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Research Article

Ischemia-Modified Albumin as a Predictor of Anemia in Hemodialysis Patients: An Exploratory Cross-Sectional Study

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Abstract

Objectives: Ischemia-modified albumin (IMA) is a biomarker of oxidative stress. Its relationship with anemia in hemodialysis (HD) patients remains unclear. This study aimed to evaluate the association between IMA and hemoglobin (Hb) in HD patients and to determine whether IMA can predict anemia.

Methods: This cross-sectional study enrolled 85 maintenance HD patients. IMA was measured using the albumin cobalt-binding assay. Anemia was defined as Hb<11 g/dL according to the KDIGO guidelines.

Results: IMA correlated inversely with Hb (r=–0.341; p=0.001). Multivariate linear regression identified Hb (β=–0.033; p=0.002) and ultrafiltration volume (β<0.001; p=0.001) as independent predictors of IMA (adjusted R^2=0.43). ROC analysis yielded an optimal IMA cutoff of ≥0.635 absorbance units (ABSU) (AUC=0.700; 95% CI, 0.582–0.817; p=0.002; sensitivity, 61.3%; specificity, 63.0%). In logistic regression, IMA≥0.635 ABSU (OR, 7.21; p=0.037) and EPO resistance (OR, 14.09; p=0.002) were independent predictors of anemia.

Conclusion: IMA levels were significantly elevated in anemic HD patients. An IMA cutoff of ≥0.635 ABSU showed moderate predictive capacity for anemia, suggesting its potential as a supplementary biomarker. Larger prospective studies are needed for validation.

Keywords: Anemia, chronic kidney disease, erythropoietin resistance, hemodialysis, ischemia-modified albumin, oxidative stress

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The worldwide burden of chronic kidney disease (CKD) continues to increase, with population-based surveys estimating that 10%–16% of adults are affected globally.[1,2] When kidney function deteriorates to end-stage kidney disease (ESKD), patients become dependent on renal replacement therapy. Among the available modalities, hemodialysis (HD) is the predominant treatment approach in numerous healthcare systems.[3]

Anemia represents one of the most prevalent and clinically consequential complications encountered in the CKD pop-

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ulation, affecting over 90% of individuals with advanced renal impairment and approximately 70% of those undergoing HD.[4] Deficient erythropoietin (EPO) synthesis by the failing kidneys constitutes the principal mechanism, although additional contributors—namely, iron depletion, chronic systemic inflammation, secondary hyperparathyroidism, and the accumulation of uremic solutes—also play important roles.[5] Notably, all of these pathways converge on enhanced oxidative stress, which has gained increasing recognition as a key driver in the pathobiology of uremic anemia. From a clinical standpoint, anemia in CKD impairs cardiac function, diminishes exercise tolerance and cognitive ability, reduces overall well-being, and independently predicts adverse outcomes, including higher rates of hospitalization and death.[6–8]

Ischemia-modified albumin (IMA) arises when the metal-binding capacity at the amino-terminal end of human serum albumin is compromised. Cobalt, nickel, and copper normally bind at this site; however, exposure to oxidative radicals, ischemic insult, hypoxic conditions, an acidotic milieu, or direct free-radical attack alters the N-terminal structure and reduces its affinity for these transition metals.[9,10] Following an ischemic episode, circulating IMA concentrations increase rapidly—within minutes—and remain elevated for roughly 6–12 hours before normalizing over 24 hours, positioning IMA as a responsive early indicator of tissue-level ischemia.[11] IMA was first shown by Sinha et al.[11] to detect myocardial ischemia before frank necrosis in the acute coronary setting and has subsequently been found to rise in diverse noncardiac disorders in which tissue oxygen delivery is compromised, such as cerebrovascular events, diabetes mellitus, and peripheral arterial disease.[12,13] Specifically within the ESKD population, Sharma et al.[14] published the earliest investigation of IMA in dialysis patients and reported that higher IMA values predicted mortality while correlating with unfavorable left ventricular structural changes. Turedi et al.[15] later confirmed that IMA concentrations measured both before and after a dialysis session exceeded those of age-matched healthy individuals. Collectively, these observations positioned IMA as a promising oxidative stress indicator warranting further study in the HD context.

A growing body of data indicates that the tissue-level oxygen deficit caused by low Hb concentrations may drive IMA elevation through enhanced oxidative modification at the albumin N-terminus.[16–18] Nevertheless, IMA has been examined in relation to anemia in the HD population by only a handful of investigators using relatively small cohorts, and a clinically useful threshold for identifying anemic patients has yet to be defined.

The present study was therefore designed to investigate whether circulating IMA concentrations correlate with Hb values in maintenance HD patients, to delineate the variables that independently determine IMA levels, and to assess the capacity of IMA to function as a predictive marker of anemia in this clinical setting.

Methods

Study Design and Population

A cross-sectional investigation was carried out in the Hemodialysis Unit affiliated with the Division of Nephrology at a tertiary university hospital in Ankara, Türkiye, from September through December 2019. The primary objective was to examine the interplay between circulating IMA concentrations, Hb values, and other routine biochemical measures in CKD patients maintained on HD.

Adults (≥18 years) with a diagnosis of CKD who were actively receiving HD, possessed a complete set of routine laboratory values dated within the previous 60 days, and consented to participation were deemed eligible. The following conditions led to exclusion: age below 18 years, unavailability of recent laboratory data, unwillingness to consent, a personal history of any malignant neoplasm, an active systemic inflammatory condition (e.g., systemic lupus erythematosus), or a confirmed episode of infection or acute cardiovascular compromise during the 3 months preceding enrollment. Eighty-five patients satisfied these criteria and were included in the analysis.

Ethical clearance was granted by the institutional clinical research ethics committee (Decision No. 2012-KAEK-15/2042, dated January 8, 2020). Every participant received a thorough verbal and written explanation of the study procedures, after which each individual provided signed informed consent.

Data Collection

Blood for IMA determination was drawn through routine venipuncture performed just before the dialysis session; no additional needle insertion was required. Five milliliters of whole blood were collected into a plain (red-top) vacutainer from each individual. Specimens were left undisturbed at ambient temperature for 20–30 minutes to allow clotting and were then centrifuged at 2000×g for 10 minutes. The resulting serum aliquots were transferred to cryovials and maintained at −80 °C pending batch analysis. All preanalytical processing was conducted in partnership with the university's allied health sciences teaching laboratory.

The following analytes were abstracted retrospectively from each patient's most recent routine workup, obtained

within 60 days of the IMA sampling date: hemoglobin (Hb), hematocrit (Htc), total leukocyte count (WBC), platelet count (PLT), blood urea nitrogen (BUN), serum creatinine, calcium, phosphorus, uric acid, albumin, C-reactive protein (CRP), serum iron (Fe), total iron-binding capacity (TIBC), transferrin saturation (TSAT), ferritin, vitamin D, parathyroid hormone (PTH), glycated hemoglobin (HbA1c), low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides.

Baseline demographic and clinical information was documented for each participant: age, sex, body mass index (BMI), tobacco use, comorbid conditions (diabetes mellitus, hypertension, coronary artery disease, peripheral artery disease, and cerebrovascular disease), type of dialysis access, presence or absence of residual kidney function, adequacy indices, EPO prescription and cumulative dose, parenteral iron supplementation history, and antihypertensive regimen.

IMA Measurement

Circulating IMA was quantified using the albumin cobalt-binding (ACB) test according to the protocol of Bar-Or et al.[9] In brief, each serum specimen was mixed with a cobalt chloride ($CoCl_2$) solution, after which dithiothreitol (DTT) and physiological saline (0.9% NaCl) were introduced. The optical density of the final reaction mixture was measured at 470 nm using a spectrophotometer. Values are reported in absorbance units (ABSU); the accepted reference interval for healthy individuals is 0–0.5 ABSU.

Definitions

A hemoglobin concentration below 11 g/dL was used to classify anemia, in accordance with the lower maintenance target endorsed by the Kidney Disease: Improving Global Outcomes (KDIGO) practice guidelines.[19] The erythropoietin resistance index (ERI) was derived by dividing the weight-adjusted weekly EPO dose (U/kg/week) by the concurrent hemoglobin level (g/dL).[20] For exploratory subgroup evaluation, EPO-treated patients were categorized into three ERI strata: <5, 5–15, and >15 U/kg/week per g/dL. Dialysis adequacy was gauged using Kt/V and the urea reduction ratio (URR).

Statistical Analysis

All computations were performed using SPSS for Windows, version 22.0 (SPSS Inc., Chicago, IL, USA). The normality of the distribution of continuous measures was assessed through graphical inspection (histograms and Q-Q plots), supplemented by the Kolmogorov-Smirnov and Shapiro-Wilk tests. Because all continuous variables departed from normality, they are reported as the mean±standard deviation, alongside the median and range (minimum–maximum). Categorical data are presented as absolute counts and proportions. Between-group differences in continuous outcomes were tested using the Mann-Whitney U test; categorical comparisons were performed using the chi-square test. The strength and direction of bivariate associations between IMA and laboratory indices were estimated using Spearman rank-order correlation coefficients.

Candidate predictors reaching $p<0.10$ in univariate testing were carried forward into a multivariable linear regression model; age, sex, cumulative EPO exposure, and coronary artery disease status were forced into the model as clinically plausible confounders. A receiver operating characteristic (ROC) curve was then constructed to evaluate whether IMA could discriminate between anemic and nonanemic patients, with calculation of the area under the curve (AUC), sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). Guided by the ROC-derived threshold, patients were recategorized and entered into a multivariable logistic regression analysis, adjusted for age and sex, to obtain odds ratios (ORs) for potential independent determinants of anemia. Two-sided p values below 0.05 were deemed statistically significant.

Results

Patient Characteristics

Eighty-five individuals constituted the final analytic sample: 50 men (58.8%) and 35 women (41.2%), with a mean age of 57.01±18.04 years and a mean BMI of 24.95±5.32 kg/m^2. Hypertension was the leading comorbidity (49.4%), followed by coronary artery disease (28.2%) and diabetes mellitus (18.8%). Thirty-two patients (37.6%) had a documented history of vascular disease, encompassing coronary artery disease (n=24), peripheral artery disease (n=11), and cerebrovascular disease (n=4). Vascular access consisted of an arteriovenous fistula (AVF) in 63 cases (74.1%) and a central venous catheter (CVC) in 22 cases (25.9%). Residual kidney function was detectable in 26 patients (30.6%), and 54 (63.5%) were receiving EPO therapy. The mean Hb level was 11.06±1.62 g/dL; 31 participants (36.5%) fulfilled the anemia criterion (Hb<11 g/dL). The cohort's mean IMA value was 0.61±0.15 ABSU (Table 1).

Correlations Between IMA and Laboratory Parameters

IMA exhibited a statistically significant inverse association with Hb ($r=-0.341$; $p=0.001$; Fig. 1) and total leukocyte count ($r=-0.235$; $p=0.030$). A direct relationship was noted between IMA and ferritin ($r=0.232$; $p=0.039$), whereas an inverse association emerged with CRP ($r=-0.279$; $p=0.011$).

Table 1. Baseline demographic, clinical, and laboratory characteristics of the study cohort (n = 85)

Characteristic	Value
Male sex, n (%)	50 (58.8)
Age (years), mean±SD	57.01±18.04
BMI (kg/m^2), mean±SD	24.95±5.32
Diabetes mellitus, n (%)	16 (18.8)
Hypertension, n (%)	42 (49.4)
Coronary artery disease, n (%)	24 (28.2)
Peripheral artery disease, n (%)	11 (12.9)
Cerebrovascular disease, n (%)	4 (4.7)
HD access: AVF, n (%)	63 (74.1)
Residual renal function, n (%)	26 (30.6)
EPO use, n (%)	54 (63.5)
Hemoglobin (g/dL), mean±SD	11.06±1.62
Hematocrit (%), mean±SD	33.99±5.03
IMA (ABSU), mean±SD	0.61±0.15
Serum albumin (g/dL), mean±SD	3.78±0.36
Ferritin (ng/mL), mean±SD	429.65±273.71
CRP (mg/dL), mean±SD	10.39±12.15
Mean UF volume (mL), mean±SD	2787±1059

AVF: Arteriovenous fistula; BMI: Body mass index; CRP: C-reactive protein; EPO: Erythropoietin; HD: Hemodialysis; IMA: Ischemia-modified albumin; UF: Ultrafiltration.

Table 2. Spearman correlation analysis between IMA and selected laboratory and clinical parameters

Parameter	r	p
Hemoglobin (g/dL)	−0.341	0.001*
WBC (K/µL)	−0.235	0.030*
CRP (mg/dL)	−0.279	0.011*
Ferritin (ng/mL)	0.232	0.039*
Mean UF volume (mL)	0.658	<0.001*
Hematocrit (%)	−0.119	0.276
BUN (mg/dL)	−0.011	0.917
Creatinine (mg/dL)	0.053	0.629
Serum albumin (g/dL)	0.098	0.373
Iron (µg/dL)	0.079	0.485
TIBC (µg/dL)	0.005	0.967
TSAT (%)	0.062	0.583
PTH (pg/mL)	0.063	0.567
Kt/V	0.172	0.120
Cumulative EPO dose (IU)	0.163	0.136

* Statistically significant (p<0.05). BUN: Blood urea nitrogen; CRP: C-reactive protein; EPO: Erythropoietin; IMA: Ischemia-modified albumin; PTH: Parathyroid hormone; TIBC: Total iron-binding capacity; TSAT: Transferrin saturation; UF: Ultrafiltration; WBC: White blood cell.

The strongest bivariate association observed was between IMA and mean ultrafiltration (UF) volume (r=0.658; p<0.001). No meaningful correlations were identified between IMA and age, BMI, albumin, calcium, phosphorus, creatinine, uric acid, iron, TIBC, TSAT, PTH, HbA1c, lipid fractions, Kt/V, URR, cumulative EPO dose, or ERI (all p>0.05; Table 2).

IMA Levels According to Clinical Subgroups

AVF users demonstrated significantly higher IMA concentrations than CVC users (p=0.015). Conversely, patients who developed intradialytic hypertension had lower IMA values (p=0.022). Among EPO-treated individuals stratified by ERI, those in the highest category (ERI>15 U/kg/week per g/dL) exhibited the greatest IMA concentrations relative to the other two strata (p=0.038). Anemic participants (Hb<11 g/dL) had markedly elevated IMA levels compared with their nonanemic counterparts (p=0.002). Sex, tobacco use, diabetes, hypertension, coronary artery disease, peripheral artery disease, cerebrovascular disease, residual kidney function, and medication categories showed no significant influence on IMA (all p>0.05).

Independent Predictors of IMA

After multivariable adjustment for age, sex, cumulative EPO dose, and coronary artery disease, Hb (β=−0.033; p=0.002) and mean UF volume (β<0.001; p=0.001) emerged as the sole independent determinants of IMA (adjusted R^2=0.43; model p<0.001; Table 3). The negative β coefficient for Hb indicates that declining hemoglobin levels are accompanied by rising IMA levels, a pattern congruent with the notion that anemia-driven hypoxia accelerates the oxidative modification of albumin.

IMA as a Predictor of Anemia: ROC Analysis

The ROC curve yielded an AUC of 0.700 (95% CI, 0.582–0.817; p=0.002), confirming that IMA possesses a statistically meaningful ability to distinguish anemic from nonanemic HD patients. At the optimal threshold of ≥0.635 ABSU, sensitivity reached 61.3%, specificity 63.0%, PPV 48.7%, and NPV 73.9% (Fig. 2).

Multivariate Logistic Regression for Anemia

Patients were then dichotomized at the ROC-derived IMA threshold, and predictors of anemia were reassessed. In the age- and sex-adjusted logistic model, two variables attained independent significance: IMA≥0.635 ABSU (OR, 7.21; 95% CI, 1.12–46.19; p=0.037) and EPO resistance (OR,

Table 3. Multivariate linear regression analysis for independent predictors of IMA levels (adjusted R^2=0.43; model p<0.001)

Variable	β coefficient	p
Hemoglobin (g/dL)	−0.033	0.002*
Mean UF volume (mL)	<0.001	0.001*
WBC (K/μL)	<−0.001	0.449
CRP (mg/dL)	−0.002	0.141
Ferritin (ng/mL)	<0.001	0.873
HD access type (AVF vs. CVC)	0.066	0.084
Vitamin D use	−0.035	0.291
Intradialytic hypertension	0.005	0.920

Adjusted for age, sex, cumulative EPO dose, and coronary artery disease status. * Statistically significant. AVF: Arteriovenous fistula; CRP: C-reactive protein; CVC: Central venous catheter; HD: Hemodialysis; UF: Ultrafiltration; WBC: White blood cell.

14.09; 95% CI, 2.69–73.95; p=0.002) (Table 4). Mean UF volume did not retain significance in this model (p=0.280).

Table 4. Multivariate logistic regression analysis for independent predictors of anemia (Hb < 11 g/dL)

Variable	OR (95% CI)	p
IMA ≥0.635 (ref: <0.635)	7.21 (1.12–46.19)	0.037*
EPO resistance (ref: ERI < 5)	14.09 (2.69–73.95)	0.002*
Mean UF volume	0.98 (0.94–1.02)	0.280

Adjusted for age and sex. * Statistically significant. CI: Confidence interval; EPO: Erythropoietin; ERI: Erythropoietin resistance index; IMA: Ischemia-modified albumin; OR: Odds ratio; UF: Ultrafiltration.

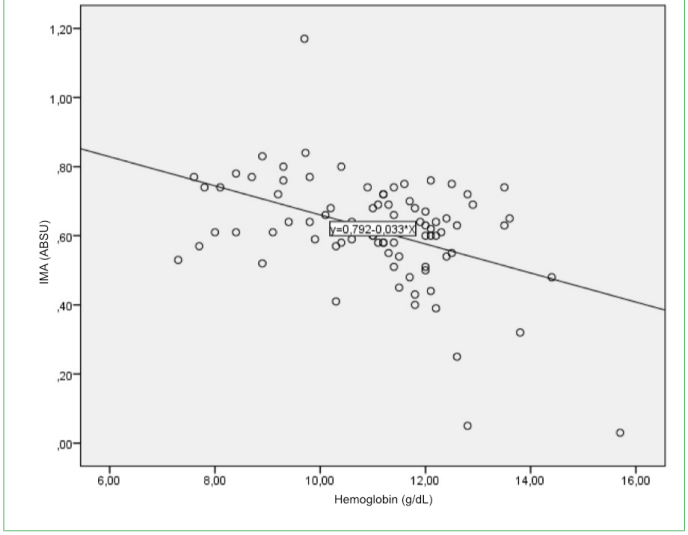

Figure 1. Scatter plot depicting the correlation between hemoglobin (Hb) and ischemia-modified albumin (IMA) levels in hemodialysis patients (r = -0.341; P = 0.001). The regression line equation: y = 0.792 - 0.033x.

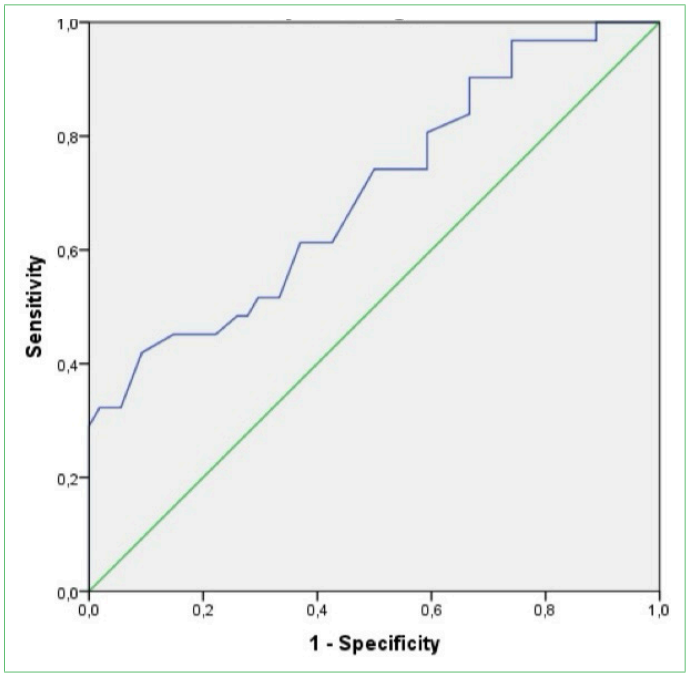

Figure 2. Receiver operating characteristic (ROC) curve for ischemia-modified albumin (IMA) as a predictor of anemia (hemoglobin < 11 g/dL) in hemodialysis patients. The area under the curve (AUC) was 0.700 (95% CI, 0.582-0.817; P = 0.002). The optimal cut-off value of ≥0.635 ABSU yielded a sensitivity of 61.3% and specificity of 63.0%.

Discussion

The present analysis of 85 maintenance HD patients revealed a robust inverse relationship between circulating IMA and Hb. After controlling for relevant confounders, Hb remained a significant independent determinant of IMA. ROC-based evaluation further established that an IMA threshold of ≥0.635 ABSU discriminated between anemic and nonanemic patients with moderate accuracy, conferring a 7.2-fold increase in anemia risk in multivariate logistic analysis.

These observations align with the work of Cichota et al.[17], who documented higher IMA concentrations and a negative IMA–Hb correlation (r=−0.344; p=0.040) in CKD patients with anemia than in healthy volunteers. In a peritoneal dialysis cohort, Su et al.[21] likewise identified an inverse IMA–Hb association (r=−0.71; p=0.024). Importantly, neither of these studies detected meaningful associations between IMA and serum calcium, phosphorus, creatinine, or uric acid—a pattern mirrored in our data. Taken together, these concordant findings reinforce the concept that diminished Hb impairs tissue oxygen delivery, thereby accelerating oxidative alteration at the albumin N-terminus and augmenting IMA generation.

One particularly noteworthy result was the strong direct association between IMA and mean UF volume (r=0.658;

p<0.001). Despite reaching statistical significance as an independent predictor in linear regression, the negligible magnitude of the UF coefficient (β<0.001) suggests limited clinical impact. Nonetheless, high intradialytic fluid removal may trigger transient intravascular volume contraction and relative tissue hypoperfusion, potentially explaining the observed link. To the best of our knowledge, no prior report has explored this specific IMA–UF relationship, and the finding merits confirmation in dedicated studies.

The direct correlation observed between IMA and ferritin (r=0.232; p=0.039) echoes the report of Awadallah et al.[16] in beta-thalassemia major. Elevated ferritin may signal excess body iron stores, which, in turn, fuel Fenton chemistry, generating hydroxyl radicals capable of oxidatively modifying albumin. Moreover, ESKD is characterized by a well-documented triad of compromised antioxidant defenses, heightened reactive oxygen species production, and chronic tissue hypoxia. Together, these derangements offer a coherent mechanistic framework for the elevated IMA concentrations observed in our cohort. Chronic anemia, sustained hypoxia, and iron-driven oxidative damage thus likely act in concert to modify the albumin N-terminus and promote IMA formation in patients with advanced kidney disease.

An unanticipated observation was the negative association between IMA and CRP (r=−0.279; p=0.011). This finding runs counter to the positive IMA–CRP relationship documented by Duarte et al.[22] in hypercholesterolemic subjects. However, Su et al.[21] similarly detected no meaningful correlation between IMA and high-sensitivity CRP in peritoneal dialysis patients. The discordance may stem from the complex bidirectional interaction between inflammation and oxidative stress in the uremic milieu, where inflammation-associated hypoalbuminemia could confound IMA interpretation. A further consideration is that our facility measured standard rather than high-sensitivity CRP, potentially underestimating subclinical inflammatory activity and contributing to the divergent result.

IMA concentrations were paradoxically higher in patients with AVF access than in those with CVC access (p=0.015), contrasting with data from Dukkipati et al.[23] and Banerjee et al.[24], who observed a greater inflammatory burden in catheter-dependent patients. The pathophysiological basis of this unexpected finding warrants further clarification.

A novel aspect of our work is the observation that patients with the highest degree of EPO resistance (ERI>15 U/kg/week per g/dL) displayed the greatest IMA levels (p=0.038). No previous investigation has directly stratified IMA across ERI categories. The finding is, however, pathophysiologically plausible: EPO hyporesponsiveness in HD patients is closely intertwined with chronic inflammation and oxidative stress, both of which favor IMA generation. Macdougall et al.[25] demonstrated that poor EPO responsiveness was accompanied by higher CRP and interleukin-6 concentrations, implying that inflammatory mediators simultaneously blunt erythroid proliferation and foster oxidative albumin modification. ERI may therefore function as a clinical surrogate for the underlying pro-oxidant environment that concurrently undermines erythropoiesis and elevates IMA.

In line with earlier observations by Sinha et al.[11] and Christenson et al.[26], neither age nor sex influenced IMA concentrations in our cohort. The transient pharmacokinetics of IMA—a rapid postischemic rise followed by normalization within a day—likely render it insensitive to fixed demographic traits.

The IMA threshold of ≥0.635 ABSU derived from our ROC analysis—although yielding only moderate sensitivity (61.3%) and specificity (63.0%)—constitutes the first such cutoff proposed specifically for CKD-associated anemia. Previous ROC-based IMA thresholds have targeted myocardial ischemia and hematologic malignancy.[11,18,27] Notably, the 0.64 ABSU cutoff reported by Erkut et al.[18] for acute leukemia (AUC=0.846; sensitivity, 65.9%; specificity, 91.7%) is strikingly similar to our value, despite being derived from a fundamentally different clinical context. No analogous threshold existed for anemia in the dialysis literature before the present study.

Several methodological constraints deserve mention. First, the cross-sectional framework prevents any causal attribution in the IMA–anemia relationship. Second, the single-center design and limited sample size (n=85) restrict external applicability and account for the broad confidence intervals in our logistic model. Third, without a healthy reference group, absolute IMA levels could not be benchmarked against those of the nonuremic population. Fourth, IMA was measured only before the dialysis session; postdialysis values, which can differ appreciably,[15] were not captured. Fifth, high-sensitivity CRP was unavailable; reliance on the standard assay may have masked low-grade inflammation.

Despite these limitations, the study furnishes preliminary evidence supporting a role for IMA as an ancillary biomarker in evaluating oxidative stress related to anemia in the HD setting.

Conclusion

IMA concentrations are substantially higher in HD patients with anemia and display an inverse relationship with Hb, most likely reflecting hypoxia-driven oxidative modification of the albumin molecule. A threshold of ≥0.635 ABSU afforded moderate discrimination of anemia in our cohort,

pointing to a potential supplementary role for IMA in clinical assessment. Relatively few studies have addressed this association, and none have previously proposed a specific diagnostic threshold. Prospective investigations enrolling larger, multisite cohorts are warranted to confirm the proposed cutoff and to delineate the added prognostic contribution of IMA in HD risk stratification.

Disclosure

Ethics Committee Approval: This study was approved by the institutional clinical research ethics committee (Decision No. 2012-KAEK-15/2042, dated January 8, 2020).

Informed Consent: Written informed consent was obtained from all participants. The study was conducted in accordance with the principles of the Declaration of Helsinki.

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References

1. Hallan SI, Coresh J, Astor BC, Asberg A, Powe NR, Romundstad S, et al. International comparison of the relationship of chronic kidney disease prevalence and ESRD risk. J Am Soc Nephrol 2006;17(8):2275–84. [CrossRef]
2. Meguid El Nahas A, Bello AK. Chronic kidney disease: the global challenge. Lancet 2005;365(9456):331–40. [CrossRef]
3. Suleymanlar G, Ates K, Seyahi N. Registry of the nephrology, dialysis and transplantation in Turkey: Registry 2017. Ankara: Turkish Society of Nephrology; 2017.
4. Kazmi WH, Kausz AT, Khan S, Abichandani R, Ruthazer R, Obrador GT, et al. Anemia: an early complication of chronic renal insufficiency. Am J Kidney Dis 2001;38(4):803–12. [CrossRef]
5. Atkinson MA, Warady BA. Anemia in chronic kidney disease. Pediatr Nephrol 2018;33(2):227–38. [CrossRef]
6. Ebben JP, Gilbertson DT, Foley RN, Collins AJ. Hemoglobin level variability: associations with comorbidity, intercurrent events, and hospitalizations. Clin J Am Soc Nephrol 2006;1(6):1205–10. [CrossRef]
7. Yang W, Israni RK, Brunelli SM, Joffe MM, Fishbane S, Feldman HI. Hemoglobin variability and mortality in ESRD. J Am Soc Nephrol 2007;18(12):3164–70. [CrossRef]
8. Gilbertson DT, Ebben JP, Foley RN, Weinhandl ED, Bradbury BD, Collins AJ. Hemoglobin level variability: associations with mortality. Clin J Am Soc Nephrol 2008;3(1):133–8. [CrossRef]
9. Bar-Or D, Lau E, Winkler JV. A novel assay for cobalt-albumin binding and its potential as a marker for myocardial ischemia-a preliminary report. J Emerg Med 2000;19(4):311–5. [CrossRef]
10. Bhagavan NV, Lai EM, Rios PA, Yang J, Ortega-Lopez AM, Shinoda H, et al. Evaluation of human serum albumin cobalt binding assay for the assessment of myocardial ischemia and myocardial infarction. Clin Chem 2003;49(4):581–5. [CrossRef]
11. Sinha MK, Roy D, Gaze DC, Collinson PO, Kaski JC. Role of "Ischemia modified albumin," a new biochemical marker of myocardial ischaemia, in the early diagnosis of acute coronary syndromes. Emerg Med J 2004;21(1):29–34. [CrossRef]
12. Sbarouni E, Georgiadou P, Voudris V. Ischemia modified albumin changes-review and clinical implications. Clin Chem Lab Med 2011;49(2):177–84. [CrossRef]
13. Piwowar A, Knapik-Kordecka M, Warwas M. Ischemia-modified albumin level in type 2 diabetes mellitus-preliminary report. Dis Markers 2008;24(6):311–7. [CrossRef]
14. Sharma R, Gaze DC, Pellerin D, Mehta RL, Gregson H, Streather CP, et al. Ischemia-modified albumin predicts mortality in ESRD. Am J Kidney Dis 2006;47(3):493–502. [CrossRef]
15. Turedi S, Cinar O, Yavuz I, Mentese A, Gunduz A, Karahan SC, et al. Differences in ischemia-modified albumin levels between end stage renal disease patients and the normal population. J Nephrol 2010;23(3):335–40. [CrossRef]
16. Awadallah SM, Atoum MF, Nimer NA, Saleh SA. Ischemia modified albumin: An oxidative stress marker in β-thalassemia major. Clin Chim Acta 2012;413(9-10):907–10. [CrossRef]
17. Cichota LC, Moresco RN, Duarte MMMF, Silva JEP. Evaluation of ischemia-modified albumin in anemia associated to chronic kidney disease. J Clin Lab Anal 2008;22(1):1–5. [CrossRef]
18. Erkut N, Mentese A, Ozbas HM, Sumer A, Orem A, Topbas M, et al. The indicator of hypoxia in acute leukemia: Ischemia-modified albumin. Cancer Biomark 2015;15(5):559–65. [CrossRef]
19. KDIGO Anemia Work Group. KDIGO clinical practice guideline for anemia in chronic kidney disease. Kidney Int Suppl 2012;2(4):279–335.
20. Kanbay M, Perazella MA, Kasapoglu B, Koroglu M, Covic A. Erythropoiesis stimulatory agent-resistant anemia in dialysis patients: review of causes and management. Blood Purif 2010;29(1):1–12. [CrossRef]
21. Su X, Zhang K, Guo F, Yuan B, Wang C, Xiao L, et al. Ischemia-modified albumin, a predictive marker of major adverse cardiovascular events in continuous ambulatory peritoneal dialysis patients. Clin Biochem 2013;46(15):1410–3. [CrossRef]
22. Duarte MM, Rocha JB, Moresco RN, Duarte T, Da Cruz IB, Loro VL, et al. Association between ischemia-modified albumin, lipids and inflammation biomarkers in patients with

hypercholesterolemia. Clin Biochem 2009;42(7-8):666–71. [CrossRef]

23. Dukkipati R, Molnar MZ, Park J, Jing J, Kovesdy CP, Kajani R, et al. Association of vascular access type with inflammatory marker levels in maintenance hemodialysis patients. Semin Dial 2014;27(4):415–23. [CrossRef]
24. Banerjee T, Kim SJ, Astor B, Shafi T, Coresh J, Powe NR. Vascular access type, inflammatory markers, and mortality in incident hemodialysis patients: the Choices for Healthy Outcomes in Caring for End-Stage Renal Disease (CHOICE) Study. Am J Kidney Dis 2014;64(6):954–61. [CrossRef]
25. Macdougall IC, Cooper AC. Erythropoietin resistance: the role of inflammation and pro-inflammatory cytokines. Nephrol Dial Transplant 2002;17(Suppl 11):39–43. [CrossRef]
26. Christenson RH, Duh SH, Sanhai WR, Wu AH, Holtman V, Painter P, et al. Characteristics of an Albumin Cobalt Binding Test for assessment of acute coronary syndrome patients: a multicenter study. Clin Chem 2001;47(3):464–70. [CrossRef]
27. Chen ZX, Wang Q, Zheng L, Bao J. [Clinical value of an improved ischemia-modified albumin assay in the diagnosis of early acute myocardial infarction]. Nan Fang Yi Ke Da Xue Xue Bao 2009;29(7):1378–80. [Chinese]