Original Article
http://mjiri.iums.ac.ir
Medical Journal of the Islamic Republic of Iran (MJIRI)

Med J Islam Repub Iran. 2025 (30 Jun);39.87. https://doi.org/10.47176/mjiri.39.87

The Comparison of Renal Osteodystrophy Indices in Hemodialysis Patients with and without Pruritus

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Received: 15 Oct 2024 Published: 30 Jun 2025

Abstract

Background: Hemodialysis (HD) patients frequently experience uremic pruritus, a condition that is both irritating and prevalent. Although its pathogenesis is not entirely understood, it is believed to be multifactorial. The objective of this investigation was to evaluate the renal osteodystrophy indices in patients undergoing hemodialysis with and without pruritus.

Methods: This cross-sectional study categorized HD patients in 3 university hospitals in Mashhad, northeast Iran, during 2022 and 2023 into 2 groups: those with and those without pruritus, as determined by the diagnostic criteria. The visual analog scale parameter was employed to evaluate the severity of pruritus. Each patient's blood urea nitrogen, creatinine, calcium, phosphorus, and intact parathyroid hormone (iPTH) levels were evaluated. The data were analyzed using SPSS software Version 16. An independent sample t test and the Mann-Whitney U test, as well as the Spearman correlation test, were used for analysis.

Results: A total of 120 participants with a mean age of 57.91 ± 16.03 years were included in the study. The findings showed that the mean blood levels of calcium ($P < 0.001$), phosphorus ($P < 0.001$), creatinine ($P < 0.001$), alkaline phosphatase ($P = 0.002$), and calcium phosphate product ($P < 0.001$) were significantly higher in the pruritic group. However, the mean blood urea nitrogen ($P = 0.458$) and iPTH levels ($P = 0.139$) did not differ significantly between the 2 groups, but there was a significant relationship between iPTH level and the severity of pruritus ($P < 0.001$).

Conclusion: The itching severity in HD patients is substantially correlated with their iPTH levels, and the majority of the indices of renal osteodystrophy are significantly higher in patients with this complication. However, additional studies are suggested.

Keywords: Renal Osteodystrophy, Hemodialysis, Pruritus, CKD-aP

Conflicts of Interest: None declared
Funding: None

Cite this article as: Zeraati D, Emadzadeh A, Zeraati AA. The Comparison of Renal Osteodystrophy Indices in Hemodialysis Patients with and without Pruritus. *Med J Islam Repub Iran.* 2025 (30 Jun);39:87. https://doi.org/10.47176/mjiri.39.87

Introduction

Chronic kidney disease (CKD) is acknowledged as a disorder that has a substantial adverse effect on public health (1, 2). The global prevalence of this condition is estimated to be around 13% (2). CKD is also prevalent in Iran (3, 4). The final episode of CKD is end-stage renal disease (ESRD), during which patients are at risk of mortality unless the uremic toxins are eliminated through renal replacement therapies, including hemodialysis (HD), peritoneal dialysis (PD), and kidney transplantation (5). It is distinguished by a variety of complications, such as uremic pruritus, which is also referred to as chronic kidney disease-associated pruritus (CKD-aP). The quality of life and survival of patients with CKD-aP are significantly affected by this condition (6, 7).

Several causes, including insufficient dialysis, xerosis, hypermagnesemia, hyperaluminemia, and secondary hyperparathyroidism, have been linked to CKD-aP (8-10). There are contradictory findings regarding some conditions, such as secondary hyperparathyroidism. Although many experts maintain that there is a correlation between

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↑What is "already known" in this topic:
Chronic kidney disease-associated pruritus (CKD-aP), also known as uremic pruritus, is very common among patients undergoing dialysis. The link between this complication and renal osteodystrophy indices is unclear.

→What this article adds:
We found that the severity of pruritus in HD patients is substantially correlated with their iPTH levels, and the majority of the indices of renal osteodystrophy are significantly higher in patients with this complication.

[DOI: 10.47176/mjiri.39.87]

the indices of renal osteodystrophy and CKD-aP (11-13), others were unable to identify any link between the indices of renal osteodystrophy and CKD-aP (14, 15). CKD-aP seems to be an underappreciated complication despite its high prevalence (16). Therefore, the purpose of this study was to assess renal osteodystrophy indices in HD patients with and without CKD-aP.

Methods

Study Design and Population

In this cross-sectional study, we compared the renal osteodystrophy indices of HD patients with and without CKD-aP. The inclusion criteria were HD patients who were ≥18 years who agreed to participate in the study. The exclusion criteria were mental illness or having a coexisting disorder that might cause pruritus. All participants were informed about the study by printed manuscripts, and then they completed the printed informed consent forms. The first author of this article also explained orally about this study to all participants.

Our sample consisted of 120 HD patients from 3 university hospitals in Mashhad, northeastern Iran, during 2022 and 2023. The study comprised 60 HD patients with CKD-aP and 60 HD patients without CKD-aP.

Measurements

Demographic data, serum levels of calcium (Ca), phosphorus (P), intact parathyroid hormone (iPTH), alkaline phosphatase (AlP), blood urea nitrogen (BUN), and creatinine (Cr) levels were recorded in the checklist, and the calcium-phosphorus product ([Ca] × [P]) was computed. In the present study, we also used a 10-cm ruler to assess the visual analog scale (VAS) for the severity of itching. In the mentioned ruler, 0 and 10 were the indicators of no pruritus and most severe pruritus, respectively (17, 18).

Statistical Analysis

We calculated the sample size based on the data in the Hu et al study (11), which reported the serum level of phosphorus in the pruritus (1.97 ± 0.57) and nonpruritus (1.65 ± 0.67) groups. Considering $\alpha = 0.05$ and $\beta = 0.2$, the sample size was calculated as 60 participants in each group. To compare the quantitative variables between the 2 study groups, we used the independent Samples t test and the Mann-Whitney U test (according to normality distribution). The Spearman correlation test was performed to assess the correlation between the score of pruritus and PTH level. The data were analyzed using SPSS Version 16 software. $P < 0.05$ was considered statistically significant.

Results

Out of the 120 patients, 60 had pruritus while the remaining 60 patients did not. There were 60 male and 60 female patients. The patients' mean age was 57.91 ± 16.03 years. The mean age of the pruritus and nonpruritus groups was 57.81 ± 15.30 and 58.01 ± 16.86 years, respectively ($P = 0.946$) (Table 1).

The patients' age, Ca, P, BUN, Cr, iPTH, AlP, [Ca] × [P], and their itching scores are depicted in Table 2. More than half of the participants in the case group had a pruritus score of >5 (median = 7; interquartile range, 5-10).

As seen in Table 2, the mean serum levels of Ca ($P < 0.001$), P ($P < 0.001$), Cr ($P < 0.001$), AlP ($P = 0.002$) and [Ca] × [P] ($P < 0.001$) were significantly higher in pruritic group, while the BUN ($P = 0.458$) and iPTH levels ($P =$

Table 1. Age and gender distribution in hemodialysis patients with (N=60) and without pruritus (N=60)

variable	Study Group	Mean	Standard Deviation	*P*-value
Age (years)	Non-Pruritus	58.01	16.86	0.946*
	Pruritus	57.81	15.3	
Gender		Male	Female	
	Non-Pruritus	27 (45%)	33 (55%)	0.361**
	Pruritus	27 (45%)	33 (55%)	

*Independent Sample t test
**Chi-square test
Data are reported as mean (SD) or frequency (percentage).

Table 2. Laboratory findings and severity of pruritus in hemodialysis patients with (N=60) and without pruritus (N=60)

Laboratory Findings	Study Group	Mean	Standard Deviation	*P*-value*
Calcium (mg/dl)	Non-Pruritus	8.33	0.868	< 0.001
	Pruritus	9.23	0.701	
Phosphorus (mg/dl)	Non-Pruritus	4.25	0.939	< 0.001
	Pruritus	5.04	1.152	
BUN (mg/dl)	Non-Pruritus	57.81	36.84	0.458
	Pruritus	62.30	28.65	
Creatinine (mg/dl)	Non-Pruritus	4.82	1.900	< 0.001
	Pruritus	7.54	3.281	
iPTH (pg/ml)	Non-Pruritus	279.34	444.317	0.139
	Pruritus	388.16	351.080	
ALP (mg/dl)	Non-Pruritus	248.22	244.036	0.002
	Pruritus	381.68	218.070	
[Ca] × [P] (mg^2/dl^2)	Non-Pruritus	35.48	8.934	< 0.001
	Pruritus	46.66	10.771	
Pruritus Score (Using Visual Analogue Scale)	Non-Pruritus	-	-	-
	Pruritus	6.96	2.652	

*Independent Sample t test
BUN: Blood Urea Nitrogen; ALP: Alkaline Phosphatase

[DOI: 10.47176/mjiri.39.87]

0.139) did not differ significantly between the 2 study groups, but there was a positive and significant correlation between iPTH and severity of pruritis (r = 0.81, $P < 0.001$).

Discussion

CKD-aP is a recognized complication of ESRD (7, 9). Makhlough et al (2013) found that serum PTH levels are significantly correlated with the severity of pruritus in HD patients, even though serum levels of Ca, P, albumin, and creatinine did not correlate with pruritus (19). Their earlier finding is consistent with the results of our study. Shahreki et al examined 100 HD patients in Zahedan, located in the southeast of Iran (14). They were unable to establish any correlation between the severity of itching in HD patients and their PTH serum levels. In their investigation, the researchers did not identify any correlation between the severity of pruritus in HD patients and their serum Ca and P levels, age, sex, and frequency or adequacy of dialysis. The discrepancy between Shahreki's research and ours may be attributed to the fact that their sample size is smaller than ours. Bolanos compared the plasma of HD patients with severe pruritus with mild/no pruritus HD patients in northern California in 2021 in an effort to discover the solutes responsible for uremic pruritus using metabolomic analysis (20). Out of the 61 individuals in their sample, 25 were eliminated, leaving just 36 patients to be included in the research. An ancillary finding in Bolanos' study was that the serum levels of Ca, P, PTH, albumin, ferritin, hemoglobin, dialysis vintage, and Kt/V for urea were similar in pruritic and non-pruritic patients. The disparity in their results from our study may be attributed to their reduced sample size and different ethnicity. Li et al investigated the impacts of neutral macroporous resin hemoperfusion on treating HD patients with refractory uremic pruritus (12). They showed that P, [Ca] × [P], and PTH levels correlate with the severity of pruritus in uremic patients. They indicated that decreasing inflammatory cytokines with macro resins could have beneficial impacts on the severity of pruritus. Most of the results of our study confirmed those of Li et al.

Hu et al studied 138 HD, 41 PD, and 203 CKD patients. They showed that there is a meaningful difference between BUN, Cr, P, [Ca] × [P], and PTH levels between the pruritus and nonpruritus groups (11). Except for BUN and PTH levels, Hu et al results confirm ours.

Uremic pruritus was substantially correlated with hyperkalemia, hyperphosphatemia, hypoalbuminemia, female sex, and a history of skin allergy, according to the study conducted in Karachi, Pakistan, in 2021 by Asghar et al. (21) However, no association was seen with the frequency of dialysis, body mass index, diabetes, hypertension, hypocalcemia, hyperparathyroidism, serum urea or creatinine, or connective tissue diseases. The differences in sample sizes and ethnicities between this research and ours may be the cause of the difference in outcomes. Narita et al found a link between several clinical factors and the onset of severe uremic pruritus. The characteristics of being male, having high pre-dialysis BUN levels, high levels of beta 2-microglobulin, Ca, P, and iPTH were all independently linked to the development of severe CKD-aP (13). Some of the data from this study, such as the association between sex and the severity of CKD-aP, do not align with our findings. However, we do see a link between i-PTH levels and itching score, which is consistent with their results. To find out whether there was a relationship between CKD-aP and certain metrics, including renal osteodystrophy indices, Shetty et al studied 120 HD patients in India (15). They did not find a positive link between pruritus and high levels of iPTH, high phosphorus, or low calcium in ESRD patients receiving HD. The differences between the results of Shetty's study and ours might be explained by the likely different nutritional status, ethnicity, and methods used in the laboratory analyses.

Strengths and Limitations

Due to the lack of sufficient data on the relationship between the renal osteodystrophy indices and CKD-aP in this region, the results of the current study might be practical for clinicians involved in the care of HD patients. Moreover, because of the cross-sectional nature of the study, we were not able to evaluate the impact of the improvement of the mentioned indices on CKD-aP.

Conclusion

Except for iPTH and BUN levels, all indices of renal osteodystrophy had meaningful differences between pruritic and nonpruritic patients in our study. We also found a positive relationship between the severity of pruritus and the serum levels of iPTH; nonetheless, further studies are warranted.

Authors' Contributions

Conceptualization: D.Z.; methodology: D.Z. and A.E.; clinical investigation: D.Z., A.E., A.A.Z.; data analysis: D.Z., A.E.; writing and original draft preparation: D.Z., A.E.; writing, reviewing, and editing: D.Z., A.E., A.A.Z.

Ethical Considerations

The Ethics Committee of the Deputy of Research and Technology of Mashhad Medical Sciences, Islamic Azad University, granted ethical permission for the study, based on the ethical code number IR.IAU.MSHD.REC. 1401.155.

Acknowledgment

This manuscript is based on the first author`s dissertation in medicine.

Conflict of Interests

The authors declare that they have no competing interests.

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[DOI: 10.47176/mjiri.39.87]