Asian Journal of Medical Principles and Clinical Practice

Volume 7, Issue 1, Page 88-95, 2024; Article no.AJMPCP.113329

Effectiveness of Intravenous Iron Therapy in Patients with Iron Deficiency Anemia Presented to Emergency Department; Retrospective Study

Muqbil Sayer Alshammari [a++*], Ahmed Almutairi [b#] and Faridah Khalaf Awadh Alharbi [c†]

[a] Saudi Board of Emergency Medicine, King Salman Specialist Hospital, Hail, Saudi Arabia.
[b] King Khalid Hospital, Majmaah, Riyadh, Saudi Arabia.
[c] Alqassim University, Buraydah, Saudi Arabia.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/113329

Original Research Article

Received: 13/12/2023
Accepted: 19/02/2024
Published: 19/02/2024

ABSTRACT

Background: Patients admitted to the Emergency Department (ED) frequently with moderate to severe iron deficiency anemia (IDA). Our goal was to investigate the safety, side effects, and results of parenteral iron treatment for IDA patients presented to HMG ALRYAN hospital in Riyadh's emergency room.

[++] Emergency Medicine Senior Registrar;
[#] Consultant of Emergency Medicine;
[†] General Physician;
**Corresponding author;*

Materials and Methods: This is a retrospective study, conducted in emergency department of HMG ALRYAN hospital Riyadh, among adult IDA patients presented to emergency department for IV iron therapy. The data was collected by authors from hospital electronic database, then entered and analysed using SPSS v 24.

Results: A total of 296 iron deficiency patients were included, their mean age was 35.3 ± 11.2. Females constitute 94.6% of study sample. Mean of baseline hemoglobin concentration was 10.6 ± 1.9. 1/12 later hemoglobin concentration mean was 12.2 ± 1.6. The baseline serum iron concentration ranged from 1 - 155.1 mcg/dL, with mean ± SD of 9.5 ± 16.1. The results showed a significant association between age regarding baseline serum iron concentration, and 1/12 later serum iron concentration, where the younger age ones had higher response to iron. The statistical analysis showed a significant association between adverse effect, and admission to hospital for adverse effect (P=0.003), where most of those who hadn't adverse effects were D/C.

Conclusion: Among included patients 5.4% had adverse effects to IV iron to treat IDA. The younger age patients had a significantly higher response to IV iron therapy.

Keywords: Emergency Department (ED); Intravenous (I.V); Iron Deficiency Anemia (IDA); Adverse Effects (AEs).

1. INTRODUCTION

Anemia is a worldwide health issue that affects children in low-income countries, childbearing age women, and the elderly [1–3]. Anemia prevalence in the Emergency Department (ED) is high [4], reflecting the global burden of a disease that affects people of all ages, genders, and geographical areas [5].

Infections, transfusion responses, immunological suppression, lung injury, alloimmunization, major cost, and the use of a limited and stressed blood supply are all issues with transfusions. When prescribed and delivered appropriately, intravenous iron is more affordable, convenient, and safe, with an estimated incidence of major adverse effects of fewer than one in 200,000 [6].

The degree of anemia, cause of blood loss, concomitant diseases, cost, availability of different iron formulations, and patient preference all influence whether intravenous or oral iron is used to treat iron deficient anemia [7]. Oral iron treatment for IDA is restricted by gastrointestinal absorption and is ineffective in the presence of other acute or chronic medical problems [8]. Intravenous iron therapy, which is supported by laboratory results, has a well-established function in the treatment of IDA when oral preparations are inefficient or unavailable [9]. Unfortunately, this technique has not yet gained acceptance in all medical settings where it should, including the emergency department [4].

Long-standing concerns regarding the safety profile of intravenous iron preparations have been allayed with the release of last-generation products [10]. Intravenous iron therapy for IDA or isolated iron deficiency (ID) has long been used in surgery to treat pre- or post-operative anemia [11], but it has recently gained popularity in other clinical settings such as obstetrics [12,13], gastroenterology [11], and cardiology for IDA or ID associated with congestive heart failure (CHF) [14]. Only a few articles on the use of intravenous iron in the ED [15–18] have been published to date; however, such investigations have piqued interest in the subject. Herein we aimed to study the safety, adverse effects, and outcomes of parenteral iron therapy in Emergency department HMG ALRYAN hospital Riyadh**.**

2. MATERIALS AND METHODS

We conducted a retrospective data analysis using computerized data during the period from Feb 2021 to April 2021. The study was conducted in emergency department of HMG ALRYAN hospital Riyadh. Adult (more than 18 years) of both gender that present to emergency department for IV iron therapy were included in the study. Data collection forms were filled by authors from electronic record and total of 296 patient data were included. Data regarding demographics was collected in addition to past medical history, pregnancy, bariatric surgery, base line and 1/12 later haemoglobin levels, serum iron and adverse effects. Statistical analysis was performed using SPSS v24, mean and standard deviation were used contentious variables, while categorical variables were presented as frequency and standard deviation. Chi square and Mann Whitney tests were used to

found the correlation between the presence of adverse effects and demographic variables as well as other variables such as (co-morbidities and laboratory measures). Paired t-test was used to examine the correlation between change in hemoglobin and serum iron by time.

3. RESULTS

A total of 296 iron deficiency patients were included in the study. Table 1 showed the demographics of our patients. Their ages ranged from fourteen to eighty-six years old, with median (IQR) of 33 (27 - 42), and mean ± SD of 35.3 ± 11.2. Approximately all of them 280 (94.6%) were females. About three-quarters of them 229 (77.4%) were healthy, while the remaining 67 (22.6%) had comorbidities. 78 (26.4%) had a previous medical history of comorbidities, while 218 (73.6%) hadn't. 93 (31.4%) of included females were pregnant. 33 (11.1%) subjected to bariatric surgery. The baseline hemoglobin concentration ranged from 5.8 to 15.7 gm/dL, with median (IQR) of 12 (11.3 - 13.3), and mean ± SD of 10.6 ± 1.9. 1/12 later hemoglobin concentration ranged from 6 – 16 gm/dL, with median (IQR) of 12 (11.3 - 13.3), and mean ± SD of 12.2 ± 1.6. The baseline serum iron concentration ranged from 1 - 155.1 mcg/dL, with median (IQR) of 4.2 (2.3 - 9.4), and mean ± SD of 9.5 ± 16.1. 1/12 later serum iron concentration ranged from 2.9 - 594.4 mcg/dL, with median (IQR) 106.7 (63.6 - 192.4), and mean ± SD of 152.9 ± 139. Approximately all of them 280 (94.6%) hadn't adverse effects, while 16 (5.4%) had. Regarding admission to hospital for adverse effects, approximately all of them 294 (99.3%) were discontinuous or discharged, 1 (0.3%) were admitted to ICU, and 1 (0.3%) were discharged against medical advice.

The statistical analysis showed a significant association between adverse effect, and admission to hospital for adverse effect (*P*=0.003), where most of those who hadn't adverse effects were D/C. There were no significant associations between adverse effects regarding the remaining parameters (Table 2).

The Pearson correlation coefficient showed a significant association between age regarding baseline serum iron concentration (Fig 1), and 1/12 later serum iron concentration, where the younger age ones had higher response to iron (Fig 2) (*P*=0.014, and 0.032, respectively). However, there were no significant association between age regarding baseline serum hemoglobin concentration, and 1/12 later serum hemoglobin concentration (*P*=0.459, and 0.603, respectively) (Table 3).

Paired t-test showed a significant association between baseline and 1/12 later hemoglobin concentration (*P*=0.000). Also, we reported a significant association between baseline and 1/12 later iron concentration (*P*=0.000) (Table 4).

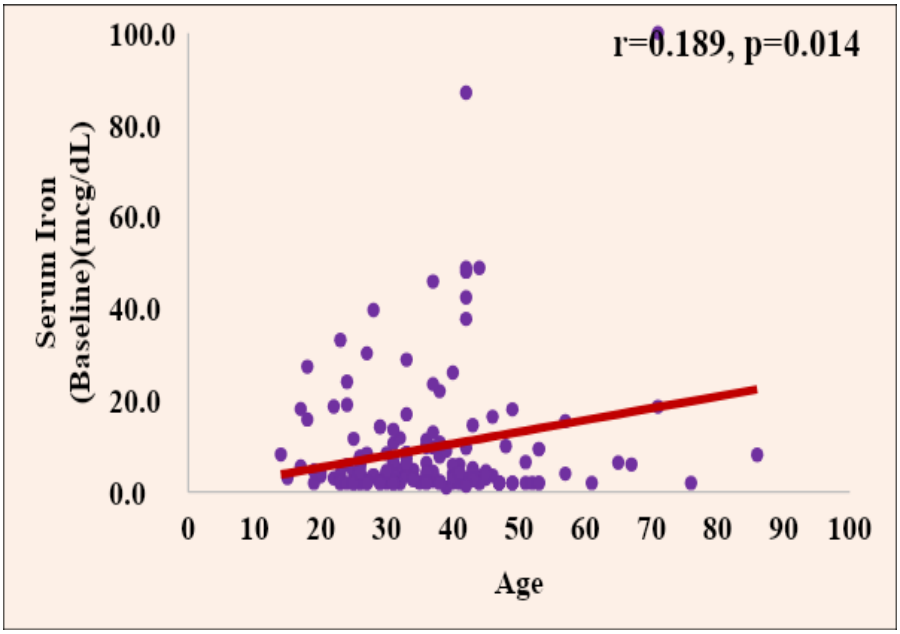

Fig. 1. Association between age regarding baseline serum iron concentration

Table 1. Description of the studied variables

	Description (n=296)
Age	
Range	14 – 86
Mean ± SD	35.3 ± 11.2
Median (IQR)	33 (27 - 42)
Sex	
Male	16 (5.4)
Female	280 (94.6)
Medical Background	
Comorbidities	67 (22.6)
Healthy	229 (77.4)
PMHx of Comorbidities	
Yes	78 (26.4)
No	218 (73.6)
(Female) Pregnant	
Yes	93 (31.4)
No	203 (68.6)
Bariatric Surgery	
Yes	33 (11.1)
No	263 (88.9)
Hb (Baseline) (gm/dL)	
Range	5.8 - 15.7
Mean ± SD	10.6 ± 1.9
Median (IQR)	12 (11.3 - 13.3)
Hb (1/12 later)(gm/dL)	
Range	6 – 16
Mean ± SD	12.2 ± 1.6
Median (IQR)	12 (11.3 - 13.3)
Serum Iron (Baseline)(mcg/dL)	
Range	1 - 155.1
Mean ± SD	9.5 ± 16.1
Median (IQR)	4.2 (2.3 - 9.4)
Serum Iron(1/12 later)(mcg/dL)	
Range	2.9 - 594.4
Mean ± SD	152.9 ± 139
Median (IQR)	106.7 (63.6 - 192.4)
Adverse Effect	
Yes	16 (5.4)
No	280 (94.6)
Admission to Hospital for (AEs)	
D/C	294 (99.3)
ICU	1 (0.3)
DAMA	1 (0.3)

4. DISCUSSION

In the emergency room, there are no clinical practice recommendations that particularly address the management of patients IDA. In this research we aimed to study the safety, adverse effects, and outcomes of parenteral iron therapy in Emergency department HMG ALRYAN hospital Riyadh.

IDA prevalence among our patients regarding to gender was higher in females (94.6%) than in males (5.4%). This ratio was higher than those reported by different studies. Spradbrow et al.,

2017 (19) also reported higher prevalence among females, but with lower ratio than ours, where 69% were female and 31% were males. However, we mismatched with Röhrig et al., 2014 (20) who reported men were found to have anemia substantially more frequently than women, with women having lower hemoglobin levels than men and men having more "mild" anemia with Hb 10 g/dL.

World Health Organization has reported that 24.8% of the general population is anemic. The prevalence of anemia among females (30.2%) is higher than among males (12.7%)

Table 2. Comparisons regarding adverse effect

	Adverse Effect		
	Yes (n=16)	**No (n=280)**	**P value**
Age			
Range	23 - 56	14 - 86	
Mean ± SD	35.5 ± 11.5	35.3 ± 11.2	0.867#
Median (IQR)	32 (26 - 48)	33 (27 - 42)	
Sex			
Male	0 (0)	16 (5.7)	1.000*
Female	16 (100)	264 (94.3)	
Medical Background			
Comorbidities	6 (37.5)	61 (21.8)	0.214*
Healthy	10 (62.5)	219 (78.2)	
PMHx of Comorbidities			
Yes	7 (43.8)	71 (25.4)	0.141*
No	9 (56.3)	209 (74.6)	
(Female) Pregnant			
Yes	3 (18.8)	90 (32.1)	0.262*
No	13 (81.3)	190 (67.9)	
Bariatric Surgery			
Yes	1 (6.3)	32 (11.4)	1.000*
No	15 (93.8)	248 (88.6)	
Hb (Baseline) (gm/dL)			
Range	7.5 - 14.7	5.8 - 15.7	
Mean ± SD	10.5 ± 2	10.6 ± 1.9	0.953#
Median (IQR)	10.4 (8.6 - 11.8)	10.3 (9.3 - 11.8)	
Hb (1/12 later)(gm/dL)			
Range	9.2 - 14.4	6 - 16	
Mean ± SD	12 ± 2	12.2 ± 1.5	0.879#
Median (IQR)	13.2 (10.3 - 13.3)	12 (11.3 - 13.2)	
Serum Iron (Baseline)(mcg/dL)			
Range	2 - 30.2	1 - 155.1	
Mean ± SD	7.8 ± 9.4	9.5 ± 16.3	0.786#
Median (IQR)	4.5 (2.8 - 7.9)	4.2 (2.1 - 9.6)	
Serum Iron(1/12 later)(mcg/dL)			
Range	2.9 - 192.4	7.6 - 594.4	
Mean ± SD	142.4 ± 93	153.5 ± 141.2	0.727#
Median (IQR)	187.1 (95 - 189.7)	105.7 (63.6 - 198.3)	
Admission to Hospital for (AEs)			
D/C	14 (87.5)	280 (100)	**0.003***
ICU	1 (6.3)	0 (0)	
DAMA	1 (6.3)	0 (0)	

**Chi square test, #Mann Whitney test*

Table 3. Correlation of age with HB & S. iron

	Age	
	r	**P**
Hb (Baseline) (gm/dL)	-0.050	0.459
Hb (1/12 later)(gm/dL)	0.042	0.603
Serum Iron (Baseline)(mcg/dL)	0.189	**0.014**
Serum Iron(1/12 later)(mcg/dL)	0.241	**0.032**

r= Pearson correlation coefficient

Table 4. Change of HB & S. iron by time

	Baseline	**1/12 later**	**P value***
Hb (Baseline) (gm/dL)			
Range	5.8 - 15.7	6 - 16	
Mean ± SD	10.6 ± 1.9	12.2 ± 1.6	**0.000**
Median (IQR)	10.3 (9.3 - 11.8)	12 (11.3 - 13.3)	
Serum Iron (Baseline)(mcg/dL)			
Range	1 - 155.1	2.9 - 594.4	
Mean ± SD	9.5 ± 16.1	152.9 ± 139	**0.000**
Median (IQR)	4.2 (2.3 - 9.4)	106.7 (63.6 - 192.4)	

**Paired t-test*

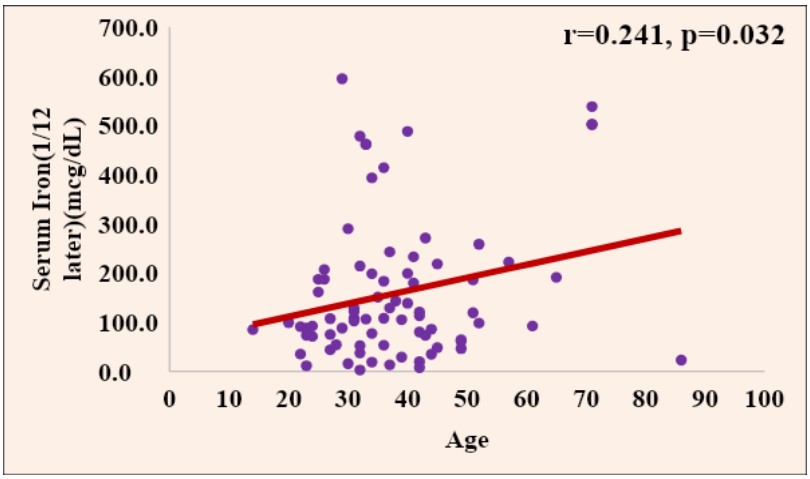

Fig. 2. Association between age regarding 1/12 later serum iron concentration

Approximately all of them 294 (99.3%) were discontinuous or discharged, 1 (0.3%) was admitted to ICU, and 1 (0.3%) was discharged against medical advice. these results mismatched with Spradbrow et al., 2017 (19) who reported 63 percent of discharged IDA patients that was referred to ED by their general physician, most frequently for transfusion or low hemoglobin. In our study, a primary care educational intervention aimed at IDA diagnostic management may have resulted in fewer ED referrals.

Nausea is the most prevalent side effect of intravenous iron. Anaphylaxis can occur with intravenous iron infusions; however, it is uncommon. Extravasation of iron solutions into the subcutaneous tissue results in brownish stains that are both persistent and unsightly for the patient (21). Among our patients 5.4% had AEs for IV iron, which was higher than this reported by Arastu et al., 2022 (21) who reported that side effect were detected in only 3.9% of all infusion cases. We showed a significant association between adverse effect, and admission to hospital for adverse effect (*P*=0.003), where most of those who hadn't adverse effects were D/C. There were no significant associations between adverse effects regarding the remaining parameters.

The existing literature demonstrates a correlation between increasing age and a reduction in hemoglobin level (22). Patel et al., 2008 (23) reported that the prevalence of anemia increases with advancing age after the age of 50 and exceeds 20% in those ≥85 years of age among community dwelling individuals. Our results, however, did not show any statistically significant difference between age regarding neither baseline hemoglobin level, nor 1/12 later level. These results matched with recent study conducted by Alsaeed et al., 2022 (24) who reported no significant association between age and hemoglobin concentration among hospitalized patients. This may be related to our specifically selected cohort. Since our study subjects all had IDA that required admission to ED for IV iron regardless of age.

We showed a significant association between age regarding baseline serum iron concentration, and 1/12 later serum iron concentration, where the younger age ones had higher response to iron. There were no similar studies to compare with our results.

Beside several strengths of the present study, which is to our knowledge the first one on this relevant subject in our country, this research has a number of limitations. First, because only IDA patients were screened, it's probable that our study undercounted the IDA prevalence in ED patients by only including iron deficiency cases. Second, because our study is based on a retrospective chart review, it is susceptible to documentation bias. Since emergency physicians may have thought of IDA or acknowledged a previously completed ferritin level but did not record, it is difficult to properly analyse documentation and identification of IDA. Even though IDA is not a life-threatening illness, there may be valid reasons—such as the patient's wishes or transfer to the primary care team for more investigation—to postpone initiating iron treatment in the ED. Moreover, our findings might not be as broadly applicable as they could be because our audit was restricted to a single centre.

5. CONCLUSION

Among our patients 5.4% had adverse effects to IV iron to treat IDA. AEs were lower among those who hadn't adverse effects were D/C. The younger age ones had a significantly higher response to IV iron.

CONSENT

It is not applicable.

ETHICAL APPROVAL

As per international standards or university standards written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that they have no known competing financial interests or non-financial interests or personal relationships that could have appeared to influence the work reported in this paper.

REFERENCES

1. Le CHH. The Prevalence of Anemia and Moderate-Severe Anemia in the US Population (NHANES 2003-2012). Collins JF, editor. PLoS One. 2016;11(11): e0166635.
2. Girelli D, Marchi G, Camaschella C. Anemia in the Elderly. HemaSphere. 2018;2(3):e40.
3. Gupta P, Perrine C, Mei Z, Scanlon K. Iron, Anemia, and Iron Deficiency Anemia among Young Children in the United States. Nutrients. 2016;8(6): 330.
4. Beverina I, Brando B. Prevalence of anemia and therapeutic behavior in the emergency department at a tertiary care Hospital: Are patient blood management principles applied? Transfus Apher Sci. 2019;58(5):688–92.
5. Kassebaum NJ, Jasrasaria R, Naghavi M, Wulf SK, Johns N, Lozano R, et al. A systematic analysis of global anemia burden from 1990 to 2010. Blood. 2014 Jan 30;123(5):615–24.
6. Chertow GM, Mason PD, Vaage-Nilsen O, Ahlmén J. Update on adverse drug events associated with parenteral iron. Nephrol Dial Transplant. 2006;21(2):378–82.
7. Boone S, Powers JM, Goodgame B, Peacock WF. Identification and Management of Iron Deficiency Anemia in the Emergency Department. J Emerg Med. 2019;57(5):637–45.
8. Goodnough LT. Iron deficiency syndromes and iron-restricted erythropoiesis (CME). Transfusion. 2012;52(7):1584–92.

9. Executive Summary. Am J Kidney Dis. 2006;47:S11–5.
10. Auerbach M, Adamson J, Bircher A, Breymann C, Fishbane S, Gafter-Gvili A, et al. On the safety of intravenous iron, evidence trumps conjecture. Haematologica. 2015;100(5):e214–5.
11. Aksan A, Işık H, Radeke HH, Dignass A, Stein J. Systematic review with network meta-analysis: comparative efficacy and tolerability of different intravenous iron formulations for the treatment of iron deficiency anaemia in patients with inflammatory bowel disease. Aliment Pharmacol Ther. 2017;45(10):1303–18.
12. Muñoz M, Stensballe J, Ducloy-Bouthors A-S, Bonnet M-P, De Robertis E, Fornet I, et al. Patient blood management in obstetrics: prevention and treatment of postpartum haemorrhage. A NATA consensus statement. Blood Transfus. 2019;17(2):112–36.
13. Lewkowitz AK, Gupta A, Simon L, Sabol BA, Stoll C, Cooke E, et al. Intravenous compared with oral iron for the treatment of iron-deficiency anemia in pregnancy: A systematic review and meta-analysis. J Perinatol. 2019;39(4):519–32.
14. Anker SD, Kirwan B-A, van Veldhuisen DJ, Filippatos G, Comin-Colet J, Ruschitzka F, et al. Effects of ferric carboxymaltose on hospitalisations and mortality rates in iron-deficient heart failure patients: an individual patient data meta-analysis. Eur J Heart Fail. 2018;20(1):125–33.
15. Quintana-Díaz M, Fabra-Cadenas S, Gómez-Ramírez S, Martínez-Virto A, García-Erce JA, Muñoz M. A fast-track anaemia clinic in the Emergency Department: feasibility and efficacy of intravenous iron administration for treating sub-acute iron deficiency anaemia. Blood Transfus. 2016;14(2):126–33.
16. Díaz MQ, Borobia AM, García Erce JA, Maroun-Eid C, Fabra S, Carcas A, et al. Appropriate use of red blood cell transfusion in emergency departments: a study in five emergency departments. Blood Transfus. 2017;15(3):199–206.
17. Khadadah F, Callum J, Shelton D, Lin Y. Improving quality of care for patients with iron deficiency anemia presenting to the emergency department. Transfusion. 2018;58(8):1902–8.
18. Beverina I, Razionale G, Ranzini M, Aloni A, Finazzi S, Brando B. Early intravenous iron administration in the Emergency Department reduces red blood cell unit transfusion, hospitalisation, re-transfusion, length of stay and costs. Blood Transfus. 2020;18(2):106–16.
19. Spradbrow J, Lin Y, Shelton D, Callum J. Iron deficiency anemia in the emergency department: over-utilization of red blood cell transfusion and infrequent use of iron supplementation. CJEM. 2017 May 7;19(3):167–74.
20. Röhrig G, Klossok W, Becker I, Benzing T, Schulz RJ. Prevalence of anemia among elderly patients in an emergency room setting. Eur Geriatr Med. 2014;5(1):3–7.
21. Arastu AH, Elstrott BK, Martens KL, Cohen JL, Oakes MH, Rub ZT, et al. Analysis of Adverse Events and Intravenous Iron Infusion Formulations in Adults With and Without Prior Infusion Reactions. JAMA Netw Open. 2022;5(3):e224488.
22. Guralnik JM, Eisenstaedt RS, Ferrucci L, Klein HG, Woodman RC. Prevalence of anemia in persons 65 years and older in the United States: evidence for a high rate of unexplained anemia. Blood. 2004;104 (8):2263–8.
23. Patel K V. Epidemiology of anemia in older adults. Semin Hematol. 2008;45(4): 210–7.
24. Alsaeed M, Ahmed SS, Seyadi K, Ahmed AJ, Alawi AS, Abulsaad K. The prevalence and impact of anemia in hospitalized older adults: A single center experience from Bahrain. J Taibah Univ Med Sci. 2022;17 (4):587–95.

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/113329