

Original Article

Non-Anaemic Iron Deficiency in Female Patients: A Multicenter Study in Islamabad

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Abstract

Objective: To assess the impact of iron status on fatigue levels in non-anemic female patients using the Fatigue Severity Scale.

Methods: A quasi-experimental study was conducted at the Department of Obstetrics and Gynaecology of Akhter Saeed Medical College, Farooq Hospital, and KRL Hospital, Islamabad, from 1st Oct 2023, to 30th Sept 2025. A total of 150 non-anaemic female patients (haemoglobin levels ≥ 12 g/dL in gynaecological patients and ≥ 11 g/dL in obstetric patients) were enrolled in the study after providing written informed consent. Fatigue was assessed using the Fatigue Severity Scale pre- and post-treatment. The primary outcome was improvement in fatigue scores after iron infusion. All collected data were entered and analysed using SPSS version 25.

Results: The baseline mean fatigue severity score was 50.96 ± 10.3 in pregnant women, which considerably decreased to 23.76 ± 6.12 after the intervention. Likewise, the baseline mean fatigue severity scale score was 52.12 ± 9 in gynaecological patients. After treatment, the level decreased to 23.42 ± 5.34 . Both groups showed a marked drop in fatigue scores after the intervention, with similar results on the Fatigue Severity Scale.

Conclusion: Even with normal haemoglobin levels, iron deficiency can lead to increased fatigue in women. When ferric carboxymaltose is administered to iron-deficient women, it efficiently decreases the severity of fatigue, highlighting the value of iron supplements in non-anaemic women with low iron stores.

Keywords: anaemia, ferritin, haemoglobin, iron, iron deficiency.

Introduction

Fatigue is a common symptom reported by non-anaemic women, particularly during pregnancy and in gynaecologic settings.¹ While iron deficiency is well known to cause anaemia, its role in non-anaemic women with iron depletion remains less explored.² Although anaemia is traditionally associated with iron deficiency, there is growing recognition that even non-anaemic individuals with low iron stores can experience fatigue.^{3,4} The Fatigue Severity Scale (FSS) has been used extensively to measure the subjective impact of fatigue, particularly in clinical settings. The FSS demonstrates high reliability, with established internal consistency (Cronbach's $\alpha = 0.81-0.94$) and test-retest reliability ($r \approx 0.84$).⁵

Iron is an essential micronutrient that plays a critical role in oxygen transport and energy metabolism. As 60% of iron stores are involved in erythropoiesis,⁶ a further 30% is integral to respiratory chain function, and 10% is incorporated into myoglobin.⁷ By the time iron deficiency is sufficiently advanced to cause anaemia, the non-erythroid compartments have already been depleted. Therefore, it is possible that iron deficiency, in the absence of anaemia, is associated with reduced functional capacity and is often accompanied by fatigue.⁸ The buildup of iron stores in non-anemic patients has been shown to improve cognitive, symptomatic, and exercise performance.⁹

Although the treatment of iron deficiency anaemia is well established, less attention has been paid to patients who are not anaemic but have low iron stores. These patients may experience symptoms, such as exhaustion, that affect their daily functioning and quality of life. Intravenous ferric carboxymaltose is widely recognised for its efficacy in restoring iron levels; however, its role in reducing fatigue in non-anemic women remains unclear. Therefore, we aimed to evaluate the efficacy of intravenous ferric carboxymaltose, a potent and rapidly acting formulation, in reducing fatigue and improving functional capacity in this specific patient group. In our local context, this condition is frequently under-recognized, resulting in delayed diagnosis and missed opportunities for timely intervention. Recent research has proposed that correcting iron deficiency in women with normal haemoglobin levels markedly reduces feelings of tiredness and restores functional capacity. A randomised trial conducted in 2021 established the advantage of intravenous iron in helping these women feel less tired.¹⁰

This study aimed to understand the effect of low iron on fatigue scores in women with normal haemoglobin, thus underscoring the value of timely diagnosis and management. The findings may also contribute to improving cognitive and physical performance and overall well-being in this population.

Materials And Methods

This quasi-experimental study was conducted in the Department of Obstetrics and Gynaecology at the Farooq Teaching Hospital and KRL Hospital, Islamabad, from 1st Oct 2023, to 30th Sept 2025.

This study was conducted in accordance with ethical standards and principles. Institutional Review Board (IRB) approval was obtained from both hospitals before the commencement of the research. Informed consent

Contributions:

SQ RR SE BR TI NA - Conception, Design
 SQ RR SE BR TI NA - Acquisition, Analysis, Interpretation
 SQ RR SE BR TI NA - Drafting
 SQ RR SE BR TI NA - Critical Review

All authors approved the final version to be published & agreed to be accountable for all aspects of the work.

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was obtained from all participants involved in the study. The research was conducted with respect for participant privacy, confidentiality, and autonomy.

Women between the ages of 18 and 45 years presenting in the outpatient and inpatient departments, with symptoms of fatigue, hemoglobin levels ≥ 12 g/dL for gynecological and ≥ 11 g/dL for obstetric patients, and serum ferritin < 12 ng/mL were included in the study.

Women with chronic illnesses, such as hypertension, diabetes mellitus, rheumatoid disease, thyroid disease, heavy menstrual bleeding, or any malignancies, were excluded from the study.

Using the WHO calculator, considering the prevalence of 10.8%,¹¹ in women with serum ferritin levels < 12 ng/mL, confidence interval 95%, and margin of error 5%, the sample size calculated came out to be 150 patients. Patients were selected by non-probability convenience sampling according to the inclusion criteria. Out of 200 recruited patients, 150 were selected from both inpatient and outpatient departments after written informed consent was obtained. All patients with fatigue had their haemoglobin and serum ferritin levels measured.

The Fatigue Severity Scale (FSS) was used to measure the level and impact of fatigue in participants. The scale consists of nine items, each rated on a 7-point Likert scale. A score of 1 indicated minimal impact or disagreement with the statement, whereas a score of 7 reflected strong agreement or severe impact. The FSS was administered to all recruited patients with serum ferritin levels < 12 ng/mL to establish a baseline (pre-intervention score). The FSS questionnaire was administered by the attending doctor, who filled out the form after conducting an interview with each patient, ensuring accuracy and consistency in responses.

A structured data collection form was used to record demographic information, including age, parity, marital status, education level, and employment status, as well as clinical data such as haemoglobin and serum ferritin levels and relevant medical history. Additionally, all participants had telephone access to facilitate follow-up and post-intervention data collection.

Patients with iron deficiency were treated with a single dose of intravenous ferric carboxymaltose 500 mg diluted in 100 ml of normal saline after a test dose, as per hospital protocol, with the cost of the medication covered by the patients as part of their standard clinical care. No additional iron supplements were administered during the study period. Following a 3-week intervention, the same questionnaire was re-administered (post-intervention score), allowing for the assessment of changes in fatigue severity. The comparison between the pre- and post-intervention scores served as an indicator of the effectiveness of the intervention. Data were double-entered to ensure accuracy, and missing or inconsistent entries were rechecked using patient contact when necessary. The statistical tests applied included the Shapiro–Wilk test for normality assessment of variables, Spearman's rho correlation analysis, and the Wilcoxon signed-rank test for comparing baseline and post-treatment scores on the Fatigue Severity Scale (FSS).

Results

The mean age of the participants was 30 ± 4.14 years, 28.44 ± 4.15 years in obstetric patients, and 31.56 ± 3.5 years in gynaecological patients. The mean parity was 2.44 (95% CI: 2.29–2.59; SD = 0.945), with a median of 2.00. The mean haemoglobin (Hb) level was 12.05 ± 0.555 g/dL, with 11.5 ± 0.3 g/dL among obstetric patients and 12.5 ± 0.3 g/dL in patients with gynaecological problems. The mean ferritin level was 8.31 ± 2.4 ng/mL, with 8.12 ± 2.44 ng/mL in obstetric cases and 8.51 ± 2.3 ng/mL in gynaecological cases. The mean baseline FSS was 51.54 ± 9.718 , and the post-treatment FSS was 23.59 ± 5.684 . The mean baseline FSS score was 50.96 ± 10.3 in obstetrics, which significantly reduced to 23.76 ± 6.0 after treatment. Similarly, the mean baseline FSS score was 52.12 ± 9.0 in gynaecological patients, which was reduced to 23.42 ± 5.34 after treatment. Both groups demonstrated a marked reduction in fatigue severity scores following treatment, with comparable post-treatment FSS values across the obstetrics and gynaecology groups.

Normality of the variables was assessed using the Shapiro–Wilk (S–W) test. The results indicated that age did not follow a normal distribution, with significant deviations observed in the S–W test (statistic = 0.978, $p = 0.016$). Similarly, parity (S–W statistic = 0.879, $p < 0.001$), haemoglobin (Hb) (S–W statistic = 0.954, $p < 0.001$), ferritin levels (S–W statistic = 0.901, $p < 0.001$), baseline fatigue severity score (FSS) (S–W statistic = 0.868, $p < 0.001$), and post-treatment FSS (S–W statistic = 0.785, $p < 0.001$) all significantly deviated from normality. Considering the above findings, none of the variables were normally distributed; therefore, we used nonparametric methods for statistical analyses.

Weak negative correlation was found between Ferritin levels and Baseline Fatigue Severity Score (FSS) ($\rho = -0.219$, $p = 0.007$), when Spearman's rho correlation analysis was done, and this indicated that low ferritin levels were related to raised fatigue severity. A weak negative correlation was also detected between ferritin levels and parity ($\rho = -0.059$, $p = 0.471$); however, this association was not statistically significant. A weak positive correlation was detected between parity and baseline FSS ($\rho = 0.262$, $p = 0.001$), which shows an inclination for advanced parity to be related to greater fatigue severity (Figure 1).

Ferritin levels were not significantly correlated with age ($\rho = -0.054$, $p = 0.511$). A weak positive correlation was detected between baseline fatigue severity scale scores and age ($\rho = 0.149$, $p = 0.069$), signifying a possible inclination for the severity of fatigue to increase with age, even though this association was not statistically significant at the 0.05 level (Figure 2).

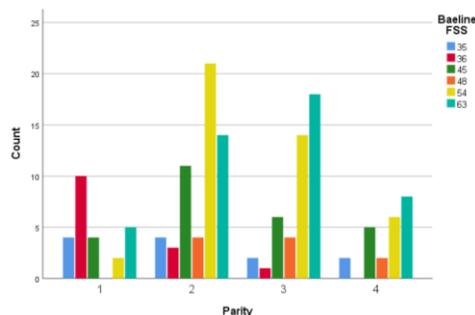


Figure 1: Correlation between age and baseline fatigue severity score (FSS)(n=150)

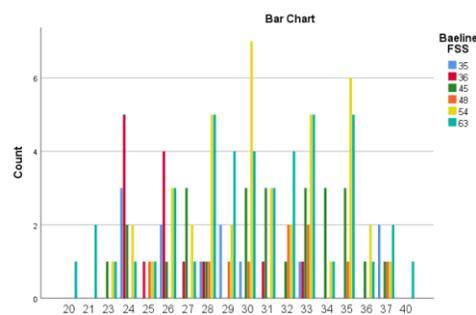


Figure 2: Correlation between age and baseline fatigue severity score (FSS)(n=150)

A Wilcoxon signed-rank test was executed to make a comparison between the reference point FSS and post-intervention Fatigue Severity Scale (FSS) scores. The findings have shown a noteworthy enhancement in the FSS scores after management. A total of 150 cases (N = 150) exhibited an enhancement in the post-treatment Fatigue Severity Scale FSS scores in comparison to the reference point, with a mean rank of 75.50 and a sum of ranks of 11325.00 (Table 1).

Table 1: Changes in Fatigue Severity Scale scores before and after iron supplementation (n=150)

	Group	Mean	Std Error mean
Baseline FSS	Obstetrics(N=75)	50.96±10.398	1.202
Post-treatment FSS		23.76±6.036	0.697
Baseline FSS	Gynaecology	52.12±9.019	1.041
Post-treatment FSS	(N=75)	23.41±5.345	0.617

The Wilcoxon signed-rank test generated a Z-value of -10.720, and the calculated p -p-value was 0.000 (2-tailed), demonstrating that the enhancement in Fatigue Severity Scale scores post-treatment is statistically significant. (Table 2).

Table 2: Wilcoxon Signed Ranks Test

		N	Mean Ranks	Sum of Ranks
Baseline FSS-Post Treatment FSS	Negative Ranks	0 ^a	00	00
	Positive Ranks	150 ^b	75.50	11325.00
	Ties	0 ^c		
	Total	150		
Baseline FSS-Post treatment FSS				
Z		-10.720b		
Asym. Sig. (2-tailed)		0.000		

a. Baseline FSS<Post Treatment FSS, b. Baseline FSS>Post Treatment FSS, baseline FSS=Post Treatment FSS

a. Wilcoxon Signed Ranks Test, b. Based on negative ranks

Discussion

The results of this study indicate the substantial effect of parenteral ferric carboxymaltose in decreasing lethargy (as measured by the Fatigue Severity Scale in women with exhausted iron reserves who had normal haemoglobin levels). In our study, both gynaecological and pregnant women experienced a considerable reduction in fatigue severity, and the outcome was more significant in women who were not pregnant.

The reference point Fatigue Severity Scale scores specified moderate to severe fatigue in both groups, with pregnant women having a slightly higher total (50.96 ± 10.3) score than non-pregnant women (52.12 ± 9). This is parallel with the existing literature, which has signified that a deficiency of iron, even when there is no haemoglobin deficiency, can result in substantial weakness because of weakened transport of oxygen, less enzymatic action, and impaired neurotransmitter regulation.^{12,13} In 2024, Jyothi et al. reported from India that non-anaemic individuals with low iron stores showed substantial improvement in fatigue scores after taking a low-dose ferrous fumarate supplement.¹² Similarly, Shamsi et al. from the UK found that iron deficiency in patients with cardiac failure was associated with decreased energy levels, and iron repletion treatment improved fatigue and exercise tolerance.¹³

Following treatment with intravenous ferric carboxymaltose, a significant reduction in FSS scores was observed in both groups (p < 0.05). The mean FSS score decreased from 50.96 ± 10.3 (combined baseline) to 23.76 ± 6 (post-treatment), representing a substantial improvement in fatigue severity. The mean fatigue score for obstetric patients decreased from 50.96 ± 10.40 at baseline to 23.76 ± 6.04 post-treatment, whereas in gynaecological patients, it decreased from 52.12 ± 9.02 to 23.41 ± 5.35.

Fatigue scores were slightly lower in gynaecological patients (28.7) than in obstetric patients (27.2), suggesting a possibly greater treatment impact. This trivial dissimilarity may be due to greater reference point fatigue or fluctuating somatic stress. However, both groups displayed comparable scores after intervention, indicating that the intervention was effective across the board. Additional enquiries could assist in elucidating what energies this difference represents to better tailor treatment.

Parenteral ferric carboxymaltose appears to be a practical choice, especially in situations in which iron is ineffective or poorly absorbed.¹¹ This was supported by group research conducted in Australia by Wyssusek et al., who reported major improvements in fatigue levels and overall well-being in females who received intravenous ferric carboxymaltose, with 82% of females reporting satisfaction with the therapy.⁹ The differential response between gynaecological and obstetric patients suggests that the underlying physiological and metabolic factors influencing fatigue may vary. Parallel benefits have also been revealed in other patient clusters, including those with prolonged lethargy.^{12,14}

Iron plays a vital role in energy synthesis, and its insufficiency can weaken muscle function and reduce somatic activity, leading to lethargy. This was reinforced by a 2024 study by Li et al., who showed that more than 60% of women with unresolved lethargy had reduced iron levels despite normal haemoglobin levels.¹⁵ The study indicated how iron insufficiency can impair energy production and disrupt mood-related neurotransmitters, including dopamine, thus instigating mutual somatic and psychological lassitude in these women.

Previous studies have revealed that iron supplementation can reduce lethargy in women with normal haemoglobin levels. A randomised controlled trial by Macher et al. 16 established that parenteral iron infusions considerably improved fatigue scores in non-anaemic women with iron deficiency.¹⁶ In their research, fatigue scores declined by an average of 8.8 points on a 100-point scale after intravenous iron therapy, with > 75% of contributors noting an obvious enhancement in daily energy levels. Likewise, research by S. Semic et al. showed that iron supplements taken by mouth treated the fatigue severity in non-anaemic women who were deficient in iron.¹⁷ This forthcoming research reported that 68% of patients had at least a 50% drop in fatigue severity in 4 weeks of treatment, supporting the proficiency of low-dose oral iron in handling the symptoms amongst this population. Research has revealed that serum ferritin levels < 50 ng/mL are associated with increased fatigue severity.¹⁸

A strong point of the research is its involvement of both admitted patients and the population attending outdoor clinics, which augments the generalisability of the results. The use of an authenticated fatigue scale (FSS) and objective follow-up ensured a reliable assessment of fatigue

levels pre- and post-treatment.¹⁹ Our research complements prevailing medicinal writings by providing native inhabitants with data on the efficiency of parenteral iron in reducing lethargy in non-anaemic women with reduced iron stores, a population often overlooked in routine clinical practice. This supports the growing body of evidence that managing iron deficiency, even in the absence of anaemia, can significantly improve energy levels and the quality of life.²⁰

Restrictions comprise a comparatively small sample size and the absence of a control cluster. Additional enquiries might also discover whether merging intravenous and oral iron supplementation could produce supplementary developments. Overall, this research highlights the significance of early detection and management of iron insufficiency, even in the absence of anaemia, as a real-world methodology to improve fatigue and the value of life in females. The outcomes uphold the incorporation of ferritin screening and targeted treatment into routine clinical care.

Conclusions

This study contributes to the growing body of evidence supporting the treatment of iron deficiency in non-anaemic patients. Intravenous ferric carboxymaltose considerably lessened fatigue in this population. Routine case selection and treatment of iron deficiency in non-anaemic women may therefore improve their quality of life and general well-being.

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