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Demographic and Clinical Profiles of Hemodialysis Patients Exhibiting Low PTH Levels and Adynamic Bone Disease

Zahra Kamiab[1,2], Gholamreza Bazmandegan[3,4], Fatemeh Jalali Khalilabadi[5,6], Mohammad Khalil Salehi[7], Mahdieh Jamshidi[6,8*]

[1]Social Determinants of Health Research Center, Rafsanjan University of Medical Sciences, Rafsanjan, Iran
[2]Department of Community Medicine, School of Medicine, Rafsanjan University of Medical Sciences, Rafsanjan, Iran
[3]Physiology-Pharmacology Research Center, Research Institute of Basic Medical Sciences, Rafsanjan University of Medical Sciences, Rafsanjan, Iran
[4]Department of Physiology and Pharmacology, School of Medicine, Rafsanjan University of Medical Sciences, Rafsanjan, Iran
[5]Non-Communicable Diseases Research Center, Rafsanjan University of Medical Sciences, Rafsanjan, Iran
[6]Department of Internal Medicine, Ali-Ibn Abi-Talib Hospital, School of Medicine, Rafsanjan University of Medical Sciences, Rafsanjan, Iran
[7]Student Research Committee, Rafsanjan University of Medical Sciences, Rafsanjan, Iran
[8]Clinical Research Development Unit, Ali-Ibn Abi-Talib Hospital, Rafsanjan University of Medical Sciences, Rafsanjan, Iran

*Corresponding Author: Mahdieh Jamshidi, Email: jamshidi.mn@gmail.com

Abstract

Introduction: Adynamic bone disease (ABD) is a condition that arises as a complication of chronic kidney disease, and biomarkers offer valuable insights into bone health in these patients. Parathyroid hormone (PTH) levels are commonly used as an indicator of bone turnover, with low PTH levels (<100 pg/mL) associated with ABD. This study described the demographic and clinical characteristics of individuals experiencing low PTH levels and evaluated the potential association between low PTH and ABD.

Methods: A cross-sectional study was conducted on 64 patients undergoing hemodialysis. The patients were divided into two groups: those with PTH levels < 100 pg/mL (n = 10) and those with PTH ≥ 100 pg/mL (n = 54). Demographic, clinical, and laboratory data, including vitamin D levels and bone biomarkers, were analyzed.

Results: Patients with reduced PTH levels demonstrated notably elevated vitamin D concentrations ($P = 0.001$) alongside decreased serum albumin levels ($P = 0.018$). No significant differences were found in other parameters, including calcium and alkaline phosphatase levels.

Conclusion: Although PTH levels are commonly used to predict bone turnover, this study acknowledges the limitation of using PTH without bone biopsy for diagnosing ABD. Additional research is required to investigate the role of vitamin D in managing ABD.

Keywords: Renal dialysis, Parathyroid hormone, Bone disease, Renal insufficiency, Chronic, Vitamin D

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Introduction

Chronic Kidney Disease (CKD) develops when the kidneys sustain damage and can no longer filter blood efficiently for a period of at least three months. As a result, excess fluids and waste accumulate in the body, potentially leading to various health complications, including heart disease, stroke, infections, and bone disorders (1, 2). In 2019, CKD ranked 15th in global mortality, resulting in 1.2 million deaths and 35.8 million disability-adjusted life years (DALYs) (3). As CKD progresses, mortality rates rise; about 50% of stage 5 CKD patients do not survive beyond five years, while ESRD patients face an even greater risk, with approximately 20% not surviving the first year of dialysis initiation (2, 4). In the U.S., ESRD remains stable at approximately 120,000 new cases annually, primarily due to diabetes and hypertension, which account for around 70% of cases (5). Chronic kidney disease (CKD) and its advanced stage, end-stage renal disease (ESRD), present significant challenges to Iran's healthcare system (6, 7). Iran similarly experiences a rise in ESRD cases, with approximately 22,000 new cases each year, driven by these factors (8). In this country, the prevalence of CKD is estimated to be 11%-15%, and recent studies have reported a rate of 23.7% in the northeast (6, 8, 9). A meta-analysis reveals that the prevalence of CKD in Iran is higher than that in other developing nations and comparable to developed countries

(10).

As kidney function declines, mineral balance becomes disrupted, influencing calcium, phosphorus, and parathyroid hormone (PTH) concentrations, which in turn impacts bone health (11, 12). This can lead to two primary bone disorders: increased bone turnover as a result of secondary hyperparathyroidism and decreased turnover associated with adynamic bone disease (ABD) (13). Secondary hyperparathyroidism is characterized by excessive PTH secretion due to hypocalcemia, often linked to CKD or conditions that impair vitamin D synthesis or action (14). In contrast, ABD is marked by reduced bone turnover resulting from suppressed activity of bone-forming cells (osteoblasts) and bone-resorbing cells (osteoclasts), which plays a crucial role in bone health. An imbalance in their function can result in bone loss and elevate the risk of fractures (15). Factors contributing to ABD include excessive suppression of PTH production, systemic inflammation, and altered bone management strategies in kidney disease patients (13, 16). ABD prevalence is notable within CKD, affecting 18% of CKD stages 3-5 patients. Diagnosing ABD typically needs a bone biopsy, not commonly performed in regular clinical practice, potentially leading to an underestimation of its prevalence (17). Symptoms of ABD, such as bone pain, muscle weakness, and mobility issues, can overlap with those of other bone disorders in CKD patients (18).

Research indicates a U-shaped relationship between low and extremely high levels of PTH and the associated risk of sudden death (14). Low PTH levels (below 50 pg/mL) are notably linked to reduced survival rates in patients undergoing hemodialysis (19, 20). Diagnosis of ABD relies on laboratory tests that measure indicators like parathyroid hormone and alkaline phosphatase, and tartrate-resistant acid phosphatase, complemented by imaging studies (13). This study aimed to investigate biomarker levels in hemodialysis patients, comparing those with ABD to those without it.

Methods

Study Design and Sample

This descriptive-analytical study employed a census sampling method to select 64 hemodialysis patients from Ali-Ibn Abi-Talib Hospital in 2021-2022.

Informed consent and ethical approval

Informed consent was obtained from all patients for the publication of their anonymized data in this article. This study received ethical approval from the Ethics Committee of Rafsanjan University of Medical Sciences (Ethical code: IR.RUMS.REC.1401.123).

Data collection

Data were collected using a researcher-made checklist to gather demographic information, including age, sex, patient weight, underlying diseases, dialysis duration, and weekly dialysis hours, all obtained from the patients' files in the dialysis department. Additionally, we recorded data on calcium, phosphorus, vitamin D, C-reactive protein (CRP), albumin, total alkaline phosphatase, creatinine (monitored monthly), and parathyroid hormone (PTH) levels (checked every three months).

Inclusion and Exclusion Criteria

Inclusion criteria encompassed all hemodialysis patients at Ali-Ibn Abi-Talib Hospital with a dialysis history exceeding three months. Exclusion criteria included patients receiving supraphysiological or therapeutic doses of calcium and vitamin D, those with incomplete medical records, and patients with acute infections, connective tissue diseases, malignancies, chronic liver diseases, thyroid disorders, recent heart attacks, trauma within the last six months, postmenopausal women, and those unwilling to participate or who had deceased (6, 13, 15).

Measures

We considered symptoms or complications such as osteoporosis, kidney stones, abdominal pain, constipation, fatigue, depression, cognitive impairment, imaging studies (ultrasound, CT, MRI), and bone mineral density (BMD) measurements (21, 22). Adynamic bone disease (ABD) was defined as a type of renal osteodystrophy associated with reduced bone turnover, reduced bone formation, and increased bone mineralization. Diagnostic criteria for ABD included a mineralized bone volume of less than 10% of the biopsy area, minimal or absent osteoblasts or osteoclasts, normal to low serum alkaline phosphatase (ALP) levels, serum PTH levels below 150 pg/mL, normal to low bone-specific alkaline phosphatase levels, and normal to low urinary deoxypyridinoline levels (21, 22).

Statistical Analysis

Statistical analyses were conducted using SPSS software version 24 (IBM SPSS Inc., Chicago, IL, USA). Quantitative data are expressed as mean ± standard deviation along with the range of values, whereas qualitative data are presented as frequencies (percentages). An independent two-sample t-test was performed to evaluate the differences in mean values of quantitative variables between the two groups. Pearson's correlation coefficients were calculated to assess the relationships between disease duration, hemodialysis duration, and laboratory parameters.

Results

The study comprised 64 participants, with 32 men (50%) and a mean age of 62.97 ± 14.93 years. The mean duration of disease and the mean duration of dialysis per week were 3.45 ± 2.83 years and 8.65 ± 1.85 hours, respectively (Table 1).

The prevalence of ABD among the participants was 15.6% (10 individuals). Independent samples t-tests were conducted to examine the distribution of variables between patients with and without ABD, as detailed in Table 2.

Among men, the prevalence of ABD was 18.8%, while it was 12.5% in women; the difference was not statistically significant ($P = 0.491$). Notably, individuals without ABD

exhibited significantly higher mean levels of serum albumin and parathyroid hormone (PTH) compared to those with ABD ($P=0.018$ and $P<0.001$, respectively). Furthermore, participants with ABD had significantly higher mean vitamin D levels than those without ABD ($P<0.001$).

A moderately strong positive correlation was observed between disease duration and serum creatinine levels ($P=0.001$). Furthermore, a weak positive and significant correlation was observed between dialysis duration and serum alkaline phosphatase levels ($P=0.017$). A notable moderate positive correlation was identified between the length of hemodialysis treatment and PTH levels (Table 3).

Table 1. Demographic and Clinical Characteristics of Hemodialysis Patients (n=64)

Variables	Mean±SD	Min-Max
Age (Years)	62.97±14.93	25-87
Weight (Kg)	63.89±11.84	37-89
Duration of disease (years)	3.45±2.83	0.33-13
Serum Albumin (g/dL)	3.71±0.41	2.4-4.4
Serum Creatinine (mg/dL)	7.29±2.28	2.61-9.6
Serum Vitamin D (ng/mL)	37.22±70.06	2-558
Serum Alkaline Phosphatase (IU/L)	313.80±184.31	133-1216
Serum Calcium (mg/dL)	8.04±0.93	5.7-9.8
Serum Phosphorus (mg/dL)	6.05±1.66	2.9-9.6
Serum C-reactive Protein (mg/L)	8.83±18.77	1-110
Serum parathyroid hormone levels (pg/mL)	596.84±422.90	53-1494
Duration of Dialysis per Week (hours)	8.65±1.85	2.50-10.50

The data were expressed as mean±standard deviation and minimum – maximum.

Discussion

ABD is a complication associated with chronic kidney disease, with biomarkers providing crucial information about bone health in affected patients (22). In the present study, 15.6% of the participants were diagnosed with ABD among hemodialysis patients. A parallel investigation conducted by Malluche et al. examined ABD prevalence among a group of U.S. hemodialysis patients, revealing an overall prevalence of 28.8%, with higher rates in older patients and those with longer dialysis durations (23). Similar studies reported ABD prevalence rates of 29.9% in African American hemodialysis patients (24). Another study by Tentori et al. investigated ABD prevalence in a large cohort of hemodialysis patients across Europe and Japan, uncovering significant variations ranging from 6.5% to 51.1% among countries (25).

In the present study, no significant gender-based difference in ABD was observed. In terms of gender, a study conducted by Uhlig et al. reported a higher prevalence of ABD in female hemodialysis patients compared to males, contrasting with our findings where a smaller percentage of female patients had ABD (13). It is important to recognize that variations in sample size, participant characteristics, diagnostic criteria, and measurement methods for bone turnover markers can influence study outcomes and lead to discrepancies between the findings.

Table 2. Comparison of Variable Distribution between Groups with and without Adynamic bone disease (n=64)

Variables	Adynamic bone disease (n=10)	Non-adynamic bone disease (n=54)	*P*-value
Age (Years)	68.30±14.76	61.98±14.88	0.222*
Duration of disease (Years)	2.60±2.20	2.83±3.68	0.129*
Duration of hemodialysis (Weeks)	7.65±2.59	8.84±1.64	0.190*
Weight (Kg)	60.20±7.03	64.57±12.45	0.287*
Serum Albumin (g/dL)	3.43±0.49	3.76±0.37	0.018*
Serum Creatinine (mg/dL)	6.67±2.87	7.38±2.17	0.429*
Serum Vitamin D (ng/mL)	72.69±170.84	30.65±24.43	0.001*
Serum Alkaline Phosphatase (IU/L)	255.20±186.23	324.64±183.63	0.277*
Serum Calcium (mg/dL)	8.35±0.72	7.98±0.96	0.254*
Serum Phosphorus (mg/dL)	5.43±1.09	6.16±1.73	0.202*
Serum C-reactive Protein (mg/L)	4.20±5.69	9.68±20.21	0.400*
Serum parathyroid hormone levels (pg/mL)	97.00±34.60	689.40±395.62	0.001*

The data were expressed as mean±standard deviation.
* *P*-value obtained from two-sample independent t-test due to normal distribution.
$P<0.05$ was considered statistically significant.

Table 3. Correlation between duration of disease and dialysis and laboratory parameters

		Albumin	Creatinine	Vit D	Alkaline phosphatase	Calcium	phosphorus	C-reactive protein	Parathyroid hormone levels
Duration of disease	Pearson Correlation	0.014	0.439*	0.009	0.298*	-0.217	0.244	0.022	0.299
	P-value	0.915	0.001	0.942	0.017	0.085	0.052	0.862	0.069
Duration of hemodialysis	Pearson Correlation	0.199	0.176	-0.109	0.299	-0.182	0.049	-0.043	0.328**
	P-value	0.115	0.165	0.389	0.069	0.150	0.700	0.737	0.008

* *P*-value obtained from correlation.
$P<0.05$ was considered statistically significant.

The findings of this study indicate a weak positive relationship between disease duration and albumin and creatinine levels. Serum albumin is recognized as an important indicator of mortality in individuals with chronic kidney disease (CKD). Previous studies have also investigated its role in ESRD development (26, 27). In a retrospective cohort analysis in the UK in 2011 that examined 1,800 individuals, serum albumin levels were identified as a crucial component in a multifactorial risk model for mortality in ESRD patients (26). In contrast, a study on Chinese hemodialysis patients in 2016 showed a negative relationship between hemodialysis duration and serum albumin levels, suggesting that longer hemodialysis was associated with lower albumin levels (28). In Japanese hemodialysis patients, reduced levels of serum albumin were linked to ABD, indicating that reduced albumin levels may heighten the risk of this condition (29). Another study in Japan also reported significantly lower serum albumin levels in ABD patients, and low albumin levels have been identified as an independent risk factor for the disease (30). These findings support the notion that low serum albumin levels could potentially increase the risk of ABD in individuals undergoing hemodialysis. It is essential to recognize that the strength and direction of these associations may be influenced by specific patient characteristics and uncontrolled variables in our study.

This study identified a slight inverse relationship between the duration of the disease and vitamin D levels, in line with the findings of Yashiro et al. regarding lower vitamin D levels in longer hemodialysis patients (31). Interestingly, our patient group displayed higher average vitamin D levels than the disease-free group, contrasting with studies from the United States and India associating low vitamin D levels with a higher risk of ABD in patients undergoing hemodialysis (32). Further investigation is needed to validate these discrepancies, considering potential differences in vitamin D supplementation and other factors.

In our study, a moderately significant positive correlation was identified between the duration of hemodialysis and PTH levels, indicating that as the disease progresses, parathyroid hormone levels tend to rise. This finding was consistent with the findings of prior research, including studies in Japanese and European cohorts (25, 33). Conversely, the correlation between disease duration and alkaline phosphatase, calcium, and CRP was weak and statistically insignificant, consistent with similar investigations (34, 35). Notably, in the group with ABD, PTH levels were noticeably lower compared to the group without the condition, contrasting with the findings of the studies associating elevated PTH levels with ABD risk, suggesting potential variations in PTH management or other influencing factors that warrant further investigation into the relationship between PTH levels and ABD (36, 37). However, it is important to highlight that increased normalized alkaline phosphatase levels have been linked to hemodialysis patients face an increased risk of hospitalization and mortality, regardless of calcium and phosphorus levels and parathyroid hormone levels, which is inconsistent with our findings (35).

Comparing variables between groups with and without ABD showed no significant difference in age, disease duration, or average weight. While some studies have linked older age and longer dialysis duration to a higher risk of ABD (36, 38), the relatively small proportion of ABD cases (15.6%) in our study suggests a need for further investigation into clinical factors. Additionally, average levels of creatinine, alkaline phosphatase, calcium, phosphorus, and C-reactive protein did not significantly differ between the patient groups, which is consistent with the findings indicating these biomarkers may not strongly predict dynamic bone disease in hemodialysis patients (39, 40).

This research has some limitations. First, the reliance on biomarker levels alone for assessing ABD may not capture the full spectrum of clinical indicators related to the condition. Second, the limited sample size and targeted demographics due to census sampling limit the generalizability of the findings to broader hemodialysis populations. Additionally, the cross-sectional design limits the ability to draw causal conclusions about the relationships between biomarkers and ABD. Variations in treatment protocols among participating hospitals may also introduce confounding variables. Future studies should address these limitations for a more comprehensive understanding of ABD in hemodialysis patients.

Conclusion

ABD is a significant clinical concern in CKD, primarily arising from decreased osteoanabolic stimulation. This study identified a positive correlation between disease duration and parathyroid hormone (PTH) and creatinine levels. Notably, patients with ABD exhibited higher vitamin D levels but lower albumin and PTH levels compared to those without ABD. Therefore, the current therapeutic strategy for dialysis patients with CKD and ABD should emphasize optimizing vitamin D management to restore PTH activity and improve overall bone health.

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Authors' Contribution

Conceptualization: Mahdieh Jamshidi, Zahra Kamiab, Gholamreza Bazmandegan.
Data curation: Mahdieh Jamshidi, Fatemeh Jalali Khalilabad, Mohammad Khalil Salehi.
Formal analysis: Zahra Kamiab.
Funding acquisition: Mahdieh Jamshidi.
Investigation: Mahdieh Jamshidi, Zahra Kamiab, Gholamreza Bazmandegan.
Methodology: Mahdieh Jamshidi, Zahra Kamiab, Gholamreza Bazmandegan.
Project administration: Mahdieh Jamshidi.
Resources: Mahdieh Jamshidi, Fatemeh Jalali Khalilabadi, Mohammad Khalil Salehi.
Software: Zahra Kamiab.

Supervision: Gholamreza Bazmandegan.
Validation: Mahdieh Jamshidi, Zahra Kamiab, Gholamreza Bazmandegan.
Visualization: Mahdieh Jamshidi, Fatemeh Jalali Khalilabadi, Gholamreza Bazmandegan.
Writing–original draft: Mahdieh Jamshidi, Zahra Kamiab, Gholamreza Bazmandegan.

Competing Interests
The authors declare that they have no conflicts of interest.

Data Availability Statement
Data used to support the findings of this study are included within the article.

Ethical Approval
This study was approved by the Ethics Committee of Rafsanjan University of Medical Sciences in Rafsanjan, Iran (Ethical code: IR.RUMS.REC.1401.123).

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