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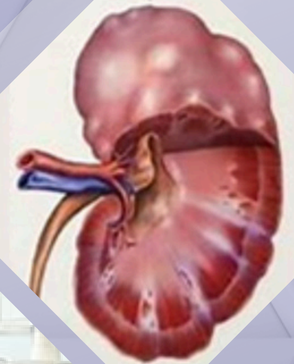

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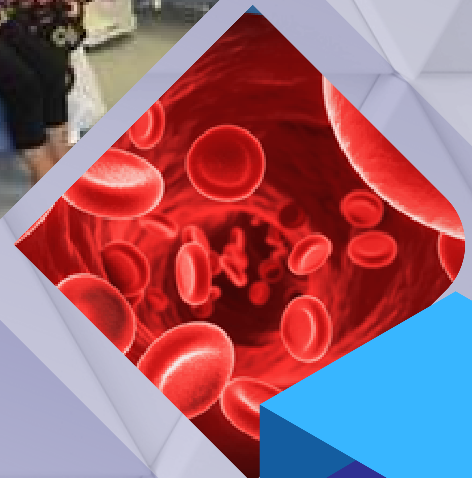

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EDITOR'S LETTER

Daerest Reader,

It is of great honor for me and my colleagues to be able to publish the first Indonesian scientific journal in nephrology, Indonesian Journal of Kidney and Hypertension (InaKidney). As we all know, Indonesia is a developing country that faces unique challenges in tackling kidney health problems and hypertension such as varying geographic characteristics, cultural diversity, universal health coverage, and dominating low-income families. We need to provide clinicians with an evidence-based recommendation in conducting the best clinical practice appropriate for our challenges. In order to achieve that, proper clinical evidence from all over the country needs to be obtained.

With the support of our international honorary editors, executive editors, and peer reviewers, we hope this journal will propel clinicians and researchers to publish their original articles. Every manuscript submitted to our journal went through a meticulous process of editing and peer review, to ensure the quality of the published paper. This journal's aim is to provide clinicians and researchers all over Indonesia, and hopefully in the future, all over the globe, not only a means to publish their original articles in nephrology but also a source of scientific pieces of evidence to help further enhance patient care.

We are well aware of the fact that this journal has many aspects that can benefit from further improvement. Any commentaries and advice by readers are much welcomed and will be of high value to better our future publications

Warm Wishes,

Best Regards,

Pringgodigdo Nugroho
Chief Editor

Greetings: Head of InaSN

Pringgodigdo Nugroho
Head of Indonesian Society of Nephrology (InaSN)

The world of nephrology in Indonesia has experienced significant progress. It is marked by the growing development of health services in the field of nephrology including dialysis, kidney transplantation, comprehensive chronic kidney disease management, as well as continuing efforts on prevention of non-communicable diseases such as hypertension.

The number of nephrologists in Indonesia has also been increasing even though the distribution is still concentrated on Java Island. However, the management of kidney disease is yet a complex problem in this country and requires substantial effort to minimize its impact on health and economy.

To support the development of nephrology and related medical technology, the Indonesian Society of Nephrology (InaSN) launched an open-access online journal, the Journal of Kidney and Hypertension (InaKidney). Through this journal, it is expected that physicians can share clinical experiences among peers throughout Indonesia, in only one click away. To complete, we are honored to have international nephrology experts as the editorial board in selecting papers published in this journal.

On behalf of InaSN, we thank all those who have worked so hard that this journal can be published and accessed by the public. We are open to all criticism and suggestions for continuous improvement. Happy reading.

Indonesian Journal of Kidney & Hypertension InaKidney

Editorial

Determinants of Nutritional Status and Quality of Life in Hemodialysis Patients

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Malnutrition is prevalent among patients undergoing hemodialysis (HD), affecting between 28% and 54% globally.[1] It is associated not only with increased morbidity and hospitalization rates but also with decreased functional status and impacts physical, emotional, and psychosocial health, ultimately leading to a lower quality of life (QoL).[2] Given the significant negative impacts of malnutrition, it is crucial for nephrologists to identify risk factors, make early diagnoses, and implement appropriate interventions for malnourished HD patients. Regular assessment of nutritional status and monitoring QoL should be integral components of standard management guidelines for HD patients, as ensuring quality assurance and continuous improvement are essential. It has been demonstrated that Health-related Quality of Life (HRQoL) significantly influences dialysis outcomes. Therefore, prioritizing both the duration and QoL for HD patients is paramount.[3]

Many factors are associated with the incidence of malnutrition in HD patients. However, in general, they can be divided into two categories. Firstly, dialysis-induced iatrogenic factors include chronic inflammation, catabolic effects of HD, loss of nutrients through the dialysis membrane, and inadequate HD, which can result in uremia and metabolic acidosis. These conditions can cause symptoms such as anorexia, nausea, and impaired food absorption.[4] Secondly, non-iatrogenic factors include poor appetite status, high monotonous eating pattern index, low diet quality, psychosocial and financial barriers,[5] lack of family support, changes in appetite, lack of knowledge,[6] and lack of physical activity.[7] Additionally, malnutrition must be considered before initiating HD treatments for patients, as it can manifest as metabolic disorders due to a progressive decrease in glomerular filtration rate, delays in access to a nephrologist, and inadequate pre-dialysis dietary care. Given the complexity of factors associated with malnutrition in HD patients, nutritional interventions should address multiple aspects. Studies by Decsa et al. and Satriyo et al., published in this journal, revealed that interventions focusing solely on one aspect, such as providing parenteral nutrition, have no impact on improving nutritional status.

In addition to frequent malnutrition, the QoL of HD patients decreases, both due to malnutrition and other reasons. Numerous studies have revealed a close relationship between malnutrition and low QoL in HD patients.[2, 8, 9]

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However, the critical aspects of QoL are extensive and complex, including employment, housing, schooling, neighborhood, cultural aspects, values, and spirituality. Health is widely regarded as one of the most critical domains of QoL. Health-related QoL encompasses various aspects related to physical, mental, emotional, and social functioning.[10] The US Food and Drug Administration (FDA) defines HRQoL as 'a multi-domain concept that represents a patient's general perception of the impact of a disease and its treatment on physical, psychological, and social aspects of life'.[11] HRQoL pertains to the physical, psychological, and social health domains unique to each individual,[12] which objective assessments and subjective perceptions of health can measure. Subjective perceptions include physical, psychological, and social health dimensions assessed by the patient, which are influenced by the individual's beliefs, life experiences, personality, and expectations.[13] Physical health dimensions (e.g., disability) can be assessed 'objectively' and provide information about the 'health status' or 'function' of the patient. HRQoL, on the other hand, assesses how the presence of physical symptoms of a disease affects a person's well-being, life satisfaction, or overall QoL. Based on this distinction, two individuals with the same physical health or disease severity can have significantly different HRQoL

How can QoL be improved in patients undergoing hemodialysis?

In principle, it is essential to assess each patient's QoL first by collecting comprehensive information to identify those who have or are at high risk of experiencing a decrease in HRQoL. This information forms the basis of clinical decision-making, rehabilitation, and individual patient management.[14] Conditions that can improve QoL are promoted, while those that worsen it are minimized or eliminated. Providing education and counseling to patients and families to increase awareness about the disease, as well as self-care activities, treatment options, complications, and rehabilitation programs can help patients lead productive lives. Management strategies may involve exercise training and addressing issues such as malnutrition, depression, anemia, and hormonal imbalances. Studies among elderly dialysis patients have demonstrated that growth hormone supplementation can improve muscle performance and HRQoL.[15] A study by Saffira et al., published in this journal, demonstrates the significant influence of physical exercise on increasing physical function, physical role, reducing physical pain, increasing vitality, and enhancing the general health of HD patients. Other studies have similarly shown that physical exercise can improve HD patients' functional capacity, respiratory muscle strength, and overall QoL.[16] Based on these results, integrating physical exercise should be a routine component of HD therapy to improve patients' QoL.[17]

Ultimately, Quality of Life Therapy (QoLT) is the only cognitive-behavioral treatment designed to enhance life satisfaction and happiness across various domains (such as self-esteem, relationships, and pleasurable activities) to improve overall QoL.[18] Improving the QoL in HD patients is the primary aim of kidney replacement therapy. The World Health Organization also emphasizes the significance of the patient's subjective perception of life within their values, standards, goals, and expectations.

Declarations

Competing interest

The author declares no conflict of interest.

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Original Article

The Administration of Intradialytic Parenteral Nutrition Does Not Affect the Anemia Status of Chronic Kidney Disease Patients Undergoing Hemodialysis

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ABSTRACT

Background: Hemodialysis (HD) patients are susceptible to malnutrition, and there is a close relationship between malnutrition and the incidence of anemia. Parenteral nutrition plays a role in treating malnutrition.
Objective: This study aims to determine the effect of parenteral nutrition on anemia in HD patients.
Methods: Quasi-experimental research which is part of the nutritional research tree at the Hemodialysis Unit of RSUP Dr. Soetomo Surabaya for 3 months. A total of 45 malnourished CKD patients (SGA B & C) undergoing routine HD were included in this study (n=26 received regular diet & education, n=17 received regular diet, education and intradialytic parenteral nutrition, and n=2 dropped out of education due to blood transfusion). Measurements of body mass index (BMI), hemoglobin (Hb), serum iron (SI), and total iron binding capacity (TIBC) were carried out before and 8 weeks after therapy. Between groups used the Mann-Whitney test, while pre and post used the Wilcoxon matched-pairs sign rank test.
Results: The treatment group was older than the control group. There was no difference in duration of HD between groups. Intradialytic parenteral nutrition had no effect on BMI (24.71±3.939 vs 24.71±4.026; p=0.3802), Hb (9.746±1.309 vs 9.162±1.960; p= 0.3525), SI (62.33±34.74 vs. 53.78±24.89; p=0.3594), and TIBC (242.8±119.0 vs. 197.3±43, 65; p=0.4258).
Conclusion: In HD patients, intradialytic parenteral nutrition for 8 weeks did not affect Hb, SI and TIBC levels. Long-term observations with larger samples are needed to confirm these findings.
Keywords: chronic kidney disease, anemia, parenteral nutrition, hemodialysis, nephrology.

Introduction

Anemia in Chronic Kidney Disease (CKD) is one of the complications that increases the risk of morbidity and mortality. The severity of anemia in CKD exacerbates particularly when patients progress to end-stage renal disease requiring kidney replacement therapy such as dialysis. The causes of anemia in CKD patients undergoing dialysis are multifactorial, including blood loss during medical procedures (dialysis, blood sampling), erythropoietin hormone deficiency, iron deficiency, inflammation, and malnutrition.[1] CKD patients undergoing hemodialysis are highly susceptible to malnutrition due to inadequate protein and calorie intake.[2] Chronic malnutrition, as we know, also exacerbates inflammation. If this continues unabated, it creates a vicious cycle where patients repeatedly undergo blood transfusions, which also carry a risk of transfusion-related infections.[3]

Nutritional improvement in CKD patients undergoing hemodialysis is crucial to break the vicious cycle and is expected to mitigate inflammation and improve nutritional status, thereby gradually improving anemia conditions.[4]

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The most fundamental approach to nutritional improvement in CKD patients undergoing hemodialysis involves diet and nutrition education by physicians and dietitians, although it takes time to achieve optimal results and requires the involvement of patients and their families.[5] Another method of nutritional improvement is through the use of parenteral nutrition during hemodialysis, especially for those who cannot tolerate oral or enteral intake due to symptoms such as nausea, vomiting, or anorexia. Previous research has shown that parenteral nutrition improves nutrition, albumin levels, BMI, and transferrin status.[3,6,7] In this study, the researchers aimed to investigate the relationship between intradialytic parenteral nutrition administration and the anemia status in CKD patients undergoing hemodialysis.

Methods

Design and participants

The research sample consisted of all CKD patients aged 21 to 60 years undergoing long-term routine hemodialysis at the hemodialysis unit of Dr. Soetomo Hospital, Surabaya. Inclusion criteria included patients with SGA category B and C scores and serum albumin levels < 3.8 g/L. Exclusion criteria encompassed unstable CKD patients, history of allergies, chronic infections and sepsis, edema, and malignancies. All research samples received the same regular diet and nutrition education. Patients receiving treatment had intradialytic parenteral nutrition administered during their scheduled dialysis sessions. The composition of the parenteral nutrition included a solution of crystalline amino acids 8.5% 500 ml (42.5 grams) with 50% dextrose 250 ml (125 grams) that could be supplemented with lipid emulsion 20% 250 ml (50 grams), electrolytes, and vitamins as needed. The parenteral nutrition was infused through a venous drip chamber during dialysis, initiated 30 minutes after HD commencement and continued throughout HD. In this study, we used a solution containing 25 grams of dextrose (250 ml D10%) and 28.8 grams of amino acids. The collected data included age, gender, duration of dialysis, body mass index (BMI), hemoglobin levels, serum iron (SI), and total iron-binding capacity (TIBC).

Statistical analysis

The data were collected and analyzed using SPSS version 25. Descriptive data included age, gender (male and female), and duration of hemodialysis. Subsequently, the observations of CKD patients undergoing hemodialysis, both those receiving intradialytic parenteral nutrition and those who did not, will be analyzed using the Mann-Whitney test (comparison between test groups) and the Wilcoxon matched-pairs signed-rank test (pre- vs. post-intervention).

Results

A total of 45 CKD patients with malnutrition (SGA B & C) undergoing routine hemodialysis at the Hemodialysis Unit of Dr. Soetomo Hospital, Surabaya, met the predefined inclusion criteria. Subsequently, 26 patients received regular diet and education (i.e., the control group), 17 patients received regular diet, education, and intradialytic parenteral nutrition (i.e., the treatment group), while 2 patients were excluded from the study due to requiring blood transfusions during the study period. Measurements of BMI, Hb levels, serum iron (SI), and TIBC were conducted on all samples in both test groups before and 8 weeks after the administration of intradialytic parenteral nutrition. The baseline data from both test groups showed that the treatment group was older than the control group (51.41±6.083 vs. 44.46± 9.118 years, p=0.0124), and there were more male patients than females (n=15/11 in the control group and n=9/8 in the treatment group). In the control group, no patients had diabetes mellitus (0%), while 15 out of 17 patients in the treatment group had diabetes mellitus (88%). In the control group, 22 out of 26 patients had hypertension (85%), while 8 out of 17 patients in the treatment group had hypertension (47%). There was no difference in the duration of hemodialysis between the two study groups (47.69±30.68 and 36.82±28.11 months,

respectively, in the control and treatment groups; p=0.2318).

Examination of vital signs in both study groups did not show statistically significant differences. For instance, the mean pulse rate of patients in the control and treatment groups were 87.38±4.392 and 87.47±4.064 beats/minute, respectively (p=0.9361). Similarly, systolic and diastolic blood pressure in both groups also did not exhibit significant differences (mean systolic: 143.8±14.99 vs. 145.3±14.19 mmHg, p=0.8205; median diastolic: 85.00 [IQR 77.50-90.00] vs. 90.00 [IQR 80.00-90.00], p=0.5317). The mean baseline BMI of patients in the control and treatment groups were 22.73±3.655 and 24.71±3.939, respectively (p=0.0976). Initial Hb levels also did not differ significantly between the control (9.227±1.654) and treatment (9.435±1.572) groups with a p-value of 0.6986. Similarly, the comparison of median SI at the beginning of the study did not show statistically significant differences with a median of 57.50 [IQR 43.25-81.25] in the control group and 50.00 [IQR 39.00-74.00] in the treatment group (p=0.3851). Likewise, the comparison of median TIBC at the beginning of the study did not show statistically significant differences with a median of 191.5 [IQR 147.8- 255.8] in the control group and 226.0 [IQR 180.0-290.5] in the treatment group (p=0.1757).

The observation results over 8 weeks in both study groups indicated that the administration of intradialytic parenteral nutrition did not affect BMI (24.71±3.939 before vs. 24.71±4.026 after; n=17; p=0.3802), Hb levels (9.746±1.309 before vs. 9.162±1.960 after; n=13; p=0.3525), serum iron (SI) levels (62.33±34.74 before vs. 53.78±24.89 after; n=9; p=0.3594), and total iron-binding capacity (TIBC) (242.8±119.0 before vs. 197.3±43.65 after; n=9; p=0.4258).

Discussion

In this study, the treatment group was older compared to the control group, and there Additionally, researchers were unable to observe the patients' food intake at home.[6,10]

were more male participants than females in both groups. Additionally, there was no difference in the duration of dialysis between the two groups. Moreover, physical examinations did not show any differences between the two groups. This finding is consistent with previous research conducted by Cano *et al*.[6]

In the treatment group, after the administration of intradialytic parenteral nutrition for 8 weeks, there was no significant increase in BMI. This finding is consistent with studies by Czekalski and Cano, which found no increase in BMI following intradialytic parenteral nutrition.[6,8] However, this contrasts with the study by Kittiskulnam, which reported an improvement in BMI after 3 months of intradialytic parenteral nutrition.[7] BMI in hemodialysis patients is influenced by various factors such as dietary intake, uremic condition, physical activity, and fluid accumulation between dialysis sessions.[9] In this study, the physical activity of patients and dietary intake did not differ pre and post-treatment. Additionally, there were no significant clinical symptoms of uremia during the study. The use of parenteral fluids may also vary between research centers.

The hemoglobin levels also did not show significant differences before and after the administration of intradialytic parenteral nutrition for 8 weeks. The hemoglobin values remained around 9. This finding is consistent with the study by Cano.[6] Similarly, there were no significant changes in serum iron (SI) and total iron-binding capacity (TIBC) values before and after the administration of intradialytic parenteral nutrition for 8 weeks. This condition is similar to the findings of the study conducted by Lu & Marsen,[9,10] where there was no improvement in SI and TIBC during the study. Despite all patients receiving monthly erythropoietin therapy in this study, there was still no improvement in hemoglobin levels. All research samples received the same regular diet and education. This could be related to the short duration of the study and possibly the socioeconomic status of the dialysis patients, who may be of lower economic status.

Conclusion

From the results of intradialytic parenteral nutrition administration over 8 weeks, there was no significant effect on Hb, SI, and TIBC levels in CKD patients undergoing hemodialysis. Longer-term observation with a larger sample size is needed to confirm these findings.

Limitations of the Study

This study may not fully reflect the entire population as it was conducted at a single healthcare center with a limited sample size. Additionally, the duration of the study was short, which may have impacted the nutritional improvements, as such improvements typically require more time.

Declarations

Competing interests

The authors declare no conflict of interest.

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Author's Contribution

Idea/concept: DMH, ADPN, AT, W, P. Design: DMH, ADPN, AT, W, P. Control/supervision: DMH, ADPN, AT, W, P. Data collection/processing: DMH, ADPN, AT, W, P. Extraction/Analysis/interpretation: DMH, ADPN, AT, W, P. Literature review: DMH, ADPN, AT, W, P. Writing the article: DMH, ADPN, AT, W, P. Critical review: DMH, ADPN, AT, W, P. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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Original Article

Providing Intradialytic Parenteral Nutrition Therapy Does Not Improve Anthropometric Status in Hemodialysis Patients with Malnutrition

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ABSTRACT

Background: Malnutrition is prevalent among hemodialysis patients and significantly impacts prognosis. It can result from reduced food intake and protein loss during hemodialysis. Nutritional status is determined through anthropometric examinations, which include upper arm circumference (UAC), body mass index (BMI), hand grip strength, bicep, and tricep fold thickness. Laboratory examinations such as total cholesterol and Malnutrition Inflammation Score (MIS) or Subjective Global Assessment (SGA) are also utilized. Intradialytic Parenteral Nutrition (IDPN) is expected to maintain or improve the nutritional status of hemodialysis patients.
Objective: To assess the impact of parenteral nutrition therapy on the anthropometric status of malnourished hemodialysis patients
Methods: This cross-sectional study, a sub-analysis of a larger nutritional therapy study, involved 24 hemodialysis patients experiencing malnutrition based on SGA B and C criteria, with 1-10 years of hemodialysis. IDPN therapy was provided, and anthropometric measurements, as well as total cholesterol levels, were taken at baseline and three months after the initiation of nutritional therapy. Data processing utilized comparative statistical analysis.
Results: The mean age was 45.33 years, with 14 males and 10 females. After 3 months, there were no significant differences in UAC (mean difference = 0.13; $p = 0.69$), BMI (mean difference = 0.13; $p = 0.50$), hand grip strength (mean difference = -0.96; $p = 0.282$), biceps skinfold thickness (mean difference = 0.13; $p = 0.69$), triceps skinfold thickness (mean difference = 0.59; $p = 0.134$), or total cholesterol (mean difference = -1.5; $p = 0.71$).
Conclusion: Three months of IDPN therapy did not improve the anthropometric status of malnourished hemodialysis patients.
Keywords: hemodialysis, intradialytic parenteral nutrition, anthropometry, chronic kidney disease.

Introduction

Patients undergoing hemodialysis (HD) frequently experience protein-energy malnutrition. The causes of protein-energy malnutrition are varied, although there is agreement on the need to assess nutritional status in HD patients using non-standard methods. Additionally, in patients with chronic kidney disease (CKD), low-grade chronic inflammation occurs, exacerbating the condition and further increasing the degree of malnutrition.[1, 2]

Anthropometric status is a key parameter for measuring improvements in malnutrition. Common anthropometric measurements used to evaluate improvements in

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malnutrition conditions include body mass index (BMI), body weight, hand grip strength, upper arm circumference, calf circumference, bicep and triceps skinfold thickness, among others. Numerous studies demonstrate that nutritional therapy can enhance the anthropometric status of HD patients.[1, 3-5]

Nutritional therapy for HD patients may involve counseling, oral supplementation, or intradialytic parenteral therapy (IDPN). Counseling therapy educates patients on managing their diet independently. Oral supplementation may include providing additional nutrients in the form of solid or liquid supplements. IDPN is administered intravenously to patients unable to tolerate enteral or oral nutrition due to gastrointestinal tract malfunction, vomiting, chronic nausea, anorexia, or those who have not responded to counseling and oral therapy.[2, 6]

Previous research suggested that IDPN did not improve the patients' clinical condition. However, contrasting findings from other studies indicated improvements in patients' quality of life and pre-albumin levels after four weeks. Few studies have linked IDPN with improvements in anthropometric status. [4,7-10] This study aimed to examine the effects of intradialysis parenteral nutrition therapy on several anthropometric parameters.

Methods

Design and participants

This cross-sectional study was a sub-analysis of a larger study conducted in 2020, investigating the provision of nutritional therapy to HD patients. It involved 24 HD patients experiencing malnutrition according to Global Assessment (SGA) B and C criteria, with a HD duration ranging from 1 to 10 years. IDPN therapy was administered to these patients, and their anthropometric status was assessed using measurements of upper arm circumference (UAC), BMI, hand grip strength, biceps and triceps skinfold thickness. Total cholesterol levels were measured through laboratory tests. Anthropometric measurements were taken at baseline and three months after nutritional therapy initiation. All patients provided informed consent before receiving nutritional therapy. This study adhered to the guidelines of Dr. Soetomo (Approval No: 0090/KEPK/XI/2020).

Statistical analysis

Statistical analysis for this study utilized SPSS version 24.0 software (Chicago, IL, USA) for data analysis. Descriptive statistics include categorical variables reported as percentages (n, %) and continuous variables presented as mean and standard deviation (mean, SD). Comparative statistical analysis was conducted using paired t-tests for normally distributed data. Alternatively, the Wilcoxon test was employed for non-normally distributed data.

Results

Patient characteristics revealed an average age of 45.33 years, with 14 males and 10 females included in the study. Among them, 10 patients reported eating three times a day, while 12 patients had a frequency of two meals per day, and only 2 patients reported eating once a day. The average dietary calorie intake was 16,490.60 kcal. The average systolic blood pressure was 144 mmHg, with a diastolic blood pressure of 82.08 mmHg, and an average duration of HD of 49.88 months. The initial mean values for anthropometric status were as follows: upper arm circumference = 25.25 cm; BMI = 23.23; hand grip strength = 22.67 kg; triceps skinfold thickness = 8.10 mm; biceps skinfold thickness = 4.52 mm (Table 1).

Table 1. Characteristics of patients receiving parenteral intradialytic nutritional therapy

	Total	Minimal	Maximum	Mean	Std. Deviation
Age	24	28	58	45.33	8.92
Sex					
Male	14				
Female	10				

Eat frequency					
1x	2				
2x	12				
3x	10				
Calori of diet	24	771,10	2390,60	1649,60	430,22
Duration HD month)	24	7	120	49,88	30,67
Heart Rate	24	78,00	96,00	87,33	4,57
Systolic blood pressure (mmHg)	24	110,00	170,00	144,16	15,29
Diastolic blood pressure (mmHg)	24	70,00	90,00	82,08	8,33
UAC(cm)	24	15,50	34,00	25,25	3,96
SfT tricep (mm)	24	2,20	16,50	8,10	4,21
SfT bicep (mm)	24	1,30	10,90	4,52	3,04
Handgrip strength (kg)	24	9,70	37,20	22,67	7,62
BMI early	24	13,27	33,20	23,23	4,39
Cholesterol (mg/dl)	24	76,00	230,00	161,42	33,66

All parameters, including UAC, BMI, hand grip strength, biceps and triceps skinfold thickness, and total cholesterol, were normally distributed. Statistical analysis utilized paired t-tests. Following the administration of IDPN therapy for 3 months, there were no significant differences observed in UAC (mean difference = 0.13; p = 0.69), BMI (mean difference = 0.13; p = 0.50), hand grip strength (mean difference = -0.96; p = 0.282), biceps skinfold thickness (mean difference = 0.13; p = 0.69), triceps skinfold thickness (mean difference = 0.59; p = 0.134), and total cholesterol (mean difference = -1.5; p = 0.71) (Table 2 and Figure 1).

Table 2. Differences in pre and post-anthropometric status 3 months after IDPN nutritional therapy

Parameter	***Mean Difference***	***Std. Deviation***	***p-value***
UAC 3rd month (cm) - UAC early(cm)	0,13	1,51	0,69
BMI 3rd month - BMI early	0,13	0,92	0,50
Handgrip strength 3rd month (kg) - Handgrip strength early (kg)	-0,96	4,26	0,28
SfT tricep 3rd month (mm) - SfT tricep early (mm)	0,59	1,85	0,13
SfT bicep 3rd month (mm) - SfT bicep early (mm)	0,13	1,51	0,69
Cholesterol 3rd month (mg/dl) - Cholesterol early (mg/dl)	-1,50	19,59	0,71

UAC: upper arm circumference; SfT: skinfold thickness; BMI: body mass index

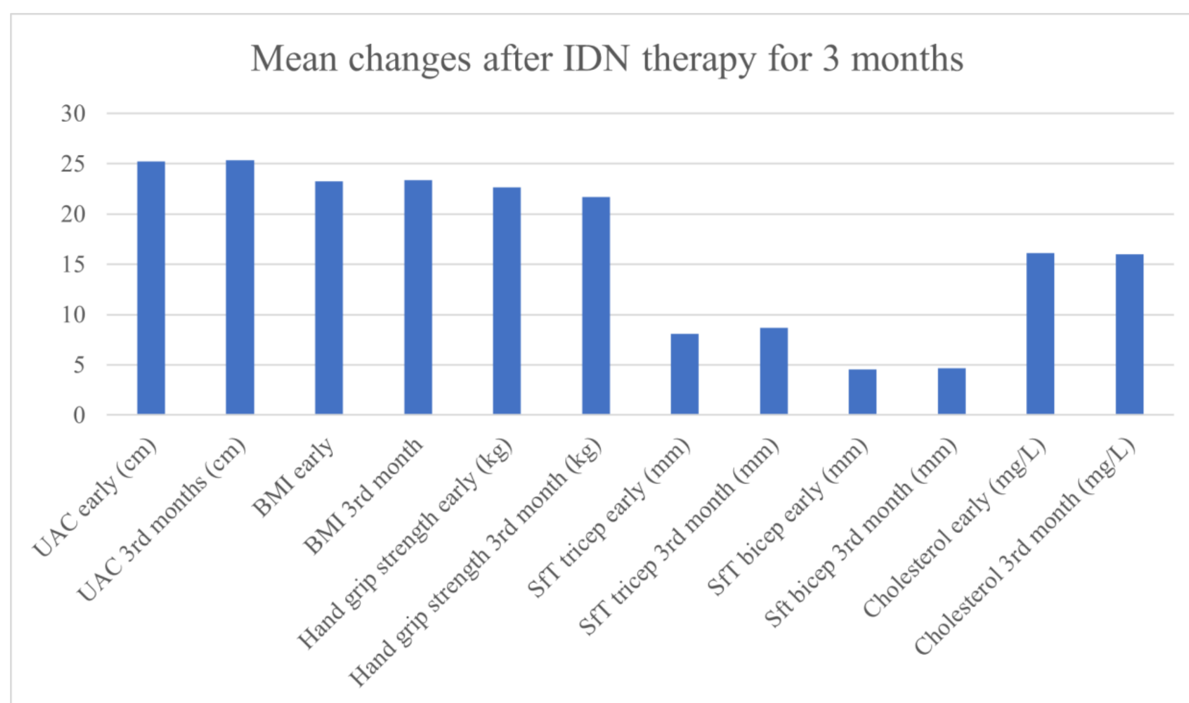

Figure 1. Changes in anthropometric status after giving IDPN therapy for 3 months

Discussion

Nearly 400,000 individuals in the United States with stage 5 CKD undergo chronic HD, facing a high annual mortality risk of 20-25%. Although cardiovascular disease is the leading cause of mortality in CKD patients, traditional cardiovascular risk factors like hypertension or hypercholesterolemia do not seem to significantly influence their mortality. Instead, insufficient protein intake, low serum albumin, weight loss, or a low BMI serve as significant indicators of high mortality risk in chronic HD patients.[12]

CKD patients often experience malnutrition, known as protein-energy wasting (PEW), due to various factors. To prevent uremia, CKD patients are typically advised to follow a low-protein diet, consuming around 0.8 grams per kilogram of body weight. Additionally, chronic inflammation present in CKD patients further contributes to PEW. During chronic HD, there is a loss of albumin and amino acids during the intradialytic process. [13, 14]

Due to its association with increased mortality risk in CKD patients, interventions aimed at improving nutritional status have the potential to enhance survival rates.

Hypoalbuminemia is commonly used as a marker for PEW in dialysis patients and is strongly correlated with mortality. IDPN, a recognized intervention for providing parenteral nutritional support during HD sessions, emerges as a potential strategy for addressing PEW conditions, particularly intradialytic hypoalbuminemia. [12]

A study by Goldstein et al. illustrated the effectiveness of IDPN in addressing organic causes of PEW among young adult and adolescent patients undergoing chronic HD. The advantage of using IDPN lies in its significant protein content, supplying 37%-42% of protein intake compared to the recommended 10% of protein from the total weekly calorie intake.[13] Research by Capelli et al. in 1994 demonstrated that the therapy group, compared to the control group, exhibited an increase in body weight. During 8 months of nutritional therapy, the therapy group showed a weight increase to 157.3 ± 40 lbs, which further continued to rise to 168.7 ± 44 lbs by the 12th month.[15,16]

Different findings emerged when comparing the effectiveness of IDPN, oral supplementation, and counseling nutritional

interventions. Compared to oral supplementation, IDPN did not show a positive impact on patient quality of life or nutrition. The French Intradialytic Nutrition Evaluation Study (FineS), a randomized controlled trial involving 186 malnourished chronic HD patients, found that one year of IDPN administration did not increase mortality rates, hospitalization rates, or reduce quality of life. In two randomized controlled trials (RCTs) examining IDPN, no significant differences were observed in improvements in BMI, serum prealbumin, serum albumin, or subjective global assessment (SGA) scores compared to oral supplementation. However, the results of these studies were limited by small sample sizes and non-compliance, with discontinuation rates ranging from 19% to 26% for oral supplements and 24% for IDPN. Additionally, there were differences in participant numbers between groups, with 17% discontinuation in the control group compared to 0% in the IDPN group. The only significant improvement in nutritional markers was observed in a small prospective cohort study (N = 20) conducted in Turkey, which reported a substantial increase in serum albumin after 4 months among patients receiving IDPN instead of oral supplements. However, this study did not directly compare intervention and control groups and was limited by lack of compliance (40% of patients switched from oral supplements to IDPN due to noncompliance) and no statistical adjustment for bias variables.[17]

A single RCT involving 107 chronic HD patients compared 16 weeks of IDPN with patients receiving 'regular dietary behavior' consultations. All patients received nutritional consultation at baseline. However, the study found that IDPN did not consistently lead to improvements in patient health or nutrition. At 4 weeks, patients receiving IDPN showed a 15% increase in serum prealbumin compared to controls (41% IDPN vs. 20.5% controls, P = 0.0415). Nevertheless, the significance of this finding is uncertain since, when considering its relation to clinical outcomes, a 15% increase remains relatively insignificant. The mean increase in serum prealbumin (26.31 mg/L) at 16 weeks did not meet the >30 mg/L threshold associated with reduced mortality, as found in Cano 2007 (48.7% vs. 31.8%, P = 0.1164). IDPN did not improve clinical outcomes regarding death (26.4% vs. 12.9%, P = 0.09), hospitalization (hospitalization rate: 59% vs. 43.2%, P = 0.15), or quality of life (change SF-12 score: -2.74 vs. 0.34, P = 1.1175). Additionally, this study has significant limitations due to its small sample size, indirect results, and lack of information about the types of interventions received by the control and potential co-intervention groups.[17]

In general, IDPN has shown to reduce mortality risk and improve mean scores on nutritional outcomes compared to the standard of care (SOC) for CKD patients. In the largest non-randomized study, the effect of IDPN on 1-year mortality was found to depend on baseline serum albumin levels. Patients with lower baseline serum albumin (≤ 3.3 g/dL) exhibited a decreased mortality rate when receiving IDPN (OR 0.61-0.72; P < 0.01). Conversely, patients with higher baseline serum albumin (>3.3 g/dL) showed either the same or increased odds of death compared to controls (OR 0.85; P = 0.10 – 2.6; P < 0.005). A smaller non-randomized study (N = 81) with a baseline serum albumin of 3.02 g/dL reported improved survival with IDPN. However, a single RCT involving 40 chronic HD patients with refractory anemia found no improvement in nutrition-related functional capacity with IDPN treatment compared to usual care. While many studies have reported improvements in mean scores across various nutritional outcomes compared to usual care, none have provided data on the proportion of patients achieving clinically significant improvements in nutritional outcomes. These studies were limited by small sample sizes (all but one with N < 100), lacked information on intervention adherence, and did not perform statistical adjustments for variable bias.[17]

A study conducted in Taiwan by Tsai et al. involving approximately 10,000 CKD patients found that changes in body composition in peritoneal dialysis (PKG) patients influenced hs-

CRP levels. CKD patients with a BMI < 23 or BMI > 23 subgroups with lower eGFR values exhibited higher hs-CRP levels compared to those with higher eGFR values. These findings suggest that improving the nutrition of CKD patients can influence body composition and potentially reduce the chronic inflammatory process.[18]

Providing nutritional therapy to HD patients can supply adequate protein and energy to enhance their nutritional status. Increases in bicep and tricep fold thickness are indicative of improved muscle mass, suggesting enhanced activity status and quality of life for HD patients. However, Demirci et al. reported no change in muscle mass following IDPN administration. It's worth noting that the response to nutritional intervention may also be influenced by the patient's inflammatory status and age.[19]

Our study's results indicated that within 3 months, IDPN did not lead to improvements in the participants' anthropometric status. However, our study was limited by the small sample size and focused solely on evaluating the anthropometric status improvement among IDPN chronic HD patients without comparison to other nutritional therapies. Future research should consider extending the observation period to at least 6 months and examining mortality rates following various nutritional interventions.

Conclusion

IDPN did not improve the anthropometric status of HD patients with malnutrition after 3 months of administration.

Limitations of the Study

The limitation of this study is that the observational period of IDPN therapy is short, only three months. Therefore, further research on nutritional therapy to improve the anthropometric status of hemodialysis patients within six months is necessary. Second, IDPN therapy in hemodialysis patients must be matched to make the comparison between groups more equal.

Declarations

Ethics approval and consent to participate

All patients in this study signed informed consent before being given nutritional therapy. This study follows Dr. Soetomo (No: 0090/KEPK/XI/2020).

Competing interests

There is no conflict of interest.

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Author's Contribution

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Original Article

Profile of Anemia and the Relationship between Hemoglobin Levels and Quality of Life in End-Stage Chronic Kidney Disease Patients undergoing Chronic Hemodialysis at Hasan Sadikin Hospital 2021-2022

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ABSTRACT

Background: Anemia is a common complication of Chronic Kidney Disease (CKD). The severity of anemia has implications for patients' quality of life.
Objective: This study aims to determine the profile of Anemia and the relationship between Hemoglobin (Hb) levels and the quality of life of end-stage CKD patients undergoing chronic Hemodialysis.
Methods: This study is analytical observational research with a cross-sectional design approach to explore the correlation between Hb levels and the quality of life of routine Hemodialysis patients at Hasan Sadikin Hospital, Bandung, throughout 2021-2022. Hb levels were continuous data. The quality of life of CKD patients was measured using the Indonesian version of the KDQOL questionnaire based on eight components. The obtained data were statistically analyzed using Spearman's Rank correlation.
Results: This study had 150 subjects, 75 male (50.0%) and an average age of 45. The most common etiology of CKD was hypertensive nephrosclerosis (52.7%). The average Hb level was 9 g/dL. The highest quality of life score was 68, and the lowest was 41.28, with a median of 50.99. The correlation analysis results showed an r of -0.157 and p of 0.057, indicating a very weak negative correlation that is not statistically significant.
Conclusion: The study's conclusion indicates no relationship between Hb levels and the quality of life of end-stage CKD patients undergoing chronic Hemodialysis.
Keywords: anemia, hemodialysis, quality of life.

Introduction

Chronic Kidney Disease (CKD) is one of the significant global health issues today. According to the United States Renal Data System, the prevalence of chronic kidney disease worldwide increases by 20-25% each year, estimating that 1 in 10 people worldwide has CKD.[1] The Indonesian Renal Registry (IRR) 2020 report noted a rise in the number of patients undergoing Hemodialysis, with 135,486 recorded in 2018, increasing to 185,901 in 2019, and declining to 130,931 in 2020. Hemoglobin (Hb) levels, as per the IRR 2020, showed a more significant number of cases with Hb < 10 gr/dl at 110,074.81%, while Hb levels ≥ 10 gr/dl accounted for 26,385.19%.[2]

CKD is characterized by kidney damage or decreased glomerular filtration rate (GFR) <60 ml/min/1.73m² for ≥ three months. CKD results in a progressive and irreversible decline in kidney function, necessitating ongoing renal replacement therapy such as dialysis or kidney transplantation.[3]

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Anemia is a common complication of CKD, primarily caused by a relative decrease in erythropoietin production that is not commensurate with the degree of Anemia. Other contributing factors to Anemia in CKD include shortened red blood cell lifespan, iron deficiency, secondary hyperparathyroidism, and infection inflammation. There is currently no national epidemiological data regarding Anemia in CKD in Indonesia. At Dr. Cipto Mangunkusumo Hospital Jakarta, in 2010, Anemia was found in 100% of new patients undergoing Hemodialysis, with an average Hemoglobin of 7.7 gr/dl.[4] Anemia leads to increased morbidity, mortality, and hospitalization rates. Additionally, it diminishes quality of life, reduces systemic hemodynamic capacity and cardiac function, increases the incidence of left ventricular hypertrophy, and impairs cognitive and sexual function. Several studies have demonstrated a strong association between Anemia and the progressive decline in kidney function.[4]

Assessment of quality of life plays a crucial role in the management of CKD patients receiving renal replacement therapy. Conducting a quality-of-life assessment before CKD patients undergo dialysis can assist doctors in selecting the appropriate type of dialysis, such as Hemodialysis or peritoneal dialysis, based on clinical indications and the patient's physical, psychological, and social conditions. The results of quality-of-life measurements can be used to evaluate the appropriateness of the therapy provided and the outcomes of healthcare efforts from the patient's perspective. Quality of life is subjective regarding the patient's feelings about their condition and the treatment they receive.[5] This research investigates the anemia profile and the relationship between hemoglobin (Hb) levels and the quality of life of CKD patients undergoing chronic hemodialysis.

Methods

Design and participants

The research design is an analytical observational design with a cross-sectional approach. This study was conducted at the Hemodialysis Installation of Hasan Sadikin Hospital in Bandung for a period of 1 year, from May 2021 to May 2022. The population of this study consists of CKD patients undergoing chronic Hemodialysis. The sample of this study comprises CKD patients with Anemia undergoing chronic Hemodialysis who meet the inclusion and exclusion criteria.

Data Collection

Inclusion criteria are CKD patients undergoing chronic hemodialysis as outpatients, aged >18 years, able to read and write, understand Bahasa Indonesia, willing to participate in the study, and signing the informed consent form voluntarily. Exclusion criteria in the study are patients with impaired consciousness such as somnolence, sopor, and coma, patients with oral communication disorders, and CKD patients undergoing chronic Hemodialysis as inpatients. The study variables consist of independent variables, namely Hb, and dependent variables, namely quality of life. The sampling in this study involves selecting all CKD patient subjects undergoing regular Hemodialysis in the Hemodialysis Installation of Hasan Sadikin Hospital in Bandung based on inclusion criteria. Research data were obtained by reviewing patients' medical records and completing questionnaires. General characteristic data such as gender and etiology of chronic kidney disease are presented on a categorical scale, while age data are presented on a numerical scale. The measured anemia profile data includes hemoglobin levels, transferrin saturation, serum iron, and TIBC (Total Iron Binding Capacity), categorized on a numerical scale. Quality of life data is measured using the Thirty-Six-item Kidney Disease Quality of Life (KDQOL-36) questionnaire, assessed based on eight components, and presented in numerical scale. The presentation of categorical scale data is in frequency with percentage. Numerical scale data are presented with mean and standard deviation if normally distributed, presented with median and minimum-maximum values if not normally distributed. Ethical approval for this study has been obtained from the ethics committee of Hasan Sadikin Hospital in Bandung.

Operational Definitions

Patients are considered anemic based on the measurement of Hb with a threshold of Hb<14 g/dL for males and Hb<12 g/dL for females.[4] Hemoglobin is a protein compound in red blood cells composed of globin chains and heme iron structures. Hb is a meta-protein of red blood cells that delivers oxygen throughout the body.[6] Quality of life is an individual's perception of their role in life according to cultural systems and values in their region. It relates to interests, life goals, aspirations, and standards to be achieved.[7]

Statistical analysis

The univariable analysis aims to describe the general characteristics and Anemia profile of CKD patients undergoing chronic Hemodialysis at Hasan Sadikin Hospital. Using Spearman's Rank correlation test, the bivariable analysis assesses the relationship between Hb and quality of life.

Results

This research was conducted at the Hemodialysis Installation of Hasan Sadikin Hospital in Bandung over one year, from May 2021 to May 2022. The study initially involved 172 respondents, but only 150 met the inclusion criteria.

Table 1. Characteristics Data of CKD Patients who have undergone Hemodialysis at RSHS Period 2021-2022.

Variable	Total
Age	
Mean±SD	44.78±14.46
Median (Min-Max)	45 (18-82)
Gender	
Male, n (%)	75(50)
Female, n (%)	75(50)
CKD Etiology	
Hypertensive Nephrosclerosis, n (%)	79(52.7)
Glomerulonephritis, n (%)	40(26.7%)
PNC, n (%)	7(4.7)
Diabetic Kidney Disease, n (%)	20(13.3)
Polycystic Kidney Disease, n (%)	2(1.3)
Unknown, n (%)	2(1.3)

Table 1 shows the general characteristics of CKD patients during the 2021-2022 period who have undergone chronic Hemodialysis, with a total of 150 patients. Based on the data above, the average age of the patients is 45 years old, with 75 male and 75 female patients. There were six recorded etiologies of CKD, dominated by hypertensive nephrosclerosis (52.7%).

Table 2. Characteristics of Anemia Profile in CKD Patients who have undergone Hemodialysis at RSHS Period 2021-2022

Variable	Total	Normality Test*
Hemoglobin		
Mean±SD	9.18±1.50	Normal (p=0,2)*
Serum Iron (µg/dL)		
Mean±SD	69.14±42.36	
Median (Min-Max)	55(18-256)	
TIBC Level (µg/dL)		
Mean±SD	198.96±14.46	
Median (Min-Max)	193.5 (41-289)	
Transferrin Saturation		
Mean±SD	43.43±62.19	
Median (Min-Max)	27.33(7.26-555.31)	

[a]Normality test using Kolmogorov-Smirnov test
**data are normally distributed*

Table 2 shows the characteristics of the Anemia profile of CKD patients in this study. The measured Anemia profile includes Hemoglobin, serum iron (Fe), TIBC levels, and transferrin saturation. Based on the data above, the patients' Hemoglobin levels are, on average, 9.18 with a standard deviation of ±1.50, and the data are normally distributed ($p>0.05$). The average Hemoglobin levels of the patients classify them as anemic according to male and female

Anemia criteria. The patients' serum iron levels are, on average, 69.14 with a standard deviation of ±42.36 and a median value of 55, with a minimum value of 18 and a maximum of 256. The patients' TIBC levels are, on average, 198.96 with a standard deviation of ±14.46 and a median value of 193.5, with a minimum value of 41 and a maximum of 289. The patients' transferrin saturation levels are, on average, 43.43 with a standard deviation of ±62.19 and a median value of 27.33, with a minimum value of 7.26 and a maximum of 555.31.

Table 3. KDQOL Score of Quality of Life in CKD Patients who have undergone Hemodialysis at RSHS Period 2021-2022

Variable	Median (Min-Max)	Normality Test*
Physical Functioning	60.91 (33-83)	
Emotional Role	100(50-100)	
Social Functioning	61.33(39-78)	
Physical Role	64(32-100)	
Pain Perception	45(20-82.5)	
Vitality	30 (16.67-63.33)	
General Health	44 (20-92)	
Mental Health	35(20-80)	
Total Score	**50.11 (40.92-67.28)**	0.001*

[a]Normality Test Kolmogorov-Smirnov
**data are not normally distributed*

Table 3 shows the KDQOL scores for each of the eight questionnaire components and overall. Based on the data above, the KDQOL scores for each element and total are not normally distributed ($p<0.05$). Overall, the KDQOL scores for patients in this study have a median value of 50.11, with a minimum value of 40.92 and a maximum value of 67.28.

Table 4. Correlation of Hemoglobin with Quality of Life Scores in CKD Patients who have undergone Hemodialysis at RSHS Period 2021-2022

	Quality of Life Score[a]	
	Correlation Coefficient r	p-value*
Hemoglobin (g/dL)	-0.130	0.057

[a]Spearman rank correlation test
**no significance (>0.05)*

Table 4 presents the correlation test results between Hemoglobin and quality of life scores in this study. Quality of life scores are not normally distributed, so the correlation analysis between Hemoglobin and quality of life scores was conducted using Spearman rank correlation. It was found that the correlation coefficient (r) is -0.157 (indicating a weak negative correlation), and the p-value is 0.057 (>0.05, not significant), meaning that the trend is negative; as Hemoglobin increases, quality of life scores decreases. However, the correlation strength is weak and insignificant, indicating no meaningful correlation or relationship. Like Figure 1, the scatterplot shows points scattered away from the curve, suggesting that the relationship between Hb and quality of life scores is weak or non-existent.

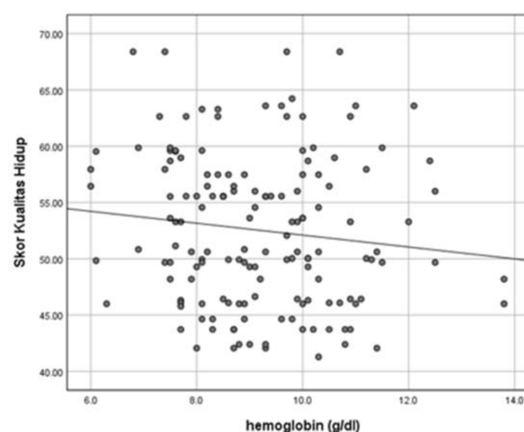

Figure 1. Scatterplot of Hemoglobin with Quality of Life Score

Discussion

This study obtained a sample of 150 patients with a mean age of 45. This is consistent with data from the Indonesian Renal Registry 2020, which shows that patients' second highest age distribution is in the 45-54 age group.

The kidney is a vital organ in the body responsible for excreting metabolic waste products, maintaining the balance of fluid and electrolytes in the blood, producing erythropoietin to stimulate red blood cell production, and synthesizing vitamin D.[8]

However, between the ages of 40 and 80, there is a decline in kidney function due to anatomical and physiological changes, including a 20% decrease in kidney mass, increased permeability of the filtration membrane, and gradual degeneration of the kidney tubules replaced by connective tissue.[9] physiological changes include electrolyte imbalance, decreased creatinine clearance, and decreased metabolites.[10] This results in most CKD patients being in the 50-59 age range. However, not only do aging processes contribute to kidney function decline, but it can also occur at younger ages due to other risk factors such as lifestyle, kidney diseases, and family history of diseases such as hypertension, diabetes mellitus, and kidney failure.[8]

The mean Hemoglobin level in the study subjects is classified as Anemia (9.18 g/dL) according to male and female Anemia criteria. Anemia is present in 80-90% of chronic kidney disease patients.[8] Renal Anemia is primarily caused by decreased erythropoietin production capacity. Other contributing factors to renal Anemia include iron deficiency (inadequate intake, repeated phlebotomy for laboratory testing, blood retention in dialysis or tubing, gastrointestinal bleeding), shortened erythrocyte lifespan, severe hyperparathyroidism, inflammation and infection, aluminum toxicity, folate deficiency, hypothyroidism, and Hemoglobinopathies.[4]

Many factors can be etiologies of Anemia in chronic kidney disease (CKD) patients. Types of Anemia based on possible etiologies found in CKD patients undergoing Hemodialysis include post-hemorrhagic Anemia, chronic disease Anemia, iron deficiency Anemia, and hemolytic Anemia. Iron deficiency Anemia in CKD consists of absolute iron deficiency Anemia when transferrin saturation (TS) is <20% and serum ferritin (SF) is <100 ng/mL (CKD-nonDialysis, CKD-Peritoneal Dialysis) and <200 ng/mL (CKD-HD). Functional iron deficiency Anemia occurs when TS is <20% and SF is ≥100 ng/mL (CKD-nonD, CKD-PD) and ≥200 ng/mL (CKD-HD). However, this study's Anemia profile results cannot determine the type of Anemia in CKD due to the lack of some data such as serum ferritin levels, erythrocyte morphology, reticulocyte count, leukocyte, and platelet levels.[4]

The analysis of KDQOL scores in CKD patients undergoing chronic Hemodialysis in this study on eight quality-of-life scales measured using the SF-36 questionnaire, namely physical function, emotional role, social function, physical role, pain, vitality, general health, and mental health, shows that most scales experience a decrease in KDQOL scores.[7] This is consistent with a study conducted by Anees (2011), where HD patients in Pakistan had poor quality of life, as seen from the decrease in physical, psychological, social, and environmental aspects.[11]

The results of the correlation analysis between Hb and quality of life obtained in the Hemodialysis Installation of Hasan Sadikin Hospital Bandung from May 2021 to May 2021 showed an r of -0.157 and p of 0.057, indicating a very weak negative correlation that is not statistically significant. Similar results were found by Nurchyati (2010) in a study of 95 respondents, which aimed to examine the relationship between Hb levels and quality of life. It was found that Hb levels were not associated with quality of life. These results are consistent with Ayoub et al.'s (2014) study on the relationship between Hb levels and quality of life using the SF-36 questionnaire in 130 respondents, which found that Hb levels were not associated with the total score of the SF-36 questionnaire.[12]

However, Haalen's (2020) study conducted in 7 countries on the relationship between Anemia and quality of life yielded different results, which found a relationship between severe Anemia and quality of life in CKD patients' daily lives.[13]

Conclusion

Based on the research findings and discussion, this study concludes that there is no relationship between Hb levels and the quality of life of patients with end-stage CKD undergoing chronic Hemodialysis.

Limitations of the Study

There are limitations to this study. The study was conducted only in one dialysis unit, leading to homogeneous subject characteristics and minimal variability. Further research in multiple dialysis units is needed to reduce bias in social and cultural aspects. Secondly, data collection was conducted through one-on-one interviews because subjects couldn't fill out questionnaires during hemodialysis treatment, potentially resulting in differences in subject interpretation of questionnaire questions. Thirdly, the type of anemia could not be determined due to the lack of examinations on serum ferritin levels, reticulocyte counts, and erythrocyte morphology.

Declarations

Ethics approval

This work was approved by the Medical Research Council [LB.02.01/X.6.5/406/2022].

Competing interests

There are no conflicts of interest.

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Author's Contribution

Idea/concept: SFH. Design: SFH. Control/supervision: AM, LS. Data collection/processing: SFH. Extraction/Analysis/interpretation: SFH. Writing the article: SFH. Critical review: AM, LS. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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Original Article

The Effect of Physical Exercise on Quality of Life in Chronic Kidney Disease Patients Undergoing Hemodialysis

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ABSTRACT

Background: Chronic kidney disease leads to a progressive and irreversible decline in kidney function, necessitating lifelong treatments such as dialysis or kidney transplantation. Patients undergoing hemodialysis (HD) often encounter challenges such as muscle weakness, which can frequently precipitate feelings of hopelessness and premature aging. These challenges can lead to medical, social, economic, and psychological issues that profoundly affect their quality of life.
Objective: This study aimed to determine the effect of physical exercise on the quality of life of patients undergoing HD.
Methods: This research was a correlational study using a cross-sectional approach. The population comprised chronic kidney disease patients undergoing HD at Anna Medika Hospital, Bekasi. There were 38 respondents who met the inclusion criteria. The analysis of the research data was conducted using the Wilcoxon test.
Results: The study yielded quality of life results after physical exercise, with both the good and moderate categories showing the same result of 47.4%, while the bad category had 5.3%.
Conclusion: There is a significant improvement in quality of life after physical training compared to before.
Keywords: quality of life, hemodialysis, chronic kidney disease.

Introduction

Chronic Kidney Disease (CKD) poses a growing global health challenge, as evidenced by increasing rates of incidence, prevalence, morbidity, and mortality. CKD is characterized by kidney damage and a decrease in glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m² for at least 3 months.[1] According to a survey by the Indonesian Nephrology Association, the prevalence of CKD in Indonesia is relatively high, at around 44.2%. This is often associated with various comorbidities, including diabetes mellitus and hypertension.[2]

Renal Replacement Therapy (RRT) can take the form of dialysis or kidney transplantation. There are two primary options for dialysis treatment: peritoneal dialysis (PD) and hemodialysis (HD). HD involves the removal of remaining metabolites from the body through diffusion to the dialysis fluid via a dialyzer tube. CKD patients undergoing HD often experience complications and problems, accompanied by changes in the form and function of body systems.[3] The problem that often occurs is muscle weakness. CKD patients experience weaker muscle strength due to reduced activity, muscle atrophy, myopathy, neuropathy, or a

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combination of these factors.[4] Weak muscles can be strengthened through physical exercise. Physical exercise entails planned, structured movements aimed at improving or maintaining one or more aspects of physical fitness. It is essential for preserving and enhancing overall body health.[5]

Physical exercise during HD increases muscle blood flow and capillary surface area, facilitating the transfer of urea and toxins from tissues to the vasculature, and subsequently to the dialyzer. It enhances body fitness, physiological function, skill, and increases lower extremity muscle strength.[6] The type of physical exercise performed is aerobic exercise, which stimulates the heart, blood circulation, and breathing. It is conducted over an extended period to yield improvements and benefits to the body.[7]

According to the WHO, quality of life is an individual's perception of their position in life within the cultural context and value system they live in, including their goals, hopes, standards, and concerns.[8] Quality of life refers to a state where an individual experiences satisfaction and enjoyment in daily activities related to physical and mental health, a sense of optimism, and the ability to actively engage in daily social activities such as work, home life, social interactions, and hobbies. Physical health is assessed based on physical function, limitations in physical roles, body pain, and perceptions of health. Mental health assessment involves evaluating social functioning and limitations in emotional roles.

The 4-5 hours HD process typically induces stress, leading some patients to experience fatigue and headaches, which can have psychological ramifications. Impaired cognitive function, lack of concentration, and disruptions in social relationships may ensue, collectively diminishing the quality of life for CKD patients undergoing HD.[6] The objective of this study was to assess how physical exercise influences the quality of life in individuals undergoing HD.

Methods

Design and participants

This research employed an observational analytical study with a cross-sectional approach, utilizing non-probability sampling. The study focused on CKD patients undergoing HD at the HD Unit of Bekasi Hospital from August to September 2019. Participants met specific criteria, including being aged over 25 years, having undergone HD for at least three months, absence of nervous system diseases or psychological disorders, stable hemodynamics, clear consciousness, doctor's approval for physical activity, good musculoskeletal health, effective communication skills, willingness to participate in the study, and readiness to engage in physical exercise—specifically, pedaling a stationary bicycle for 15 minutes twice a week during HD.

Statistical analysis

Univariate analysis was performed on the research data, involving scoring of the quality of life questionnaire before and after physical exercise. The results of this data analysis are presented using a scoring system. Bivariate analysis was conducted to assess the impact of physical exercise on the quality of life of CKD patients undergoing HD. The statistical test employed in this research was the Wilcoxon test method. Data analysis was performed using SPSS version 2.3.

Results

This research data are primary data observed and measured directly by researchers. There are 38 patients who met the criteria. The research was conducted twice weekly for 6 weeks, from 6 August to 14 September 2019. Kidney Disease Quality of Life SF-36 (KDQOL SF-36) questionnaire data was collected in the first and sixth weeks; then, physical exercise was carried out in the second to fifth weeks.

Table 1. Characteristics of Respondents

Characteristics	Amount (%)
Gender	
Man	25 (66)
Woman	13 (34)
Age	

≤40	5 (13)
41-50	11 (29)
51-60	11 (29)
61-70	8 (21)
≥70	3 (8)
Length of HD (years)	
≤1	2 (6)
1-2	18 (47)
≥2	18 (47)

Male participants accounted for 66%, while the remaining percentage consisted of females. The two largest age groups were 41-50 and 51-60, respectively, each 29%. The duration of undergoing HD, which was 1-2 years and more than two years, was also the same, at 47% (Table 1).

The quality of life level assessment was conducted using the KDQOL SF-36 questionnaire of 24 questions focused on the current quality of life. According to the total scoring results, there are three levels of quality, namely very good (331-361), moderate (301-330), and poor (269-300). Quality of life scoring before physical exercise was good at 18.4%, moderate at 41.2%, and poor at 39.5%. Meanwhile, after physical exercise, the same number of good and moderate criteria were found, namely 47.4% and 5.3% poor (Table 2).

Table 2. Quality of life scoring before and after physical exercise

Quality of life scoring	Before (n and %)	After (n and %)
Good (331-361)	7 (18.4)	18 (47.4)
Medium (301-330)	16 (41.2)	18 (47.4)
Poor (269-300)	15 (39.5)	2 (5.3)

The assessments measured when respondents physically exercise using a stationary bike are time, distance, calories, speed, and vital signs. The results of each assessment category are different for each respondent because the respondent's physical condition influences them at that time. After 4 weeks of physical training, there was an increase in time of 69%, distance of 87%, calories of 61%, and speed of 55% (Table 3).

Table 3. Distribution of assessment results on physical training for 4 weeks

Evaluation	Increase (n and %)	Stable (n and %)	Decrease (n and %)
Time	26 (69)	7 (18)	5 (13)
Distance	33 (87)	0	5 (13)
Calories	23 (61)	2 (5)	13 (34)
Speed	21 (55)	3 (8)	14 (37)

The difference was found between the questionnaires before and after physical exercise. When before is subtracted from after with a negative result (negative rank), the questionnaire after is lower than before; there are no respondents. A positive rank indicates that the questionnaire after was higher than before, totaling 37 respondents, while the number with the same value or no change was 1 respondent. The analysis revealed *the p-value* was 0.000 <0.01 ($\alpha + 1\%$), meaning there was a significant difference in quality of life observed between the periods before and after engaging in physical exercise.

Table 4. Measurement of vital signs

Vital Signs	Before	After
Pulse		
<60	5 (13.1)	8 (21)
61-99	32 (84.2)	28 (73.8)
>100	1 (2.7)	2 (5.2)
Systolic blood pressure (mmHg)		
<120	16 (42.1)	8 (21.1)
121-159	19 (50)	21 (71)
>160	3 (7.9)	3 (7.9)
Diastolic blood pressure (mmHg)		
<80	29 (76.3)	23 (60.5)
81-99	7 (18.4)	12 (31.5)
>100	2 (5.3)	3 (8)
Respiratory frequency		
<20	12 (31.5)	10 (26.4)
>20	26 (68.5)	28 (73.6)

Discussion

The number of respondents who participated in the research is 38, with the majority being male at 66%. The research is the same as other research and data from the 2018 Indonesian Renal Registry, which found more

male patients than female. Clinically, men have a risk of experiencing CKD 2 times greater.[2,4,10] This may be because women pay more attention to health and maintain a healthy lifestyle than men.[10]

The percentages for the 41-50 and 51-60 age categories are the same, at 29%. This research aligns with other researchers who found the most significant age category in the 18-45 years group (46%) and an age category of 45-60 years (74.1%).[11,12] Patients aged >60 years have a 2.2 times greater risk of experiencing CKD than those aged <60 years. Kidney function will decrease with increasing age. After 40 years, there will be a progressive decrease in GFR until 70 years, approximately 50% of normal.[13]

The duration of undergoing HD was 1-2 years and >2 years; the results were the same, respectively 47%. This study aligns with other studies, with results showing that the duration of HD is≥12 months (66%).[11] Several studies have found a relationship between the duration of HD and quality of life.[14] However, some state that there is no relationship between HD duration and the patient's quality of life.[15,16]

Research shows that the quality of life for patients undergoing HD >5 years is notably poorer in both physical and mental aspects compared to ≤5 years.[17] This finding is associated with being on HD for longer and older patient age, factors that indirectly influence patient quality of life.[18] As patients undergo hemodialysis for a more extended period, their adherence to the treatment tends to increase. Usually, the patient has reached the acceptance stage and received education about the disease from nurses and doctors.

The normality test for physical exercise on time, distance, and calories showed abnormal results, so the Wilcoxon test was used. While the speed of spread was normal, so the paired t-test was used. The Wilcoxon test results for the time, distance, and calorie components showed a Sig. (*2*-tailed) value <0.05, meaning a significant difference between the first and fourth weeks. The time, distance, and calories were higher in the fourth week than during the first week. Meanwhile, the paired t-test for the speed component showed a Sig. (*2*-tailed) value of >0.05, meaning there was no significant difference between the speed of the first and fourth weeks.

The Wilcoxon test tested the normality of vital sign components such as pulse rate, respiratory rate, TDS, and TDD, which are not distributed normally. It was found that the pulse and TDD had a Sig. value (*2*-tailed*)* <0.05. There is a significant difference between pulse and TDD at week 4 and week 1. The pulse and BBP in the first week were higher than in the fourth week, meaning there was a significant decrease in the pulse and BBP in the fourth week. Meanwhile, TDS and respiratory frequency did not significantly differ between the fourth and first weeks with Sig. values (*2*-tailed*)* ≥0.05.

The Spearman test shows no significant relationship between time, distance, calories, and speed in quality of life, as seen from the Sig. value (2-tailed) ≥0.05 (α=5%). Likewise, in the correlation test of vital signs with quality of life, there was no significant relationship between pulse rate, TDS, TDD, and respiratory frequency and quality of life with the Sig. value (*2*-tailed) ≥0.05 (α=5%).

The data collected for the first week using a questionnaire before physical exercise on 38 respondents was then analyzed using the Wilcoxon test due to the non-normal distribution of the data as determined by the normality test. The results revealed the quality of life was categorized as poor for 39.5% of participants, moderate for 41.2%, and good for 18.4%. The data collected in the sixth week using the same questionnaire after physical exercise showed that the quality of life was poor, 5.3%, moderate, and good, at the exact figures, 47.4% each.

Although HD can improve the quality of life for CKD patients, HD cannot stand alone in improving the patient's quality of life. Several studies show a decline in patient's quality of life after a long period of HD treatment. This is associated with the effect of HD on decreased muscle structure and function due to uremia, resulting in reduced physical activity, muscle atrophy, difficulty in walking, physical work ability, and impaired function.[19]

Strength training is one type of physical exercise required by regular HD patients.[19]

Researchers use stationary bicycles to carry out physical exercises. Patients were required to train their lower extremities, strengthening the muscles and working harder against resistance forces. Muscle strength is needed and is the basis for performing other physical abilities. Physical exercise can improve functional capacity, respiratory muscle strength, and quality of life among hemodialysis patients.[20] Johansen recommends incorporating physical exercise into the HD routine, which is essential for enhancing the quality of life of CKD patients. This can exert a significant effect on improving physical function, reducing physical pain, increasing vitality and general health, and improving the quality of life of HD patients.[21]

Conclusion

Before engaging in physical exercise, the quality of life for CKD patients undergoing HD is moderate. However, after physical exercise, the patient's quality of life improves. This shows the influence of physical exercise on the quality of life in CKD patients undergoing HD.

Limitations of the Study

This study is subject to several limitations, including a small number of respondents and the lack of literature discussing physical exercise in HD patients.

Declarations

Ethics approval

All respondents filled out a written willingness to participate in research. Passed research ethics eligibility is (No. 187/KEP-UY/BIA/X/2019).

Competing interests

None.

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Author's Contribution

Idea/concept: LA. Control/supervision: EP, HN. Data collection/processing: SHM. Extraction/Analysis/interpretation: SHM. Editor: MLU. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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Review Article

The Role of Physical Activity in Improving QOL of Patients Undergoing Hemodialysis

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ABSTRACT

Patients undergoing hemodialysis (HD) experience increased mortality rates and decreased physical activity, which has an impact on patients' low quality of life (QOL). Physical activity has positively affected cardiovascular function, strength, and overall health status. On the other hand, physical activity has not been proven to cause any health hazards in HD patients. However, physical activity has not become a routine practice for HD patients, and there are no clear guidelines for physical activity in HD patients. Due to the inherent condition, intradialytic aerobic exercise appears to be the most suitable physical activity method for HD patients. However, research is still needed to assess the effectiveness and safety of intradialytic exercise (IDE) for HD patients in the long term. Research results can be used as a reference in developing the most appropriate IDE guidelines for HD patients.
Keywords: end-stage renal disease, intradialytic exercise, aerobic exercise, quality of life.

Introduction

Hemodialysis (HD) is the predominant treatment approach for patients with end-stage renal failure (ESKD). Compared with those who are physically active regularly, HD patients who are classified as sedentary have a chance of dying by more than 60% every year. [1] HD patients who sit more tend to experience lower quality of life (QOL), and a decrease in VO2 max is connected to a higher risk of mortality.[1–3] A strong association exists between increased mortality and lower levels of objective, self-reported physical functioning.[4]

Physical activity methods in HD patients vary greatly, and they can be done intradialytic (IDE) or interdialytically. Until now, specific guidelines for physical activity in HD patients have not been established. The Kidney Disease Improving Global Outcomes (KDIGO) guidelines advise incorporating regular physical activity into the everyday routine of patients with chronic kidney disease (CKD) (minimum of 30 minutes/day, five times/week) and should be tailored to each individual's cardiovascular health as well as tolerance level.[5] International physical activity (PA) guidelines provide guidelines for performing 150 minutes/week of moderate-intensity aerobic PA in patients with chronic

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conditions.[6] The most appropriate physical activity for HD patients appears to be the IDE aerobic method. However, other recommendations include resistance exercise, interdialytic aerobic exercise, and a combination of resistance and aerobic exercise.[7] In principle, IDE focuses on increasing the patient's physical endurance and strength by addressing a range of psychosocial and physiological parameters.[8] IDE has been proven to positively affect the overall health and readmission rates for HD patients,[9,10], and improved QOL.[11–14] General guidelines recommend performing aerobic IDE within the first 2 hours of an HD session, with moderate to high intensity based on VO2 max assessment 10, for 30 minutes, lasting five weeks to 6 months, while most programs are 12 weeks long.[15] Apart from that, a health service team is also needed that involves many experts apart from nephrologists, including cardiologists, physiotherapists, exercise physiologists, renal dietitians, and nurses.[16] Special equipment also needs to be available, such as an ergometer connected to a bed or HD chair so that HD patients can benefit from aerobic exercise. This review is primarily concerned with assessing the benefits of physical activity and identifying the most suitable IDE methods for HD patients to improve their QOL

Benefits of Physical Activity in Improving Quality of Life

Compared with those who do not undergo HD, CKD patients who undergo HD have lower functional abilities. This is associated with lower physical activity levels, ultimately affecting their QOL.[17] A strong relationship exists between physical function and patient outcomes, including health-related QOL (HRQOL) and mortality.[4,18] Reduced physical function and low muscle strength impact their QOL, reducing their ability to carry out daily activities.[19,20] Compared with healthy people, CKD patients show a significantly lower ability to perform daily activities and reduced capacity to participate in social, entertainment, or independent exercise.[17] Sedentary HD patients had a greater than 60% chance of dying annually in contrast to those who engaged in regular physical activity.[1] It has been shown that self-reported physical activity is strongly associated with lower mortality and HRQOL in HD patients.[21] Likewise, QOL results according to SF-36, Physical Component Summary (PCS), and Mental Component Summary (MCS) results obtained can act as predictors of mortality and hospitalization rates.[22] Other studies also prove that physical activity is an independent predictor of death in HD patients.[23] In contrast, increased physical activity was linked to a decreased mortality risk.[24] Even participating in light physical activity is linked to a reduced mortality risk.[25] Importantly, regular physical activity is advantageous in every stage of kidney disease, enhancing physical fitness, muscle strength, and HRQOL.[26]

So, based on the evidence above, it is clear that physical activity affects the QOL of HD patients.[17] Therefore, to improve QOL in HD patients, one significant effort is increasing their physical activity.[27] However, it must be realized that carrying out and assessing physical activity in HD patients also presents numerous challenges.[28] Therefore, it is necessary to consider many things in determining the method of physical activity and the assessment that is most appropriate individually, primarily related to the resources and capabilities possessed by each dialysis unit.

Physical Activity Methods in Hemodialysis Patients

Many various exercise methods for HD patients whose efficacy and weaknesses have been studied. These include resistance exercise, aerobic exercise, a blend of resistance and aerobic exercise, range of motion, respiratory muscle training, stretching exercise, electrical muscle stimulation, walking exercise, peripheral muscle training, and sham exercise/usual care.[10] Among the various exercise methods, aerobic exercise is proven effective in improving QOL, whereas stretching exercise significantly reduces QOL compared to usual care.[10] Since HD patients have several typical limitations, aerobic exercise seems to be the most suitable method. However, combining resistance with aerobic exercise can also be an alternative if the patient can tolerate

the program. Resistance exercise, as a form of physical activity, trains muscles to contract against the equipment used to increase strength, endurance, mass, size, and muscle hypertrophy. Incorporating progressive resistance into an exercise program improved muscle strength.[7] Based on biochemical and molecular physiology analysis, combining resistance exercise with aerobic exercise improves exercise capacity, VO2 max, and 6-min walk test (6MWT). Combining resistance exercise and aerobic exercise is the method that has the most significant impact on 6MWT.[10] Resistance exercise promotes the number of muscle mitochondria, increases oxidative phosphorylation, and triggers mitochondrial biogenesis by activating the peroxisome proliferator-activated receptor g coactivator 1a signaling pathway in reaction to increased intracellular Ca2+ and reactive oxygen species. Increases in cyclic adenosine monophosphate (AMP) and p38 mitogen-activated protein kinase occur due to adenosine triphosphate (ATP) breakdown and increased adrenergic stimulation.[10,29]

Outcomes of Aerobic Intradialytic Exercise in Hemodialysis Patients

Most dialysis patients experience decreased muscle strength and aerobic power, making them less capable of tolerating the energy demands of various daily activities.[15] They also start with a lower exercise tolerance, which can hinder integrating an exercise program into their usual treatment. Indeed, the effects of exercise during HD remain a controversial issue.[30] Some studies have not observed notable changes in self-reported HRQOL after IDE programs. However, most have discovered significant positive physical impacts in programs lasting from 5 weeks to 6 months, with many programs being 12 weeks long.[15] Increasingly, many studies have shown that even light exercise can positively affect patients' mental and physical health. These benefits include improvements in lower extremity muscle strength, aerobic capacity, lipid metabolism, and systolic blood pressure, and they also show benefits from HRQOL.[15] Based on a systematic review and meta-analysis, aerobic IDE has a notable beneficial impact on QOL, both MCS and PCS.[8,10]

Taking into account the conditions inherent in HD patients and the many benefits if carried out on HD days, aerobic IDE seems to be the most reasonable choice. Some of the benefits of IDE include that it is an easy intervention, does not involve additional time, increases compliance, provides encouragement within an organized environment, and can be directly monitored by medical staff.[31,32] IDE causes increased muscle blood flow, and a more significant amount of open capillary surface area in the working muscle will facilitate a higher flux of urea and related toxins from the tissue to the vascular compartment and subsequent removal through the dialyzer.[33] IDE can also increase dialysis efficiency by reducing solute rebound, which occurs due to increased perfusion of skeletal muscle, which in turn has the potential to improve its health.[34] Besides increasing dialysis efficiency, IDE has also been shown to improve VO2 max and QOL.[11–14]

Aerobic Intradialytic Exercise Regimens to Improve QoL

There are many variations in the implementation of aerobic IDE in HD patients. The following are several examples of IDE aerobic programs from several researchers that have been proven to provide an increase in QOL, including:

- The exercise program consists of warming up for 5 minutes and cycling for 10-15 minutes for three months with an intensity of 12-16 points on the Borg scale. This program resulted in a percentage change in the total QOL score of 37.7%.[35]
- Patients receive IDE passively using electrically powered pedaling at a moderate speed for 30 minutes per session (3 times 10-minute exercises with a 20-minute recovery period) within the first 2 hours of the dialysis session. After the 8-week washout, the patient actively pedaled in the same way for eight weeks. This exercise program resulted in a change in the total QOL-SF-36 score of 20.8%.[30]

- The exercise program includes a warm-up, aerobic exercise, and cool-down. Warm up by passive stretching of the lower extremities and aerobic activity using a bicycle at a speed of 0.5 km/hour (approximately 35 rpm) for 5 minutes. Following that, the conditioning phase involved 30 minutes of exercise within the first 2 hours of dialysis, with intensity based on the 11- and 13-point Borg scales. The cool-down phase consisted of 2 minutes of cycling with a minimum load at 35 rpm and passive stretching of the lower extremities. This exercise program resulted in a change in the total QOL-SF-36 score of 14.7%.[36]
- The exercise program involves cycling for 45 minutes at a speed of 45–50 rpm during the 2nd and 3rd hours of the 4-hour HD session. Training resistance was set to range between 65% and 75% of maximum power capacity (in watts), evaluated at the start of training, reassessed, and adjusted every two weeks with a submaximal cycling test. Every training session incorporated a warm-up and cool-down of 5 minutes each. The program led to a 25% improvement in QOL, primarily resulting from changes in physical health rather than mental health. [33]

Conclusion

Patients undergoing HD who are classified as sedentary generally have a low QOL. Physical activity has been shown to affect the overall health of HD patients positively. However, physical activity has not become a routine or an integral part of managing HD patients. Considering the existing limitations, with lower exercise tolerance, the IDE aerobic program appears to be the most appropriate physical activity method for HD patients. However, further research is necessary to examine the effectiveness and safety of IDE in the long term, which can be used as a reference in developing the best physical activity guidelines for HD patients, especially regarding the type of exercise and equipment, intensity, duration, and exercise modality.

Declarations

Competing interests

The authors declare no conflict of interest.

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Author's Contribution

Idea/concept: ARF, NS. Design: ARF, NS. Control/supervision: NS. Data collection/processing: ARF, NS. Extraction/Analysis/interpretation: ARF, NS. Literature review: NS. Writing the article: ARF, NS. Critical review: NS. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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Case Report

Nephrogenic Ascites in End-Stage Renal Disease Patients Undergoing Hemodialysis: Case Series

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ABSTRACT

Ascites occurring in individuals with chronic kidney disease (CKD) undergoing hemodialysis (HD) are referred to as nephrogenic ascites (NA). The pathogenesis of NA remains uncertain but involves many interrelated factors. These factors include inadequate dialysis, low ultrafiltration, poor nutrition, increased peritoneal membrane permeability, and impaired peritoneal lymphatic reabsorption. Frequent accompanying complaints are leg edema, nausea, decreased appetite, weakness, and complaints due to hypotension during HD. NA generally carries a poor long-term prognosis, likewise, with complex therapeutic options, both medical and surgical. Management of NA includes education regarding fluid restrictions, a high protein diet, intensive HD, as well as therapeutic modalities with continuous ambulatory peritoneal dialysis (CAPD) and kidney transplantation. CAPD has been proven to improve quality of life and recovery from ascites. The NA in this case report was all related to the patient's low level of compliance against fluid intake restrictions, particularly while experiencing oliguria or anuria. In this case, intensive education regarding limiting fluid intake and high-protein nutrition seems essential for better patient outcomes. On the other hand, the presence of infectious complications gives poor outcomes. Two patients presented with umbilical hernia, which could be an obstacle for CAPD.
Keywords: nephrogenic ascites, dialysis adequacy, low protein intake.

Introduction

Nephrogenic ascites (NA) are ascites that occur in patients with end-stage kidney disease (ESRD) undergoing hemodialysis (HD). The cause of NA is multifactorial and can be a combination of low patient compliance, inadequate dialysis, ultrafiltration failure due to hypotension, poor nutrition, and increased peritoneal membrane permeability. In general, NA carries a worse long-term prognosis for HD patients.[1] Management of NA is very complicated, including medical and surgical therapy. Education about limiting fluid intake and a high-protein diet must be periodically reviewed. This report presents 3 case series of HD patients with NA, with varying underlying causes of ESRD and patient outcomes.

Case Illustration

Case 1

A 51-year-old man complained of abdomen enlargement for the last 3 months, accompanied by a feeling of fullness, nausea, decreased appetite, and sometimes coughing. The patient has undergone HD 2 times a week for 2 years, with hypertension and diabetes mellitus (DM) as underlying ESRD. He often experiences hypotension, requiring crystalloid fluid therapy at

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the end of HD. The patient's hemoglobin (Hb) level also frequently decreases, requiring a transfusion. Compliance with fluid restrictions is also low; on the other hand, there is oliguria.

The patient's dry weight was 55 to 60 kg, with an average gain of 5 to 6 kg. Using Cimino as HD access, the ultrafiltration rate is 500-750 cc/hour; blood flow rate (QB) starts from 180-210 ml/min, and dialysate flow rate (QD) is 500 ml/min. Blood pressure (BP) was 180/100 mmHg, heart rate 100x/min, respiratory rate 24x/min, temperature 36.5^{o}C, and SpO2 100% in room air. There was an enlarged left heart, as well as ascitic fluid. No abnormalities were found in other organs.

Laboratory: Hb was 7.6 g/dl, serum urea and creatinine levels were 130 mg/dl and 6.5 mg/dl respectively, albumin levels were 2.9 mg/dl, electrolyte levels were normal, and markers for viral hepatitis were negative.

Patients hospitalized with loop diuretic IV, transfusions of blood, and albumin. After the transfusion, Hb and albumin levels approached normal. Another therapy is ascites puncture, with a total of 3 liters of fluid. Re-education was also conducted regarding continuous ambulatory peritoneal dialysis (CAPD), protein diet, and fluid restrictions. There was an improvement after 4-5 months, with a dry weight of around 60 to 62 kg, minimal leg edema, and ascites. However, Hb levels often fall, necessitating frequent transfusions.

Case 2

A 53-year-old woman complained of abdomen enlargement since the previous month, accompanied by worsening shortness of breath, nausea, and frequent coughing from the last week. The patient has been undergoing HD for 2 years, twice a week, with an underlying ESRD hypertension. Compliance with diet and fluid restriction is low, and there is anuria condition. On the other hand, on average, the patient often receives blood transfusions once a month. Dry weight is 58 kg, with an average weight gain of 7-8 kg. Using double lumen catheter for HD access for 4-5 hours, ultrafiltration 300-500 cc/hour QB starting from 170-200 ml/min, and QD 500 ml/min.

The patient looked pale, had poor nutritional status, and had hypotony in both arms. BP was 200/100 mmHg, heart rate 110x/min, respiratory rate 30x/min, temperature 36.5°C, and SpO2 98% with O2 4 lpm nasal cannula. There was swelling in both legs and signs of left heart enlargement. The abdomen showed prominent ascites, while other organs were within normal limits.

Laboratory: Hb was 6.9 g/dl, leukocytes 13,500/ul, serum urea and creatinine levels 180 mg/dl and 10.5 mg/dl respectively, albumin level was 2.3 mg/dl, electrolyte levels were normal, and viral hepatitis markers were negative. Chest X-ray results showed pneumonia.

The patient was hospitalized and given ceftriaxone 1 gram BID, furosemide IV, and blood and albumin transfusions. Hb levels have increased to 9.2 mg/dl, while albumin levels remained low. Additionally, ascites paracentesis of 1 liter within 24 hours was performed. However, despite treatment efforts, the patient’s condition deteriorated, leading to death after 5 days, primarily due to sepsis.

Case 3

A 31-year-old man complained of abdomen enlargement for the last 2 weeks. He also experienced weakness, shortness of breath, dry cough, and increasing weight loss. The patient underwent HD for 2 years, twice a week, with underlying ESRD was glomerulonephritis. The patient's compliance with diet and fluid restriction is low, with anuria condition. The dry weight was 60 kg, with an average weight gain of up to 8 kg, making it challenging to achieve dry weight. Using double lumen catheter for HD access, lasting 4-5 hours, ultrafiltration 500-750 cc/hour; QB starting from 180-200 ml/min, and QD 500 ml/min. The patient often experienced hypotension during HD and complained of muscle cramps, dizziness, and nausea. Giving 0.9% NaCl fluid at the end of HD made achieving the UF goal difficult.

On physical examination, the patient appeared weak, with poor nutritional status and hypotony in both arms. BP was 150/80 mmHg, heart rate 100x/m regular, respiratory rate 24x/minute, temperature 36.2°C, and SpO2 98%

room air. The conjunctiva was pale, swollen in both legs and left heart enlargement. The abdomen showed massive ascites and an umbilical hernia, while other organs were normal.

Laboratory: Hb was 10.5 g/dl, serum urea and creatinine levels were 131 mg/dl and 10.6 mg/dl respectively, albumin level was 3.2 mg/dl, electrolytes were normal, and viral hepatitis markers were negative. Chest X-ray radiology suggested an active specific process.

The patient was hospitalized and received standard treatment, including furosemide IV and symptomatic therapy. Paracentesis, 1 liter of ascites per 24 hours, was also performed. After 7 days of treatment, the condition improved, and the follow-up was outpatient, with re-education regarding compliance with diet and fluid intake.

Discussion

In general, the complaints and clinical conditions of the patients above are relatively the same, namely an enlarged abdomen and slight leg edema. There was no history of other organ abnormalities or malignancy, but there was 1 case of pneumonia, and umbilical hernias were found in 2 patients, which were associated with massive ascites. All patients had heart enlargement related to HD and its comorbidities.

Ascites associated with HD are referred to as nephrogenic ascites (NA).[4] The cause of NA is still unclear, but it is thought to involve a combination of interrelated factors, including poor nutritional status, patient non-compliance, and late initiation of renal replacement therapy (RRT). The pathophysiology underlying the occurrence of NA includes hepatic vein hydrostatic pressure, changes in the permeability of the peritoneal membrane caused by the inflammatory effects of uremic toxins, obstruction of lymphatic channels caused by inflammatory infiltrates resulting in changes in peritoneal fluid absorption, and accumulation of ascitic fluid. Other predisposing factors may include hypoalbuminemia, hyperparathyroidism, effective in controlling ascites formation and therapy against ascites (Table 1).[9]

heart failure, constrictive pericarditis, pancreatitis, and cirrhosis with portal hypertension.[5]

Diaz-Mancebo stated that the theory underlying the pathophysiology of NA is as follows[6]:

- Increased hepatic vein hydrostatic pressure
- Excess fluid intake
- Increased peritoneal membrane permeability, caused by uremic toxins, long-term use of dialysate solutions, immune complexes, activity of the renin-angiotensin-aldosterone (RAA) system, and hemosiderosis
- Disruption of peritoneal lymphatic drainage

The four pathogenesis mechanisms above have different roles in causing NA, but they are all related.[5]

The diagnosis of NA is carried out by exclusion, which requires a complete examination to exclude liver and heart function, infection, and malignant causes. The history and physical examination generally show ascites with minimal leg edema. Patients usually also have a history of anorexia and cachexia and experience hypotension during HD. In addition to kidney function, the recommended laboratory evaluation includes markers for viral hepatitis B and C and albumin or protein levels.

The prognosis of HD patients with accompanying ascites is relatively poor, with low quality of life (QOL). Life expectancy in HD patients with nephrogenic ascites ranges from 7 to 10.7 months on average, with a 44% chance of dying within 15 months of diagnosis. The clinical course of patients with recurrent NA is characterized by cachexia and, ultimately, progression to death.[5] Management of NA is complex and includes various medical and surgical modalities.[7] In the early stages, salt intake and fluid restriction are limited, intensive HD with ultrafiltration is administered, and intravenous albumin with a high protein diet is administered to control ascites and prevent hypotension. CAPD, peritoneovenous shunt (PVS), and kidney transplantation appear to be

Table 1. Treatment options for nephrogenic ascites, following advantages and disadvantages

Intervention	Advantages	Disadvantages
Restriction of drinking and salt accompanied by intensive hemodialysis and ultrafiltration	Ascites is reduced	Hypotension
Hyperalimentation therapy	Increased nutrition	Untested
Repeated paracentesis	Symptoms decrease	Losing large amounts of protein
CAPD	Reduced ascites and nutrition increase	Early protein loss
Peritoneo-venous shunt	Ascites reduced, dialysis	Shunt
Kidney transplantation	The best therapy for Ascites	Can recur at times kidney damage

Conclusion

Case series of NA have been reported, all of which were associated with low levels of patient compliance with fluid intake restrictions. More intensive education regarding limiting fluid intake and high-protein nutrition seems essential for better patient outcomes. NA is a condition that accompanies ESRD undergoing HD with a poor prognosis. Many factors are caused and are interrelated, including poor nutritional status, low compliance, and late initiation of RRT. The therapy of choice consists of intensive HD, a high-protein diet, kidney transplantation, PVS, and paracentesis. CAPD is also an option because it has been proven to improve QOL and recovery from ascites.

Declarations

Competing interests

The authors declare no conflict of interest.

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