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Research Article

PHARMACOVIGILANCE INSIGHTS: A RARE COHORT STUDY ON HYPERSENSITIVITY REACTIONS TO INTRAVENOUS IRON SUCROSE IN POSTPARTUM ANEMIC WOMEN AT TERTIARY CARE HOSPITAL, TAMILNADU

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ABSTRACT

Objectives: This study aims to investigate the incidence, severity, and timeline of hypersensitivity reactions (HSRs) associated with intravenous (IV) iron sucrose and to evaluate the effectiveness of management strategies in postpartum anemic (PPA) women using a structured pharmacovigilance approach.

Methods: The 2-year, single-center, prospective observational cohort study was conducted in obstetrics and gynecology at a tertiary care hospital in Tamil Nadu. Among 238 PPA women, 129 received a standard dose of iron sucrose and were categorized into adverse drug reaction (ADR, n=11) and non-ADR (n=118) groups. To identify potential risk factors for HSRs, we performed a nested case–control analysis, comparing the 11 cases who experienced HSRs with the 118 controls from the same cohort who did not. A Delphi panel assessed ADRs and graded HSRs using the World Health Organization-Uppsala Monitoring Centre causality scale and Ring–Messmer classification, respectively. The data were analyzed using Fisher's exact test.

Results: The HSR incidence was 8.5%. Most of the patients experienced Grade 2 HSR (63.64%) moderate ADR, followed by Grade 3, severe, potentially life-threatening (27.27%), requiring emergency management, with no fatalities. Demographics showed no significant association with ADRs ($p>0.05$). Patients with severe anemia appeared to increase the likelihood of ADRs (odds ratio = 2.77; 95% confidence interval: 0.573–13.42; $p=0.204$, though statistically non-significant. Over half of HSRs (54.5%) occurred after multiple doses, and 72.7% developed within 15 min of infusion. One medication error caused recurring reactions. Most ADRs (91%) were classified as probable/likely.

Conclusion: This study highlights the critical need for active pharmacovigilance in tracking, managing rare and unpredictable ADRs of IV iron sucrose, necessitating pre- and post-infusion risk assessments, immediate intervention, and infusion policy optimization in the future.

Keywords: Adverse drug reactions, Hypersensitivity, Iron sucrose, Medication errors, Pharmacovigilance, Postpartum anemia.

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INTRODUCTION

According to the data from the National Family Health Survey-3, anemia is a significant health issue in India, with approximately 50% of pregnant women affected, and it contributes to 20–40% of maternal deaths. India accounts for 80% of maternal deaths due to anemia in the South Asian region [1]. The World Health Organization (WHO) defines postpartum anemia (PPA) as a condition where hemoglobin (Hb) concentration is <11 g/dL, 1 week after delivery, and <12 g/dL, within the 1st postpartum year [2]. This is common among new mothers and can persist into the 1st postpartum year.

Studies indicate that anemic mothers are more prone to depression, fatigue, and impaired cognition, which may affect mother–infant bonding [3,4]. Short intervals between pregnancies or repeated pregnancies spaced <2 years, especially when iron stores are not fully replenished, are major contributors to PPA, apart from the poor nutritional status of the mother. Treatment typically includes iron supplementation for 100 days postpartum to restore iron levels or, in severe cases, blood transfusions. Oral iron formulations are effective but have a slower onset of action than parenteral iron. There are studies mentioning that parenteral iron formulations, such as iron sucrose infusion, outperform oral iron supplements in terms of safety and efficacy, despite the risk of adverse effects, which is addressed in this study considering the hypersensitivity reactions (HRSs). These reactions range from mild reactions, such as a metallic taste, gastrointestinal discomfort, and nausea, to severe, but rare, potentially life-threatening anaphylaxis, which occurs in fewer than 1 in 200,000 administrations [5,6].

Most research elaborates on the comparative safety and efficacy of parenteral iron formulations such as dextrose, maltose, and sucrose. However, studies examining iron sucrose-related adverse drug reactions (ADRs) severity, reaction timeline, and real-time monitoring in PPA women are limited. Therefore, this study applies a structured pharmacovigilance framework, combining prospective observation, Delphi consensus, and validated ADR causality and HSR severity scales, to evaluate the incidence and management outcomes of HRSs in this population.

MATERIALS AND METHODS

The single-center, prospective observational cohort study of PPA women was conducted between December 2022 and December 2024 at a tertiary care hospital in Erode, Tamil Nadu, India. To identify potential risk factors for HSRs, we performed a nested case–control analysis, comparing the 11 cases who experienced HSRs with the 118 controls from the same cohort who did not experience HSRs. We used the Strengthening of the Reporting of Observational Studies in Epidemiology (STROBE) cohort reporting guidelines for the study [7].

Ethical statement

The study was approved by the Institutional Ethics Committee (IEC). Certificate number JKKNCP/IEC-CER/1422123/Ph.D. All participants provided written informed consent before participating, and their confidentiality and privacy were protected.

Inclusion and exclusion criteria

Inclusion criteria: Inpatient PPA women aged 18 years and above who underwent vaginal or cesarean section delivery in the obstetrics and gynecology department, and received at least one dose of intravenous (IV) iron sucrose infusion.

Exclusion criteria: Patients with a known allergy or hypersensitivity to parenteral iron sucrose, those with iron overload, and mild anemic patients who did not receive iron sucrose infusions were excluded.

Sample size and sampling techniques

In this study, a convenience sampling technique was used, as ADRs are unpredictable and iron sucrose-induced HSRs are rare, making probability-based sampling impractical. This method involves enrolling eligible patients based on availability and is a widely accepted non-probability approach in clinical research, particularly useful for accessing target populations when studying infrequent or unpredictable events [8]. Although convenience sampling can introduce bias, selection bias was minimized by consecutively including all eligible PPA inpatients. HSRs were prospectively monitored and documented by a clinical pharmacist during or immediately after infusion, reducing recall and reporting bias.

Formal power calculations were not performed, as HSRs to IV iron sucrose are rare and unpredictable, making such estimation impractical. Instead, the sample size was calculated using Food and Drug Administration (FDA) clinical trial and post-marketing data, which report mild HSRs in approximately 2–5% of patients and serious reactions in <0.01% [5]. Using a 5% expected incidence, 95% confidence level, and ±5% margin of error, the minimum required sample size was estimated as 73 patients. A total of 238 postpartum anemic patients were enrolled initially. Of these, 129 were treated with iron sucrose; among them, 11 experienced HSRs. With 129 participants included, the sample was considered adequate to capture rare HSRs within the study population.

Data collection

The relevant data, such as details of the IV iron sucrose infusion (dosing, infusion time, dilution, and infusion rate) and additional information on patient demographics, medical, medication, and allergic histories, were collected during ward rounds and post-ward rounds through in-depth case sheet reviews and patient history interviews. A detailed overview of patient enrolment, as well as the causality assessment of ADRs [9] and grading of HSRs [10], is presented in the STROBE flowchart (Fig. 1).

Standard parenteral iron sucrose therapy and outcome measures

The standard recommended dose of iron sucrose (100–200 mg) is administered as a slow IV push injection or infusion for 15–30 min. All the patients received 100 mg/5 mL iron sucrose diluted in 100 mL 0.9% saline for 30 min. None of the patients received the test dose as the study site protocol did not require any test dose [5].

Rapid infusion of iron sucrose can lead to several adverse reactions, including hypotension, dyspnea, headache, nausea, vomiting, dizziness, joint pain, paraesthesia, abdominal and muscle pain, edema, and, in severe cases, cardiovascular collapse. These reactions usually occur within 30 min of administration and may manifest after the first or subsequent doses. Many of these symptoms can be managed by administering IV fluids, hydrocortisone, and/or antihistamines. In certain instances, slowing down or temporarily pausing the infusion rate may be necessary [5,6].

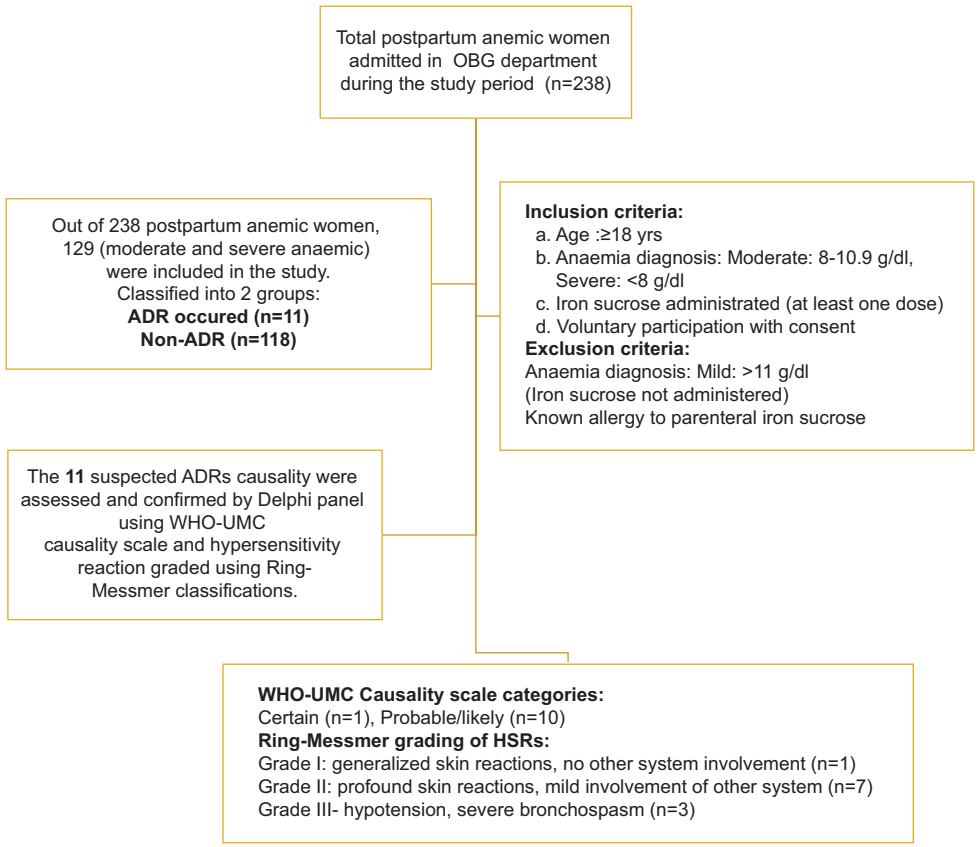

Fig. 1: Strengthening of the Reporting of Observational Studies in Epidemiology Flowchart – patient enrolment and causality assessment of adverse drug reaction with hypersensitivity reaction grading

Delphi causality assessment

All patients who received iron sucrose infusion were closely monitored for any occurrence of ADRs by a clinical pharmacist. A clinical pharmacist is uniquely positioned to monitor, report, and prevent ADR and medication errors, and support safe medication use. The observed HSRs were analyzed and confirmed by an expert Delphi panel (consisting of a clinical pharmacist, physician, and nurse). The Delphi panel assessed the causal relationship between the suspected drug and ADRs using the WHO-Uppsala Monitoring Centre (WHO-UMC) causality scale.

The Delphi panel also examined information on dechallenge (withdrawal of suspected drug) and rechallenge (reintroduction of suspected drug), onset lag-time, infusion-related symptoms, and outcomes of ADRs (such as life-threatening events, hospitalization prolongation, temporary/permanent organ damage, or fatal outcomes). These patients were monitored until complete recovery, followed up to discharge. The Delphi panel's advice was promptly adopted for the effective management of ADRs. The Delphi panel ensured consistency in ADR causality assessments through a structured consensus process. Each panelist independently assessed the causality of reported ADRs based on standard causality criteria, i.e., the WHO-UMC causality scale. Their responses were compared to identify any differences. In case of any disagreements or confusion, the panel resolved them in a consensus meeting, with external consultation when necessary. The panel's inter-rater reliability was assessed by comparing causality ratings, and consensus was reached before finalizing conclusions.

Outcome measures

The primary outcome measures included evaluating the incidence and severity of infusion reactions, ADR timelines, and the effectiveness of various management strategies for HSRs, such as ceasing iron sucrose infusion and administering antihistamines and corticosteroids.

Statistical analysis

The statistical analysis of data was performed using Statistical Package for the Social Sciences version 30.0. The categorical variables (e.g., age group, body mass index [BMI] category, gravida (G), anemia severity, comorbidities, etc.) of ADR and non-ADR groups were compared by the Chi-square test (if the cell counts ≥5) or Fisher's Exact test. Variables with $p<0.05$ were considered statistically significant. In a cohort study, relative risk (RR) is defined in general. When the event is a rare occurrence, it is preferable to monitor the odds ratio (OR) to approximate RR. Risk estimation (effects of variables on ADR risk) was analyzed by OR with a 95% confidence interval (CI). All other variables were expressed in percentages and numbers.

RESULTS

A total of 238 PPA patients were enrolled in this study based on the eligibility criteria, and 129 patients received iron sucrose and were monitored for iron sucrose-induced ADRs. The sociodemographic and basic characteristics of all the patients at the time of HSRs development are detailed in Table 1. ADR occurrence data showed that among the 11 patients with HSRs, the majority of the participants were within the younger age groups of 18–22 years and 23–27 years.

The BMI data revealed a concerning trend: out of 11 women, only four were of normal weight, one was underweight (BMI <18.5), with OR=0.085; 95% CI: 0.004–1.632; p-value of 0.102, and the remaining individuals were classified as overweight or obese. The obstetric history indicated that four women were primigravida, whereas the remaining were multigravida. Most of the postpartum women (81.81%) had moderate anemia, whereas a smaller portion (18.18%) had severe anemia. Among these severe anemia subgroups, two had ADRs, and the observed OR was 2.774 with a 95% CI of 0.573–13.421, and a p-value of 0.204. Although not statistically significant, this suggests a possible trend toward higher ADR risk in severely anemic women, requiring studies over a larger population. All the demographic data showed no significant association with ADRs (*p>0.05).

The comorbid status revealed that pre-eclampsia (27.27%) was the most common in the study. In addition, one woman had a known case of rheumatic heart disease, and two had hypothyroidism. The medical history revealed that two patients had received parenteral iron therapy for treating iron deficiency anemia, and pre-eclampsia was treated effectively with oral labetalol. Postpartum hemorrhage is a major complication that requires immediate attention, since it can exacerbate anemia and can lead to maternal mortality and morbidity. In the ADR-occurring group, 10 patients had a cesarean delivery, and one patient had a normal vaginal delivery. Metronidazole and ampicillin antibiotics were given together to prevent infection since their spectrum of activity varies.

According to the Ring and Messmer classification, a system is used to grade the severity of anaphylaxis and other HSRs. This study found that the majority of patients experienced moderate (Grade 2: 63.64%) to severe (Grade 3: 27.27%) HSRs (Table 2).

As shown in Table 3, 11 subjects in this cohort study experienced ADRs. The most common symptoms were chills and rigor, reported by 63.63% (seven out of 11 patients). Dyspnea (shortness of breath) was the second most frequent reaction, occurring in 36.36% (four out of 11 cases).

The onset lag time refers to the time taken for an adverse reaction to occur after IV initiation. The onset lag time data revealed significant variability among the subjects, with the majority (72.72%) experiencing ADR onset within 1 to 15 min, a relatively short period. 18.18% (n=2), exhibited an onset lag time ranging from 16 to 30 min, whereas only a single subject (9.09%) had a delayed onset lag time between 31 and 60 min. (Fig. 2).

ADRs occurred even at the first dose in three patients, showing that reactions can happen early during treatment. The highest number of ADRs (six patients) was reported in those receiving the 3rd dose or beyond, indicating a potential increase in risk with repeated infusions. The mechanism behind delayed reactions and immediate reactions is suspected to be dose-independent, which is justified, as anaphylactic reactions can even occur at the first dose and, in certain instances, at the 6th dose (two patients) (Fig. 3).

The management strategies employed in this study demonstrate a clear trend in the effectiveness of various treatment combinations for recovery among the subjects. Notably, all the patients (100%) who discontinued iron therapy experienced recovery, suggesting that the cessation of IV iron sucrose played a crucial role in alleviating adverse reactions. Among the management strategies, the combination of chlorpheniramine maleate (CPM) and dexamethasone was the most commonly used treatment (36.36%), indicating that this approach may be particularly beneficial in managing symptoms. Dexamethasone alone also resulted in a significant recovery rate of 27.27%, reinforcing its potential as an effective intervention (Table 4).

In this cohort, one suspected ADR was categorized under the "certain" category, and the rest of them were "probable/likely" (Fig. 4). The "certain" case involved a patient who accidentally received parenteral iron sucrose due to an administration error by a healthcare professional, despite the Delphi panel's recommendation to discontinue therapy. This unintentional positive rechallenge led to a recurrence of hypersensitivity symptoms, thereby confirming a causal relationship that met the WHO-UMC criteria for a "certain" classification. All patients were treated immediately and stabilized.

DISCUSSION

The current study has found an 8.5% incidence of HSRs following IV iron sucrose administration in PPA women, slightly higher than the previous report [6]. Saroj and Shiralee's study among PPA patients reported that iron sucrose caused 26% ADRs, without any serious adverse effects, but these results differ in terms of severity from the current study [11]. The majority of reactions occurred rapidly, within 15 min, underscoring the critical window for close patient monitoring

Table 1: ADR versus non-ADR in postpartum anemic women

Total postpartum anemic women (n=238)					
Total postpartum anemic women given iron sucrose (n=129)					
Variable	**ADR cases (n=11)**	**Non-ADR cases (n=118)**	**OR**	**95% CI (lower-upper)**	***p-value**
Age group (in years)					
18–22	4	42	1.000	0.234–4.264	1.000
23–27	4	48	1.142	0.269–4.855	0.856
28–32	1	11	1.047	0.106–10.342	0.968
>33	2	17	0.809	0.135–4.841	0.816
BMI (kg/m^2)					
Underweight (<18.5)	1	1	0.085	0.004–1.632	0.102
Normal (18.5–25)	4	47	1.000	0.236–4.236	1.000
Overweight (25–29.9)	3	38	1.078	0.227–5.113	0.924
Obese (30–35)	3	32	0.907	0.190–4.332	0.903
Gravida					
Primigravida (G1)	4	41	1.000	0.234–4.271	1.000
Multigravida (G2)	5	55	1.073	0.271–4.247	0.919
Multigravida (≥G3)	2	22	1.073	0.181–6.330	0.937
Menstrual history					
Regular	6	70	1.000	0.307–3.251	1.000
Irregular	5	48	0.822	0.237–2.850	0.758
**Anemia severity					
Moderate (8–10.9 g/dL)	9	73	1.000	0.375–2.662	1.000
Severe (<8 g/dL)	2	45	2.774	0.573–13.421	0.204
Comorbidities					
Asthma	1	13	1.444	0.147–14.139	0.752
Pre-eclampsia	3	36	1.333	0.278–6.387	0.718
Hypothyroidism	2	23	1.277	0.216–7.548	0.786
Rheumatic heart disease	1	10	1.111	0.111–11.089	0.928
None	4	36	1.000	0.232–4.309	1.000
Postpartum complications					
Postpartum hemorrhage	3	39	1.344	0.252–7.150	0.728
Postpartum pre-eclampsia	3	31	1.069	0.199–5.727	0.937
Gestational diabetes mellitus	2	25	1.293	0.199–8.368	0.787
Infection	2	20	1.034	0.158–6.764	0.971
None	3	29	1.000	0.186–5.371	1.000
Comedications					
Levothyroxine	1	12	1.118	0.132–9.427	0.917
Labetalol	3	34	1.056	0.278–4.004	0.935
Salbutamol	1	15	1.398	0.168–11.608	0.756
Ferrous sulfate	11	118	1.000	0.417–2.396	1.000
Previous iron therapy	2	27	1.258	0.263–6.010	0.773
Antibiotics†	11	118	1.000	0.417–2.396	1.000
Metformin	2	26	1.211	0.253–5.798	0.809
Insulin	1	14	1.305	0.156–10.881	0.805

Chi-square test or Fisher's exact test. *p≤0.05 is statistically significant, *p>0.05 is non-significant. †Antibiotics (metronidazole, ampicillin). **Exclusion criteria: Patients with a known allergy or hypersensitivity to parenteral iron sucrose, those with iron overload, and mild anemic patients who did not receive iron sucrose infusions were excluded. ADR: Adverse drug reaction, BMI: Body mass index, OR: Odds ratio, CI: Confidence interval

Table 2: Ring and Messmer classification of hypersensitivity

Grade of hypersensitivity	**No. of subjects (n=11)**	**Percentage**
Grade 1 (Mild)	1	9.09
Grade 2 (Moderate)	7	63.64
Grade 3 (Severe)	3	27.27

Table 3: Adverse drug symptoms/reactions

Type of reactions	**No. of subjects (n=11)**	**Percentage**
Pyrexia	3	27.27
Itching/Rashes	2	18.18
Dyspnea	4	36.36
Tachycardia	3	27.27
Hypotension	2	18.18
Chills, rigor	7	63.63

during infusion. These findings reaffirm the need for vigilance during parenteral iron therapy. Statistical analysis revealed no significant association between demographic or clinical variables (age, BMI, gravida, and comorbidities) and ADR occurrence, consistent with the unpredictable nature of these reactions.

The rate and dose of IV iron sucrose administration are the critical factors in HSRs. All the patients received the same dosage strength and rate of iron infusion, but the patients experienced varying degrees of HSRs with different timelines. Hence, continuous patient monitoring throughout the treatment course is mandatory. The variability in reaction timelines and severity suggests potential inter-subject differences, which may be due to individual physiological or metabolic factors, variability in response to the drug, or other extrinsic factors, and it makes predicting HSRs a challenge.

All patients received immediate treatment following ADR onset, primarily with corticosteroids and CPM, resulting in effective recovery in all cases. Anaphylactic reactions necessitated cessation of iron sucrose infusion to prevent further complications, and only a minority of patients required supplemental oxygen. These management

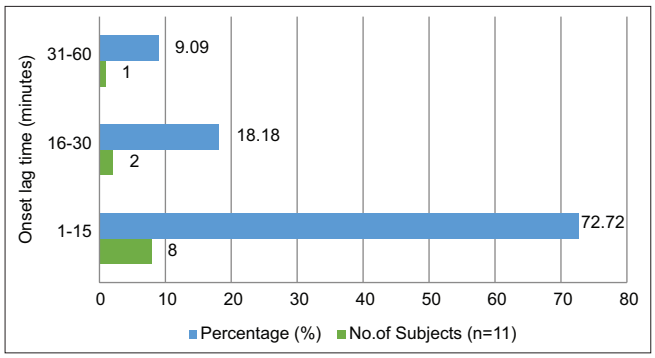

Fig. 2: Onset lag time (time taken for the reactions to occur after intravenous initiation)

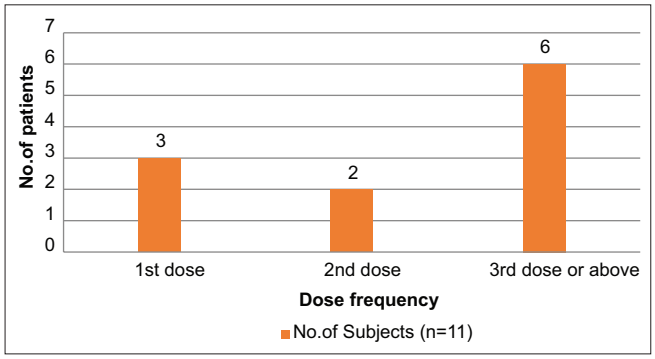

Fig. 3: Dose frequency of infusion and reaction occurrence

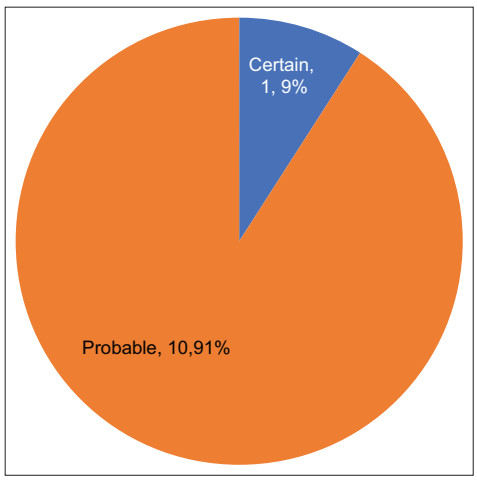

Fig. 4: World Health Organization-Uppsala monitoring centre causality assessment of adverse drug reaction

outcomes reveal the effectiveness of current treatment protocols and the potential benefit of combination therapy of antihistamine and corticosteroids. In our cohort, pre-medication with antihistamines or corticosteroids was not administered before IV iron sucrose infusion. Although recent trends suggest that prophylactic use of these agents can reduce ADRs associated with iron formulations, their routine use for all patients receiving parenteral iron remains debatable. Instead, pre-medication should be reserved for cases with clear clinical indications. This underscores the critical role of pharmacovigilance and regulatory oversight to promote evidence-based practice and avoid unnecessary medication use.

A comparative study on iron sucrose and dextrose by Hsia *et al* revealed that no significant difference was observed in the incidence of total or

Table 4: Management of ADRs and their outcomes

Management strategy	Outcome	No. of subjects (n=11)	Percentage
Administration of chlorpheniramine maleate+dexamethasone	Recovered	4	36.36
Dexamethasone	Recovered	3	27.27
Hydrocortisone	Recovered	2	18.18
Chlorpheniramine maleate+hydrocortisone	Recovered	2	18.18
Supportive care			
Oxygen supplementation	Recovered	2	18.18
Discontinuation of iron therapy	Recovered	11	100.00

ADR: Adverse drug reaction

immediate adverse reactions; however, the risk of delayed reactions was comparatively greater in the iron sucrose group [12]. In contrast, Auerbach and Ballard, Critchley and Dunbar studies have suggested that high-molecular-weight iron dextran has a higher incidence of ADRs than iron sucrose [13,14]. No major ADR or HSRs were seen in the Karwasara *et al.* study [15]. ADR usually happens at normal doses and is unpredictable; reactions may be dose-dependent or independent.

The underlying mechanisms of HSRs to iron sucrose are not fully elucidated but differ from those associated with iron dextran. Iron dextran-related reactions often involve anti-dextran antibodies, which can trigger immediate hypersensitivity and complement activation-related pseudo-allergy (CARPA). In contrast, iron sucrose does not form immune complexes with anti-dextran antibodies, and immunoglobulin E (IgE)-mediated (Type I) mechanisms are considered less likely because no evidence supports the presence of specific anti-iron sucrose antibodies.

Instead, non-IgE-mediated mechanisms, particularly CARPA, are thought to play a major role. In this pathway, the iron-sucrose complex can activate the complement system, generating anaphylatoxins (C3a and C5a) that induce mast cell and basophil activation, resulting in pseudo-allergic reactions clinically indistinguishable from true anaphylaxis.

An additional hypothesis suggests that hypersensitivity may rely on free iron, non-transferrin-bound iron (NTBI) in the circulation. This can be explained physiologically: when total iron input exceeds the binding capacity of transferrin, it appears transiently in plasma. NTBI can promote oxidative stress, complement activation, and the release of inflammatory mediators such as histamine and cytokines, amplifying HSRs. Transferrin levels, however, vary between individuals depending on iron status, inflammation, liver function, and pregnancy, meaning that the risk of free iron–mediated reactions can differ among patients. In this study, patients received both oral ferrous sulfate and IV iron sucrose, which could theoretically increase circulating free iron if dosing exceeds individual binding capacity, contributing to hypersensitivity risk. [16,17] In dose-dependent mechanisms, the risk of hypersensitivity increases with higher doses of iron sucrose. A case report on iron sucrose-induced hypersensitivity, Mishra *et al* revealed that an ADR occurs at the first dose after a few minutes of iron sucrose infusion, suggesting a HSR rather than an immediate dose-related toxicity [18]. As the growing concern of HSR, it is better to avoid the same IV iron formulation again in severe HSR cases. The recent reports of Karwasara *et al*., Nagaratnam *et al*., Parikh *et al*., and Kamath *et al.* say that Ferric carboxy maltose can be considered a safe and effective alternative to iron sucrose [15,19-21].

The present study revealed that it is essential to calculate iron requirements based on the patient's body weight and Hb levels; otherwise, concomitant administration of oral ferrous sulfate alongside

IV iron sucrose can lead to iron overdose and toxicity. FDA suggests that the simultaneous use of oral and IV iron may reduce iron absorption [5], emphasizing the need for individualized iron supplementation strategies.

The majority of adverse events are immediate and severe anaphylactic reactions, so rechallenge was not necessary. Prophylactic antibiotic use was universal in this cohort; similar results were observed in Sharma *et al.*'s study [22]. This is consistent with WHO recommendations (broad-spectrum antibiotics such as cefazolin, first-generation cephalosporins, or penicillin-based combinations such as amoxicillin with clavulanic acid or metronidazole) based on local practices and availability for cesarean and assisted delivery procedures to prevent postpartum infections [23-25]. Although they are effective, their widespread use raises concerns about antimicrobial resistance. This finding calls for continued vigilance in antibiotic stewardship and further research to optimize prophylaxis while minimizing resistance risk.

Limitations

Limitations of this study include the relatively small sample size, and the use of convenience sampling may limit generalizability. The sample size in this study was determined based on an expected 5% incidence of HSRs, which was sufficient to estimate the incidence of HSRs following IV iron sucrose administration. However, the limited number of HSR cases (n=11) substantially reduced the statistical power to detect significant associations between potential risk factors and rare HSR occurrence. With only 11 HSR cases, the study was underpowered for multivariate analysis, as indicated by the wide confidence intervals for several odds ratios (e.g., 0.573–13.42 for severe anemia).

The analysis was therefore limited to univariate, unadjusted odds ratios, which are susceptible to confounding by unmeasured variables such as parity or delivery type. The observational design does not allow for establishing causality beyond associations, and confounding factors may have influenced the results. Finally, the study population was limited to postpartum women at a single center, which may limit applicability to other patient groups or settings. However, HSRs to iron sucrose are rare, making our findings valuable for generating hypotheses despite the limited number. Although the association between severe anemia and HSRs was not statistically significant, the elevated odds ratio (2.77) suggests a possible relationship that warrants further investigation in a larger population. Given the rarity of HSRs to iron sucrose, these exploratory findings remain valuable and highlight the need for larger, multicenter studies with more diverse populations to confirm these observations and better identify risk factors.

Recommendations

The current study also highlights the urgent need for a nationwide medication error reporting system in India. Such a system is essential to enhance drug safety and reduce preventable medication errors, which remain a significant challenge in clinical practice. One administration error in the cohort led to a confirmed ADR, which was potentially life-threatening, underscoring critical gaps in medication safety. Timely action by the clinical pharmacist in withholding the IV re-administration has prevented fatality. Encouraging clinical pharmacist involvement and constituting a Delphi panel can address these challenges by improving medication error prevention, enhancing ADR detection and management, and supporting healthcare provider and patient education. Integrating clinical pharmacy expertise with emerging disciplines such as pharmacogenomics, pharmacovigilance, and precision medicine can pave the way for a new era of safe drug practices.

CONCLUSION

The study highlights the critical need for pharmacovigilance in tracking and managing rare and unpredictable ADRs of IV iron sucrose in postpartum anemic women. The individual patients require pre- and post-infusion risk assessments, and immediate intervention with emergency treatment is essential for managing such rare incidents. Future studies should prioritize identifying patient-specific risk factors that predispose to early or delayed ADR, and optimizing infusion protocols to minimize adverse outcomes.

AUTHORS' CONTRIBUTIONS

All authors contributed equally. KR: Concept, study design, review of literature, data collection, interpretation of results, statistical analysis, draft, and revision of manuscript.

SP: Concept, Design, Methodology, Results interpretation, manuscript correction, and finalization.

CONFLICT OF INTEREST STATEMENT

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