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The association Malnutrition-Inflammation Score with chronic kidney disease-associated pruritus and quality of life in hemodialysis patients: a multicenter cross-sectional study

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Malnutrition is prevalent among hemodialysis patients, negatively impacting their quality of life (QoL) and chronic kidney disease-associated pruritus (CKD-aP). This study investigates the association between the Malnutrition-Inflammation Score (MIS) and CKD-aP, as well as QoL, in hemodialysis patients. This cross-sectional study was conducted on 479 HD patients (279 males and 200 females) referred to eight dialysis centers. A food frequency questionnaire (FFQ), Kidney Disease Quality of Life Short Form (KDQOL-SF™), and Yosipovitch Itch Questionnaire (YIQ) were used to assess nutritional status, QoL, and CKD-aP, respectively. Anthropometric indices, body mass index (BMI), biochemical parameters, and adequacy of dialysis (Kt/V) were also measured in all patients. Significant differences were observed across MIS quartiles in terms of age, dialysis vintage, dialysis time, and urine volume ($p < 0.05$ for all). QoL scores showed significant differences, with the physical component score and symptoms/problems score being lower in higher MIS quartiles ($p < 0.05$ for all). Multivariate analyses revealed that higher MIS quartiles were significantly associated with worse QoL scores, including symptoms/problems and physical component scores, even after adjusting for confounders ($p < 0.05$ for all). Moreover, the pruritus VAS score, as well as the burden of kidney disease and mental component, had a significant negative association with MIS after adjusting for confounders ($p < 0.05$ for all). This study demonstrates that higher MIS, indicating poorer nutritional status, is associated with impaired QoL, particularly in the symptoms/problems, physical, and mental components among hemodialysis patients. However, no significant association was found between MIS and CKD-aP.

Keywords Malnutrition-Inflammation Score, CKD-aP, Pruritus, Quality of life, Hemodialysis

Abbreviations

CKD-aP	Chronic Kidney Disease-Associated Pruritus
QoL	Quality of Life
MIS	Malnutrition-Inflammation Score

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FFQ	Food Frequency Questionnaire
KDQOL-SF™	Kidney Disease Quality of Life Short Form
YIQ	Yosipovitch Itch Questionnaire
BMI	Body Mass Index
CKD	Chronic Kidney Disease
SBP	Systolic Blood Pressure
DBP	Diastolic Blood Pressure
PCS	Physical Component Summary
MCS	Mental Component Summary
VAS	Visual Analog Scale
TIBC	Serum Total Iron Binding Capacity

Malnutrition is highly prevalent among dialysis patients, with studies reporting rates ranging from 18 to 56%[1,2]. The severity of malnutrition is also an important factor; as more severe forms confer greater mortality risk. In dialysis patients, two distinct forms of malnutrition have been identified. The first variant is typified by diminished nutritional status, depletion of fat-free mass, and maintained serum albumin levels. Conversely, the second form is marked by inflammation and atherosclerosis, evidenced by reduced serum albumin levels despite adequate food consumption. Research indicates that a notable portion of hemodialysis individuals fail to meet the prescribed protein and energy requirements. Consequently, their consumption of essential nutrients is suboptimal, leading to prevalent occurrences of protein-energy malnutrition and inflammation within this patient population[3,4]. The intricate interplay between malnutrition and inflammation in dialysis patients reveals a complex web of physiological disturbances that can significantly impact disease. In the realm of dialysis management, the Malnutrition-Inflammation Score (MIS) emerges as a valuable tool for assessing the nutritional and inflammatory status of patients[5,6]. The research literature has shown that higher scores on the MIS are correlated with poorer survival rates and an increased risk of mortality among dialysis patients. This finding underscores the critical importance of addressing issues of malnutrition and inflammation to improve the clinical outcomes and prognosis for individuals undergoing dialysis treatment[7,8]. Malnourished dialysis patients have diminished physiological reserves and reduced resilience to withstand the stresses of illness, hospitalization, and other medical interventions[9]. Studies have shown that nutritional status was significantly correlated with all generic quality of life (QoL) sub-scales, and malnutrition was the most significant predictor of impaired scores on the kidney disease quality of life instrument (KDQOL-SF)[10,11]. Hemodialysis (HD) patients generally have a moderate QoL compared to the general population, caregivers, and post-kidney transplantation patients, indicating a lower QoL in HD patients[12–14]. Research indicates that individualized dietary interventions significantly improve nutritional parameters such as serum albumin and BMI, which are closely linked to both physical and mental health outcomes in this population[15,16]. Malnutrition, often prevalent among hemodialysis patients, correlates negatively with QoL, highlighting the importance of nutritional assessments in predicting health outcomes[17]. Furthermore, complications during hemodialysis sessions and side effects like pruritus have been correlated with malnutrition in these patients[18]. However, it is important to note that many of these findings are derived from cross-sectional studies, which primarily identify statistical associations rather than causal relationships. Therefore, while these factors appear to correlate with QoL improvements, further longitudinal research is needed to establish definitive causal links and better inform clinical practices. Research indicates that pruritus, particularly uremic pruritus, is a common and distressing symptom among dialysis patients, significantly affecting their QoL. Previous studies have reported the prevalence of chronic kidney disease-associated pruritus (CKD-aP) in patients undergoing hemodialysis, ranging from 40 to 70%, with 37% experiencing moderate-to-severe itching[19,20]. Studies have shown that pruritus is associated with alterations in calcium/phosphorus metabolism, hyperparathyroidism and elevated plasma phosphorus levels[21]. Additionally, the opioid system is a significant target for many treatments aimed at alleviating uremic pruritus, indicating its central role in the pathophysiology of this symptom[21]. Despite technological advances in dialysis sessions and better treatment for chronic kidney disease, low QoL and CKD-aP remain common problems, often underdiagnosed. The current multicenter cross-sectional study examined the association between MIS, QoL, and CKD-aP in hemodialysis patients. By examining the nutritional and inflammatory status using MIS, we seek to gain a deeper understanding of the potential underlying the development of pruritus in chronic kidney disease (CKD) patients and its effect on their overall well-being. Understanding this association could provide valuable insights for the development of targeted interventions to improve the management of CKD-aP and enhance the QoL for hemodialysis patients.

Method

We conducted a cross-sectional study at eight medical facilities (five governments and three private) in Ahvaz, Shushtar, and Shiraz. All participants had a history of CKD and were undergoing regular hemodialysis for at least six months. Out of 755 patients initially screened, 268 were excluded for not meeting eligibility criteria or declining participation. An additional eight participants were excluded due to extreme calorie intake reporting. Ultimately, 479 CKD patients were included in the study (Fig. 1). The inclusion criteria were: undergoing regular hemodialysis for at least six months and being over 18 years of age. The exclusion criteria included: enteral or parenteral feeding, cognitive or communication problems, severe neurological or mental disorders, active neoplastic disease, severe alcohol or drug addiction, major amputation (lower/upper extremities), diagnosis of cancer, acute or chronic pancreatitis, irritable bowel syndrome, and hepatic insufficiency. The study adhered to the principles outlined in the Declaration of Helsinki. All participants provided written informed consent after being fully informed. Approval for this research was granted by the Ethics Committee of Shoushtar Faculty of Medical Sciences in Shoushtar, Iran (Registration no: IR.SHOUSHTAR.REC. 1403.035).

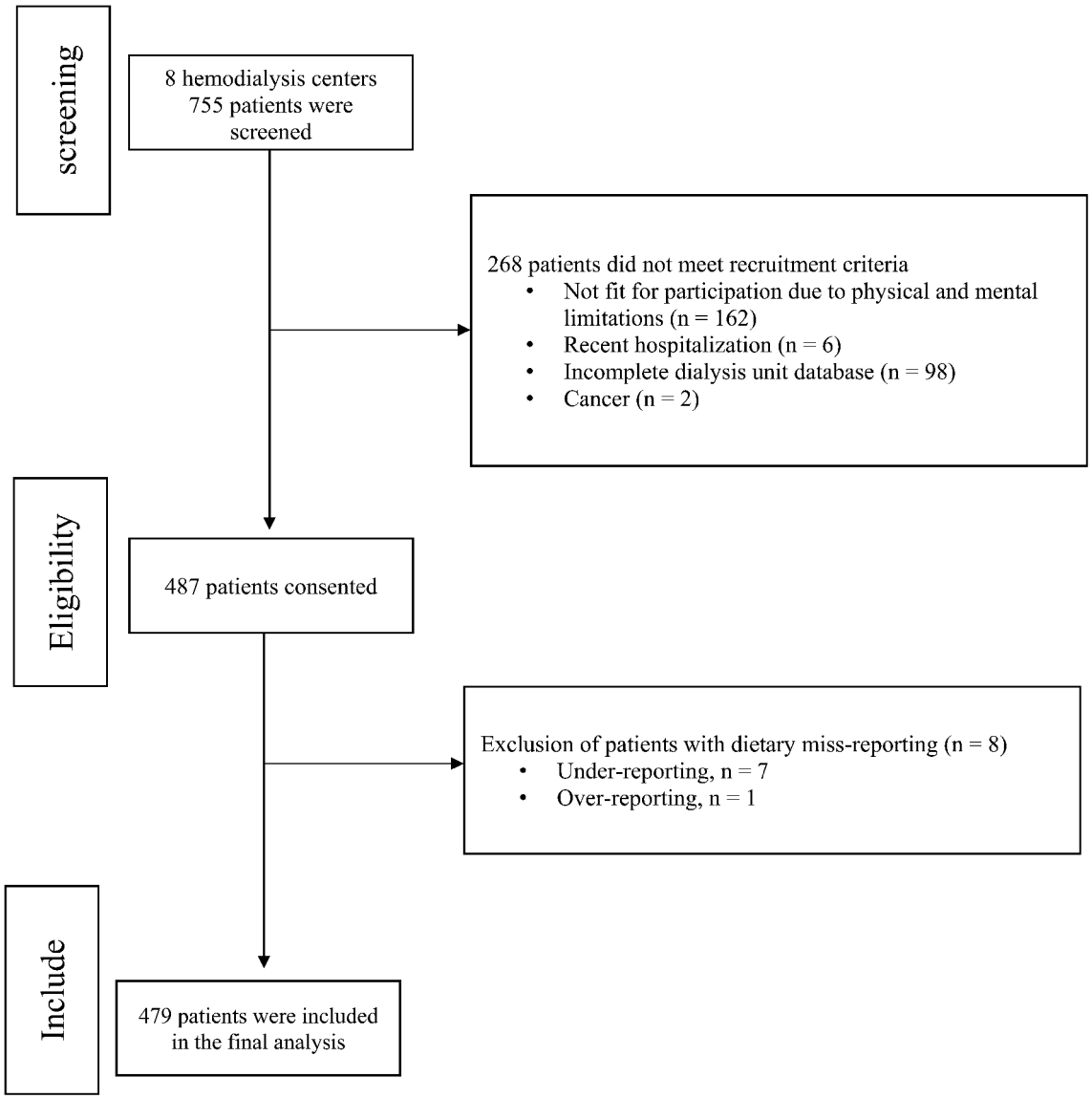

Fig. 1. Participant flow chart.

Data collection

We extracted various variables from medical records at baseline, including age, gender, marital status, jobs, duration of dialysis treatment, frequency of dialysis sessions, urea reduction ratio (URR), urea kinetics (Kt/V), and the primary etiology of renal failure. Biochemical markers, such as serum albumin, calcium, phosphate, creatinine, potassium, serum total iron binding capacity, and urea nitrogen, were assessed using data from the dialysis unit's records for the same month. Furthermore, detailed medical histories were recorded, including the history of medication prescriptions, and the presence of hypertension and diabetes mellitus. Hypertension was defined as a systolic blood pressure (SBP) of 130 mmHg or higher, a diastolic blood pressure (DBP) of 80 mmHg or higher, or the use of antihypertensive medication[22]. Diabetes was defined as a fasting glucose level of 7.0 mmol/L or higher, a glycated hemoglobin level of 6.5% or higher, or the use of antidiabetic medication[23].

Malnutrition-Inflammation Score (MIS)

The MIS is a validated tool used to assess the malnutrition-inflammation status of patients. It consists of 10 components, each with severity levels ranging from 0 (normal) to 3 (severely abnormal). These components include aspects like medical history, physical examination, BMI, and laboratory parameters like serum albumin level and Serum total iron binding capacity (TIBC). The total MIS score can range from 0 (normal) to 30 (severely malnourished), with a higher score indicating a more severe degree of malnutrition and inflammation. Based on the MIS score, the participants were categorized into three groups: normal nutritional status (MIS score 0–7), mild to moderate malnutrition (MIS score 8–18), and severe malnutrition (MIS score 19–30)[24,25].

Dietary food intake

Dietary intake was evaluated using a reliable and validated semi-quantitative food frequency questionnaire (FFQ) consisting of 168 food items, specifically designed for the Iranian population. The FFQ's ability to accurately depict the dietary habits of Iranians has been supported by previous research[26,27]. Trained dietitians conducted face-to-face interviews with patients to assist with questionnaire completion and to determine the frequency of consumption for each food item, ranging from daily to yearly, over the past year. The reported consumption frequency was standardized to daily intake equivalents. The serving sizes for individual food items were converted from household units to grams for consistency. Nutritional analysis was performed using Nutritionist IV software to calculate total energy, macronutrients, and micronutrients.

Quality of life assessment

QoL was assessed using the KDQOL-SF™ 1/3, a 36-item questionnaire that measures health-related QoL in CKD patients. It comprises two main sections: 12 generic items that gauge overall mental and physical well-being and 24 specific items related to CKD, focusing on symptoms, impacts, and the challenges posed by kidney disease. Participants rated item frequency or severity on a 5-point Likert scale. Responses were transformed into five subscale scores (0-100): Physical Component Summary (PCS), Mental Component Summary (MCS), Burden of Kidney Disease, Symptoms and Problems of Kidney Disease, and Effects of Kidney Disease, with higher scores indicating better QoL. The KDQOL-SF™ 1/3 is a valid and reliable tool for assessing QoL among Iranian HD patients[28]. It is responsive to QoL changes, easy to administer, and straightforward to interpret.

Assessment of pruritus

To evaluate the severity of itching in dialysis patients, the Yosipovitch Itch Questionnaire (YIQ) was employed. This well-established and validated instrument was developed by Yosipovitch and colleagues in 2001[29] and is modeled on the McGill pain questionnaire. The YIQ encompasses 8 sections comprising 23 questions that comprehensively assess the following dimensions: history of itching, history of anti-itching medication use, impact of itching on sleep, impact of itching on daily activities, impact of itching on QoL, emotional dimensions of itching (e.g., frustration, anger), intensity of itching based on the VAS in three scenarios, and location of itching. Scoring involves assigning a score of 1 for "yes" responses, 0 for "no" responses, 2 for "always" responses, 1 for "sometimes" responses, and 0 for "never" responses. To calculate the score for each section, the scores of the individual questions within that subscale are summed. Higher scores on each section of the YIQ indicate a greater severity of itching.

Anthropometric assessment

For anthropometric measurements, the patient's height was recorded barefoot using a non-stretchable tape measure with a precision of 0.1 cm. Dry weight, measured post-dialysis with minimal clothing and without shoes, was captured using a calibrated digital floor scale with a precision of 0.1 kg, ensuring the absence of signs of fluid depletion or overload. BMI was calculated by dividing dry weight by the square of the height.

Statistical analyses

To compare study variables, participants were categorized into quartiles based on their MIS scores. Continuous variables were presented as mean ± SD, while categorical variables were expressed as frequency (%). The Shapiro–Wilk test was used to evaluate the normality of continuous variables. Differences in continuous variables across MIS quartiles were compared using one-way ANOVA with post hoc (LSD). Categorical variables were compared across the MIS quartiles using the Chi-square or the Fisher's exact tests. In multivariate linear regression, the relationship between continuous dependent variables (CKD-aP and QoL) and MIS quartiles (as an independent variable) was examined in both crude and multivariable-adjusted models. The first adjusted model accounted for confounding factors such as age, sex, BMI, physical activity, diabetes, hypertension, smoking, occupation, marital status, education, income level, intradialytic weight gain, dialysis vintage, dialysis duration, frequency of hemodialysis sessions, fluid intake, and urine output. Model 2 additionally controlled for energy intake and medication prescriptions. Statistical analyses were performed using SPSS software (Version 26.0; Chicago, IL), with p-values < 0.05 considered statistically significant.

Results

Study population

As shown in Table 1, significant differences were observed across quartiles of MIS for age, BMI, center type, and medication prescriptions for calcium carbonate, sevelamer hydrochloride, calcitriol, and furosemide (all p values < 0.05). Patients in higher MIS quartiles (Q4) were older (mean age 58.25 ± 15.54 years; $p < 0.001$) and had a lower BMI ($p = 0.001$). A significant association was also found between MIS quartiles and the type of center where patients received care ($p = 0.001$), with a higher proportion of patients in higher MIS quartiles receiving care at governmental centers. Additionally, patients in higher MIS quartiles received higher doses of calcium carbonate ($p = 0.01$), sevelamer hydrochloride ($p = 0.01$), calcitriol ($p = 0.004$), and furosemide ($p = 0.04$). Although not statistically significant, there was a trend towards higher rates of diabetes and hypertension in patients with higher MIS quartiles ($p \geq 0.05$).

Dialysis parameters and nutritional intake at baseline across MIS quartiles

In Table 2, significant differences were observed across MIS quartiles in terms of dialysis vintage, dialysis time, and urine volume. Patients in the lowest MIS quartile (Q1) had a shorter duration of dialysis treatment (mean dialysis vintage 69.48 ± 63.83 months) compared to other quartiles. While, the highest quartile had longer dialysis times (mean 3.86 ± 0.51 h). The study also found that dietary intake varied significantly across quartiles,

Characteristics, mean (SD) or *N* (%)	MIS quartiles				*P* value
	Q1(*N* = 116)	Q2(*N* = 106)	Q3(*N* = 152)	Q4(*N* = 105)	
Age, y	49.00 ± 14.24[a, b,c]	53.75 ± 13.45[e]	54.38 ± 15.20[f]	58.25 ± 15.54	**< 0.001**
Male (%)	71 (61.2)	63 (60.0)	90 (59.6)	54 (51.4)	**0.04**
BMI, kg/m^2	26.87 ± 4.32[b, c]	25.9 ± 4.33[d, e]	23.76 ± 4.87	23.8 ± 12.6	**0.001**
Diabetes (n, %)	63 (54.3)	54 (50.9)	89 (58.6)	64 (61.0)	0.44
Hypertension (n, %)	28 (24.1)	28 (26.4)	35 (23.0)	30 (28.6)	0.76
Center type (N) (%)					**0.001**
Governmental	37 (31.9)	63 (59.4)	112 (73.7)	90 (85.7)	
Private	79 (68.1)	43 (40.6)	40 (26.3)	15 (14.3)	
Job, N (%)					0.25
Unemployed	17 (14.7)	23 (21.7)	22 (14.5)	12 (11.4)	
Housekeeper	34 (29.3)	34 (32.1)	54 (35.5)	47 (44.8)	
Retired	28 (24.1)	25 (23.6)	37 (24.3)	24 (22.9)	
Employee	13 (11.2)	6 (5.7)	7 (4.6)	4 (3.8)	
Self-employment	15 (12.9)	13 (12.3)	25 (16.4)	15 (14.3)	
Others	9 (7.8)	5 (4.7)	7 (4.6)	3 (2.9)	
Marital status, N (%)					0.58
Married	88 (75.9)	83 (78.3)	111 (73.0)	75 (71.4)	
Single	23 (19.8)	16 (15.1)	31 (20.4)	14 (13.3)	
Divorced	4 (3.4)	3 (2.8)	3 (2.0)	7 (6.7)	
Dead spouse	1 (0.9)	4 (3.8)	7 (4.6)	9 (8.6)	
Education, N (%)					0.60
< 12 years	83 (71.6)	86 (81.1)	123 (80.9)	90 (85.7)	
≥ 12 years	33 (28.4)	20 (18.9)	29 (19.1)	15 (14.3)	
Income status, N (%)					0.58
< 5 million Rials	34 (29.3)	45 (42.5)	51 (33.6)	34 (32.4)	
5–10 million Rials	44 (37.9)	37 (34.9)	60 (39.5)	43 (41.0)	
10–20 million Rials	32 (27.6)	19 (17.9)	30 (19.7)	23 (21.9)	
> 20 million Rials	6 (5.2)	5 (4.7)	11 (7.2)	5 (4.8)	
Medication prescriptions					
Calcium carbonate 500 mg, time/day	1.00 ± 1.48[b]	1.04 ± 1.61[d]	1.61 ± 2.11	1.23 ± 1.52	**0.01**
Sevelamer hydrochloride 800 mg, time/day	1.05 ± 1.81[c]	0.83 ± 1.50	0.81 ± 1.24	0.59 ± 1.20	**0.01**
Calcitriol 0.25 mcg, time/day	0.40 ± 0.86[b]	0.61 ± 1.08[d]	0.90 ± 1.36	0.69 ± 1.00	**0.004**
Furosemide time/day	0.60 ± 1.25[a, b,c]	0.33 ± 0.79	0.35 ± 0.81	0.28 ± 0.72	**0.04**
Corticosteroids, N (%)	110 (94.9)	105 (99.1)	143 (94.1)	100 (95.2)	0.25
Lipid-lowering drugs, N (%)	95 (81.9)	93 (87.7)	121 (79.6)	87 (82.9)	0.40

Table 1. The characteristics at baseline across quartiles of MIS ($n = 479$). Data for quantitative variables are presented as means ± SD, obtained from ANOVA, Post hoc (LSD) according to the pattern. Data for qualitative variables are presented as frequencies (percentages) and analyzed using chi-square tests. BMI, body mass index; MIS, Malnutrition-Inflammation Score. [a]Significant difference between quartiles 1 and 2. [b]Significant difference between quartiles 1 and 3. [c]Significant difference between quartiles 1 and 4. [d]Significant difference between quartiles 2 and 3. [e]Significant difference between quartiles 2 and 4. [f]Significant difference between quartiles 3 and 4.

with the higher energy and protein intake observed in Q1 compared to Q3 and Q4 ($p = 0.01$ and $p = 0.001$, respectively).

MIS, CKD-aP, and QoL at baseline across MIS quartiles

Table 3 presents a comprehensive analysis of various characteristics across four quartiles (Q1 to Q4) of the MIS. The MIS score significantly differed across quartiles, with Q1 having a mean score of 1.21 (± 0.75) and Q4 showing the highest mean score of 11.39 (± 2.35) ($p < 0.001$). The distribution of nutritional status among the participants was as follows: 335 were well-nourished, 135 had mild-to-moderate malnutrition. The prevalence of severe malnutrition was highest in the CKD-aP group, with no significant difference in distribution across the quartiles (p-value = 0.43). The CKD-aP Score ranged from 3.83 ± 2.03 in Q1 to 4.61 ± 2.21 in Q4. The visual analogue scale (VAS) score did not show significant differences across quartiles (p-value = 0.60). In terms of QoL, the QoL Score was significantly lower in Q4 compared to the other quartiles, with a mean score of 53.63 ± 13.15 ($p = 0.01$). Additionally, the Symptoms/Problems Score and the Physical Component Score also

Characteristics, mean (SD) or *N* (%)	MIS quartiles				*P* value
	Q1(*N* = 116)	Q2(*N* = 106)	Q3(*N* = 152)	Q4(*N* = 105)	
Urine volume					
< 500 ml	67 (57.8)	75 (70.8)	121 (79.6)	82 (78.1)	**< 0.001**
≥ 500 ml	49 (42.2)	31 (29.2)	31 (20.4)	23 (21.9)	
Dialysis parameters					
Intradialytic Weight Gain, kg	1.85 ± 1.18[c]	2.02 ± 1.1	1.99 ± 1.31	2.28 ± 1.06	0.05
Dialysis vintage, month	19.73 ± 17.67[a, b,c]	45.86 ± 50.25[e]	57.73 ± 73.53	69.48 ± 63.83	**< 0.001**
Dialysis time, hours	3.55 ± 0.45[b, c]	3.67 ± 0.55[e]	3.69 ± 0.44[f]	3.86 ± 0.51	**< 0.001**
Frequency dialysis per week, Time/week	2.84 ± 0.43	2.84 ± 0.43	2.91 ± 0.57	2.78 ± 0.62	0.28
Dietary intake					
Energy, kcal/d	2374.2 ± 845.6[b, c]	2182.4 ± 931.2	2151.7 ± 818.8	2017.4 ± 773.3	**0.01**
Carbohydrates intake, g	357.0 ± 142.2	321.6 ± 143.6	324.4 ± 128.0	310.0 ± 130.7	**0.06**
Protein intake, g	87.8 ± 36.5[b, c]	79.3 ± 37.4	74.1 ± 31.1	71.0 ± 29.4	**0.001**
Total fat intake, g	68.4 ± 33.1	66.6 ± 38.6	64.8 ± 35.7	57.6 ± 33.7	0.12
Fluid intake, ml	1235 ± 1288	1279 ± 1023	1158 ± 733	1094 ± 866	0.52
PA, met-min/wk	361.66 ± 530.67	391.32 ± 1060.94	352.25 ± 1086.22	785.24 ± 4229.32	0.37

Table 2. The mean (SD) or N (%) of dialysis parameters and nutritional intake at baseline across quartiles of MIS ($n = 479$). Data for quantitative variables are presented as means ± SD, obtained from ANOVA, Post hoc (LSD) according to the pattern. Data for qualitative variables are presented as frequencies (percentages) and analyzed using chi-square tests. PA, physical activity. [a]Significant difference between quartiles 1 and 2. [b]Significant difference between quartiles 1 and 3. [c]Significant difference between quartiles 1 and 4. [d]Significant difference between quartiles 2 and 3. [e]Significant difference between quartiles 2 and 4. [f]Significant difference between quartiles 3 and 4. [d]Significant difference between quartiles 2 and 3. [e]Significant difference between quartiles 2 and 4. [f]Significant difference between quartiles 3 and 4.

Characteristics, mean (SD) or *N* (%)	TOTAL (*N* = 479)	MIS quartiles				*P* value
		Q1(*N* = 116)	Q2(*N* = 106)	Q3(*N* = 152)	Q4(*N* = 105)	
MIS						
Well-nourished, N (%)	335 (69.93)	116 (100)	106 (100)	113 (74.34)	0	**< 0.001**
Mild-to-moderate malnutrition, N (%)	135 (28.18)	0	0	39 (25.65)	96 (91.42)	
Severe malnutrition, N (%)	9 (1.87)	0	0	0	9 (8.57)	
MIS Score	5.59 ± 3.88	1.21 ± 0.75[a, b,c]	3.42 ± 0.49[d, e]	6.46 ± 1.14[f]	11.39 ± 2.35	**< 0.001**
CKD-aP						
No, N (%)	286 (59.70)	74 (63.79)	57 (53.77)	94 (61.84)	61 (58.09)	0.43
Yes, N (%)	193 (40.29)	42 (36.20)	49 (46.22)	58 (38.15)	44 (41.90)	
CKD-aP Score	4.07 ± 2.13	3.83 ± 2.03	3.89 ± 1.97	4.00 ± 2.24	4.61 ± 2.21	0.29
VAS Score	3.22 ± 3.20	3.59 ± 3.70	2.89 ± 3.12	2.98 ± 2.82	3.54 ± 3.29	0.60
Quality of Life						
Quality of Life Score	57.08 ± 13.09	59.39 ± 13.26[c]	57.33 ± 14.05[e]	57.54 ± 11.84[f]	53.63 ± 13.15	**0.01**
Symptoms/problems	82.36 ± 13.87	85.50 ± 13.38[b, c]	83.65 ± 12.61[d, e]	82.14 ± 13.75[f]	77.94 ± 14.80	**< 0.001**
Effects of kidney disease	75.46 ± 18.86	75.73 ± 20.19	76.71 ± 20.34	75.99 ± 16.14	73.18 ± 19.55	0.54
Burden of kidney disease	44.02 ± 29.81	46.39 ± 29.89	43.39 ± 32.76	45.23 ± 27.89	40.29 ± 29.32	0.44
Physical component	40.10 ± 11.74	45.24 ± 9.89[a, b,c]	41.59 ± 11.84[e]	39.07 ± 11.06[f]	34.41 ± 11.85	**< 0.001**
Mental component	43.45 ± 12.63	44.09 ± 13.14	41.30 ± 11.53	45.25 ± 12.53	42.33 ± 13.02	0.06

Table 3. The mean (SD) or N (%) of MIS, CKD-aP and Quality of Life at baseline across quartiles of MIS ($n = 479$). Data for quantitative variables are presented as means ± SD, obtained from ANOVA, Post hoc (LSD) according to the pattern. Data for qualitative variables are presented as frequencies (percentages) and analyzed using chi-square tests. MIS, Malnutrition-Inflammation Score; CKD-aP, chronic kidney disease-associated pruritus. [a]Significant difference between quartiles 1 and 2. [b]Significant difference between quartiles 1 and 3. [c]Significant difference between quartiles 1 and 4. [d]Significant difference between quartiles 2 and 3. [e]Significant difference between quartiles 2 and 4. [f]Significant difference between quartiles 3 and 4.

showed a similar trend, with Q4 reporting mean scores of 77.94 ± 14.80 and 34.41 ± 11.85, respectively, both significantly lower than those in the other quartiles ($p < 0.001$), while the mental component score showed no significant differences across quartiles ($p = 0.06$).

Clinical and laboratory values at baseline across MIS quartiles

The clinical and laboratory values at baseline across quartiles of the MIS Score are summarized in Table 4. Mean fasting blood sugar (113.41 ± 48.20 mg/dL) and hemoglobin (11.24 ± 1.80 g/L) were within normal ranges, with no significant differences across quartiles. However, iron levels were significantly higher in the lowest quartile (90.82 ± 83.49 mg/dL) compared to other quartiles (63.90-71.25 mg/dL, $p = 0.001$) and sodium was lower in the Q2 (138.42 ± 4.42 mmol/L) compared to Q1 and Q4 (140.58 ± 6.00 and 139.97 ± 4.86, $p = 0.012$). Phosphate and Ca x P levels were notably lower in the highest quartile (4.80 ± 1.20 mg/dL and 40.44 ± 10.85 mg2/dL2, respectively) than Q1 and Q2 ($p = 0.002$ and $p = 0.006$, respectively).

MIS score relationship with quality of life (QoL) and chronic kidney disease-associated pruritus (CKD-aP)

Based on the multivariate linear regression analyses presented in Table 5, the results were adjusted for various covariates across three models. In Model 0, which only accounted for MIS quartiles as an independent variable, the β coefficients for Q2, Q3, and Q4 were 0.06 (SE = 0.44, $p = 0.88$), 0.17 (SE = 0.43, $p = 0.70$), and 0.78 (SE = 0.45, $p = 0.09$) respectively, showing no significant association with CKD-aP. However, in Model 1 and Model 2, where MIS quartiles were entered as an independent variable and adjusted for additional variables such as demographic factors and dialysis-related parameters, the associations remained non-significant with similar β coefficients and p-values. The visual analog scale (VAS) Score showed a significant negative association in both Model 1 and Model 2 after adjustments. For instance, in Model 1, the β coefficients for Q2-Q4 were −1.58 (SE = 0.65, $p = 0.01$), -1.71 (SE = 0.75, $p = 0.02$), and −1.22 (SE = 0.84, $p = 0.15$), indicating a worsening of VAS scores with higher MIS quartiles. Regarding KDQOL-SF dimensions such as QoL Score and Symptoms/Problems Score, significant negative associations were observed in higher quartiles when compared to Q1 in both Model 1 and Model 2 after adjustments for confounders like age, sex, BMI, comorbidities, socioeconomic status, and dialysis-related factors. For instance, in the QoL Score assessment using Model 2, the β coefficients for Q3 and Q4 were −1.80 (SE = 1.74, $p < 0.001$) and −6.39 (SE = 2.02, $p < 0.001$) respectively. In the Symptoms/Problems Score assessment using the same model, the β coefficients for Q3 and Q4 were −2.24 (SE = 1.90, $p = 0.24$) and −6.54 (SE = 2.21, $p < 0.001$). Furthermore, significant decrements were observed in Physical Component Scores across all models with increasing MIS quartiles; for example in Model 2: Q2 (-3.20 SE = 1.43, $p = 0.03$), Q3 (-5.05 SE = 1.48, $p < 0.001$), Q4 (-8.93 SE = 1.72, $p < 0.001$). In contrast to physical components, Mental Component Scores did not show a consistent pattern in Model 0. However, in Models 1 and 2, significant associations were observed with Q4 ($p < 0.05$). Moreover, the Burden of Kidney Disease showed a significant negative association in Model 1 for Q4 (-11.14 SE = 4.79, $p = 0.02$, p-trend = 0.01).

Characteristics, mean (SD) or *N* (%)	MIS quartiles				*P* value
	Q1(*N* = 116)	Q2(*N* = 106)	Q3(*N* = 152)	Q4(*N* = 105)	
FBS, mg/dL	113.41 ± 48.20	120.34 ± 58.00	110.00 ± 43.03	114.819 ± 52.17	0.437
Hemoglobin, g/L	11.24 ± 1.80	10.94 ± 1.90	11.21 ± 2.00	11.47 ± 1.85	0.254
Iron, mg/dL	90.82 ± 83.49[a, b,c]	71.25 ± 51.25	65.96 ± 43.55	63.90 ± 43.20	**0.001**
Ferritin, ng/mL	236.82 ± 242.75[c]	261.62 ± 268.27[e]	281.68 ± 259.48[f]	408.44 ± 359.5	**0.001**
Serum total iron binding capacity ,µg/dL	337.7 ± 74.14[b, c]	331.75 ± 79.83[d, e]	289.65 ± 94.74[f]	229.69 ± 103.77	**0.001**
Hematocrit, %	34.90 ± 6.98	34.33 ± 5.34	34.88 ± 5.98	34.51 ± 7.63	0.883
Platelets, 10*3/µg	202.85 ± 64.60	192.47 ± 67.48	185.44 ± 72.82	183.99 ± 70.51	0.140
Calcium, mg/dL	8.43 ± 0.94	8.39 ± 0.90	8.41 ± 0.99	8.41 ± 0.77	0.990
Sodium, mmol/L	140.58 ± 6.00[a]	138.42 ± 4.42[e]	139.63 ± 4.35	139.97 ± 4.86	**0.012**
Potassium, mmol/L	4.94 ± 0.76[b, c]	5.03 ± 0.73[e]	5.11 ± 0.91	5.14 ± 0.84	0.256
Phosphate, mg/dL	5.44 ± 1.09[b, c]	5.29 ± 1.54[e]	5.06 ± 1.38	4.80 ± 1.20	**0.002**
Ca x P, mg^2/dL^2	45.74 ± 9.52[b, c]	44.37 ± 13.74[e]	42.62 ± 12.34	40.44 ± 10.85	**0.006**
Albumin, g/ dL	4.26 ± 0.39	4.26 ± 0.39	4.26 ± 0.39	4.26 ± 0.39	0.54

Table 4. The mean (SD) Clinical and laboratory values at baseline across quartiles of MIS ($n = 479$). Data for quantitative variables are presented as means ± SD, obtained from ANOVA, Post hoc (LSD) according to the pattern. Data for qualitative variables are presented as frequencies (percentages) and analyzed using chi-square tests. FBS: fasting blood sugar; Ca: calcium; P: phosphate. [a]Significant difference between quartiles 1 and 2. [b]Significant difference between quartiles 1 and 3. [c]Significant difference between quartiles 1 and 4. [d]Significant difference between quartiles 2 and 3. [e]Significant difference between quartiles 2 and 4. [f]Significant difference between quartiles 3 and 4.

		Q1		Q2		Q3		Q4		
		β (SE)	*p*	β (SE)	*P*	β (SE)	*p*	β (SE)	*p*	*p*-Trend
CKD-Ap										
CKD-aP Score	Model 0	Ref.	-	0.06(0.44)	0.88	0.17(0.43)	0.70	0.78(0.45)	0.09	0.09
	Model 1	Ref.	-	-0.37(0.44)	0.41	-0.35(0.52)	0.49	0.38(0.59)	0.52	0.50
	Model 2	Ref.	-	-0.37(0.45)	0.40	-0.30(0.52)	0.56	0.38(0.59)	0.52	0.46
VAS Score	Model 0	Ref.	-	-0.70(0.67)	0.30	-0.61(0.64)	0.34	-0.05(0.69)	0.94	0.98
	Model 1	Ref.	-	-1.58(0.65)	**0.01**	-1.71(0.75)	**0.02**	-1.22(0.84)	0.15	0.19
	Model 2	Ref.	-	-1.61(0.65)	**0.01**	-1.43(0.75)	0.06	-1.17(0.85)	0.17	0.26
Quality of life										
Quality of Life Score	Model 0	Ref.	-	-2.06(1.74)	0.24	-1.85(1.59)	0.24	-5.76(1.74)	**<0.001**	**0.003**
	Model 1	Ref.	-	-1.54(1.76)	0.38	-2.66(1.81)	0.14	-7.10(2.10)	**<0.001**	**0.001**
	Model 2	Ref.	-	-1.40(1.68)	0.30	-1.80(1.74)	**<0.001**	-6.39(2.02)	**<0.001**	**0.003**
Symptoms/problems	Model 0	Ref.	-	-1.85(1.83)	0.31	-3.36(1.68)	0.05	-7.57(1.83)	**<0.001**	**<0.001**
	Model 1	Ref.	-	-0.98(1.88)	0.60	-2.58(1.94)	0.18	-6.27(2.25)	**0.01**	**0.006**
	Model 2	Ref.	-	-1.37(1.84)	0.46	-2.24(1.90)	0.24	-6.54(2.21)	**<0.001**	**0.005**
Effects of kidney disease	Model 0	Ref.	-	0.98(2.53)	0.70	0.26(2.32)	0.91	-2.54(2.53)	0.32	0.33
	Model 1	Ref.	-	0.51(2.6)	0.84	0.47(2.68)	0.86	-3.08(3.11)	0.32	0.37
	Model 2	Ref.	-	0.69(2.56)	0.76	1.49(2.64)	0.57	-2.35(3.07)	0.44	0.55
Burden of kidney disease	Model 0	Ref.	-	-2.99(3.99)	0.45	-1.16(3.66)	0.75	-6.09(4.00)	0.13	0.21
	Model 1	Ref.	-	-0.88(4.01)	0.83	-4.71(4.13)	0.25	-11.14(4.79)	**0.02**	**0.01**
	Model 2	Ref.	-	-0.14(3.89)	0.97	-2.85(4.01)	0.48	-9.00(4.66)	0.05	0.05
Physical component	Model 0	Ref.	-	-3.65(1.49)	0.01	-6.17(1.37)	**<0.001**	-10.83(1.50)	**<0.001**	**<0.001**
	Model 1	Ref.	-	-3.27(1.49)	**<0.001**	-5.54(1.54)	**<0.001**	-9.59(1.79)	**<0.001**	**<0.001**
	Model 2	Ref.	-	-3.20(1.43)	**0.03**	-5.05(1.48)	**<0.001**	-8.93(1.72)	**<0.001**	**<0.001**
Mental component	Model 0	Ref.	-	-2.79(1.68)	0.10	1.16(1.54)	0.45	-1.75(1.69)	0.30	0.90
	Model 1	Ref.	-	-3.09(1.66)	0.06	-0.92(1.71)	0.59	-5.4(1.99)	**0.01**	**0.03**
	Model 2	Ref.	-	-2.97(1.64)	0.07	-0.33(1.69)	0.84	-5.15(1.97)	**0.01**	**0.04**

Table 5. Multivariate linear regression of the association Chronic kidney disease-associated pruritus, and Quality of life and Malnutrition-Inflammation Score (MIS) ($n = 479$). Model 0: Calculated using multivariate linear regression, MIS quartiles entered as an independent variable. In this test, bold values indicate the significance level below 0.05 is defined ($p < 0.05$). Model 1: Calculated using multivariate linear regression, MIS quartiles entered as an independent variable, and adjusted for the effect of age, sex, BMI, physical activity, diabetes, hypertension, smoking, job, marital status, education, income status, inter-dialysis weight gain, dialysis vintage, dialysis time, frequency of hemodialysis sessions, fluid intake, and urine volume. Model 2: Calculated using multivariate linear regression, MIS quartiles entered as an independent variable, and adjusted for the effect of age, sex, BMI, physical activity, diabetes, hypertension, smoking, job, marital status, education, income status, inter-dialysis weight gain, dialysis vintage, dialysis time, frequency of hemodialysis sessions, fluid intake, urine volume, energy intake, and medication prescriptions. CKD-aP, chronic kidney disease-associated pruritus; VAS: visual analog scale.

Discussion

Despite the acknowledged significance of nutritional status in HD patients, the exploration of the association between malnutrition, QoL, and CKD-aP remains an underexplored area in the literature. The results of this study demonstrate that patients in the highest MIS quartile (Q4) were older, had a longer dialysis vintage, longer weekly dialysis times, and a higher percentage of patients with low urine volume. This is consistent with previous research showing that older age and longer dialysis duration are associated with an increased risk of malnutrition and inflammation in this patient population[30]. The observed differences in dialysis parameters across MIS quartiles likely reflect the complex interplay between malnutrition, inflammation, and declining kidney function in this patient group. Furthermore, the present study demonstrates varying degrees of nutritional status among dialysis patients. Mild-to-moderate malnutrition was prevalent in 28% of participants, while severe malnutrition was present in 5.3%. These findings align with previous studies, such as that by Harun et al. (2021)[5], which reported significantly different MIS scores in hemodialysis patients. Additionally, another study conducted on HD patients showed that 25% of patients were normally nourished, 54.3% were mildly malnourished, 20.8% were moderately malnourished, and none were severely malnourished[30]. The pathogenesis of malnutrition in CKD is multifaceted, including alterations in metabolism and nutrient processing. The catabolic effects of uremia and chronic inflammation associated with CKD accelerate muscle wasting and protein-energy malnutrition. Additionally, the frequent dialysis sessions in hemodialysis treatment can lead to the loss of essential nutrients and proteins[10,31]. Our findings are consistent with prior research indicating that the MIS is associated with

adverse outcomes in this population. The present study found significant associations between QoL scores, particularly in the symptoms/problems domain and the physical component, with MIS. There are limited studies on the association between MIS and QoL in HD patients. Visiedo et al. (2022)[10] demonstrated that malnutrition is associated with lower scores on various QoL sub-scales, including the kidney disease summary component, the physical component summary, and the mental component summary. In addition, Ali et al. (2024)[32] reported a significant correlation between malnutrition and lower QoL scores among elderly patients, those with pitting edema, and individuals with diabetes. In contrast, Shahrin et al. (2019)[33] found no significant association between nutritional status and burden of kidney disease, symptom/problem list, and effects of kidney disease except for a correlation between protein intake and the physical composite subscale of QoL. In addition to the findings mentioned earlier, this study revealed a significant negative correlation between the risk of malnutrition and the physical and mental composites of QoL. The differential impact of nutritional status on physical and mental components of QoL is well-demonstrated. While malnutrition may primarily affect physical functioning and symptoms, its influence on mental well-being can vary. The varying significance of the mental component across different models can be attributed to the intricate nature of health and the complexity of adjustments made in the regression analysis. The inclusion of additional covariates in Model 1 and Model 2 highlights the multifaceted influence of factors such as age, sex, BMI, physical activity, comorbidities, and medication prescriptions, which may alter the observed associations. Research suggests that factors such as age, gender, education level, marital status, and living conditions can all influence an individual's mental QoL[34,35]. Possible mechanisms may include the important role of dietary protein intake in the catabolic process in HD patients, which helps prevent muscle wasting and decrease the risk of infection. Furthermore, poor nutrition can result in nutrient deficiencies, such as low levels of iron, zinc, magnesium, and omega-3 fatty acids, which are crucial for brain function and development. These deficiencies can lead to irritability, lack of concentration, and cognitive impairments[36,37]. Another important finding is that multivariate linear regression analysis did not reveal a significant association between CKD-aP and MIS quartiles, even after adjusting for demographic factors and dialysis-related parameters. However, the VAS score exhibited a significant negative association with higher MIS quartiles after adjusting for multiple variables. The VAS score is used to assess the severity of pruritus. Research suggests a correlation between elevated blood lead levels and inflammation, as well as poor nutritional status, which may intensify pruritus in HD patients[38]. Conversely, patients with pruritus frequently present with analytical parameters indicative of malnutrition, including low albumin levels and elevated C-reactive protein[21]. In a study of anorexia nervosa patients, pruritus was assessed using a structured questionnaire, VAS, clinical examination, and serological markers. The study demonstrated pruritus as a clinical manifestation of anorexia nervosa, associated with low weight and resolving with weight restoration[39]. The disparity between our findings and those reported may be attributed to differences in the study population and variable assessment methods. Previous studies primarily focused on changes in body mass index or albumin and C-reactive protein levels, while our study employed the MIS, which evaluates a comprehensive array of laboratory parameters. In our study, the fluctuating significance of the VAS Score across different models could be attributed to the intricacies of adjusting for various covariates in the regression analysis. While Model 1 demonstrates a significant association between higher MIS quartiles and worse VAS scores after adjusting for several demographic and clinical factors, the inclusion of additional covariates in Model 2 might have diluted this association. Factors such as energy intake and medication prescriptions included in Model 2 could potentially mediate the relationship between MIS quartiles and subjective well-being, thereby affecting the significance of the VAS Score. This study contributes to a deeper understanding of how nutritional and inflammatory status can affect dialysis patients and emphasizes the need for targeted interventions in this vulnerable population. However, it is important to note that our study was not without limitations. First, its cross-sectional design precludes the establishment of causal relationships between MIS and the outcomes of interest. Longitudinal studies are needed to determine the temporal relationship between these variables. Second, the sample size, although relatively large, may not be sufficient to detect small or moderate effects, particularly in subgroup analyses. Third, the dietary intake data were collected using a FFQ, which relies on self-reporting and may be subject to recall bias and measurement error. Finally, the study was conducted in a specific geographic region and may not be generalizable to other populations or settings.

Conclusion

This multicenter cross-sectional study demonstrates a significant association between the MIS and various dimensions of QoL among hemodialysis patients. The results indicate that higher MIS quartiles are linked to poorer QoL, particularly in physical health, symptoms/problems and the burden of kidney disease, with substantial differences observed across quartiles. Specifically, patients in the lowest MIS quartile reported significantly better health-related QoL compared to those in the highest quartile. Despite these findings, no significant correlation was found between MIS and CKD-aP scores across quartiles, suggesting that while nutritional status impacts QoL, it may not directly influence the severity of pruritus in this population. Furthermore, clinical parameters such as iron levels and phosphate concentrations varied significantly across MIS quartiles, highlighting the complex interplay between nutrition, inflammation, and overall health in hemodialysis patients. These findings underscore the critical need for routine assessment of nutritional status using tools like the MIS to identify at-risk patients early and implement targeted interventions. Addressing malnutrition and inflammation may enhance patient outcomes and improve QoL for individuals undergoing hemodialysis. Future research should explore the longitudinal effects of nutritional interventions on both QoL and CKD-aP to further elucidate these relationships.

Data availability

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

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Author contributions

Study concept and design: H.R and M.A; acquisition of data: P.T, K.K, H.S and S.S; analysis and interpretation of data: H.B and F.F; drafting of the manuscript: H.R, A.Z and H.B; critical revision of the manuscript for important intellectual content: S.K and S.S; statistical analysis: H.B and M.A; administrative, technical, and material support: S.B & S.S; study supervision: M.A and A.Z.

Declarations

Competing interests

The authors declare no competing interests.

Additional information

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