Experience in Using Intravenous Iron: A Retrospective Study on Outcome of Intravenous Iron in Medical Ward of a Tertiary Hospital

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ABSTRACT

Introduction:
Numerous studies have highlighted the efficacy and safety of intravenous (IV) iron in treating iron deficiency anaemia (IDA), particularly in reducing the need for blood transfusions. This study aimed to evaluate the effectiveness and safety of IV iron and to determine the factors influencing the achievement of target haemoglobin (Hb) levels.

Methods:
Data from hospitalized adult patients who received IV Iron over a one-year period were analyzed. A total of 120 patients were recruited using convenience sampling method. The study endpoints include the increment in Hb level and mean corpuscular volume (MCV), as well as the predictors and adverse drug reactions (ADRs) associated with IV iron used.

Results:
The Hb and MCV increased significantly from 8.28±1.12 g/dL to 10.53±1.76 g/dL and 77.31±10.66fL to 82.19±9.04 fL, respectively. Additionally, 49.2% of patients achieved an increase in Hb ≥2g/dL, and 13.3% achieved normalization of Hb. Minor ADRs were reported in only 2.8% of patients. Four significant predictors affecting the use of IV iron to achieve an increase in Hb ≥2g/dL were baseline Hb (aOR 0.541; 95% CI 0.348 – 0.843), baseline ferritin ≤30 µg/dL (aOR 3.059; 95% CI 1.136 – 8.240), non-diabetes mellitus (aOR 0.317; 95% CI 0.130 – 0.772) and blood disorder (aOR 5.195; 95% CI 1.024 – 26.358).

Conclusion:
Hospitalized patients with lower baseline Hb, baseline ferritin ≤30 µg/dL, non-diabetes mellitus, and underlying blood disorders were identified as predictors for the use of IV iron in the treatment of IDA to achieve an Hb increase of ≥2g/dL.

Keywords:
Iron deficiency anaemia, intravenous iron, effectiveness, safety, and factors

INTRODUCTION

Anaemia is a global public health problem, and iron deficiency causes anaemia in 32.9 % of the world's population.[1,2] The National Health and Morbidity Survey (NHMS) reported that the prevalence of anaemia among Malaysians was 21.3%.[3] Anaemia can develop during hospitalization (due to blood sampling, complications, or major surgery) and persist after discharge. Untreated anaemia impairs long-term function.[4] Allogeneic blood transfusion (ABT) is frequently used to restore haemoglobin (Hb) levels rapidly and effectively, but the benefits are temporary.[5] ABT increases the risk of infection, cardiac complications, prolonged hospitalization, and death.[6] Oral iron is typically the first-line treatment for Iron Deficiency Anaemia (IDA) patients because it is inexpensive and readily available.[1] However, oral iron correction is limited by gastrointestinal absorption and is ineffective in the presence of acute or chronic medical conditions.[7] Due to the limitations of oral iron and the adverse effects of ABT, interest in using parenteral iron therapy to treat IDA has increased.

A large systematic review and meta-analysis of the safety and efficacy of parenteral iron has shown that intravenous (IV) iron is effective at increasing Hb concentration and decreasing the risk of ABT.[7] In one randomised controlled trial, patients who received a cumulative dose of 1000 mg IV iron were more likely to have a ≥2 g/dL increase in Hb at week 5.[8] As a result, recent guidelines promote the safe use of IV iron to improve patient outcomes.[4] Beverina et al. found that early IV iron administration in the Emergency Department reduces red blood cell transfusions, hospitalisation, re-transfusion, length of stay, and cost.[9] A study in a Spanish tertiary hospital proved that early anaemia management with IV iron in a fast-track anaemia clinic is safe, durable, and cost-effective.[10]

In Malaysia, the use of IV iron is determined by the accessibility of IV iron in various settings, the prescriber's experience, the duration given for iron deficiency correction (emergency or elective surgeries), and the patient's allergenic profile.[4] In most public healthcare facilities, it is primarily prescribed in public healthcare for obstetrics, gynaecology, and dialysis patients. IV iron is also used in surgeries to correct pre- or post-operative anaemia in orthopaedic, cardiac, colorectal, and major abdominal surgeries. Recently, its use has expanded to gastroenterology and cardiology for IDA or iron deficiency in congestive heart failure.

This study aimed to evaluate the effectiveness and safety of IV iron and to determine the factors influencing the achievement of target Hb levels. The findings from this study can guide practitioners in prescribing IV iron to IDA patients in medical settings, potentially reducing the use of ABT. Additionally, understanding the factors contributing to achieving target Hb levels after IV iron therapy may help practitioners identify the target population and optimise treatment choices.

METHODS

Study Design

This was a single-centre, retrospective observational study conducted in the medical wards of Hospital Kuala Lumpur (HKL). All adult patients prescribed with IV iron from January 2021 to December 2021 were identified through a record bin card in the Pharmacy Department at HKL, and eligible patients were recruited into the study. This study included adult patients aged 18 years and above who were prescribed IV iron in the medical wards of HKL. The exclusion criteria for this study were incomplete data, pregnant women, and patients with acute bleeding. The convenience sampling method was used in this study. The sample size was calculated using the online Raosoft® software. The population size of IDA patients in the medical wards of HKL was estimated to be 2100, and the percentage of study events was set at 26.3%, based on the results published in a study that reported the percentage of the efficacy of IV iron in achieving a target Hb of ≥2 g/dL following iron infusion for the treatment of IDA. Assuming a type 1 error rate (α) of 0.05 and a power (β) of 80%, the calculated sample size needed for this study was at least 261 patients.

Outcome Measurement

The primary efficacy outcome of this study was the mean change in Hb and MCV from baseline. Baseline Hb and MCV levels for the IV iron group were collected before IV iron administration. However, for the blood transfusion and IV iron group, baseline Hb and MCV levels were collected post-blood transfusion. The highest Hb and MCV readings for the IV iron group were collected between weeks 1 to 12, while for the blood transfusion and IV iron group, they were collected between weeks 4 to 12 to avoid the post-blood transfusion effect. The effectiveness of IV iron was determined by an Hb increase of ≥2 g/dL from baseline to the highest Hb reading, or normalization of Hb (≥13 g/dL for males and ≥12 g/dL for females) at weeks 7–12 after the initial treatment.[8,13] For safety outcomes, all ADRs occurring post-IV iron throughout the admission and documented by any healthcare workers in the patient's medical record were collected, regardless of whether the events were reported as ADRs to the facility. Further analysis was performed to determine the predictors affecting the effectiveness of IV iron in achieving an Hb increase of ≥2 g/dL.

Data Collection

The patients' medical records were traced from the Records Office at HKL. The laboratory parameters were traced from the Laboratory Information System (LIS). The investigator created a data collection form to extract the required information from the patients' medical records. The data collection form consists of four parts: (A) Patient demographics, (B) Pharmacotherapy treatment, (C) Treatment outcome, and (D) Adverse Drug Reactions (ADRs).

Statistical Analysis

Data analyses were conducted using IBM® SPSS® Statistics Version 26. Descriptive analysis for continuous data was expressed as the mean and standard deviations (SD) or median and interquartile range (IQR), depending on the distribution, whereas categorical data were reported as frequencies and percentages. The paired t-test was used to determine significant changes in Hb and MCV levels from baseline pre- and post-IV iron. Pearson's Chi-square or Fisher's exact test was used to determine the proportion of patients who achieved an increase in Hb of at least 1 g/dL and 2 g/dL. Logistic regression (LR) models were performed to analyze the predictors affecting the efficacy of IV iron in achieving an Hb increase of ≥2 g/dL. Variables with a P-value < 0.25 from the simple LR analysis were included in the multiple LR model to assess the independent predictors that affect the efficacy of IV iron in achieving an Hb increment of ≥2 g/dL. LR results were presented as odds ratios with a 95% confidence interval. All statistical tests with a P-value < 0.05 denote statistical significance.

RESULTS

Patient Demographic and Baseline Characteristics

The study profile is summarized in Figure 1. A total of 120 patients were recruited, with baseline demographics and clinical characteristics detailed in Table 1. Most patients were female (65.8%, n=79), Malay (57.5%, n=69), with a mean age of 56.5 ± 17.3 years. Of all patients, 56.7% (n=68) were treated with IV iron, while 43.3% (n=52) received both blood transfusion and IV iron. Admissions were mainly due to anaemia (71.7%, n=86) and infection (55.0%, n=66), with 15.8% (n=19) testing positive for COVID-19.

A total of 92.5% (n=111) had pre-existing co-morbidities, with the top three being hypertension (60.8%, n=73), diabetes mellitus (49.2%, n=59), and blood disorders (15.0%, n=18). Most patients (98.3%, n=118) received low-molecular-weight iron dextran (LMW-ID). The majority were given a 1000 mg iron dose (47.5%, n=57), and most presented with moderate anaemia (62.5%, n=75).

The median baseline ferritin level was 183.40 µg/L (19.10 - 700.50), with 40.0% (n=48) ≤100 µg/L. The median transferrin saturation (TSAT) level was 11.6% (6.4 - 16.6), with 80.0% (n=96) ≤20%. C-reactive protein (CRP) data was unavailable for 70.8% (n=85) of patients, while 22.5% (n=27) had positive CRP. Baseline iron status showed that 39.2% (n=47) had TSAT ≤20% and serum ferritin ≤100 µg/L or TSAT ≤20% and serum ferritin >100 µg/L, and 15.0% (n=18) had TSAT >20% and serum ferritin >100 µg/L.

Efficacy Outcomes

The frequency of safety and efficacy outcomes following IV iron therapy is summarised in Table 2. The mean highest Hb level and MCV after IV iron infusion were 10.53 g/dL (± 1.76) and 82.19 fL (± 9.04), respectively. Most of the patients (49.2%, n=59) achieved an increment of Hb level from baseline to ≥2 g/dL, followed by 25.8% (n=31) of patients with ≥1 g/dL. Most patients did not have data on Hb at week 7 and beyond (47.5%, n=57), and only 13.3% (n=16) of the patients achieved normalisation of Hb at week 7 and beyond.

The Hb concentration increased significantly from 8.28 ± 1.12 g/dL to 10.53 ± 1.76 g/dL, with a mean difference of 2.25 (1.92–2.58) (P < 0.001). The MCV level also increased significantly from 77.31 ± 10.66 fL to 82.19 ± 9.04 fL, with a mean difference of 4.88 (3.64–6.13) (P < 0.001). (Table 3)

The study showed the proportion of patients achieving an increase in Hb of at least 1 g/dL and 2 g/dL based on baseline iron status, treatment status, IV iron dose, and severity of anaemia. Among patients with ferritin levels ≤100 µg/L, 60.4% (n=29) achieved an Hb increase of ≥2 g/dL (P=0.032). Additionally, among those receiving ≥1000 mg of IV iron, 82.1% (n=55) achieved a significant Hb increase of ≥1 g/dL (P=0.044). (Table 4)

Safety Outcomes

A total of 215 patients received iron infusion in the ward. Six patients (2.8%) experienced ADRs, with five cases (2.3%) resulting in the discontinuation of the infusion. Only one case (16.7%) was reported to the Malaysian Adverse Drug Reactions Advisory Committee (MADRAC). One patient experienced a severe adverse event (seizure), while the others had mild ADRs: shortness of breath (n=1), hypotension (n=1), fever (n=2), rigors (n=2), nausea (n=1), and knee joint pain (n=1).

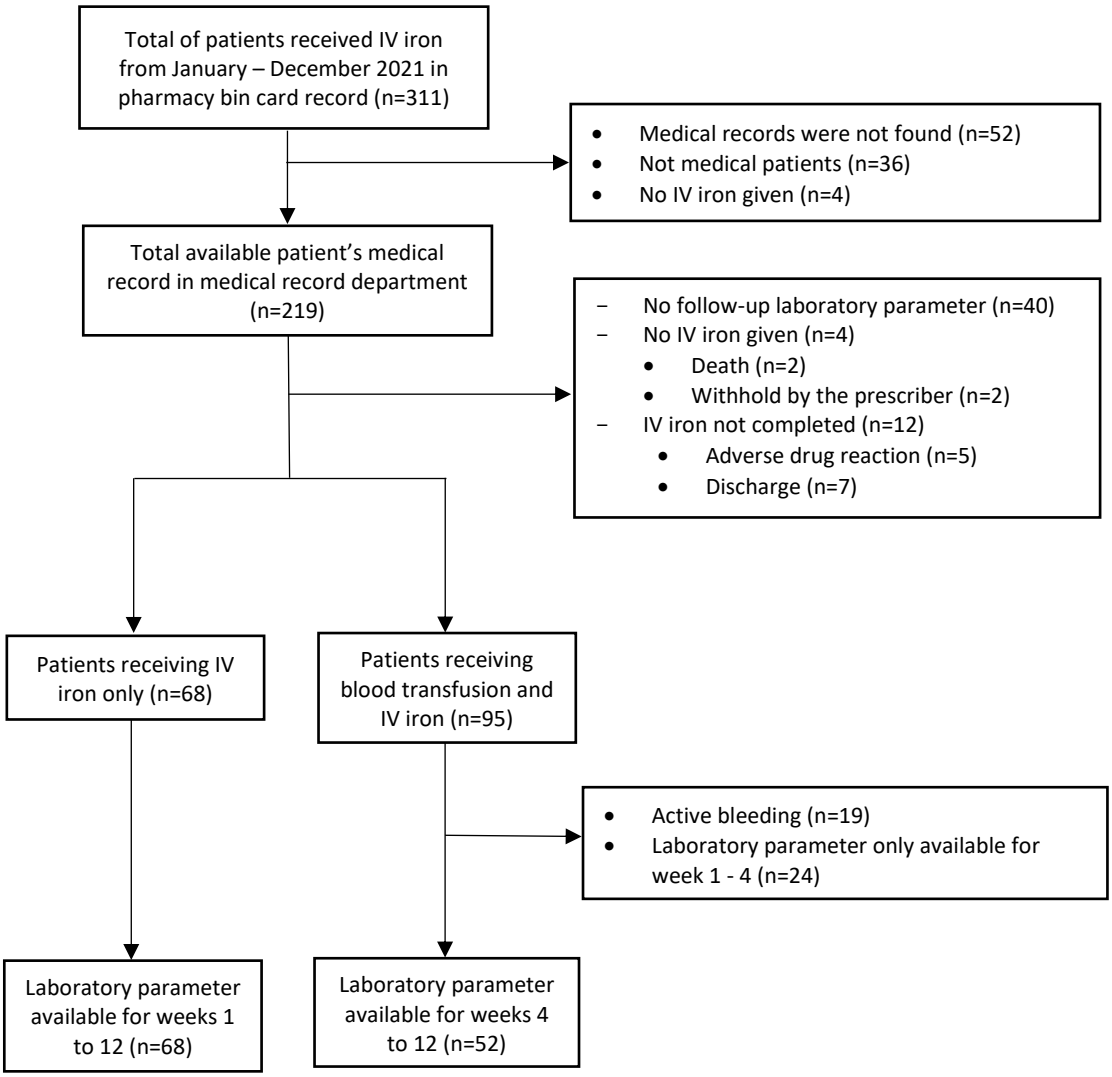

Figure 1. Study flowchart

Table 1. Baseline Demographic and Clinical Characteristic of all eligible subjects (n = 120)

Variables	n (%)
Age (years)	
Mean (SD)	56.50 (17.3)
Range	18.10–88.00
< 65	76 (63.3)
≥ 65	44 (36.7)
Gender	
Male	41 (34.2)
Female	79 (65.8)
Race	
Malay	69 (57.5)
Chinese	23 (19.2)
Indian	24 (20.0)
Foreigners	4 (3.3)
Treatment status	
Intravenous iron	68 (56.7)
Blood transfusion and intravenous iron	52 (43.3)
Length of hospitalisation (days)	
Median (IQR)	11 (7 – 18)
Range	2 - 101
Discharge status	
Discharged	117 (97.5)
Death	3 (2.5)
Diagnosis upon admission	
Anaemia	86 (71.7)
Infection	66 (55.0)
Co-morbidities	
No known comorbidity on admission	9 (7.5)
Chronic kidney disease	
Diabetes mellitus	16 (13.3)
Hypertension	59 (49.2)
Coronary heart disease	73 (60.8)
Heart failure	17 (14.2)
Cancer	8 (6.7)
Gastrointestinal disease	10 (8.3)
Blood disorder	16 (13.3)
Uterine fibroid	18 (15.0)
Infection	6 (5.0)
Cerebral vascular accident	3 (2.5)
Others	15 (12.5)
	33 (27.5)
COVID-19 PCR status	
Detected	19 (15.8)
Not detected	101 (84.2)
IV Iron type	
Iron dextran	118 (98.3)
Iron sucrose	2 (1.7)
Total dose (mg)	
< 1000	53 (44.2)
1000	57 (47.5)
> 1000	10 (8.3)
Vitamin B12 deficiency	
Yes	2 (1.7)
No	91 (75.8)
No data	27 (22.5)
Folate acid deficiency	
Yes	10 (8.3)
No	83 (69.2)
No data	27 (22.5)
Severity of anaemia[a]	
Mild	8 (6.7)
Moderate	75 (62.5)
Severe	37 (30.8)
Baseline Hb level (g/dL)	
Mean (SD)	8.28 (1.12)
Range	4.10–11.60
Baseline MCV level (fL)	
Mean (SD)	77.31 (10.66)
Range	52.80–119.10
Baseline ferritin level (µg/L)	
Median (IQR)	183.40 (19.10-700.50)
Range	2.60-9130.00
≤ 100 µg/L	48 (40.0)
> 100 µg/L	65 (54.2)
Not available	7 (5.8)
Baseline TSAT level (%)	
Median (IQR)	11.10 (6.40–16.60)
	0.90-61.60
Range	96 (80.0)
≤ 20	18 (15.0)
> 20	6 (5.0)
Not available	
Baseline iron level (µg/L)	
Median (IQR)	3.90 (3.00–5.50)
Range	1.40–20.20
Baseline CRP level	
Negative (≤ 5 mg/L)	8 (6.7)
Positive (> 5 mg/L)	27 (22.5)
Not available	85 (70.8)
Blood transfusion	
Yes	52 (43.3)
No	68 (56.7)
Baseline iron status	
TSAT ≤ 20% and serum ferritin ≤ 100 µg/L	47 (39.2)
TSAT > 20% and serum ferritin ≤ 100 µg/L	0 (0.0)
TSAT > 20% and serum ferritin > 100 µg/L	18 (15.0)
TSAT ≤ 20% and serum ferritin > 100 µg/L	47 (39.2)
No complete data	8 (6.7)

[a] Mild anaemia: Hb 11.0 – 12.9 g/dL (Male); 11.0 – 11.9 g/dL (Female);
Moderate anaemia: Hb 8.0 – 10.9 g/dL;
Severe anaemia: Hb < 8.0 g/dL

Predictors for Achieving Hb Increase of ≥2 g/dL

The predictors for achieving an increment in Hb ≥2 g/dL are shown in Table 5. Simple LR was performed as the initial step. Variables with a P-value < 0.25 were included in the multiple LR analysis (Table 5). Multiple LR analyses identified four significant predictors that affect the use of IV iron to achieve an increment of ≥2 g/dL. The four significant predictors were underlying diabetes mellitus (aOR 0.317, 95% CI 0.130 – 0.772, P = 0.011), underlying blood disorder (aOR 5.195, 95% CI 1.024 – 26.358, P = 0.047), baseline Hb (aOR 0.541, 95% CI 0.348 – 0.843, P = 0.007), and baseline ferritin ≤30 µg/dL (aOR 3.059, 95% CI 1.136 – 8.240, P = 0.027).

Table 2. Efficacy and safety outcomes following intravenous iron therapy (n = 120)

Variables	n (%)
Highest Hb level[a] (g/dL)	
Mean (SD)	10.53 (1.78)
Range	(7.10–14.80)
Hb increment from baseline (g/dL)	
< 0.5	15 (12.5)
0.5 – 0.9	15 (12.5)
1.0 – 1.9	31 (25.8)
≥ 2.0	59 (49.2)
Achievement of Hb (g/dL)	
< 2	61 (50.8)
≥ 2	59 (49.2)
Normalisation of Hb at week 7 and above[b]	
Yes	16 (13.3)
No	47 (39.2)
No data	57 (47.5)
Highest MCV level (fL)	
Mean (SD)	82.19 (9.04)
Range	51.70 – 107.30
ADR (n=215)	
Yes	6 (2.8)
No	209 (97.2)
ADR reported (n=6)	
Yes	1 (16.7)
No	5 (83.3)
ADR resulting in IV iron discontinuation (n=215)	
Yes	5 (2.3)
No	210 (97.7)
Description of ADRs	
Fitting	1
Hypotension	1
Fever	2
Knee joint pain	1
Rigors	2
Nausea	1
Shortness of breath	1

[a] Patient with iron therapy (week 1-12); Patients with iron therapy and blood transfusion, Hb level after iron transfusion (weeks 4-12); [b] Male ≥ 13.0 g/dL and Female ≥ 12.0 g/dL

Table 3. Haematological laboratory parameters before and after treatment with intravenous iron

Variables	Pre-treatment Mean (SD)	Post-treatment Mean (SD)	Mean difference (95% CI)	*t* statistic *(df)*	*P* -value[a]
Hb (g/dL)	8.28 (1.12)	10.53 (1.76)	2.25 (1.92-2.58)	13.54 (119)	<0.001
MCV (fL)	77.31 (10.66)	82.19 (9.04)	4.88 (3.64-6.13)	7.77 (119)	<0.001

[a] Paired t-test

Table 4. The proportion of patients achieving an increase in Hb of at least 1 g/dL and 2 g/dL by baseline iron status, treatment status, the dose of IV Iron and severity of anaemia

Variables	Total (N)	Achieving Hb Increase of ≥ 1 g/dL		Achieving Hb Increase of ≥ 2 g/dL	
		n (%)	*P*-value[a]	n (%)	*P*-value[a]
Baseline iron status					
TSAT ≤ 20% and serum ferritin ≤ 100 µg/L	47	40 (85.1)	0.078	29 (61.7)	0.052
TSAT > 20% and serum ferritin > 100 µg/L	18	12 (66.7)		7 (38.9)	
TSAT ≤ 20% and serum ferritin > 100 µg/L	47	31 (66.0)		18 (38.3)	
TSAT ≤ 20%	96	73 (76.0)	0.392[b]	48 (50.0)	0.387
TSAT > 20%	18	12 (66.7)		7 (38.9)	
Ferritin ≤ 100 µg/L	48	40 (83.3)	0.060	29 (60.4)	0.032
Ferritin > 100 µg/L	65	44 (67.7)		26 (40.0)	
Treatment status					
IV Iron only	68	49 (72.1)	0.395	34 (50.0)	0.835
Blood transfusion and IV iron	52	41 (78.8)		25 (48.1)	
Dose of IV iron					
< 1000 mg	53	35 (66.0)	0.044	21 (39.6)	0.063
≥ 1000 mg	67	55 (82.1)		38 (56.7)	
Severity of anaemia					
Mild and moderate anaemia	83	58 (69.9)	0.052	38 (45.8)	0.267
Severe anaemia	37	32 (86.5)		21 (56.8)	

[a] Pearson's Chi-square; [b] Fisher's Exac

Table 5. Simple and multiple logistic regression analyses of the predictor of achieved increment Hb ≥ 2 g/dL (n = 120)

Predictor variables	Simple Logistic Regression		Multiple Logistic Regression	
	OR (95% CI)	*P*-value	aOR (95% CI)	*P*-value
Age	0.965 (0.943-0.987)	0.002†		
Gender				
Male	Reference	0.656		
Female	0.842 (0.395-1.793)			
Race				
Malay	Reference			
Chinese	0.387 (0.145-1.033)	0.058†		
Indian	0.518 (0.202-1.328)	0.171†		
Foreigners	0.242 (0.024-2.442)	0.229†		
Blood transfusion				
Yes	0.926 (0.450-1.907)	0.835		
No	Reference			
Total dose of IV iron				
<1000 mg	Reference			
=1000 mg	1.950 (0.913-4.168)	0.085†		
>1000 mg	2.286 (0.575-9.083)	0.240†		
With co-morbidities				
Yes	0.758 (0.193-2.972)	0.691		
No	Reference			
Co-morbidities				
Chronic kidney disease	0.198 (0.053-0.735)	0.016†		
Coronary heart disease	0.378 (0.124-0.150)	0.087†		
Gastrointestinal disease	2.567 (0.833-7.908)	0.101†		
Cancer	1.037 (0.284-3.785)	0.956		
Diabetes mellitus	0.289 (0.137-0.613)	0.001†	0.317 (0.130-0.772)	0.011
Hypertension	0.321 (0.149-0.691)	0.004†		
Heart failure	0.600 (0.137-2.632)	0.498		
Blood disorder	10.977 (2.392-50.629)	0.002†	5.195 (1.024-26.358)	0.047
Uterine fibroid	2.145 (0.378-12.183)	0.389		
Cerebral vascular accident	0.331 (0.099-1.105)	0.072†		
Other co-morbidities	1.138 (0.511-2.538)	0.751		
COVID status				
Negative	Reference			
Positive	0.713 (0.265-1.920)	0.503		
Severity of anaemia				
Mild	Reference			
Moderate	0.829 (0.193-3.566)	0.801		
Severe	1.312 (0.284-6.067)	0.728		
Baseline Hb	0.595 (0.411-0.860)	0.006†	0.541 (0.348-0.843)	0.007
Baseline MCV	0.987 (0.954-1.021)	0.451		
Baseline TSAT				
≥20%	Reference			
<20%	1.571 (0.562-4.396)	0.389		
Baseline Ferritin				
>30µg/dL	Reference		Reference	
≤30µg/dL	3.071 (1.316-7.166)	0.009†	3.059 (1.136-8.240)	0.027
Baseline iron	1.071 (0.950-1.208)	0.263		
Baseline CRP				
≤5mg/L	Reference			
>5mg/L	0.253 (0.048-1.319)	0.103†		
Diagnosis				
Anaemia	1.125 (0.508-2.491)	0.772		
Infection	0.547 (0.264-1.132)	0.104†		
Others	1.475 (0.570-3.814)	0.423		

†Variables included in the multivariate logistic regression. Backward stepwise LR multiple logistic methods were applied in all analyses. No interactions and multicollinearity were detected. Hosmer-Lemeshow Test $\chi 2 = 11.49$, df = 8, $P = 0.176$; Overall classification table = 71.7%; Area under ROC curve = 78.9%. The reference group for co-morbidities and diagnoses is participants without these conditions.

DISCUSSION

The study revealed that anaemia was treated either with intravenous (IV) iron alone or a combination of blood transfusion and IV iron, depending on the patient's clinical condition and the physician's judgement. The effects of blood transfusion are typically transient; once the patient's condition was stabilised, IV iron was administered to address the underlying cause.[14]

Most of our patients are under 65 years old. In contrast, an observational study conducted in a Portuguese internal medicine ward found that anaemia prevalence mainly occurs in elderly patients.[15] This discrepancy could be explained by the insufficient sample size, which may not have accurately reflected the entire population due to missing data. Our study yielded a similar result to the NHMS report and the study by Palareti et al., showing that anaemia is more common in females, primarily due to menstruation and poor nutrition.[3,15]

In the medical ward, the prescribing rate for LMW-ID is higher than iron sucrose because the administration of LMW-ID is more convenient, and it can be given as a total dose infusion. Most of our patients were administered LMW-ID as a one-gram infusion, which is recommended by clinical studies as an adequate dose for most patients.[16]

Most of our patients had TSAT ≤20%; however, half of these patients had ferritin levels ≤100 µg/L, while the other half had levels >100 µg/L. A low serum ferritin level indicates depleted iron stores. However, ferritin is also a positive acute-phase reactant, so an elevated value does not always rule out iron deficiency.[4] The high ferritin levels observed in our study can be attributed to the fact that most patients were diagnosed with infections and underlying chronic diseases that cause inflammation, such as coronary heart disease, chronic kidney disease, and cancer.[12]

For the efficacy outcome, our study demonstrated significant mean changes in Hb from baseline, aligning with most studies that found IV iron to be effective in increasing Hb concentration.[7,12,14,16,17] However, some of these studies reported a significantly higher mean Hb difference compared to our findings. This discrepancy could be attributed to variations in the doses and preparations of IV iron used, the potential effects of erythropoiesis-stimulating agents, and relatively lower mean baseline TSAT and serum ferritin levels (indicating depleted iron stores) or underlying severe IDA, which may influence the treatment response.[7,14,16] Additionally, our study showed that IV iron significantly increased MCV concentration from baseline, consistent with the findings of Koutroubakis et al.17

Another efficacy outcome was defined as achieving an increment in Hb of ≥2 g/dL. One study using a one-gram dose of LMW-ID reported an increase in Hb of ≥2 g/dL in 26.3% of patients.[12] Our study reported a higher percentage of patients achieving this outcome compared to that study.[17] Another study using a one-gram dose of LMW-ID found that 51.1% of patients achieved an Hb increase of ≥2 g/dL, which was almost identical to the result of our study. A separate study using a total dose of ferumoxytol infusion showed that 58.0% of patients experienced an Hb increase of >2 g/dL.[16] This study reported a greater outcome than ours; however, its mean baseline TSAT and serum ferritin levels were relatively lower, which may have influenced the treatment response.

In terms of Hb normalization, a study using a total dose of ferric carboxymaltose infusion found that 56.8% of patients achieved an Hb level of more than 12.0 g/dL by the end of the study.[14] In comparison, only a small proportion of our patients achieved Hb normalization after IV iron therapy. This may be because most patients did not have a follow-up appointment at our facility, resulting in a lack of follow-up laboratory data.

Additionally, our study found that patients who received IV iron doses of ≥1000 mg were significantly more likely to achieve an Hb increment of ≥1 g/dL, and a higher proportion of these patients achieved an Hb increase of ≥2 g/dL. This is consistent with the findings of Reinisch et al., which recommend a higher dose of 1000 mg IV iron for a more pronounced Hb response without compromising safety.[18]

For safety outcomes, our study was consistent with other studies, showing that IV iron is safe.[12,19] Only 2.8% of patients experienced ADRs, leading to discontinuation in five cases. There was only one serious adverse event (seizure) and no deaths reported. However, only one out of six ADRs was reported to MADRAC. This should alert healthcare professionals to the importance of reporting and recording ADRs in the institution's system. Additionally, patients should be given an ADR card to prevent unintended administration.

Our study identified predictors for IV iron use to achieve an Hb increment ≥2 g/dL. Our findings were consistent with other studies showing baseline Hb as a significant predictor, with lower baseline Hb levels resulting in a greater response.[14,18,20] Two studies found CRP to be a significant predictor of response [18,20], while the 2007 DRIVE study showed CRP had no effect.[21] However, due to limited CRP data in our study and a small sample size, we could not conclude whether CRP is a significant predictor, and the results might not be statistically significant.

Studies, including the DRIVE study, found that ferritin levels do not predict IV iron responsiveness, except when ferritin is low (≤300 µg/L).[20-22] TSAT levels (<19% or ≥19%) did not impact IV iron responsiveness.[21] Our study confirmed that high ferritin levels had no significant effect, while low ferritin (≤30 µg/dL) predicted treatment response and indicated iron deficiency. These findings align with the DRIVE study's conclusion that baseline TSAT levels do not affect IV iron responsiveness.

In addition, our study found that among the underlying comorbidities, blood disorders were a significant predictor of an Hb increment ≥2 g/dL. This is associated with the fact that anaemia, idiopathic thrombocytopenic purpura, haemophilia, warm autoimmune haemolytic anaemia, and Evans syndrome were the blood disorders identified in this study. Patients with these conditions may have a low baseline Hb level.

Furthermore, our study found that patients with underlying diabetes mellitus had a lower chance of achieving an Hb increment ≥2 g/dL after IV iron compared to those without diabetes. Studies have shown that elevated serum ferritin and iron are risk factors for type 2 diabetes, which may explain why diabetes mellitus can reduce the treatment response to IV iron.[23,24]

Study Limitation

There were a few limitations to this study. Firstly, data were obtained from medical records and the electronic system, which may affect data quality due to omissions in documentation and missing information. Secondly, we cannot determine if patients received blood transfusions at other hospitals or if they were exposed to iron before admission or after discharge, which could impact the treatment response. Additionally, we did not define iron deficiency as part of our inclusion criteria, although the majority of our patients met laboratory criteria for it. Given the wide variation in practice patterns in the real-world setting, these findings are more likely to reflect actual clinical practice. Lastly, the study's power may be limited due to the small sample size.

CONCLUSION

This study showed that IV iron significantly increases haemoglobin and MCV levels without causing significant adverse events. Lower baseline haemoglobin, ferritin ≤30µg/L, non-diabetes mellitus, and underlying blood disorder are identified as significant predictors for the use of IV iron in the treatment of IDA to achieve an increment of haemoglobin ≥2 g/dL. These predictors may help identify the target population to optimize treatment. The study findings showed positive safety and efficacy of IV iron in patients in general medical wards.

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CONFLICT OF INTEREST

The authors declare no conflict of interests.

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ETHICAL APPROVAL

The study was conducted in accordance with the ethical standards of the Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia, and the University's Ethics Committee, with compliance to the Guidelines on Good Clinical Practice (GCP) and the Declaration of Helsinki. Ethics approval was obtained from MREC (NMRR ID-22-00034-V7P (IIR)) and the University's Ethics Committee (UKM PPI/111/8/JEP-2022-258) prior to the commencement of the study.

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