Correlational Analysis of Physiological and Psychological Factors with Fatigue on Chronic Kidney Disease Patients Undergoing Hemodialysis

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A B S T R A C T

Fatigue is a major problem commonly experienced by chronic kidney disease patients undergoing hemodialysis. However, currently, the factors that correlate with fatigue on chronic kidney diseases patients undergoing hemodialysis are not comprehensive studies and there are still contradictory results from previous studies in Indonesia. This study aims to investigate correlational analysis of physiological and psychological factors with fatigue on chronic kidney disease patients undergoing hemodialysis. This studi use a cross-sectional study with a sample count of 80 patients undergoing hemodialysis in Yarsi Public Hospital Pontianak, Indonesia. The sampling was carried out using the total sampling approach. A FACIT fatigue scale tool and depression and anxiety stress scale (DASS) 42 were employed to measure fatigue and depression, while hemoglobin and urea levels were taken based on medical history. The Spearman's Rho test shows the physiological factor from the urea level had an insignificant correlation with fatigue (p-value 0.585). The physiological factor of hemoglobin level had a weak positive correlation (p value 0.001 and r= 0.349) with fatigue. The psychological factor of depression had a strong negative correlation (p-value 0.000 and r = -0.812) with fatigue. The psychological factor of depression was the dominant factor causing fatigue than other factors based on the standardized coefficient beta value of -0.717. Factors that correlate with fatigue on chronic kidney disease patients undergoing hemodialysis are hemoglobin levels and depression. The most dominant factor influencing fatigue in chronic kidney disease patients undergoing hemodialysis is depression.

A B S T R A K

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Kelelahan merupakan masalah utama yang sering dialami oleh pasien gagal ginjal kronik yang menjalani hemodialisis. Namun, saat ini faktor-faktor yang berkorelasi dengan kelelahan pada pasien gagal ginjal kronik yang menjalani hemodialisis belum diteliti secara komprehensif dan masih terdapat hasil yang kontradiktif dengan penelitian-penelitian sebelumnya di Indonesia. Penelitian ini bertujuan untuk mengetahui analisis korelasi faktor fisiologis dan psikologis dengan kelelahan pada pasien gagal ginjal kronis yang menjalani hemodialisis. Penelitian ini menggunakan studi potong lintang dengan jumlah sampel 80 pasien yang menjalani hemodialisis di RSU Yarsi Pontianak, Indonesia. Pengambilan sampel dilakukan dengan menggunakan pendekatan total sampling. Alat FACIT *Fatigue Scale dan depression and anxiety stress scale* (DASS) 42 digunakan untuk mengukur kelelahan dan depresi, sementara kadar hemoglobin dan urea diambil berdasarkan riwayat medis. Uji Spearman's Rho menunjukkan faktor fisiologis dari kadar urea tidak terdapat korelasi dengan kelelahan (p-value 0,585). Faktor fisiologis kadar hemoglobin memiliki korelasi positif yang lemah (p value 0,001 dan r= 0,349) dengan kelelahan. Faktor

psikologis depresi memiliki korelasi negatif yang kuat (p-value 0,000 dan r = -0,812) dengan kelelahan. Faktor psikologis depresi merupakan faktor dominan penyebab kelelahan dibandingkan faktor lainnya berdasarkan nilai koefisien standar beta sebesar -0,717. Faktor yang berhubungan dengan kelelahan pada pasien penyakit ginjal kronik yang menjalani hemodialisis adalah kadar hemoglobin dan depresi. Faktor yang paling dominan mempengaruhi kelelahan pada pasien penyakit ginjal kronis yang menjalani hemodialisis adalah depresi.

INTRODUCTION

Chronic kidney diseases is often a major problem and develops with an incidence of 10.8%-16% worldwide and in 2016 it reached more than 21 million cases with a mortality rate of 98% (Hill et al., 2016; Xie et al., 2018; Yuan et al., 2019). In Indonesia, in 2013 the incidence of chronic kidney diseases reached 0.2% or as many as 499,800 cases and increased to 0.38% or as many as 980,400 cases in 2018 (Riskesdas, 2018).

The high incidence of chronic kidney disease makes patients have to be given medical treatment to maintain life(Chilcot et al., 2016). Dialysis therapy is very necessary and is still the main choice for patients with end-stage kidney disease because the kidneys have decreased function so that dialysis therapy assistance is needed (Kalantar-Zadeh & Fouque, 2017; Pu et al., 2019).Although currently hemodialysis can help patients with kidney disorders, hemodialysis therapy in the long term will result in complications and affect physical, psychological, social, spiritual and emotional aspects that cannot be controlled by individuals (Tavassoli et al., 2019).

Fatigue is a major problem commonly experienced by chronic kidney diseases patients undergoing hemodialysis by 78%-83.8%, putting fatigue as the leading issue on patients with hemodialysis(Ali & Taha, 2017; Bossola et al., 2018).Generally, the fatigue prevalence on chronic kidney disease patients undergoing hemodialysis therapy is astronomically high, i.e., 44,7-97%, from the mild to severe level(Joshwa & Campbell, 2017).

Fatigue is an objective feeling from troublesome experiences in patients' life (Joshwa & Campbell, 2017; Picariello et al., 2017).Patients can experience the worst fatigue of energy loss, decreased concentration, decreased activity, or hypotension after hemodialysis (Davey et al., 2019; Fuentes-Márquez et al., 2017).

Fatigue is also associated with poor life quality increasing cardiovascular disease risk and substantially increase the hospitalization and mortality rate (Kim & Kim, 2019; Pu et al., 2019; Wang et al., 2016).These are factors worsening patients' condition, putting challenges to nurses in administering treatments(Tavassoli et al., 2019).

Fatigue can develop depending on factors such as accumulation of waste products (creatine, urea, uric acid), impaired function metabolic and endocrine, fluid electrolyte disturbances, changes in cardiovascular function, inadequate ultrafiltration, anemia, sleep disorders and depression(Bossola et al., 2018; Joshwa & Campbell, 2017; Wang et al., 2015).

Based on the unpleasant symptoms theory classified into the theory of middle range, fatigue is affected by physiological and psychological factors(Lenz & Pugh, 2018).Physiological factors include hemoglobin and urea levels, while the psychological factor is depression(Jhamb et al., 2009; Joshwa & Campbell, 2017; Wang et al., 2015).However, results from several studies remain controversial due to their different outcomes. Therefore, further studies are required concerning factors causing fatigue(Bai et al., 2015; Bossola et al., 2018; Chilcot et al., 2016; Mathias et al., 2020; Wang et al., 2016; Zyga et al., 2015).

Further complications of fatigue in patients on hemodialysis include impaired concentration, intradialytic hypotension, decreased quality of life and prolonged lethargy (Fuentes-Márquez et al., 2017; Vasilopoulou et al., 2016).This will certainly increase the suffering of patients and affect their decision making, compliance in undergoing treatment and quality of life(Kim & Kim, 2019).

The importance of understanding factors that correlate with fatigue is a strategy of nurses in optimizing interventions and improving patients' life quality. However, currently, the factors that correlate with fatigue on patients undergoing hemodialysis are not comprehensive studies and there are still contradictory results from previous studies in Indonesia. Thus, this study aimed to investigate correlational analysis of physiological and psychological factors with fatigue on on patients undergoing dialysis intervention at Yarsi Public Hospital in Pontianak-Indonesia.

METHOD

Study design and participants

The research was conducted to study the factors that correlate with fatigue using a cross-sectional method, including physiological factors such as hemoglobin and urea levels and psychological factors such as depression. The dependent variable in this study was fatigue, whereas the independent variables were urea levels, hemoglobin levels, and depression. The study was carried out from February 2021 to March 2021 at the Hemodialysis Room of Yarsi Public Hospital in Pontianak, Indonesia.Inclusion criteria in this study included: (i) age > 18 years; (ii) composmentist consciousness; (iii) undergoing hemodialysis for at least 1 month; (iv) able to communicate well. Exclusion criteria in this study included: (i) patients diagnosed with schizophrenia; (ii) experiencing motor, sensory or global aphasia. Drop out criteria in this study included: (i) patients who did not fill out the questionnaire completely.

Sampling procedures

The study employed the total sampling technique where the samples were acquired from the whole chronic kidney disease patient population undergoing hemodialysis at Yarsi Public Hospital in Pontianak, Indonesia, i.e., 80 people. Total

sampling was utilized due to the limited population number, dropout risk, and patients failing to fulfill study requirements.

Data collection

The researchers utilized documentation to observe the age, medical history, hemoglobin level, and urea level as patients' characteristics. Urea and hemoglobin levels were taken from the last 3-month laboratory outcome from the available medical record at Yarsi Public Hospital in Pontianak, Indonesia. This is because human red blood cells have a life span of 3 months (Li et al., 2019).If more than one urea and hemoglobin level examination occurs during a three-month period, the researcher uses the most recent examination results.

FACIT Fatigue Scale tool is a questionnaire to identifies individual fatigue within the past week. The questionnaire comprises 13 questions ranging from 0 to 52, with a score ≥ 30 indicates mild fatigue and a score <30 indicates severe fatigue (Joshwa & Campbell, 2017; Sihombing et al., 2016).FACIT Fatigue Scale has been tested and is proven valid, with r calculation over r table of 0.279 on each question, and the score ranges between 0.331-0.636. It is reliable, examined from the Cronbach's alpha value of 0,646(Sihombing et al., 2016).

Depression, Anxiety Stress Scale (DASS) 42 is a questionnaire demonstrating one's depression level(Kia-Keating et al., 2017).Depression status assessment using the DASS 42 questionnaire depicted worsening condition when the score goes higher (Basha & Kaya, 2016).DASS 42 is evidently reliable to measure depression with Cronbach's Alpha value(0.96)and factor load ranges from (0,36 to 0,80) for depression, calculated in construct validity. It is concluded that DASS 42 has high reliability and validity(Basha & Kaya, 2016).

Procedure

Respondents willing to be study subjects signed informed consent as the approval. Then, the researchers administered DASS 42 and FACIT Fatigue Scale questionnaires to measure depression and fatigue scores. The researchers also conducted a documentation study based on medical records to obtain the urea level, hemoglobin level, age, and medical history from respondents and validated them to nurses of the hemodialysis unit or respondents or associated respondent families.

Data analysis

SPSS 19 for Windows was used to analyze the results.The univariate analysis (see table 1) on the numerical data scale variable was determined on the mean value, standard deviation, and range value. Meanwhile, the percentage value was utilized on the categorical data scale variable. On the bivariate analysis (table 2), data were tested using normality (Kolmogorov-Smirnov test), demonstrating that data did not distribute normally. Therefore, the bivariate analysis used a non-parametric test, i.e., Spearman's Rho test, with a predetermined significance value, i.e., p-value <0,05. The Spearman correlation test strength was observed from the correlation coefficient value (r) with negligible correlation (0,00-0,10), weak(0,10-0,39), moderate(0,40-0,69), strong (0,70-0,89), and very strong (0,90-1.0)(Schober & Schwarte, 2018). The multivariate analysis (see table 3) employed a multiple linear regression analysis test. However, an assumption test was conducted to discover the feasibility, consistency, and accuracy of the multiple linear regression test consisting of multicollinearity, independence, homoscedasticity, and normality tests(Uyanɪk & Güler, 2013).

RESULTS

Respondents' characteristics (table 1) undergoing hemodialysis were mostly female, i.e., 42 people (52.5%). Based on age, the average respondent age was 52.08 years, with the youngest age being 22 and the oldest was 75. Based on the hemoglobin level, the average was 8,569 g/dl, where the lowest was 5,7 g/dl, and the highest was 11,9 g/dl. The average urea level was 129.44 mg/dl; the lowest was 66 mg/dl, and the highest was 231 mg/dl. Based on comorbiditiesof respondents, hypertension dominated by 49 (61.2%). On the depression score from the DASS 42 questionnaire, the average depression score was 11.24, where the lowest was 2, and the highest was 28. Meanwhile, the fatigue score from the FACIT Fatigue Scale obtained an average score of 35.01, the lowest score of 17, and the highest score of 49.

Table 1.
Respondent's characteristics (*n*=80)

Variables	*n* (%)	Mean (±SD)	Range
Age (Years)		52,08 (11,579)	22-75
Gender			
Male	38 (47,5)		
Female	42 (52,5)		
Comorbidities			
Diabetes Mellitus	21 (26,3)		
Hypertension	49 (61,2)		
Other	10 (12,5)		
Hemoglobin Level(g/dl)		8,569 (1,2843)	5,7-11,9
UreaLevel (mg/dl)		129,44 (29,171)	66-231
Depression (DASS 42)		11,24 (6,291)	2-28
Fatigue (FACIT Fatigue)		35,01 (9,173)	17-49

Note: *n*: Frequency (%)

The Spearman's Rho test results of the correlation between the variables (table 2) show no correlation between a physiological factor of urea level (p value 0.585, r = 0.062)with fatigue. However, a weak positive correlation was

present between a physiological factor of hemoglobin level (p value 0.001, r = 0.349), concluding that a higher hemoglobin level will increase the FACIT Fatigue Scale score and tend to decrease fatigue symptoms. The psychological factor of depression measured using DASS 42 shows a strong negative correlation (p-value 0,000 and r = -0,812), concluding that a higher depression level will decrease the FACIT Fatigue Scale score, leading to increased fatigue correlation

Table 2.
Correlationbetween HB level, urea level and depression with fatigue

Variables	r	p value
Physiological Factor		
HemoglobinLevel(g/dl)	0,349	0,001[*]
UreaLevel (mg/dl)	0,062	0,585
Psychological Factor		
Depression (DASS 42)	-0,812	0,000[*]

Note: Spearman's Rho test
r: Correlation coefficient
*Significant value 0.05 level

A multicollinearity test is declared fulfilling requirements when a strong correlation (multicollinearity) is absent, observed from a maximum variance inflation factors (VIP) value of 10, and a tolerance value over 0.4. The multicollinearity test in this study obtained a 1.115 VIF value and 0.897 tolerance value; hence, assumptions were met. An independence is conducted to discover whether each variable is independent and is declared fulfilling requirements if the Durbin Watson falls between -2 and + 2. In this study, the Durbin Watson value was 1.835; therefore, independence assumptions were me. The homoscedasticity test in the study obtained a homoscedasticity scatterplot distribution point around zero, constantly distributing and not creating a particular pattern. Thus, it is concluded that the data was homogeneous and fulfilled the requirements. The normality test shows that data were distributing and following the diagonal line; hence, the normality test was fulfilled.

The multiple linear regression test (table 3) demonstrates a significant effect from the physiological factor of hemoglobin level (p-value 0,049) and psychological factor of depression (0,000) on fatigue with standardized coefficient beta values of 0.151 and -0.717, respectively. It illustrates the strong effect and effective contribution from independent variables on fatigue, where a higher standardized coefficient beta value will increase the effect of independent variables on the dependent variable.

The anova test result (table 3) shows a simultaneous effect from hemoglobin level and depression on fatigue with p-value (anova) 0,000 and R^2 = 0,779. It indicates that independent variables directly affected the dependent variable by 77.9%. The unstandardized coefficient B and std. error-values were present on hemoglobin level (1,140 and 0,571) and depression (-1,108 and 0,116).

Table 3:
Multiple linear regression analysis of factors correlated with fatigue

Model	Unstandardized Coefficient		Standardized Coefficient Beta	p value	p value (Anova)
	B	Std. error			
Constant	37,687	5,495		0,000	
HemoglobinLevel (g/dl)	1,140	0,571	0,151	0,049	0,000
Depression (DASS 42)	-1,108	0,116	-0,717	0,000	

Note : R^2 = 0,779
DASS: Depression, Anxiety Stress Scale; g/dl : grams per decilitre; B: Beta

DISCUSSION

The study results demonstrate a weak correlation between the physiological factor of hemoglobin level (p-value 0,001 and r = 0,349, averagely 8,6 g/dl) and fatigue in patients undergoing hemodialysis. It follows several studies discovering a significant correlation between hemoglobin level and fatigue score, where a lower hemoglobin level potentially increases fatigue(Jhamb et al., 2013; Kodama et al., 2020; Prochaska et al., 2017).Anemic condition with an average hemoglobin level of < 11 g/dl may increase fatigue in patients undergoing hemodialysis(Chilcot et al., 2016; Kodama et al., 2020; Yang & Lu, 2017).Anemia reduces oxygen delivery to body organs and tissues, increasing fatigue symptoms. It limits physical activities to compensate

for reduced functional capacity(Fishbane & Spinowitz, 2018; Jhamb et al., 2013).

In kidney disease populations undergoing hemodialysis, anemia may occur due to insufficient erythropoietin production by kidneys(Joshwa & Campbell, 2017).Reduced erythropoietin reduces hemoglobin level and oxygen supply to body cells, triggering fatigue and reducing activity levels, conditions, and functional status(Chilcot et al., 2016; Prochaska et al., 2017).In this study, on average, patients experienced anemia with a hemoglobin level of 8.6 g/dl, indicating an over-normal reduction. The study results discover an association between anemia and decreased energy, headache symptoms, and limited physical activities, constituting most complaints discovered in patients undergoing hemodialysis. It may trigger fatigue.

The study results did not discover an association between the physiological factor of urea level (p-value 0,585 and r = 0,062, averagely 129,44 mg/dl) and fatigue on patients undergoing hemodialysis at Yarsi Public Hospital in Pontianak, Indonesia. It contrasts precedent studies revealing a significant correlation between urea level and fatigue on patients undergoing hemodialysis, with an average urea level exceeding normal of >83 mg/dl to 180 mg/dl, termed uremia(Bossola et al., 2014; Zuo et al., 2018).

Uremic toxin accumulation causes mitochondria dysfunction, reducing energy consumption and generating fatigue(Artom et al., 2014).Patients withuremic, usually complain of nausea, vomiting, dyspepsia, anorexia, weight loss, and change of mental status, which may increase the fatigue risk due to nutritional disorders that reduce energy(Dioguardi et al., 2016; Lisowska-Myjak, 2014; Meyer & Hostetter, 2014).Our study did not find ancorrelation between urea level and fatigue, contradictory to several studies. It may be caused by other dominant factors or differences in the sample number. Also, most uremic symptoms were not discovered in patients undergoing hemodialysis at Yarsi Public Hospital in Pontianak, Indonesia.

The study results obtained a correlation between the psychological factor of depression (p-value 0,000) and fatigue. Depression also has a strongcorrelation with fatigue obtained from the correlation coefficient value (r = -0,812). Depression also possess the most dominant effect on fatigue among other variables with a standardized coefficient beta value of -0.717. It follows several studies that discovered a significant association between depression and fatigue(Jhamb et al., 2013; Royani et al., 2017; Wang et al., 2015).Depression is often linked to fatigue since fatigue is documented on 76-93% of individuals experiencing depression with many adverse complications, including worsenedquality of life(Aghakhani & Fattahi, 2019; Farragher et al., 2019).

Depression in chronic kidney disease patients relates to peripheral activation from the immune-inflammation pathway contributing to nerve inflammation, continuous neuro progressive change, and reduced neurotransmitter expression.(Bossola et al., 2014; Ting et al., 2020)Therefore, it shows that an activated immune-inflammation pathway, e.g., interleukin-6 (IL-6), may contribute to fatigue(Bossola et al., 2014; Ting et al., 2020).Several studies discovered a significant association between IL-6 level and fatigue, where a higher IL-6 level will increase fatigue by > 31%(Brys et al., 2020; Pedraz-Petrozzi et al., 2020).Our study results, a higher depression score increased fatigue. Depression often manifests in lethargy, weakness feeling, and reduced enthusiasm and motivation; hence, it can be associated with energy reduction on hemodialysis patients to perform regular activities.

The study implication is to provide an illustration to nurses to identify factors causing fatigue on respondents that may be affected by physiological and psychological factors. It becomes nurses' base to administer treatments with a holistic approach. Moreover, nurses are expected to perform promotive and preventive measures by considering various associated factors affecting fatigue so that patients can control fatigue that may increase the disease's morbidity and mortality.

LIMITATION OF THE STUDY

This study has a limitation where it was conducted during a pandemic era, affecting the study. During the pandemic, the hospital applied health protocols, i.e., distancing between nurses and patients. Therefore, the interview process was disrupted, particularly on elderly patients with decreased hearing function.

CONCLUSIONS AND SUGGESTIONS

The study concludes an insignificant correlation between the physiological factor of urea level and fatigue; however, there is a significant association between the physiological factor of hemoglobin level and psychological factor of depression with fatigue on patients undergoing hemodialysis at Yarsi Public Hospital in Pontianak, Indonesia. Depression is the most dominant factor affecting fatigue based on the multiple linear regression analysis.

The study results are expected to be an illustration to nurses to identify factors causing fatigue based on risk factors. Thus, nurses may perform interventions, promotive, and preventive measures to control increased fatigue that potentially increases the disease's morbidity and mortality.Therefore, the recommendation for hemodialysis nurses are to develop standard operating procedures that aim to minimize psychological problems in patients, so that they can be used to improve the quality of life and health status of hemodialysis patients.

ETHICAL CONSIDERATIONS

This study has acquired an ethical-clearance from the Ethics Committee of the Faculty of Medicine, Tanjungpura University, Pontianak with a register number of 1405/UN22.9/TA/2021. Date : 11 February 2021

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