

Factors Affecting Urem Levels In Chronic Kidney Failure Patients

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Abstract

The prevalence of chronic kidney failure in Indonesia increases with age. The condition of kidney failure characterized by very high plasma urea levels is called uremia. Kidney failure is caused by age, gender, and a history of hypertension, diabetes, and metabolic disorders that result in decreased kidney function. Supplements such as psych stimulants (caffeine and amphetamines) can affect kidney function.

The purpose of this study was to determine the characteristics of research respondents based on gender, age and history of indications in patients with chronic kidney failure. The design of this study is an analytical observational study with a research sample of 160 using univariate, bivariate (chi-square) analysis and regression tests.

Patients with chronic renal failure by gender were 100 patients (62.5%) male and 60 female (37.5%). The range of age groups in patients with chronic renal failure are 46-45 years old, 46 patients (28.75%), 56-65 years old, 45 patients (28.13%) and age 76-85 3 patients (1, 87%). Indications for the cause of chronic kidney failure patients were hypertension = 58 patients (36.3%), Diabetes Mellitus (DM) = 52 patients (32.5%), Gout = 16 patients (10%), Lipid Profile = 13 patients (8.1%), Supplements = 9 patients (5.6%), Medicines 5 = patients (3.1%) and Descendants = 7 patients (4.4%).

Background

Chronic Kidney Disease (CKD) is a kidney disorder characterized by structural and functional abnormalities that last for more than three months. The development of kidney damage is characterized by an increase in one of the important chemicals in the blood, namely urea. Urea is the end product of protein and amino acid metabolism produced by the liver and distributed through the intracellular and extracellular fluids into the blood to be filtered by the glomerulus and partially reabsorbed in conditions where urine is disturbed. The condition of kidney failure which is characterized by very high plasma urea levels is known as uremia. This situation can be dangerous and requires hemodialysis or a kidney transplant (Verdiansyah, 2016).

According to the United Stages Renal Data System (Saran et al., 2020) from 2016 to 2017, increased from 13.8% to 14.5%. The results of basic health research data in 2018 the prevalence of chronic kidney failure in Indonesia is 0.38%, increasing with increasing age 35-44 years (0.331%),

45-54 years (0.564%), 55-64 years (0.721%) (Risksdas, 2018). Meanwhile, the number of new patients undergoing hemodialysis in Indonesia doubled in 2018 compared to 2017 (Pernefri, 2018).

Kidney failure can be caused by age, gender and a history of hypertension, diabetes and diseases with metabolic disorders that result in decreased kidney function (Pranandari & Supadmi, 2015). People with diabetes are also more at risk of developing chronic kidney disease than patients who do not have diabetes. Kidney failure can also be caused by an increase in serum uric acid levels. Increased uric acid levels in the serum will form uric acid crystals in the kidneys. They can settle in the renal medullary interstitial, tubules or collecting system, which will eventually cause kidney failure (Nur, Anggunan, & Wulandari, 2019).

Supplements that have compositions such as psych stimulants (caffeine and amphetamines) can be proven to affect kidney function. Amphetamines can narrow the arteries to the kidneys so that blood going to the kidneys decreases and lacks food and oxygen intake. Drugs such as analgesics can cause kidney damage or nephropathy (Pranandari & Supadmi, 2015). CKD patients with these causes receive medical attention. Therefore, it is necessary to research to determine the factors that influence the level of urea in patients with chronic kidney failure.

Research methods

The design of this study was an analytic observational study by tracing the history of patients with chronic renal failure undergoing hemodialysis. The study sample was patients diagnosed with experienced chronic kidney failure known through medical records. The patient routinely performs hemodialysis. The age of the research respondents starts from 15 to 75 years and is willing to be a respondent study. The number of research respondents was 160 samples. The analysis was carried out using SPSS with univariate test then followed by bivariate analysis (chi-square) and continued with logistic regression test to see the most influential variable.

Results and Discussion

1. Characteristics of Respondents by Gender

Table 1.1. Kidney Failure Research Respondents by Gender

Gender	Frequency (f)	Percentage (%)
Man	100	62.5%
Woman	60	37.5%
Total	160	100%

Characteristics of research respondents based on gender showed that the male sex was 100 patients (62.5%) and the female was 60 patients (37.5%) with a total of 160 patients (100%). Thus, the male sex men constitute the majority of the research respondents than the female gender. The results of this study are in line with the results of research (Aisara, Azmi, & Yanni, 2018) with the results of the majority of research being men (56.7%) who have Chronic Kidney Disease (CKD), the results of Adhiatma's research, (Adhiatma, Wahab, Fajar, & Widyantara, 2014) the results of the Chronic Kidney Disease research are also the majority of men (62.1%) and the results of the Pinzon study, (Pinzon, Padmanaba, & Esdras Ardi Pramudita, 2016) it was found that the male gender was the majority of respondents in the CKD research, which was 65.2%. Male sex is more affected by CKD than the female caused by several things, namely men who have a terrible lifestyle or quality of life that can affect their health such as smoking, consuming coffee, alcohol and taking supplements that can trigger disease. Systemic disease can cause a decrease in kidney function, so that it has an impact on the quality of life (Ipo, Aryani, & Suri, 2016).

The large proportion of sex who suffers from Chronic Kidney Failure who undergo hemodialysis therapy is due to an increase in creatinine which is influenced by muscle mass and muscle breakdown. The male sex tends to have more muscle mass so that the blood creatinine level is higher in men than women (Kurniawati & Asikin, 2018). Creatinine results from the breakdown of muscle phosphate and is produced by the body constantly depending on muscle mass. Creatinine can be related to muscle mass and reflects changes in creatinine and kidney function. The diagnosis of kidney failure can be made when the serum creatinine value increases above the normal value. In renal failure and uremia conditions, creatinine excretion by the glomerulus and renal tubules decreases (Verdiansyah, 2016).

The female sex has a lower risk of developing kidney disease because women have more estrogen than men. The hormone estrogen can affect calcium levels in the body by inhibiting the formation of certain cytokines that can inhibit osteoclasts so they don't absorb too much bone and balance calcium levels. Calcium has a protective effect by preventing the absorption of oxalate which can form kidney stones as one of the causes of chronic kidney failure (Wahyuni, Kartika, & Asrul, 2019).

2. Characteristics of Respondents Based on Age

Table 2.1. Kidney Failure Research Respondents Based on Age Range

Age (years)	Frequency (f)	Percentage (%)
16 – 25	6	3.75%

26 – 35	16	10%
36 – 45	25	15.63%
46 – 55	46	28.75%
56 – 65	45	28.13%
66 – 75	19	11.87%
76 - 85	3	1.87%
Total	160	100%

The characteristics of research respondents according to age group were grouped into age groups: 16-25 years, 26-35 years, 36-45 years, 46-55 years, 56-65 years, 66-75 years and 76-85 years. Research data based on age group shows that the majority of research respondents are from the age group of 46 - 45 years, namely 46 patients (28.75%) which are then followed by the age group of 56 - 65 years, namely 45 patients (28.13%) and respondents the least research was shown in the age group of 76-85 years, namely three patients (1.87%).

Decreasing kidney function is a normal process with every human age. Increasing age shows a progressive decrease in Glomerular Filtration Rate (GFR) and Renal Blood Flow (RBF) with a decrease occurring around 8 ml/min/1.73m² every decade since the age of 40 years (Aisara et al., 2018). The number of nephrons formed after birth cannot be reformed so that if any are damaged, the number of them will decrease in function. After 40, the number of nephrons will generally reduce by 10% every ten years (Kurniawati & Asikin, 2018). A person after 40 years will experience a progressive decline in the glomerular filtration rate until the age of 70 years by approximately 50% of normal function and tubular function including the ability to reabsorb and concentrate is also reduced so that it will trigger kidney failure (Dewi, 2015; Anita & Novitasari, 2011). After the age of 30 years, the kidneys will atrophy (the size of the kidneys shrinks from normal size) and the thickness of the renal cortex will decrease by about 20% every decade. Other changes that will occur with age are thickening of the glomerular basement membrane, expansion of the mesangium-glomerulus and matrix protein deposits extracellular causing glomerulosclerosis or damage to the glomerulus (Arifa et al., 2017).

The results of the research conducted by Delima (Delima & Tjitra, 2017) obtained the results of the study of CKD patients in the age range of 61 - 85 years, namely 118 cases of CKD patients. Older people have a higher risk of death due to a lower glomerular filtration rate (GFR). The GFR value for the elderly with CKD is an average of 15 mL/minute per 1.73 m², while the GFR value for adults with CKD is an average of 45 mL/minute per 1.73 m². Ageing will cause a decrease in the value of GFR and renal blood flow (RBF) progressively. A reduction in GFR will cause a

decrease in the average plasma flow and coefficient in the glomerular capillaries. Decreased resistance to arterioles afferents is associated with increased hydraulic pressure in the glomerular capillaries and change hemodynamics. This occurs due to changes in kidney structure with ageing such as loss of renal mass, hyalinization on arteriole afferent, increased glomerular sclerotic and tubulointerstitial fibrosis (Anita, 2015).

3. Characteristics of Respondents Based on History of Indications

Table 3.1 Kidney Failure Research Respondents Based on History of Indications

Indication	Frequency (f)	Percentage (%)
Hypertension	58	36.3%
Diabetes Mellitus (DM)	52	32.5%
Gout	16	10%
Lipid Profile	13	8.1%
Supplement	9	5.6%
Drug	5	3.1%
Descendants	7	4.4%
Total	160	100%

Table 3.2 Chi-square

Chi-square	Sig
Hypertension	0.026
Diabetes Mellitus (DM)	0.023
Gout	0.026
Lipid Profile	0.038
Supplement	0.011
Drug	0.026
Descendants	0.819

Table 3.3 Variable in the equation

Variable in equation	Sig
Hypertension	0.629
Diabetes Mellitus (DM)	0.563

Gout	0.285
Lipid Profile	0.279
Supplement	0.217
Drug	0.120

Characteristics of research respondents, according to indications showed the majority were hypertension as many as 58 patients (36.3%) then followed by indications of Diabetes Mellitus (DM) as many as 52 patients (32.5%), uric acid as many as 16 patients (10%), Lipid Profile as many as 13 patients (8.1%), Supplements as much as 9 patients (5.6%), Medication as many as 5 patients (3.1%) and Descendants as many as 7 patients (4.4%). The study results reported that the sig chi-square value of hypertension, diabetes mellitus, uric acid, lipid profile, supplements, and drugs was sig < 0.05. It could be interpreted that the history of indications affected urea levels in patients with kidney failure. Meanwhile, heredity with sig 0.819 > 0.05 means that heredity does not affect urea levels in patients with kidney failure.

Variable in the equation is used to assess which variables affect the dependent variable. The factors that affect urea levels can be seen in Table 3.3. It can be seen that hypertension (sig 0.629), diabetes mellitus (sig (0.563), uric acid (0.285), lipid profile (sig 0.279), supplements (sig 0.217), drugs (sig 0.120), sig value > 0.05, so it means that there is no historical factor indicating the most effect on urea levels.

Hyperglycemia is often accompanied by the onset of metabolic syndrome, one of which is hypertension. High sugar levels will stick to the walls of blood vessels. The following process is oxidation, where blood sugar reacts with proteins from blood vessel walls which will cause AGEs (Advanced Glycosylated Endproducts), which are substances formed from excess sugar and protein that bind to each other. The situation that arises will damage the inner walls of blood vessels and attract saturated fat or cholesterol to stick to the walls of blood vessels, resulting in an inflammatory reaction. Leukocytes, platelet cells, and other materials join together to form a plaque that causes the walls of blood vessels to become rigid, stiff, and eventually blockages arise, resulting in changes in blood pressure or hypertension (Winta, Setiyorini, & Wulandari, 2018).

Based on the results of research by Nur (Nur et al., 2019), it was found that the average uric acid level in chronic kidney failure patients who underwent hemodialysis was 7.49 mg/dl with an SD of 1.34 mg/dl. Decreased kidney function in CKD patients will cause various complications, one of which is hyperuricemia or an imbalance between the productions of uric acid secretion. This imbalance will cause uric acid hyper saturation, namely the solubility of uric acid in serum that exceeds the threshold to stimulate the accumulation of urate in the form of its salt (monosodium

urate) in various tissues. The condition of hyperuricemia is caused by two main factors: the high production of uric acid levels in the body due to excessive uric acid synthesis and decreased excretion of uric acid in the distal tubule of the kidney.

Patients with chronic kidney disease have impaired lipid and lipoprotein profile (dyslipidemia) due to impaired maturation and changes in HDL composition and impaired metabolism of lipoprotein-rich triglycerides, which causes their composition to increase in the blood. Dyslipidemia is a lipid metabolism disorder characterized by an increase or decrease in the lipid fraction in plasma. The main lipid fraction abnormalities were an increase in total cholesterol, LDL cholesterol and triglycerides and a decrease in HDL cholesterol. LDL cholesterol is the lipoprotein that contains the most cholesterol. The LDL cholesterol will be carried to the liver and steroidogenic tissues, one of which is the adrenal glands. In patients with CKD, Small dense LDL is highly elevated and is rich in immature and easily oxidized triglycerides and can cause blockages in the blood vessels due to the fats that stick to the blood vessels. High levels of LDL cholesterol will trigger the accumulation of cholesterol in cells which causes atherosclerosis (hardening of the arteries) and expansion of plaque on the walls of blood vessels. If atherosclerosis occurs, the blood supply to the kidneys will decrease and cause disturbances in GFR and reduced kidney function. Dyslipidemia can accelerate the process of kidney disease through several mechanisms; the first is the reabsorption of fatty acids, phospholipids and cholesterol contained in proteins filtered by tubular epithelial cells, the second is the accumulation of lipoproteins in the mesangium. High levels of LDL cholesterol will trigger the accumulation of cholesterol in cells which causes atherosclerosis (hardening of the walls of the arteries) and accumulation of plaque on the walls of blood vessels. If atherosclerosis occurs, the blood supply to the kidneys will be reduced and can cause disturbances in GFR and decreased kidney function. Dyslipidemia can accelerate the process of kidney disease through several mechanisms; the first is the reabsorption of fatty acids, phospholipids and cholesterol contained in proteins filtered by tubular epithelial cells, the second is the accumulation of lipoproteins in the mesangium. High levels of LDL cholesterol will trigger the accumulation of cholesterol in cells which causes atherosclerosis (hardening of the walls of the arteries) and accumulation of plaque on the walls of blood vessels. If atherosclerosis occurs, the blood supply to the kidneys will decrease and cause disturbances in GFR and decreased kidney function. Dyslipidemia has the potential to accelerate the process of kidney disease through several mechanisms. The first is the reabsorption of fatty acids, phospholipids and cholesterol contained in proteins filtered by tubular epithelial cells. Second is the accumulation of lipoproteins in the mesangium glomerulus (Ahmad, Bandu, & Artha, 2018; Sagita, Setiawan, & Hardian, 2018; Senge, Moeis, & Sugeng, 2017). The research results conducted by Bhagaskara (Bhagaskara, Liana,

& Santoso, 2015) found that the results of research respondents in CKD patients with high LDL cholesterol results as much as 82.8% and low HDL cholesterol results as much as 89.2%.

Risk factors that influence the incidence of chronic kidney failure are the use of analgesic drugs, NSAIDs (Non-steroidal Anti-Inflammatory Drugs) and herbal medicines. Analgesic drugs are paracetamol and antalgic, while NSAIDs are mefenamic acid, diclofenac sodium, diclofenac potassium, piroxicam, tenoxicam, meloxicam, ibuprofen, ketoprofen. Epidemiological evidence suggests an association between excessive use of analgesics and non-steroidal anti-inflammatory drugs and the incidence of kidney damage. The clinical use of analgesic drugs > 10 years of service gives a 1.4 times greater chance of experiencing chronic kidney failure, indicating that the duration of analgesic use > 10 years increases the risk of kidney failure. Patients who use more than 500 tablets of analgesic drugs have a 23 times greater risk of chronic kidney failure. The use of acetaminophen more than 5,000 tablets for five years can increase the incidence of end-stage renal failure. Non-steroidal anti-inflammatory drugs inhibit prostaglandin synthesis, which causes vasoconstriction in the renal medulla. Clinically, patients who use NSAIDs more than 5000 tablets have a 12 times greater risk of chronic kidney failure. A combination of analgesics and NSAIDs can increase the risk of chronic kidney failure 5.1 times. Consumption of herbal medicines does not yet have standardization regarding safety and the correct dose and cannot be ascertained. Supervision of herbal medication also tends to be loose, but in the investigation, many found hazardous chemical substances in herbal medicines that can harm the body's organs, especially the kidneys. These are types of dangerous metals or medicinal chemicals that aggravate and reduce kidney function. These chemicals and drugs cause kidney damage by forming crystals to form tubular injury.

Supplements are synthetic vitamins resulting from chemical products that are not free from carcinogenic substances, and if consuming excessive supplement drinks will aggravate the work of the kidneys. Supplemental drinks contain harmful substances such as taurine. Taurine is a detoxifying amino acid that has a glycine-like effect in neutralizing all kinds of toxins. Consumption of taurine in supplements that exceeds the limit of 40-400 mg / day can make the kidneys work harder. If consumed for an extended time, these substances can narrow the arteries to the kidneys to reduce the blood going to the kidneys (Muharni, Dewi, & Yolanda, 2019). The results of research conducted by Ariyanto (Ariyanto et al., 2018) The use of energy drink supplements > 4 times per week can cause the risk of chronic kidney disease stage V by 2.9 times compared with people who consume <4 times per week.

People with diabetes are also more at risk of developing chronic kidney disease than patients who do not have diabetes. High blood sugar levels cause the kidneys to have to work harder in the

blood filtering process, which as a result, can leak in the kidneys. The results of research conducted by Santosa, Trijayanto and & Endiyono (2017) showed that a person would get diabetes more quickly if he has a maternal lineage and will tend to get diabetes more easily if he has a history of diabetes from his father and mother at the same time, which is due to the decrease in genes while in the womb is more significant in the mother compared to the father.). These genes will be responsible for insulin sensitivity and increased glucose uptake along with an increase with age. Estrogen levels in women will decrease, which in turn will reduce the activation of ER gene expression so that insulin sensitivity and glucose uptake will also decrease (Santosa, Trijayanto, & Endiyanto, 2017).

Conclusion

From the male gender, as many as 100 patients (62.5%) and female as many as 60 patients (37.5%) are patients with chronic kidney failure. The range of age groups in patients with chronic renal failure is 46-45 years old, 46 patients (28.75%), 56-65 years old, 45 patients (28.13%) and age 76-85, 3 patients (1, 87%).

Indications for the cause of chronic kidney failure patients were Hypertension 58 patients (36.3%), Diabetes Mellitus (DM) 52 patients (32.5%), Gout 16 patients (10%), Lipid Profile 13 patients (8.1%), Supplements 9 patients (5.6%), Medicines 5 patients (3.1%) and Descendants 7 patients (4.4%). Indications of the cause of patients with kidney failure do not affect urea levels.

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