The Role of Osteocalcin, TRAP, and TNF-α in Predicting Anemia Severity in Patients with Chronic Kidney Disease

Shahad Luay Abdulkareem Al-Abdali, PhD* Raid J. Mohammed Al-Timimi, PhD* Arif Sami MALIK, M.B.ch.B, F.I.C.M.S**

ABSTRACT

Anemia is a major and challenging complication in patients with chronic kidney disease, especially those undergoing maintenance hemodialysis. Bone-derived and inflammatory markers such as osteocalcin, TRAP, and TNF-α may contribute to anemia severity through multiple pathways. This study aimed to determine the predictive value of these biomarkers in assessing anemia severity among hemodialysis patients at Hamida Al-Masfah Dialysis Center, Al-Imamain Al-Kadhimain Teaching Hospital, Baghdad. A cross-sectional study was conducted over six months, from November 1, 2023 to April 20, 2024, involving 100 adult patients. Patients were classified according to KDIGO guidelines into mild, moderate, and severe anemia groups. Results revealed significantly higher mean levels of osteocalcin, TRAP, and TNF-α in patients with mild anemia compared to those with moderate and severe forms (p = 0.019, 0.008, and <0.001, respectively). ROC analysis showed that TNF-α had the highest diagnostic accuracy (AUC = 0.731), followed by osteocalcin and TRAP. These findings suggest that elevated levels of osteocalcin, TRAP, and TNF-α are associated with anemia and may serve as useful biomarkers in predicting anemia severity in CKD patients undergoing hemodialysis.

Keywords: Chronic kidney disease, Anemia, Hemodialysis, Osteocalcin, TRAP, TNF-α, Biomarkers

INTRODUCTION

Anemia represents a significant complication in individuals with chronic kidney disease (CKD), especially among those receiving maintenance hemodialysis. The condition arises from a complex interplay of factors, including reduced erythropoietin (EPO) production, diminished red blood cell (RBC) lifespan, iron deficiency, chronic inflammation, and suppression of bone marrow[1]. Conventional methods for managing anemia in chronic kidney disease (CKD) have emphasized iron supplementation and erythropoietin (EPO) therapy. Resistance to erythropoiesis-stimulating agents (ESA) continues to pose a considerable clinical challenge, highlighting the need for further investigation into additional pathophysiological mechanisms[2,3]. Recent evidence underscores the potential contributions of inflammation and disrupted bone metabolism to the pathogenesis of renal anemia. Tumor necrosis factor-alpha (TNF-α) is a notable inflammatory marker recognized for its inhibitory effects on erythropoiesis[4]. TNF-α is a pro-inflammatory cytokine produced by activated monocytes and macrophages in reaction to uremia and immune activation induced by dialysis[5]. It inhibits the differentiation of erythroid progenitors, suppresses the expression of the EPO gene, and promotes oxidative stress and apoptosis in hematopoietic tissues[6]. In patients with chronic kidney disease (CKD), elevated levels of TNF-α have been linked to reduced hemoglobin levels and a diminished response to erythropoiesis-stimulating agent (ESA) therapy[7].

Simultaneously, there is increasing interest in bone-derived biomarkers as factors contributing to anemia in chronic kidney disease (CKD). The bone marrow is closely linked to the skeletal system, and disturbances in bone remodeling can negatively impact hematopoietic niches[8]. Osteocalcin is a non-collagenous protein hormone predominantly synthesized by osteoblasts in the process of bone formation. This process is implicated in matrix mineralization and has demonstrated a regulatory role in energy metabolism and potentially hematopoiesis, mediated by signaling pathways related to insulin sensitivity and interactions with bone marrow[9,10]. Dysregulated osteocalcin levels may indicate altered bone turnover states that hinder erythropoietic support in patients with chronic kidney disease[11].

Tartrate-resistant acid phosphatase 5b (TRAP-5b) is an enzyme secreted by active osteoclasts and is widely acknowledged as a marker of bone resorption[12]. Increased levels of TRAP-5b suggest heightened osteoclast activity, potentially affecting erythropoiesis indirectly through mechanisms such as bone marrow remodeling, fibrosis, or impaired stromal support for hematopoietic progenitors[13]. TRAP-5b may interact with inflammatory pathways, thereby establishing a connection between bone health and the pathophysiology of anemia[14]. While TNF-α, osteocalcin, and TRAP-5b have been individually investigated in the context of CKD-related bone or inflammatory disorders, there is a paucity of research on their collective diagnostic or predictive significance in evaluating anemia severity. Comprehending these associations could improve the clinical management of renal anemia and refine the targeting of therapies beyond traditional EPO and iron supplementation[15].

PATIENTS AND METHODS

This cross-sectional study was conducted in the Hamida Al-Masfah Dialysis Center, Al-Imamain Al-Kadhimain Teaching Hospital in Baghdad, Iraq, over a six-month duration from November 1, 2023, to April 20, 2024. Ethical approval was secured from the Institutional

* Department of Chemistry and Biochemistry
College of Medicine, Al-Nahrain University
Baghdad, Iraq.
Email: shahadly141@gmail.com
** Department of Medicine, College of Medicine
Al-Nahrain University, Baghdad, Iraq.

Review Board (IRB) of the College of Medicine, Al-Nahrain University. Informed permission was obtained in writing from all subjects enrolled in the study.

One hundred adult patients, aged 18 years or older, on maintenance hemodialysis for a minimum of three months and receiving erythropoiesis-stimulating drugs (ESAs), were recruited. Patients were excluded if they exhibited the following:
(1) Active infection, malignancy, or recent hemorrhage within the preceding 3 months.
(2) Iron deficiency anemia (serum ferritin <100 ng/mL and transferrin saturation <20%).
(3) Hemoglobinopathies such as thalassemia or sickle cell disease.
(4) Malnutrition (albumin <2.5 g/dL or BMI <18.5 kg/m²); or (5) incomplete clinical or laboratory data.
According to the KDIGO recommendations, there were 15 patients (15%) with mild anemia, 39 patients (39%) with moderate anemia, and 46 patients (46%) with severe anemia. Demographic and clinical information, including age, gender, body mass index (BMI), length of dialysis, and medical history, was documented. Blood samples were obtained prior to dialysis sessions for laboratory examination.

Laboratory Assessments: Hematological parameters were evaluated with the Phoenix Hematology Analyzer (Japan). Biochemical indicators, including serum calcium, phosphate, creatinine, and albumin, were quantified with automated chemistry analyzers. Iron indicators, such as serum ferritin and transferrin saturation (TSAT), were assessed utilizing recognized methodologies. Vitamin D and Vitamin K concentrations were measured with ELISA kits from Cloud-Clone Corp (USA). Bone turnover markers, such as osteocalcin and tartrate-resistant acid phosphatase 5b (TRAP-5b), together with the inflammatory marker TNF-α, were quantified utilizing Cloud-Clone Corp ELISA kits on the HUMAN ELISA Reader system (Germany). The coagulation profile, encompassing prothrombin time (PT) and international normalized ratio (INR), was assessed utilizing the STart Max® Coagulometer (Stago, France).

Sample preparation entailed centrifugation with a high-speed centrifuge (Bioneer, Korea), and pipetting executed with precision pipettes (BOECO, Germany). Temperature-regulated incubation was conducted utilizing Cypress Diagnostic incubators. The weekly ESA dose (Eprex®) was recorded in international units (IU). All analyses were performed within 1–2 hours of blood collection.

Statistical Analysis: All data were input and analyzed utilizing SPSS version 26. Descriptive statistics were presented as means ± standard deviations for continuous variables and as frequencies and percentages for categorical variables. Group comparisons were performed utilizing independent samples t-tests and Chi-square tests, with a p-value of ≤0.05 being statistically significant[16,17].

RESULTS

This cross-sectional study comprised 100 individuals with chronic kidney disease (CKD) receiving regular hemodialysis. The average age of participants was 51.41 ± 14.18 years (range: 19–85 years), comprising 64% male and 36% female individuals.

Severity of Anemia

Based on KDIGO guidelines, 15% of patients had mild anemia, 39% had moderate anemia, and 46% had severe anemia.

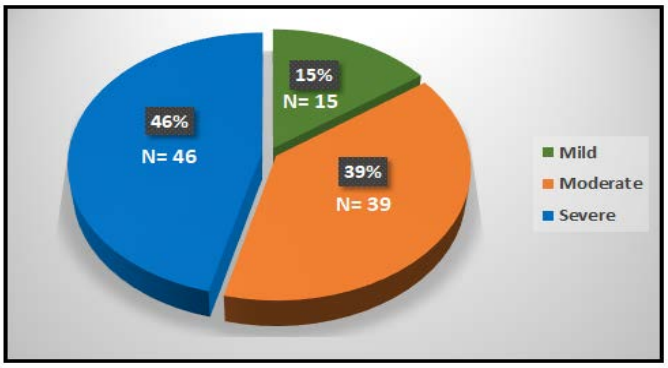

Figure 1. Distribution of anemia severity among CKD patients]

Demographic and Anthropometric Characteristics

There were no statistically significant variations were seen in age, gender, occupation, weight, height, BMI, smoking, or alcohol status between the anemia severity groups. Despite the observation of male preponderance and a marginally elevated BMI in the severe group, these findings did not achieve statistical significance ($p > 0.05$).

Clinical and Dialysis-Related Characteristics

The etiology of CKD, transplantation history, length of ESRD, dialysis duration, and frequency were not significantly correlated with the severity of anemia. ESA frequency had a significant correlation ($p = 0.017$); patients with mild anemia were more inclined to take ESA three times weekly, whereas those with severe anemia mostly received it once weekly.

Hematological Parameters

Transferrin saturation exhibited a significant difference among hematological indices between groups ($p = 0.012$), with the highest levels observed in the severe anemia group. The PT and INR values were considerably elevated in the mild anemic cohort ($p = 0.021$ and 0.023, respectively). Other measures, such as ferritin, UIBC, iron, TIBC, and transferrin, exhibited no significant differences.

Biochemical Markers

No notable variations were detected in calcium, phosphorus, creatinine, albumin, or 25(OH) vitamin D levels across the groups. Vitamin D levels were considerably reduced in participants with mild anemia compared to those with moderate and severe anemia ($p = 0.021$).

Bone and Inflammatory Biomarkers

Levels of osteocalcin, TRAP, and TNF-α were significantly higher in the mild anemia group compared to moderate and severe groups ($p = 0.019$, 0.008, and <0.001, respectively).

Diagnostic Performance of Biomarkers

ROC analysis indicated that TNF-α had the greatest diagnostic efficacy in distinguishing mild anemia from both moderate and severe anemia (AUC = 0.761 and 0.731, respectively). Osteocalcin and TRAP show moderate diagnostic efficacy in anemia stratification.

DISCUSSION

This cross-sectional study examined 100 patients with chronic kidney disease receiving regular hemodialysis, evaluating the severity of anemia in relation to bone and inflammatory biomarkers, specifically

Table 1. Demographic and anthropometric characteristics by anemia severity

Variables	Mild (n=15)	Moderate (n= 39)	Severe (n= 46)	p-value
Age, years				
Mean±SD	56.33±14.34	49.72±17.93	51.24±11.21	0.309
Range	27-85	19-85	20-75	
Sex				
Male	9(60%)	22(56.41%)	33(71.74%)	0.321
Female	6(40%)	17(43.59%)	13(28.26%)	
Occupation				
Free job	3(20%)	4(10.26%)	9(19.57%)	0.683
Retired	4(26.67%)	6(15.38%)	7(15.22%)	
Unemployed	3(20%)	11(28.21%)	13(28.26%)	
Housewife	4(26.67%)	17(43.59%)	13(28.26%)	
Employed	1(6.67%)	1(2.56%)	4(8.7%)	
Weight, kg				
Mean±SD	69.47±13.71	71.92±18.37	76.63±18.81	0.300
Range	45-90	41-142	51-144	
Height, cm				
Mean±SD	161.73±8.69	163.46±9.22	166.8±8.8	0.090
Range	147-172	130-177	150-190	
BMI, kg/m²				
Mean±SD	26.51±4.72	26.79±6.0	27.36±5.19	0.898
Range	17.58-35.63	18.22-52.16	18.69-44.44	
Smoking				
Never	10(66.67%)	26(66.67%)	29(63.04%)	0.931
Ex/current	5(33.33%)	13(33.33%)	17(36.96%)	
Alcohol				
Never	14(93.33%)	34(87.18%)	41(89.13%)	0.810
Ex/current	1(6.67%)	5(12.82%)	5(10.87%)	
GFR				
Mean±SD	8.0±1.96	8.26±4.52	8.2±4.2	0.979
Range	5.0-11.0	4.0-26.0	3.0-25	

osteocalcin, tartrate-resistant acid phosphatase (TRAP), and tumor necrosis factor alpha (TNF-α). The results revealed that 46% of patients experienced severe anemia, 39% moderate anemia, and 15% mild anemia, aligning with prior studies that report a high prevalence of anemia in end-stage renal disease (ESRD) patients receiving dialysis, attributed to compromised erythropoiesis and inflammation-induced resistance to erythropoietin[1,18,19]. An examination of demographic and clinical characteristics revealed no significant correlation with anemia severity, consistent with prior research by Rostami et al., which indicated that demographic factors such as age, gender, and BMI do not independently forecast anemia progression in dialysis patients[20]. Nonetheless, the frequency of erythropoiesis-stimulating agents (ESAs) exhibited a strong correlation, with mildly anemic individuals receiving ESAs more often. This may indicate improved treatment adherence or responsiveness in the initial stages of anemia[21]. Notably, transferrin saturation was markedly elevated in the severe anemia cohort among hematological indicators. This may indicate functional iron overload resulting from chronic inflammation and inadequate iron use, as corroborated by prior research in hemodialysis cohorts[22]. PT and INR levels were markedly raised in the mild anemic cohort, potentially indicating impaired hepatic synthetic function or anticoagulant use in certain individuals, although not directly associated with the pathogenesis of anemia[23].

Vitamin D levels were markedly reduced in the mild anemia group in comparison to the moderate and severe anemia groups. This contrasts with other research indicating that vitamin D deficiency is more prevalent in severe anemia; nevertheless, inconsistencies may arise from variations in supplementing protocols or test errors[24,25]. Concurrently, levels of calcium, phosphate, creatinine, and albumin exhibited no significant variations, consistent with previous research suggesting that these indicators are less responsive to the severity of anemia when within normal limits[26].

The primary finding of the study is the notable increase in osteocalcin, TRAP, and TNF-α among the mild anemia cohort. These indicators exhibited gradually reduced levels with escalating anemia severity. TNF-α, a pro-inflammatory cytokine, is recognized for its suppression of erythropoiesis and inhibition of erythropoietin activity; nevertheless, its reduction in severe anemia may signify immunological exhaustion or adaptability, as shown in chronic inflammatory conditions[27,28]. Osteocalcin and TRAP, both indicators of bone turnover, were elevated in mild anemia, possibly indicating increased bone activity that decreases as anemia intensifies and bone metabolism decelerates due to malnutrition-inflammation complex syndrome[29].

ROC analysis revealed that TNF-α had the greatest diagnostic efficacy in differentiating mild from severe anemia, with moderate sensitivity and specificity. This underscores the efficacy of TNF-α as a non-invasive biomarker for the early detection and monitoring of anemia in CKD patients, along with previous studies that emphasize the predictive potential of inflammatory cytokines in renal anemia[30]. Osteocalcin and TRAP demonstrated considerable diagnostic accuracy, indicating their potential as surrogate markers for the evolution of anemia, particularly in the context of renal osteodystrophy[31,32].

This work demonstrates that osteocalcin, TRAP, and TNF-α are inversely correlated with anemia severity, suggesting that their assessment could enhance early diagnosis and stratification of anemia in dialysis-dependent CKD patients. Additional longterm investigations

Table 2. Clinical and dialysis-related parameters by anemia severity

Variables	Mild (n=15)	Moderate (n= 39)	Severe (n= 46)	p-value
Cause of CKD				
Diabetes	3(20%)	5(12.82%)	7(15.22%)	
Hypertension	2(13.33%)	9(23.08%)	6(13.04%)	
DM+HTN	3(20%)	9(23.08%)	15(32.61%)	
ADPKD	1(6.67%)	1(2.56%)	7(15.22%)	
HTN+analgesic	0(0%)	4(10.26%)	2(4.35%)	
Neurogenic B.	1(6.67%)	4(20.26%)	2(4.35%)	0.318
Renal atrophy	0(0%)	2(5.13%)	3(6.52%)	
Others	5(33.33%)	5(15.82%)	4(8.7%)	
Kidney transplant				
No	13(86.67%)	36(92.31%)	44(95.56%)	0.484
Yes	2(13.33%)	3(7.69%)	2(4.35%)	
ESRD duration				
Mean±SD	7.46±7.9	6.15±5.0	7.26±9.27	
Median	4.0	4.0	5.0	0.904
Range	2.0-33.0	1.0-24.0	0.5-59.0	
HD duration, yrs				
Mean±SD	3.5±3.05	4.0±2.76	3.47±2.57	
Median	3.0	3.0	2.75	0.470
Range	0.3-12.0	0.6-11.0	0.25-12.0	
HD frequency/wks				
Once	0(0%)	1(2.56%)	0(0%)	
Twice	3(20%)	4(10.26%)	5(10.87%)	0.623
Thrice	12(80%)	34(87.18%)	41(89.13%)	
ESA duration				
Mean±SD	3.0±2.51	4.78±3.41	3.7±2.73	
Median	2.0	3.75	3.0	0.075
Range	0.3-9.0	0.7-15.0	0.5-12.0	
ESA frequency				
Once	7(46.67%)	27(69.23%)	38(82.61%)	
Twice	3(20%)	9(23.08%)	9(19.57%)	**0.017**
Thrice	5(33.33%)	3(7.69%)	3(6.52%)	

Table 3. Hematological parameters by anemia severity

Variables	Mild (n=15)	Moderate (n= 39)	Severe (n= 46)	p-value
Ferritin				
Mean±SD	555.8±319.1	539.1±279.0	461.8±280.1	0.357
Range	114-1200	134-1200	44-1200	
UIBC				
Mean±SD	184.0±85.9	177.5±63.5	159.1±78.3	0.384
Range	40-310	28-303	34-355	
Iron				
Mean±SD	70.8±33.3	78.3±43.6	82.1±26.6	0.555
Range	31.8-175	31-275	30-174	
TIBC				
Mean±SD	244.0±77.5	253.8±59.8	241.2±68.8	0.678
Range	114-363	96-381	112-425	
Transferrin				
Mean±SD	36.8±356.6	36.0±43.0	38.4±23.8	0.949
Range	12.7-152.2	12.2-286.5	14.5-155.4	
Transferrin saturation, %				
Mean±SD	43.2±8.8[a]	49.4±9.9[ab]	53.2±12.8[b]	**0.012**
Range	22-57	32-76	26-87	
PT				
Mean±SD	16.3±2.4[a]	15.1±1.5[b]	14.8±1.9[b]	**0.021**
Range	13.9-23.7	12.4-18.8	11.8-21	
INR				
Mean±SD	1.5±0.23[a]	1.4±0.13[b]	1.33±0.18[b]	**0.023**
Range	1.24-2.2	1.1-1.7	1.05-1.9	

Table 4. Biochemical markers by anemia severity

Variables	Mild (n=15)	Moderate (n= 39)	Severe (n= 46)	p-value
Calcium				
Mean±SD	8.71±0.86	8.8±0.79	8.74±1.08	0.951
Range	6.8-10.10	6.8-10.72	3.6-11.0	
Phosphorus				
Mean±SD	5.13±1.75	4.81±1.41	5.1±1.7	0.670
Range	2.8-9.0	1.81-7.6	2.8-13.7	
Creatinine				
Mean±SD	7.35±2.13	7.77±2.43	8.12±3.24	0.630
Range	3.9-11.7	2.7-12.4	2.8-19.3	
Albumin				
Mean±SD	3.89±0.59	4.13±1.124	4.14±0.86	0.678
Range	2.35-4.8	2.94-9.4	3.2-7.9	
Vitamin D				
Mean±SD	54.7±27.57[a]	70.0±18.35[b]	69.95±16.71[b]	0.021
Range	6.54-89.48	38.48-108-58	37.93-102.48	
25(OH) vitamin D				
Mean±SD	20.95±4.87	21.03±5.04	21.86±4.71	0.682
Range	12.21-28.97	12.24-30.75	12.3-32.06	
Vitamin K				
Mean±SD	983.19±288.63	1010.93±282.7	970.68±335	0.660
Range	277.9-1427.2	389.1-1937.2	149.95-1968.7	

Table 5. Bone and inflammatory biomarkers by anemia severity

Variables	Mild (n=15)	Moderate (n= 39)	Severe (n= 46)	p-value
Osteocalcin				
Mean±SD	10.33±2.61[a]	8.97±1.55[b]	8.95±1.42[b]	0.019
Range	7.27-17.27	3.19-11.06	5.94-11.59	
TRAP				
Mean±SD	4.13±1.33[a]	3.68±0.[43ab]	3.49±0.5[b]	0.008
Range	2.86-7.3	2.79-4.7	2.55-4.77	
TNF-α				
Mean±SD	188.39±63.24[a]	139.1±27.2[b]	141.88±27.18[b]	<0.001
Range	100.45-325.49	91.8-208.08	38.49-213.26	

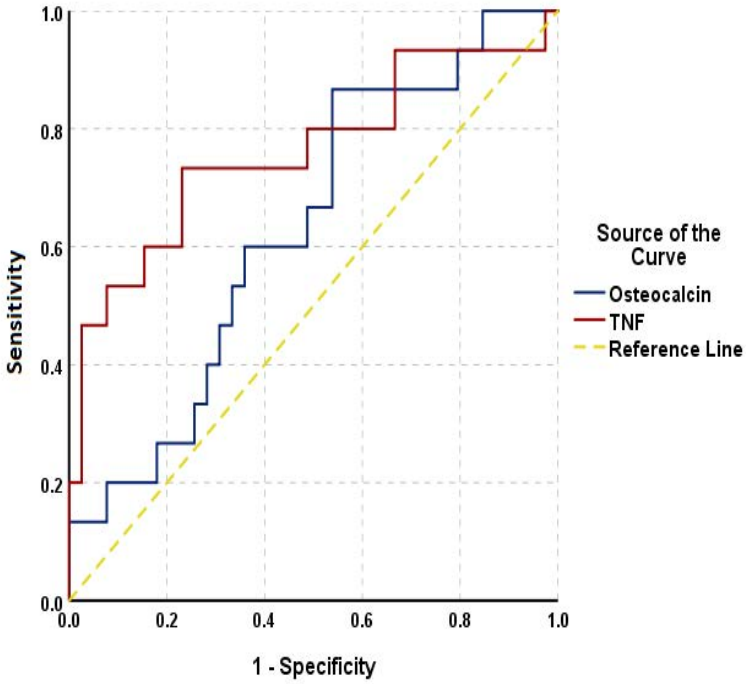

Figure 2. Receiver operating characteristic curve of osteocalcin and TNF-α in the context of discrimination between mild and moderate anemia in patients with CKD undergoing hemodialysis

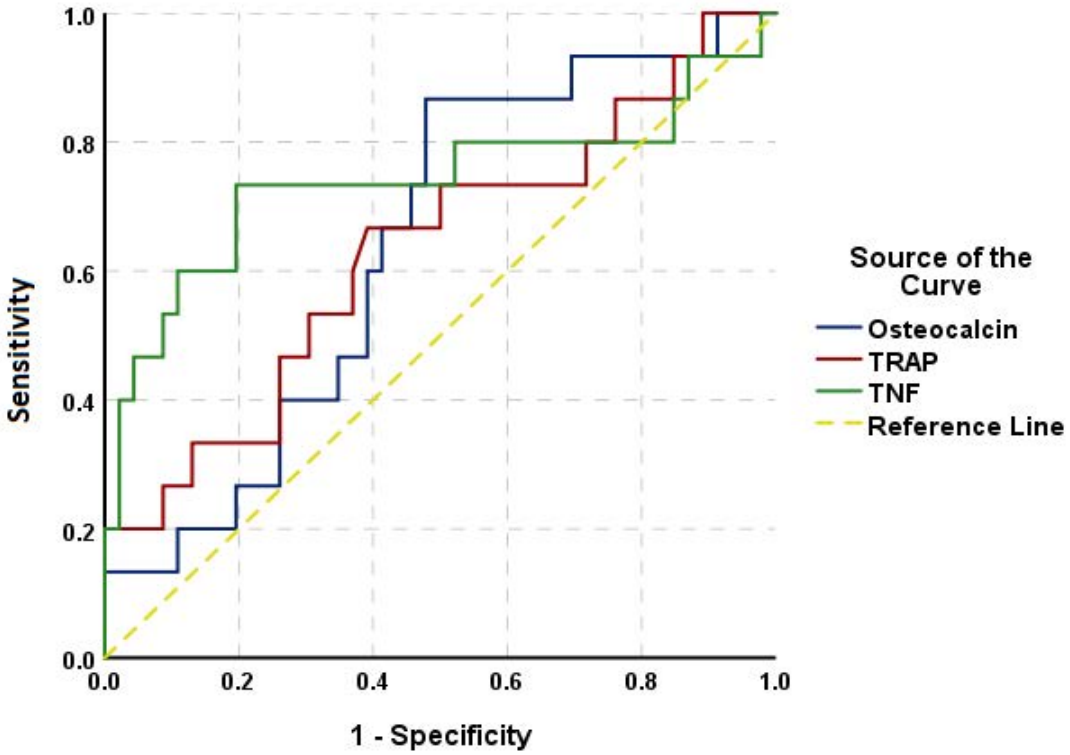

Figure 3. Receiver operating characteristic curve of osteocalcin, TARP and TNF-α in the context of discrimination between mild and moderate anemia in patients with CKD undergoing hemodialysis

are necessary to confirm these findings and evaluate their prognostic significance.

RECOMMENDATION

This study advocates for the inclusion of osteocalcin, TRAP, and TNF-α as auxiliary biomarkers in assessing anemia severity in patients with chronic renal disease receiving hemodialysis. TNF-α exhibited enhanced diagnostic efficacy and may function as an early marker for the advancement of anemia. An integrated assessment of these biomarkers with conventional criteria may improve risk categorization and facilitate more personalized anemia therapy. Modifying ESA therapy according to biomarker profiles may enhance treatment efficacy. Additional extensive, prospective investigations are advised to confirm these results and investigate their therapeutic relevance.

CONCLUSION

This study revealed that elevated levels of osteocalcin, TRAP, and TNF-α were strongly correlated with milder forms of anemia in hemodialysis patients. These findings indicate that bone-derived and inflammatory biomarkers may function as significant indications for the early detection and stratification of anemia. TNF-α demonstrated that the most significant diagnostic efficacy. Integrating these indicators into standard assessments may improve clinical decision-making in the management of anemia in patients with chronic renal disease. Additional prospective investigations are required to validate these correlations and investigate their therapeutic implications.

Authorship Contribution: All authors share equal effort contribution towards (1) substantial contributions to conception and design, acquisition, analysis and interpretation of data; (2) drafting the article and revising it critically for important intellectual content; and (3) final approval of the manuscript version to be published. Yes.

Potential Conflicts of Interest: None

Competing Interest: None

Acceptance Date: 18 August 2025

REFERENCE

1. Portolés J, Martín L, Broseta JJ, et al. Anemia in Chronic Kidney Disease: From Pathophysiology and Current Treatments, to Future Agents. Front Med (Lausanne) 2021;8:642296.
2. Gutiérrez OM. Understanding the connection between bone and anemia in CKD. Clin J Am Soc Nephrol 2022;17(3):423–31.
3. Babitt JL, Lin HY. Mechanisms of anemia in CKD. J Am Soc Nephrol 2012;23(10):1631–4.
4. Díaz-Murillo R, Aljama P. Inflammation and resistance to ESA in CKD. Nefrología 2020;40(1):15–22.
5. Tarng DC, Huang TP. The role of inflammation in anemia in hemodialysis. Blood Purif 2021;50(2):128–36.
6. Zhao Y, Wang C, Song Y, et al. TNF-α impairs erythropoiesis via JAK2/STAT5. J Cell Physiol 2020;235(11):8847–56.
7. Locatelli F, Bárány P, Covic A, et al. Kidney Disease: Improving Global Outcomes anemia guidelines. Kidney Int Suppl 2012;2(4):288–91.
8. Yu B, Wang CY. Osteoblastogenesis in hematopoietic regulation. J Bone Miner Res 2020;35(11):2132–49.
9. Lee NK, Sowa H, Hinoi E, et al. Endocrine regulation of energy metabolism by the skeleton. Cell 2007;130(3):456–69.

10. Kanazawa I. Osteocalcin as a hormone regulating glucose metabolism. World J Diabetes 2021;12(8):1220–34.
11. Gifre L, Ruiz-Gaspà S, Monegal A, et al. Hemodialysis and bone turnover markers. Clin Nephrol 2021;95(3):163–70.
12. Ivaska KK, Gerdhem P, Väänänen HK, et al. TRAP-5b as a marker of bone resorption. Clin Chem 2010;56(11):1914–20.
13. Evenepoel P, Cunningham J, Ferrari S. Bone histomorphometry in CKD. Nat Rev Nephrol 2021;17(12):685–701.
14. Duque EJ, Crispilho SF, Oliveira IB, et al. Osteoimmunology and bone marrow niche. Rev Bras Reumatol 2022;62(3):309–17.
15. Tungsanga S, Bello AK. Prevention of CKD complications in older adults. Drugs Aging 2024;41(7):565–76.
16. Manna MJ, Baqir LS, Abdulamir HA. The assessment of the antimicrobial effect of gemfibrozil alone or in combination with ceftriaxone or gentamycin on several types of bacteria. Acta Pharm Sci 2024;62(3):565-74.
17. The role of VEGF levels in the differentiation between malignant and benign breast tumor. J Res Pharm 2024; 28(3): 603-11.
18. Santos EJF, Dias RSC, Lima JFB, et al. Erythropoietin Resistance in Patients with Chronic Kidney Disease: Current Perspectives. Int J Nephrol Renovasc Dis 2020;13:231-37.
19. Badura K, Janc J, Wąsik J, et al. Anemia of Chronic Kidney Disease-A Narrative Review of Its Pathophysiology, Diagnosis, and Management. Biomedicines 2024;12(6):1191.
20. Hizomi Arani R, Fakhri F, Naeimi Tabiee M, et al. Prevalence of anemia and its associated factors among patients with type 2 diabetes mellitus in a referral diabetic clinic in the north of Iran. BMC Endocr Disord 2023;23(1):58.
21. Wong BC, Ravani P, Manns BJ, et al. Association of a change in erythropoiesis-stimulating agent dose during hospitalization and subsequent hemoglobin levels and transfusions in hemodialysis patients. Am J Kidney Dis 2013;62(5):947-52.
22. Chinnadurai R, Macdougall IC, Kalra PA. Treatment of anaemia in end-stage renal disease: A double-edged iron sword? EBioMedicine 2019;40:31-2.
23. Jessica C, Kevin V, Marie VA, et al. A comparative study on the haemostatic changes in kidney failure patients: Pre- and post- haemodialysis and haemodiafiltration. Thromb Res 2024;242:109120.
24. Kim YL, Kim H, Kwon YE, et al. Association between Vitamin D Deficiency and Anemia in Patients with End-Stage Renal Disease: A Cross-Sectional Study. Yonsei Med J 2016;57(5):1159-64.
25. Kim JS, Hwang HS. The role of vitamin D in anemia among CKD patients. Korean Circ J 2021;51(12):961–82.
26. Elendu C, Elendu RC, Enyong JM, et al. Comprehensive review of current management guidelines of chronic kidney disease. Medicine (Baltimore) 2023;102(23):e33984.
27. Ramseyer VD, Garvin JL. Tumor necrosis factor-α: regulation of renal function and blood pressure. Am J Physiol Renal Physiol 2013;304(10):F1231-42.
28. Santos EJF, Dias RSC, Lima JFB, et al. Erythropoietin Resistance in Patients with Chronic Kidney Disease: Current Perspectives. Int J Nephrol Renovasc Dis 2020;13:231-7.
29. Vervloet MG, Brandenburg VM; CKD-MBD working group of ERA-EDTA. Circulating markers of bone turnover. J Nephrol 2017;30(5):663-70.
30. Badura K, Janc J, Wąsik J, et al. Anemia of Chronic Kidney Disease-A Narrative Review of Its Pathophysiology, Diagnosis, and Management. Biomedicines 2024;12(6):1191.
31. Kan C, Lu X, Zhang R. Effects of hypoxia on bone metabolism and anemia in patients with chronic kidney disease. World J Clin Cases 2021;9(34):10616-25.
32. Amnuay K, Srisawat N, Wudhikarn K, et al. Factors associated with erythropoiesis-stimulating agent hyporesponsiveness anemia in chronic kidney disease patients. Hematol Rep 2019;11(3):8183.