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Frequency and Determinants of Visual Impairment Among Adults with Iron Deficiency Anemia at a Tertiary Care Hospital in Pakistan: Implications for Multidisciplinary and Rheumatology Care

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Abstract: **Background:** Iron deficiency anemia is common in Pakistan and may affect ocular tissues through reduced oxygen delivery, altered retinal microcirculation, and impaired neural function. Pakistani evidence on objectively measured visual impairment among adults with laboratory-confirmed iron deficiency anemia remains limited.
Objective: To determine the frequency and pattern of visual impairment among adults with iron deficiency anemia and to identify clinical, hematological, retinal, and optical coherence tomography factors associated with visual impairment. **Methods:** This prospective hospital-based observational study enrolled 272 consecutive non-pregnant adults with laboratory-confirmed iron deficiency anemia at Saidu Teaching Hospital, Pakistan. Participants underwent complete blood count and iron-status assessment, structured symptom evaluation, best-corrected visual acuity testing, color vision and contrast sensitivity assessment, slit-lamp examination, dilated fundus examination, and spectral-domain optical coherence tomography. Visual impairment was defined as best-corrected visual acuity worse than 6/12 in the better eye. Associations were assessed using chi-square or Fisher exact tests, as appropriate, and multivariable binary logistic regression. **Results:** The mean age was 34.5 ± 9.9 years, and 232 participants (85.3%) were women. Visual impairment was present in 48 of 272 participants (17.6%; 95% confidence interval, 13.6% to 22.6%). Mild impairment was present in 39 participants, moderate impairment in eight, and severe impairment in one. Retinal abnormalities were identified in 36 participants (13.2%), and retinal nerve fiber layer thinning was identified in 66 (24.3%). Hemoglobin below 8 g/dL, symptom duration of at least six months, and retinal abnormalities remained independently associated with visual impairment. **Conclusion:** Visual impairment affected approximately one in six adults with iron deficiency anemia in this hospital-based cohort. Severe anemia, prolonged symptoms, and retinal abnormalities were independently associated with visual impairment. These findings support consideration of ophthalmic assessment in patients with severe or persistent iron deficiency anemia and warrant confirmation in larger multicenter and longitudinal studies.

Keywords: iron deficiency anemia; visual impairment; retinal nerve fiber layer; anemic retinopathy; optical coherence tomography; Pakistan

INTRODUCTION

Anemia is defined by a hemoglobin concentration below an age-, sex-, and physiological-status-specific threshold, with consideration of relevant measurement and population factors [1]. The World Health Organization continues to identify anemia as a major public health problem, particularly among young children, pregnant and postpartum women, and menstruating adolescent girls and women [2]. Global Burden of Disease estimates indicate that anemia affected approximately 1.92 billion people in 2021 [3]. Dietary iron deficiency remains one of the leading contributors to the worldwide anemia burden [4].

Pakistan continues to carry a substantial burden of anemia and iron deficiency. Studies among women of reproductive age in Quetta and Karachi have documented frequent anemia and iron deficiency [5,6]. National analyses also show persistent geographic and socioeconomic inequalities despite some improvement in anemia prevalence over time [7]. Iron deficiency may result from inadequate dietary intake, menstrual or gastrointestinal blood loss, repeated pregnancies, or impaired absorption, while interpretation of ferritin can be complicated by concurrent inflammation [8].

The eye is a metabolically active organ with high oxygen requirements, making the retina and optic nerve potentially vulnerable to sustained reductions in oxygen delivery. Reported ocular manifestations of severe anemia include conjunctival pallor, retinal hemorrhages, cotton wool spots, Roth spots, venous dilatation, optic disc edema, ischemic optic neuropathy, and, rarely, retinal vascular occlusion [9]. These abnormalities provide biological plausibility for visual dysfunction in patients with severe or prolonged iron deficiency anemia.

Structural retinal changes have also been demonstrated using optical coherence tomography (OCT). A 2024 systematic review and meta-analysis found significantly lower mean retinal nerve fiber layer (RNFL) thickness in individuals with iron deficiency anemia than in controls [10]. Individual adult studies from India and Egypt similarly reported reduced peripapillary RNFL thickness [11-13]. Structural retinal or choroidal differences have also been described in women and children with iron deficiency anemia [14-16]. Importantly, a longitudinal study reported increases in choroidal and RNFL thickness after parenteral iron replacement, suggesting that at least some OCT changes may be reversible [17].

Optical coherence tomography angiography (OCT-A) studies have extended these observations to the retinal microcirculation. Reduced macular and radial peripapillary capillary vessel density has been reported in adults with iron deficiency anemia [18,19], while altered retinochoroidal vascular plexus measurements have been demonstrated in women with iron deficiency anemia [20]. Similar vessel-density changes have been described in children [21]. Microvascular alterations have also been observed in pregnancy-associated anemia, although that population is clinically distinct from non-pregnant adults with iron deficiency anemia [22].

Functional evidence is less extensive than structural and microvascular evidence. A recent population-based analysis of US women reported associations between iron status and visual field loss, but its cross-sectional design did not establish causality [23]. In Pakistan, most anemia research has focused on prevalence, nutritional determinants, pregnancy-related outcomes, or hematological features [5-7]. The frequency of objectively measured visual impairment among Pakistani adults with laboratory-confirmed iron deficiency anemia therefore remains insufficiently characterized.

Iron deficiency is clinically relevant in rheumatology because anemia in patients with chronic inflammatory and autoimmune disorders is often multifactorial. Iron deficiency may coexist with anemia of inflammation, chronic gastrointestinal blood loss, nutritional deficiency, or treatment-related factors. Distinguishing these mechanisms is particularly important because ferritin may be elevated or appear falsely reassuring in inflammatory states. Ocular symptoms in such patients may also arise from the underlying rheumatic disease, treatment effects, or systemic anemia. Therefore, understanding anemia-associated visual abnormalities may have practical relevance to multidisciplinary rheumatology care.
The present study aimed to estimate the frequency and pattern of visual impairment among adults with laboratory-confirmed iron deficiency anemia and to examine its relationship with anemia severity, symptom duration, retinal abnormalities, and retinal nerve fiber layer thinning.

OBJECTIVES

Primary objective

To determine the frequency of visual impairment among adults with laboratory-confirmed iron deficiency anemia at a tertiary care hospital in Pakistan.

Secondary objectives

To describe the severity of visual impairment and the

pattern of visual complaints and ocular abnormalities.
To determine the frequency of retinal abnormalities and retinal nerve fiber layer thinning.
To compare visual impairment across mild, moderate, and severe iron deficiency anemia.
To identify independent predictors of visual impairment after adjustment for demographic and clinical factors.
To evaluate the potential relevance of anemia-associated ocular abnormalities to rheumatology practice, particularly where iron deficiency may coexist with chronic inflammation.

MATERIALS AND METHODS

Study design and setting
A prospective hospital-based observational study was conducted at Saidu Teaching Hospital, Pakistan, through the Departments of Medicine/Hematology and Ophthalmology over a 12-month period. Participants were enrolled consecutively, and ophthalmic outcomes were assessed at enrollment. The manuscript was prepared in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement [24].

Study population
The study included non-pregnant adults aged 18 to 60 years with newly diagnosed or untreated iron deficiency anemia. Recruitment occurred before initiation of definitive iron replacement whenever clinically safe and feasible.

Diagnostic criteria for iron deficiency anemia
Anemia was defined using the applicable World Health Organization hemoglobin threshold [1]. Iron deficiency was confirmed by a serum ferritin level below 15 ng/mL. When inflammation was clinically suspected, iron deficiency was accepted with ferritin below 30 ng/mL together with transferrin saturation below 20%, after clinical review, in keeping with contemporary diagnostic recommendations that emphasize cautious interpretation of ferritin in inflammatory states [8]. Microcytosis and hypochromia supported, but did not independently establish, the diagnosis.

Inclusion criteria
Eligible participants were aged 18 to 60 years, had laboratory-confirmed iron deficiency anemia, provided written informed consent, and were able to complete visual acuity testing and ophthalmological examination.

Exclusion criteria
Participants were excluded for pregnancy, known diabetes mellitus, uncontrolled hypertension, glaucoma, visually significant cataract or corneal opacity, inherited retinal disease, previous retinal vascular occlusion, optic neuritis, known neurological disease affecting vision, intraocular surgery within the preceding six months, current vitamin B12 or folate deficiency, hemoglobinopathy, active malignancy, chronic kidney disease stage 4 or 5, or inability to complete a reliable visual assessment.

Sampling technique and sample size
Non-probability consecutive sampling was used. Because no robust Pakistani estimate was available for visual impairment specifically among adults with confirmed iron deficiency anemia, an expected frequency of 20% was used for sample-size estimation. At a 95% confidence level and 5% absolute precision, the minimum required sample size was 246. After allowing approximately 10% for incomplete examinations, the planned sample size was 272 participants.

Hematological assessment
Complete blood count included hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, red cell distribution width, leukocyte count, and platelet count. Ferritin and transferrin saturation were measured. C-reactive protein was requested when inflammation was suspected. Anemia was classified as mild, moderate, or severe according to the applicable World Health Organization hemoglobin thresholds [1].

Ophthalmic assessment
Distance visual acuity was assessed in each eye separately using a standard Snellen or logMAR chart, both as presenting acuity and after best correction. Refraction was performed when presenting acuity was reduced. Near vision, pupillary reactions, ocular motility, color vision using Ishihara plates, and contrast sensitivity using the Pelli-Robson chart were assessed. Slit-lamp examination documented conjunctival pallor and anterior-segment findings. Intraocular pressure was measured, and a dilated fundus examination was performed. Color fundus photography was obtained when available.

Optical coherence tomography
Peripapillary RNFL thickness and macular ganglion cell parameters were measured using spectral-domain OCT. Scans were repeated when signal quality was below the manufacturer's recommended threshold or when segmentation was clearly incorrect. RNFL thinning was defined as an average or sectoral thickness below the fifth percentile of the device normative database in at least one eye, after exclusion of common ocular causes.

Primary and secondary outcomes

The primary outcome was visual impairment, defined for this study as best-corrected visual acuity worse than 6/12 in the better eye. Severity was graded as mild (worse than 6/12 to 6/18), moderate (worse than 6/18 to 6/60), severe (worse than 6/60 to 3/60), and blindness (worse than 3/60). Secondary outcomes included visual complaints, abnormal contrast sensitivity, color-vision abnormality, retinal abnormalities, and RNFL thinning.

Data quality

Investigators used a standardized case report form. Ophthalmic examinations were performed by an ophthalmologist or by a trained examiner under the supervision of an ophthalmologist. A 10% sample of study records was compared with source records, and classification discrepancies were resolved by consensus.

Statistical analysis

Data were analyzed using IBM SPSS Statistics for Windows, version 29.0 (IBM Corp., Armonk, NY, USA). Continuous variables were summarized as mean ± standard deviation or median with interquartile range, according to distribution. Categorical variables were summarized as frequencies and percentages. The frequency of visual impairment was reported with a 95% Wilson confidence interval. Categorical associations were evaluated using the chi-square test or Fisher exact test, as appropriate. Multivariable binary logistic regression was used to identify independent predictors of visual impairment. Adjusted odds ratios with 95% confidence intervals were reported. All tests were two-sided, and $p < 0.05$ was considered statistically significant.

Ethical considerations

The study protocol was reviewed by the Institutional Review Board/Ethics Committee of Saidu Teaching Hospital, which granted a waiver of full ethical review. Written informed consent was obtained from all participants before enrollment. The study was conducted in accordance with the principles of the Declaration of Helsinki [25] and applicable institutional requirements. Participant confidentiality was protected through de-identification of study records and restricted access to research data. Participants with severe anemia, retinal hemorrhage, optic disc edema, or significant visual impairment were referred promptly for appropriate medical and ophthalmological management.

RESULT

Participant characteristics

A total of 286 potentially eligible patients were screened. Fourteen were excluded, including six with diabetes mellitus, three with visually significant cataract, two with vitamin B12 deficiency, two who could not complete reliable acuity testing, and one who declined participation. The final analysis included 272 participants. The mean age was 34.5 ± 9.9 years, and 232 participants (85.3%) were women. The median duration of anemia-related symptoms was 5.8 months (interquartile range, 3.3 to 9.5 months). Mean hemoglobin was 9.26 ± 1.81 g/dL, and median serum ferritin was 9.4 ng/mL (interquartile range, 6.0 to 11.7 ng/mL). Mild anemia was present in 57 participants (21.0%), moderate anemia in 159 (58.5%), and severe anemia in 56 (20.6%).

Table 1. Demographic and hematological characteristics, n = 272

Characteristic	Value
Age, years, mean ± SD	34.5 ± 9.9
Women, n (%)	232 (85.3)
Rural residence, n (%)	125 (46.0)
Symptom duration, months, median (IQR)	5.8 (3.3 to 9.5)
Hemoglobin, g/dL, mean ± SD	9.26 ± 1.81
Serum ferritin, ng/mL, median (IQR)	9.4 (6.0 to 11.7)
Mild anemia, n (%)	57 (21.0)
Moderate anemia, n (%)	159 (58.5)
Severe anemia, n (%)	56 (20.6)

IQR, interquartile range; SD, standard deviation.

Frequency and severity of visual impairment

Best-corrected visual impairment in the better eye was present in 48 of 272 participants, corresponding to a frequency of 17.6% (95% confidence interval, 13.6% to 22.6%). Mild visual impairment was present in 39 participants (14.3% of the total cohort), moderate impairment in eight (2.9%), and severe impairment in one (0.4%). No participant met the study definition of blindness. Visual complaints were reported by 83 participants (30.5%), most commonly blurred or reduced vision, difficulty reading or performing near work, reduced contrast, and transient visual obscurations.

Table 2. Frequency and pattern of visual impairment

Outcome	n	%
Any best-corrected visual impairment	48	17.6
Mild visual impairment	39	14.3
Moderate visual impairment	8	2.9
Severe visual impairment	1	0.4
Blindness	0	0.0
Any visual complaint	83	30.5
Blurred or reduced vision	61	22.4
Difficulty reading or near work	44	16.2
Transient visual obscurations	18	6.6
Photopsia or visual field complaint	11	4.0

Visual impairment categories were based on best-corrected visual acuity in the better eye.

Ophthalmological and optical coherence tomography findings

Conjunctival pallor was the most frequent examination finding and was present in 219 participants (80.5%). Abnormal contrast sensitivity was identified in 78 (28.7%), and abnormal color vision in 31 (11.4%). Retinal abnormalities were identified in 36 participants (13.2%) and included venous dilatation or tortuosity, retinal hemorrhages, cotton wool spots, Roth spots, and optic disc edema; some participants had more than one finding. RNFL thinning was identified in 66 participants (24.3%).

Table 3. Ocular and retinal findings

Finding	n	%
Conjunctival pallor	219	80.5
Abnormal contrast sensitivity	78	28.7
Retinal nerve fiber layer thinning	66	24.3
Abnormal color vision	31	11.4
Any retinal abnormality	36	13.2
Retinal venous dilatation or tortuosity	19	7.0
Retinal hemorrhage	11	4.0
Cotton wool spots	4	1.5
Roth spots	3	1.1
Optic disc edema	2	0.7

Retinal subcategories may overlap.

Factors associated with visual impairment

Visual impairment was significantly more frequent among participants with symptom duration of at least six months, hemoglobin below 8 g/dL, ferritin below 5 ng/mL, retinal abnormalities, and RNFL thinning. Age, sex, and rural residence were not significantly associated with the primary outcome in univariable analysis.

Table 4. Univariable associations with visual impairment

Variable	Visual impairment present, n/N (%)	Visual impairment absent, n/N (%)	p value
Age 40 years or older	12/83 (14.5)	71/83 (85.5)	0.458
Female sex	41/232 (17.7)	191/232 (82.3)	1.000
Rural residence	19/125 (15.2)	106/125 (84.8)	0.414
Symptoms for at least 6 months	30/129 (23.3)	99/129 (76.7)	0.032
Hemoglobin below 8 g/dL	25/56 (44.6)	31/56 (55.4)	<0.001
Ferritin below 5 ng/mL	20/52 (38.5)	32/52 (61.5)	<0.001
Any retinal abnormality	16/36 (44.4)	20/36 (55.6)	<0.001
Retinal nerve fiber layer thinning	20/66 (30.3)	46/66 (69.7)	0.004

P values were derived from the chi-square test or Fisher exact test, as appropriate.

Multivariable analysis

After adjustment, hemoglobin below 8 g/dL was associated with fourfold higher odds of visual impairment. Retinal abnormalities were associated with approximately 3.6-fold higher odds, and symptom duration of at least six months was associated with approximately twofold higher odds. Ferritin below 5 ng/mL and RNFL thinning did not remain independently significant after adjustment for anemia severity and retinal findings.

Table 5. Multivariable logistic regression for visual impairment

Predictor	Adjusted odds ratio	95% confidence interval	p value
Age, per year	1.01	0.97 to 1.05	0.588
Female sex	1.03	0.39 to 2.75	0.953
Symptoms for at least 6 months	2.12	1.04 to 4.33	0.038
Hemoglobin below 8 g/dL	4.00	1.48 to 10.80	0.006
Ferritin below 5 ng/mL	1.56	0.56 to 4.37	0.398
Any retinal abnormality	3.60	1.52 to 8.52	0.004
Retinal nerve fiber layer thinning	1.31	0.59 to 2.93	0.507

The dependent variable was best-corrected visual impairment in the better eye.

DISCUSSION

In this hospital-based cohort, visual impairment was present in approximately one in six adults with iron deficiency anemia. The frequency was higher among participants with severe anemia, prolonged symptoms, retinal abnormalities, and RNFL thinning in univariable analyses. After adjustment, hemoglobin below 8 g/dL, symptom duration of at least six months, and retinal abnormalities remained independently associated with visual impairment. Because the study was conducted at a single tertiary-care center, the observed frequency should be interpreted as a clinical cohort estimate rather than a population prevalence for Pakistan.

The structural findings are consistent with the broader OCT literature. The 2024 meta-analysis by Ghasemi and colleagues demonstrated lower pooled RNFL thickness in patients with iron deficiency anemia compared with controls [10]. Joshi and Ingle reported reduced average peripapillary RNFL thickness in adults with iron deficiency anemia [11], while Das Gupta and colleagues found similar reductions in nutritional-deficiency anemia, including the iron-deficiency subgroup [12]. El-Gamal and colleagues also reported peripapillary RNFL differences in iron deficiency anemia [13]. Studies in children and women have described related structural retinal and choroidal abnormalities [14-16].

The microvascular literature provides a complementary mechanism. Koca and colleagues reported reduced macular and radial peripapillary vessel density on OCT-A in adults with iron deficiency anemia [18]. Düzgün and colleagues identified altered retinochoroidal vascular plexus measurements in affected women [20], and Kocer and colleagues demonstrated reduced radial peripapillary capillary density that correlated with hematological indices [19]. Pediatric OCT-A data have likewise shown lower peripapillary and macular vessel density [21]. Findings from pregnancy-associated anemia also demonstrate that systemic anemia can be accompanied by quantifiable retinal microvascular changes, although pregnancy represents a distinct physiological state and should not be directly generalized to the present cohort [22].

The association between hemoglobin below 8 g/dL and visual impairment is clinically plausible. Severe anemia reduces arterial oxygen-carrying capacity and may compromise retinal oxygen delivery, particularly when chronic or accompanied by microvascular abnormalities. Retinal hemorrhages, cotton wool spots, disc edema, and rare retinal arterial occlusion have been described in severe iron deficiency anemia [9]. The finding that retinal abnormalities remained independently associated with visual impairment in the present analysis further supports the clinical relevance of fundus assessment when visual symptoms occur.

The relationship between RNFL thinning and visual impairment was more nuanced. RNFL thinning was associated with visual impairment in univariable analysis but did not remain significant after adjustment. This may indicate confounding by anemia severity or coexisting retinal abnormalities, or it may reflect limited power to distinguish overlapping

structural pathways. Importantly, Coban and colleagues documented increases in RNFL and choroidal thickness after parenteral iron replacement [17], raising the possibility that some structural changes may be at least partially reversible. Longitudinal studies linking correction of anemia to repeat visual function and OCT measurements are therefore needed.

Functional outcomes have been studied less extensively than structural imaging. A 2025 NHANES analysis reported an inverse association between transferrin saturation and visual field loss among US women aged 40 to 49 years, and iron deficiency definitions were associated with higher odds of visual field loss [23]. Those data are not directly comparable with the present study because of differences in population, exposure definition, and visual outcome, but they reinforce the need to examine functional as well as structural ocular consequences of impaired iron status.

Pakistani anemia research has predominantly focused on women of reproductive age, nutritional determinants, and geographic or socioeconomic variation [5-7]. Women also constituted most of the present cohort, which is consistent with the recognized clinical burden of iron deficiency among women of reproductive age. However, the relatively small male subgroup limits sex-specific inference, and the single-center design restricts generalizability across regions and healthcare settings.

These findings may have particular relevance to rheumatology practice, where anemia is frequently multifactorial and iron deficiency may coexist with anemia of inflammation. In patients with chronic inflammatory or autoimmune disorders, ferritin can be difficult to interpret because it behaves as an acute-phase reactant, making assessment of transferrin saturation and inflammatory markers clinically important. In addition, visual complaints in patients attending rheumatology services may have several potential explanations, including ocular manifestations of the underlying rheumatic disorder, treatment-related effects, and systemic hematological abnormalities. Recognition of severe or persistent iron deficiency may therefore help identify patients who warrant formal ophthalmological assessment. The present cohort was not selected according to rheumatic diagnosis, so these observations should be interpreted as clinically relevant, hypothesis-generating evidence rather than disease-specific rheumatology findings [8].

More broadly, experimental and clinical studies in other inflammatory and metabolic settings have shown that antioxidant or metabolic interventions can modify inflammatory and oxidative-stress pathways [26,27]. These studies do not establish a mechanism for anemia-related visual impairment and were not conducted in rheumatology cohorts. They are cited only as broader biological context for the interaction between systemic metabolic or inflammatory states and tissue oxidative stress, an area that warrants direct investigation in anemia and ocular disease.

This study had several strengths. Iron deficiency was laboratory confirmed, major alternative causes of visual impairment were excluded, best-corrected rather than presenting visual acuity was used for the primary outcome, and participants underwent fundus examination and OCT. Important limitations include the absence of a non-anemic control group, potential referral bias from a single tertiary center, possible inflammation-related misclassification of ferritin, the predominantly female sample, and the cross-sectional timing of the ophthalmic assessment. The observational design cannot establish that iron deficiency caused the visual abnormalities observed.

Future multicenter studies should include non-anemic comparison groups and standardized assessment of inflammatory markers, visual fields, contrast sensitivity, and OCT/OCT-A. Longitudinal reassessment after correction of iron deficiency would be particularly valuable. Demonstration that visual or structural abnormalities improve in parallel with hematological recovery would strengthen causal inference and help identify which ocular changes are clinically reversible.

CONCLUSION

Visual impairment was identified in 17.6% of adults with laboratory-confirmed iron deficiency anemia in this hospital-based cohort. Hemoglobin below 8 g/dL, symptom duration of at least six months, and retinal abnormalities were independently associated with visual impairment. These findings support heightened attention to visual symptoms and consideration of formal ophthalmic assessment in patients with severe or prolonged iron deficiency anemia. Larger multicenter and longitudinal studies are needed to determine generalizability and to assess whether correction of iron deficiency improves visual outcomes. These observations may be particularly relevant to multidisciplinary and rheumatology care, where iron deficiency can coexist with chronic inflammation and where visual complaints may have overlapping systemic, inflammatory, and ocular causes. Future studies specifically enrolling patients with rheumatic diseases are warranted to determine whether anemia severity and iron status are associated with ocular abnormalities in these populations.

DECLARATIONS

Ethics approval and consent to participate: The study protocol was reviewed by the Institutional Review Board/Ethics Committee of Saidu Teaching Hospital, which granted a waiver of full ethical review. Written informed consent was obtained from all participants before enrollment. The study was conducted in accordance with the Declaration of Helsinki and applicable institutional ethical requirements. Participant confidentiality was maintained through de-identification and restricted access to study data.

Consent for publication: Not applicable. The manuscript does not contain identifiable individual patient information, images, or other personal data requiring separate consent for publication.

Availability of data and materials: The de-identified data generated and analyzed during the study are not publicly available because of institutional, ethical, and patient-confidentiality requirements. De-identified data may be made available from the corresponding author upon reasonable request, subject to institutional and ethical approval.

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Research integrity and transparency: The authors affirm that all numerical findings reported in this manuscript were derived from the enrolled clinical cohort and analyzed according to the methodology described in the study. The authors take responsibility for the accuracy, completeness, and integrity of the reported data and analyses.

Use of artificial intelligence: Generative artificial intelligence tools were used solely to assist with language refinement, organization, and editorial improvement of the manuscript. Artificial intelligence was not used to generate, modify, or fabricate patient data, clinical outcomes, or statistical results. All scientific content, statistical findings, interpretations, references, and final manuscript text were critically reviewed and verified by the authors, who retain full responsibility for the accuracy and integrity of the work.

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