

Correlation between Degree of HT with Degree of Albuminuria in Non-dialysis Chronic Kidney Disease Patients at Hypertension Kidney Polyclinic Dr. Soetomo General Hospital

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Abstract

Background: Hypertension (HT) in chronic kidney disease (CKD) occurs through increased activity of the Renin Angiotensin Aldosterone System (RAAS) which causes increased renin and angiotensin II hypersecretion. According ISH 2020, degree of HT is divided into grade 1 and 2. Uncontrolled HT cause glomerular capillary damage so that albuminuria increases. According KDIGO 2013, degree of albuminuria is divided into mild, moderate, and severe. Albuminuria that lasts more than 3 months indicates CKD. Dialysis in CKD can cause intradialytic HT and increased albumin levels. Until now, research on correlation between degree of HT with degree of albuminuria is still limited. This study aims to determine correlation between degree of HT with degree of albuminuria in non-dialysis CKD patients at Hypertension Kidney Polyclinic Dr. Soetomo General Hospital. **Methods:** Analytical observational study with cross sectional design using medical records of non-dialysis CKD patients at Hypertension Kidney Polyclinic Dr. Soetomo General Hospital for period of May-October 2021, according to inclusion and exclusion criteria. Correlation test using spearman test. **Results:** There were 75 study subjects with male (61.3%), age 46-65 years old (42.7%), comorbidities other than HT were DM (32%), HT duration <5 years (58.7%), controlled HT (66.7%), taking 1 anti-HT (74.7%), ARB (26.7%), severe albuminuria (50.7%). This study showed that there was no correlation between degree of HT and degree of albuminuria in non-dialysis CKD patients (p-value=0.982, correlation coefficient=0.003). **Conclusion:** There is no correlation between degree of HT with degree of albuminuria in non-dialysis CKD patients at Hypertension Kidney Polyclinic Dr. Soetomo General Hospital.

Keywords: Chronic Kidney Disease; Hypertension; Degree of Hypertension; Albuminuria; Degree of Albuminuria

1. Introduction

Chronic kidney disease (CKD) is a global public health problem that is increasing in terms of prevalence, incidence of kidney failure, morbidity and mortality rates, poor prognosis and high medical costs (Kemenkes RI, 2017). CKD is an abnormality of kidney structure or function that lasts for more than 3 months and has health implications. CKD is diagnosed if there is a decrease in the estimated glomerular filtration rate (eGFR) <60 ml/minute/1.73 m² for 3 months or more with or without kidney damage (KDIGO, 2013). The prevalence of CKD globally is 13.4% and the highest is in male (Kemenkes RI, 2017). In 2017, CKD caused 1.2 million deaths and the world's 12th leading cause of death (Carney, 2020). Causes of CKD include DM (Diabetes Mellitus), HT, glomerulonephritis, chronic tubulointerstitial nephritis, plasma cell neoplasms, sickle cell nephropathy (SCN) (Vaidya and Narothona, 2020). Complications of CKD include cardiovascular

disease, HT, anemia, bone and mineral abnormalities, water and salt retention, electrolyte disturbances and metabolic acidosis (Bello et al., 2017).

HT is a condition of increasing systolic blood pressure 140 mmHg and diastolic blood pressure 90 mmHg after two measurements in separate visits (ISH, 2020). The prevalence of HT in 2015 globally ranged from 13% - 41% and was highest in male (Zeng et al., 2020). HT consists of primary/essential HT and secondary HT. In about 95% of primary HT, the cause is unknown, while secondary HT in about 5% occurs in HT patients and causes include renal artery stenosis, CKD, sleep apnea, and adrenal disease (Delacroix et al., 2014). HT grades include HT grade 1: 140-159 mmHg and/or 90-99 mmHg, HT grade 2: 160 mmHg and/or 100 mmHg. Complications of HT include myocardial infarction, coronary heart disease, congestive heart failure, stroke, CKD, hypertensive encephalopathy, hypertensive retinopathy (Nuraini, 2015). Pharmacological or anti-HT therapy includes Angiotensin converting enzyme (ACE) inhibitors, Angiotensin Receptor Blockers (ARBs), calcium channel blockers (CCBs), diuretics, beta blockers (ISH, 2020).

Albuminuria is the presence of albumin in the urine with levels above normal (KDIGO, 2013). Albuminuria that lasts more than 3 months indicates kidney damage (Ahmed et al., 2013). Causes of albuminuria DM, HT, systemic lupus erythematosus (SLE), vasculitis, amyloidosis, myeloma, congestive heart failure. SLE is an autoimmune disease that often causes complications in the kidney in the form of lupus nephritis which is characterized by albuminuria (Khoerrunisah et al., 2021; Haider and Ahsan, 2020). In DM there is an increase in transforming growth factor beta-1 (TGF- β 1) which will induce an increase in the extracellular matrix resulting in thickening of the glomerular basement membrane (GBM). Thickening and changes in kidney structure can cause albuminuria (Elfiani et al., 2019). Degree of albuminuria based on albumin creatinine ratio (ACR) includes light/normal albuminuria: <30 mg/g, moderate albuminuria: 30-300 mg/g, severe albuminuria: >300 mg/g (KDIGO, 2013).

HT in CKD is associated with increased activity of the Renin Angiotensin Aldosterone System (RAAS). There is decreased blood flow in the peritubular capillaries from glomerular sclerosis, resulting in hypersecretion of renin and an increase in angiotensin II. Angiotensin II can increase vascular resistance and blood pressure (Ku et al., 2019). An increased degree of HT will cause damage to the renal blood vessels or capillaries. This damage results in glomerular dysfunction, thereby reducing the ability of the kidneys to filter (Asmayawati et al., 2018; Sardi and Pusparini, 2019). Damage to the glomerular filtration barrier will change the permeability of the glomerular basement membrane, resulting in albuminuria. Albumin that penetrates the barrier will cause tubular dysfunction due to albumin overload (Haider and Ahsan, 2020). Systolic blood pressure has a greater effect on increasing levels of albuminuria (Jung et al., 2016). An increase in systolic blood pressure causes intraglomerular pressure to increase and this contributes to the release of transmembrane proteins resulting in albuminuria (Xie et al., 2018). Albuminuria is a marker of increased glomerular capillary pressure and a predictor of progressive loss of kidney function (Yan et al., 2012). HT can also cause CKD due to the intake of fat into blood vessel cells so that blood vessel walls thicken, narrow and kidney damage occurs (Giena et al., 2018).

Dialysis is the process of removing waste and extra water from the blood and it is a replacement therapy for kidney function in cases of kidney failure. Dialysis can only replace kidney function to a certain extent, namely by diffusion and ultrafiltration activity. Dialysis therapy is usually used in stage 5 CKD or end stage renal disease (ESRD) (Vadakedath and Kandi, 2017). Dialysis can cause intradialytic HT complications and cause increased albumin levels (Ferdianan et al., 2019; Arinta et al., 2014).

Based on data regarding the high prevalence of CKD and HT and continues to increase every year, this study aims to determine correlation between degree of HT with degree of albuminuria in non-dialysis CKD patients at Hypertension Kidney Polyclinic Dr. Soetomo General Hospital.

2. Methods

2.1. Data Collecting

An analytical observational study with a cross sectional design. The data used are secondary data of non-dialysis CKD patients at Hypertension Kidney Polyclinic Dr. Soetomo General Hospital in May–October 2021. The sampling technique was carried out by consecutive sampling. The minimum sample size is 41 ($\alpha = 0.05$ $\beta = 0.2$ $r = 0.428$).

$$n = \left[\frac{(Z_{\alpha} + Z_{\beta})}{0,5 \ln \left(\frac{1+r}{1-r} \right)} \right]^2 + 3$$

a. Inclusion criteria

1. Patients aged 18 years and over
2. CKD patients with comorbid HT
3. Never had dialysis

b. Exclusion criteria

1. Incomplete patient data

2.2. Data Analysis

Presentation of data in tabular form with explanations that clarify. The correlation between degree of HT with degree of albuminuria was analyzed using a bivariate analysis of the spearman correlation test, p-value < 0.05 was considered significant and calculated using SPSS. This research was approved by the Health Research Ethics Committee of Dr. Soetomo General Hospital.

3. Result

Data retrieval with medical records of non-dialysis CKD patients at Hypertension Kidney Polyclinic Dr. Soetomo General Hospital, May – October 2021. Based on the data, 75 samples were obtained that met the inclusion criteria.

Table 1. Distribution of CKD Patients by Gender

| Gender | n (amount) | % (percentage) | Total |
|--------|------------|----------------|-------|
| Male | 46 | 61,3 | 75 |
| Female | 29 | 38,7 | |

Table 1 shows that most CKD patients are experienced by male (61.3%), female (38,7%).

Table 2. Distribution of CKD patients by age

| Age | n | % | Minimum | Maximum | Total | Mean |
|-----------------|----|------|---------|--------------|-------|-------------------|
| 17-25 years old | 13 | 17,3 | 18 | 81 years old | 75 | 50,0933 years old |
| 26-45 years old | 12 | 16,0 | | | | |
| 46-65 years old | 32 | 42,7 | | | | |
| >65 years old | 18 | 24,0 | | | | |

Table 2 shows the most CKD patients at the age of 46-65 years old (42.7%), >65 years old (24,0%), 17-25 years old (17,3%), 26-45 years old (16,0%). The youngest age is 18 years old and the oldest age is 81 years old. The mean age is 50.0933 years old.

Table 3. Distribution of CKD Patients by Comorbidities

| Comorbidities | n | % | Total |
|-------------------------|----|------|-------|
| HT | 29 | 38,7 | 75 |
| HT + DM | 24 | 32,0 | |
| HT + SLE | 7 | 9,3 | |
| HT + DM + SLE | 2 | 2,7 | |
| HT + other disease | 11 | 14,7 | |
| HT + DM + other disease | 2 | 2,7 | |

Table 3 shows the most comorbidities CKD patients were HT (38.7%), HT + DM (32.0%), HT + DM (32,0%), HT + other disease (14,7%), HT + SLE (9,3%), HT + DM + SLE (2,7%), HT + DM + other disease (2,7%).

Table 4. Distribution of CKD patients by HT duration

| HT Duration | n | % | Total |
|-------------|----|------|-------|
| <5 years | 44 | 58,7 | 75 |
| ≥5 years | 31 | 41,3 | |

Table 4 shows that the longest HT duration in CKD patients was <5 years (58.7%), ≥5 years (41,3%).

Table 5. Distribution of CKD Patients by Degree of HT

| | Controlled HT | HT Grade 1 | HT Grade 2 | Total |
|---|---------------|------------|------------|-------|
| n | 50 | 20 | 5 | 75 |
| % | 66,7 | 26,7 | 6,7 | |

Controlled HT= <140/<90 mmHg, HT grade 1= 140-159/90-99 mmHg, HT grade 2= 160/≥100 mmHg

Table 5 shows degree of HT in CKD patients at most is controlled HT (66.7%), HT grade 1 (26,7%), HT grade 2 (6,7%).

Table 6. Distribution of CKD patients based on the Number of Anti-HT Drugs Consumed

| Number of Anti-HT | n | % | Total |
|-------------------|----|------|-------|
| 1 drug | 56 | 74,7 | 75 |
| 2 drugs | 17 | 22,7 | |
| 3 drugs | 2 | 2,7 | |
| > 3 drugs | 0 | 0 | |

Table 6 shows the number of anti-HT drugs consumed by CKD patients at most was 1 drug (74.7%), 2 drugs (22.7%), 3 drugs (2.7%), >3 drugs (0%).

Table 7. Distribution of CKD Patients by Type of Anti-HT Drugs Consumed

| Type of Anti-HT Drugs | n | % | Total |
|-----------------------------------|----|------|-------|
| ACE inhibitors | 17 | 22,7 | 75 |
| ARBs | 20 | 26,7 | |
| CCBs | 16 | 21,3 | |
| Diuretics | 0 | 0 | 9,3 |
| Beta blockers | 3 | 4,0 | |
| ACE inhibitors + CCBs | 7 | 9,3 | |
| ARBs + CCBs | 6 | 8,0 | 0 |
| ACE inhibitors + Diuretics | 0 | 0 | |
| ARBs + Diuretics | 0 | 0 | |
| ACE inhibitors + Beta blockers | 1 | 1,3 | 4,0 |
| ARBs + Beta blockers | 3 | 4,0 | |
| CCBs + Diuretics | 0 | 0 | |
| CCBs + Beta blockers | 1 | 1,3 | 0 |
| ACE inhibitors + CCBs + Diuretics | 0 | 0 | |
| ARBs + CCBs + Diuretics | 0 | 0 | |
| ARBs + CCBs + Beta blockers | 1 | 1,3 | |

Table 7 shows that the most type of anti-HT drugs consumed by CKD patients were ARBs (26.7%), ACE inhibitors (22.7%), CCBs (21.3%), ACE inhibitors + CCBs (9.3%), ARBs + CCBs (8.0%), beta blockers and ARBs + beta blockers (4.0%), ACE inhibitors + beta blockers, CCBs + beta blockers, and ARBs + CCBs + beta blockers (1.3%).

Table 8. Distribution of CKD patients based on degree of albuminuria experienced

| | Normal/mild Albuminuria | Moderate Albuminuria | Severe Albuminuria | Total |
|---|----------------------------|-------------------------|-----------------------|-------|
| n | 7 | 30 | 38 | 75 |
| % | 9,3 | 40,0 | 50,7 | |

Table 8 shows degree of albuminuria experienced by CKD patients is the most severe albuminuria (50.7%), moderate albuminuria (40.0%), normal/mild albuminuria (9.3%).

Table 9. Correlation Test between Degree of HT with Degree of Albuminuria

| Variable | Correlation Coefficient | p-value | n |
|---------------------------------------|----------------------------|---------|----|
| Degree of HT Degree of albuminuria | 0,003 | 0,982 | 75 |

*Spearman correlation test

Table 9 shows the results of the spearman correlation test between degree of HT with degree of albuminuria has a p-value = 0.982 (p-value >0.05), meaning that there is no correlation between the two variables. The correlation coefficient of 0.003 indicates a unidirectional relationship between the two variables and the relationship is very low.

4. Discussion

Analytical observational study with a cross sectional design on the correlation between degree of HT and degree of albuminuria of non-dialysis CKD patients at Hypertension Kidney Polyclinic, Dr. Soetomo General Hospital in May–October 2021. Based on the data of this study, it was shown that male (61.3%) experienced more CKD. This is in line with previous studies which stated that more male experience CKD due to poor lifestyle and quality of life, and have risk factors for kidney disease progression in the form of proteinuria, poor blood pressure control, smoking, alcohol consumption (Ipo et al., 2016; Baroleh et al., 2019; Chang et al., 2016). Male have a faster development of proteinuria and have a higher risk of developing HT (Fachrunnisa et al., 2014).

HT often occurs in men because they are more likely to have a job, consume alcohol, and are less likely to receive and take HT drugs (Aristotle, 2018; Choi et al., 2017). Male often have HT in their late thirties, while female are after menopause. This is because in female the hormone estrogen will decrease at menopause. The hormone estrogen plays a role in increasing levels of High Density Lipoprotein (HDL) which protects against cardiovascular disease before menopause (Aristoteles, 2018).

In this study, subjects who experienced CKD were mostly 46-65 years old (42.7%), followed by age >65 years old (24.0%), with the most common comorbidity being HT. This is in accordance with previous research which stated that HT often occurs at the age of 45 years old because with increasing age there will be changes in the arteries to become stiff which causes the capacity and blood recoil to decrease so that blood pressure increases (Nuraeni, 2019; Cahyo et al., 2021; Tamamilang et al., 2018). At the age of 55 years old, the artery walls will thicken due to the accumulation of collagen in the muscle layer so that the blood vessels become narrow and stiff. Blood is forced through narrow blood vessels so that blood pressure increases and sclerosis of the kidney blood vessels can occur which results in vasoconstriction and obstruction. Glomerulus and tubules will be damaged so that the nephrons are damaged (Cahyo et al., 2021; Tamamilang et al., 2018).

The most common comorbidities experienced by CKD patients in this study were HT (38.7%), followed by HT + DM (32.0%). This is in line with previous studies which showed that HT was the highest comorbidities in CKD, followed by DM (Baroleh et al., 2019; Dasari et al., 2014). High blood glucose can damage the blood vessels of the kidney, thus affecting kidney function. In a state of high blood pressure and high blood glucose, the kidney have difficulty carrying out their functions (Baroleh et al., 2019). In this study, only a few subjects with comorbidities SLE were HT + SLE (9.3%), HT + DM + SLE (2.7%). This is in accordance with previous studies that comorbidities CKD are HT (57.7%), DM (25.0%), UTI (10.0%), urinary tract stones (8.0%), SLE (2.3%).) (Hervinda et al., 2014; Tjekyan, 2014). SLE can cause complications in the kidney in the form of lupus nephritis with symptoms of albuminuria (Khoerrunisah et al., 2021).

The longest HT duration in CKD patients in this study was <5 years (58.7%). This is in accordance with previous studies which showed that HT <5 years had the highest incidence of CKD (Medistra, 2017; Hidayati et al., 2008). The variation in the HT duration until the onset of CKD is influenced by lack of exercise intensity, high salt intake, non-adherence to HT therapy, genetic factors, and the time of diagnosis of HT. Many HT patients are asymptomatic so that the diagnosis of HT is made when HT is grade 2 or very high and may have HT for a long time (Medistra, 2017).

The highest degree of HT in this study was controlled HT (66.7%) <140 mmHg/<90 mmHg. This is in line with the research of Tamburian et al., 2016 which showed that controlled HT was more than uncontrolled HT, and there were more patients without complications. The study of Dramawan, 2017 also shows that HT is controlled more and the highest age group is 46-55 years old, meaning that the older you are, the wiser you will be and there will be more information about the disease. The number of controlled HT is more because it has high compliance in undergoing HT treatment such as adherence to anti-HT consumption, healthy lifestyle, reducing salt and coffee intake (Tamburian et al., 2016; Dramawan, 2017).

The number of anti-HT consumed by CKD patients in this study was at most 1 drug or monotherapy (74.7%). This is in accordance with previous studies which showed that the use of anti-HT monotherapy was more widely used in prehypertension, controlled HT, and grade 1 HT (Tandililing et al., 2017; Fadhilla and Permana, 2020; Tamburian et al., 2016; Liu et al., 2016; Marinier et al., 2019). Anti-HT monotherapy can still treat controlled HT and HT grade 1, while HT grade 2 requires combination therapy (Tandililing et al., 2017; Marinier et al., 2019). The use of monotherapy aims to help achieve treatment compliance, milder side effects, and the majority of controlled HT is resolved with monotherapy (Damayanti, 2020). According to ISH, 2020, the first step in HT therapy is a combination of 2 low-dose drugs, consider monotherapy in low-risk HT grade 1 or very old age.

The type of anti-HT consumed by CKD patients in this study was mostly ARB (26.7%), then ACE inhibitors (22.7%). This is consistent with previous research that ARBs are the first line of therapy for HT and CKD (Dewi et al., 2018; Burnier et al., 2019). The study of Tandililing et al., 2017 stated that ACE inhibitors are often used as monotherapy and are effective for mild, moderate, and severe HT. ARBs have renoprotective properties, overcome proteinuria, beneficial effects on heart disorders (Dewi et al., 2018). ACE inhibitors can reduce proteinuria and intraglomerular pressure, inhibiting the development of CKD (Muchtar et al., 2015). The study of Liu et al., 2019 stated that the majority of HT in CKD were given ARBs monotherapy or ACE inhibitors because they had kidney and cardiovascular protective effects. According to ISH, 2020, the first line of HT therapy is an ACE inhibitors or ARBs because it can control blood pressure and reduce albuminuria.

The highest degree of albuminuria experienced by CKD patients in this study was heavy albuminuria (50.7%) >300 mg/g. This is in accordance with the study of Aipassa et al., 2021 which divided albuminuria +1: 20 mg/dL, +2: 50 mg/dL, and +3: 100 mg/dL indicating that albuminuria +2 and +3 had the highest number. Aipassa research showed that the majority of HT grade 2, HT was treated as monotherapy, less compliant with anti-HT drugs consumption, >70 years old, at that age there was a decrease in organ function, elasticity of blood vessels, and cells were unable to regenerate. The study of Sardi and Pusparini, 2019 divided negative albuminuria: <150 mg/day, albuminuria +1 to +3: >200 mg/day showed that negative and positive albuminuria had the same number of subjects. In this study, Sardi and Pusparini took subjects aged 40-70 years, the most positive albuminuria was at 50-59 years old, and the highest number of positive albuminuria was in HT grade 2.

In this study, based on the spearman correlation test between degree of HT with degree of albuminuria, it has a p-value = 0.982 (p-value > 0.05), correlation coefficient = 0.003, meaning that there is no correlation between the two variables. This is in accordance with the study of Herrera et al., 2010 in Cuba with 2762 subject, stated that the highest prevalence of patients with positive albuminuria was in the prehypertension group. Herrera research took data from CKD subjects who were diligent in active screening, controlled, healthy lifestyle, only a few DM comorbidities, and subjects experiencing CKD who later experienced HT as a complication of CKD. However, in contrast to the study of Poudel et al., 2012 in Nepal with 106 subject and the study of Sardi and Pusparini, 2019 in Jakarta with 40 subject, stated that there is a correlation between the degree of HT and levels of albuminuria, positive albuminuria mostly occurred in HT grade 2.

5. Conclusion

Based on the results of research on non-dialysis CKD patients at the Kidney Hypertension Polyclinic at Dr Soetomo Surabaya Hospital, it can be concluded that there is no correlation between the degree of HT and the degree of albuminuria. The degree of HT that is high or increasing does not affect the increase in the level or degree of albuminuria. Thus, a high degree of HT has no effect on the severity of CKD.

6. Recommendations

Future studies are expected to add other variables such as blood sugar levels, eliminate confounding variables, add primary data to determine the patient's lifestyle, and albuminuria levels using continuous data, especially if the levels are >300 mg/g.

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