Original Article

Assessment of Iron Parameters of Obstetricians and Gynecologists in Pakistan: It's not only our Patients who Suffer

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Abstract

Objectives: To determine the iron status of Obstetricians, effect of intravenous ferric carboxymaltose on hemoglobin level and iron status. To evaluate the effect of increase in hemoglobin on quality of life and to determine association between serum ferritin and hemoglobin level

Study Design: Cross-sectional study

Place and Duration of Study: Society of Obstetricians and Gynecologists of Pakistan (SOGP) annual meeting held in Islamabad, Pakistan, from 5th to 7th December 2014

Methodology: Venous blood samples of the participants were collected after informed consent and assessed for hemoglobin concentration, MCV, MCH and serum ferritin. Intravenous ferric carboxymaltose was offered to participants with serum ferritin <100 ng/mL. Repeated assessments of the core laboratory values were performed at 2 and 4 weeks post infusion and participants were asked about feeling of wellbeing using a non-validated, questionnaire.

Results: The mean age of 174 participants was 43.4±9.7 years. Mild to moderate anemia was present in 41% (72). Serum ferritin <15ng/mL was observed in 26.43% (46) with average serum ferritin level of 66.65±82.91ng/mL. An increase of hemoglobin 1.6g/dl was observed 2-4 weeks post infusion in 28 participants who opted to receive IV ferric carboxymaltose. Serum ferritin levels increased from 23.9 ng/mL to 152.9 ng/ml, with 70% of recipients having a value >100 ng/ml. Better state of health was reported post infusion by 89% participants.

Conclusion: Hemoglobin estimation is not true reflection of Iron deficiency. It not only affects poor, illiterate, and least aware population but also health care professionals who are well aware, educated and of good socioeconomic status. Carboxymaltose infusion significantly increased hemoglobin and serum ferritin level and improved feeling of wellbeing.

Key Words: Anemia, Ferric carboxymaltose, Gynecologist, Iron deficiency, Obstetricians, Serum ferritin.

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Introduction

Anemia is a major health problem affecting 1.62 billion people globally.[1] It is more prevalent in developing countries. According to World Health Organization, Pakistan falls into the category of moderate prevalence,

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affecting more people than any other condition and constituting a public health condition of epidemic proportions.[2,3] The health consequences are stealthy but devastating, invisibly eroding the development potential of individuals, societies and national economies.

The symptoms of anemia vary according to the severity from asymptomatic to generalized weakness, fatigue, irritability, palpitations and breathlessness. Iron Deficiency (ID) is one of the most common causes of anemia. Iron is used not only for storage and transport of oxygen but also for metabolism of skeletal and cardiac muscles as component of oxidative enzymes and mitochondrial functioning.[4] Iron deficiency adversely affects the physical performance, cognitive function, quality of life and immune status.[5,6] In a recent study conducted in Taiwan of more than 32,000 patients the overall cancer risk was significantly elevated among patients with Iron Deficiency Anemia (IDA) and was hypothesized to be related to altered immune activities associated with IDA.[7]

On average, it is estimated that humans have 3,000-4,000mg iron.[8] On daily basis the loss is approximately 1-2mg which is compensated by absorption of a similar amount through dietary sources and hence any reduction in either intake or increase in loss may lead to ID.[8] Women are at greater risk of developing ID due to inadequate iron supplementation or poor nutrition (especially where vegetarian diets apply), heavy menstruation, repeated child birth, shortened inter-pregnancy interval and lack of antenatal care.[9] It is anticipated that up to 40% of women enter pregnancy in an ID state.[10]

Children born to mothers with ID have a greater risk for developing ID. Due to the importance of iron in the early stages of development, ID adversely affects the cognitive function, physical growth and capacity of infants and children.[11]

Serum ferritin levels lower than 15ng/mL confirm ID however due to fluctuations between individuals, a value of >100ng/mL is required to exclude iron deficiency.[12] In patients suffering from chronic inflammatory diseases, serum ferritin may be less reliable and in such cases; transferrin saturation (TSAT) may be the more appropriate marker.[13] Asia Pacific expert recommendations state that normal hemoglobin levels do not equate to normal iron levels.[14] Treatment of anemia secondary to iron deficiency involves treating the underlying cause and iron replacement by oral or parenteral route. The aim of iron therapy is to replenish body iron deficits.[15]

As prevalence of ID with and without anemia is very high in Pakistan.[3] Hence this study has taken a unique approach to assess the iron status of the obstetricians and gynecologists treating patients at high risk of iron deficiency i.e. pregnant women and/or those with other conditions often associated with iron deficiency such as heavy menses. The aim of the study was to determine the iron status of Obstetricians, effect of Intravenous (IV) ferric Carboxymaltose on Hb level and Iron status. In addition, the effect of increase in Hb on quality of life and association between serum ferritin and Hb level was calculated.

Methodology

This cross-sectional study was performed on healthy volunteers that gave their consent during the Society of Obstetricians and Gynecologists of Pakistan (SOGP) annual meeting held in Islamabad from 5 –7 December 2014. All the participants were female health care professionals related to the field of Obstetrics and Gynecology. Male obstetricians and gynecologists were excluded from the study. It was reviewed and approved by Ethical reviewer Board of Sir Ganga Ram Hospital/ Fatima Jinnah Medical University, Lahore.

Clinicians and health care providers donated venous blood sample for assessments of hemoglobin concentration, MCV, MCH and serum ferritin. Blood samples were collected during the meeting between the hours of 10am to 2pm reducing diurnal variances that may be otherwise observed. Assessments of laboratory parameters were performed at Aga Khan University Hospital laboratory services.

The WHO criteria to diagnose iron deficiency anemia, was applied. Additionally, weight and age were captured for each participant. All the variables were quantitative and measured using mean and standard deviation. On the basis of hemoglobin levels, study participants were divided into 2 groups: anemic (Hb <12g/dL) and non-anemic (Hb ≥12g/dL) for further analyses and comparisons.

The diagnosis of iron deficiency was determined using criteria per Guyatt et al; namely serum ferritin <15ng/mL is confirmed ID; 15-100ng/mL is potential ID & >100ng/mL excludes ID. [11]

IV ferric carboxymaltose was offered to participants of the survey with serum ferritin <100 ng/mL. For subjects accepting therapy, repeated assessments of the core laboratory values were performed at approximately 2 and 4 weeks post infusion and a simple, non-validated, questionnaire was administered to enquire from the

participants whether they feel better or worse post therapy.

Overall missing values accounted for less than 5% of data and were left blank. Analysis was performed using Eeviews software for statistical analysis. Quantitative variables like, age of participants, Hb level, MCV, MCH, Serum ferritin were calculated as mean and standard deviation. Qualitative variables like quality of life assessment were given in percent. Student t test was applied as test of significance and p value, ≤0.05 is considered significant.

Results

Overall 174 female clinicians and health care providers donated blood samples for assessment of iron parameters. The mean age of the participants was 43.4±9.7 (24-72) years and the average body weight was 69.2±12.8Kg (46.0 to 120.0Kg).

The average hemoglobin concentration of participants was 12.3±1.37g/dL (8.0 g/dL to 16.1g/dL). In total, 41% participants had mild to moderate anemia (Hb<12g/dL). Iron deficiency (serum ferritin <15ng/mL) was observed in 26.43% (46) of the population surveyed, with average serum ferritin level of 66.65+ 82.91ng/mL (2.5ng/mL – 734.0 ng/mL) and only 21.83% (38) of participants had a serum ferritin >100ng/mL. (Table I)

Table I: Iron parameters in anemic & non anemic groups (n=174)

Parameters	Total	Hb ≥12 g/dL (Non-anemic)	Hb <12 g/dL (Anemic)
Group	174	102 (59%)	72 (41%)
Age (Years)	43.4 ± 9.67	44.5 ± 9.7	41.8 ± 9.24
Hb. (gm/dL)	12.32 ± 1.36	13.15 ± 0.87	11.15 ± 1.04
MCV	80.7 ± 15.75	85.22 ± 4.99	74.28 ± 22.34
MCH	24.86 ± 4.97	26.49 ± 1.50	22.54 ± 6.92
S. Ferritin ng/mL	66.65 ± 82.91	89.27 ± 96.06	34.63 ± 42.99

The mean serum ferritin was 89.27±96.06 (4.2-734) ng/mL and 34.63±42 (2.5 to 210) ng/mL for the non-anemic and anemic groups respectively. The percentage of patients with serum ferritin <15ng/mL was 45.83% (33) and 12.74% (13) in the anemic and non-anemic groups whilst 6.94% (5) and 32.35% (33) had serum ferritin levels greater than 100ng/mL in 2 groups respectively (Figure I and II) .

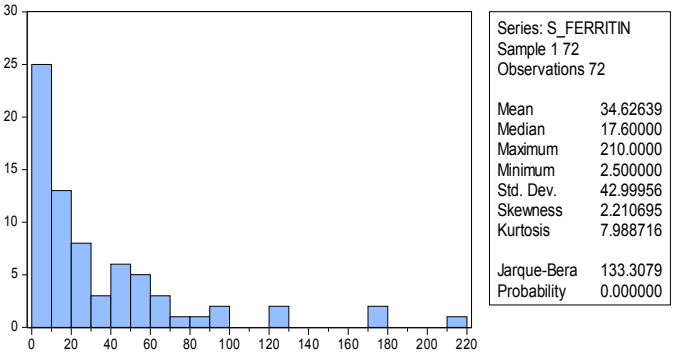

Figure I. Serum Ferritin in Anemic Group

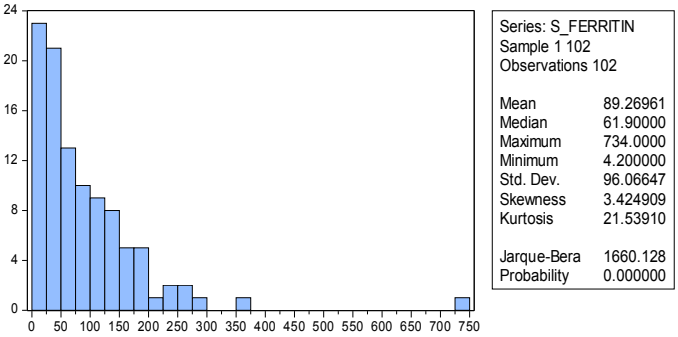

Figure II: Serum ferritin in non- anemic group

The correlation coefficient r=0.37 indicating the weak positive correlation of hemoglobin with serum ferritin. The both variable weak positive correlation indicates that if hemoglobin is increased then s. ferritin level will also increase and vice versa. (Figure III)

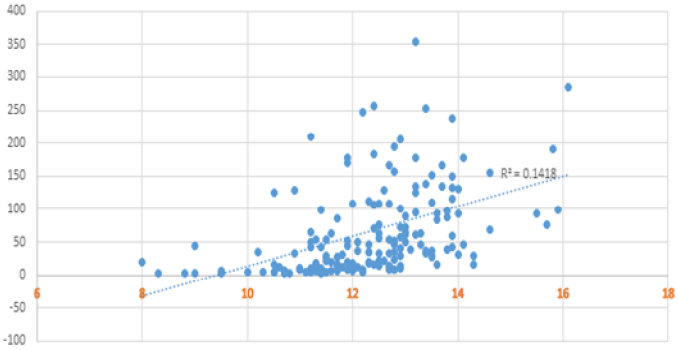

Figure III: Scattor plot of serum Ferritin and Hb concentration

Post assessments, 28 HCP's elected to receive IV Ferric Carboxymaltose (FCM) to correct their iron deficiency. Between 500 and 1000mg iron (average dose: 643mg iron) as FCM was administered as an intravenous infusion over ~15 minutes with dilution in normal saline. The baseline and 2-4 weeks post infusion Hb and serum ferritin of recipients have been

show in Table II. 70% of women had a value >100 ng/mL and all had a value greater than 50ng/mL (Figure IV).

Table II: Comparison of iron parameters pre & post infusion FCM

Parameters	Pre infusion FCM	Post infusion FCM	P value
No. of subjects	28	28	
Hb. Gm/dl	11.25 ± 1.40	12.80 ± 1.01	<0.0001
Serum ferritin ng/mL	23.87 ± 21.53	147.47 ± 93.6	<0.0001
FCM dose	642.8± 230		

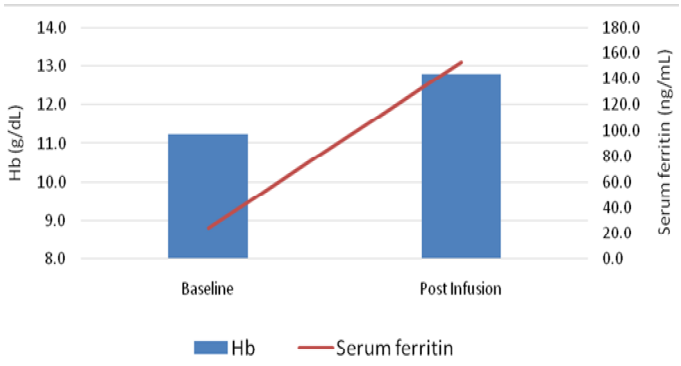

Figure IV. Change in Hb and serum ferritin 2-4 post FCM infusion

A simple non-validated quality of life (QoL) questionnaire was filled by all who received FCM with 89% of the participants reported feeling a little or much better post infusion and the remaining with no change (Figure V). No adverse events related to IV FCM were recorded in these otherwise healthy women post infusion.

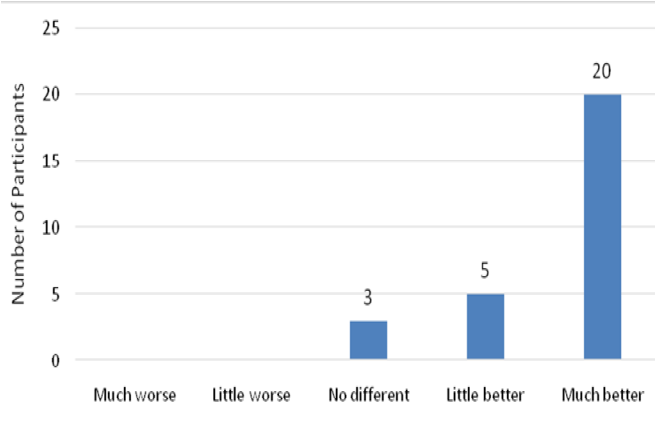

Figure V. Quality of Life response 2-4 weeks post infusion FCM

Discussion

Anemia is a major health problem in Pakistan with iron deficiency remaining the primary cause.[3, 16]

In this study, 41% of the health care professionals surveyed, had mild to moderate iron deficiency anemia. Moreover significant proportion of the surveyed population were iron deficient, 45.8 % having serum ferritin levels <15ng/mL and only 21% having levels >100ng/mL (which would exclude iron deficiency).[12] This data reflects the extent of ID in our population and is suggestive of the need to closely monitor the iron levels along with hemoglobin of not only our patients but the care givers (and general population) as well. Detection of anemia in 41 % of the study participants is not only alarming but also indicates ignorance about self-wellbeing. Despite being highly educated, well aware of ID causes and with a generally higher socioeconomic status (compared to many patients) never thought of taking iron supplementation.

Significantly high proportion of Iron deficiency detected in our study participants may also reflect the different nutritional and dietary habits of Pakistani population versus other ethnic nationals. Whilst nutritional deficiencies and lack of knowledge about Iron absorption inhibitors and promoters explain many of the cases from this study, it is worth noting that other causes may exist in the populations presenting with IDA. For instance, hookworm infestation is common due to poor sanitation.[16] Both malarial control and parasitic disease can be improved via health services and improved sanitation.[17]

Treatment of iron deficiency is an easy task with several options available to clinicians. Firstly, appropriate dietary amendments may offer a simple solution although are often the most difficult to implement. A national action plan based on appropriate dietary modification, food fortification, improved sanitation and iron supplementation should be formulated and implemented.[16] Awareness about iron inhibitors and promoters can help people to modify their dietary habits. Role of fruit juices to enhance iron absorption and tea to inhibit iron absorption needs to be emphasized. Encourage consumption of milk and dairy products as between meal snacks rather than at meal time.[18-21]

Therapeutic interventions, such as oral and intravenous iron, are also widely available. Oral iron remains the first line therapy but the main issue is the poor compliance and tolerance due to GI side effects and possibly the long duration required to replenish iron

stores. Additionally, the effectiveness of oral iron in patients with underlying inflammatory conditions may be of limited benefit due to difficulties with absorption.[22] Parenteral iron offers rapid repletion and a shorter duration of treatment. It is useful in patients at high or urgent need of their iron replenishment i.e. at late stage of pregnancy, within 4 weeks of planned surgery (to aid in reducing unnecessary transfusions), when excessive blood loss exceeds intake of iron (such as heavy menstruation) or when iron is not being absorbed by the GI system (e.g. inflammatory bowel disease).[23]

In this study, 28 subjects diagnosed as iron deficient had parenteral iron repletion using ferric carboxymaltose. A significant increase was observed for both serum ferritin (confirming appropriate repletion of the iron stores) and Hb concentration (or correction of anemia) within 4-6 weeks similar to other published studies.[24, 25] Iron treatment in subjects with low serum ferritin improves symptoms like fatigue, physical performance and quality of life even in cardiac patients.[26-28] Quality of life survey filled by our participants, majority (89%) reported improvement. A randomized placebo-controlled study revealed that a single 1000mg iron infusion of ferric carboxymaltose effectively improved the fatigue symptoms, cognitive functions and quality of life in iron deficient women with normal or borderline haemoglobin.[29]

Conclusion

It is concluded that anemia affects more than 40% of the female health care providers caring for the Pakistani society. This suggests that iron deficiency anemia is a problem affecting not only the poor, illiterate and least aware population of Pakistan but also the highly educated, well aware community with better socioeconomic status who, ironically, treat the high risk population. Hemoglobin estimation is not true reflective of Iron deficiency anemia. Iron deficiency should be assessed on a more frequent basis, especially in women with otherwise unexplained fatigue. Oral and parenteral formulations may be warranted when ID is diagnosed.

References

1. De Benoist B, McLean E, Egli I, Cogswell M, Cogswell M. WHO global database on anaemia. Geneva: WHO. 2008:1993-2005.
2. Kassebaum NJ, Jasrasaria R, Naghavi M, Wulf SK, Johns N, Lozano R, Regan M, Weatherall D, Chou DP, Eisele TP, Flaxman SR. A systematic analysis of global anemia burden from 1990 to 2010. Blood. 2014;123(5):615-24.
3. Akhtar S, Ahmed A, Ahmad A, Ali Z, Riaz M, Ismail T. Iron status of the Pakistani population-current issues and strategies. Asia Pacific journal of clinical nutrition. 2013;22(3):340-347.
4. Jankowska EA, von Haehling S, Anker SD, Macdougall IC, Ponikowski P. Iron deficiency and heart failure: diagnostic dilemmas and therapeutic perspectives. European heart journal. 2012. DOI: http://dx.doi.org/10.1093/eurheartj/ehs224 ehs224
5. Johnson TA. Anaemia. In: Luesley DM, Bakker PN, editors. Obstetrics and Gynaecology an evidence- based text for MRCOG 2nd ed. London: Hodder Arnold. 2010; 139-143.
6. Camaschella C. Iron deficiency Anemia. N Engl J Med.2015; 372:1832-1843.
7. Hung N, Shen CC, Hu YW, Hu LY, Yeh CM, Teng CJ, et al.. Risk of cancer in patients with iron deficiency anemia: a nationwide population-based study. PloS one. 2015 ;10(3):e0119647.
8. Waldvogel-Abramowski S, Waeber G, Gassner C, Buser A, Frey BM, Favrat B, Tissot JD. Physiology of iron metabolism. Transfusion Medicine and Hemotherapy. 2014;41(3):213-221.
9. Naz H, Begum B. Prevalence and associated risk factors of anaemia in pregnant women in a teaching hospital, Korangi Industrial Area. Pak J Surg. 2013;29(2):131-133.
10. Milman N. Prepartum anemia: prevention and treatment. Ann Hematol 2008; 87(12):949-959.
11. Noronha JA, Khasawenh E, Seshan V, Ramasurbramaniam S, Raman S. Anemia in Pregnancy-consequences and challenges: A review of literature. J S Asian Fed Obstet Gynecol.2012; 4(1):64-70.
12. Guyatt et al. Laboratory diagnosis of iron deficiency anemia: an over view. J Gen Intern Med.1992;7(2): 145-153.
13. Zahu a, Kaneshiroin, Kaunitz JD. Evaluation and Treatment of Iron deficiency Anemia: A Gastroenterological Perspective. Dig Dis Sci.2010; 55:548-559.
14. Breymann C, Bian XM, Blanco-Capito LR, Chong C, Mahmud G, Rehman R. Expert recommendations for the diagnosis and treatment of iron-deficiency anemia during pregnancy and the postpartum period in the Asia-Pacific region. Journal of perinatal medicine. 2011;39(2):113-21.
15. Pasricha SR, Drakesmith H, Black J, Hipgrave D, Biggs BA. Control of iron deficiency anemia in low-and middle-income countries. Blood. 2013 Apr 4;121(14):2607-17.
16. Balarajan Y, Ramakrishnan U, Özaltin E, Shankar AH, Subramanian SV. Anaemia in low-income and middle-income countries. The Lancet. 2012;378(9809):2123-2135.
17. Goodnough LT, Schrier SL. Evaluation and management of anemia in the elderly. Am J Hematol 2014; 89(1):88-96.
18. WHO and UNICEF, Focusing on Anaemia: Towards an Integrated Approach for Effective Anaemia Control, WHO, Geneva, Switzerland, 2004.
19. Akhtar S, Asghar A. Mineral fortification of whole wheat flours an overview. In: Preedy VR, Watson RR, Patel VB, editors. Fortification of flours and breads and their metabolic effects. Boston: Elsevier/academic Press; 2011. 263-271.
20. Goddard AF, James MW, Mclntyre AS, et al. Guidelines for the management of iron deficiency anaemia. Gut 2011; 60:1309. Gut doi:10.1136/gut.2010.228874
21. Recommendations to prevent and control iron deficiency in the United States. Centers for Disease Control and prevention. MMWR Morb Mortal Wkly Rep 1998; 47:1.
22. Khalafallah A, Dennis A, Bates J, et al. A prospective randomized, controlled trial of intravenous versus oral iron for moderate iron deficiency anaemia of pregnancy. J Intern Med. 2010; 268-286.
23. Krayenbuehl PA, Battegay E, Breymann C, Furrer J, Schulthess G. Intravenous iron for the treatment of fatigue in nonanemic, premenopausal women with low serum ferritin concentration. Blood. 2011 Sep 22;118(12):3222-3227.
24. Breymann C, Gliga F, Bejenariu C, Strizhova N. Comparative efficacy and safety of intravenous ferric carboxymaltose in the treatment of postpartum iron deficiency anemia. International Journal of Gynecology & Obstetrics. 2008 ;101(1):67-73.

25. Barish CF, Koch T, Butcher A, Morris D, Bregman DB. Safert and efficacy of Intravenous Ferric Carboxymaltose(750mg) in the Treatment of Iron Deficiency Anemia: Two Randomized Controlled Trials. Anemia 2012.
26. Vaucher P, Druais PL, Waldvogel S, Favrat B. Effect of iron supplementation on fatigue in nonanemic menstruating women with low ferritin: a randomized controlled trial. Canadian Medical Association Journal. 2012 Aug 7;184(11):1247-1254.
27. Garvican LA, Saunders PU, Cardoso T, Macdougall IC, Lobigs LM, Fazakerley R, Fallon KE, Anderson B, Anson JM, Thompson KG, Gore CJ. Intravenous iron supplementation in distance runners with low or suboptimal ferritin. Medicine and science in sports and exercise. 2014;46(2):376-385.
28. Gaber R, Kotb NA, Ghazy M, Nagy HM, Salama M, Elhendy A. Tissue Doppler and strain rate imaging detect improvement of myocardial function in iron deficient patients with congestive heart failure after iron replacement therapy. Echocardiography. 2012;29(1):13-18.
29. Favrat B, Balck K, Breymann C, Hedenus M, Keller T, Mezzacasa A, Gasche C. Evaluation of a single dose of ferric carboxymaltose in fatigued, iron-deficient women–PREFER a randomized, placebo-controlled study. PLoS One. 2014 9(4):e94217.