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Original Article

Correlation Between RET-He and Quality of Life in Chronic Kidney Disease Patients with Routine Hemodialysis: A Study at Ulin General Hospital Banjarmasin

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ABSTRACT

Background: The 2018 Riskesdas report revealed that the incidence of chronic kidney disease (CKD) affects 0.38% of Indonesia's population. Anemia frequently complicates CKD, especially in patients undergoing regular hemodialysis. Reticulocyte hemoglobin equivalent (RET-He) assesses hemoglobin content in reticulocytes, indicating iron availability for erythropoiesis in the bone marrow. CKD significantly impacts patients' socio-economic status, heightening morbidity and mortality while diminishing quality of life. The relationship between RET-He and the quality of life in CKD patients on routine hemodialysis remains unclear.
Objective: To investigate the correlation between RET-He and quality of life in CKD patients undergoing routine hemodialysis.
Methods: A cross-sectional observational analytical study with data from medical records of CKD patients receiving routine hemodialysis between October 1st and October 30th, 2021. The Spearman correlation test was used for analysis.
Results: This study included 92 patients, consisting of 40 males and 52 females, with a median age of 50 years and RET-He values at 31. Quality of life metrics included physical function (800, range: 0-1000), physical limitations (300, range: 0-400), body pain (175, range: 75-255), general health (475, range: 225-600), vitality (320, range: 200-400), social function (175, range: 75-200), emotional limitations (300, range: 100-300), and mental health (380, range: 160-500). The correlation analysis revealed no significant relationships: physical function (p=0.359), physical limitations (p=0.813), body pain (p=0.373), general health (p=0.547), vitality (p=0.616), social function (p=0.828), emotional limitations (p=0.482), and mental health (p=0.136).
Conclusion: There is no significant correlation between RET-He levels and the quality of life in CKD patients undergoing regular hemodialysis.
Keywords: RET-He, chronic kidney disease, quality of life.

Introduction

Chronic Kidney Disease (CKD) continues to pose a significant challenge in the medical field. Approximately 80% of CKD patients live in countries with large elderly populations and readily accessible healthcare systems.[1] The 2018 Riskesdas report indicated an increase in non-communicable diseases, including stroke, cancer, diabetes mellitus, chronic kidney disease, and hypertension,

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compared to the 2013 data. In Indonesia, CKD affects 0.38% of the population, amounting to 713,783 individuals out of 252,124,458.[2, 3]

Anemia is prevalent among CKD patients, particularly those undergoing routine hemodialysis. This condition is primarily due to inadequate endogenous erythropoietin production, with iron deficiency also playing a significant role.[4] In these patients, iron deficiency can result from gastrointestinal bleeding, blood retention in the dialysis circuit, requent blood draws, and malnutrition. Poor dietary intake, absorption issues, and the use of anticoagulants further increase the risk of bleeding. Chronic blood loss within the dialysis circuit and frequent blood tests further deplete iron levels. Functional iron deficiency may also occur when inflammation or other factors impair the use of iron for red blood cell production, even if total body iron levels are normal. Managing this involves regular monitoring of iron status, nutritional support, minimizing blood loss, and optimizing iron therapy.[5]

Various biochemical markers, including serum ferritin, serum transferrin saturation (TSAT), percentage of hypochromic erythrocytes (%HYPO), reticulocyte hemoglobin content (CHr), erythrocyte zinc protoporphyrin (Er-ZPP), and reticulocyte hemoglobin equivalent (RET-He), are used to diagnose iron deficiency anemia (IDA) in CKD patients. Serum ferritin reflects iron stores, TSAT measures iron availability, %HYPO indicates hypochromic erythrocytes, CHr assesses hemoglobin content in reticulocytes, Er-ZPP levels reflect decreased iron availability for heme synthesis, and RET-He evaluates iron-restricted erythropoiesis. These markers, often used together, help clinicians assess iron status, considering factors like inflammation and erythropoiesis-stimulating agents that can affect individual marker interpretation.[6]

RET-He measures the hemoglobin content in reticulocytes, providing insight into iron availability for erythropoiesis in the bone marrow. Reticulocytes, being less mature than erythrocytes, circulate more rapidly and can be more sensitive indicators of ongoing erythropoietic activity. This sensitivity makes RET-He a valuable marker for assessing iron status and erythropoietic activity, particularly in CKD, where anemia is prevalent and monitoring iron levels is crucial for effective management.[7, 8] Given the challenges in accurately assessing iron status in this population, particularly with confounding factors such as inflammation and erythropoiesis-stimulating agents, RET-He is a valuable tool for diagnosing and managing IDA in hemodialysis patients. Integrating RET-He into routine clinical practice could streamline monitoring efforts and enhance treatment strategies for anemia in this population.[5, 7, 9]

CKD significantly affects patients both medically and socio-economically, leading to decreased quality of life and increased morbidity and mortality rates. The disease often necessitates frequent medical visits, treatments such as dialysis or kidney transplantation, and medications, imposing a financial burden on patients and their families. Additionally, CKD may cause complications such as cardiovascular disease, anemia, bone disease, and neurological issues, further diminishing patients' overall well-being and functionality. CKD can also impair their ability to work, resulting in potential loss of income and disruption of social and professional lives. Addressing the socio-economic impacts of CKD is crucial for comprehensive care, improving patient outcomes, and enhancing quality of life.[1, 10, 11]

A patient's quality of life is a multidimensional concept encompassing physical health, mental status, independence, social relationships, and environmental confidence. It reflects their overall perception of their life situation, including their goals, hopes, standards, and concerns. In CKD, maintaining or improving quality of life is a key treatment goal. This involves managing physical symptoms and complications while addressing psychosocial and environmental factors affecting the well-being of the patients.[12]

Research on the relationship between RET-He levels and quality of life among CKD patients undergoing routine hemodialysis remains limited. Previous studies have highlighted RET-He as a promising alternative parameter for diagnosing IDA in routine hemodialysis patients. This study aims to provide valuable insights into how RET-He, a marker of iron availability for erythropoiesis, may impact the overall well-being and quality of life of CKD patients receiving hemodialysis. The expected benefit of this research lies in enhancing our understanding of the relationship between RET-He and quality of life, providing clinicians with additional insights for better assessment and management of anemia in CKD patients undergoing routine hemodialysis. By elucidating this correlation, healthcare providers could be better equipped to tailor treatment strategies, improving both hematologic status and quality of life for these patients.

Methods

Design and participants

This study is a non-experimental analytical observational study utilizing a cross-sectional approach. It was conducted at the hemodialysis unit at Banjarmasin Ulin General Hospital from October 1st to October 30th, 2021, focusing on CKD patients undergoing routine hemodialysis. The participants were selected using non-probability sampling, specifically consecutive sampling, where individuals are enrolled sequentially as they become available. The minimum sample size was set at 74 patients, allowing for the inclusion of CKD patients receiving hemodialysis treatment during the study period. The objective was to analyze the relationship between RET-He levels and the quality of life in this patient population, providing valuable insights into their health status and well-being.

The final sample comprised 92 patients who met the inclusion criteria: diagnosed with CKD, aged between 18 and 65 years, and undergoing routine hemodialysis for more than 3 months with a frequency of two sessions per week. The exclusion criteria are incomplete medical records, current hospitalization, acute infection confirmed by physical examination, malignant disease, ongoing immunosuppressant or steroid therapy, use of non-steroidal anti-inflammatory drugs (NSAIDs), and autoimmune conditions. Data were obtained from medical records and included demographic information (gender, age), hemodialysis duration, and RET-He levels. The RET-He variable is numerical. Quality of life data were obtained through the Short Form-36 (SF-36) questionnaire, which measures mental health, emotional limitations, social function, vitality, general health, body pain, physical limitations, and physical function. The quality of life variable is also numerical.

Table 1. Research variable

Variable Name	Definition	Measurement Procedure	Measurement Results	Data Scale
RET-He	Iron content in reticulocytes in the blood circulation.[7]	Obtained from patient biochemical data	The amount of iron in the patient's reticulocytes	Numerical
Quality of life of CKD patients	CKD patient's perception of their position in life, goals, hopes, standards, and concerns.[12]	Completed SF-36 questionnaire	Numerical values describing various aspects including mental health, emotional limitations, social function, vitality, general health, body pain, physical limitations, and physical function	Numerical

Statistical analysis

Statistical data analysis was performed using SPSS software. Descriptive analysis was computed to summarize basic patient characteristics. The Kolmogorov-Smirnov normality test was used to assess the normality of distributions for patient age, RET-He levels, and SF-36 subscales. The Pearson correlation test was used to assess correlation when both datasets were normally distributed, and the Spearman correlation test was used when the datasets were not normally distributed. Significance was defined based on a p-value of <0.05.

Results

The study included 92 subjects, with 40 males and 52 females. Data on the age of CKD patients undergoing routine hemodialysis range between 16 and 65 years (Table 2).

Table 2. Profile of research subjects

Variable Name	N	Min-Max	Mean	Standard deviation
Age	92	16 – 65	49.01	10,833
RET-He	92	20 – 37	31.09	3,434
Physical function	92	0 – 1000	741.30	214,400
Physical limitations	92	0 – 400	287.77	81,999
Body aches	92	75 – 255	167.01	36,847
General health	92	225 – 600	448.10	104,055
Vitality	92	200 – 400	302.83	56,846
Social function	92	75 – 200	164.73	34,580
Emotional limitations	92	100 – 300	255.43	54,196
Mental function	92	160 – 500	371.25	92,545

A data normality test was carried out using the Kolmogorov-Smirnov method. It was found that data on patient age, RET-He, mental health, emotional limitations, social function, vitality, general health, body pain, physical limitations, and physical function were not normally distributed, requiring the use of the Spearman correlation test for these variables (Table 3).

Table 3. Kolmogorov-Smirnov normality test results

Variable Name	Statistics	DF	SIG.
Age	0,097	92	0,031
RET-He	0,137	92	0,000
Physical function	0,201	92	0,000
Physical limitations	0,298	92	0,000
Body aches	0,217	92	0,000
General health	0,119	92	0,003
Vitality	0,195	92	0,000
Social function	0,205	92	0,000
Emotional limitations	0,371	92	0,000
Mental function	0,115	92	0,005

The data were analyzed using the Spearman correlation test to determine their significance. It was found that RET-He did not affect the patient's quality of life as described by mental health, emotional limitations, social function, vitality, general health, body pain, physical limitations, and physical function ($p>0.05$) (Table 4).

Table 4. Spearman correlation test results

	RET-HE	
	P VALUE	R
Physical function	0,359	-0,097
Physical limitations	0,813	-0,025
Body aches	0,373	-0,094
General health	0,547	-0,064
Vitality	0,616	0,053
Social function	0,828	0,023
Emotional limitations	0,482	-0,074
Mental function	0,136	-0,157

Discussion

Health-related quality of life is known to be reduced in patients with CKD, with anemia often exacerbating this decline. RET-He measures the iron content in reticulocytes, young red blood cells, and provides a more accurate reflection of iron availability over the 120-day lifespan of erythrocytes. This study examined the relationship between RET-He and quality of life in CKD patients undergoing routine hemodialysis. The Spearman correlation test was used for this analysis, but the results revealed no significant relationship between these variables. Although low RET-He values can indicate iron deficiency in CKD patients with anemia and potentially worsen their overall condition, our study found that low RET-He levels did not affect their quality of life. This outcome may be influenced by factors such as the duration of hemodialysis, the patient’s age, comorbidities, and the environmental support.

In contrast to our findings, a study by Krishnan et al. in 2020 reported that about two-thirds (68%) of CKD patients undergoing routine hemodialysis experienced a decline in their quality of life compared to those who had undergone kidney transplantation.[13] This is consistent with Pretto et al., who identified common causes for reduced quality of life in these patients, including symptoms of depression, complications such as recurrent infections, headaches, pain, anemia, and post-hemodialysis fatigue.[14] The differences between these studies and our research could be due to variations in sample size, with larger samples potentially including patients with longer histories of hemodialysis and more complex complications.

The SF-36, used to assess the quality of life in CKD patients, includes measures of mental health, emotional limitations, social function, vitality, general health, body pain, physical limitations, and physical function. Several studies have reported a high prevalence of depression among CKD patients, negatively impacting their mental health. Depression in CKD patients is often linked to poor clinical conditions, comorbidities, complications from the disease and its treatment, and prolonged hospital stays.[15, 16] A 2018 study by Souweine et al. highlighted that post-dialysis weakness could also affect physical function, associated with protein-energy wasting, and reduced physical activity.[17]

Research from Iran has shown a significant positive association between medication adherence and overall quality of life scores. This highlights the importance of personalized educational interventions to enhance patients' understanding of their condition and the importance of treatment adherence.[18] The study concluded that failing to adhere to treatment properly would increase the perception of disease symptoms and negatively impact the patient's physical function, psycho-emotional limitations, and social function. These studies did not find a significant correlation between RET-He and patients' physical function, emotional limitations, or social function, possibly due to some patients already being well-informed about their condition and adhering to treatment.

In this study, the non-significant relationship between RET-He and quality of life suggests that anemia and other CKD complications can contribute to deteriorating kidney function. Observational data can make it challenging to disentangle the specific impact of anemia from other influencing factors. However, data from larger patent cohorts with multiple variables could offer deeper insights. This research indicates that the quality of life of CKD patients is not solely determined by RET-He levels, which describe the patient's iron deficiency anemia. The patient's condition is multifaceted and influenced by various factors, such as age, duration of hemodialysis, complications from diseases and treatments, individual comorbidities, and environmental support. Addressing iron deficiency anemia in CKD patients through appropriate therapy can improve their condition and reduce complications associated with CKD. Comprehensive patient care, including education for patients and their families, is crucial for maintaining quality of life and preserving mental health. Therefore, multiple factors must be addressed to improve and maintain the quality of life for CKD patients.

Conclusion

The study found no significant relationship between RET-He and the quality of life in CKD patients undergoing routine hemodialysis. Various factors, including the patient's age, the duration of hemodialysis treatment, individual disease and treatment complications, diverse comorbidities, and environmental support, likely influence this outcome.

Limitations of the Study

Several confounding factors not examined in this research could have impacted the results. Further research is needed to better understand the relationship between RET-He and quality of life in CKD patients undergoing routine hemodialysis.

Declarations

Ethics approval and consent to participate

This study adhered to all ethical guidelines set forth by the research site.

Competing interests

The authors declare no conflict of interest related to this article. The research and results are presented impartially and objectively.

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Author's Contribution

Idea/concept: MR, RK. Design: MR. Control/supervision: TW, NP. Data collection/processing: AF. Analysis/interpretation: AF. Literature review: AF, NP, TW, RK. Writing the article: AF, MR, RK, Critical review: MR, RK. 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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