The efficacy of the heme bound iron supplement (Optifer®) in treatment of iron deficiency anemia with Pregnancy

**ABSTRACT**

**Background:** The World Health Organization defined hemoglobin below 11 gm/ dl as anemia. Iron deficiency is the most common cause of anemia among other nutritional deficiencies. The iron requirements during pregnancy are higher, and it increases furthermore during the second, and third trimesters. Maternal anemia is a leading cause of perinatal morbidity, and adverse outcome in obstetrics.

**Objectives:** This comparative study designed to evaluate the efficacy, and tolerability the heme bound iron supplement (Optifer®) in treatment of iron deficiency anemia during pregnancy.

**Patients and methods:** One hundred and ten pregnant (110) women with hemoglobin level below 10 gm/dl due to iron deficiency anemia will included in this comparative study, after approval of the study, and after informed consent. Studied women will be receive the heme bound iron supplement (Optifer®) tablets for correction of iron deficiency anemia during pregnancy twice daily till hemoglobin level of 11-12 gms/dl, then one tablet daily as maintenance. Studied women will asked during each ante-natal care visit for any side effects related to Optifer® as gastrointestinal upset, metallic taste, constipation and/or intolerance. Treatment efficacy of Optifer® will checked by comparing the pre-treatment hemoglobin, ferritin, reticulocytes, MCV, and MCH by the 3 months` post-treatment values. Primary outcome measures: the efficacy, of the heme bound iron supplement (Optifer®) in treatment of iron deficiency anemia during pregnancy. While the secondary outcome measures; the tolerability, and the side effects related to the Optifer®.

**Key words:** Heme, iron, Optifer®, deficiency, pregnancy.

**INTRODUCTION**

The World Health Organization defined hemoglobin below 11 gm/ dl as anemia [1]. Iron deficiency is the most common cause of anemia among other nutritional deficiencies (B12, and folic acid) [2].

The iron requirements during pregnancy are higher, and it increases furthermore during the second, and third trimesters [3]. In addition, a blood loss of ≥1 Liter occurs in 7% of vaginal deliveries, and 23% of cesarean deliveries associated with 1000-1500 ml blood loss [4-5].

Maternal anemia is a leading cause of perinatal morbidity, and adverse outcome in obstetrics [6-9]. Adequate, and effective iron supplementation is crucial during pregnancy to reduce the perinatal morbidity related to iron deficiency anemia [10].

Oral iron therapy is safe, cost-effective treatment for iron deficiency anemia during pregnancy. The conventional non-heme iron preparations given on empty stomach, and associated with gastric discomfort, constipation, which adversely affect the compliance, and the treatment outcome [11-12].

The heme iron is effective, well tolerable oral iron preparation, its use during pregnancy improves the compliance, and ensures continuous iron intake during pregnancy [11-13].

*Nissenson et al, concluded* that theuse of hem iron for 6 months in hemodialysis patients was effective in treatment of iron deficiency anemia, and replaced the intravenous iron preparations [14].

*Abdelazim et al,* concluded that the heme iron is safe, effective, well tolerable oral iron preparation as well as intravenous iron saccharate for treatment of iron deficiency during pregnancy [13,15].

In addition, *Hoppe at el,* conducted a 12 weeks intervention study to investigate the possibility of using heme iron as a diet-based treatment to improve the iron status of women of reproductive age. *Hoppe at el,* concluded that the dietary-based treatment containing heme iron has few side effects, and can be used efficiently to improve the iron status of women of reproductive age [16].

Optifer® is a new genuine heme bound iron supplement made under HACCP (hazards analysis, and critical control points) standards in Sweden. So, this comparative study designed to evaluate the efficacy, and tolerability of the new heme bound iron supplement (Optifer®) in treatment of iron deficiency anemia during pregnancy.

**PATIENTS AND METHODS**

This comparative study will be carried out in Ahmadi hospital, Kuwait Oil Company (KOC) over the next 6 months, after approval of the study by the Obstetrics and Gynecology department ethical committee. This study will include One hundred and ten pregnant (110) women with hemoglobin level below 10 gm/dl due to iron deficiency anemia, after informed consent. Studied women will be receive Optifer® tablets for correction of iron deficiency anemia during pregnancy.

Inclusion criteria includes pregnant women ≥20 years, 14-26 weeks` gestation with hemoglobin level between 8-10 gm/dl. Pregnant women with anemia due to causes other than iron deficiency, and pregnant women received blood transfusion during current pregnancy will excluded from this study. The Diagnosis of iron deficiency anemia based on; hemoglobin concentration (gm/dl), serum ferritin (ug/l), mean Corpuscular Volume (MCV), and mean corpuscular hemoglobin (MCH) [7-9].

The heme bound iron supplement (Optifer®) tablets, (L`Avenir Med., MediTec FerroCare., Sweden) (contain 12 mg heme bound iron in Canada, while it contain 18 mg heme bound iron, and 80 mg vitamin C in Middle east). The heme iron content of the Optifer® tablets has a unique carrier intestinal receptors Heme Carrier Protein-1 (HCP-1). According to the manufacturer instructions, the studied women will receive Optifer® tablets twice daily (1 tablet morning, and 1 tablet evening) not related to meals till hemoglobin level of 11-12 gms/dl, then one tablet daily as maintenance dose [14].

After oral intake, tablets, the iron content of the tablets absorbed by the HCP-1 receptors of the small intestine, and the serum peak of iron reached within 2-4 hours. Each tablet of Optifer® increases the serum iron by 3.15 mg [9]. Studied women will receive oral folic acid with Optifer® to avoid folic deficiency, and participants will asked during each ante-natal care visit for any side effects related to Optifer® as gastrointestinal upset, metallic taste, constipation and/or intolerance. Treatment efficacy of Optifer® will checked by comparing the pre-treatment hemoglobin, ferritin, reticulocytes, MCV, and MCH by the 3 months` post-treatment values [17,18].

Primary outcome measures: the efficacy, of the heme bound iron supplement (Optifer®) in treatment of iron deficiency anemia during pregnancy. While the secondary outcome measures; the tolerability, and the side effects related to the Optifer®.

**Sample size:** The required sample size calculated using data from previous studies [15,16], and G Power software version 3.17 for sample size calculation (Heinrich Heine Universität; Düsseldorf; Germany), setting α -error probability at 0.05, power (1- β error probability) at 0.95%, and effective sample size (w) at 0.3. The effective sample ≥ 110 women needed to produce a statistically acceptable figure.

**Statistical analysis**

Collected data will statistically analyzed using Statistical Package for Social Sciences (SPSS); computer software version 20 (Chicago, IL, USA). Numerical variables will be presented as mean, and standard deviation (±SD), while categorical variables will presented as number (n) and percentage (%). Student (t) test will used to compare the pre-treatment hemoglobin, ferritin, reticulocytes, MCV, and MCH by the 3 months` post-treatment values to evaluate the efficacy of the Optifer® in treatment of iron deficiency anemia during pregnancy. The significance level set as *P*<0.05.

**REFERENCES**

[1]. Güleç UK, Özgünen FT, Evrüke IC, Demir SC. Anemia in Pregnancy. Arch Med Rev J. 2013: 22 (3); 300-316. [Google Scholar]

[2]. WHO. Hemoglobin Concentrations for the Diagnosis of Anemia and Assessment of Severity. Vitamin and Mineral Nutrition Information System. World Health Organization, Geneva. 2011 (WHO/NMH/NHD/MNM/11.1) <http://apps.who.int/iris/bitstream/10665/85839/3/WHO_NMH_NHD_MNM_11.1_> eng.pdf?ua=1

[3]. Bothwell T H. Iron Requirements in Pregnancy and Strategies to Meet Them. [Am J Clin Nutr.](https://www.ncbi.nlm.nih.gov/pubmed/10871591) 2000;72(1 Suppl):257S-264S. [PubMed]

[4]. Stafford I, Dildy GA, Clark SL, Belfort MA. Visually estimated and calculated blood loss in vaginal and cesarean delivery. Am J Obstet Gynecol. 2008; 199 (5): 519. e1-7. doi: 10.1016/j.ajog.2008.04.049. [PubMed]

[5]. Barut A and Harma M. Intravenous iron treatment for iron deficiency anemia in pregnancy. J Turkish-German Gynecol Assoc. 2009; 10: 109-15. [Google Scholar]

[6]. Kalaivani K. Prevalence & consequences of anaemia in pregnancy. Indian J Med Res. 2009; 130 (5): 627-633. [PubMed]

[7]. Shafi D, Purandare SV, Sathe AV. Iron Deficiency Anemia in Pregnancy: Intravenous Versus Oral Route. J Obstet Gynaecol India. 2012; 62 (3): 317-321. doi: 10.1007/s13224-012-0222-0. [PubMed]

[8]. Abdelazim IA, Abu-Faza M, Sanchez VJ. Iron Therapy in Treatment of Iron Deficiency Anemia Before Delivery: Intravenous Versus Oral Route. J Gynecol Obstet Med. 2014; 1: 1-7. doi: 10.13140/RG.2.1.4678.8644. [Google Scholar]

[9]. Abdelazim IA, Abu-Faza ML, Hamdan SB. Intravenous Iron Saccharate Infusion for Treatment of Iron Deficiency. ARC J Gynecol Obstet. 2016; 1: 16-20. http://dx.doi.org/10.20431/2456-0561.0103004 [Google Scholar]

[10]. EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS) (2010) Scientific Opinion on the Safety of Iron (Blood Peptonates) for the Proposed Uses as a Source of Iron Added for Nutritional Purposes to Foods for the General Population, Including Food Supplements. EFSA Journal 2010; 8: 1585. [www.efsa.europa.eu](http://www.efsa.europa.eu). [Google Scholar]

[11]. Pavord S, Myers B, Robinson S, Allard S, Strong J, Oppenheimer C. UK Guidelines on the Management of Iron Deficiency in Pregnancy. [Br J Haematol.](https://www.ncbi.nlm.nih.gov/pubmed/22512001) 2012;156(5):588-600. <https://doi.org/10.1111/j.1365-2141.2011.09012.x>. [PubMed]

[12]. Johnson-Wimbley TD, Graham DY. Diagnosis and Management of Iron Deficiency Anemia in the 21st Century. [Therap Adv Gastroenterol.](https://www.ncbi.nlm.nih.gov/pubmed/21694802) 2011;4(3):177-84. doi: 10.1177/1756283X11398736. [PubMed]

[13]. Abdelazim IA, Abu-Faza M, Elbiaa AAM, Othman HS, Alsharif DA, Elsawah WF. Heme Iron Polypeptide (Proferrin®-ES) Versus Iron Saccharate Complex (Ferrosac) for Treatment of Iron Deficiency Anemia during Pregnancy. Acta Medica International. 2017;4(1): 55-60. doi: 10.5530/ami.2017.4.11.doi: 10.5530/ami.2017.4.11. [Google Scholar]

[14]. Nissenson AR and Charytan C. Controversies in Iron Management. Kidney International. 2003; 64: S64-S71. <https://doi.org/10.1046/j.1523-1755.64.s87.10.x>. [PubMed]

[15]. Abdelazim IA, Abu-Faza M, Elbiaa A, Osman H, Alsharif D, Elsawah W. Heme iron to correct Iron deficiency anemia with pregnancy. Clin Obstet Gynecol Reprod Med. 2017; 3(3), 1–3. <https://doi.org/10.15761/COGRM.1000186>. [Google Scholar]

[16]. [Hoppe M](https://www.ncbi.nlm.nih.gov/pubmed/?term=Hoppe%20M%5BAuthor%5D&cauthor=true&cauthor_uid=22951158), [Brün B](https://www.ncbi.nlm.nih.gov/pubmed/?term=Br%C3%BCn%20B%5BAuthor%5D&cauthor=true&cauthor_uid=22951158), [Larsson MP](https://www.ncbi.nlm.nih.gov/pubmed/?term=Larsson%20MP%5BAuthor%5D&cauthor=true&cauthor_uid=22951158), [Moraeus L](https://www.ncbi.nlm.nih.gov/pubmed/?term=Moraeus%20L%5BAuthor%5D&cauthor=true&cauthor_uid=22951158), [Hulthén L](https://www.ncbi.nlm.nih.gov/pubmed/?term=Hulth%C3%A9n%20L%5BAuthor%5D&cauthor=true&cauthor_uid=22951158). Heme iron-based dietary intervention for improvement of iron status in young women. [Nutrition.](https://www.ncbi.nlm.nih.gov/pubmed/22951158) 2013 Jan;29(1):89-95. doi: 10.1016/j.nut.2012.04.013. [PubMed]

[17]. Yee J, Besarab A (2002) Iron sucrose: the oldest iron therapy becomes new. Am J Kidney Dis. 2002; 40 (6): 1111-1121. [PubMed]

[18]. Teucher B, Olivares M, Cori H. Enhancers of iron absorption: ascorbic acid and other organic acids. Int J Vitam Nutr Res. 2004; 74 (6): 403-419. [PubMed]