

An Observational Comparative Study of Oral and Intravenous Iron Therapy for Iron Deficiency Anemia in a Tertiary Care Hospital

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ABSTRACT

Background: Iron Deficiency Anemia (IDA) is one of the most prevalent nutritional disorders in the world associated with substantial morbidity. Intravenous iron therapy has been considered as a more efficacious alternative to standard oral iron therapy because of its rapid correction of iron deficiency, improved tolerability, and better compliance among patients. **Objectives:** This study aimed to compare the efficacy, safety, and cost-effectiveness of intravenous iron with oral iron in the treatment of IDA. **Materials and Methods:** A Prospective observational study was conducted at tertiary care hospital, over a six-month among 84 adult patients diagnosed with IDA who received oral iron or intravenous iron therapy. Hemoglobin levels before and after iron therapy were compared using paired *t*-tests. Analysis of Covariance (ANCOVA) was performed to compare post treatment hemoglobin after adjustment for baseline hemoglobin as covariate and two-way repeated-measures ANOVA evaluated changes over time and between groups. A *p*-value <0.001 was considered statistically significant. **Results:** The study comprises 9 males and 75 females, with a predominance of premenopausal women. Hemoglobin levels increased significantly in both groups following iron therapy. Patients receiving intravenous iron therapy demonstrated a significant increase in hemoglobin 2.13 g/dL compared with oral iron therapy 0.56 g/dL. ANCOVA demonstrated a significant difference in post treatment hemoglobin between groups $F(1,81)=5.71, p=0.019$. ANOVA showed significant effects of time $F(1,82)=139.1, p<0.001$, and significantly time $\times$ treatment interaction $F(1,82)=47.4, p<0.001$, indicating superior hematological improvement with intravenous iron therapy. Gastrointestinal adverse effects occurred in 21.4% participants receiving oral iron therapy, whereas mild hypersensitivity reactions in 11.90% in patients administered with intravenous iron therapy. The Incremental Cost-Effectiveness Ratio (ICER) for intravenous iron therapy was ₹4076.43 per additional g/dL increase in haemoglobin. **Conclusion:** Both intravenous and oral iron therapy significantly improve hemoglobin levels, with greater improvement observed in intravenous therapy, offering a safe and efficient alternative to patients with moderate to severe iron deficiency anemia. The between group difference remained significant after adjustment for baseline hemoglobin.

Keywords: Cost-effectiveness, Ferric carboxy maltose, Hemoglobin, Intravenous iron therapy, Iron deficiency anemia, Oral iron therapy.

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INTRODUCTION

Anemia is a common hematological clinical condition marked by a decrease in hemoglobin concentration or circulating red blood cell bulk, resulting in decreased oxygen delivery to bodily tissues. According to the World Health Organization, anemia is

defined as hemoglobin levels lowering below 13 g/dL in men and 12 g/dL in women. The condition represents a broad spectrum of disorders that differ in underlying mechanisms, including reduced erythrocyte production, abnormal red cell development, or increased loss or destruction of red blood cells (DiPiro *et al.*, 2023). Iron Deficiency Anemia (IDA) is the most widespread form of anemia globally, impacting an estimated 1.6 billion people and notably contributing to maternal and pediatric morbidity and mortality (Bairwa *et al.*, 2017). IDA, the most prevalent type of nutritional impairment, results from a sustained negative iron balance caused by factors such as inadequate nutrition, chronic blood loss, malabsorption, or increased physiological demands (Das *et al.*, 2020).



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The clinical consequences are profound, impacting oxygen transport, energy metabolism, and cognitive function, underscoring the critical need for effective treatment strategies to replenish iron stores and restore hemoglobin levels (Kumari *et al.*, 2024). It primarily presents as a microcytic hypochromic anemia caused by low iron availability for production of hemoglobin. Iron homeostasis is a tightly regulated process involving intestinal absorption, plasma transport, tissue storage, and recycling, with disruption at any level potentially leading to deficiency (DiPiro *et al.*, 2023). Iron depletion often develops gradually and may remain clinically silent before progression to overt anemia. Timely recognition through appropriate laboratory evaluation is essential, as untreated iron deficiency can adversely affect physical performance, cognitive function, and overall quality of life (DiPiro *et al.*, 2023).

Historically, oral iron therapy has been the mainstay of treatment for IDA due to its convenience, low cost, and ease of administration. However, its effectiveness is frequently compromised by several limitations. Poor gastrointestinal absorption, a high incidence of adverse effects including constipation, nausea, and epigastric pain, and the resultant poor patient adherence often undermine treatment success, requiring several months of consistent use to fully replenish iron stores (Das *et al.*, 2020). These challenges have prompted a search for more reliable alternatives, particularly in settings where rapid correction of anemia is desired or oral therapy has failed. Intravenous (IV) iron therapy has emerged as a compelling option, offering a direct route of administration that bypasses the gastrointestinal tract. Modern IV iron formulations have demonstrated improved safety profiles compared to their predecessors, facilitating more rapid and significant increases in hemoglobin and ferritin level (Kumari *et al.*, 2024). While IV iron offers advantages in terms of safety and efficacy, it is associated with higher costs, requires healthcare infrastructure for administration, and carries a small risk of infusion-related reactions. Consequently, the choice between oral and IV iron therapy involves a careful assessment of clinical urgency, patient tolerance, and resource availability (Kumari *et al.*, 2024).

The present research was undertaken to comparatively evaluate efficacy and safety of oral and intravenous iron therapy in iron deficiency anemia patients. By evaluating their short-term effectiveness in improving hemoglobin level, assessing their adverse drug reactions and evaluating cost-effectiveness, this study aims to provide evidence-based guide to healthcare workers in optimizing treatment strategies thereby improving patient care.

MATERIALS AND METHODS

Study design, place and duration

A prospective, observational, comparative study was conducted in the Department of General Medicine at a tertiary care teaching hospital, for a period of six months. Treatment response was

assessed at baseline and after 14 days of initiation of the respective iron therapy.

Inclusion Criteria

The study included patients of either gender >18 years of age with confirmed diagnosis of IDA on treatment with either oral or intravenous iron therapy, willing to participate and provide informed consent. Patients with mandatory Hb < 12g/dL (Females) or Hb < 13g/dL (Males) and Serum ferritin <30 ng/mL laboratory results to confirm IDA and Transferrin saturation < 20% additionally were included.

Patients with heart failure, chronic kidney disease, acute kidney injury, inflammatory bowel disease were also included in the study as these conditions are common causes or contributors to iron deficiency anemia in clinical practice excluding them will create generalization which contradicts to the real-world setting.

Exclusion Criteria

Patients with anemia due to other etiologies such as hemolytic, aplastic or megaloblastic anemia and patients with known history of hypersensitivity to iron formulations, pediatric patients were excluded.

Sample size calculation

Sample size was calculated using the formula $N = (Z_{\alpha/2} + Z_{1-\beta})^2 \times (\sigma^2) / d^2$ where, Significance level (α)=0.05 Confidence level=95%, Power=80%, Standard deviation (σ)=0.349, Expected difference (d)=0.20, $Z_{\alpha/2}$ =1.96 and $Z_{1-\beta}$ =0.84. It calculated as 47.77, approximately 48 participants per group, 96 participants in total. However, due to constraint study time period and predefined inclusion and exclusion criteria a total of 84 participants were included comprising 42 in each group receiving oral and intravenous iron therapy respectively.

Study Population and group allocation

During the study, all eligible participants who met the predefined inclusion, exclusion criteria and provided informed consent were included in the study. Patients were not randomly assigned to oral or intravenous iron therapy groups. Instead, they were categorized into the respective treatment groups according to the iron therapy they received as part of their clinical management. All the participants enrolled in the study were required to have hemoglobin and serum ferritin levels before initiation of iron therapy as both parameters were essential for the confirmation of iron deficiency anemia. Transferrin saturation was additionally assessed to support the overall diagnosis.

Study groups

Oral iron therapy group ($n=42$) patients received oral iron supplementation in the form of iron salts. The majority of patients ($n=41$) were prescribed Ferrous Ascorbate 100 mg once

daily, while one patient ($n=1$) received Ferrous Sulphate 200 mg once daily. The prescribed doses refer to the iron salt preparation not the exact elemental iron content. The dose and type of oral iron preparation was decided by the treating physician based on patient's clinical condition and laboratory parameters. As per the treatment regimen oral iron therapy was planned for 3 months with hemoglobin assessment at 14 days. Treatment continued and the outcome of this study reflects hemoglobin status at day 14 only not treatment completion.

Intravenous (IV) iron therapy group ($n=42$) patients received intravenous iron supplementation in the form of iron carbohydrate complex belonging to class colloidal nanoparticles. The majority of patients ($n=41$) were administered Ferric Carboxy Maltose (FCM) in the varying doses of 400 mg, 500 mg, 1000 mg, individualized based on patients' clinical condition and serum ferritin levels, while one patient ($n=1$) received Iron Sucrose 200 mg intravenously. The dose and type of intravenous iron preparation was decided by the treating physician based on patient's clinical condition and laboratory parameters. The prescribed doses do not refer to the exact elemental iron content. Hemoglobin was assessed after 14 days of intravenous iron therapy as a part of this study. During the 14 days study period the patient was not switched to oral iron preparation.

All participants were followed up for a period of 14 days following initiation of iron therapy. At baseline, Hemoglobin and serum ferritin was assessed for all participants, while transferrin saturation assessed only for participants whose laboratory record was available. Baseline serum iron and Total Iron Binding Capacity (TIBC) although was planned originally but as these parameters were consistently not performed across all the participants and could not be reliably reported so was dropped. At the day 14 hemoglobin was the only parameter which was reassessed to evaluate the hematological response to iron therapy in both treatment groups, as serum ferritin and transferrin saturation were not repeated.

Ethical Approval

The study was approved by Institutional Review Board (IRB) of Apollo Institute of Medical Sciences, Jubilee Hills, Film Nagar, Hyderabad, Telangana IRB Approval No: AIMSR/ARB/RC/2025/05/33. The study was conducted in accordance with the principles of the Declaration of Helsinki. Patient confidentiality and data privacy were maintained throughout the study.

Data collection

Data were collected using a self-designed Case Report Form (CRF), developed based on the study objectives and relevant literature. The CRF captured patient demographics, past medical history, medication history, allergy history, menstrual history, prescribed medications, laboratory parameters, and anemia management details.

Adverse Drug Reaction (ADR)

Adverse Drug Reactions (ADRs) were monitored throughout the study period using both spontaneous reporting by patients and active monitoring at follow-up. Patients were encouraged to report any unexpected symptoms or discomfort.

Statistical Analysis

Data collected from all participants were entered into Microsoft Excel and analyzed using Jamovi statistical software (version 2.7.24). Categorical variables were summarized as frequencies and percentages, while continuous variables were expressed as mean $\pm$ Standard Deviation (SD). A paired t -test was used to compare hemoglobin within each treatment group before and after therapy. Because baseline hemoglobin differed between two groups, Analysis of Covariance (ANCOVA) was performed to compare post treatment hemoglobin levels between treatment groups with baseline hemoglobin as a covariate in preference to an unadjusted independent t -test. A two-way repeated-measures Analysis of Variance (ANOVA) was used to evaluate the effects of treatment (oral iron vs. intravenous iron), time (pre-treatment vs. post-treatment), and their interaction on hemoglobin levels. Cost-effective analysis was calculated using Incremental Cost-Effectiveness Ratio (ICER) (KG, 2016), as difference in cost between intravenous and oral iron therapies divided by difference in effectiveness between two groups. A p -value of <0.001 was considered statistically significant for all analyses.

RESULTS

A total of 84 patients diagnosed with iron deficiency anemia who fulfilled the inclusion criteria were included in the study, with 42 patients into oral iron therapy and intravenous iron therapy group. The study population comprised majorly of females 75 (89.29%) and males 9 (10.71%), suggesting higher prevalence of IDA among females, predominately pre-menopause females (Table 1). The mean age of the study population was 36.7 years, ranging from 19 to 66 years. The highest proportion of patients belonged to the 19 - 28 and 39 - 48 years age groups, comprising 25 (29.76%) patients, followed by the 29 - 38 years age group with 22 (26.19%) patients. The majority of patients receiving oral iron therapy belonged to the 19-28 years age group 13 (30.95%), whereas the majority of patients receiving intravenous iron therapy belonged to the 39-48 years age group, 14 (33.33%).

Among the study population, the most common etiologies of IDA were menorrhagia, chronic blood loss, and nutritional deficiency. The most common associated comorbid conditions included gastrointestinal diseases, such as hemorrhoids, peptic ulcer disease, and Crohn's disease, followed by chronic kidney disease/acute kidney injury, thyroid disorders, cardiovascular disease, and pregnancy, while several patients also presented with concurrent infectious illnesses (Table 2). The most frequently reported clinical manifestation was shortness of breath ($n=26$),

followed by dizziness ($n=15$), fatigue ($n=11$), generalized weakness ($n=9$), nausea and vomiting ($n=8$), and palpitations ($n=5$). Pica was the least frequently reported symptom, occurring in only one patient (Table 3).

Baseline laboratory tests included Hemoglobin (Hb) and serum ferritin. The mean baseline hemoglobin level before treatment was 8.21 ± 1.01 g/dL for oral iron therapy and 6.40 ± 1.35 g/dL for IV iron therapy. According to the severity distribution, the majority of patients in both groups have moderate anemia (60, 71.43%), while intravenous iron therapy patients had a higher proportion of severe anemia. When comparing serum ferritin levels, the majority of patients receiving oral iron therapy had severe ferritin deficiency, whereas moderate to severe ferritin deficiency predominated in intravenous iron therapy (Table 4).

Following 14 days of treatment, significant improvement was observed in both treatment groups. The mean hemoglobin increased to 8.77 ± 0.93 g/dL after oral iron therapy and 8.53 ± 0.92 g/dL in after IV iron therapy. The mean hemoglobin increment

was 0.56 g/dL and 2.13 g/dL in the oral and intravenous therapy groups, respectively. Paired t -test analysis showed a statistically significant increase in mean hemoglobin levels from baseline to post-treatment in both oral ($t=-10.0$, $p<0.001$) and intravenous iron therapy groups ($t=-9.63$ $p<0.001$) (Table 5).

As baseline hemoglobin levels differed substantially between oral and IV group, Analysis of Covariance (ANCOVA) was performed with baseline hemoglobin as covariate. After adjustment of baseline hemoglobin, statistically significant difference in post-treatment haemoglobin was observed in both the treatment groups, $F(1,81)=5.71$, $p=0.019$, partial $\eta^2=0.066$. Baseline hemoglobin was significant covariate $F(1,81)=32.83$, $p<0.001$, partial $\eta^2=0.288$ (Table 6).

Repeated-measures Analysis of Variance (ANOVA) demonstrated a highly significant time effect, indicating that hemoglobin levels increased significantly from pre-treatment to post-treatment irrespective of treatment group ($F(1,82)=139.1$, $p<0.001$, partial $\eta^2=0.629$). A significant group effect was also observed,

Table 1: Demographic characteristics of the study population.

Category	Oral Iron Therapy $n=42$ (%)	IV Iron Therapy $n=42$ (%)	Overall $n=84$ (%)
Age Group (years)			
19-28	13 (30.95)	12 (28.57)	25 (29.76)
29-38	11 (26.19)	11 (26.19)	22 (26.19)
39-48	11 (26.19)	14 (33.33)	25 (29.76)
49-58	5 (11.90)	4 (9.52)	9 (10.71)
59-68	2 (4.76)	1 (2.38)	3 (3.57)
Gender			
Female	36 (85.71)	39 (92.86)	75 (89.29)
Male	6 (14.29)	3 (7.14)	9 (10.71)
Menstrual status among females			
Pre-menopause	56 (74.67) of females		
Menopause	19 (25.33) of females		

IV=Intravenous.

Table 2: Clinical presentation of study population.

Clinical Presentation	Oral Iron Therapy ($n=42$)	IV Iron Therapy ($n=42$)	Overall ($n=84$)
SOB	10	16	26
Dizziness	8	7	15
Fatigue	5	6	11
Generalized weakness	3	6	9
Nausea and vomiting	5	3	8
Palpitations	1	4	5
Pica	0	1	1

IV=Intravenous, SOB=Shortness of breath, Categories are not mutually exclusive, a patient may report more than one clinical presentation, so count do not sum for $n=84$.

Table 3: Underlying associated condition of the study population.

Condition	Oral Iron Therapy (n=42)	IV Iron Therapy (n=42)	Overall (n=84)
GI Diseases	5	2	7
Secondary to Blood loss	4	3	7
Menorrhagia	4	3	7
Secondary to nutritional	2	4	6
CKD / AKI	1	3	4
Pregnancy	1	0	1
Heart disease	1	0	1
With other comorbid conditions	24	27	51

IV=Intravenous, GI=Gastrointestinal, CKD=Chronic Kidney Disease, AKI=Acute Kidney Injury, Categories are not mutually exclusive, a patient may have more than 1 associated condition, so count do not sum for n=84.

Table 4: Distribution of laboratory data among study population.

Severity	Oral Iron Therapy n=42 (%)	IV Iron Therapy n=42 (%)	Overall n=84 (%)
Serum Hb (g/dL)			
Severe (3.9-6.2 g/dL)	2 (4.76)	15 (35.71)	17 (20.24)
Moderate (6.2-8.5 g/dL)	38 (90.48)	22 (52.38)	60 (71.43)
Mild (8.5-10.8 g/dL)	2 (4.76)	5 (11.91)	7 (8.33)
Serum Ferritin (µg/mL)			
Severe (3-13 µg/mL)	27 (64.29)	19 (45.24)	46 (54.76)
Moderate (13-23 µg/mL)	14 (33.33)	20 (47.62)	34 (40.48)
Mild (23-33 µg/mL)	1 (2.38)	3 (7.14)	4 (4.76)

IV=Intravenous, Hb=Hemoglobin.

demonstrating an overall difference in hemoglobin response between patients receiving intravenous iron therapy and oral iron therapy ($F(1,82)=25.4$, $p<0.001$, partial $\eta^2=0.237$). Furthermore, the significant time $\times$ group interaction ($F(1,82)=47.4$, $p<0.001$, partial $\eta^2=0.367$) indicated that the magnitude of hemoglobin improvement over time differed significantly between the treatment groups, with patients receiving IV iron therapy demonstrating a greater increase in hemoglobin compared with those receiving oral iron therapy (Table 7).

A total of 14 Adverse Drug Reactions (ADRs) were reported among the study population receiving oral and IV iron therapy. Nine ADRs occurred in the oral iron group, whereas five occurred in the intravenous group. Gastrointestinal adverse effects predominated among patients receiving oral iron therapy and included constipation ($n=2$, 4.76%), metallic taste ($n=2$, 4.76%), diarrhea ($n=1$, 2.38%), heartburn ($n=1$, 2.38%) and vomiting ($n=1$, 2.38%). Overall, ($n=33$, 78.57%) patients receiving oral iron therapy reported no adverse effects. In the intravenous iron group ($n=5$, 11.9%), experienced hypersensitivity reactions characterized by urticaria, rash, and facial swelling were reported in five patients. All reported ADR were mild in severity and were

managed symptomatically with no treatment discontinuation or mortality attributable to iron therapy was observed (Table 8).

Cost-effective analysis was performed using Incremental Cost-Effective Ratio (ICER). The total cost of oral iron therapy was ₹100 per treatment course, whereas intravenous iron therapy cost ₹6,500 per treatment course, resulting in a Difference in Cost (DC) of ₹6,400. The mean hemoglobin improvement was 0.56 g/dL in the oral iron group and 2.13 g/dL in the intravenous group, with a Difference in Effect (DE) of 1.57g/dL. The Incremental Cost-Effectiveness Ratio (ICER) was calculated to be ₹4,076.43 per additional unit of hemoglobin gained, indicating that an additional expenditure of ₹4,076.43 was required to achieve one additional unit of therapeutic benefit with intravenous compared with oral iron therapy (Table 9).

DISCUSSION

The current study compared the efficacy, safety, and cost-effectiveness of oral iron therapy to intravenous iron therapy in Iron Deficiency Anemia (IDA) patients. After 14 days of iron therapy, both treatment groups showed a significant improvement in hemoglobin levels, increase was significantly larger in patients receiving intravenous iron, indicating a faster hematological

response. This could potentially be attributed to the direct administration of iron into the blood stream with intravenous therapy, leading to an increase in immediate delivery of iron for erythropoiesis and replenishment of iron reserves, whereas the effectiveness of oral iron varies depending on gastrointestinal absorption and treatment adherence.

The increased efficacy of intravenous iron observed in the current study is consistent with previous research studies (Das *et al.*, 2020) observed that intravenous iron sucrose was more effective, safer, and cost-effective than oral iron in the rapid correction of hemoglobin and serum ferritin levels in patients with moderate IDA. Similarly (Zhang *et al.*, 2024), in a multicentre randomized trial involving 338 patients, observed that high dose intravenous iron resulted in faster improvement in hemoglobin and iron metabolism than oral iron while recommending for further evaluation of long-term safety, patient experience, and cost-effectiveness. The results of the present study support these observations by significantly greater improvement in hemoglobin with intravenous iron over a short treatment period compared to oral iron therapy. The effectiveness of intravenous iron has also been observed in specific patient populations.

The effectiveness of intravenous iron has also been established in select patient populations. (Schröder *et al.*, 2005) observed that intravenous iron sucrose was more GI tolerable than oral iron in patients with inflammatory bowel disease. Likewise, (Khalafallah *et al.*, 2010) also showed that intravenous iron polymaltose produced greater correction of hemoglobin and replenishment of

iron stores than oral iron in pregnant women with moderate IDA while having favourable safety profile. In postpartum women (Mangnale *et al.*, 2022), found that intravenous iron preparations achieved faster correction of hemoglobin and restoration of iron stores than oral therapy, confirming the consistent therapeutic advantage of intravenous iron across different clinical settings.

Our study is also consistent with (Panchal *et al.*, 2015) who compared oral and intravenous iron formulations stating significant improvements in hemoglobin, serum ferritin with intravenous iron sucrose than with oral ferrous sulfate or ferrous ascorbate. Their study also demonstrated a lower incidence of gastrointestinal adverse effects with intravenous therapy, which is comparable to the adverse event profile observed in the present study.

The present study observed clinical presentations such as shortness of breath, dizziness, fatigue, and generalized weakness, typical characteristics of iron deficiency anemia reported in published literatures. The study also reported that Menorrhagia and chronic blood loss were the leading causes for iron deficiency anemia emphasizing the importance of identifying and correcting the underlying causes to correct iron deficiency.

With regard to safety, GI adverse effects were observed in patients receiving oral iron therapy, and hypersensitivity reactions in the intravenous iron group. Although all reactions were successfully treated without complication, emphasizing that intravenous iron should be administered under medical supervision.

Table 5: Comparison of pre and post-treatment haemoglobin levels within oral and intravenous iron therapy.

Group	N	Pretreatment Hb (g/dL)	Post-treatment Hb (g/dL)	Mean increase in Hb (g/dL)	t value	p value	Effect size (Cohen's d)
Oral Group	42	8.21±1.01	8.77±0.93	0.56	-10.0	<0.001	-1.55
IV Group	42	6.40±1.35	8.53±0.92	2.13	-9.63	<0.001	-1.49

Hb=Hemoglobin, IV=Intravenous, t=t-statistic, p=p-value, Cohen's d=effect size.

Table 6: Comparison of post-treatment haemoglobin levels between oral and intravenous iron therapy using ANCOVA adjusted for baseline hemoglobin.

Source	Sum of Squares	d _f	Mean Square	F	p	Partial η ²
Treatment groups (Oral vs IV)	3.53	1	3.527	5.710	0.019	0.066
Baseline Hb	20.28	1	20.282	32.83	<0.001	0.288
Residuals	50.04	81	0.618	-	-	-

ACNOVA=Analysis of covariance, Hb=Hemoglobin, IV=Intravenous, F=F-statistic, p=p-value, Partial η²=Partial eta squared.

Table 7: Effect of treatment group and time on hemoglobin response: ANOVA Results.

Effect	d _f	F value	p value	Effect Size η ² _p
Time (Pre- treatment vs Post-treatment)	1,82	139.1	<0.001	0.629
Treatment Group (IV vs Oral)	1,82	25.4	<0.001	0.237
Time x Group Interaction	1,82	47.4	<0.001	0.367

IV=Intravenous, ANOVA=Analysis of Variance, d_f=degrees of freedom, F=F-statistic; P=P-value, η²_p=Partial eta squared.

Table 8: Adverse drug reactions reported in the study population with severity, management and outcome.

Treatment Group	Adverse Drug Reaction	n (%)	Severity	Management	Outcome
Oral Iron Therapy (n=42)	Constipation	2 (4.76)	Mild	Symptomatic management with Syp Lactulose	Resolved
	Metallic taste	2 (4.76)	Mild	Reassurance, no intervention	Resolved
	Nausea	2 (4.76)	Mild	Symptomatic management	Resolved
	Diarrhea	1 (2.38)	Mild	Symptomatic management with ORS and probiotics	Resolved
	Heartburn	1 (2.38)	Mild	Symptomatic management with Inj. Pantoprazole	Resolved
	Vomiting	1 (2.38)	Mild	Symptomatic management with Inj Ondansetron	Resolved
	No adverse effects	33 (78.57)			
Intravenous Iron (n=42)	Allergic reaction (urticaria/rash/facial swelling)	5 (11.90)	Mild	Symptomatic management with Inj Pheniramine and Inj Hydrocortisone	Resolved
	No adverse effects	37 (88.10)			

Syp=Syrup; Inj=Injection.

Another important factor in the management of IDA is treatment satisfaction in the study (Ghamri *et al.*, 2024) reported that patients receiving intravenous iron expressed greater treatment satisfaction primarily because the treatment avoided the swallowing difficulties, gastrointestinal intolerance, and adherence issues associated with oral iron therapy. These findings support the medication adherence is associated with intravenous iron therapy during clinical practice.

The clinical advantages of intravenous iron are also supported by this study's cost-effective analysis. Intravenous iron showed better clinical efficacy compare with oral iron therapy but is associated with higher treatment cost. An Incremental Cost-Effectiveness Ratio (ICER) of ₹4076.43 per additional g/dL increase in hemoglobin was found to be for intravenous iron therapy compare to oral iron therapy. This indicates that the additional therapeutic benefit of intravenous iron therapy can be obtained by added incremental investment. These findings are comparable with the economic study conducted by (Argüelles-Arias *et al.*, 2022) reported that oral iron was the least expensive therapy but was limited by lower efficacy, GI adverse effects, and poor adherence. Their observations concluded that FCM was the most cost-effective intravenous formulation despite its higher initial cost due to its greater therapeutic effectiveness and potential to improve quality of life while reducing healthcare utilization.

The broad literature supports intravenous iron's long-term therapeutic advantages. A meta-analysis by (Mei *et al.*, 2022) found that intravenous iron dramatically improved exercise capacity and quality of life in patients with heart failure and iron deficiency, although while more research is needed to determine long-term safety and effectiveness. These data, together with the

findings of the current investigation, reaffirm the importance of intravenous iron as a viable treatment alternative for quick correction of iron deficiency anemia, particularly in patients who require immediate restoration of iron stores or who are intolerant to oral iron therapy.

LIMITATION

The current study was constrained by its observational design and non-randomized treatment allocation, as treatment was prescribed by the physician which may have resulted in the difference in the baseline hemoglobin and residual confounding between the treatment groups, although this difference was addressed using ANCOVA. A small number of patients with heart failure, CKD/AKI, inflammatory bowel disease and pregnancy were included, as these conditions are common causes or contributors to iron deficiency anemia in clinical practice excluding them will create generalization which contradicts to the real-world setting hence due to small size study limits to draw firm conclusions from this subgroups, but this conditions may acted as confounding factors influencing both treatment allocation and hemoglobin response. Overall, relatively small sample size, short study duration with follow-up period of 14 days, limiting assessment of long-term hematological response, iron store replenishment, recurrence of anemia, delayed adverse events, and lack of post-treatment iron profile assessment, including serum ferritin and transferrin saturation. Additional large-scale, multicentre studies with longer follow-up are needed to assess the long-term safety, effectiveness, and cost-effectiveness of intravenous iron therapy in a wide range of patient populations, including those with chronic kidney disease, inflammatory bowel disease, pregnancy, and other chronic conditions associated with iron deficiency anemia.

Table 9: Incremental Cost Effectiveness Ratio (ICER) of Iron therapy.

Alternatives	Cost (C), ₹	Difference in Cost (DC), ₹	Effect (g/dL)	Difference in Effect (DE) (g/dL)	ICER (₹/g/dL)
Oral Iron	100	-	0.56	-	-
IV Iron	6,500	6,400	2.13	1.57	4076.43

ICER= $(C_{IV} - C_{Oral}) / (E_{IV} - E_{Oral})$, where ICER, incremental cost-effectiveness ratio; C=treatment cost; E=mean increase in hemoglobin (g/dL), IV=Intravenous.

CONCLUSION

The current study indicates that both intravenous and oral iron therapy significantly improves hemoglobin levels in iron deficiency anemia patients with greater mean increase in hemoglobin in intravenous iron therapy. This between group difference remained statistically significant $p=0.019$ after baseline hemoglobin adjustment using ANCOVA indicating therapeutic benefit of intravenous therapy is not simply an artifact of the more severe anemia in that group.

Intravenous iron therapy is generally well tolerated. although GI adverse effects such as constipation, diarrhoea, heartburn, nausea, vomiting, and metallic taste, were found to be more common with oral iron therapy, few patients developed hypersensitivity reaction such as urticaria, rash, and facial swelling following intravenous iron administration and were managed without serious complications.

Although intravenous iron is associated with a higher acquisition cost than oral iron therapy, the incremental cost-effectiveness ratio of ₹4076.43 per additional g/dL of hemoglobin gained, indicating that the additional cost is associated with incremental hemoglobin benefit. The rapid correction of anemia, improved adherence, and potential reduction in the need for blood transfusions and other healthcare resource which may further enhance its long-term economic value.

Overall, intravenous iron therapy may represent a safe, effective, and clinically valuable alternative to oral iron therapy, particularly for patients with moderate to severe iron deficiency anemia, intolerance to oral iron, poor treatment adherence, or those requiring rapid replenishment of iron stores.

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ABBREVIATIONS

ADR: Adverse Drug Reaction; **AKI:** Acute Kidney Injury; **ANCOVA:** Analysis of covariance; **ANOVA:** Analysis of Variance; **CKD:** Chronic Kidney Disease; **CRF:** Case Report Form; **FCM:** Ferric Carboxy Maltose; **GI:** Gastrointestinal; **Hb:** Hemoglobin; **ICER:** Incremental Cost-Effectiveness Ratio; **IDA:** Iron Deficiency Anemia; **IRB:** Institutional Review Board; **IV:** Intravenous; **SD:** Standard Deviation; **SOB:** Shortness of Breath; **TIBC:** Total Iron-Binding Capacity.

CONFLICT OF INTEREST

The authors declare that there is conflict of interest.

AUTHORS CONTRIBUTION

Kasagani Bhavani, Thummala Harshini Reddy and Tummanpally Hima Bindu: Conceptualization study design, development of methodology, data collection, data curation, statistical analysis, interpretation of results, writing of the original draft, and review and editing of the final manuscript.

Dr. Ayesha Fatima: Supervision, guidance on study conceptualization and methodology, statistical oversight, interpretation of findings, and critical review and editing of the manuscript.

Dr. Srikar and Dr. Nagendar Devulapally: Provided clinical support, expert guidance, and reviewed the manuscript.

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