

RELATIONSHIP AND COMPARISON OF HYPERTENSION GRADE 1 AND 2 TO THE EVENT OF CHRONIC RENAL FAILURE

Abstract

Hypertension is an increase in systolic and diastolic blood pressure above average, which can increase the occurrence of chronic kidney failure. Age, gender, genetics, nutrition, stress, activity, and lifestyle are risk factors for this problem. This study aims to determine the relationship and comparison of hypertension grades 1 and 2 to the incidence of chronic kidney failure at UKI General Hospital by looking at medical record data. This research was conducted with an analytical observational method and a cross-sectional approach. The sample consists of 73 respondents, and the sample selection using a simple random sampling technique. The results showed that the most criteria were age > 40 years (74.0%), the most gender was female (58.9%), and the highest body mass index (BMI) was mild overweight (43.8%). In this study, there was a significant relationship between hypertension and chronic kidney failure $p=0.002$ ($p<0.05$), and respondents with grade 2 hypertension had a higher risk of chronic kidney failure compared to grade 1 hypertension (95.6%).

Keywords: *Chronic Kidney Failure, hypertension, UKI General Hospital.*

Introduction

“Hypertension increases systolic and diastolic blood pressure above normal. The Joint National Committee (JNC) 8 classifies human blood pressure into normal, prehypertension, grade 1 hypertension, and grade 2 hypertension” [1]. “Hypertension is now a global problem because of its increasing prevalence. According to the American Heart Association, after suffering from hypertension for 20 years, the American population has reached up to 74.5 million, and almost 90-95% of cases are unknown. Hypertension is a degenerative disease that is a serious problem today. Hypertension is categorized as a silent disease or a silent killer because the patient does not know he has hypertension or does not know before checking his blood pressure. The incidence of hypertension increases with age” [2]. “The national hypertension prevalence in 2013, was 25.8%. The highest was in the Bangka Belitung Islands (30.9%), while the lowest was in Papua Island (16.8%). Based on these data, only 1/3 were diagnosed, and the remaining 2/3 were undiagnosed. Data shows that only 0.7% of people with high blood pressure take antihypertensive drugs. It shows that most people with hypertension are unaware that they have hypertension or are getting treatment. Hypertension kills nearly 8 billion people worldwide and 1.5 million people annually in the East-South Asia region. About a third of adults in South-East Asia suffer from hypertension. In addition, hypertension often occurs in patients with an age range of 35-44 years (6.3%), 45-54 years (11.9%), and age 55-64 (17.2%). Meanwhile, according to economic status, the highest proportion of hypertension is at the lower middle level (27.2%) and middle (25.9%)” [3].

“The danger of uncontrolled hypertension can cause dangerous complications, such as coronary heart disease, stroke, chronic kidney failure, brain disorders, and visual disturbances. Target organ damage due to hypertension will depend on the magnitude of the increase in blood pressure and the length of time the condition of increased blood pressure is undiagnosed or untreated” [4]. “In 2013 shows that the Indonesian population suffering from kidney failure is 0.2% or 2 per 1000. The highest prevalence of kidney failure is in Central Sulawesi Province, at 0.5%. More than 2 million people worldwide receive treatment with dialysis or kidney transplantation, and only about 10% experience these treatments” [3]. At first, chronic kidney failure does not show typical symptoms, so it is often too late to detect.

Signs and symptoms from kidney failure are widespread and can be found in other diseases, one of which is hypertension. Hypertension is the second most common cause of end-stage renal failure after diabetes mellitus. In fact, according to several studies, hypertension is one of the risk factors for increasing death in hemodialysis patients [5]. "Hypertension, better known as high blood pressure, is a condition where a person's blood pressure is above the average or optimal limit of 120 mmHg for systolic and 80 mmHg for diastolic, which occurs chronically (in the long term). This disease is categorized as silent because the patient does not know he has hypertension before checking his blood pressure" [1; 2]. "In the early stages, most hypertensive patients show an increased cardiac output followed by an increase in peripheral resistance, which results in a persistent increase in blood pressure. Increased peripheral resistance in essential hypertension occurs gradually over time, while autoregulation occurs in a short time" [1].

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"Hypertension is now a global problem because of its increasing prevalence. Hypertension can be divided into three groups, namely systolic hypertension, diastolic hypertension, and mixed hypertension. Systolic hypertension (isolated systolic hypertension) is an increase in systolic pressure without an increase in diastolic pressure and is generally found in the elderly. Systolic pressure is related to the high pressure in the arteries when the heart contracts (heart rate). Systolic pressure is the maximum pressure in the arteries" [6]. "Diastolic hypertension (diastolic hypertension) is an increase in diastolic pressure without an increase in systolic pressure, usually found in children and young adults. Diastolic hypertension occurs when small blood vessels narrow abnormally, increasing blood flow and diastolic pressure resistance. Diastolic blood pressure is related to arterial pressure when the heart is relaxed between beats. Mixed hypertension is an increase in systolic and diastolic pressure". [6]

"Based on the cause, hypertension is divided into primary hypertension and secondary hypertension" [7]. "According to The Seventh Report of The Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-8), the classification of blood pressure in adults" [8]. "Risk factors for hypertension are divided into two, namely factors that cannot be controlled (age, gender, and family history of hypertension) [9] and factors that can be controlled (nutritional status - Body Mass Index, smoking, food intake, stress, and obesity, and physical activity)" [10; 11; 12]. There are many causes of hypertension. It cannot be explained by only one causal factor. But in the end, it will all relate to controlling sodium (Na) in the kidneys so that blood pressure increases. Four causative factors dominate the occurrence of hypertension [7]: a) The role of intravascular volume; b) The role of autonomic nervous control; c) The role of renin-angiotensin-aldosterone (RAA); and d) The role of the vascular walls of blood vessels.

"Diagnosis of hypertension with the most accurate physical examination using a mercury sphygmomanometer. It is advisable to take more than one measurement in a sitting position with the elbows bent on the table with the palms facing up, and the arms should be at heart level. Measurements were carried out in a calm state. Patients are expected not to

consume foods and beverages that can affect blood pressure, such as coffee, soda, foods high in cholesterol, alcohol, and so on” [13]. Patients diagnosed with hypertension can take further action, namely: [13; 14] a) Determine the extent of hypertension suffered; b) Isolating the cause, and c) Search for additional risk factors. Another critical aspect of the examination is the search for additional risk factors that should be addressed. After being diagnosed with hypertension, essential examinations such as cardiology, radiology, laboratory tests, electrocardiography (ECG), and X-rays will be carried out. The tests performed include a) a special X-ray (angiography) which includes the injection of a contrast agent (iodine), which is used to visualize the aortic, renal, and adrenal artery tissue; and b) Examine sensory and peripheral nerves with an electroencephalography (EEG) device, this tool resembles an electrocardiography (ECG).

The main goal of hypertension treatment is to achieve and maintain the target BP. If the target BP is not achieved within one month of treatment, the initial dose may be increased, or by adding a second drug from one of the classes (thiazide diuretic, CCB, ACEI, or ARB). The combination of two low-dose drugs is recommended for conditions where BP is >20/10 mmHg above target and not controlled by monotherapy. Physiologically the concept of a combination of 2 drugs (dual therapy) is quite logical because counter-activation mechanisms often limit the response to a single drug. For example, the loss of water and sodium by thiazides will be compensated by the Renin Angiotensin Aldosterone System (RAAS) so that it will limit the effectiveness of thiazides in lowering blood pressure. The recommended combination of 2 classes of low-dose drugs is RAAS inhibitor + diuretic and RAAS + CCB inhibitor. It is important to remember not to use a combination of ACEI and ARB in the same patient. If the BP target cannot be achieved using two antihypertensive drugs in the recommendations above or because of contraindications or more than three drugs are needed to achieve the BP target, antihypertensive drugs from other classes can be used. Referral to a hypertension specialist may be indicated for patients whose BP targets cannot be achieved using the above strategies or for complex patient management that requires further consultation. The JNC VIII guidelines recommend a combination of ACE inhibitors or ARBs with CCBs and thiazides [15]. There are five groups of first-line drugs commonly used for the initial treatment of hypertension, namely diuretics, beta-adrenergic receptor blockers (β -blockers), angiotensin-converting enzyme (ACE-inhibitors), angiotensin receptor blockers (ARBs), and calcium antagonists. In addition, three drugs are considered second-line: adrenergic nerve blockers, central α_2 agonists, and vasodilators.

“Hypertension that occurs over a long time will be dangerous, causing complications. These complications can attack various target organs, namely the brain, eyes, heart, peripheral arteries, and kidneys. As a result of the occurrence of hypertension complications, patients' quality of life is low, and the worst possibility is death in patients due to hypertension complications” [16]. “Hypertension can cause organ damage either directly or indirectly. Several studies have found that the cause of damage to these organs can be through an increase in blood pressure in organs or indirect effects, including the presence of autoantibodies against angiotensin II receptors, oxidative stress, down-regulation, and so on. Other studies have shown that a high-salt diet and sensitivity to salt play a significant role in the occurrence of target organ damage, such as blood vessel damage due to increased expression of transforming growth factor- β (TGF- β)” [13]. “Kidney failure can occur due to progressive damage due to high pressure on the renal capillaries, the glomerulus. In damage to the glomerulus, blood flowing to the functional units of the kidney and nephrons will be disrupted and can progress to hypoxia and death. In damage to the glomerular membrane, protein will be excreted through the urine to reduce the plasma colloid osmotic pressure, causing edema, which is often found in chronic hypertension” [15].

“Chronic renal failure is a pathophysiological process with various etiologies, resulting

in a progressive decline in kidney function and generally ending in kidney failure. Kidney failure is a clinical condition characterized by an irreversible decline in kidney function and requires renal replacement therapy in the form of dialysis or kidney transplantation” [17]. “In addition, chronic kidney failure can also be defined as the occurrence of kidney damage (renal damage) that occurs for more than three months, in the form of structural or functional abnormalities, with or without a decrease in the glomerular filtration rate (GFR), with manifestations of pathological abnormalities, kidney disorders such as abnormalities in blood or urine composition as well as abnormalities in imaging tests and a glomerular filtration rate (GFR) of less than 60 ml/min/1.73 m²” [13].

“Chronic kidney failure is a progressive and irreversible kidney function disorder in which the body's ability fails to maintain metabolism and fluid and electrolyte balance, causing uremia or retention of urea and other nitrogenous wastes in the blood” [15]. “Chronic kidney disease occurs when both kidneys cannot maintain a suitable internal environment for survival. Causes of chronic kidney failure include infectious diseases, inflammatory diseases, hypertensive vascular diseases, connective tissue disorders, congenital and hereditary disorders, metabolic diseases, toxic nephropathy, and obstructive nephropathy” [18; 19]. “Chronic kidney failure is also defined as a form of kidney function failure, especially in the nephron unit, which progresses slowly due to long-lasting, persistent causes that result in the accumulation of metabolites or uremic toxic residues” [13]. The classification of chronic kidney disease is based on two things: a) based on the degree (stage) of the disease; b) based on an etiologic diagnosis. Classification based on the degree of disease made based on the glomerular filtration rate (GFR), which is calculated using the Cockcroft-Gault formula as follows:

$$\text{LFG (ml/mnt/(1,73m}^2\text{))} = \frac{(140 - \text{age}) \times \text{Weight}}{72 \times \text{Plasma Creatinine (mg/dl)}}$$

Notes = for girls X with 0,85

Table 1. Classification of chronic renal failure disease based on glomerular filtration rate.

Degrees	Explanation	LFG (ml/minute/1,73m ²)
1	Kidney damage with average GFR /↑	≥90
2	Kidney damage with GFR drops slightly	60-90
3	Kidney damage with moderately low GFR	30-59
4	Kidney damage with severe GFR drop	15-29
5	Kidney failure	<14

“The most common causes of chronic kidney failure are divided into eight classifications: intestinal tubular infections, inflammatory diseases, hypertensive vascular diseases, connective tissue disorders, congenital and hereditary disorders, metabolic diseases, toxic nephropathy, and obstructive nephropathy. Chronic renal failure is caused by several factors, including impaired renal clearance, decreased glomerular filtration rate, fluid and sodium retention, acidosis, calcium and phosphate imbalance anemia, and uremic bone disease” [20]. The pathophysiology of chronic renal failure initially depends on the underlying disease. The normal kidney has about one million nephrons contributing to the GFR value. The occurrence of an injury or kidney damage can still be maintained by cleaning dissolved plasma substances by the kidneys with compensation in the form of hypertrophy mediated by molecules such as cytokines and growth factors [21]. Nephron hypertrophy will be followed by the process of glomerular hyperfiltration, which causes an increase in capillary pressure and glomerular blood flow. This adaptation process is brief and will be

followed by a maladaptation process in the form of sclerosis of the remaining nephrons, causing a progressive decline in nephron function, even though the underlying disease is no longer active. Increased glomerular capillary pressure will damage the capillaries and cause Focal Segmental Glomerulosclerosis (FSGS), which can progress to global glomerulosclerosis damage [21].

Hyperfiltration will activate the Renin-Angiotensin-Aldosterone System (RAAS), which is mediated by transforming growth factor (TGF- β). Increased RAAS plays a role in the occurrence of hypertension, and increased glomerular permeability plays a role in proteinuria. Several factors, such as hypertension, albuminuria, hyperlipidemia, hyperglycemia, hyperphosphatemia, and uncontrolled diabetes, can increase the progression of chronic renal failure. It causes glomerular and tubulointerstitial sclerosis and fibrosis [15]. Decreased kidney function is characterized by decreased GFR and increased serum urea and creatinine levels. A decrease in GFR by 60% or chronic renal failure stage 1-3 with normal or slightly elevated serum urea and creatinine levels usually does not cause clinical symptoms (asymptomatic). A decrease in GFR < 30 mL/min/1.73m² (stage 4-5) begins to cause complaints in the form of nocturia, weakness, nausea, lack of appetite, and weight loss to cause signs of uremia such as anemia, hypertension, phosphorus metabolism disorders, and calcium, pruritus and so on. At GFR <15%, kidney failure will occur and require renal replacement therapy [13]. Decreased GFR will cause anemia, hypertension, proteinuria, acidosis, hyperphosphatemia, hyponatremia, uremia, hyperkalemia, and other manifestations. Kidney damage will reduce erythropoietin production so that erythrocytes are not formed, which causes anemia with symptoms of paleness, fatigue, and reduced physical activity [16]. Proteinuria is a sign of kidney damage. Decreased kidney function will cause increased glomerular permeability, so protein molecules such as albumin will be free to pass through the filtration membrane. In addition, impaired filtration function will lead to the accumulation of urea in the blood (uremia) [18].

“Chronic kidney failure is the final stage of kidney failure, where the body fails to maintain metabolism, fluid, and electrolyte balance which causes high urea (uremia), namely retention of urea and other nitrogenous wastes in the blood” [22]. So, urea level is one of the results for assessing kidney function properly and one of the signs or symptoms to determine the stage of the disease course in patients with chronic kidney failure. Chronic kidney failure is divided into three stages: a) The mild stage is a decrease in kidney reserves. During this stage, serum creatinine and blood urea nitrogen (BUN) levels are normal, and the patient is asymptomatic; b) Moderate stage of renal insufficiency, more than 75% of the functioning tissue has been damaged. At this stage, BUN levels begin to rise above normal limits. The increase in the concentration of BUN is different because it depends on the protein content in the diet. At this stage, serum creatinine levels also rise above normal levels. Azotemia is usually mild unless the patient, for example, is under stress from infection, heart failure, or dehydration. Nocturia and polyuria appear at this stage of renal insufficiency, and c) Severe and terminal stages of chronic renal failure are called end-stage renal failure or uremia. End-stage renal failure is seen when about 90% of the nephron mass has been destroyed, or only about 200,000 nephrons are still intact. GFR values are only 10% of normal, and creatinine clearance maybe 5-10 ml per minute or less. In this situation, serum creatinine and BUN levels will increase suddenly in response to a slightly decreased GFR. Urine becomes isoosmotic with plasma at a constant specific gravity of 1.010. Patients usually become oliguria (urinary output of fewer than 500 ml/day) due to glomerular failure, even though the disease initially attacks the renal tubules. The complex of biochemical changes and symptoms called uremic syndrome affects every system in the body. In the final stages of kidney failure, the patient will surely die unless he gets treatment through a kidney transplant or dialysis [22].

Hypertension is one of the causes of Chronic Kidney Failure through a process that results in the progressive and irreversible loss of many functional nephrons. Chronic increase in pressure and strain in the arterioles and glomeruli is believed to cause sclerosis of the glomerular blood vessels or glomerulosclerosis. The decrease in the number of nephrons will cause adaptive processes, namely increased blood flow, GFR (Glomerulus Filtration Rate), and urine output in the surviving nephrons. This process involves nephron hypertrophy, vasodilation, and functional changes that decrease vascular resistance and tubular reabsorption in the surviving nephrons. Changes in kidney function over a long period can further damage existing nephrons. The sclerotic lesions that form more and more can cause glomerular obliteration, which results in a further decline in renal function, and creates a slowly growing vicious cycle that ends in Terminal Kidney Failure. The effect of hypertension severity on the kidneys depends on the high blood pressure and the duration of hypertension. The higher the blood pressure for a long time, the more severe the complications that can be seen [13; 15].

Based on the background described above, a problem can be formulated: how is the relationship and comparison between hypertension grades 1 and 2 to the incidence of chronic kidney failure? The study aimed to determine the relationship and comparison between hypertension grades 1 and 2 on the incidence of chronic kidney failure.

Methodology

This study uses an analytic observational research design to determine the causal relationship between two variables in an observational way, where the relationship can be in the form of differences, relationships, or influences. In this study, a cross-sectional approach was used. Cross-sectional is a study in which the variables are measured only once so that it does not require follow-up or follow-up. This research was conducted at UKI General Hospital, East Jakarta, and was carried out from August to October 2019. The population in this study were all inpatients suffering from hypertension grades 1 and 2 at UKI General Hospital, East Jakarta, from January to December 2018. Large Samples in cross-sectional studies can be calculated using the Lemeshow formula, where the population size (n):

$$n = \frac{Z_{\alpha}^2 PQ}{d^2}$$

$$n = \frac{(1,96 \times 1,96) \times 0,258 \times 0,742}{(0,1 \times 0,1)}$$

- n : Number of samples required
- Z α : Level of significance / normal standard derivative 1.96
- d : Acceptable error 10%
- P : Prevalence is estimated at 25.8%
- Q : 1-p = 1 - 0,258 = 0,742

Based on the calculation of the formula above, the number of samples in this study obtained was 73. Sampling using a simple random sampling technique, where each member or unit of the population has the same opportunity to be selected as a sample. The data collection method that will be carried out is secondary data obtained from medical records of inpatients at UKI General Hospital, East Jakarta, from January to December 2018. Data processing includes the stages of editing, coding, and scoring then the data is entered into the program. SPSS for WINDOWS and the calculated frequency are then shown in the table. Data analysis was carried out using univariate and bivariate analysis methods.

RESULTS AND DISCUSSION:

The results of grouping medical record data from UKI General Hospital can be grouped according to age, as shown in Table 2.

Table 2. Distribution by patient age

Age (years)	Frequency	Percent
<40	19	26,0
>40	54	74,0
Total	73	100,0

Based on Table 2, it can be seen that from 73 hypertensive patients, there were 19 patients (26.0%) with an age range of fewer than 40 years and 54 patients (74.0%) with an age range of more than 40 years. Increasing age is an essential factor in hypertension because, after the age of 40 years, the walls of arteries will experience thickening due to a buildup of collagen substances in the muscle layer, so that blood vessels will gradually narrow and become stiff, causing the elasticity of blood vessels to decrease in proportion to increasing age [6].

The results of grouping medical record data from UKI General Hospital can be grouped by gender according to Table 2.

Table 3. Distribution by gender

Gender	Frequency	Percent
Male	30	41,1
Female	43	58,9
Total	73	100,0

Based on Table 3, it can be seen that of 87 patients with hypertension, 36 patients (41.4%) were male, and 51 patients (58.6%) were female. The risk factors for hypertension based on sex are more common in women, the cause is not yet known, but one of the factors is because, at the time of menopause, it causes reduced production of the hormone estrogen [8].

The results of grouping medical record data from UKI General Hospital can be grouped according to BMI as Table 3.

Table 4. Distribution by body mass index

BMI	Frequency	Percent
<18,5	4	5,5
18,5-25,0	21	28,8
25,1-27,0	32	43,8
>27	16	21,9
Total	73	100,0

Based on Table 4, it can be seen that from 73 hypertensive patients, four patients (5.5%), normal (18.5-25.0), were found with a low BMI (<18.5). ,8%), moderately overweight (25.1-27.0), as many as 32 patients (43.8%), and severely overweight (>27), as many as 16 patients (21.9%). Research shows that the most BMI status is mild overweight because being overweight above normal requires more oxygen to meet metabolic needs, resulting in increased blood volume and pressure to meet metabolic needs caused by excess body weight. In addition, an increase in the amount of free fatty acids will narrow the blood vessels, so that blood pressure will increase, which also increases blood pressure and blood volume, an increase in peripheral resistance, an increase in catecholamines due to increased sympathetic nerve activity, an increase in insulin and aldosterone levels in plasma causing retention of Na in the blood. These things can increase blood volume causing hypertension [12].

The analysis of medical record data from UKI General Hospital can be related to the degree of hypertension with chronic kidney failure, as shown in Table 4.

Table 5. The relationship between the degree of hypertension and chronic renal failure

		Chronic kidney failure		Total	P Value
		Yes	No		
Blood Pressure	Hypertention Grade 1	3	2	5	0,002
	Hypertention Grade 2	65	3	68	
Total		68	5	73	

Based on Table 5 above, it was found that two patients with Hypertention Grade 1 did not experience chronic kidney failure, and three patients with Hypertention Grade 2 did not experience chronic kidney failure, or it can be said that 5 of the patients with hypertension did not experience chronic kidney failure. In addition, three patients with Hypertention Grade 1 had chronic kidney failure, 65 stage-2 hypertensive patients had chronic kidney failure, and 68 hypertensive patients with chronic kidney failure. Based on the Chi-Square test, there was a significant relationship between the degree of hypertension and the incidence of chronic kidney failure because of $p=0.002$ ($p<0.05$). Hypertension is one of the causes of Chronic Kidney Failure through a process that results in the progressive and irreversible loss of many functional nephrons. Chronic increase in pressure and strain in the arterioles and glomeruli is believed to cause sclerosis of the glomerular blood vessels or glomerulosclerosis. The decrease in the number of nephrons will cause adaptive processes, namely increased blood flow, GFR (Glomerulus Filtration Rate), and urine output in the surviving nephrons. This process involves nephron hypertrophy, vasodilation, and functional changes that decrease vascular resistance and tubular reabsorption in the surviving nephrons [13; 15].

The analysis of medical record data from UKI General Hospital can be compared with the degree of hypertension with chronic kidney failure, as shown in Table 5.

Table 6. Comparison of the degree of hypertension with chronic renal failure

		Chronic Kidney Failure		Total
		Yes	No	
Blood Pressure	Hypertention Grade 1 percentage (%)	3 60,0%	2 40,0%	5 100,0%
	Hypertention Grade 2 percentage (%)	65 95,6%	3 4,4%	68 100,0%
Total		68	5	73
Percentage (%)		93,2%	6,8%	100,0%

Table 6 shows that of the six patients with grade 1 hypertension, three (60.0%) suffered from hypertension with chronic kidney failure, and two (40.0%) suffered from hypertension but were not followed by chronic kidney failure. Meanwhile, of the 68 patients with grade 2 hypertension, 65 patients (95.6%) had hypertension with chronic renal failure, and three patients (4.4%) had hypertension but were not followed by chronic renal failure. The effect of hypertension severity on the kidneys depends on the high blood pressure and the duration of hypertension. The higher the blood pressure for a long time, the more severe the complications that can be caused due to decreased kidney function that occurs [15].

Conclusion

Based on the results and discussion, conclusions can be drawn: there is a significant relationship between hypertension grades 1 and 2 with the incidence of chronic kidney failure in hospitalized patients suffering from hypertension at UKI General Hospital for January-December 2018. The research carried out still has several weaknesses of various factors. The data comes from medical record data which is often incomplete, and many data need to be found. Limited time is also an obstacle, so checking and recording data is not in-depth. Further research can produce more valid research by considering factors related to subjects and objects that can affect research.

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