

PAPER DETAILS

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Relation of parathyroid hormone with malnutrition in peritoneal dialysis patients

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ABSTRACT

Aims: Protein-energy wasting syndrome is a risk factor specific to ESRD is protein-energy wasting (PEW) syndrome. Clinical and experimental studies have suggested that secondary hyperparathyroidism plays a vital role in increasing energy expenditure in patients with ESRD. The geriatric nutritional risk index (GNRI) is used to evaluate nutritional status in various pathological conditions. Considering the effect of parathormone on malnutrition and studies indicating that parathyroid hormone causes weight loss, we aimed to investigate the relationship between malnutrition and parathyroid hormone (PTH) in our patients using GNRI.

Methods: Forty-nine patients without known malignancy, liver disease, or chronic inflammatory disease who underwent peritoneal dialysis were included in the study. Patient data were recorded from these files. Height and weight were measured. GNRI was calculated by the formula $14.89 \times \text{serum albumin (g/dL)} + [41.7 \times \text{bodyweight/ideal body weight}]$

Results: Forty-nine patients (29 females, 59.2%) were included in the study. Three (6.1%), seven (14.3%), and seven (14.3%) patients had severe, moderate, and mild malnutrition, respectively. GNRI was positively correlated with albumin, hematocrit, and calcium levels ($r=0.757$, $r=0.355$, $r=0.423$; $p<0.05$, respectively). GNRI was negatively correlated with dialysis vintage ($r=-0.303$, $p=0.038$) and PTH ($r=-0.287$; $p=0.046$).

Conclusion: This study demonstrated a relationship between malnutrition and hyperparathyroidism. Increased PTH levels may cause phenotypic switching from white to brown fat via PTH receptors.

Keywords: Peritoneal dialysis, protein-energy malnutrition, secondary hyperparathyroidism

INTRODUCTION

The risk of mortality in people with chronic kidney disease, especially those receiving renal replacement therapy for end-stage renal disease (ESRD), is too high to be explained by traditional risk factors alone.¹ One risk factor for ESRD is protein-energy wasting (PEW) syndrome, which is characterized by malnutrition and changes in body composition.²⁻⁴ PEW is common in patients with ESRD and is associated with a risk of hospitalization and death.⁵⁻⁷ Therefore, new therapeutic approaches are needed to prevent and treat PEW. Previous clinical and experimental studies have suggested that secondary hyperparathyroidism plays a vital role in increasing energy expenditure in ESRD.⁸⁻¹⁰

The geriatric nutritional risk index (GNRI), calculated only by body weight, height, and serum albumin level, is used to evaluate the nutritional status in various

pathological conditions.^{11,12} It has been used in chronic hemodialysis,¹²⁻²¹ and peritoneal dialysis (PD)²²⁻²⁴ patients in the association between malnutrition and all-cause mortality and cardiovascular (CV) events.

Considering the effect of parathormone on malnutrition and studies indicating that parathyroid hormone causes weight loss, we aimed to investigate the relationship between malnutrition and PTH in our patients using the GNRI.

METHODS

The study was initiated with the approval by the Health Sciences University Haseki Training and Research Hospital Clinical Researches Ethics Committee (Date: 01.03.2023, Decision No: 217-2022). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

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This was a retrospective cross-sectional study. A total of 49 patients who were followed up in the peritoneal dialysis unit of the Haseki Research And Training Hospital for four years without known malignancy, liver disease, chronic inflammatory disease, and who did not receive nutritional support were included in the study. An informed consent form was obtained from all patients. Demographic and laboratory data were recorded from their files. Height and weight were measured. GNRI was calculated according to the formula $14.89 \times \text{serum albumin (g/dl)} + [41.7 \times \text{bodyweight/ideal body weight}]$. If body weight exceeded the ideal body weight, the body weight/ideal body weight was taken as 1. The GNRI was evaluated as <82 severe, 82-92 moderate, 92-98 mild malnutrition risk; and >98, normal.

SPSS for windows 20.0 package program was used for statistical analysis. The Shapiro–Wilk test was used to detect the normality of the parameters. For normally distributed parameters, variance analysis and Tukey's multiple comparison tests were used to compare more than two groups. To compare two groups in independent parameters, a t-test was used, and results are presented as mean \pm standard deviation. For the parameters not customarily distributed, more than two groups were compared using the Kruskal–Wallis test, and Dunn's multiple comparison tests were used. The Mann-Whitney U test compares two groups, and the results are presented as median (25%-75%) values. The chi-square test was used for the analysis of the cross tables. Spearman and Pearson's test was used for the analysis of correlation. The parameters that were found to be correlated were evaluated using linear regression analysis.

RESULTS

Forty-nine patients (29 females, 59.2%), with a mean age of 51 ± 13 years, were included in the study. The etiology of ESRD was as follows: glomerulonephritis, 26.5% (13 patients); diabetes in 22.4% (11 patients); hypertension in 20.4% (10 patients); pyelonephritis in 14.3% (4 patients); polycystic kidney disease, 10.2% (5 patients); Alport in 2% (1 patient); and amyloidosis, 4.1% (2 patients). Thirty-one patients underwent CAPD, while 18 underwent APD (36.7%). The mean laboratory values of patients are shown in [Table 1](#).

Mean GNRI was 102.16 ± 14.53 . According to the GNRI scores, three patients had severe (6.1%), seven (14.3%) had moderate, and seven (14.3%) had mild malnutrition. Thirty-two patients were not malnourished.

Table 1. Demographic values and laboratory measurements of the patients

Parameter	Value
Male/female	20/29
Age (years)	51 ± 13
Dialysis vintage(years)	4 ± 3
Primary disease	
Glomerulonephritis	13(26.5%)
Diabetes mellitus	11(22.4%)
Hypertension	10(20.4%)
Polycystic disease	5(10.2%)
Pyelonephritis	7(14.3%)
Amyloidosis	2(4.1%)
Alport	1(2%)
Dialysis modality	
CAPD	31(63.3%)
APD	18(36.7%)
Urea (mg/dl)	98 ± 25
Creatinine (mg/dl)	7.8 ± 2.7
Albumin (gr/dl)	3.6 ± 0.5
Ca (mg/dl)	8.9 ± 0.8
Phosphorus (mg/dl)	5 ± 1
PTH(μ G/dl)	551 ± 507
Hematocrit	31 ± 6
Ferritin	$318(16-2326)$
Uric acid (mg/dl)	5.8 ± 1
Residual renal volume (ml)	$639(0-2800)$
BMI (kg/m ²)	25.88 ± 5.28
GNRI	102.16 ± 14.53

PTH: parathyroid hormone, BMI: Body Mass Index, GNRI: Geriatric nutritional risk index

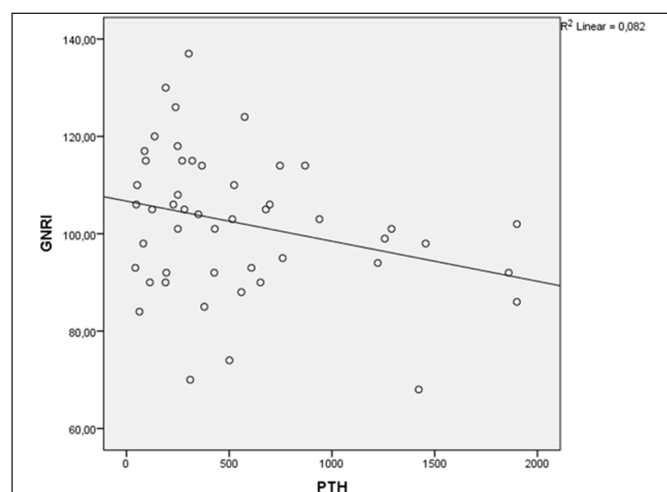
Patients were divided into two groups based on the presence of malnutrition. PTH levels were increased in the malnutrition group. Seventeen patients had malnutrition, and 32 patients did not have malnutrition. The mean age was 53 ± 12 years in the malnutrition group and 50 ± 14 years in the non-malnutrition group. Albumin levels were significantly higher in patients without malnutrition (3.8 ± 0.3 vs 3.1 ± 0.3 , $p < 0.05$). Dialysis vintage, residual renal function, and urea and creatinine levels were not significantly different ([Table 2](#)). Creatinine was 7.8 ± 2.9 vs. 7.6 ± 2.2 in normal and malnutrition groups, respectively ($p > 0.05$). The hematocrit level was significantly lower in the malnutrition group than in the non-malnutrition group (30 ± 5 vs. 32 ± 5 ; $p < 0.05$). Uric acid, phosphorus, and ferritin levels did not differ between the groups ([Table 2](#); $p < 0.05$). PTH levels were found to be increased in the malnutrition group, but this was not statistically significant (659 ± 594 vs. 494 ± 453 ; $p > 0.05$). Calcium levels were higher in patients with normal nutritional status (9.2 ± 0.6 vs. 8.4 ± 1.0 ; $p < 0.05$). Body mass index was lower in the malnutrition group (21.55 ± 3.3 vs. 28.35 ± 4.19 ; $p < 0.05$).

Table 2. Comparison of groups according to presence of malnutrition

	Malnutrition (-)	Malnutrition (+)	p
Male/female	12/20	8/9	p>0.05
Age (years)	50±14	53±12	p>0.05
Dialysis vintage	4±3	5±3	p>0.05
Urea (mg/dl)	97±17	100±23	p>0.05
Creatinin (mg/dl)	7.9±2.9	7.6±2.2	p>0.05
Albumin (gr/dl)	3.8±0.3	3.1±0.3	p<0.05
Ca (mg/dl)	9.2±0.6	7.6±2.2	p<0.05
Phosphor (mg/dl)	5±1	5±1	p>0.05
PTH (µg/dl)	494 (48-1900)	659±594 (43-1900)	p>0.05
Hematocrit	32±5	30±5	p<0.05
Ferritin	281 (46-1038)	384 (16-2326)	p>0.05
Uric acid (mg/dl)	5.9±1.1	5.6±0.9	p>0.05
Residual renal volume (ml)	772 (0-2800)	289±427 (0-1200)	p>0.05
BMI(kg/m ²)	28.35±4.39	21.55±3.3	p<0.05

PTH: parathyroid hormone, BMI: Body Mass Index, GNRI: Geriatric nutritional risk index

The GNRI was positively correlated with albumin, hematocrit, and calcium levels ($r=0.757$, $r=0.355$, and $r=0.423$, respectively; $p < 0.05$). GNRI was negatively correlated with dialysis vintage ($r=-0.303$, $p=0.038$) and PTH ($r=-0.287$; $p=0.046$) (Figure) (Table 3).

**Figure.** correlation of GNRI with PTH

PTH: parathyroid hormone, BMI: Body Mass Index, GNRI: Geriatric nutritional risk index

Table 3. Correlations of GNRI with studied parameters

	R	P
Dialysis vintage	-0.303	0.038
Hematocrit	-0.355	0.012
PTH	-0.287	0.047
Albumin	-0.757	0.00
Ca	0.423	0.002
Residual renal volume	0.404	0.004

Regression analysis revealed that albumin, RRV, and PTH levels were significant independent determinants of GNRI (Table 4).

Table 4. Regression analysis of GNRI

	B	Beta	t	Sig.
(Constant)	39,874		2,596	,013
Albumin	19,660	,719	6,315	,0001
Dialysis vintage	-,276	-,054	-,557	,580
Residual renal volume (ml)	,005	,227	2,416	,020
Htc	,190	,069	,704	,485
Ca	-1,373	-,079	-,726	,472
PTH	-,006	-,194	-2,036	,048

PTH: parathyroid hormone, BMI: Body Mass Index, GNRI: Geriatric nutritional risk index

DISCUSSION

The main finding of this study was that PTH, albumin, and RRV were the major determinants of the GNRI.

Some studies have examined the GNRI in hemodialysis patients. One study reported that 31.6% of dialysis patients had malnutrition that could be detected using the GNRI.¹² Evidence suggests that the GNRI is a nutritional assessment tool that can be used for dialysis patients. It has been shown that GNRI can be used as a predictor of mortality in dialysis patients as well as its importance in the diagnosis of malnutrition.¹²⁻²⁴ Malnutrition is common in chronic kidney disease (CKD)^{12,20} with approximately 18-75% of patients with CKD receiving maintenance dialysis, with evidence of malnutrition.²⁰ In our patient group, 34.7% of patients had malnutrition.

Serum calcium levels were significantly lower in malnourished patients. This decrease may be because we did not measure ionized calcium levels, and decreased albumin levels may have caused decreased total calcium levels. In addition, the vitamin D levels could not be measured. Decreased vitamin D levels can lead to reduced calcium levels.

Correlation analysis showed that the GNRI was negatively correlated with the RRV. This significance was obtained after the regression analysis. RRV may lead to patients eating independently. In addition, preservation of RRF was found to be associated with decreased inflammation, which is a component of the malnutrition syndrome.^{25,26}

Chronic kidney disease and mineral and bone disorders increase mortality and morbidity.²⁷ The mechanism for this appears to be crosstalk between the bone and vascular wall. Malnutrition is associated with cardiovascular diseases. Although many factors can cause malnutrition in patients with CKD, inflammation is one of the most important causes.²⁸⁻³⁰ Inflammation increases atherosclerosis.

The main finding of this study was the relationship between the GNRI and PTH levels. In the malnutrition group, the PTH levels tended to be higher, but this increase was not statistically significant. In the

correlation analysis, GNRI was negatively correlated with PTH levels. Decreased protein intake, as well as increased energy expenditure, is one of the contributing factors to PEW. Increased resting energy expenditure (REE) is caused by increased protein and fat catabolism. As a result, loss of adipose tissue and muscle tissue occurs. In a study of hemodialysis patients, İkizler et al.³¹ showed that the REE was higher in dialysis patients than in healthy controls. In addition, in this study, the REE increased even more during dialysis in the patient group.

An increase in REE occurs with a phenotypic transition from white to brown adipose tissue, which is called adipose tissue browning.³² In a study by Cuppari et al.⁹ the REE of patients was measured, and PTH was shown that PTH is an independent marker of REE.

After adjustment for lean body mass, REE was higher in patients with severe hyperparathyroidism than in patients with mild and moderate hyperparathyroidism and healthy individuals. In addition, the investigators measured the REE before and six months after parathyroidectomy (PTx) in patients with severe hyperparathyroidism. They found a 23% decrease in REE after surgery, parallel with a significant decrease in PTH levels. Therefore, these data suggest that severe SHPT may contribute to PEW by increasing the REE of ESRD patients and that PTx may reverse this condition.

Kir et al.¹⁰ reported that PTH and PTH-related peptides (PTHrPs), which share the same receptor, act as mediators of fat tissue and muscle mass loss in mouse models of cancer and renal failure. In a previous study, Kir et al.³³ In cancer cachexia, PTHrP causes browning and wasting of adipose tissue by inducing the expression of UCP and other genes involved in thermogenesis and energy expenditure.

Tumor-bearing mice were then injected with antibodies that neutralized PTHrP. They observed that adipose tissue browning and the loss of muscle mass and strength were reversed. Since PTH and PTHrP share the same receptor, they conducted a study with 5/6 nephrectomized mice to understand the role of PTH in cachexia, which occurs in renal failure.¹⁰ Fat browning and cachexia associated with secondary hyperparathyroidism developed in nephrectomized rats. Fat browning and muscle atrophy did not occur after nephrectomy in mice with PTH/PTHrP receptor deletion in the adipose cells. These data suggest that PTH and PTHrP may cause malnutrition via the PTH receptor. They also explained why PEW is common in secondary hyperparathyroidism and why it improves with hyperparathyroidism treatment.

This study had some limitations. First, the number of patients included in this study was low. Second, this was a cross-sectional study, so we could only discuss the status at that time. Third mortality and hospitalizations are not included in this population

CONCLUSION

As a result, PTH levels were negatively correlated with the GNRI values in our study. This may be caused by increased PTH, causing phenotypic switching from white adipose tissue to brown fat by PTH receptors. Therefore, the treatment of secondary hyperthyroidism may prevent and reverse malnutrition and wasting. Follow-up studies with larger cohorts are required to address this issue.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was initiated with the approval by the Health Sciences University Haseki Training and Research Hospital Clinical Researches Ethics Committee (Date: 01.03.2023, Decision No: 217-2022).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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