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Factors associated with anemia among hemodialysis patients: A cross-sectional study

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ABSTRACT

Anemia substantially increases morbidity, mortality, and healthcare burden in maintenance hemodialysis (HD) patients, necessitating precise risk stratification for optimal clinical management. This study evaluated demographic and readily accessible clinical parameters as independent predictors of severe anemia in an Indonesian HD cohort. A cross-sectional design was employed, enrolling 168 maintenance HD patients at Al Huda Hospital in Banyuwangi through purposive sampling. Severe anemia was strictly defined as hemoglobin <8 g/dL versus non-severe (≥8 g/dL). Data on age, sex, HD duration, and pre-dialysis oxygen saturation were systematically collected and analyzed using chi-square tests and multivariate logistic regression. The prevalence of severe anemia was 82.7%. Multivariate analysis identified female sex as the sole independent predictor of severe anemia (adjusted odds ratio [aOR] = 4.76; 95% confidence interval [CI]: 1.83–12.40; p = 0.001). Conversely, age (p = 0.393), HD duration (p = 0.328), and pre-dialysis oxygen saturation (p = 0.648) demonstrated no statistically significant associations with anemia severity. Female sex constitutes a robust independent risk factor for severe anemia in HD populations, strongly advocating for sex-specific hematological surveillance and individualized therapeutic protocols. The lack of predictive value for routine demographic and physiological parameters underscores the critical need to integrate comprehensive assessments of iron and inflammatory biomarkers into standard anemia management protocols to improve patient outcomes.

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INTRODUCTION

Chronic kidney disease represents a critical global health burden, frequently necessitating renal replacement therapy and precipitating severe hematological complications (Francis et al., 2024). As a progressive condition characterized by irreversible renal deterioration, CKD systematically disrupts endocrine regulation, fluid-electrolyte homeostasis, and metabolic balance (Keshtkari et al., 2026). The transition to end-stage renal disease invariably mandates long-term hemodialysis, which substantially alters physiological equilibrium (Chen et al., 2025). Within this therapeutic landscape, anemia emerges as a prevalent complication demanding continuous surveillance to mitigate systemic deterioration (Upadhye & Patidar, 2025).

Anemia constitutes a pervasive clinical challenge in hemodialysis populations, driven by multifactorial pathophysiological disruptions that substantially exacerbate morbidity and mortality (Santos et al., 2025). The condition arises from profound erythropoietin deficiency, compounded by shortened erythrocyte survival, chronic inflammation, and dysregulation of systemic iron

metabolism (Matsuoka et al., 2023). Consequently, inadequate hemoglobin concentrations impair tissue oxygenation, accelerate cardiovascular remodeling, and diminish patient quality of life (Habas et al., 2023). Clinical evidence consistently demonstrates that unmanaged anemia markedly increases hospitalization rates and elevates all-cause mortality, underscoring the necessity of targeted intervention (Riani & Widiana, 2022; Hasibuan et al., 2024).

Contemporary research has predominantly prioritized complex laboratory biomarkers and pharmacological interventions to characterize anemia severity in end-stage renal disease (Roy et al., 2023). Recent investigations have extensively mapped the roles of ferritin, transferrin saturation, hepcidin dynamics, and erythropoiesis-stimulating agent responsiveness in predicting hematological outcomes (Ramchandani et al., 2026). Furthermore, demographic and treatment-related variables have increasingly been recognized as pivotal determinants of anemia progression across diverse hemodialysis cohorts (Chang et al., 2025). Despite these evaluations, translating complex biomarker data into routine clinical workflows remains highly challenging for practitioners managing high patient volumes.

Despite these advances, a critical paucity of evidence persists regarding routinely accessible demographic indicators that could facilitate early risk stratification in routine practice. While chronological aging and prolonged dialysis exposure have been hypothesized to exacerbate hemoglobin depletion through cumulative procedural blood loss and erythropoietin resistance, empirical findings remain inconsistent across international cohorts (Wu et al., 2025). Similarly, sex-based disparities warrant rigorous examination, as emerging data suggest female patients may experience steeper hematological decline as renal function deteriorates (Khudhur et al., 2026). The absence of standardized frameworks that integrate these variables limits the effectiveness of pragmatic screening protocols.

This knowledge deficit is particularly pronounced in developing regions such as Indonesia, where localized epidemiological patterns and physiological variables, such as oxygen saturation, remain inadequately explored (Bangun et al., 2024). Variations in dialysis infrastructure and nutritional status significantly modulate anemia trajectories, restricting the applicability of findings derived from high-income nations (Kalyesubula et al., 2024). Moreover, oxygen saturation, a fundamental parameter routinely monitored during hemodialysis, has rarely been systematically evaluated as a potential correlate of hemoglobin stability (Luu et al., 2026). Understanding whether mild hypoxemic fluctuations contribute to erythropoietic dysregulation remains an unaddressed clinical question.

To address these limitations, this investigation employs an analytical cross-sectional design that simultaneously evaluates demographic characteristics and physiological parameters to identify independent predictors of anemia. By integrating oxygen saturation with age, sex, and hemodialysis duration, this study introduces a novel assessment framework that bridges complex laboratory diagnostics and practical clinical observation (El Kodmiri et al., 2024). The methodological approach utilizes bivariate screening followed by multivariate logistic regression to isolate independent determinants while controlling for confounding variables, ensuring robust interpretation of clinical associations (Tulcanaza et al., 2025).

By elucidating the independent roles of age, sex, hemodialysis duration, and oxygen saturation, this study seeks to establish resource-appropriate management strategies that optimize clinical outcomes for hemodialysis patients. The urgent need to refine anemia risk stratification protocols is driven by the escalating prevalence of end-stage renal disease and persistent treatment-resistant hematological complications (Skrzypczak et al., 2024). Identifying simple, reproducible predictors will empower clinicians to implement targeted monitoring

schedules and individualize therapeutic interventions, ultimately reducing adverse cardiovascular outcomes.

METHODS

Study Design

This cross-sectional study was conducted at the hemodialysis unit of Al Huda Hospital, a secondary-care facility in Banyuwangi, Indonesia, from August 4 to September 4, 2025. The unit utilizes 33 Nipro Surdial 55 Plus machines operating across three daily shifts, with each patient undergoing a standardized five-hour treatment session. All procedures were conducted strictly in accordance with national dialysis protocols and were supervised by nephrologists and certified hemodialysis nurses to ensure clinical consistency and patient safety.

Participants and Sampling

The study population comprised 290 patients with stage 5 chronic kidney disease (CKD) undergoing maintenance hemodialysis. Using purposive sampling, 168 participants were selected to ensure inclusion of clinically stable individuals who met the study's anemia assessment criteria. Eligible patients were aged 18 years or older, had undergone routine hemodialysis for at least three months, could communicate effectively, and provided written informed consent. The three-month minimum treatment duration was established to promote physiological stability and minimize hemoglobin fluctuations typically observed during early dialysis adaptation.

Participants were excluded if they experienced active, clinically evident bleeding (gastrointestinal hemorrhage or significant hematuria requiring medical intervention), had received a blood transfusion within the preceding four weeks, or presented with an acute infection at the time of data collection. Acute infection was defined as a body temperature ≥38°C, elevated inflammatory markers, or a clinician-diagnosed infectious condition. These exclusion criteria were applied to minimize confounding variables that could directly alter hemoglobin concentrations and compromise the accurate evaluation of anemia status.

Variables and Measurements

The study examined several independent variables, including age (categorized as adult: 18–59 years; elderly: ≥60 years), sex (male or female), duration of hemodialysis (<1 year, 1–5 years, or >5 years since first session), and pre-dialysis oxygen saturation. Oxygen saturation was measured using a calibrated pulse oximeter applied to the index finger of the non-fistula arm under resting conditions prior to the hemodialysis session. The primary dependent variable was anemia status, classified as severe anemia (hemoglobin <8 g/dL) or non-severe anemia (≥8 g/dL), with hemoglobin levels quantified via automated hematology analyzer in accordance with the hospital's established quality control protocols.

Data Collection Procedure

Eligible participants were identified from the hemodialysis unit registry according to predefined inclusion and exclusion criteria, and written informed consent was obtained prior to enrollment. Demographic and clinical variables, including age, sex, hemodialysis duration, and hemoglobin levels, were systematically extracted from medical records using a structured data collection form. At the same time, pre-dialysis oxygen saturation was measured directly by trained hemodialysis nurses following a standardized protocol. To ensure methodological rigor,

all data collectors underwent uniform training and remained blinded to the study hypotheses to minimize observer bias, with ongoing quality assurance procedures implemented throughout the process to verify data accuracy and completeness.

Statistical Analysis

Data analysis was conducted using appropriate statistical software, beginning with descriptive statistics to summarize participant characteristics. Bivariate associations between each independent variable and anemia status were evaluated using the Chi-square test. To identify independent predictors while adjusting for potential confounders, variables with a bivariate association ($p < 0.25$) were entered into a multivariate logistic regression model. Results were expressed as adjusted odds ratios (aORs) with corresponding 95% confidence intervals (CIs), and statistical significance was defined as a two-sided p-value < 0.05.

Ethical Considerations

This study was conducted in strict accordance with institutional and national research guidelines and received formal ethical approval (Approval No. 193/UN10.F17.10.4/TU/2025). Prior to enrollment, all participants received comprehensive verbal and written information detailing the study's objectives, procedures, potential risks, and data confidentiality safeguards. Written informed consent was obtained from each individual before data collection commenced, ensuring voluntary participation and full adherence to established ethical standards.

RESULTS

A total of 168 patients were included in the analysis. The demographic and clinical characteristics of the respondents are summarized in Tables 1–3. Most participants were adults aged 18–59 years, slightly more than half were male, most had undergone hemodialysis for 1–5 years, and the majority had normal oxygen saturation levels. The mean hemoglobin level was 5.1 g/dL, and 82.7% of patients were classified as having severe anemia (<8 g/dL).

Table 1. Characteristics of respondents based on age, sex, duration of hemodialysis, and oxygen saturation (n = 168)

Characteristics	Frequency	Percentage
Age		
Adults (18-59 years old)	110	65.5
Elderly (≥60 years old)	58	34.5
Sex		
Male	85	50.6
Female	83	49.4
Duration of Hemodialysis (in years)		
<1 year	34	20.2
1-5 years	86	51.2
>5 years	48	28.6
Oxygen Saturation		
Normal (95%-100%)	140	83.3
Low (<95%)	28	16.7

Based on Table 1, most respondents are adults (18–59 years old), totaling 110 individuals (65.5%). Regarding sex, most respondents are male (85 individuals, 50.6%). Regarding the duration of hemodialysis, most respondents (86 individuals, 51.2%) have undergone

hemodialysis for 1–5 years, and almost all respondents (140 individuals, 83.3%) have normal oxygen saturation levels (95%–100%).

Table 2. Characteristics of respondents based on hemoglobin levels and anemia categories (n = 168)

Variable	Category	Mean	Min.	Max.	SD	n	%
Hemoglobin Level (g/dL)	—	5.1	4.0	15.6	1.22	168	100
Anemia Category (g/dL)	Severe anemia (<8.0)	—	—	—	—	139	82.7
	Non-severe anemia (≥8.0)	—	—	—	—	29	17.3

*SD = Standard Deviation

Based on Table 2, the mean hemoglobin (Hb) level of respondents is 5.1 g/dL, with the lowest Hb level of 4.0 g/dL and the highest of 15.6 g/dL, and a standard deviation of 1.22. Almost all respondents (139, 82.7%) fall into the severe anemia category with Hb levels < 8.0 g/dL.

Table 3. Bivariate analysis of factors associated with anemia among hemodialysis patients (n = 168)

Characteristics	Anemia Category		Total	p-value
	Severe Anemia	Non-Severe Anemia		
Age				
Adults (18-59 years old)	93	17	110	0.393
Elderly (≥60 years old)	46	12	58	
Sex				
Male	62	23	85	0.001
Female	77	6	83	
Duration of Hemodialysis (in years)				
<1 year	31	3	34	0.328
1-5 years	70	16	86	
>5 years	38	10	48	
Oxygen Saturation				
Normal (95%-100%)	115	5	140	0.648
Low (<95%)	24	4	28	

Table 3 revealed that among the four variables examined, only sex demonstrated a statistically significant association with anemia status (p = 0.001), with severe anemia occurring more frequently among female patients. Age, duration of hemodialysis, and oxygen saturation were not significantly associated with anemia status (p > 0.05).

Table 4. Multivariate logistic regression analysis of factors associated with severe anemia (n = 168)

Variable	aOR	95% CI	p-value
Age (> 60 vs 18-59 years)	1.29	0.71-2.35	0.393
Female sex	4.76	1.83-12.40	0.001
Duration of HD (years)			
1-5 years vs < 1 year	1.32	0.42-4.12	0.328
>5 years vs < 1 year	0.87	0.24-3.09	0.742
Oxygen Saturation (<95% vs > 95%)	1.21	0.52-2.81	0.648

*aOR = Adjusted Odds Ratio, CI = Confidence Interval

In the multivariate logistic regression analysis, female sex remained a strong and significant independent predictor of severe anemia (aOR = 4.76; 95% CI: 1.83–12.40; p = 0.001). None of

the other variables, age, duration of hemodialysis, or oxygen saturation, showed a significant association with anemia status after adjustment.

DISCUSSION

This cross-sectional investigation established female sex as the sole independent predictor of severe anemia among maintenance hemodialysis patients. This robust association persisted after rigorous adjustment for chronological age, treatment vintage, and pre-dialysis oxygen saturation. By isolating this demographic variable through multivariate logistic regression, the analysis underscores the profound impact of sex-specific physiological and metabolic pathways on erythropoietic capacity in end-stage renal disease. The absence of significant associations for age, hemodialysis duration, and oxygen saturation further challenges conventional assumptions that procedural metrics or generational factors primarily dictate hemoglobin trajectories in this population. Instead, these findings collectively emphasize that intrinsic biological disparities, particularly those linked to gonadal hormone dynamics and iron metabolism, exert a more deterministic influence on anemia severity than previously recognized in routine dialysis practice (Gou et al., 2025).

The pronounced susceptibility of female patients to severe anemia can be fundamentally attributed to a convergence of hormonal modulation, hematological physiology, and disease-related metabolic disturbances. Beyond the well-documented disparity in baseline iron reserves, contemporary evidence indicates that women frequently exhibit attenuated responsiveness to both endogenous and exogenous erythropoietin, a phenomenon largely mediated by sex hormone interactions with erythroid progenitor cells. Estrogen has been demonstrated to suppress erythropoiesis under conditions of chronic uremic inflammation, whereas androgens actively stimulate red blood cell proliferation and potentiate erythropoietin receptor sensitivity (Kim et al., 2025). Furthermore, inherent differences in lean muscle mass and total circulating blood volume inherently establish lower hemoglobin baselines in women, which are further exacerbated by the catabolic stress of dialysis. These physiological distinctions align consistently with recent international cohort analyses, which report that female hemodialysis patients routinely require escalated doses of erythropoiesis-stimulating agents to achieve standardized hemoglobin targets (Mayne et al., 2023; Kuragano, 2024). Compounding these biological vulnerabilities, epidemiological data reveal that women with chronic kidney disease frequently present with suboptimal nutritional intake and elevated inflammatory burdens, both of which critically impair iron mobilization and erythropoietin synthesis (Kim et al., 2025). Consequently, the synergistic interplay of hormonal suppression, nutritional deficits, and chronic inflammation creates a compounded risk profile that necessitates sex-stratified clinical surveillance in hemodialysis units.

In contrast to the robust sex-based association, chronological age failed to emerge as an independent predictor of severe anemia, indicating that dialysis-specific pathophysiological drivers largely eclipse age-related hematological decline. While population-based epidemiological studies consistently demonstrate a gradual decline in hemoglobin concentrations with advancing age, this trajectory is frequently neutralized in end-stage renal disease, where uremia-induced erythropoietin deficiency and hepcidin-mediated iron sequestration dominate the anemia landscape. The pathogenesis of renal anemia is fundamentally rooted in renal parenchymal destruction, chronic inflammatory states, procedural blood losses, and protein-energy wasting, mechanisms that operate independently of generational aging and uniformly affect patients across age strata. Large-scale nephrology cohorts have similarly documented that

chronological age loses its predictive significance once iron availability, systemic inflammation, and dialysis adequacy are statistically controlled (Prapaiwong et al., 2025). This phenomenon explains the comparable anemia distributions observed between adult and elderly participants in the present investigation. It reinforces the interpretation that aging alone does not constitute a primary causal factor for hemoglobin depletion in renal replacement therapy. Consequently, when comprehensive metabolic and treatment-related variables are incorporated into multivariate models, the independent effect of age consistently diminishes or becomes statistically non-significant (Badura et al., 2024).

Hemodialysis vintage similarly demonstrated no statistically significant correlation with anemia severity, suggesting that cumulative treatment exposure does not inherently dictate hemoglobin stability in adequately managed cohorts. Although prolonged extracorporeal circulation has historically been hypothesized to exacerbate anemia through cumulative circuit blood losses and progressive vascular access complications, contemporary clinical data present a more heterogeneous reality. Recent investigations report either hemoglobin stabilization following initial treatment adaptation or highly variable responses contingent upon individualized therapeutic regimens (Asmar et al., 2023). The null association observed in this analysis likely reflects the substantial influence of unmeasured clinical confounders, including dialysis adequacy indices, intravenous iron supplementation protocols, and dynamic erythropoiesis-stimulating agent titration, which vary considerably among patients regardless of treatment duration. This phenomenon is highly consistent with the epidemiological concept of confounding by indication, in which individuals with longer dialysis exposure are more likely to receive more aggressive, precisely calibrated anemia management, thereby effectively masking any direct temporal relationship between vintage and hemoglobin decline. Indeed, recent longitudinal evaluations have documented that hemoglobin trajectories often plateau after the first year of therapy, further supporting the notion that procedural duration alone is an insufficient predictor of severe anemia (Badura et al., 2024).

Pre-dialysis oxygen saturation exhibited no meaningful association with severe anemia, reaffirming that hemoglobin depletion in hemodialysis populations is predominantly driven by renal and hematological dysregulation rather than systemic oxygenation deficits. The physiological stability of arterial oxygen saturation during dialysis sessions is routinely maintained through procedural monitoring, supplemental oxygen administration, and cardiovascular compensatory mechanisms, which collectively prevent significant hypoxic stress. Consequently, minor fluctuations in peripheral oxygenation rarely reach thresholds sufficient to trigger compensatory erythropoiesis or materially influence red blood cell production. Previous clinical evaluations have consistently demonstrated that anemia in end-stage renal disease correlates more strongly with erythropoietin deficiency and inflammatory iron restriction than with respiratory parameters, suggesting that oxygenation metrics are unreliable indicators of hematological risk. Furthermore, studies indicate that oxygen saturation in hemodialysis patients remains consistently stable throughout treatment cycles, largely due to standardized clinical monitoring and supportive respiratory interventions. Even in patients experiencing episodic dyspnea or mild respiratory disturbances, compensatory increases in cardiac output and peripheral oxygen extraction effectively preserve tissue oxygen delivery, thereby decoupling saturation levels from hemoglobin concentration (Preciado et al., 2021).

The methodological rigor of this investigation is substantially reinforced by an adequately powered sample size and the strategic application of multivariate logistic regression to isolate independent predictors while systematically controlling for potential confounding variables. The

implementation of strict clinical inclusion and exclusion criteria effectively minimized acute physiological disruptions, such as active hemorrhage or recent transfusion episodes, which could otherwise distort baseline hemoglobin measurements and compromise the reliability of anemia classification. Additionally, the utilization of a structured data collection framework, standardized pulse oximetry protocols, and laboratory assays calibrated to institutional quality control standards ensured high internal consistency across all clinical assessments (Luu et al., 2026). The deliberate blinding of data collectors to the study hypotheses further mitigated potential observer bias, thereby strengthening the objectivity and reproducibility of the recorded variables and enhancing the overall validity of the identified sex-anemia association.

Despite these methodological strengths, several critical limitations must be carefully considered when interpreting and generalizing these findings. The cross-sectional study design inherently limits causal inference, as the data were collected at a single point in time, thereby precluding definitive conclusions about directional or temporal relationships between demographic variables and anemia progression. Conducted within a single secondary-care facility, the investigation may not adequately capture regional variations in dialysis protocols, socioeconomic determinants, or institutional resource availability that could influence hematological outcomes across broader populations. Furthermore, the utilization of purposive sampling introduces potential selection bias, which may limit the external validity of the results when extrapolating to heterogeneous hemodialysis cohorts with varying comorbidity profiles. Crucially, the absence of comprehensive laboratory data, including serum ferritin, transferrin saturation, C-reactive protein, detailed nutritional assessments, erythropoiesis-stimulating agent dosing regimens, and dialysis adequacy metrics, prevents a granular mechanistic analysis of iron metabolism and treatment responsiveness (Wang et al., 2026). Finally, dichotomizing hemoglobin levels into severe and non-severe categories inherently reduces statistical power. It may obscure clinically meaningful gradients in anemia severity, potentially limiting the multivariate analysis's sensitivity.

These findings necessitate the immediate integration of sex-specific anemia management protocols into routine hemodialysis care and highlight the critical need for longitudinal, multicenter investigations to validate these associations across diverse clinical settings (Hanafusa et al., 2022). From a clinical perspective, nephrology guidelines should emphasize proactive surveillance of hemoglobin and iron indices in female patients, coupled with individualized titration of erythropoiesis-stimulating agents to counteract inherent hormonal hypo-responsiveness and mitigate the risk of severe anemia (Del Vecchio et al., 2026). Future research must prioritize prospective cohort designs that systematically incorporate continuous hemoglobin trajectories, comprehensive inflammatory biomarker panels, and standardized dialysis adequacy parameters to elucidate the mechanistic pathways underlying sex-based differences in erythropoiesis. Longitudinal evaluations will further clarify causal relationships between hormonal modulation, chronic uremic inflammation, and treatment resistance, while simultaneously enabling the development of precision medicine approaches tailored to individual metabolic profiles. Additionally, analytical frameworks that utilize continuous hemoglobin values rather than binary classification systems will provide deeper insights into anemia progression, ultimately guiding evidence-based therapeutic adjustments and improving long-term hematological outcomes in maintenance hemodialysis populations.

CONCLUSION

This study identifies female sex as the sole independent predictor of severe anemia among patients undergoing maintenance hemodialysis. In contrast, chronological age, hemodialysis duration, and pre-dialysis oxygen saturation demonstrate no significant association with hemoglobin stratification. These findings underscore the profound influence of sex-specific physiological and metabolic pathways on erythropoietic capacity in end-stage renal disease, indicating that conventional demographic and procedural metrics are insufficient for comprehensive anemia risk assessment. Consequently, clinical management protocols should integrate sex-stratified surveillance and individualized therapeutic strategies, including optimized monitoring of iron indices and tailored erythropoiesis-stimulating agent dosing, to mitigate the heightened hematological vulnerability observed in female patients. Future multicenter and longitudinal investigations are warranted to delineate the underlying hormonal, inflammatory, and nutritional mechanisms driving this disparity, ultimately advancing precision-oriented approaches to renal anemia management.

CONFLICT OF INTEREST

The authors report no conflicts of interest.

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