

Original Research Article

Factors associated with blood pressure in end stage renal disease patients receiving regular hemodialysis at Wangaya general hospital, Denpasar

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ABSTRACT

Background: Hypertension is common findings in end-stage renal disease (ESRD) patients receiving hemodialysis, around two third among them are poorly controlled. We analyzed factors affecting blood pressure in patients undergoing regular hemodialysis.

Methods: A single center cross-sectional study conducted including 65 patients receiving regular hemodialysis at hemodialysis unit Wangaya general hospital, Bali, Indonesia. Ordinal regression test was performed to analyze the relationship between factor associated with blood pressure in regular hemodialysis patients.

Results: Among subjects included, 64 (98.5%) subject had hypertension and 22 (34.4%) subjects had well controlled blood pressure (<140/90 mmHg), 20 (31.3%) subjects had blood pressure between 140/90 to 160/100 mmHg and 22 (34.4%) subjects had blood pressure >160/100 mmHg. Univariate analysis showed statistically significant associated factors were higher number of antihypertensive medications ($p=0.002$), higher level of hemoglobin ($p=0.008$), hematocrit ($p=0.012$) and urea ($p=0.041$). Multivariate analysis showed higher amount of anti-hypertensive medications and year of dialysis were statistically significant associated with blood pressure in regular hemodialysis patients.

Conclusions: Significant factors associated with blood pressure in regular hemodialysis patients were higher amount of anti-hypertensive medications and increased year of dialysis.

Keywords: ESRD, Hemodialysis, Blood pressure, Hypertension

INTRODUCTION

Hypertension is a very common findings in patients with ESRD receiving hemodialysis as renal replacement therapy. Hypertension in hemodialysis patients is diagnosed when pre-dialysis blood pressure is >140/90 mmHg or post-dialysis blood pressure is >130/80 mmHg.¹ Although recent evidence suggests that out-of-dialysis blood pressure measuring are better than pre and post-dialysis BP in diagnosing hypertension, guiding the management and predicting risk of cardiovascular event

and death, the practice is often difficult in low resource settings. In patients with ESRD receiving renal replacement therapy, the prevalence of hypertension was found to be 80-90%.² Since hypertension is the major contributing factor to the cardiovascular event risk reduction in this population, blood pressure control will improve survival rates. Achieving blood pressure control using anti-hypertensive drugs result in 30% risk reduction of cardiovascular events and death, but in fact adequate control in only achieved in 27.4% of regular hemodialysis with hypertension.^{3,4}

Multiple mechanisms have been described to involve in progression of hypertension in regular hemodialysis patients. The main pathogenic mechanism considered are volume and sodium overload. Other contributing mechanisms such as sympathetic nervous systems and renin-angiotensin-aldosterone axis activation, alteration of arterial wall increased arterial stiffness, chronic inflammation, endothelial dysfunction results in imbalance of endothelial-derived vasodilators and vasoconstrictors and drugs such as erythropoietin-stimulating agents are interact with each other in development hypertension in regular hemodialysis patients.⁵

Achievement of target blood pressure is affected by individual characteristics including age, gender and various laboratory parameters.^{6,7} This study aimed to assess the factors that influence blood pressure in patients undergoing regular hemodialysis. This study will provide a deeper understanding of the factors that play a role in the progression of hypertension in regular hemodialysis patients.

METHODS

We performed a cross-sectional study at hemodialysis unit Wangaya general hospital, Bali, Indonesia from February 2021 to April 2021. Total of 65 patients who underwent regular hemodialysis twice weekly were included in this study. This study ethically accepted by the ethics committee of Wangaya general hospital with a register number 012/III.4/KEP/RSW/2021. Patients aged 18 years and over who had undergone regular hemodialysis for at least 12 months, without being hospitalized during the study were included as study subjects.

Analysis of blood pressure related to patients' characteristics, medical and dialytic variables were done in this study. Patient's age, duration of hemodialysis, primary renal disease contributing to ESRD, anti-hypertensive medication profile, pre and post-dialysis blood pressures and ultrafiltration removed were obtained from hemodialysis records. Blood pressure and ultrafiltration removed values were obtained based on the mean measurements for 1 month while the patient was undergoing regular hemodialysis. Hypertensive, hemoglobin, hematocrit, serum urea and creatinine were measured during regular check-up on hemodialysis unit.

Hypertensive status was analyzed based on pre-dialysis blood pressure measurement. Hypertension is defined as pre-dialysis blood pressure measurement >140/90 mmHg and/or taking anti-hypertensive medication on regular basis. Among those who had hypertension, blood pressure than classified into 3 categories which are well control (<140/90 mmHg), class II (between 140/90 mmHg and 160/100 mmHg) and class III (>160/100 mmHg). Univariate and multivariate analysis of pre-dialysis blood pressures with patient's characteristic, hemodialysis factors and anti-hypertensive medication were done by ordinal regression test. Statistically significant is shown with $p < 0.05$, with a 95% confident interval. All statistical analyzes were performed by SPSS version 25.0 to determine factors related to blood pressure in regular hemodialysis patients.

RESULTS

Here we presented baseline characteristic of the study in Table 1. Mean duration of hemodialysis was 3.9 years. Among these population, 64 (98.5%) subject had hypertension. Hypertensive nephrosclerosis (41.5%) and diabetic kidney disease (35.4%) were highest primary renal disease contributing to ESRD. The mean pre-dialysis systolic (SBP) and diastolic blood pressures (DBP) were 148.5 and 78.6 mmHg, while the mean post-dialysis SBP and DBP were 151.0 and 79.8 mmHg. Most patients with hypertension were taking combination of two or more antihypertensive medication. Calcium channel blockers were the most prescribed antihypertensive medication (86.2%), followed by angiotensin-II receptor blocker (81.5%), β -blocker (33.8%), nitrate (6.2%), angiotensin-converting enzyme inhibitor (4.6%) and α -2 agonist (3.1%). Systolic and diastolic blood pressure is in increasing trend by duration of hemodialysis as shown in Figure 1.

Ordinal regression test was performed to analyzed the relationship between factor associated with hypertension in regular hemodialysis patients. Univariate analysis shown statistically significant factors were higher number of antihypertensive medications prescribed (0.928, $p=0.002$), higher level of hemoglobin (-0.425, $p=0.008$), hematocrit (-0.115, $p=0.012$), and urea (0.0016, $p=0.041$). Significant factors associated with blood pressure in multivariate analysis are only higher amount of anti-hypertensive medications prescribed and increased year of dialysis.

Table 1: Baseline characteristic of regular hemodialysis patients in Wangaya general hospital.

Variables	N (%)
Age	52.65±13.8
Sex	
Male	48 (73.8)
Female	17 (26.2)

Continued.

Variables	N (%)
Duration of hemodialysis (in years)	3.9±2.9
Hypertension	64 (98.5)
Well controlled (<140/90 mmHg)	22 (34.4)
Class II (between 140/90 mmHg and 160/100 mmHg)	20 (31.3)
Class III (>160/100 mmHg)	22 (34.4)
Pre-dialysis blood pressure	
SBP (mmHg)	148.5±19.6
DBP (mmHg)	78.6±11.1
Post-dialysis blood pressure	
SBP (mmHg)	151.0±22.5
DBP (mmHg)	79.8±8.7
Ultrafiltration removed (liter)	2.8±0.8
Hemoglobin	10.1±1.6
Hematocrit (%)	31.1±5.6
Urea (mg/dl)	107.2±32.9
Creatinine (mg/dl)	10.22±3.2
Primary renal disease	
Diabetic kidney disease	23 (35.4)
Hypertensive nephrosclerosis	27 (41.5)
Chronic pyelonephritis	7 (10.8)
Chronic glomerulonephritis	4 (6.2)
Polycystic kidney disease	1 (1.5)
Systemic lupus erythematosus	1 (1.5)
Other	2 (3.1)
Anti-hypertensive medication profile	
Number of anti-hypertensives	
1	13 (20)
2	30 (46.2)
3	17 (26.2)
4	4 (6.2)
Class of anti-hypertensive	
ACE inhibitor	3 (4.6)
ARB	52 (81.5)
B-blocker	22 (33.8)
CCB	56 (86.2)
Nitrate	4 (6.2)
α-2 agonist	2 (3.1)

Table 2: Univariate and multivariate analysis of factor associated with hypertension in regular hemodialysis patients in Wangaya general hospital.

Variables	Univariate		Multivariate	
	Coefficient	P value	Coefficient	P value
Age	-0.16	0.351	-0.027	0.186
Sex	-0.472	0.367	-0.097	0.878
Duration of hemodialysis	0.157	0.058	0.268	0.013
Ultrafiltration removed	0.252	0.388	0.011	0.976
Number of anti-hypertensive medication	0.928	0.002	0.992	0.005
Hemoglobin	-0.425	0.008	-0.076	0.082
Hematocrit	-0.115	0.012	-0.139	0.348
Urea	0.016	0.041	0.015	0.134
Creatinine	-0.003	0.963	-0.054	0.614

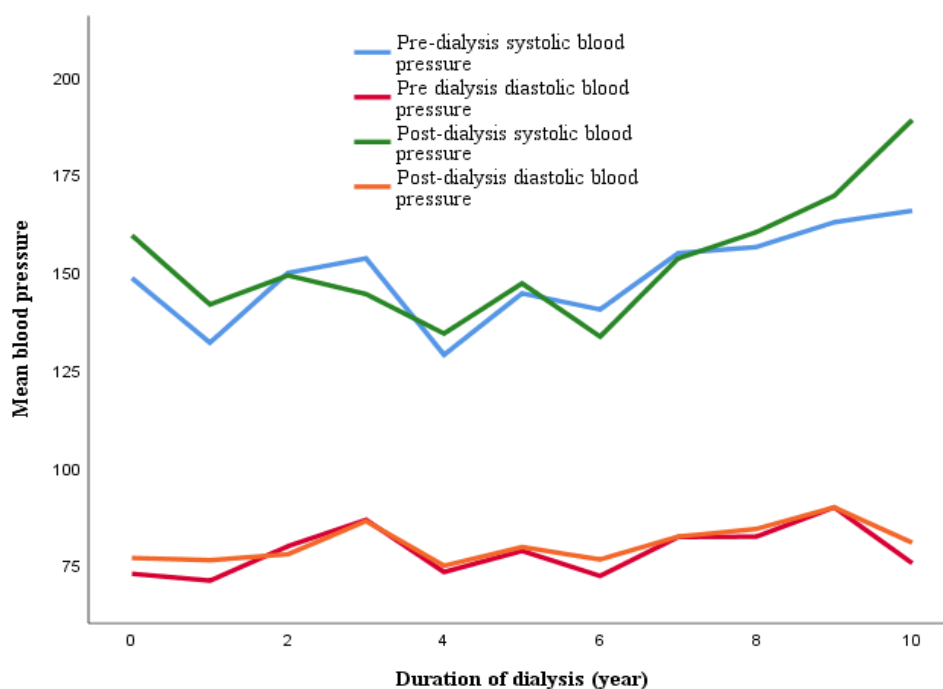


Figure 1: Mean SBP and DBP by duration of dialysis (year) in regular hemodialysis patients in Wangaya general hospital.

DISCUSSION

Hypertension is a condition that is commonly found in patients on regular hemodialysis. In our study, hypertension was found in 98.5% of patients on regular hemodialysis. Blood pressure target in patients on regular hemodialysis is still a matter of debate. There are still no guidelines that clearly define optimal blood pressure targets in regular hemodialysis patients. Several guidelines state that optimal blood pressure is pre-dialysis blood pressure <140/90 mmHg and post-dialysis blood pressure <130/90 mmHg, but all those guidelines note that there is insufficient evidence to support these targets.^{1,8,9} Here we found regular hemodialysis patients with hypertension who met the blood pressure target only reached 34.4%.

Blood pressure is linked to a number of factors in regular hemodialysis patients, univariate analysis found hemoglobin, hematocrit, serum urea levels and the number of antihypertensive medications prescribed were significant factors (Table 2). Number of anti-hypertensive medications prescribed is also significant factor associated with blood pressure in multivariate analysis, along with the duration of hemodialysis.

Lower hemoglobin level was associated with lower blood pressure. Anemia is also a common finding in hemodialysis patients that occurred through several mechanism. Anemia can increase production of nitric oxide which result in decrease of systemic vascular resistance due to nitric oxide-mediated vasodilation,

reduces blood viscosity. Hemoglobin levels were also found to be linked to arterial stiffness in regular hemodialysis patients. Thus, increase arterial stiffness in higher hemoglobin levels can also contributes to the increase in blood pressure in regular hemodialysis patient.¹⁰ Lower hemoglobin level will be directly proportional to lower hematocrit level and red blood cell counts. Lower hematocrit will lead to less viscous blood. Increased hematocrit was discovered to be an independent risk factor for hypertension, with every 1% rise in hematocrit associated with a 7% increase in hypertension risk.^{11,12}

Urea concentration in patients with chronic renal disease reported to increase oxidative stress and reactive oxygen species (ROS). Endothelial pro-inflammatory pathways and inactivation of prostacyclin (PGI₂) synthase will be triggered by this urea-induced ROS.¹³ Increased urea concentration also reported to have positive correlation with pulse wave velocity, reflecting increase in arterial stiffness.¹⁴ This combined mechanism of endothelial dysfunction, impaired vasodilation, and increased arterial stiffness was thought to be the mechanism of urea concentration altering blood pressure.

Increasing number of antihypertensive medications was associated with higher blood pressure in univariate and multivariate analysis in this study. These finding is similar with previous studies.^{4,6,15} Despite the fact that the amount of anti-hypertensive drugs prescribed has increased, blood pressure management has remained unsatisfactory and it

may suggest that underlying mechanism sustaining hypertension in regular hemodialysis patients is not addressed adequately with current medications. In ESRD patients on regular hemodialysis, complex pathways and interactions of multiple factors play a role in the pathogenesis of hypertension. Volume and sodium overload is a major pathogenic factor of hypertension as the result of minimally functioning kidney in ESRD patients. Improvement in excessive fluid and sodium removal can result in better blood pressure control, this can be achieved through individualized, slow and more frequent hemodialysis.^{16,17} This effect can't be observed in this study because of a standardized twice a week hemodialysis performed in all subjects in this study.

In multivariate analysis, significant factor besides number of antihypertensive medications which positively associated with blood pressure in regular hemodialysis patients is increased duration of hemodialysis. Previous study analyzed arterial stiffness measurement through pulse wave velocity (PWV) in patient with hemodialysis. Hemodialysis population is associated with early and rapid progression of vascular stiffness. PWV value was 24% higher in regular hemodialysis population than in healthy population and more than twofold higher yearly increase. Increased duration of the patients receiving hemodialysis was associated with increased of PWV in rate of 1.78 ± 0.510 cm/sec per month. The speed of arterial pressure waves passing through the aorta and large arteries is measured as PWV, it is usually calculated by dividing distance between two points of recording arteries with its pressure wave transit time at those points. Increased arterial stiffness can result as hypertension. This evidence came from as PWV could predict the onset of hypertension and progression of blood pressure in hypertensive populations.¹⁸

Presence of CKD is related with chronic inflammatory state. Chronic inflammatory status is prevalent among CKD patients and its increase accompanying with further decline in renal function and dialysis patients. The pathophysiology of chronic inflammation development in patient with CKD is thought to be multifactorial, including dialysis membranes and central venous catheter exposure, oxidative stress, cellular senescence, chronic fluid and sodium overload, retention of uremic toxins and immune dysfunction.¹⁹ Chronic inflammation have been linked to hypertension and participate to its development. A study found that higher and sustained inflammatory state were associated with higher annual elevation of blood pressure.²⁰ This chronic inflammatory state in regular hemodialysis patient also could contribute to higher blood pressure in patients with more year on receiving dialysis.

This research had a number of limitations. First, as it is cross-sectional design, it only showed association between variables and couldn't explain causality of the variables. Second, blood pressure measurement and classification were done in hemodialysis unit, pre- and post-dialysis. As several studies mention that this measurement was not as

sensitive as ambulatory blood pressure monitoring or home blood pressure measurement to diagnose hypertension in regular hemodialysis population.

CONCLUSION

This study shows that majority of the population on regular hemodialysis has hypertension and only one third among them is controlled. Increased amount of anti-hypertensive drugs prescribed and duration patients receiving hemodialysis are significant factors associated with increased blood pressure in daily hemodialysis patients. More studies should be performed in defining mechanisms of hypertension in hemodialysis population and individualized effort needed to be delivered to achieve optimal blood pressures target in hemodialysis patient.

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