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Studies on Erythrocyte Sedimentation Rate, Serum Iron / Total Iron Binding Capacity, and Progesterone in Women with Uterine Fibroid in Imo State

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ABSTRACT

Uterine fibroids are the most common benign tumors of the female reproductive tract and are frequently associated with heavy menstrual bleeding, inflammation, and hormonal dysregulation. These features predispose affected women to iron deficiency and related hematological alterations. However, data integrating inflammatory markers, iron indices, and progesterone levels in women with uterine fibroid in South-Eastern Nigeria remain limited. This study evaluated erythrocyte sedimentation rate (ESR), serum iron, total iron-binding capacity (TIBC), transferrin saturation, and serum progesterone levels in women diagnosed with uterine fibroid in Imo State, Nigeria. This analytical cross-sectional study included 30 women with ultrasound-confirmed uterine fibroid and 30 age-matched apparently healthy controls. ESR was determined using the Westergren method, serum iron and TIBC were measured colorimetrically, transferrin saturation was calculated, and serum progesterone was assayed using ELISA. Data were analyzed using independent sample *t*-tests, one-way ANOVA, correlation analysis, and effect size estimation. Statistical significance was set at $p < 0.05$. Women with uterine

fibroid had significantly higher ESR compared with controls (70.37 ± 36.53 vs 10.93 ± 9.52 mm/hr; $p < 0.0001$). Serum iron levels were significantly reduced in the fibroid group (12.05 ± 4.14 vs 27.78 ± 9.53 $\mu\text{mol/L}$; $p < 0.0001$), while TIBC was significantly elevated (153.33 ± 77.51 vs 71.54 ± 26.03 $\mu\text{mol/L}$; $p < 0.0001$). Mean transferrin saturation was markedly lower among women with fibroid (10.08%) compared with controls (45.23%), with 86.7% of fibroid patients exhibiting transferrin saturation $< 20\%$. Serum progesterone levels were significantly higher in the fibroid group (31.44 ± 20.47 vs 6.18 ± 7.15 ng/mL; $p < 0.0001$). Effect size analysis demonstrated very large differences for ESR (Cohen's $d = 2.23$) and serum iron ($d = -2.14$). Age-stratified analysis showed no significant differences across age groups for ESR, iron indices, or progesterone ($p > 0.05$). Women with uterine fibroid in Imo State exhibit significant inflammatory activity, profound iron deficiency, and elevated progesterone levels compared with healthy controls. The high prevalence of reduced transferrin saturation highlights the clinical importance of routine iron status assessment in fibroid management. These findings underscore the need for integrated inflammatory, hematological, and hormonal evaluation in women with uterine fibroid, particularly in resource-limited settings.

Keywords: Uterine fibroid, erythrocyte sedimentation rate, iron deficiency, transferrin saturation, progesterone

1. INTRODUCTION

Uterine fibroids, also referred to as uterine leiomyomas, are the most prevalent benign tumors of the female reproductive tract and represent a leading cause of gynecological morbidity among women of reproductive age worldwide. They arise from the smooth muscle cells of the myometrium and are characterized by clonal proliferation, excessive extracellular matrix deposition, and altered tissue architecture. Although fibroids are benign, their clinical significance lies in their high prevalence, chronic course, and capacity to impair quality of life through symptoms such as heavy menstrual bleeding, pelvic pain, pressure symptoms, infertility, and recurrent pregnancy loss (Bulun *et al.*, 2025; Yang *et al.*, 2022).

The burden of uterine fibroids is disproportionately high among women of African descent, with earlier age at onset, more aggressive growth patterns, and increased symptom severity compared with other populations. In low- and middle-income settings such as Nigeria, delayed presentation, limited access to specialist care, and reliance on surgical intervention further compound disease burden. In Imo State, uterine fibroids remain one of the most common indications for gynecological consultation and myomectomy, yet local biochemical and inflammatory profiling of affected women remains underexplored, despite its relevance to clinical decision-making and peri-operative optimization.

One of the most clinically significant consequences of uterine fibroids is abnormal uterine bleeding, particularly heavy menstrual bleeding, which has been formally classified as a structural cause under the FIGO PALM-COEIN system (Munro *et al.*, 2011). Chronic excessive menstrual blood loss predisposes affected women to progressive iron depletion and iron-deficiency anemia, conditions that are frequently underdiagnosed or inadequately managed in gynecological practice. Donnez *et al.* (2022) emphasized that uterine disorders, especially fibroids, constitute a major yet often overlooked contributor to iron-deficiency anemia in women, underscoring the need for routine evaluation of iron status in this population.

Assessment of iron metabolism using serum iron and total iron-binding capacity (TIBC) provides valuable insight into the severity and pattern of iron depletion associated with chronic

blood loss. Serum iron reflects circulating iron bound to transferrin, while TIBC serves as an indirect measure of transferrin availability and iron-binding reserve. In iron-deficiency states secondary to heavy menstrual bleeding, serum iron levels are typically reduced, with a compensatory elevation in TIBC and reduced transferrin saturation (Sholzberger *et al.*, 2025).

Recent studies have demonstrated a high prevalence of undiagnosed iron deficiency among gynecology patients, even in the absence of overt anemia, highlighting the importance of early biochemical screening to prevent functional impairment and improve clinical outcomes (Goldberg *et al.*, 2025).

Beyond bleeding-related iron loss, emerging evidence suggests that uterine fibroids are biologically active lesions associated with inflammatory and immune-mediated pathways. Fibroid tissues exhibit increased expression of pro-inflammatory cytokines, growth factors, and extracellular matrix-modulating enzymes, suggesting that chronic low-grade inflammation may contribute to fibroid growth, symptom expression, and disease progression (Ishikawa *et al.*, 2024; Dolmans *et al.*, 2024).

In this context, the erythrocyte sedimentation rate (ESR), a long-standing nonspecific marker of systemic inflammation, may provide additional clinical information. ESR reflects alterations in plasma protein composition that promote erythrocyte aggregation and accelerated sedimentation, and while nonspecific, it remains a widely accessible and cost-effective marker in routine clinical practice, particularly in resource-limited settings (Athan *et al.*, 2025).

Hormonal regulation remains central to the pathophysiology of uterine fibroids. While estrogen has historically received greater attention, contemporary evidence highlights the pivotal role of progesterone in fibroid initiation and growth. Progesterone promotes fibroid cell proliferation, inhibits apoptosis, and enhances extracellular matrix accumulation through progesterone receptor-mediated signaling pathways (Aliet *et al.*, 2023).

Fibroid tissues consistently demonstrate increased progesterone receptor expression compared with adjacent normal myometrium, providing a mechanistic basis for the effectiveness of progesterone-modulating therapies (Bulun *et al.*, 2025). However, circulating progesterone levels vary across the menstrual cycle, and the relationship between systemic progesterone concentration and fibroid-related symptomatology remains incompletely understood, particularly in African populations.

In women with uterine fibroids, alterations in progesterone dynamics may influence menstrual regularity, bleeding severity, and reproductive outcomes. Evaluating serum progesterone levels, when appropriately timed within the menstrual cycle, may therefore offer insight into endocrine status, ovulatory function, and the hormonal milieu supporting fibroid growth. When interpreted alongside inflammatory markers and iron indices, progesterone assessment contributes to a more integrated understanding of the systemic effects of uterine fibroids.

Against this backdrop, the present study seeks to evaluate erythrocyte sedimentation rate, serum iron, total iron-binding capacity, and progesterone levels in women with uterine fibroids in Imo State. By integrating inflammatory, hematological, and hormonal parameters, this study aims to generate locally relevant data that reflect the multifaceted biological impact of uterine fibroids.

Such evidence may support earlier identification of iron depletion, improve peri-operative management, inform individualized treatment strategies, and contribute to the global discourse on fibroid biology from an underrepresented population.

2. MATERIALS AND METHODOLOGY

2. 1. Study Area

This study was conducted at the Imo State Specialist Hospital, Owerri, Imo State, Nigeria. Owerri is the capital city of Imo State and lies within the south-eastern region of Nigeria. The city comprises three Local Government Areas: Owerri Municipal, Owerri North, and Owerri West. The Imo State Specialist Hospital serves as a major referral center for gynecological, hematological, and clinical chemistry services, making it suitable for this study.

2. 2. Study Design

An analytical cross-sectional study design was adopted. The study was carried out in September 2024 to evaluate erythrocyte sedimentation rate (ESR), serum iron, total iron-binding capacity (TIBC), and serum progesterone levels in women diagnosed with uterine fibroids. Cross-sectional designs are widely used for biomarker assessment and prevalence-based clinical investigations where exposure and outcome are measured simultaneously (Setia, 2016).

2. 3. Study Population

The study population comprised women aged 18 years and above with ultrasound-confirmed uterine fibroids attending the gynecology clinic of the Imo State Specialist Hospital. Apparently healthy women without clinical or radiological evidence of uterine fibroids were recruited as controls. Control participants were age-matched women with no history of abnormal uterine bleeding, iron supplementation, hormonal contraceptive use, or hormonal therapy within three months preceding the study, in order to minimize confounding effects on iron and hormonal parameters (Munro *et al.*, 2011).

2. 4. Method of Recruitment

Participants were recruited consecutively from eligible patients attending gynecology clinics during routine hospital visits. The objectives and procedures of the study were explained to prospective participants in clear and understandable language. Only participants who met the inclusion criteria and voluntarily provided informed consent were enrolled, in line with established ethical guidelines for human research (World Medical Association, 2013).

2. 5. Selection Criteria

Inclusion Criteria

- Women aged 18 years and above
- Ultrasound-confirmed diagnosis of uterine leiomyoma
- Provision of informed consent

Exclusion Criteria

- Refusal to give consent
- Presence of other gynecological conditions such as endometriosis or ovarian cysts
- Chronic systemic diseases known to affect hematological or iron parameters

- Current or recent use of hormonal therapy, iron supplements, or medications affecting iron metabolism or progesterone levels

2. 6. Sample Size Determination

Sample size was determined using the formula described by Araoye (2004) at a 95% confidence level and 5% precision, assuming a prevalence of 2%.

$$n = Z^2 \frac{(1-P)P}{D^2}$$

where;

n = the minimum sample size

Z = the standard normal deviation, usually set at 1.960 which corresponds to the 95% confidence interval

P = the assumed prevalence rate in the study area

D = degree of precision required

Q = (1-P)

The required sample size is calculated as follows:

Assumed prevalence = 2.0% = 2/100 = 0.02

$$n = Z^2 \frac{(1-P)P}{D^2}$$

$$n = 1.96^2 \frac{1-0.02) 0.02}{0.05^2}$$

$$n = 3.8416 \frac{(0.98)0.02}{0.0025}$$

$$n = \frac{3.8416 \times 0.0196}{0.0025}$$

$$n = \frac{0.07529536}{0.0025}$$

$$n = 30$$

Based on this calculation, a minimum sample size of 30 participants was obtained. Although modest, this sample size was considered adequate for exploratory analysis and preliminary evaluation of inflammatory, iron, and hormonal biomarkers, consistent with similar hospital-based clinical studies in resource-limited settings (Pourhoseingholiet *al.*, 2013).

2. 7. Sample Collection

Eight milliliters (8 mL) of venous blood were collected aseptically from each participant using standard venipuncture techniques. Two milliliters (2 mL) were dispensed into EDTA-

anticoagulated tubes for ESR determination, while six milliliters (6 mL) were dispensed into plain tubes for serum separation. The plain tubes were allowed to clot and centrifuged at 3,000 rpm for 10 minutes to obtain serum. All sample handling procedures followed standard clinical laboratory protocols to ensure sample integrity and analytical reliability (Whitehead *et al.*, 2019).

2. 8. Laboratory Analysis

2. 8. 1. Determination of Serum Progesterone

Serum progesterone levels were determined using an enzyme-linked immunosorbent assay (ELISA) technique based on antigen–antibody reactions, following the manufacturer’s instructions. ELISA remains a validated and widely accepted method for quantitative progesterone measurement in clinical and research settings (Wild, 2013).

To reduce physiological variability, blood samples for progesterone analysis were collected during the mid-luteal phase of the menstrual cycle (days 21–23) in participants with regular menstrual cycles, corresponding to peak progesterone secretion (Filicori, 1984). In participants with irregular cycles, progesterone values were interpreted cautiously.

2. 8. 2. Determination of Erythrocyte Sedimentation Rate

ESR was determined using the Westergren method, the international reference standard for ESR measurement. EDTA-anticoagulated blood was introduced into a Westergren tube and allowed to stand vertically for one hour, after which the sedimentation distance was measured in millimeters per hour (mm/hr) (Westergren, 1921; Whitehead *et al.*, 2019). ESR was selected due to its wide availability, low cost, and established role as a nonspecific indicator of systemic inflammation in routine clinical practice, particularly in resource-limited settings (Brigden, 1999).

2. 8. 3. Determination of Serum Iron

Serum iron concentration was measured using a colorimetric method based on the ferrozine principle. Iron was dissociated from transferrin, reduced to the ferrous form, and reacted with a chromogen to produce a colored complex measurable spectrophotometrically. This method is widely used in clinical chemistry for assessment of iron status (Andrews, 2000).

2. 8. 4. Determination of Total Iron-Binding Capacity

Total iron-binding capacity was determined by saturating serum transferrin with excess iron, removing unbound iron, and quantifying transferrin-bound iron using a colorimetric technique. TIBC provides an indirect measure of transferrin concentration and is routinely employed in the evaluation of iron deficiency states (Abbaspour *et al.*, 2014).

2. 9. Ethical Considerations

Ethical approval was obtained from the Health Research Ethics Committee of the Imo State Specialist Hospital, Owerri. Written informed consent was obtained from all participants prior to enrollment. All procedures complied with the ethical principles outlined in the Declaration of Helsinki for research involving human subjects (World Medical Association, 2013).

2. 10. Statistical Analysis

Data obtained from the study were coded and entered into Microsoft Excel and subsequently analyzed using the Statistical Package for the Social Sciences (SPSS) software, version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were summarized using descriptive statistics and presented as mean $\pm$ standard deviation. Prior to inferential analysis, data distributions were assessed for approximate normality to justify the use of parametric statistical tests.

Comparisons of mean erythrocyte sedimentation rate (ESR), serum iron, total iron-binding capacity (TIBC), and serum progesterone levels between women with uterine fibroid and healthy controls were performed using independent sample *t*-tests. The same statistical approach was applied for subgroup analyses involving menopausal and non-menopausal women with uterine fibroid. Associations between serum progesterone and inflammatory and iron parameters (ESR, serum iron, and TIBC) were evaluated using Pearson's correlation coefficient. In addition to hypothesis testing, effect size analysis was conducted using Cohen's *d* to quantify the magnitude of differences between fibroid and control groups, thereby providing a measure of clinical relevance beyond statistical significance. All statistical tests were two-tailed, and a *p*-value of less than 0.05 was considered statistically significant (Kim, 2015).

3. RESULTS

3. 1. Comparison of ESR, Serum Iron, TIBC, and Progesterone between Women with Uterine Fibroid and Healthy Controls

Table 1 summarizes the mean values of erythrocyte sedimentation rate (ESR), serum iron, total iron-binding capacity (TIBC), and serum progesterone in women diagnosed with uterine fibroid and apparently healthy controls. Differences between groups were assessed using an independent sample *t*-test. Diagrammatical representation of the results are shown in Figures 1, 2 and 3.

Table 1. Mean Values of ESR, Serum Iron, TIBC, and Progesterone in Women Diagnosed with Uterine Fibroid and Healthy Controls (Mean $\pm$ S.D).

Parameters	Test (N = 30)	Control (N = 30)	t-value	p-value
Age (years)	34.43 $\pm$ 5.30	34.43 $\pm$ 5.30	0.000	1.0000
ESR (mm/hr)	70.37 $\pm$ 36.53	10.93 $\pm$ 9.52	8.624	< 0.0001*
Serum Iron (μ mol/L)	12.05 $\pm$ 4.14	27.78 $\pm$ 9.53	-8.296	< 0.0001*
TIBC (μ mol/L)	153.33 $\pm$ 77.51	71.54 $\pm$ 26.03	5.479	< 0.0001*
Progesterone (ng/mL)	31.44 $\pm$ 20.47	6.18 $\pm$ 7.15	6.382	< 0.0001*

Key: ESR – Erythrocyte Sedimentation Rate; TIBC – Total Iron-Binding Capacity; S.D – Standard Deviation; *= significant *p* value

Mean Erythrocyte Sedimentation Rate in Women with Uterine Fibroid and Healthy Controls

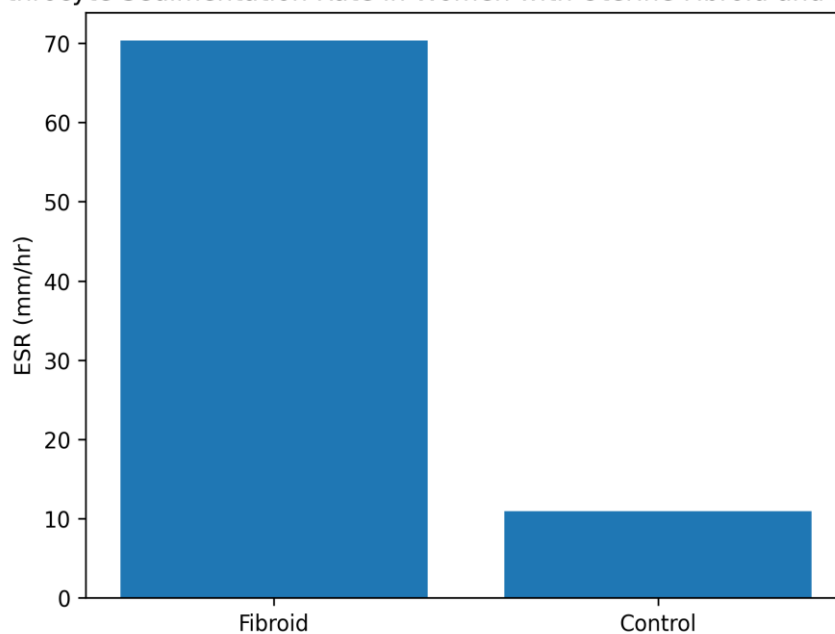


Figure 1. Mean Erythrocyte Sedimentation Rate (ESR) in Women with Uterine Fibroid and Healthy Controls.

Distribution of Serum Iron in Women with Uterine Fibroid and Healthy Controls

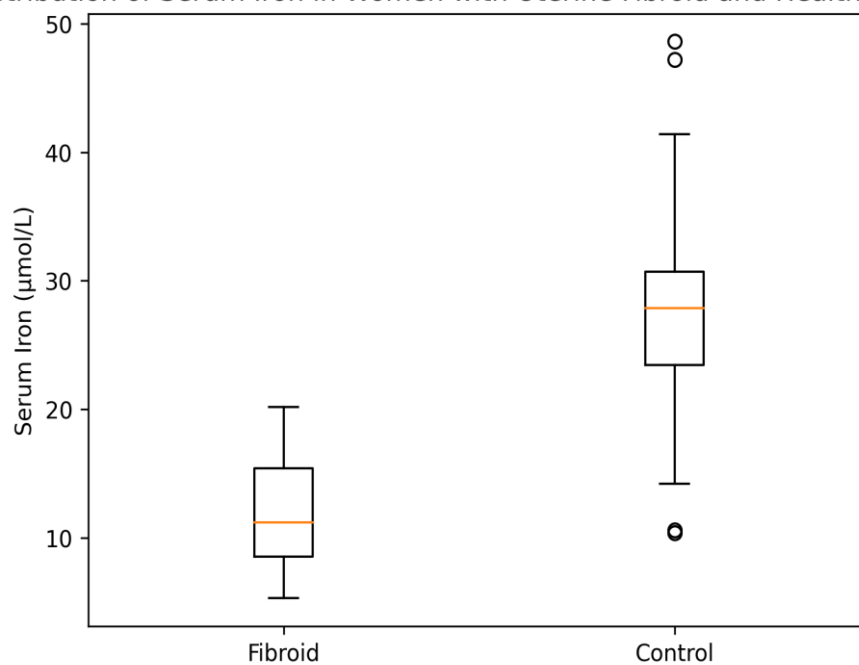


Figure 2. Box Plot of Serum Iron Distribution in Women with Uterine Fibroid and Healthy Controls.

Distribution of Total Iron-Binding Capacity in Women with Uterine Fibroid and Healthy Controls

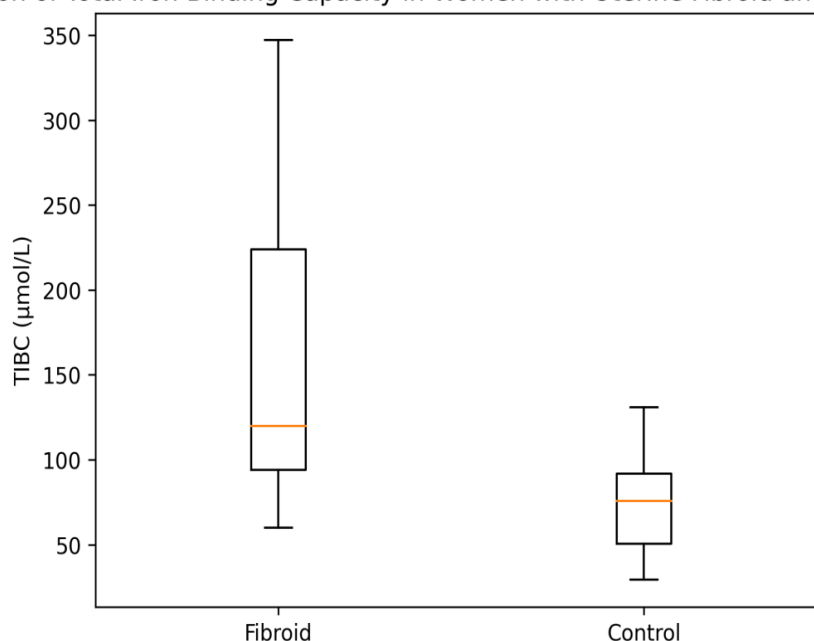


Figure 3. Total Iron Binding Capacity in women with Uterine Fibroid and Healthy Controls.

3. 2. Comparison of ESR, Serum Iron, TIBC, and Progesterone between Menopausal and Non-Menopausal Women with Uterine Fibroid

Table 2 presents the comparison of ESR, serum iron, TIBC, and progesterone levels between menopausal and non-menopausal women with uterine fibroid.

Table 2. Mean Values of ESR, Serum Iron, TIBC, and Progesterone in Women with Uterine Fibroid (Mean $\pm$ S.D).

Parameters	Menopausal Women (N=15)	Non Menopausal Women (N=15)	t-value	p-value
ESR (mm/hr)	70.37 $\pm$ 36.53	70.37 $\pm$ 36.53	0.00	1.000
Serum Iron (μ mol/L)	12.05 $\pm$ 4.14	78.98 $\pm$ 10.45	-32.61	<0.0001*
TIBC (μ mol/L)	153.33 $\pm$ 77.51	341.34 $\pm$ 24.56	-12.67	<0.0001*
Progesterone (ng/mL)	31.44 $\pm$ 20.47	6.89 $\pm$ 2.85	6.50	<0.0001*

Key: ESR – Erythrocyte Sedimentation Rate; TIBC – Total Iron-Binding Capacity; S.D – Standard Deviation; *= significant p value

3. 3. Correlation of Progesterone with ESR, Serum Iron, and TIBC in Women Diagnosed with Uterine Fibroid

Table 3 shows the correlation between serum progesterone levels and ESR, serum iron, and TIBC in women diagnosed with uterine fibroid. Diagrammatic representation is shown in Figure 4.

Table 3. Correlation of Progesterone with ESR, Serum Iron, and TIBC in Women Diagnosed with Uterine Fibroid.

Parameters	N	R	p-value
ESR (mm/hr)	30	0.077	0.6850
Serum Iron ($\mu\text{mol/L}$)	30	0.047	0.8047
TIBC ($\mu\text{mol/L}$)	30	-0.130	0.4923

Key: ESR – Erythrocyte Sedimentation Rate; TIBC – Total Iron-Binding Capacity; S.D – Standard Deviation; *= significant p value.

Relationship Between Progesterone and ESR in Women with Uterine Fibroid

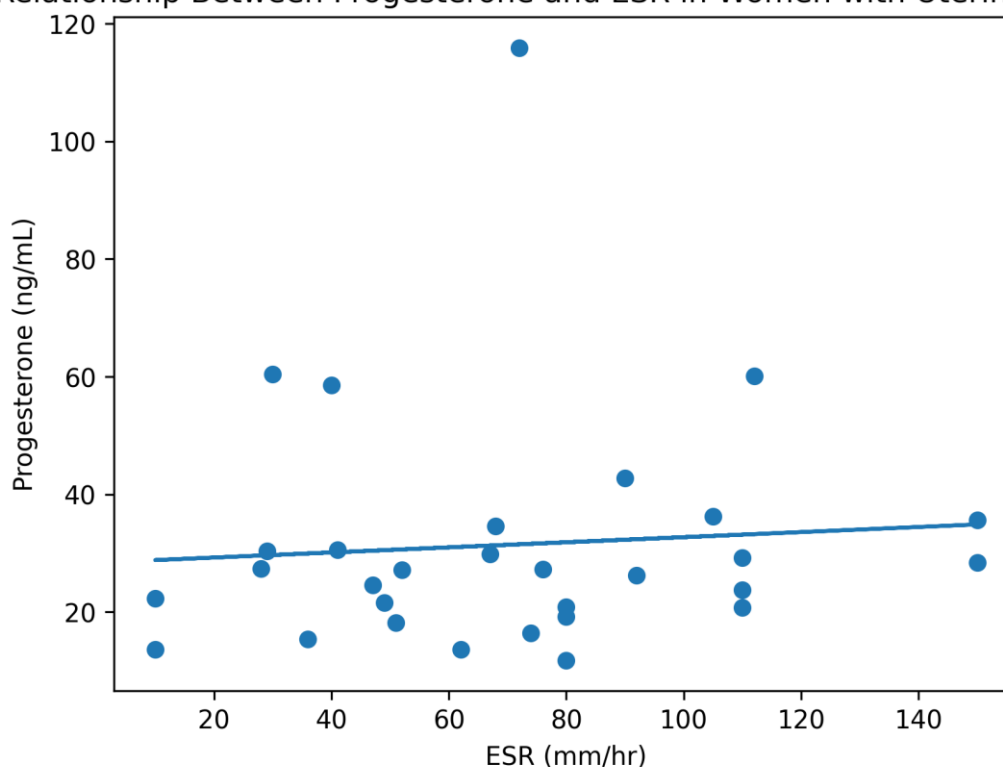


Figure 4. Scatter Plot of Serum Progesterone versus ESR in Women with Uterine Fibroid.

3. 4. Transferrin Saturation (%) in Women with Uterine Fibroid and Healthy Controls

Transferrin saturation (TSAT) was calculated for all participants using serum iron and total iron-binding capacity. Women with uterine fibroid demonstrated markedly lower mean transferrin saturation compared with healthy controls, indicating reduced iron availability in the fibroid group. The results are shown in Table 4 and Figure 5

Table 4. Mean Transferrin Saturation (%) in Women with Uterine Fibroid and Healthy Controls.

Group	N	Mean TSAT (%)
Uterine Fibroid	30	10.08
Control	30	45.23

Mean Transferrin Saturation (%) in Women with Uterine Fibroid and Healthy Controls

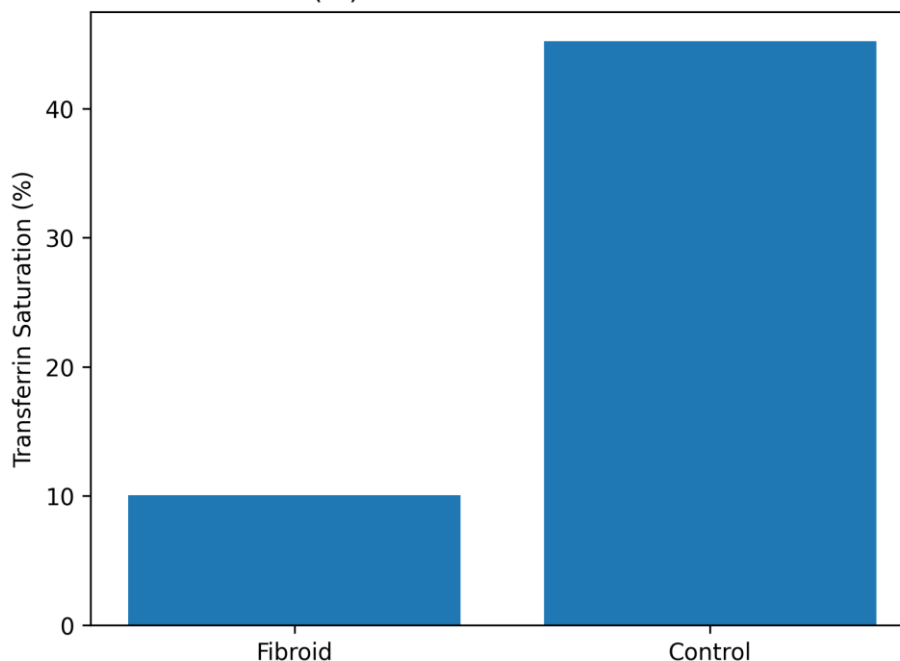


Figure 5. Mean Transferrin Saturation (%) in women with Uterine Fibroid and Healthy Controls.

3. 5. Prevalence of Iron Deficiency and Elevated ESR among Women with Uterine Fibroid

Using transferrin saturation <20% as a criterion for iron deficiency and ESR >20 mm/hr as a marker of elevated inflammatory activity, the prevalence of these abnormalities was determined among women with uterine fibroid. The results are shown in Table 5.

Table 5. Prevalence of Iron Deficiency and Elevated ESR in Women with Uterine Fibroid.

Parameter	Criterion	Frequency (n)	Percentage (%)
Iron Deficiency	TSAT < 20%	26	86.7
Elevated ESR	ESR > 20 mm/hr	28	93.3

3. 6. Effect Size (Cohen's d) of Differences between Fibroid and Control Groups

Effect size analysis was conducted to determine the magnitude of differences between women with uterine fibroid and healthy controls for the studied parameters. The results are shown in Table 6.

Table 6. Effect Size (Cohen's d) for Key Study Parameters.

Parameter	Cohen's d	Magnitude
ESR	2.23	Very large
Serum Iron	-2.14	Very large
TIBC	1.41	Large
Progesterone	1.65	Large

3. 7. ESR-Stratified Subgroup Analysis among Women with Uterine Fibroid

Women with uterine fibroid were stratified according to ESR levels to explore trends in iron indices and progesterone across varying degrees of inflammatory activity. The results are shown in Table 7.

Table 7. Distribution of ESR Categories among Women with Uterine Fibroid.

ESR Category (mm/hr)	Frequency (n)	Percentage (%)
≤20	2	6.7
21–50	7	23.3
51–100	11	36.7
>100	10	33.3

3. 8. Progesterone-Based Subgroup Analysis in Women with Uterine Fibroid

Participants were categorized into low and high progesterone groups using the median progesterone value to examine distributions of inflammatory and iron parameters. The results are shown in Table 8.

Table 8. Progesterone-Based Subgroup Distribution among Women with Uterine Fibroid.

Progesterone Group	Criterion	Frequency (n)	Percentage (%)
Low Progesterone	< Median	15	50.0
High Progesterone	≥ Median	15	50.0

4. DISCUSSION

This study assessed erythrocyte sedimentation rate (ESR), iron indices (serum iron, total iron-binding capacity, and transferrin saturation), and progesterone levels in women diagnosed with uterine fibroid in Imo State compared with age-matched healthy controls. The findings demonstrate a consistent pattern of elevated ESR, reduced circulating iron with compensatory increases in iron-binding capacity, markedly reduced transferrin saturation, and higher progesterone levels among women with uterine fibroid. These alterations collectively reflect the inflammatory, hematological, and hormonal milieu associated with leiomyoma pathophysiology and its clinical manifestations, particularly heavy menstrual bleeding and iron depletion (Bulun *et al.*, 2025; Yang *et al.*, 2022; Donnezet *et al.*, 2022).

The significantly elevated ESR observed in women with uterine fibroid suggests increased systemic inflammatory activity and/or hematological changes that promote erythrocyte aggregation. ESR is a well-established but nonspecific marker influenced by plasma acute-phase proteins, particularly fibrinogen, as well as red blood cell characteristics, and it rises in both inflammatory states and certain hematologic conditions (Brigden, 1999; Tishkowski and Gupta, 2023).

Emerging evidence indicates that uterine fibroids are associated with a pro-inflammatory uterine environment characterized by dysregulated cytokine signaling, immune cell infiltration, and extracellular matrix remodeling, all of which contribute to fibroid growth and symptomatology (Bulun *et al.*, 2025; Regidor *et al.*, 2025; Yang *et al.*, 2022). Studies examining inflammatory markers in women with fibroids and related gynecologic disorders have reported associations between fibroids and systemic inflammatory changes, although the magnitude of these associations varies across populations (Gleason *et al.*, 2022; Ishikawa *et al.*, 2024).

The very high ESR values recorded in this cohort may therefore reflect a combination of inflammatory signaling intrinsic to fibroid biology and secondary effects of iron deficiency or anemia, both of which are known to augment ESR values (Brigden, 1999; Donnezet *et al.*, 2022). A central finding of this study is the significant reduction in serum iron and transferrin saturation, accompanied by elevated TIBC, in women with uterine fibroid. This pattern is characteristic of iron deficiency, where depletion of iron stores leads to increased hepatic

synthesis of transferrin and reduced circulating iron availability (Al-Naseem *et al.*, 2021; Peyrin-Biroulet *et al.*, 2015).

Transferrin saturation provides a clinically meaningful assessment of iron availability, and thresholds below approximately 20% are widely used to indicate iron deficiency in diverse clinical settings (Peyrin-Biroulet *et al.*, 2015; Hands *et al.*, 2024). The high prevalence of transferrin saturation below this threshold in the fibroid group underscores a substantial burden of iron deficiency in this population.

The most plausible explanation for this finding is leiomyoma-associated heavy menstrual bleeding, which represents one of the leading causes of iron deficiency and iron deficiency anemia among women of reproductive age (Munro *et al.*, 2011; Donnez *et al.*, 2022). Contemporary clinical guidance emphasizes that iron deficiency may be present even before overt anemia develops and that reliance on hemoglobin alone can underestimate iron depletion in women with abnormal uterine bleeding (Al-Naseem *et al.*, 2021; Munro, 2023).

In addition, chronic low-grade inflammation associated with fibroid pathology may contribute to functional iron restriction via hepcidin-mediated mechanisms, further reducing serum iron availability despite increased iron-binding capacity (Donnez *et al.*, 2022; Regidor *et al.*, 2025). The significantly higher serum progesterone levels observed in women with uterine fibroid are consistent with the well-established role of progesterone in fibroid development and growth. Uterine leiomyomas exhibit increased expression of progesterone receptors, and progesterone signaling promotes smooth muscle cell proliferation, inhibition of apoptosis, and extracellular matrix accumulation within fibroid tissue (Kim and Sefton, 2012; Ali *et al.*, 2023). Clinical trial evidence further supports the centrality of progesterone signaling in fibroid biology, as selective progesterone receptor modulators such as ulipristal acetate have demonstrated efficacy in reducing fibroid-related bleeding and improving symptoms (Donnez *et al.*, 2012a; Donnez *et al.*, 2012b). These therapeutic effects reinforce the biological plausibility of elevated progesterone levels in women with fibroids.

Nevertheless, interpretation of circulating progesterone concentrations warrants caution, as progesterone levels vary markedly across the menstrual cycle and are sensitive to the timing of sample collection. In addition, immunoassay-based hormone measurements may exhibit analytical variability, particularly at lower concentrations (Stanczyk *et al.*, 2003; Handelsman *et al.*, 2017). These factors should be considered when interpreting hormonal differences, and future studies would benefit from standardized cycle-phase sampling or advanced analytical methods such as mass spectrometry.

Stratified analyses based on ESR and progesterone levels suggest that iron deficiency and inflammatory changes are not confined to a narrow subset of fibroid patients but are distributed across varying levels of inflammatory and hormonal activity. This observation aligns with current understanding that fibroids represent a heterogeneous condition in terms of molecular features and symptom severity, yet often converge on shared clinical consequences such as heavy menstrual bleeding and iron depletion (Yang *et al.*, 2022; Sefah *et al.*, 2023).

Age-stratified analysis and one-way ANOVA revealed no statistically significant differences in ESR, iron indices, or progesterone levels across age groups within the fibroid cohort. This finding suggests that once fibroids are established and symptomatic, associated biochemical disturbances may occur across a broad reproductive age range rather than being restricted to a particular age group (Bulun *et al.*, 2025; Uimari *et al.*, 2022).

The demonstration of widespread iron deficiency and elevated inflammatory markers among women with uterine fibroid in this setting has important clinical implications.

Iron deficiency, even in the absence of severe anemia, is associated with fatigue, reduced physical performance, impaired cognitive function, and increased perioperative risk (Al-Naseem *et al.*, 2021; Munro, 2023).

International guidelines for the management of heavy menstrual bleeding and symptomatic leiomyomas emphasize the need for structured evaluation, including assessment of iron status and timely correction of iron deficiency alongside fibroid-directed therapy (Munro *et al.*, 2011; Bird *et al.*, 2019; ACOG, 2021). The findings of this study support the incorporation of iron studies particularly transferrin saturation—into routine evaluation of women presenting with uterine fibroid in similar resource-constrained settings.

A key strength of this study lies in the integrated assessment of inflammatory, iron, and hormonal parameters, supplemented by transferrin saturation, prevalence estimates, effect size analysis, and subgroup stratification. These approaches enhance clinical interpretability beyond simple mean comparisons.

Limitations include the absence of ferritin and inflammatory biomarkers such as C-reactive protein or hepcidin, which would allow clearer differentiation between absolute iron deficiency and inflammation-driven iron restriction. In addition, variability in menstrual cycle phase at the time of progesterone sampling may have influenced hormone measurements (Stanczyk *et al.*, 2003; Handelsman *et al.*, 2017).

Future research should incorporate ferritin and inflammatory markers, document bleeding severity and fibroid characteristics, and standardize hormonal sampling to further elucidate the complex interplay between inflammation, iron metabolism, and hormonal regulation in uterine fibroid disease (Donnezet *et al.*, 2022; Vannucciniet *al.*, 2024; Bulun *et al.*, 2025).

5. CONCLUSION

This study demonstrates that women with uterine fibroid in Imo State exhibit a distinct pattern of systemic alterations characterized by elevated erythrocyte sedimentation rate, marked iron deficiency evidenced by reduced serum iron and transferrin saturation with compensatory elevation of total iron-binding capacity, and significantly higher circulating progesterone levels compared with age-matched healthy controls. These findings highlight the multifactorial biological impact of uterine fibroids, encompassing inflammatory activity, disordered iron metabolism, and hormonal dysregulation.

The high prevalence of reduced transferrin saturation underscores a substantial burden of iron deficiency among women with uterine fibroid, likely driven by chronic menstrual blood loss and potentially compounded by inflammation-related alterations in iron handling. Importantly, iron deficiency was evident irrespective of age, emphasizing that biochemical consequences of fibroids are not restricted to specific reproductive age groups. Elevated ESR further suggests that fibroid pathology is associated with systemic inflammatory changes, which may coexist with or be amplified by iron depletion.

Although progesterone levels were significantly higher in women with uterine fibroid, the absence of significant correlations between progesterone and inflammatory or iron parameters indicates that progesterone may primarily exert its effects through local tissue-level mechanisms rather than directly influencing systemic inflammation or iron status. This observation aligns with current understanding of progesterone-driven leiomyoma growth mediated by receptor-dependent signaling within fibroid tissue.

Overall, these findings support the need for integrated evaluation of inflammatory markers, iron indices, and hormonal status in the clinical management of women with uterine fibroid, particularly in resource-limited settings where anemia and its consequences remain underrecognized. Routine assessment of iron status, including transferrin saturation, may facilitate earlier identification and correction of iron deficiency, improve quality of life, and optimize peri-operative outcomes. Further studies incorporating ferritin, hepcidin, and additional inflammatory biomarkers are warranted to better delineate the mechanisms linking inflammation, iron metabolism, and hormonal regulation in uterine fibroid disease.

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