OPEN ACCESS Potravinarstvo Slovak Journal of Food Sciences

potravinárstvo® Slovak Journal of Food Sciences

Potravinarstvo Slovak Journal of Food Sciences
vol. 13, 2019, no. 1, p. 891-897
https://doi.org/10.5219/1193
Received: 18 September 2019. Accepted: 30 October 2019.
Available online: 28 November 2019 at www.potravinarstvo.com

ISSN 1337-0960 (online)

MACRONUTRIENTS, MICRONUTRIENTS INTAKE AND INFLAMMATION IN HEMODIALYSIS PATIENTS

Siti Fatonah, Moh Sulchan, Muchlis Achsan Udji Sofro

ABSTRACT

Inflammation in hemodialysis patients occurs since before undergoing hemodialysis. Inflammation is associated with an increase in oxidative stress. Hemodialysis patients are at risk for macronutrients and micronutrients deficiencies which can influence the increase in oxidative stress and inflammation. The purpose of this study was to evaluate the intake of micronutrients and inflammatory status in hemodialysis patients. This study was a cross-sectional study with 76 hemodialysis patients (40 male and 36 female) who attended in two hemodialysis centers of Kendal, Indonesia. After obtaining the written consent, then patients were interviewed food intake consisting of macronutrient and micronutrient intake. Macronutrient and micronutrient intake are obtained by the semi quantitative food frequency method and classified as a deficit (<100% adequacy level) and normal/ more (≥100% adequacy level), according to specific recommendations for individuals undergoing dialysis. Serum albumin was examined using the Brom Cresol Purple (BCP) method with a low category (<3.5 $mg.dL^{-1}$) and normal (3.5 – 4.5 $mg.dL^{-1}$). The hs-CRP serum was examined using the ELISA method and categorized as low (<1 $mg.L^{-1}$), moderate (1 – 3 $mg.L^{-1}$) and high (> 3 $mg.L^{-1}$). A descriptive analysis was performed. The results of this study showed that 88.2% deficit energy intake, 84.2% deficit protein intake, 85.5% deficit of vitamin A intake, 85.5% deficit of vitamin C intake, 100% deficit of vitamin E intake, 98, 7% deficit zinc intake , 92.1% deficit copper intake. 63.2% subjects are low level of serum albumin and 61.8% subjects is high level of hs-CRP serum. Macronutrient and micronutrient intake in most hemodialysis patients shows deficit. The serum albumin of most hemodialysis patients shows low level. Serum hs-CRP most hemodialysis patients show high level.

Keywords: macronutrients; micronutrients; albumin; hs-CRP; inflammation

INTRODUCTION

End stage renal disease patients have high mortality rates which are not only caused by traditional risk factors of cardiovascular disease, but other factors such as inflammation and protein energy malnutrition (PEM) **(Kalantar and Kopple., 2001)**. End stage renal disease is characterized by a decrease in irreversible kidney function with a glomerular filtration rate below 15/mL/min/1.73 m^2 and must undergo renal replacement therapy **(Hill et al., 2016)**. A continuous decrease in glomerular filtration rate will worsen the condition of chronic kidney disease (CKD) patients and will increase their mortality **(Panichi et al., 2008)**. Hemodialysis patients will experience inflammation that occurs since before undergoing hemodialysis **(Kalantar et al., 2004)**. **Yao et al. (2009)** stated that oxidative stress will affect the occurrence of inflammation in hemodialysis patients. Oxidative stress in CKD patients occurs early in the disease and increases gradually with the development of kidney disorders **(Yao et al., 2009)**. Hemodialysis patients will experience an increase in proinflammatory cytokines such as elevated serum hs-CRP **(Verhave et al., 2005; Panichi et al., 2008)**. The hs-CRP serum is part of the process of atherosclerosis and has a direct effect on endothelial cells, monocyte-macrophages and smooth muscle cells and supports the occurrence of atherogenenesis **(Stevinkel et al., 2005)**. Hemodialysis patients will also experience increased levels of urea which results in the occurrence of uremia. Urea levels in the blood will cause feelings of nausea and vomiting **(Kalantar et al., 2004)**. This will cause a decrease in appetite that can reduce nutrient intake. This in turn will cause nutrient intake to also decrease. Hemodialysis patients will also have poor eating behaviour such as high sugar, fat, low cereal, fruit and vegetables **(Lou et al., 2007)**. Hemodialysis patients had lower calorie, protein, and fiber intakes than recommendations **(Bossola et al., 2013)**. Decreased macronutrient intake will be in line with a decrease in micronutrient intake. Low micronutrient intake will also cause antioxidant intake to decrease. Antioxidants play a role in reducing oxidative stress **(Sahni et al., 2012)**. High oxidative stress in hemodialysis patients indicates inflammation and will increase cardiovascular complications, mortality and increase the need for antioxidants **(Miura et al., 2002; Locatelli et al., 2002)**. Antioxidants in food ingredients are found in various active ingredients including vitamins C, E, pro-vitamin A, zinc, cooper, selenium, α-tocopherol, organosulfur, flavonoids, thymoquinone, statins, niacin, phycocyanin, etc. **(Sahni et al., 2012)**. Vegetables and fruits contain a lot of antioxidants, but hemodialysis patients sometimes limit vegetables and fruits because of high potassium. Whereas a diet high in fruits and vegetables is not only good for improving lipid profiles, but also reduces oxidative stress and inflammation **(Bossola et al., 2013)**. Hemodialysis patients will overhydrate and protein loss through urine and dialysate which can result in a decrease in albumin **(Gama et al., 2012)**. Low albumin is associated with increased lipid peroxidation and supports oxidative stress in hemodialysis patients **(Castro et al., 2014)**. **Kaysen et al. (2002)** states that low serum albumin in dialysis patients is strongly associated with inflammation. The aim of this study is to evaluate the intake of macronutrients, micronutrients and inflammatory status in hemodialysis patients.

Scientific hypothesis

We investigate several hypotheses in our study:

a. The intake of macronutrients (energy and protein of hemodialysis patients shows inadequacy

b. The intake of micronutrients (vit A, C, E, zinc, copper) of hemodialysis patients shows inadequacy

c. Albumin levels of hemodialysis patients show low levels

d. The levels of hs-CRP hemodialysis patients show high levels

MATERIAL AND METHODOLOGY

This research is a descriptive study with a cross sectional approach conducted from March to April 2019 in two hemodialysis centers in the city of Indonesia state. The study population was all patients undergoing outpatient care in two hemodialysis centers. Research subjects were all patients with chronic kidney disease undergoing hemodialysis at two hemodialysis centers were taken by consecutive sampling and obtained as many as 76 people. Inclusion criteria are hemodialysis patients who are aware and can communicate well and are willing to participate in research by signing an informed consent. Exclusion criteria were chronic kidney disease patients who have never undergone hemodialysis and patients who had sepsis.

The size of the sample with a confidence level (α) of 95%, a proportion of 13.4%, a degree of error of 10% so the minimum number of samples is 45 subjects. Samples who participated in this study were 76 people. This research has obtained ethics from the Ethics Research Commission of the Faculty of Medicine, Diponegoro University Semarang number 55/EC/FK UNDIP/II/2019.

The variables studied included macronutrient intake (which consists of energy, protein), micronutrient intake (which consists of vitamins A, C, E zinc, copper), serum albumin and hs-CRP serum. The research tool used was a semi quantitative food frequency questionnaire. Before dialysis, the patients' height and weight were measured with a health scale, respectively. All measurements are carried out according to standard instructions when the subject is not wearing heavy clothes and no shoes. The weight and heights were recorded with accuracy of 100 g and 1 cm, respectively. Ideal body weight is used to calculate nutritional requirements according to recommendations for patients undergoing hemodialysis. This study was conducted by researchers assisted by an enumerator who is a nutritionist. Blood sampling is performed by nurses on duty in the hemodialysis unit before the research subjects conduct the hemodialysis process. Serum albumin concentration was measured by using the Brom Cresol Purple (BCP) method. Hs-CRP concentrations were measured with enzyme-linked immunosorbent assay (ELISA) kits (DRG International Inc, USA). Serum albumin is divided into two criteria: low (<3.5 $mg.dL^{-1}$) and normal (3.5 – 4.5 $mg.dL^{-1}$). Inflammatory status of serum hs-CRP is divided into three namely low risk (<1 $mg.L^{-1}$), moderate (1 – 3 $mg.L^{-1}$), high (>3 $mg.L^{-1}$) **(Myers et al., 2004)**. The level of sufficient energy, protein, vitamins A, C, zinc and copper was obtained by interviewing food intake using a semiquantitative food frequency questionnaire. The data obtained is processed by performing a recapitulation of the frequency of the use of types of food and converted into grams and then processed using the nutrisurvey program. The adequacy levels of energy, protein, vitamins A, C, E, zinc and cooper are obtained by calculating the percentage of total intake divided by dietary requirement individual (DRI). Adequacy levels are categorized into deficits (<100% DRI) and normal / more (≥100% DRI).

Statistic analysis

Data were analysed using the version 16.0 of Stastitical Package for the Social Sciences (SPSS). Data distribution and normality were seen using the Kolmogorov Smirnov test ($p \geq 0.05$). A. descriptive analysis of each variable was carried out in which the categorical variables were expressed as frequencies and percentages and the continuous variables as mean and standard deviation or median (min – max). Result were expressed as mean ±*SD* (for normally distributed data) otherwise it expressed as median(min – max).

RESULTS AND DISCUSSION

This research was carried out on 76 subjects consisting of 52.6% men and 47.4% women. Hemodialysis patients are mostly male because the average glomerular filtration rate (GFR) and serum creatinine values in men are higher than those in female **(Hecking et al., 2014)**. The mean age of hemodialysis patient was 49.12 years, with the highest percentage (34.2%) at age 45 – 54 years followed by age 55 – 64 years (26.3%). Hemodialysis patients after the age of 40 the kidney will progressively decrease the glomerular filtration rate **(Kalantar and Kopple, 2001)**.

Age more fourthy years there will be a decrease of ±10% the number of functional nephrons every ten years after patients aged 40 years due to nephrosclerosis and glomerulosclerosis. As a result of nephrosclerosis and glomerulosclerosis will cause elderly patients experiencing chronic kidney failure and must be treated hemodialysis. Hemodialysis patients have a high prevalence of comorbidities **(Sarnak et al., 2003)**.

In this study the most common comorbid is hypertension (53.9%) and followed by cardiovascular disease (31.6%).

Table 1 Characteristics of hemodialysis patients.

Characteristics (n = 76)	n (%)	Mean ±*SD*
Gender		
Male	40 (52.6)	
Female	36 (47.4)	
Age (years)		
25-34	6 (7.9)	
35-44	20 (26.3)	49.12 ±10.03*
45-54	26 (34.2)	
55-64	20 (26.3)	
65-74	4(5.3)	
Comorbid		
Hypertension	41 (53.9)	
Diabetes	6 (7.9)	
Cardiovascular disease	24 (31.6)	
Serebrovascular disease	3 (3.9)	
Gastrointestinal disease	1 (1.3)	
Tuberculosis	1 (1.3)	
The number of comorbid		
1 comorbid	32 (42.1)	
>1 comorbid	34 (44.7)	
>2 comorbid	9 (11.8)	
>3 comorbid	1 (1.3)	
Frequency hemodialysis		
One per week	9 (11.8)	
Two per week	67 (88.2)	
Time of hemodialysis (months)		
< 6 months	26 (34.2)	10 (1 – 105)**
6 – 12 months	16 (21.1)	
>12 months	34 (44.7)	

Note: * Mean ±Standar deviation; ** Median (minimum–maximum).

Table 2. Kolmogorof smirnov test

Variable	*p*
Adequacy level of Energy	0.048
Adequacy level of Protein	0.175*
Adequacy level of Vitamin A	0.000
Adequacy level of Vitamin C	0.000
Adequacy level of Vitamin E	0.000
Adequacy level of Zink	0.200*
Adequacy level of Copper	0.001

Note : **p*-value ≥0.05 = normally distributed data.

The kidney damage especially the cortex will stimulate the production of the hormone renin which will encourage increased blood pressure resulting in hypertension **(Sarnak et al., 2003)**.

This study shows that 44.7% of study subjects had two comorbidities. **Steven et al. (2010)** states that the more comorbid hemodialysis patients have will affect physical function. This study shows that patients who have more than one comorbid have difficulty breathing problems, edema, lack of balance, difficulty walking, restlessness, using a wheelchair.

Hemodialysis is a kidney replacement therapy which is done 2 – 3 times a week with a length of 4 – 5 hours, which aims to remove the remnants of protein metabolism and correct disruption of fluid and electrolyte balance **(Daugirdas et al., 2015)**. In this study 88.2% did hemodialysis twice a week and 12.8% once a week. Despite hemodialysis, not all uremic toxins can be excreted. This can lead to various kinds of comorbidities.

Hemodialysis on schedule will reduce the accumulation of toxins. In this study the frequency of hemodialysis subjects was determined by the doctor and in accordance with kidney damage experienced. So, it will reduce nausea and increase appetite. At the time of the study there were one subject who did not keep the hemodialysis schedule due to being busy, so the subjects felt very nauseous, edema and have difficulty breathing problems.

Subjects of this study had undergone hemodialysis with different lengths of hemodialysis. The highest percentage is 12 months (44.7%) with a time span of 1 – 105 months. **Kalantar and Kopple (2001)** says that the provision of dialysis therapy in terminal kidney failure patients aims to prolong life and control uremia symptoms and maintain quality of life. Hemodialysis patients have experienced chronic inflammation since not undergoing hemodialysis **(Panichi et al., 2008)**. Hemodialysis patients will experience an increase in free radical production and lipid peroxidation which in turn will increase inflammation **(Bianchi, 2009)**. Dietary macronutrients and micronutrients may be especially important in protecting against human diseases associated with free radical damage to cellular DNA, lipids, and proteins **(Barakat et al., 2017)**.

Kolmogorov Smirnov test shows that the adequacy level of protein and zinc is normally distributed because of *p*-values ≥0.05. While the adequacy level of energy, vitamins A, C, E and zinc shows data not normally distributed as indicated by p <0.05. Table 2 compares macronutrients and micronutrient intake with recommendations for hemodialysis patients. As It was seen that the intake of macronutrients and micronutrients in most hemodialysis patients is deficit. This research shows that 88.2% of the subjects experienced a deficit of energy and 84.2% deficit of protein. Macronutrient and micronutrient intake is very important to prevent the occurrence of protein energy malnutrition (PEM) that often occurs in hemodialysis patients **(Kalantar and Kopple, 2001)**. PEM is the state of decreased body pools of protein with or without fat depletion or a state of diminished functional capacity, caused at least partly by inadequate nutrient intake relative to nutrient demand and/or which is improved by nutritional repletion.

Indicators of PEM in maintenance hemodialysis patients include decreased dietary protein and energy intake. In this study there were 57.9% of subjects showed nausea so that food intake decreased, and nutritional adequacy was not fulfilled. The subject said that nausea made it difficult to accept food. The patient limits the protein to prevent increased in creatinine urea serum. PEM are associated with chronic inflammation **(Kalantar and Kopple, 2001)**. PEM in hemodialysis patients not only shows deficit of energy and protein. But it also deficit micronutrients that the body needs **(Kalantar and Kopple, 2001)**. This research shows there is a deficit of micronutrients needed by hemodialysis patients such as vitamins A, C, E, zinc and copper. **Slee (2012)** state about hemodialysis patients will experience a phase called anorexia cachexia syndrome (ACS).

Table 2 Intake macronutrients and micronutrients in hemodialysis patient.

Variables	N (%)	Average ±*SD*	Recomendation[2]
Energy			
Deficite	67 (88.2)	60.95 (28.5 – 128.3)**	30 – 35 kcal/kg bw/day (≥60 year)
Normal/ Higher	9 (11.8)		35 kcal/kgbw/day (<60 year)
Protein			
Deficite	64 (84.2)	69.36 ±30.3564*	1.2 gr/kgbw/day
Normal/ Higher	12 (15.8)		
Vitamin A			
Deficite	65 (85.5)	41.95 (1.2 – 143.7)**	≥900 µg/day (male)
Normal/ Higher	11 (14.5)		≥700 µg/day(female)
Vitamin C			
Deficite	65 (85.5)	42.4 (4.8 – 150.3)**	90 mg/day (male)
Normal/ Higher	11 (14.5)		75 mg/day (female)
Vitamin E			
Deficite	76 (100)	18.35 (2 – 64)**	15 mg/day
Normal/ Higher	-	-	
Zink			
Deficite	75 (98.7)	34.637 ±17.305*	≥10 mg/day (male)
Normal/ Higher	1 (1.3)		≥8 mg/day (female)
Cooper			
Deficite	70 (92.1)	53.3 (6.7 – 166.7)**	1.5 mg/day
Normal/ Higher	6 (7.9)		

Note:* Mean ±standar deviation; ** Median (min-max).

ACS is a collection of symptoms characterized by decreased appetite (anorexia) and increased resting energy expenditure (REE) accompanied by increased protein breakdown. Hemodialysis patients will also experience catabolism so that they need more calories than healthy people. Patients undergoing hemodialysis will usually experience an increase in uremic toxins that can reduce appetite and even loss of appetite due to nausea. Decreased appetite occurs because of an increase in proinflammatory cytokines and their effects peripherally on the skeletal muscle pathway that regulates turnover protein and centrally on the neurons in the hypothalamus that regulate appetite. ACS causes a negative energy balance in hemodialysis patients due to decreased food intake. Increased proinflammatory cytokines will increase the development of ACS, so that the activity of leptin and ghrellin may be disrupted. Leptin is anoxygenic peptide which can reduce appetite, while ghrellin is orexigenic peptide which increases appetite. Both are pathways regulating appetite in the brain/hypothalamus. In the normal pathway, neurons in the hypothalamus center produce melanocortins (proopiomelanocortin (POMC)/ cocaine and amphetamine-regulated transcript (CART)) activated by leptin, which have anorexic and catabolic effects. Whereas neuronpeptide Y (NPY) and angouti-related protein (AgRP) express neurons activated by ghrellin which have orexigenic effects. In hemodialysis patients, there is a disturbance in the circulation of leptin and ghrellin where the POMC/CART activity remains while the NPY/AgRP decreases. This has an impact on increasing resting energy expenditure and decreasing appetite. Besides that, the increase in creatinine urea also has the effect of reducing appetite. Decreased appetite is what will cause decreased food intake. **Barakat et al. (2017); Therrien, Byham and Beto (2015)** shows the same thing that hemodialysis patients are at risk of nutrient deficiency due to nutrient intake under the recommendation of KDOQI. Table 2 shows that the intake of vitamin A most (85.5%) of respondents showed a deficit. **Sahni et al., (2012)** shows that vitamin A intake in hemodialysis patients lower than healthy control groups . This study also showed that the median level of vitamin A adequacy was 41.95% with a minimum value of 1.2% and a maximum of 143.7 %. A range that is too far away indicates that there are study subjects who have very low and very high levels of sufficiency. According to KDOQI, the need for vitamin A in CKD patients with hemodialysis is 900 µg in males and 700 µg in females. Food sources that contain lots of vitamin A include all kinds of milk, butter, eggs, fish oil, vegetables with green and yellow leaves, fruits and liver **(Kalantar and Fouque, 2017)**. Subjects with deficit intake of vitamin A said they were afraid to eat vegetables and fruit because they thought it was high in potassium so they worried that blood potassium would increase. The study subjects only ate 1 – 2 tablespoons of vegetables each meal. Vitamin A is mostly contained in green and orange vegetables and fruits. Green vegetables and orange fruits are usually high in potassium which is automatically reduced by hemodialysis patients **(Bossola et al., 2014)**. The study subjects also did not consume liver containing high vitamin A. **Vas et al. (2014)** stated that the intake of vitamin A was only 373.98 (257.57 – 649.50) mcg from 700 to 900 mcg recommended. This shows a deficit intake vitamin A in hemodialysis patients. **Vas et al. (2014)** showed that 81.4% of subjects had inadequate vitamin A intake. This research also shows that most 85.5% had a sufficient level of vitamin C deficit. **Barakat et al. (2017)** which states that vitamin C intake in hemodialysis patients usually tends to be low because of the limitation of potassium in diets recommended for hemodialysis patients. Hemodialysis patients restrict vegetables and fruit for fear of increasing potassium. **Kalantar and Kopple (2001)** states that hemodialysis patients have significantly lower intakes of vitamin C, fiber, potassium and carotenoids than healthy people. The Dietary Reference Intake Panel of the Institute of Medicine recommends a recommended vitamin C diet of 90 mg per day for men and 75 mg per day for women **(Kalantar and Fouque, 2017)**. The inadequacy of vitamin C in this study was due to the fact that most of the subjects thought that vegetables and fruits contained lots of potassium and should be avoided. Adequacy levels of vitamin E in study subjects showed that 100% had a deficit. **Kooshki, Samadipour and Akbarzadeh (2015)** points out the same thing that vitamin E intake is less than the recommendation. Vitamin E is found in many grains. **Lou et al. (2007)** said that hemodialysis patients also limit potassium intake by avoiding vegetables, fruit and seeds. The subject of this study also conducted restrictions on grains. This will cause the intake of vitamin E is also not enough to meet nutritional needs. Based on interviews with research subjects, they limited their intake of legumes such as tofu, tempeh, peas, green beans, cashews for fear of creatinine urea increasing. The need for Vitamin E in both male and female CKD patients is 15 mg/day **(Kalantar and Fouque, 2017)**. Sources of vitamin E are vegetable oils, unprocessed grains, nuts, fruits, vegetables and meat **(Kopple, 2001)**. Most of the research subjects (98.7%) had a zinc adequacy level classified as deficit. **Sahni et al., (2012)** states that the average zinc intake was found to be less than the recommendation for hemodialysis patients. **Sahni et al. (2012)** states that zinc is a mineral that has strong potential as an antioxidant, usually obtained from foods rich in protein. Low protein intake is significantly correlated with low zinc intake. The low zinc intake in the study subjects was due to the protein intake of the subjects also showing a deficit with the average protein intake of 69.361 ±30.356%. Zinc is found in many foods such as meat, fish, cheese, chicken, eggs and milk products, beans, almonds and parsley. This research shows that copper adequacy level was mostly (92.1%) indicating a deficit. **Szpanowska, Chowaniec and Kolarzyk (2008)** stated that copper intake was very low, less than 40% of the recommended. This research subjects carried out a restriction in their diet, especially those containing protein for fear that their creatinine urea had increased. Graph 1 shows that most (63.2%) had a relatively low albumin because it was less than 3.5 g.dL^{-1}. Low serum albumin is a sign of protein energy malnutrition. Protein energy malnutrition when energy and protein requirements are not met as needed. Deficit of food intake in hemodialysis patients in the long run will cause protein energy malnutrition. Low protein intake will cause hypoalbuminemia **(Kaysen et al., 2002)**. This study shows that the intake of macronutrients and micronutrients in most subjects is deficit. The origin of PEM appears to precede dialysis treatment, and it is engendered progressively as glomerular filtration rate (GFR) decreases to less than 55 mg.min^{-1} **(Kalantar and Kopple, 2001)**. Hypoalbuminemia have been shown to develop along with the progression of CKD stages. Serum albumin will decrease with decreasing glomerular filtration rate (GFR). Hemodialysis patients show a decrease in glomerular filtration rate up to <15 mL/min/1.72m^2. Serum albumin is a negative acute phase reactant as a marker of inflammation **(Kaysen et al., 2002)**. Graph 2 shows that most (61.8%) subjects had serum hs-CRP in the high-risk category because it was more than 3 mg.L^{-1}. Based on recommendations from the Centers for Disease Control and Prevention (CDC) cut offs point hs-CRP levels >3 mg.L^{-1} indicate a group at high risk of cardiovascular disease **(Myers et al., 2004)**.

This study also found that the median hs-CRP level was 4.85 mg.L^{-1} with a minimum level of 0.29 mg.L^{-1} and a maximum of 20.30 mg.L^{-1}. Increased levels of CRP as a consequence of the chronic inflammatory process that is found in conditions such as kidney disorders. The inflammatory process in hemodialysis is caused by the involvement of various factors such as accumulation of uremia toxin, malnutrition, oxidative stress, volume overload, carbonyl stress, decreased levels of antioxidant, low production of anti-inflammatory cytokines, comorbid, dialysis treatment **(Kalantar et al., 2003)**. Hemodialysis patients often experience a condition of uremia. Uremia in hemodialysis patients will increase proinflammatory cytokine levels associated with increased mortality. In addition, the dialysis process also contributes to the increase in cytokine secretion at the end of hemodialysis. In this case,

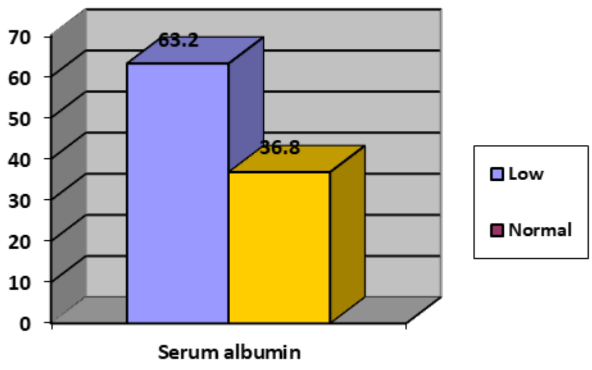

Figure 1 Frequency serum albumin level.

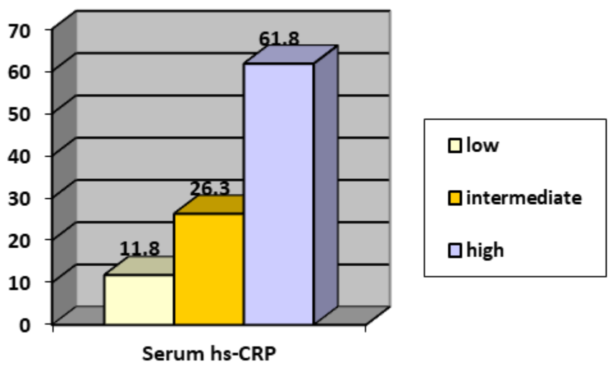

Figure 2 Frequency serum hs-CRP level.

the dialysis membrane can stimulate increased cytokine release. Increased proinflammatory cytokines can reduce appetite so that food intake decreases **(Kalantar et al., 2003)**. Decreased food intake such as energy and protein are likely to cause PEM which will increase inflammation by increasing hs-CRP levels. In this study the majority of hemodialysis patients showed micronutrient intake that was classified as deficit. vitamins A, C, E, zinc, copper are micronutrients that act as antioxidants. Malnourished dialysis patients may be deficient of antioxidant such as vitamin C or carotenoids which may lead to increased oxidative stress leading to inflammation **(Kalantar and Kopple, 2001)**. Antioxidants are very important to protect the body from free radical attack which can increase oxidative stress. Increased lipid peroxidation (LP) and reduced enzymatic antioxidant defence have been observed in predialysis patients. Loss or deficiency of antioxidant activity could also contribute to enhanced oxidative stress in uremia **(Kalantar et al., 2003; Tarko et al., 2013)**. Oxidative stress defines an imbalance between formation of reactive oxygen species (ROS) and anti-oxidative defence mechanisms. It occurs when there is excessive free radical production and/or low antioxidant defence and results in chemical alterations of bio-molecules, causing structural and functional modifications **(Sahni et al., 2012)**. Oxidative stress and inflammation status are well-known interrelated factors in hemodialysis patient with common underlying mechanisms including endothelial dysfunction and common complications, such as cardiovascular disease and death **(Bianchi, 2009)**. Serum hs-CRP is an inflammatory marker that is associated with an increased risk of death due to cardiovascular disorders **(Stevinkel et al., 2005)**.

CONCLUSION

This study shows that intake of macronutrients and micronutrients in hemodialysis patients is deficit. This research concludes that 88.2% deficit of energy and 84.2% deficit of protein. In addition, micronutrient intake also shows 85.5% deficit of vitamin A, 85.5% deficit of vitamin C, 100% deficit of vitamin E. Zinc intake at 98.7% showed a deficit and copper intake at 92.1% also showed a deficit. There were 63.2% of subjects had low albumin serum and 61.8% of subjects had high hs-CRP serum.

REFERENCES

Barakat, R., Haviv, Y. S., Geva, D., Vardi, H., Shahar, D. R. 2017. Macro and micronutrients deficiencies within hemodialysis patient's dietary intake, should we re-consider our recommendations? *SL Nutr. Metab.*, vol. 1, no. 1, p. 115.

Bianchi, M. E. 2009. HMGB1 loves company. *J. Leukoc. Biol.*, vol. 86, p. 573-576. https://doi.org/10.1189/jlb.1008585

Bossola, M., Di Stasio, E., Viola, L., Carlomagno, G., Monteburini, T., Cenerelli, S., Santarelli, S., Boggi, R., Miggiano, G., Vulpio, C., Mele, C., Tazza, L. 2014. Dietary intake of trace elements, mineral, and vitamins of patients on cgronic hemodialysis. *Int. Urol. Nephrol.*, vol. 46, no. 4, p. 809-815. https://doi.org/10.1007/s11255-014-0689-y

Bossola, M., Leo, A., Viola, A., Carlomagno, G., Mounteburini, T., Cenerelli, S., Santarelli, S., Boggi, R., Miggiano, G., Vulpio, C., Mele, C., Tazza, L. 2013. Dietary intake of macronutrients and fiber in mediteranian patients on chronic hemodialysis. *J. Nephrol.*, vol. 26, no. 5, p. 912-918. https://doi.org/10.5301/jn.5000222

Castro, L. L., Martins, M. C. C., Garcez, A. M., Pacheco, J. F. R., Cunha, F. V. M., Neto, J. M. M., Freitas, M. C. L., Cunha, L. A. M. 2014. Hypoalbuminemia and oxidative stress in patients on renal hemodialysis program. *Nutr. Hosp.*, vol. 30, no. 4, p. 952-959. https://doi.org.10.3305/nh.2014.30.4.7667.

Daugirdas, J. T., Depner, T. A., Inrig, J., Mehrotra, R., Rocco, M. V., Suri, R. S., Weiner, D. E. 2015. KDOQI clinical practice quidline for hemodialysis adequacy: 2015 update. *AJKD*, vol. 66, no. 5, p. 884-930. https://doi.org/10.1053/j.ajkd.2015.07.015

Gama, A. T., Heimburger, O., Stevinkel, P., Barany, P., Lindholm, B., Qureshi, A. R. 2012. Serum albumin as predictor of nutritional status in patients with ESRD. *Clin. J. Am. Soc. Nephrol.*, vol. 7, no. 6, p. 1446-1453. https://doi.org/10.2215/CJN.10251011.

Hecking, M., Bieber, B. A., Either, J., Kautzky-Willer, A., Sunder-Plassmann, G., Saemann, M. D., Ramirez, S. P., Gillespie, B. W., Pisoni, R. L., Robinson, B. M., Port, F. K. 2014. Sex-specific differences in hemodialysis prevalence and practices and the male to female mortality rate : The dialysis outcomes and practice patterns study (DOPPS). *PLOS Med*, vol. 11, no. 10. https://doi.org./10.1371/journal.pmed.1001750.

Hill, N. R., Fatoba, S. T., Oke, J. L., Hirst, J. A., O'Callaghan, C. A., Lasserson, D. S., Hobbs, F. D. R. 2016. Global prevalence of chronic kidney disease- A systematic review and meta analysis. *PloS One*, vol. 11, no. 7, p. 1-18. https://doi.org/10.1371/journal.pone.0158765

Kalantar, Z. K., Fouque, D. 2017. Nutritional Management of Chronic Kidney Disease. *New England Journal of Medicine*, vol. 37, no. 18, p. 1765-1776. https://doi.org/10.1056/NEJMra1700312.

Kalantar, Z. K., Kopple, J. D. 2001. Relative contribution of nutrition and inflammation to clinical outcome in dyalisis patients. *Am. J. Kidney Dis.*, vol. 38, no. 6, p. 1343-1350. https://doi.org/10.1053/ajkd.2001.29250

Kalantar, Z. K., Mcallister, C. M., Block, G., Humphreys, M. H. 2004. Appetide and inflammation, nutrition, anemia and clinical outcome in hemodialysis patients. *Am. J. Clin. Nutr.*, vol. 80, no. 1, p. 299-307. https://doi.org/10.1093/ajcn/80.2.299

Kalantar, Z. K., Stenvinkel, P., Pillon, L., Kopple, J. D. 2003. Inflammation and nutrition in renal insufficiency. *Adv. Ren. Replace Ther.*, vol. 10, no.3, p. 155-169. http://doi.org/10.1053/j.arrt.2003.08.008.

Kaysen, G. A., Dubin, J. A., Muller, H. G., Mitch, W. E., Rosales, L. M., Levin, N. W. 2002. Relationships among inflammation nutrition and physiologic mechanisms establishing albumin levels in hemodyalisis patient. *Kidney Int.*, vol. 61, no. 6, p. 2240-2249. https://doi.org/10.1046/j.1523-1755.2002.00076.x

Kooshki, A., Samadipour, E., Akbarzadeh, R. 2015. The association between serum C-reactive protein and macronutrients and antioxidants intake in hemodialysis patients. *J. Med. Life*, vol. 8, no. 2, p. 43-46.

Kopple, J. D. 2001. National Kidney Foundation K/DOQI Clinical Practice Gudelines for Nutrition in Chronic Renal Failure. *Am. J. Kidney Dis.*, vol. 37, no. 1, p. S66-70. https://doi.org/10.1053/ajkd.2001.20748

Locatelli, F., Fouque, D., Heimburger, O., Drueke, T. B., Cannata, A. J. B., Horl, W.,H. Ritz, E. 2002. Nutritional status in dialysis patient. *Nephrol. Dial. Transpl.*, vol. 17, no. 4, p. 563-572. https://doi.org/10.1093/ndt/17.4.563

Lou, L. M., Campos, B., Gimeno, J. A., Boned B. 2007. Nutrien intake and eating habits in hemodialysis patients:

Comparison with a model based on mediterranean diet. *Nefrologia*, vol. 27, no. 1, p. 38-45.

Miura, Y., Nakai, K., Suwabe, A., Sera, K. 2002. Trace element in renal disease. *Nucl. Instr. Meth. Phys. Res.*, vol. 189, no. 1-4, p. 443-449. https://doi.org/10.1016/S0168-583X(01)01122-3

Myers, G. L., Rifai, N., Tracy, R. P., Roberts, W. L., Alexander, R. W., Biasucci, L. M., Catravas, J. D., Cole, T. G., Cooper, G. R., Khan, B. V., Kimberly, M. M., Stein, E. A., Taubert, K. A., Warnick, G. R., Waymack, P. P. 2004. Application to clinical and public health practice: Report from the laboratory science discussion group. In Proceeding of CDC/AHA workshop on markers of inflammation and cardiovascular disease. *Circulation*, vol. 110, p. e545-e549. https://doi.org/10.1161/01.CIR.0000148980.87579.5E

Panichi, V., Rizza, G. M., Paoletti, S., Bigazzi, S., Aloisi, M., Barsotti, G., Rindi, P., Donati, G., Antonelli, A., Panicuci, E. 2008. Chronic inflammation and mortality in hemodialysis: effect of different renal replacement therapies. Results from the Riscavid study. *Nephrol. Dial. Transpl.*, vol. 23, no. 7, p. 2337-2343. https://doi.org/10.1093/ndt/gfm951

Sahni, N., Gupta, K. L., Rana, V. S., Prasad, R., Bhalla, A. K. 2012. Intake of antioxidants and their status in chronic kidney disease patients. *J. Ren. Nutr.*, vol. 22, no. 4, p. 389-399. https://doi.org/10.1053/j.jrn.2011.09.002

Sarnak, M. J., Levey, A. S., Schoolwerth, A. C., Coresh, J., Culleton, B., Hamm, L. L., McCullough, P. A., Kasiske, B. L., Kelepouris, E., Klag, M. J., Parfrey, P. 2003. Kidney disease as a risk factor for development of cardiovascular disease. *Circulation*, vol. 108, p. 2154-2169. https://doi.org/10.1161/01.CIR.0000095676.90936.80

Slee, A. D. 2012. Exploring metabolic dysfunction in chronic kidney disease. *Nutr. Metab.*, vol. 9, no. 36, p. 1-16. https://doi.org/10.1186/1743-7075-9-36.

Steven, L. A., Li, S., Wang, C., Huang, C., Becker, B. N., Bomback, A. S., Brown, W. W., Burrows, N. R., Jurkovitz, C. T., McFariane, S. I., Norris, K. C., Shilpak, M., Whaley, A. T. C., Chen, S. C., Bakris, G. L., McCullough, P. A. 2010. Prevalence of Chronic Kidney Disease and Comorbid Illness in Elderly Patients in United States: Result From the Kidney Early Evaluation Program (KEEP). *Am. J. Kidney Dis.*, vol. 55, no. 302, p. S23-S33. https://doi.org/10.1053/j.ajkd.2009.09.035

Stevinkel, P., Ronco, C., Brendolan, A., Levin, N. W. 2005. Inflammation in end stage renal disease a fire that burns within. *Contrib Nephrol.*, vol. 149, p. 185-199. https://doi.org/10.1159/000085525

Szpanowska, A. W., Chowaniec, E., Kolarzyk, E. 2008. Estimation of intake of zinc, copper and iron in the diet of patients with chronic renal failure treated by hemodialysis. *Biological Trace Element Research*, vol. 124, no. 2, p. 97-102. https://doi.org/10.1007/s12011-008-8131-x

Tarko, T., Duda-Chodak, A., Satora, P., Zając, N. 2013. Antioxidant activity of goji berries and bilberry at particular digestion stages in an in vitro model simulating the human alimentary tract. *Potravinarstvo*, vol. 7, no. 1, p. 235-238.

Therrien, M., Byham, G., Beto, J. 2015. A Review of Dietary Intake Studies in Maintenance Dialysis Patients. *J. Ren. Nutr.*, vol. 25, no. 4, p. 329-338. https://doi.org/10.1053/j.jrn.2014.11.001.

Vas, I. M. F., Freitas, A. T. V. S., Peixoto, M. R. G., Ferraz, S. F., Compos, M. I. V. A. M. 2014. Food intake in patients on hemodialysis. *Revista de Nutricao*, vol. 27, no. 6, http://doi.org/10.1590/1415-52732014000600002

Verhave, J. C., Hillege, H. L., Burgerhof, J. G. M., Gansevoort, R. T., Zeeuw, D. D., Jong, P. E. D. 2005. The association between atherosclerotic risk factor and renal function in the general population. *Kidney Int.*, vol. 67, no. 5, p. 1967-1973. https://doi.org/10.1111/j.1523-1755.2005.00296.x

Yao, Q., Pecoits, F. R., Lindholm, B., Stevinkel, P. 2009. Traditional and non-traditional factors as contributors to atherosclerotic cardiovasculer disease in end stage renal disease. *Scandinavian journal of urology and nephrology*, vol. 38, no. 5, p. 405-416. https://doi.org/10.1080/00365590410031715.

Acknowledgments:

The author wish to Department of Nutrition Science, Faculty of Medicine Diponegoro University, Semarang, Indonesia, laboratory of National Diponegoro Hospital, Semarang, Indonesia and laboratory of dr. H. Soewondo Hospital, Kendal, Indonesia for entirely supporting this research.

Contact address:

*Siti Fatonah, Diponegoro University, Faculty of Medicine,Department of Nutrition Science, Semarang, Indonesia 50275, Tel: +6281325713642,
E-mail: syifakendal@gmail.com
ORCID: https://orcid.org/0000-0001-9922-7798

Moh Sulchan, Diponegoro University, Faculty of Medicine, Department of Nutrition Science, Semarang, Indonesia 50275, Tel: +62816655235,
E-mail: mohsulchan@gmail.com
ORCID: https://orcid.org/0000-0002-6961-2780

Muchlis Achsan Udji Sofro, Diponegoro University, Faculty of Medicine, Department of Internal Medicine, dr. Kariadi Hospital, Semarang, Indonesia 50244, Tel: +628122916803,
E-mail: muchlis.aus@gmail.com
ORCID: https://orcid.org/0000-0003-0164-4863

Corresponding author: *