

## Treatment Evaluation of Hemodialysis Patients in General Public Hospital in Indonesia

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### ABSTRACT

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Patients with Chronic Kidney Disease (CKD) in the final stages are indicated to obtain renal replacement therapy, namely dialysis. Dialysis is meant both peritoneal dialysis and hemodialysis. The purpose of this study is to analyze treatment in CKD patients undergoing outpatient hemodialysis at RS X. This type of research is an observational study with a cross sectional (retrospective) approach using medical record documents and patient treatment data. Analysis of the treatment uses descriptive statistic. Research data is quantitative data. The sample of the study is 74 patients. The results indicate the accuracy of the indication (100%), the accuracy of the patient (76.65%), the accuracy of the drug (79.55%), and the accuracy of the dose (96.57%).

#### Keywords:

Evaluation of Treatment, Hemodialysis, Chronic Kidney Disease

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## 1. INTRODUCTION

The main text Chronic Kidney Disease (CKD) is a global health issue indicated by the increasing number of prevalence and incidence of kidney failure, appalling prognosis and high expense. The prevalence of CKD is increasing as number of veteran increase as well as diabetes disease and hypertension cases that increase. Around 1 per 10 of global population has suffered from CGK at certain stadium/level.[11]

According to Global Burden of Disease (2010), CKD was ranked equal to 27 with respect to lethal causes in 1990 and enhanced to 18 in rank in 2010. In Indonesia, treatment on kidney disease contributes to the second highest expense after heart disease (BPJS).[11]

Chronic Kidney Disease (CKD) is a pathophysiological process with various causes that results in a progressive decline in kidney function and kidney failure. Currently, CKD cases are increasing rapidly, especially in developing countries and become a major health problem in the world because it is a risk factor for cardiovascular disease. [16] Kidney failure can be caused by several factors, namely hypertension, uric acid levels, levels creatinine, diabetes, and many others. [7]

A patient diagnosed with final stadium of chronic kidney disease is indicated to receive renal replacement therapy, namely dialysis which are either peritoneal or hemodialysis. [22]

Based on the 8th Annual Report of Indonesian Renal Registry (IRR), number of both active and newly-indicated hemodialysis patients keeps increasing from 2007 to 2015. There were 4,977 new patients and 1,885 active patients in 2017 while in 2015, number of 21,050 new patients and 30,554 active patients of hemodialysis were observed. Chronic kidney disease or terminal/ESRD patients were outnumbered (89%). [18] The end stage renal disease (ESRD) which is characterized by irreversible kidney damage is a chronic exhausting disease that suffers about 14000 Iranian patients. ESRD could have a significant impact on patient's quality of life, both mental and physical health status. [3]

PGK is the progressive abnormality of either kidney's structure or function for more than 3 months which might lead to terminal kidney failure. Other factors causing PGK are Albuminuria, presence of urine sediment, abnormality of electrolyte caused by tubular disease, kidney transplantation trail, and decrease of GFR value less than 60 ml/minute /1.73 square meter. Patient with GFR value less than 15 ml/minute//1.73 square meter is required to undergo hemodialysis initiation and kidney transplantation. [10]

The substance extracted especially through kidney excretion may cause toxicity to kidney failure patient. [27] All applied therapies to CKD patients require concern both from pharmacokinetics and pharmacodynamics. A patient with kidney failure may undergo certain condition of which the reduction of clearance of hydrophilic and metabolite substances occur. As a result, accumulation of potential toxic occurs which may lead to the reduction of glomerulus filtration acceleration and worsen kidney condition.

## 2. METHOD

### Equipment

Patient data sheet, RS X formularies, KDOQI guide and the renal handbook (RDH).

### Materials

Medical and treatment record of Hospital X.

### Method

This research is quantitative descriptive research.

### Data Analysis

This research applies univariate analysis with SPSS program

Table 1. Characteristic of Sociodemography of Hemodialysis Patients in Hospital X

Characteristic of Sociodemography	Frequency (n=74)	Proportion (%)
<b>Age</b>		
Range	22-70	-
Median	53	-
Mean (SD)	50.36	-
18-25 Years	4	5.41
26-35 Years	6	8.11
36-45 Years	11	14.86
46-55 Years	26	35.14
56-65 Years	23	31.08
> 65	4	5.41
<b>Gender</b>		
Male	44	59.46
Female	30	40.54
<b>Level of Education</b>		
Uneducated	1	1.35
Elementary School	8	10.81
SMP	14	18.92
SMA	44	59.46
Perguruan tinggi	7	9.46
<b>Status Pekerjaan</b>		
Bekerja	51	68.92
Tidak bekerja	23	31.08
<b>Penyakit Penyerta/Komplikasi</b>		
Anemia	72	97.30
Hipertensi	68	91.89
Diabetes Mellitus	11	14.86
Kardiovaskular	24	32.43
Tidak ada	2	2.70

Table 2. Treatment Profile of Hemodialysis Patients at X Hospital

Kelas Terapi	Golongan Obat	Nama Generik	Nama Dagang	Jumlah Pasien (n = 74)	Proporsi (%)	
<b>Antihipertensi</b>	Calcium Canal Blocker (CCB)	Amlodipin		72	97.30	
		Nifedipin	Adalat oros	48	64.86	
		Diltiazem	Herbesser CD	1	1.35	
	β- Blocker	Bisoprolol		Concor	20	27.03
				V-Bloc	11	14.86
		Propanolol		Blorece	4	5.41
					1	1.35
	Angiotensin II Reseptor Blocker (ARB)	Candesartan			17	22.97
		Valsartan			36	48.65
		Telmisartan	Micardis		2	2.70
	Antagonis α2-pusat	Clonidine			7	9.46
		Loop Diuretik	Furosemide		67	90.54

	ACE Inhibitors	Captopril		5	6.76
		Ramipril		1	1.35
<b>Gagal Jantung</b>	Glikosida jantung	Digoxin		2	2.70
<b>Antidiabetik</b>	Antidiabetik Parenteral	Analog Insulin	Levemir	8	10.81
	Sulfonilurea		Novorapid	1	1.35
		Glimepiride		1	1.35
		Glikazid	Glucodex	2	2.70
<b>Antiangina</b>	Nitrat	Isosorbide	Farsorbid	21	28.38
		Dinitrat			
		Gliseril Trinitrat	Nitrokaf	13	17.57
			Nitral	3	4.05
<b>Antianemia</b>	Anemia defisiensi asam folat	Asam folat	Star folat	74	100.00
	Anemia defisiensi Fe	Iron Sucrose	Rinofe	47	63.51
	Anemia defisiensi Erithropoetin	Erithropoetin Alpha	Epotrex	73	98.65

### 3. RESULTS AND DISCUSSION

#### 3.1 Socio-demography Characteristic of Patient

##### 3.1.1. Age

As seen on table 1, numbers of patients who obtain hemodialysis treatment (based on age) range from 46 to 55 years old are 26 patients (35.14%), and those with age range from 56 to 65 years old are 23 patients (31.08%). The data is equivalent to IRR data (2015) in which most CKD patients are 45 to 54 years old (29.46%) followed by 55 to 64 years old (27.31%).

The degradation of kidney function that occurs to people over 40 years old is part of human degenerative process. Each kidney possesses around 1 million nephrons at early stage of childbirth. However, kidney size and number of nephrons are diminished once someone reaches 40 yo. As a result, people over 40 yo tend to have chronic kidney issue. The case has changed nowadays as people below 40 yo also suffer from kidney disease due to lifestyle in consuming uncontrolled fat food and carbonated drink. Age affects the way one perceives upcoming things in the future, issues solving and decision making [21]. Besides, age is correlated with prognosis of a disease, complication of the disease as well as compliance to treatment therapy.

##### 3.1.2. Gender

As observed on table 1, number of male patients with CKD to receive hemodialysis is more (40 patients or equal to 59.46%) compared to female patients (30 patients or equal to 40.54%). The data is equivalent to IRR data (2015) in which chronic kidney disease mostly to male (54.70%).

According to a research conducted by Dana (2015) at Dr. Mintoharjo hospital in 2014, sample characteristics indicated male patients were more compared to female patients (56.82% and 43.18% respectively). Walker, R and Edward, C once stated that number of CKD male patients is 1.5 times bigger than the female [21] Reports of pregnant patients with chronic kidney disease on hemodialysis (ERCHD) with successful births are becoming more frequent. [8]

Urinary system problems may occur to either male or female. Both are susceptible to the disease. It may occur due to progressive reduction of kidney function and changing in lifestyle [4] Regarding the lifestyle, high risk is on males who tend to suffer from chronic kidney disease. Smoking and alcohol drinking may cause tension on kidney of which it forces the kidney to work harder than usual. Nicotine substance from the tobacco will be passed into the body with other hazardous chemical substances such as carbon monoxide. Alcoholic substance and nicotine combined will impact to changing of heart beats, respiration and blood pressure. Carcinogenic substance, alcohol in this case that is excreted out of the body throughout the urinary will affect DNA to change and destroy kidney cells. This alteration may affect kidney function and trigger to chronic kidney disease. [21] Probability that the group of patients with chronic renal failure with the female gender has a probability of living higher than the group of patients gender to male.

##### 3.1.3 Concomitant Diseases

CKD patients (hemodialysis treatment recipients) possess several concomitant diseases. In X Hospital, number of CKD patient who suffer from Anemia, hypertension, cardiovascular and diabetes mellitus are 72, 68, 24 and 11 patients respectively.

Greater number of patients with Anemia as concomitant disease is caused by the lack of Erythropoietin production or lack of Iron (fe), followed by Hypertension which also may cause kidney failure or vice versa, kidney failure may lead to hypertension. Long time hypertension may affect changing in arterial within the whole body causing fibrosis and hialinasi on blood vessel wall. On kidney, arteriosclerosis is due to long time hypertension may lead to nephrosclerosis. This disruption contributes to Iskemia which is caused by narrow of lumen on the intra-renal

blood vessel. Due to artery and arterial narrowing process, glomerulus and atrophy tubulus are harmed causing all nephrons in damage and chronic kidney disease occur as a result. Therefore, blood pressure of CKD patients shall be in control with aim to prevent and decline kidney damage of which CKD patients' blood pressure shall be less than 140/90 mmHg [4] In kidney disease populations undergoing hemodialysis, anemia may occur due to insufficient erythropoietin production by kidneys. [19]

Another concomitant disease is cardiovascular including Heart Failure and Congestive Heart Failure (CHF), which are the main lethal causes at chronic kidney disease stage. It occurs due to the reduction of intravascular or cardiac output known as cardio-renal syndrome. The cardio-renal syndrome is reduction in kidney function due to heart failure, and vice versa renocardiac syndrome is reduction in heart function due to kidney failure.

Diabetes mellitus is ranked 4 in concomitant disease to chronic kidney disease. Uncontrolled diabetes may lead to nephropathy diabetes which is one of the causes to kidney failure. High blood sugar level will force kidney to operate harder in blood filtration process and so, leakage of kidney glomerulus may occur. At the beginning, patient will face albumin leakage excreted through urine and developed to a worst condition in which filtration function of kidney is disrupted.

### 3.2 Treatment Profile

As seen on table 2, the most consumed medicine is folic acid (74 patients with 100% in percentage). Consumption of epotrex by 73 patients (98.65%), Amlodipin by 72 patients (97.30%), Furosemide by 67 patients (90.54%) and the least consumed medicines are Diltiazem, propranolol, ramipril and glimepiride by 1 patient respectively(1.35%).

Profile of medicine consumption is all groups of medicines consumed by ckd patients (hemodialysis patients) with concomitant disease, in which each cure objective of each group of medicines. Both routine precautions and education of the unit staff will be necessary to reduce the viral transmission in the hemodialysis unit. <sup>(Lusida, 2012)</sup> The dosage of erythropoietin varies depending only on changes in the patient's weight. [17]

#### 3.2.1 Cardiovascular System Medicines

Cardiovascular diseases play a serious health issue to elder patients. One of them is called hypertension which is one of the main causes of chronic kidney disease. Type of cardiovascular medicine delivered to the CKD patients are classified as anti-hypertension therapy, antidiuretic and lipid/cholesterol reduction medicine. The cardiovascular medicines are the most consumed. Intradialytic hypertension is a major complication during hemodialysis and implicates increased cardiovascular complications and death. [13]

With respect to type of medicines consumption by CKD patients at X hospital in 2017, the most consumed medicine was anti-hypertension (292 consumption) covered 54.38%. It was due to hypertension as concomitant disease and the consumption varied from one or more type of more.

The pattern of the recipe of anti-hypertension medicines (at Hospital X in 2017) included Calcium Canal Blocker (CCB) of 121 times (22.54%), group of Angiotensin II Receptor Blocker (ARBs) as much as 55 times (10.24%),  $\beta$ -Blocker of 36 times (6.7%), Loop Diuretic of 67 times (12.48%), and group of Antagonis  $\alpha$ 2-center and ACE Inhibitors of 7 times (1.30%) and 6 times (1.12%) respectively.

During chronic kidney stage, anti-hypertension medicines could accumulate in blood and worsen the function of the kidney. Therefore, special awareness shall be presented in order to choose the safest anti-hypertension medicines.

Talking on treatment pattern, the most distributed medicine is Amlodipine of 72 times (97.30%) which is classified as CCB group. This group plays an important role in prevention of calcium distribution into the blood which will lead to vasodilatation that reduces peripheral pressure. It also assists in relaxation of arterial muscles, but not to vascular vein and so, does not lead to pre-load. [5]

According to Hypertension therapy guidance of CKD patients (hemodialysis recipient), once blood pressure target level is achieved, the patient is recommended for an additional treatment using  $\beta$ -blocker. Further evaluation on hypertension root causes shall be conducted if the treatment does not work. Combination of two medicines (ACEI group or ARB with CCB) is fully recommended for patients with type II hypertension (without concomitant diseases). If the expected blood pressure is not achieved,  $\beta$ -blocker shall be considered to be consumed as well.

In either kidney diabetes related disease or non-related, ACEI and ARC have effects on kidney protection (reno-protective). One of both medicines shall be used during first stage of therapy in order to control blood pressure and to maintain kidney function. [5] Combination of  $\beta$ -Blocker consumption such as bisoprolol (for patient of kidney failure) will assist in controlling blood pressure level as well as to prevent from infarction, coronary heart disease, oxygen reduction, and to stabilize myocardium. [5]  $\beta$ -Blocker medicine is effective to 50–70% of light to medium hypertension patients. [15] Mostly, adrenoreceptor beta-1 is proven to be effective in reducing blood pressure. Bisoprolol is the  $\beta_1$  inhibitor which is produced in liver for a long period of time and as for that reason, this medicine may only be consumed once daily. Combination of CCB group works as inhibitor for calcium influx on vascular blood muscles and myocardium, and can also be consumed to cure angina. For diuretic combination therapy, furosemide works by preventing the contraceptors  $\text{Na}^+$ ,  $\text{K}^+$  dan  $\text{Cl}^-$  and applied to cure edema.

### Endocrine System Medicines

There were 12 recipients who took anti-diabetes medicines including Levemir, Novorapid, Glimepiride and Glikazid. Novorapid (insulin aspartate) is used for therapy of both type 1 and 2 diabetes mellitus while levemir (insulin detemir) is used for type 2 diabetes.

This research applied Glimepiride and Glikazid for oral anti-diabetes therapy. Both medicines are classified as oral hypoglycemic (second derivatives of sulfonylurea group) which work by stimulating insulin secretion in the pancreas, and so only effective for diabetes patients whose pancreas  $\beta$  cells are still properly functioning. The consumption of the second derivative sulfonylurea is more compared to its first generation which has side effects that rarely occur and lack of interaction with other medicines. [6]

### 3.2.2 Vitamin and Mineral

CKD patients (hemodialysis recipients) often experience Anemia. Anemia is caused by erythropoietin and Iron (fe) deficiency. [9] One of kidney functions is to produce erythropoietin hormone which stimulates spinal cord to produce erythrocytes. Chronic kidney disease contributes to reduction of erythropoietin production and thus resulting in Anemia. Therefore, erythropoietin hormone is also crucial to prevent Anemia.

There were 74 patients who consumed vitamin and mineral medicines (100%), as anemia is the concomitant disease. Vitamin and mineral are crucial for metabolism. Vitamin is an organic compound required by the body (in small amount) to maintain health and also work sometimes as co-factor during enzyme metabolism, whereas mineral is an-organic compound which is a critical part of the enzyme. Mineral assist in regulating lots of biological function and required by the body with respect to growth and maintenance of tissues including bones. Anti-anemia group of medicine commonly used is folic acid. As observed, 80-90% of CKD patients have anemia. It is caused by several factors, yet the insufficiency of erythropoietin production plays the key role. [23] In general, anemia becomes worst during the reduction of kidney function. As kidney function got decreased (stadium leveling up and GFR decreases), the higher prevalence of anemia may occur. [9] Hemodialysis patients are in high risk of experiencing folic acid deficiency as folic acid is being extracted out of plasma, while the HD procedure runs. [13]

Calporosis ( $\text{CaCO}_3$ ) is usually applied as buffer in handling metabolic acidosis that mostly occurs on CKD patients due to difficulty of acid secretion resulted from metabolism inside the body. [25] Calcium carbonate is also used to handle hiperfosfatemia condition. The condition occurs as phosphate is released from the cells due to metabolic acidosis and uremic. Calcium carbonate works by tightening phosphate throughout the digestive track resulting in reduction of phosphate absorption. [12] In chronic kidney disease, calcium level inside the blood becomes high, and in order to resolve the unbalanced of the mineral, calcium, vitamin and electrolyte are given. [12]

## 4. CONCLUSION

To conclude, the most consumed medicines are folic acid and Amlodipine. Treatment evaluation covers 100% exact indication, 79.55% exact medicines, 96.57% exact dosage and 76.65% of exact patient. Current applied treatment has complied with the regulated standard namely Formularium of Hospital X and KDOQI Guidance. The medicines that are not qualified as per Formularium of Hospital X are Acarbose and Digoksin, whereas the medicines that do not comply with KDOQI Guidance (with respect to implementation guidance) are Clonidine, Digoksin and Furosemide.

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