggers RAAS activation which then results in an increase in blood pressure (Wulan *et al.*, 2018). Fourth is the stress and anxiety conditions patients during the treatment. This condition will trigger a sympathetic response that causes an increase in blood pressure (Dharmapatni, 2020).

Additionally, the limitations of the study may also have an effect on the insignificant results. The limitation in some questions is the adherence measurement instrument (ProMAS questionnaire) which is subjective, making it difficult to measure the patient's honesty when filling out the questionnaire. Also, the limited population in this study will have an impact on the measurement results of the ProMAS questionnaire because it is based on previous research by Kleppe *et al.* (2015) and Pratama *et al.* (2019), with significant results using more than 200 respondents.

CONCLUSION

Most of the respondents involved in this study were male (70.13%), aged <65 years (80.52%), duration of disease <5 years (89.61%), had primary education (57.14%), and without complications (57.10%). About 61.04% of patients had a high level of medication adherence and 66.23% of patients had uncontrolled blood pressure. The results showed that there was no significant relationship between medication adherence and blood pressure control (p=0.478). However, the results supported that high medication adherence has a positive impact on improving blood pressure control in patients with ESRD.

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