

Assessment of systemic inflammatory and immune biomarkers and alterations in calcium and parathyroid hormone in hemodialysis patients with type 2 diabetes mellitus

 Funda Bulut Arıkan*¹,  Hakkı Öztürk²

¹Department of Physiology, Faculty of Medicine, Kırıkkale University, Kırıkkale, Türkiye

²Infectious Diseases Epidemiologist, Dialysis Physician, Private Ankara Balgat Dialysis Center, Ankara, Türkiye

Cite this article as: Bulut Arıkan F, Öztürk H. Assessment of systemic inflammatory and immune biomarkers and alterations in calcium and parathyroid hormone in hemodialysis patients with type 2 diabetes mellitus. *Intercont J Int Med.* 2026;4(2):28-33. doi:10.51271/ICJIM-0072

Received: 15.03.2026

Accepted: 20.04.2026

Published: 26.05.2026

ABSTRACT

Aims: Chronic systemic inflammation and mineral metabolism disturbances are prevalent in hemodialysis (HD) patients. The presence of type 2 diabetes mellitus (T2DM) may further exacerbate inflammatory burden and disrupt calcium-parathyroid hormone (Ca-PTH) homeostasis. This study aimed to perform a comparative assessment of systemic and immune-inflammatory indices together with Ca-PTH levels in HD patients with and without T2DM, to assess the impact of diabetes on these parameters.

Methods: This retrospective multicenter study included 211 maintenance HD patients, including 97 with T2DM and 114 without diabetes. Inflammatory and immune-related indices, including the PIV, SIRI, SII, NLR, PLR, LMR, NMR, MPVLR, MHR, SII/albumin ratio, and CRP/albumin ratio were evaluated together with hematological parameters, biochemical markers, and mineral metabolism parameters.

Results: SIRI, PIV, MHR, IMA, and monocyte concentrations were notably elevated in the T2DM group compared to their non-diabetic counterparts ($p < 0.05$). ROC analysis showed modest discriminatory performance for SIRI (AUC=0.586) and PIV (AUC=0.583), with PIV demonstrating 71% sensitivity at a cut-off value of 25.28. In contrast, serum calcium and PTH levels were lower in the T2DM group, with calcium exhibiting the negative association among the studied parameters. SIRI and PIV were positively associated with leukocyte-related inflammatory markers, whereas calcium and PTH correlated with hemoglobin, hematocrit, potassium and phosphorus.

Conclusion: In hemodialysis patients, T2DM may be associated with an increased systemic inflammatory burden and a relative suppression of the Ca-PTH axis. Lower calcium and PTH levels could potentially reflect alterations in mineral metabolism and may be suggestive of a tendency toward adynamic bone disease. These observations may highlight the potential value of integrating inflammatory indices with Ca-PTH parameters to better characterize diabetes-associated inflammatory activity and disturbances in mineral metabolism in this patient population.

Keywords: Diabetes, hemodialysis, systemic inflammatory and immune indices, parathyroid hormone, calcium, mineral metabolism

INTRODUCTION

Maintenance hemodialysis (HD) cohorts are increasingly defined by a striking prevalence of type 2 diabetes mellitus (T2DM), an overarching comorbidity that imposes a multifaceted cardiovascular, metabolic, and psychosocial strain.¹ The survival of diabetic dialysis patients is significantly worse than that of dialysis patients without diabetes.² Cohort studies conducted in HD populations have reported that approximately 45-74% of HD patients have diabetes, and diabetes has been shown to be associated with a higher comorbidity burden and an approximately 72% increased risk of mortality.¹ Systemic inflammation serves as a pivotal mechanistic link in the underlying pathophysiology of both HD and T2DM. In HD patients, contact between blood and dialysis membranes promotes platelet adhesion and activation, contributing to chronic subclinical inflammation and immune dysregulation.^{3,4} Platelet activation represents

one of the earliest steps in the inflammatory cascade observed in HD patients and triggers multiple events that lead to chronic subclinical inflammation and immune dysfunction. Notably, platelet activation is considered a central mechanism that initiates chronic low-grade inflammation and contributes to immune system dysregulation in this population.³⁻⁵ In HD patients, dysfunction has been demonstrated in both the innate and adaptive immune systems. This condition is characterized by impaired anti-inflammatory responses, including reduced synthesis of IL-10 and caspase-8, as well as T-cell abnormalities such as a reduction in CD73⁺ T-cell subsets.^{5,6} Alterations in innate immune cells, such as neutrophils and monocytes, as well as adaptive immune components including T and B lymphocytes, are partly associated with exposure to uremic toxins and repeated extracorporeal blood circulation. These changes are positively associated with systemic inflammation,

*Corresponding Author: Funda Bulut Arıkan, funbulut@kku.edu.tr



increased susceptibility to infections, and an elevated risk of cardiovascular complications.^{4,5,7} In particular, the accumulation of uremic toxins, which is common in HD patients, increases leukocyte activity and promotes inflammation.⁷ Chronic low-grade inflammation is both a driver and a consequence of diabetes, particularly T2DM, and is closely linked to oxidative stress and metabolic dysfunction. Sustained inflammation in diabetes mellitus is linked to insulin resistance and increased glucose concentrations, which is evidenced by elevated levels of inflammatory biomarkers.⁸ In addition, chronic hyperglycemia and insulin resistance observed during the diabetic process lead to the pathological accumulation of advanced glycation end products (AGEs) in tissues, thereby disrupting bone homeostasis. This metabolic dysfunction suppresses bone turnover by inhibiting osteoblastic activity and limits the physiological adaptive capacity of the parathyroid gland in response to altered homeostatic demands.^{9,10}

In this context, in this context, the present study aimed to assess the effect of T2DM on inflammatory status among individuals undergoing HD by analyzing systemic inflammatory and immune-inflammatory indices, together with calcium (Ca) and parathyroid hormone (PTH) levels.

METHODS

Ethics

This study was conducted with the approval of the Kırıkkale University Ethics Committee for Non-interventional Researches (Date: 14.05.2025, Decision No: 2025.05.07). Permission to access clinical data was granted by Private Ankara Balgat Dialysis Center. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Study Design

This retrospective, multicenter study included 211 patients receiving maintenance HD who were followed at the Department of Internal Medicine, Kırıkkale University Faculty of Medicine, and the Private Ankara Balgat Dialysis Center between January 2020 and January 2025. According to diabetes status, patients were categorized into two groups: those with T2DM (n=97) and those without diabetes (n=114). The study included patients with a confirmed diagnosis of T2DM and a disease duration of at least 10 years, all of whom were diagnosed with diabetic nephropathy based on hospital records. The mean age of the study population was 62.7±11 years. All participants were receiving maintenance HD due to end-stage kidney disease with a glomerular filtration rate (GFR) of 15 ml/min/1.73 m² or lower. The diagnosis of T2DM was established in accordance with the criteria of the American Diabetes Association (ADA).

In this study, inflammatory and immune-related indices—including the Pan-Immune-Inflammation Value (PIV), Systemic Immune-inflammation Index (SII), Systemic Inflammation Response Index (SIRI), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR), neutrophil-to-monocyte ratio (NMR), mean platelet volume-to-lymphocyte ratio (MPVLR), monocyte-to-high-density lipoprotein cholesterol ratio (MHR), SII/albumin ratio, and CRP/albumin ratio were evaluated. Hematological parameters included

leukocyte, neutrophil, lymphocyte, monocyte, and platelet counts, plateletcrit, hemoglobin, hematocrit, and mean platelet volume (MPV). Biochemical markers comprised C-reactive protein (CRP), ferritin, ischemia-modified albumin (IMA), high-density lipoprotein cholesterol (HDL-C), non-HDL cholesterol, alanine aminotransferase (ALT), and albumin. Parameters related to electrolyte and mineral metabolism, including PTH, sodium (Na), potassium (K), Ca, and phosphorus (P), were also recorded. Patient demographics and laboratory datasets were compiled retrospectively by accessing medical archives.

Inclusion and Exclusion Criteria

Patients aged 18 years or older were eligible for inclusion, were receiving maintenance HD for end-stage kidney disease (GFR≤15 ml/min/1.73 m²), had been on regular HD for at least 6 months.

Patients were excluded if they had been receiving HD for less than 6 months; had an active infection, sepsis, or any acute inflammatory condition at the time of blood sampling; had a known malignancy or active autoimmune or rheumatologic disease; were pregnant; had missing key clinical or laboratory data that could compromise the reliability of the analyses; or were younger than 18 years of age. Patients with severely impaired glycemic control or acute critical conditions were excluded from the study.

Statistical Analyses

All data analyses were conducted with IBM SPSS Statistics for Windows (version 27.0; IBM Corp., Armonk, NY, USA). Normality of the data was examined using the Shapiro-Wilk test. According to the distribution characteristics, intergroup differences were analyzed using the Student's t-test for normally distributed variables or the Mann-Whitney U test for non-normally distributed variables. The discriminative ability of inflammatory biomarkers was evaluated using receiver operating characteristic (ROC) curve analysis, and the area under the curve (AUC) was used to assess diagnostic accuracy. The optimal cut-off value was determined using the Youden index (sensitivity+specificity-1) to identify the point that provided the best balance between sensitivity and specificity.

Correlations among variables were examined using either Pearson or Spearman correlation tests, as appropriate. Statistical significance was defined as a two-tailed p value of less than 0.05.

RESULTS

Hematological and Inflammatory Parameters

A statistically significant difference in monocyte counts was observed between the groups (p=0.045). In contrast, no statistically significant differences were detected in leukocyte, neutrophil, lymphocyte, platelet counts, plateletcrit, hemoglobin, hematocrit, or MPV (p>0.05), (Table 1). Regarding inflammatory and immune-related indices, significant differences in PIV, SIRI, and MHR were observed between the groups (p=0.044, p=0.040, and p=0.004, respectively). However, no significant differences were found for SII, NLR, PLR, LMR, NMR, MPVLR, or the ratios of SII/albumin and CRP/albumin (p>0.05), (Table 2).

Table 1. Hematological, biochemical, and mineral metabolism parameters in hemodialysis patients with T2DM

| Categories/parameters | HD with T2DM (mean±SD/IQR) | HD (mean±SD/IQR) | P |
|-------------------------------------------|----------------------------|---------------------|--------|
| Gender (female) | 46 (47.4%) | 44 (38.6%) | 0.21 |
| Gender (male) | 51 (52.6%) | 70 (61.4%) | |
| Hematological parameters (mean±SD) | | | |
| Leukocyte (10 ³ /μL) | 6.95±2.1 | 6.56±2.2 | 0.14 |
| Neutrophil (10 ³ /μL) | 4.71±1.7 | 4.32±1.7 | 0.12 |
| Lymphocyte (10 ³ /μL) | 1.44±0.5 | 1.37±0.5 | 0.37 |
| Monocyte (10 ³ /μL) | 0.67±0.4 | 0.58±0.2 | 0.045* |
| Platelet (10 ³ /μL) | 198.3±67.6 | 194.9±56.1 | 0.69 |
| Plateletcrit (%) | 0.64±3.4 | 0.25±0.1 | 0.24 |
| Hemoglobin (g/dl) | 11.36±1.6 | 11.36±1.7 | 0.97 |
| Hematocrit (%) | 34.67±6.4 | 35.09±6.4 | 0.64 |
| MPV (fL) | 11.12±1.1 | 10.96±1.0 | 0.30 |
| Biochemical markers (median (IQR)) | | | |
| CRP (mg/L) | 10.3 (5.4-23.2) | 9.6 (4.6-16.6) | 0.35 |
| Ferritin (ng/ml) | 618 (400-760.2) | 732 (514-851.5) | 0.29 |
| IMA (ABSU) | 0.711 (0.595-0.818) | 0.619 (0.507-0.753) | 0.044* |
| HDL-C (mg/dl) | 40 (29-46) | 38.50 (34-44.2) | 0.20 |
| non-HDL-C (mg/dl) | 139 (120.7-179.2) | 136 (120.5-172.7) | 0.92 |
| ALT (U/L) | 14 (11-18.7) | 13 (9-17.2) | 0.55 |
| Alb (g/dl) | 3.7 (3.4-3.9) | 3.7 (3.5-4) | 0.51 |
| Mineral metabolism | | | |
| PTH (pg/ml) (median (IQR)) | 198.5 (110.2-309) | 203.5 (129.7-406.7) | 0.007* |
| Na (mEq/L) (mean±SD) | 137.8±3.1 | 138.2±4.2 | 0.45 |
| K (mEq/L) (mean±SD) | 5.13±0.8 | 5.28±0.8 | 0.18 |
| Ca (mg/dl) (mean±SD) | 8.34±0.8 | 8.74±0.9 | 0.002* |
| P (mg/dl) (mean±SD) | 5.12±1.4 | 5.18±1.4 | 0.77 |

T2DM: Type 2 diabetes mellitus, IQR: Interquartile range, SD: Standard deviation, MPV: Mean platelet volume, CRP: C-reactive protein, Ferritin: Ferritin, IMA: Ischemia-modified albumin, HDL-C: High-density lipoprotein cholesterol, ALT: Alanine aminotransferase, Alb: Albumin, PTH: Parathyroid hormone, Na: Sodium, K: Potassium, Ca: Calcium, P: Phosphorus (IQR: 25th-75th percentile)

Table 2. Comparison of inflammatory indices between groups

| Parameter | HD with T2DM median (IQR) | HD median (IQR) | P |
|---------------|---------------------------|-----------------------|--------|
| PIV | 34 (21.40-62.58) | 26.9 (14.03-61.21) | 0.044* |
| SII | 647.8 (413.21-909.02) | 586.7 (366.74-976.95) | 0.20 |
| SIRI | 2.03 (1.38-3.15) | 1.6 (1.16-2.51) | 0.040* |
| NLR | 3.14 (2.42-4.50) | 3.2 (2.40-4.49) | 0.13 |
| PLR | 143.9 (104.34-192.75) | 138.6 (112.88-190.60) | 0.63 |
| LMR | 2.14 (1.56-3.26) | 2.3 (1.80-3.28) | 0.39 |
| NMR | 8.6 (5.24-10.69) | 7.4 (5.85-9.44) | 0.40 |
| MPVLR | 8.03 (6.26-11.13) | 7.8 (6.37-10.36) | 0.45 |
| MHR* | 0.020 (0.010-0.020) | 0.010 (0.010-0.020) | 0.004* |
| SII/Alb ratio | 170.5 (104.10-229.00) | 159.9 (98.46-258.75) | 0.89 |
| CRP/Alb ratio | 2.6 (1.68-5.10) | 2.4 (1.16-3.99) | 0.22 |

T2DM: Type 2 diabetes mellitus, IQR: Interquartile range, PIV: Pan-Immune-Inflammation Value, SII: Systemic Immune-inflammation Index, SIRI: Systemic Inflammation Response Index, NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, LMR: Lymphocyte-to-monocyte ratio, NMR: Neutrophil-to-monocyte ratio, MPVLR: Mean platelet volume-to-lymphocyte ratio, MHR: Monocyte-to-high-density lipoprotein cholesterol ratio. Data are presented as median (IQR: 25th-75th percentile)

The diagnostic performance evaluation demonstrated that SIRI and PIV were significantly elevated in the diabetic group (p<0.05). The AUC values for SIRI (0.586) and PIV (0.583)

indicated a modest but significant discriminatory capacity for identifying diabetic status. Specifically, PIV showed a sensitivity of 71% at a cut-off value of 25.28, suggesting screening potential. Correlation analysis revealed that both PIV and SIRI were significantly and positively associated (p<0.001) with neutrophil and leukocyte (WBC) counts, as well as with NLR and SII, while showing a highly significant inverse correlation with LMR (p<0.001).

Biochemical Markers and Mineral Metabolism

A statistically significant difference in IMA concentrations was identified between the groups (p=0.044), whereas no significant differences were observed for CRP, ferritin, HDL-C, non-HDL-C, ALT, or albumin (p>0.05). Notably, PTH and serum Ca levels differed significantly between the groups (p=0.007 and p=0.002, respectively), being significantly lower in the diabetic group. No significant differences were detected in sodium, potassium, or phosphorus levels (p>0.05), (Table 1).

Receiver operating characteristic (ROC) analyses and curves are presented in Table 3 and Figure. ROC curve analysis suggested that Ca might serve as a negative predictor for T2DM (Table 3). This finding suggests that decreased Ca levels may be inversely associated with T2DM occurrence. In the present cohort, the observed relationship between lower PTH and Ca levels and an increased prevalence of T2DM may reflect a complex interplay between Ca homeostasis and glucose metabolism. Correlation analysis showed that PTH was positively correlated with LMR (p<0.001), hematocrit (p=0.001), hemoglobin (p=0.016), phosphorus (p<0.001), and potassium (p=0.015). Similarly, serum Ca levels were significantly and positively associated with hematocrit (p=0.205, p=0.003) and phosphorus (p=0.182, p=0.008), (Table 4).

DISCUSSION

The pathophysiological framework of both HD and T2DM is inextricably tied to systemic inflammation. In the present study, the T2DM subgroup exhibited substantially higher values for SIRI, PIV, MHR, IMA, and monocytes, whereas a physiological suppression was observed in Ca and PTH levels when compared with their non-diabetic counterparts. Consistent with our findings, previous studies have identified SIRI as a independent prognostic marker in diabetic HD patients. Elevated SIRI levels were associated with an approximately fourfold increase in mortality risk, and a SIRI-based predictive model has been proposed as a valuable tool for clinical risk stratification in this population.^{11,12} There is a limited number of studies evaluating the MHR in diabetic HD patients. However, findings from related populations support our results. In a study conducted among patients with diabetic nephropathy, the association between MHR and disease severity was evaluated in the subgroup with severe albuminuria, and MHR levels were found to be significantly elevated.¹³ The PIV index has not previously been examined in HD patients with T2DM. In contrast, earlier research demonstrated significantly higher SII and PIV levels in female HD patients compared with their male counterparts.¹⁴ The PIV index, which integrates neutrophil, monocyte, platelet, and lymphocyte counts, reflects both inflammatory activation and immune dysregulation.¹⁵ In patients undergoing HD, the presence of T2DM may further increase PIV levels due

Table 3. ROC analysis of biomarkers for T2DM in hemodialysis patients

| Variable | AUC (95% CI) | p-value | Cut-off | Sensitivity (%) | Specificity (%) |
|--------------|-----------------------|---------|---------|-----------------|-----------------|
| SIRI | 0.586 (0.509-0.663) | 0.028 | 2.01 | 49.5 | 67.5 |
| PIV | 0.583 (0.505-0.661) | 0.036 | 25.29 | 71.0 | 49.6 |
| Parathormone | 0.420 (0.341 - 0.498) | 0.04 | 46.50 | 97.9 | 8.3 |
| Calcium | 0.382 (0.307-0.457) | 0.002 | 6.80 | 96.9 | 3.5 |

ROC: Receiver operating characteristic, T2DM: Type 2 diabetes mellitus, AUC: Area under the curve, CI: Confidence interval, PIV: Pan-Immune-Inflammation Value, SIRI: Systemic Immune-inflammation Index, SII: Systemic Inflammation Response Index

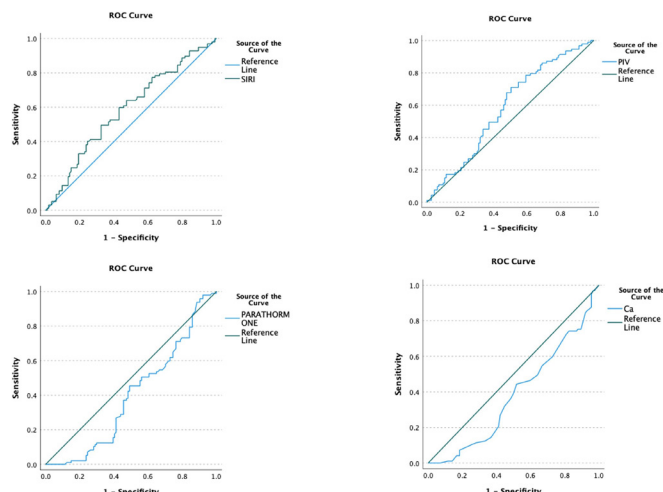


Figure. ROC curve analyses

ROC: Receiver operating characteristic

to possibly driven by intensified systemic inflammation, endothelial impairment, and oxidative stress.

Although not identical to the population included in the present study, similar outcomes have been reported in studies involving patients with diabetic nephropathy, where monocyte levels were significantly higher compared with healthy controls.¹⁶ These results support the hypothesis that monocyte-mediated inflammatory pathways may contribute to the inflammatory milieu observed in diabetic kidney disease and HD patients with T2DM.

Diabetes mellitus is well known to exert detrimental effects on both innate and acquired immune responses, leading to significant immune dysfunction.¹⁷ Hyperglycemia and AGEs in diabetes increase the release of monocytes from the bone marrow and prolong their survival in circulation.¹⁸ In the literature, non-classical pro-inflammatory monocytes (CD14⁺CD16⁺) have been reported to be increased particularly in patients with diabetic nephropathy.¹⁶

Recent evidence indicates that when diabetes and chronic kidney disease coexist, monocytes undergo epigenetic and metabolic reprogramming, resulting in a pro-inflammatory phenotype through a mechanism referred to as “trained immunity.” Hyperglycemia-induced metabolic stress and AGEs affect hematopoietic stem cells and myeloid progenitors, thereby increasing the production of pro-inflammatory monocytes and promoting a persistent inflammatory response in these cells.^{19,20} Furthermore, the chronic inflammatory milieu associated with uremia and HD alters monocyte functional properties and contributes to persistent activation of the innate immune response.^{7,17} In our study, the pronounced increase in monocyte levels in T2DM patients undergoing HD may be attributable to impaired chemotactic receptor function, which may limit the migration of these cells from the vascular compartment to tissues, thereby prolonging their persistence in circulation. In addition, chronic inflammation may promote immune aging (immunosenescence), further contributing to the accumulation of circulating monocytes. Indeed, it has been reported that immunosenescence in chronic kidney disease

Table 4. Correlation analysis of inflammatory and biochemical parameters

| Parameters | SIRI | Monocyte | PIV | MHR | Ca ⁺⁺ | PTH | NLR | SII | CRP | Alb |
|------------------|------------------------|-----------------------|------------------------|-----------------------|------------------------|------------------------|------------------------|-----------------------|-----------------------|-----------------------|
| SIRI | 1 | .628** ($<.001$) | .400** ($<.001$) | .437** ($<.001$) | -.088 (.204) | -.359** ($<.001$) | .685** ($<.001$) | .735** ($<.001$) | .134 (.052) | -.066 (.338) |
| Monocyte | .628** ($<.001$) | 1 | .061 (.384) | .745** ($<.001$) | .003 (.968) | -.219** (.002) | .464** ($<.001$) | .001 (.988) | .107 (.122) | -.002 (.980) |
| PIV | .400** ($<.001$) | .061 (.384) | 1 | .017 (.811) | -.244** ($<.001$) | -.114 (.10) | .523** ($<.001$) | .488** ($<.001$) | .866** ($<.001$) | .052 (.458) |
| MHR | .437** ($<.001$) | .745** ($<.001$) | .017 (.811) | 1 | .014 (.836) | -.138 (.050) | .396** ($<.001$) | .341** (.002) | -.130 (.060) | -.112 (.108) |
| Ca ⁺⁺ | -.088 (.204) | .003 (.968) | -.244** ($<.001$) | .014 (.836) | 1 | .146* (.040) | -.020 (.777) | -.120 (.082) | -.097 (.161) | .330** ($<.001$) |
| PTH | -.319** ($<.001$) | -.219** (.002) | -.124 (.076) | -.138 (.050) | .146* (.040) | 1 | -.246** ($<.001$) | -.201** (.004) | -.032 (.647) | .134 (.055) |
| NLR | .685** ($<.001$) | .464** ($<.001$) | .523** ($<.001$) | .396** ($<.001$) | -.020 (.777) | -.246** ($<.001$) | 1 | .832** ($<.001$) | .288** ($<.001$) | -.144* (.042) |
| SII | .735** ($<.001$) | .001 (.988) | .488** ($<.001$) | .341** (.002) | -.120 (.082) | -.201** (.004) | .832** ($<.001$) | 1 | .081 (.241) | .041 (.563) |
| CRP | .134 (.052) | .107 (.122) | .866** ($<.001$) | -.130 (.060) | -.097 (.161) | -.032 (.647) | .288** ($<.001$) | .081 (.241) | 1 | -.026 (.713) |
| Alb | -.066 (.338) | -.002 (.980) | .052 (.458) | -.112 (.108) | .330** ($<.001$) | .134 (.055) | -.144* (.042) | .041 (.563) | -.026 (.713) | 1 |

SIRI: Systemic Inflammation Response Index, PIV: Pan-Immune-Inflammation Value, MHR: Monocyte-to-high-density lipoprotein cholesterol ratio, Ca: Calcium, PTH: Parathyroid hormone, NLR: Neutrophil-to-lymphocyte ratio, SII: Systemic Immune-Inflammation Index, CRP: C-reactive protein, Alb: Albumin

leads to the accumulation of functionally altered but highly pro-inflammatory monocyte and macrophage populations in the circulation.²¹ This phenomenon may reflect the presence of an “aged” immune cell pool characterized by reduced tissue infiltration capacity but increased inflammatory activity, which may represent an important mechanism underlying the chronic inflammatory state observed in diabetic HD patients. In the present study, lower Ca and PTH levels observed in HD patients with T2DM may be associated with adynamic bone disease, a condition characterized by low bone turnover that is frequently reported in diabetic patients with chronic kidney disease.²² Chronic hyperglycemia, accumulation of AGEs, and insulin resistance may suppress osteoblast function, thereby reducing bone turnover and impairing the physiological responsiveness of the parathyroid gland.⁹ Consistent with this mechanism, previous studies have reported lower PTH levels and a higher prevalence of low bone turnover patterns in diabetic nephropathy patients.¹⁰

The present study demonstrates that SIRI (AUC: 0.586, $p=0.028$) and PIV (AUC: 0.583, $p=0.036$) exhibit statistically significant but modest discriminatory performance for identifying T2DM status. Although SIRI achieved a specificity of 67.5% at a cut-off value of 2.01 and PIV showed a sensitivity of 71.0%, the proximity of their lower confidence intervals to the 0.50 threshold indicates that their clinical applicability should be interpreted with caution.

In contrast, parathormone (AUC: 0.420) and Ca (AUC: 0.382) demonstrated limited diagnostic performance, suggesting a weak inverse association with T2DM rather than meaningful predictive utility. Given their suboptimal AUC values and particularly the low specificity observed for Calcium, these markers do not currently satisfy the criteria for independent clinical biomarkers in this setting.

Overall, these findings should be considered preliminary evidence of altered mineral metabolism in the diabetic nephropathy rather than definitive diagnostic indicators, and they warrant validation in larger, adequately powered prospective cohorts.

Limitations

This study’s retrospective design limited our ability to fully adjust for confounding factors like medication history and comorbidities via multivariable analysis. Although HbA1c was not recorded, it is often a suboptimal marker in HD patients due to altered erythrocyte turnover. To minimize these constraints, we applied strict inclusion criteria, including a T2DM history of ≥ 10 years and a stable dialysis vintage of ≥ 6 months. Future prospective studies are required to validate the independent predictive value of these markers.

CONCLUSION

As a result, HD patients with T2DM exhibit a complex biochemical profile characterized by elevated SIRI and PIV levels, as well as a decline in Ca and PTH concentrations. Although SIRI and PIV showed statistically significant but modest discriminatory performance, their diagnostic utility necessitates cautious interpretation. Furthermore, the inverse patterns observed for Ca and PTH suggest a potential suppression of the mineral bone axis possibly reflecting low bone turnover states such as adynamic bone disease within the context of diabetic nephropathy. Collectively, these findings

provide preliminary evidence of a link between systemic inflammation and altered mineral metabolism. Further high-powered, prospective studies are essential to validate these associations and to clarify their prognostic significance in the diabetic nephropathy population.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study was conducted with the approval of the Kırıkkale University Ethics Committee for Non-interventional Researches (Date: 14.05.2025, Decision No: 2025.05.07).

Informed Consent

This retrospective study used pre-existing anonymized patient data. No additional intervention was performed, and there was no direct patient contact. The study was approved by the Ethics Committee, and the requirement for written informed consent was waived by the ethics committee.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

Financial Disclosure

The authors received no financial support for the conduct or publication of this research.

Author Contributions

Concept: FBA; Design: FBA; Control: FBA, HÖ; Data Collection and/or Processing: FBA, HÖ; Analysis and/or Interpretation: FBA; Literature Review: FBA; Article Writing: FBA; Critical Review: FBA, HÖ.

REFERENCES

- Al-Ghamdi SMG, Bieber B, AlRukhaimi M, et al. Diabetes prevalence, treatment, control, and outcomes among hemodialysis patients in the Gulf Cooperation Council countries. *Kidney Int Rep.* 2022;7(5):1093-1102. doi:10.1016/j.ekir.2022.02.012.
- Drechsler C, Krane V, Ritz E, März W, Wanner C. Glycemic control and cardiovascular events in diabetic hemodialysis patients. *Circulation.* 2009;120(24):2421-2428. doi:10.1161/CIRCULATIONAHA.109.857268
- Ilyas D, Blackburn E, Herbert A, et al. #2866 The CompAct-HD trial reports a persistent inflammatory profile in patients undergoing haemodialysis, acutely exacerbated with each treatment. *Nephrol Dial Transplant.* 2024;39(Supplement_1):gfae069-0159-2866. doi:10.1093/ndt/gfae069.159
- Campo S, Lacquaniti A, Trombetta D, Smeriglio A, Monardo P. Immune system dysfunction and inflammation in hemodialysis patients: two sides of the same coin. *J Clin Med.* 2022;11(13):3759. doi:10.3390/jcm11133759
- Dawood A, Fiedler R, Markau S, Girndt M, Ulrich C. Polysome profiling proves impaired IL-10 and caspase-8 translation in PBMCs of hemodialysis patients. *Biomolecules.* 2025;15(3):335. doi:10.3390/biom15030335
- Xiang F, Sun L, Cao X, et al. CD73 as a T cell dysfunction marker predicting cardiovascular and infection events in patients undergoing hemodialysis. *Clin Chim Acta.* 2024;555:117791. doi:10.1016/j.cca.2024.117791
- Diaz-Ricart M, Torramade-Moix S, Pascual G, et al. Endothelial damage, inflammation and immunity in chronic kidney disease. *Toxins (Basel).* 2020;12(6):361. doi:10.3390/toxins12060361
- Cecerska-Heryć E, Engwert W, Michałow J, et al. Oxidative stress markers and inflammation in type 1 and 2 diabetes are affected by BMI, treatment type, and complications. *Sci Rep.* 2025;15(1):23605. doi:10.1038/s41598-025-05818-z
- Evenepoel P, Stenvinkel P, Shanahan C, Pacifici R. Inflammation and gut dysbiosis as drivers of CKD-MBD. *Nat Rev Nephrol.* 2023;19(10):646-657. doi:10.1038/s41581-023-00736-7

10. Dempster DW, Evenepoel P, Nickolas TL, et al. Osteoporosis and CKD-metabolic bone disease under the same umbrella: insights from a joint scientific symposium. *Kidney Int Rep.* 2026;11(5):106362. doi:10.1016/j.ekir.2026.106362
11. Zhang Z, Zhao L, Zhou X, Meng X, Zhou X. Role of inflammation, immunity, and oxidative stress in hypertension: new insights and potential therapeutic targets. *Front Immunol.* 2023;13:1098725. doi:10.3389/fimmu.2022.1098725
12. Zhu J, Shi R, Li X, et al. Association between neutrophil percentage-to-albumin ratio and mortality in hemodialysis patients: insights from a prospective cohort study. *BMC Nephrol.* 2025;26(1):112. doi:10.1186/s12882-025-04027-0
13. Yang W, Zhong Y, Zhou P, Lu D. Monocyte to high-density lipoprotein cholesterol ratio as a marker of the presence and progression of diabetic kidney disease. *Ren Fail.* 2025;47(1):2438846. doi:10.1080/0886022X.2024.2438846
14. Arıkan FB, Öztürk H. Inflammatory indices in hypertensive hemodialysis patients: clinical implications of MPV and MPVLR. *J Med Palliat Care.* 2025;6(5):569-574. doi:10.47582/jompac.1773774
15. Arıkan FB, Sağsöz N. Enhancing diagnostic accuracy in polycystic ovary syndrome using novel inflammatory indices. *Kırıkkale Uni Med J.* 2025;27(2):217-224. doi:10.24938/kutfd.1718713
16. Chen Y, Men K, Meng CM, Ma J, Guo JC. Changes in TLR-4 expression level and CD14+CD16+ monocyte ratio in the peripheral blood of patients with early diabetic nephropathies. *ScienceAsia.* 2020;46(2):206-212. doi:10.2306/scienceasia1513-1874.2020.022
17. Trandafir MF, Savu OI, Gheorghiu M. The complex immunological alterations in patients with type 2 diabetes mellitus on hemodialysis. *J Clin Med.* 2024;13(13):3687. doi:10.3390/jcm13133687
18. Jin X, Liu L, Zhang Y, et al. Advanced glycation end products enhance murine monocyte proliferation in bone marrow and prime them into an inflammatory phenotype through MAPK signaling. *J Diabetes Res.* 2018;2018:2527406. doi:10.1155/2018/2527406
19. Netea MG, Domínguez-Andrés J, Barreiro LB, et al. Defining trained immunity and its role in health and disease. *Nat Rev Immunol.* 2020;20(6):375-388. doi:10.1038/s41577-020-0285-6
20. Bekkering S, Arts RJW, Novakovic B, et al. Metabolic induction of trained immunity through the mevalonate pathway. *Cell.* 2018;172(1-2):135-146.e9. doi:10.1016/j.cell.2017.11.025
21. Espi M, Koppe L, Fouque D, Thauinat O. Chronic kidney disease-associated immune dysfunctions: impact of protein-bound uremic retention solutes on immune cells. *Toxins (Basel).* 2020;12(5):300. doi:10.3390/toxins12050300
22. Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Update Work Group. KDIGO 2017 clinical practice guideline update for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease-mineral and bone disorder (CKD-MBD). *Kidney Int Suppl (2011).* 2017;7(1):1-59. doi:10.1016/j.kisu.2017.04.001