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THE CORRELATION BETWEEN HS-CRP LEVEL AND NUTRITION STATUS TO THE QUALITY OF LIFE OF PATIENTS WITH CHRONIC KIDNEY DISEASE WHO UNDERWENT HEMODIALYSIS IN HAJI ADAM MALIK CENTRAL GENERAL HOSPITAL MEDAN

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Abstract

Chronic kidney disease (CKD) is a global health problem with global prevalence ranging from 11-13%. The process of chronic inflammation and malnutrition in CKD patients undergoing hemodialysis (HD) is a medical condition that affects the quality of life. This study aims to determine the correlation of hs-CRP levels and nutritional status with quality life of CKD patients undergoing HD. This research is an analytical study, cross sectional design, conducted in December 2019 - March 2020 at Haji Adam Malik General Hospital Medan. Based on the fisher's exact test of 37 samples, a significant correlation was found between hs-CRP and physical health ($p = 0.037$, PR 1.6) and with psychological well-being ($p = 0.045$; PR 1.78). There was no correlation found between hs-CRP with social relations ($p = 0.091$; PR 1.7) and the environment ($p = 0.078$; PR 1.54). A significant correlation was found between nutritional status and several domains including physical health ($p = 0.038$; PR 1.6), psychological well-being ($p = 0.005$; PR 2.09), social correlations ($p = 0.011$; PR 2.48), and the environment ($p = 0.012$; PR 2.02). The study determined that there was correlation found between hs-CRP levels with physical health and psychological well-being and between nutritional status with all domains of quality of life.

Introduction

Chronic kidney disease (CKD) is a global health problem with a global prevalence that reaches between 11-13%. [1] Indonesian Renal Registry (IRR) reported an increase in CKD cases from 2007 to 2016. There was a total of 1885 CKD patients in 2007, while in 2016, this number increase to a total of 52,385. Hemodialysis measures increased from year to year and in 2017 a very drastic increase in trials with support residents who take part in the National Health Insurance (JKN) program that they have full access and financing for undergoing chronic hemodialysis (HD). In 2007 the number of HD conducted in Indonesia was 114,220 times, and in 2012 the data became 623,181 times and increased dramatically as many as 1,694,432 HD conducts in 2017. [2] The inflammatory process is often found in CKD patients. Biomarkers that can be used to assess inflammation in dialysis patients are high levels of C-reactive protein (hs-CRP) produced by the liver and regulate various kinds of cytokines. [3] hs-CRP is a polypeptide molecule from the pentraxins group which is an acute phase protein. [4] Increased concentrations of hs-CRP over a long period of time play a role in the development of cardiovascular and cerebrovascular diseases and affect the quality of life in CKD patients. [5] In addition to experiencing chronic inflammation, CKD patients also experience protein energy malnutrition or protein energy wasting (PEW). [6] Poor nutritional status in CKD patients is due to several factors including impaired protein metabolism, excess hydration (overhydration), protein loss and inflammation. [7] The process of chronic inflammation and malnutrition in CKD patients undergoing HD is a medical condition that affects the quality of life of CKD patients. [8,9]

Several studies have shown that CKD patients undergoing HD have a lower quality of life, even lower than CKD patients undergoing peritoneal dialysis, kidney transplantation or the general population. A systematic review and meta-analysis by Ghiasi et al that reviewed 45 studies with a total sample of 17,200 people using various questionnaire instruments in the form of SF-36, HRQOL, and KDQOL-SF concluded that the average quality of life of CKD patients undergoing routine HD is lower than controls. [10] Other studies found a strong correlation between nutritional status (as measured by a malnutrition-inflammatory score) and quality of life (KDQOL-SF36) in CKD patients undergoing routine HD. This is evidenced by the correlation coefficient ($r =$



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0.705 and p value <0.001. [9] Based on the background above, the researcher wanted to look for the correlation between the inflammatory factors (CRP levels) and nutritional status (MIS scores) with the quality of life (WHOQOL-BREF) of CKD patients undergoing HD at the Haji Adam Malik General Hospital in Medan. The absence of prior research that seeks a correlation between these variables encourages researchers to conduct this study.

Method

Research design

This research is an analytical study, cross sectional design, conducted in December 2019 - March 2020 at Haji Adam Malik General Hospital Medan (HAM). The population in this study were all patients undergoing therapeutic treatment at HAM Hospital and during December 2019 - March 2020. The study sample was part of an affordable population that met the inclusion criteria for male and female patients aged ≥ 18 years, final stage CKD patients who underwent hemodialysis therapy with a duration of dialysis ≥ 3 months and agreed to be included in the study. Exclusion criteria were when there was an acute infection (clinically found: fever, coughing, urination during urination, abdominal pain, diarrhea), the patient had fever, the patient was unstable, the patient received parenteral nutrition when examined. Patients who fit the criteria were asked to participate in the study. Participants then filled out the consent letter after receiving an explanation.

Hs-CRP examination

Blood samples were taken before hemodialysis and was then sent to the laboratory. The hs-CRP examination was carried out in the laboratory of Haji Adam Malik General Hospital using the turbidimetric immunoassay method (Architect c8000, Chicago). The results of the hs-CRP examination are shown in numbers in mg / dl units. Blood sampling was carried out before hemodialysis took place. This was because the hemodialysis procedure can trigger inflammation that can be marked by a significant increase in hsCRP levels. [11] Increased levels of hsCRP could cause bias in this study.

Nutrition Status Check

Examination of nutritional status was done by filling out a malnutrition-inflammatory questionnaire. The questionnaire was filled out by researchers based on interviews with patients, conducted physical examinations in the form of measurements of height, weight and BMI calculation, looking at signs of subcutaneous fat loss and signs of loss of muscle mass. Laboratory tests in the form of serum albumin and TIBC levels were also performed to complete this questionnaire. Blood samples were taken after HD and sent to the laboratory.

Quality of Life Status Check

Quality of life checks were carried out using the WHOQOL-BREF questionnaire. The questionnaire was filled out by the research subjects or assisted by researchers by conducting interviews on the research subjects based on the questions on the questionnaire. Scores on each component were summed and shown as numbers.

Result

From the 37 samples obtained, the number of male patients with CKD who underwent hemodialysis were 24 samples (64.9%) and female were 13 samples (35.1%). Patients under the age of 51 years amounted to 20 samples (54.1%) and above the same as 51 years amounted to 17 samples (45.9%). Based on body mass index, from 37 samples, 28 samples (75.7%) were classified as underweight (IMT <18.5 kg / m²) and 9 samples (24.3%) were classified as normoweight (IMT 18.5 -22.9 kg / m²). Of the 37 samples, 23 (62.2%) had diabetes mellitus and 14 (37.8%) did not have diabetes mellitus. The number of samples who had hypertension comorbidities were 19 samples (51.4%) and those without hypertension comorbidities were 18 people (48.6%). The number of samples that have uric acid nephropathy (UAN) comorbidities were 20 samples (54.1%) and those without UAN comorbidities were 17 samples (45.9%). The number of samples that had comorbidity of Obstructive Kidney Disease (PGOI) were 14 people (37.8%) and who did not have PGOI concomitant diseases were 23 samples (62.2%). Of the 37 samples, 19 samples (51.4%) underwent hemodialysis for less than 50 weeks and 18 people (48.6%) underwent hemodialysis for above equal to 50 weeks

The patients' quality of life assesment included physical health, psychological well-being, social relations and the environment. Based on fisher's exact test in this study, there was found a significant correlation between hs-CRP on physical health (p = 0.037, PR 1.6) and psychological well-being (p = 0.045; PR 1.78). There was no



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correlation found between hs-CRP and social relations ($p = 0.091$; PR 1.7) and the environment ($p = 0.078$; PR 1.54). Based on the fisher's exact test in this study, there was found a significant correlation between nutritional status with physical health ($p = 0.038$; PR 1.6), psychological well-being ($p = 0.005$; PR 2.09), social correlations ($p = 0.011$; PR 2.48), and the environment ($p = 0.012$; PR 2.02).

Discussion

This study aims to assess the quality of life of patients in the WHOQOL-BREF questionnaire domain for the presence or absence of inflammatory processes in CKD patients as seen from hs-CRP levels and also for nutritional status. In the domain of physical health, an assessment was made on how often patients need medical help to reduce pain, need energy, rest, sleep, mobilization, activity, treatment and work so that they can function well in daily life. In the domain of psychological well-being, several aspects were found, such as positive and negative feelings, ways of thinking, self-esteem, body image, and spiritual which can influence CKD patients. In the domain of social relations, an assessment was made on social relations between individuals, social support, sexual activity and patient satisfaction with the support obtained from the surrounding environment. In the environmental domain includes physical security, home environment, financial resources, health facilities, ease of getting information, health, recreation, and transportation that he receives in undergoing regular hemodialysis. Based on the fisher's exact test in this study, there was found a significant correlation between hs-CRP on the quality of life of the physical health domain ($p = 0.037$, PR 1.6). This is in line with research conducted by Kumar et al (2015) where HsCRP levels were found to be increased in patients with CKD compared to the control group. There is a significant correlation between decreased GFR and hs-CRP concentration indicating inflammatory activity in patients with CKD. [12] Some other studies also showed that CKD patients undergoing HD had a low quality of life, even lower than CKD patients undergoing peritoneal dialysis, kidney transplantation or the general population. In line with the results, a research conducted by Joshie et al and Dabrowska- Bender et al, quality of life assessed using the WHOQOL-BREF questionnaire was found to decrease from all domains, both the physical, social, psychosocial and environmental domains. [13,14]

Based on the fisher's exact test in this study, there was found a significant correlation between hsCRP and the quality of life of the psychological welfare domain ($p = 0.045$; PR 1.78). This is in line with a research conducted by Liukkonen et al (2006) which stated that there was an increased risk of depressive episodes 1.7 to 3.1 times in samples that showed increase levels of hs-CRP (95% CI, 1.1-8.8). [15] According to Kim et al (2018), inflammation has been known to have a correlation with mental health and quality of life. Psychological conditions are related to the endocrine and immune systems, especially inflammation and regulation of the HPA axis. Stress causes an inflammatory response and affects the HPA axis, resulting in anti-inflammatory regulation. There are many studies on the correlation between depression and inflammation, and this correlation is very complex and interactive. In general, depression is associated with increased inflammation which correlates with ideas and suicide attempts. In addition, inflammation can reduce the quality of life due to decreased sense of excitement. In that research, one did not find any correlation between hsCRP concentration with stress, depression and sleep disorders. However, the hsCRP concentration was associated with an increased incidence of suicidal ideation in adults. [16]

Based on the fisher's exact test in this study, no significant correlation was found between hsCRP and the quality of life of the social relations domain ($p = 0.091$; PR 1.7). Social correlations are very important for well-being and health. Social isolation is a picture of a decrease in the size of social correlations and lack of social contact. Social isolation is associated with increased blood pressure, CRP and fibrinogen, as well as increased inflammatory and metabolic responses to stress. [17] This contradicts the research conducted by Pavela et al. They found little evidence that social isolation could increase the risk of increased CRP hs concentrations. [18] There was no correlation between hsCRP and environmental quality in this study ($p = 0.078$; PR 1.54). As far as literature studies are conducted, there is still little research to support this. However, in a study conducted by Shen et al (2009) that looked at the influence of genetic and environmental factors on the hsCRP concentration, they found genetic variations in the CRP locus and other loci, as well as dietary and lifestyle factors influencing the variability in concentration interindividual CRP hs plasma. [19] Based on the fisher's exact test in this study, there was found a significant correlation between nutritional status and quality of life in the physical health domain ($p = 0.038$; PR 1.6). This is in line with a cohort study conducted in Southern California in 2009. The study was conducted on 809 outpatients with a diagnosis of chronic kidney disease who underwent regular HD for 8 weeks, carried out an assessment of quality of life using a short form-36 questionnaire instrument or better known as SF-36 and assessment of malnutrition status were established through malnutrition-inflammatory



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scoring (MIS). The results of the study found that there was significant correlation between malnutrition and quality of life, specifically on the dimensions of physical health ($p < 0.001$). [20] Physical health is one of the things found in CKD patients that had decreased in its function to assess the quality of life of patients, especially those who have nutritional status that was lacking/malnutrition. This indicates that the condition of malnutrition can cause a decrease in a person's capacity to perform daily physical activities as simple as helping oneself to walk or move flexibly independently. [21]

Based on the fisher's exact test in this study, there was found a significant correlation between nutritional status and quality of life of the psychological welfare domain ($p = 0.005$; PR 2.09). This is in accordance with the study of Rambo et al in 2009 which stated that scoring nutritional status using MIS on regular HD patients had a significant correlation with the mental and psychological aspects of the quality of life of respondents assessed by the SF- 36 instrument. [20] The high mortality rate in patients undergoing regular HD seems to be one of the reasons that has an influence on the mental condition and psychological aspects of CKD patients who routinely undergo hemodialysis. [20] As is well known, CKD patients who routinely undergo hemodialysis experience a physiological stress every day. Such pressure certainly affects the quality of life, especially in mental conditions that are also influenced by anxiety and depression. Campbell et al found that there were clinically significant changes, one of which was the psychological nature in question, when an intervention was performed in the nutrition of kidney failure patients undergoing hemodialysis ($p = 0.069$). [21] From this research it can be understood that support and intervention both in nutrition and psychologically in CKD patients undergoing regular HD is indeed beneficial in improving the quality of life of patients.

Based on the fisher's exact test in this study found a significant correlation between nutritional status on the quality of life of the social relations domain ($p = 0.011$; PR 2.48). This is in line with the results of Campbel et al's study which stated that there was significance between the nutritional conditions of kidney failure patients who undergo daily social functions (p value = 0.02). Patients with poorer nutritional conditions exhibit lower social functioning than those with good nutritional conditions or who are given nutritional interventions during the observation period. [21]

Based on the fisher's exact test in this study, there was found a significant correlation between nutritional status and quality of life in the environmental domain ($p = 0.012$; PR 2.02). As is known, environmental conditions include physical security, home environmental conditions, health facilities, financial resources, recreation and transportation. [22] Previous studies conducted in Taiwan in 2013 stated that there was a positive influence between the history of residence and air polluted environment with the incidence of protein energy wasting (PEW) in patients with routine renal failure hemodialysis (p value = 0.041). The study stated that in addition to paying attention to nutritional factors in patients with kidney failure, environmental factors also need to be given full attention by clinicians in improving functional patients who routinely run hemodialysis, and also that between nutritional factors and environmental factors found a correlation that affects each other. [23]

Conclusion

There is a significant correlation between hs-CRP levels with the quality of life in domain of physical health and psychological well-being. There is also a significant correlation between nutritional status and quality of life in domain of physical health, psychological well-being, social relations and the environment. As far as literature studies are conducted, there is still very little research on inflammatory status and quality of life in CKD patients undergoing hemodialysis, especially in Indonesia. For this reason, further research is needed to evaluate the correlation of hsCRP and nutritional status to quality of life in CKD patients. Further research is needed with a larger sample size and more varied sample characteristics given the high number of CKD patients undergoing routine hemodialysis with various comorbidities accompanying it. Furthermore, it is necessary to analyze other factors that influence nutritional status and hs-CRP levels on quality of life in patients undergoing hemodialysis.

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Table 1.1 Distribution of Research Subjects based on Demographic Characteristics

Variable	Total (n)	Percentage (%)
Gender		
Male	24	64,9
Female	13	35,1
Age		
< 51 tahun	20	54,1
≥ 51 tahun	17	45,9
IMT		
<i>Underweight</i>	28	75,7
<i>Normoweight</i>	9	24,3
Diabetes Melitus		
Yes	23	62,2
No	14	37,8
Hypertension		
Yes	19	51,4
No	18	48,6
Uric Acid Nephropathy		
Yes	20	54,1
No	17	45,9
Obstruction Infection Kidney Disease		
Yes	14	37,8
No	23	62,2
Duration undergoing HD		
< 50 weeks	19	51,4
≥ 50 weeks	18	48,6

Data presented as total (n) and percentage (%)



Table 1.2 Effects of hs-CRP on Quality of Life

Quality of Life	hs-CRP		p-value <i>fisher's</i> <i>exact test</i>	PR
	Inflamatio n	No Inflammation		
Physical health				
Good	1 (4%)	3 (33%)	0.037	1.60
Poor	27 (96%)	6 (67%)		
Psychological well-being				
Good	3 (13%)	4 (44%)	0.045	1.78
Poor	25 (89%)	5 (56%)		
Social relations				
Good	6 (21%)	5 (56%)	0.091	1.70
Poor	22 (79%)	4 (44%)		
Environment				
Good	4 (14%)	4 (44%)	0.078	1.54
Poor	24 (86%)	5 (56%)		

Table 1.3 Effects of Nutrition Status on Quality of Life

Quality of Life	Nutritional Status		p-value <i>fisher's</i> <i>exact test</i>	PR
	Malnutrit ion	No Malnutrition		
Physical health				
Good	1 (4%)	3 (33%)	0.038	1.6
Poor	27 (96%)	6 (67%)		
Psychological well-being				
Good	2 (7%)	5 (56%)	0.005	2.09
Poor	26 (93%)	4 (44%)		
Social relations				
Good	5 (18%)	6 (67%)	0.011	2.48
Poor	23 (82%)	3 (33%)		
Environment				
Good	3 (11%)	5 (56%)	0.012	2.02
Poor	25 (89%)	4 (44%)		