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# Lactoferrin with Ferrous Gluconate versus Ferrous Gluconate for Treatment of Iron Deficiency Anaemia during Pregnancy

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## **Abstract**

**Background:** Iron deficiency is the most common single-nutrient deficiency worldwide. According to the US Centers for Disease Control and Prevention (CDC) recommendations, the diagnosis of anemia during pregnancy must be based on hemoglobin (Hb) values lower than 11 mg/dl during the first and the third trimester or lower than 10.5 mg/dl during the second trimester. Ferrous gluconate that has to be administered to patients with iron deficiency anemia in large quantities due to the poor bioavailability of inorganic iron. Moreover, oral administration of ferrous gluconate causes many side effects, including gastrointestinal discomfort, nausea, vomiting, diarrhea and constipation. Lactoferrin is a multifunctional iron-binding protein possessing anti-inflammatory and anti-microbial effects.

**Aim of the Study:** The study aims to compare between lactoferrin with ferrous gluconate versus ferrous gluconate alone in treatment of iron deficiency anemia during pregnancy.

**Patients and Methods:** This was a randomized controlled clinical trial that was conducted in Ain Shams University Maternity Hospital (ASUMH) from March 2023 to November 2023 on 40 pregnant women who had iron deficiency anemia during pregnancy recruited from inpatient/outpatient antenatal clinic of ASUMH.

**Results:** Group B had a significant increase in hemoglobin, hematocrit and serum ferritin level, group A had significantly more nausea than group B ( $p = 0.013$ ), while there was no significant difference between the groups in terms of constipation or non-compliance ( $p > 0.05$ ), there is no significant difference between the groups in terms of age or gestational age.

**Conclusion:** In our study we compared between lactoferrin with ferrous gluconate versus ferrous gluconate in treatment of iron deficiency anemia during pregnancy. Accordingly, we found that Oral lactoferrin with ferrous gluconate is better tolerated with higher increase in mean hemoglobin and lower side effects (nausea) when compared to oral iron therapy alone.

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## **INTRODUCTION**

Iron is a necessary trace element for all mammals and involved in many essential metabolic processes such as oxygen transport, mitochondrial respiration and enzymatic activities (1).

Anemia is characterized by a decreased quantity of red blood cells, often accompanied by diminished hemoglobin levels or altered red blood cell morphology. Anemia is pathophysiologically diverse and often multifactorial (2).

Iron deficiency (ID) is the most common micronutrient deficiency worldwide with >20% of women experiencing it during their reproductive lives. Physiological adaptation in pregnancy leads to physiological anemia of pregnancy. This is because the plasma volume expansion is greater than red blood cell (RBC) mass increase which causes hemodilution (3).

The British Committee for Standards in Hematology guidelines defines pregnancy anemia as hemoglobin level < 11 g/L in the first trimester, < 10.5 g/L in the second trimester, and < 10 g/L during the postpartum period (4).

Lactoferrin is a glycoprotein from the transferrin family consist of 691 amino acids. It is a component of exocrine secretions such as milk and saliva and is present in neutrophil granules. Lactoferrin was identified in 1939 in bovine milk and isolated in 1960 from both human and bovine milk (5).

LF is a multifunctional protein that deserves to be called a “miracle molecule”, exhibiting a number of other beneficial properties such as anti-pathogenic, anti-cancer, anti-inflammatory, immunomodulatory and DNA-regulatory activities (5).

Lactoferrin has two times higher affinity for iron than serum transferrin. Besides, it

permits iron export from tissues to the blood by interplaying with ferroportin and hepcidin which are key proteins in iron homeostasis. Lactoferrin does not provoke adverse gastrointestinal side effects (6).

Oral iron supplementation is an inexpensive and effective option for treating ID in stable outpatients. The recommended dose of elemental iron for treatment of iron deficiency is 100-200mg daily. Higher doses should not be given, as absorption is saturated and side effects increased. Iron salts such as ferrous gluconate, ferrous sulfate, and ferrous fumarate remain the standard first-line therapy for treating ID (4).

The oral dose for iron deficiency anemia should be 40-80mg of elemental iron daily. Ferrous Gluconate Tablets 300mg contain 35mg of elemental iron taken 1-2times/day. If taken correctly, oral iron supplements will give a rise in Hb of 20g/l every 3 weeks.

## **AIM OF THE WORK**

The study aims to compare between lactoferrin with ferrous gluconate versus ferrous gluconate alone in treatment of iron deficiency anemia during pregnancy.

## **PATIENTS AND METHODS**

This was a randomized controlled clinical trial that was conducted in Ain Shams University Maternity Hospital (ASUMH) from March 2023 to November 2023 on 40 pregnant women who had iron deficiency anemia during pregnancy recruited from inpatient/outpatient antenatal clinic of ASUMH.

### **Inclusion criteria:**

Pregnant women with single fetus, microcytic hypochromic anemia, gestational age (14 - 35 weeks), serum ferritin level <24 ng/dl, ages eligible for study: 20 years to 40 years.

### **Exclusion Criteria:**

Associated chronic medical disorder (CKD, liver disease, peptic ulcer and chronic blood

loss), associated bleeding disorder, anaemia requiring blood transfusion (Hb < 7gm/dL), hypersensitivity to iron preparations, haemoglobinopathies (G6PD, thalassemias, sickle cell disease).

This study included two groups: group I: 20 patients were given ferrous gluconate 300 mg (Ferrous-Gluconate®, tab.300mg, glucofer, Egypt) two times daily, group II: 20 patients were given lactoferrin 100mg (Pravotin-sachets®,100mg, Hygint, Egypt) with ferrous gluconate twice daily.

Hematological parameters (rise in hemoglobin), (rise in serum ferritin) and the adverse effects of both drugs were studied at registration and after 4 weeks.

### **Study Procedures:**

#### ***All patients will undergo the following:***

Informed consent will be obtained from all the participants in this study before enrolling in this study and all participants will be subjected to a detailed clinical assessment including: a detailed history, general, abdominal examinations, Investigations.

#### ***1-History taking:***

Personal history: name, age, occupation and address, menstrual and obstetric history: Date of LMP, expected date of delivery which will be calculated according to Naegle's rule and gestational age. In addition to history of presence of any menstrual irregularities, duration. Past History: of Anemia in previous pregnancy, other diseases like Thalassemia, sickle cell anemia, liver or renal diseases or any other condition that may affect hemoglobin.

#### ***2-Medical examination:***

General: Assessment of complexion and vital data (blood pressure, pulse, capillary refill), abdominal examination to assess fundal height.

***3-Investigations*** to perform will include:

Laboratory: Complete blood count (microcytic hypochromic anemia)

Imaging: Ultrasound to assess biometry to exclude fetal growth restriction.

Women will be divided in two groups with 20 in each group, the first group will receive one tab of ferrous gluconate 300mg administered orally twice per day for 4 weeks and the second group will receive lactoferrin sachets 100mg with ferrous gluconate 300mg twice per day for 4 weeks.

Patients were assigned to take the medication orally; once daily before breakfast, and Parvotin (100 sachets were be dissolved each in ¼ glass of water and taken before breakfast). Patients were advised to avoid the intake of tea, coffee, milk, milk products, antacids and calcium preparation within 2 hours before or after iron capsules. Women will be told to record side effects as nausea, vomiting, abdominal discomfort and constipation. Women will have a blood sample (CBC) withdrawn after 4 weeks to assess rise in pregnant anemia.

#### ***Ethical Considerations:***

The study gained the approval from the ethical committee of the department of Obstetrics and Gynecology, faculty of medicine, Ain Shams University. Informed consent was taken after explaining the study purpose and methods to the subjects.

#### ***Data Management and Analysis:***

The collected data was revised, coded, tabulated and introduced to a PC using Statistical package for Social Science (SPSS 25). Data was presented and suitable analysis was done according to the type of data obtained for each parameter.

## RESULTS

**Table 1: Comparison between group A and group B regarding age and gestational age**

	Group A	Group B	t test		
	Mean ± SD	Mean ± SD	t	p value	sig.
Age	32.4 ± 10.16	28.45 ± 6.39	1.47	0.151	NS
gestational age	30.47 ± 3.5	30.5 ± 3.68	-0.03	0.980	NS

This table shows that there is no significant difference between the groups in terms of age or gestational age.

**Table 2: Mixed design ANOVA for Hemoglobin levels among the 2 groups**

HB	Pre	Post	p value	sig.
Group A	9.59 ± 0.14	9.86 ± 0.19	0.172	NS
Group B	9.41 ± 0.14	10.09 ± 0.19	0.001	S
p value	0.359	0.416		
sig.	NS	NS		

The table shows the results of a mixed design ANOVA for hemoglobin levels among the two groups of patients. The table indicates that there was no significant difference in hemoglobin levels between the two groups before or after the treatments, group B had a significant increase in hemoglobin.

**Table 3: Mixed design ANOVA for Hematocrit levels among the 2 groups**

Hematocrit	Pre	Post	p value	sig.
Group A	29.77 ± 0.56	30.29 ± 0.67	0.504	NS
Group B	28.9 ± 0.56	31.77 ± 0.67	0.001	S
p value	0.278	0.124		
sig.	NS	NS		

The table shows the results of a mixed design ANOVA for hematocrit levels among the two groups of patients. The table shows that there was no significant difference in hematocrit levels between the two groups before or after the treatments, but group B had a significant increase in hematocrit from pre to post treatment.

**Table 4: Mixed design ANOVA for MCV levels among the 2 groups**

MCV	Pre	Post	p value	sig.
Group A	79.44 ± 1.64	82.58 ± 1.56	<0.001	S
Group B	75.53 ± 1.64	77.81 ± 1.56	0.043	S
p value	0.100	0.037		
sig.	NS	NS		

The table shows the results of a mixed design ANOVA for mean corpuscular volume (MCV) levels among the two groups of patients. The table shows that there was a significant difference in MCV levels between the two groups after the treatments, with group A having a higher MCV than group B. The table also shows that both groups had a significant increase in MCV levels from pre to post treatment, indicating that the treatments affected the red blood cell size in both groups.

**Table 5: Mixed design ANOVA for MCH levels among the 2 groups**

MCH	Pre	Post	p value	sig.
Group A	25.67 ± 0.71	26.85 ± 0.62	<0.001	S
Group B	24.9 ± 0.71	24.45 ± 0.62	0.035	S
p value	0.447	0.009		
sig.	NS	S		

The table show the results of a mixed design ANOVA for mean corpuscular hemoglobin (MCH) levels among the two groups of patients. The table shows that there was a significant difference in MCH levels between the two groups after the treatments, with group A having higher MCH than group B. The table also reveals that both groups had significant changes in MCH levels from pre to post, with group A increasing and group B decreasing their MCH.

**Table 6: Mixed design ANOVA for Ferritin levels among the 2 groups**

Ferritin	Pre	Post	p value	sig.
Group A	12.3 ± 0.94	19.9 ± 2.56	<0.001	S
Group B	14.55 ± 0.94	35.15 ± 2.56	<0.001	S
p value	0.097	<0.001		
sig.	NS	S		

The table shows the results of a mixed design ANOVA for ferritin levels among the two groups of patients. The table indicates that both groups had a significant increase in ferritin levels after the treatments, but group B had a much higher increase than group A. The table also shows that there was no significant difference in ferritin levels between the two groups before the treatments, but there was a significant difference after the treatments, with group B having higher levels than group A.

**Table 7: Comparison between group A and group B regarding Nausea, Constipation and Non-compliance**

	Group A	Group B	Chi square		
	N (%)	N (%)	X <sup>2</sup>	p value	sig.
Nausea	9 (45%)	2 (10%)	6.14	0.013	S
Constipation	8 (40%)	3 (15%)	3.14	0.077	NS
Non-compliance	6 (30%)	5 (25%)	0.13	0.723	NS

The table shows that group A had significantly more nausea than group B ( $p = 0.013$ ), while there was no significant difference between the groups in terms of constipation or non-compliance ( $p > 0.05$ ).

## **DISCUSSION**

Anemia is defined as a condition in which the Haemoglobin (Hb) level in the body is lower than normal, which results in a decreased oxygen-carrying capacity of red blood cells to tissues (7). It affects all age groups, but pregnant women and children are more vulnerable (8).

According to the WHO guidelines, anemia

in pregnancy is defined as a hemoglobin level < 11 g/dL in the first trimester and less than 10.5 g/dl in the second and third trimesters (9, 10).

In addition, according to WHO, anemia affects approximately 1.5 billion people worldwide (11). Anemia has the highest prevalence in 3 groups: children aged <5 years, pregnant women, and women of reproductive age (12).



Anemia is one of the most prevalent complications during pregnancy (13). It is commonly considered a risk factor for poor pregnancy outcomes and can result in complications that threaten the life of both mother and fetus, such as preterm birth, low birth weight (14).

Pregnancy increases maternal iron demand for three reasons. Maternal plasma and blood volumes are increased during pregnancy (15). Each extra gram of hemoglobin that the mother synthesizes requires an addition 3.46 milligram of elemental iron.

In addition, the fetus requires iron for its own metabolic and oxygen delivery needs as well as the loading of its comparatively large endogenous iron stores that will be utilized in the first six months of postnatal life (16).

There are a wide variety of iron supplements in use around the world, and their quality varies. Oral iron therapy is the treatment of choice for the most of patients with iron deficiency anemia (3,17). Conventional iron in form of ferrous sulphate is limited by gastro intestinal complaints. The use of ferrous gluconate as an alternative to these conventional ferrous salts offer less gastro intestinal upsets (18).

Lactoferrin is a naturally existing iron-binding multifunctional protein; it is present at high concentrations in human milk and in the milk of other mammals. It is also present in other body fluids such as tears, saliva, bile, pancreatic juice, genital and nasal secretions, and circulating neutrophils (19).

Therefore, oral administration of bovine lactoferrin as an iron-supplying molecule is an appealing therapeutic strategy, even if to date studies have shown conflicting results, reporting either enhancement or inhibition of intestinal iron delivery (20).

The main aim of this study was to compare between lactoferrin with ferrous gluconate versus ferrous gluconate in treatment of iron deficiency anemia during pregnancy.

This prospective randomized controlled study was conducted in Ain shams University Maternity Hospital. This study was conducted on 40 women divided into: Group I: 20 patients were given ferrous gluconate 300 mg (Ferrous-Gluconate®, tab.300mg glucofer, Egypt) two times daily. Group II: 20 patients were given lactoferrin 100mg (Pravotin-sachets®, 100mg, Hygint, Egypt) with ferrous gluconate twice daily.

In agreement with our results, Bayoumy et al., (21) who aimed to assess the compliance, efficacy and safety of lactoferrin in comparison to ferrous sulfate in Treatment of Nutritional Iron Deficiency Anemia during Second Trimester among Egyptian Ladies. They found that in Lactoferrin (N=70) group, Age (years) Mean  $\pm$  SD was 26.4 $\pm$ 4.2 with range 20.0–34.0 and the GA (in weeks) Mean  $\pm$  SD was 19.3 $\pm$ 2.7 with range 12.0–25.0. Parity Median (1st–3rd IQ) was 1.0 (0.0–2.0) with range 0.0–4.0, Parity; Primi was 20 (28.6%) while Multi was 50 (71.4%). While in Ferrous sulphate (N=70) group, Age (years) Mean  $\pm$  SD was 27.4 $\pm$ 4.5 with range 20.0–35.0 and the GA (in weeks) Mean  $\pm$  SD was 19.0 $\pm$ 2.5 with range 14.0–24.0. Parity Median (1st–3rd IQ) was 1.0 (0.0–3.0) with range 0.0–4.0, Parity; Primi was 20 21 (30.0%) while Multi was 49 (70.0%). There was no significant difference between the Lactoferrin group and ferrous sulfate group in terms of age or gestational age and as regard Parity Median (1st–3rd IQ) and Parity (Primi and Multi).

Also, Rezk et al., (22) who aimed to evaluate the efficacy and safety of lactoferrin in comparison to ferrous sulphate for the treatment of iron deficiency anemia (IDA) during pregnancy. They reported that in Group 1 (Lactoferrin group), Age was 26.4  $\pm$  5.18, GA at inclusion was 16.32  $\pm$  1.76 and Parity 1.42  $\pm$  1.37. While in Group 2 (Ferrous group), Age was 26.5  $\pm$  5.65, GA at inclusion was 16.01  $\pm$  1.82 and Parity 1.50

$\pm 1.29$ . There was no significant difference regarding age, GA and Parity between Lactoferrin group and Ferrous group.

As well, El-Nasr et al., (23) who aimed to evaluate the effectiveness, safety and acceptability of ferrous sulphate alone in comparison to combination of ferrous sulphate and lactoferrin for the treatment of iron deficiency anemia during pregnancy and their effect on neonatal iron store. Their study was conducted on 300 pregnant women from the second trimester with IDA who separated on 2 groups; ferrous sulphate group: 150 pregnant women received 150 mg of dried ferrous sulphate capsules. Combined ferrous sulphate and lactoferrin group: 150 pregnant women received combined 200 mg lactoferrin and 30 mg iron once daily for eight consecutive weeks. They found that there was no significant difference between the two groups as regard age and GA and Parity (PG and multipara).

In our study, we reported that group A had significantly more nausea than group B ( $p = 0.013$ ), while there was no significant difference between the groups in terms of constipation or non-compliance ( $p > 0.05$ ).

In consistent with our results, Rezk et al., (22) they reported that Gastrointestinal adverse events occurred more frequently with ferrous sulphate than the lactoferrin group.

Also, El-Nasr et al., (23) they revealed that there was statistically a significant difference between ferrous sulphate alone and combined ferrous sulphate and lactoferrin group regarding gastrointestinal side effects.

As well, Balsha et al., (24) who aimed to compare the safety, tolerability, efficacy and hematological response of lactoferrin in treatment of iron deficiency anemia during pregnancy versus ferrous sulfate capsules. They demonstrated that the adverse effects of treatment; there was a significant difference between the two groups, being the least

among the lactoferrin group.

In contrast with our results, Bayoumy et al., (21) they found that Maternal adverse effects as nausea, vomiting, abdominal pain, constipation and heart burn were significantly less frequent in lactoferrin group than in ferrous sulfate group. Therefore, compliance with lactoferrin treatment was significantly higher than in ferrous sulphate group.

In our study, as regard the results of a mixed design ANOVA for hemoglobin levels between the two groups of patients, there was no significant difference in hemoglobin levels between the two groups before or after the treatments, group B had a significant increase in hemoglobin.

In consistent with our results, Bayoumy et al., (21) they found that as regard basal and follow up Hemoglobin (gm/dL), in Lactoferrin (N=70) group, Basal Hb; Mean  $\pm$ SD was  $9.0 \pm 0.6$  ranged from 8.0 to 9.9, at Follow up Hb; Mean  $\pm$ SD was  $10.2 \pm 0.6$  ranged from 9.1 to 11.2 and the change (after-before) in Hb; Mean  $\pm$ SD  $1.2 \pm 0.2$  ranged from 0.2 to 1.3. There was a significant difference in Lactoferrin group before and after the treatment. While as regard basal and follow up Hemoglobin (gm/dL); in Ferrous sulphate (N=70), Basal Hb Mean  $\pm$ SD was  $9.1 \pm 0.6$  ranged from 8.0 to 9.9; at Follow up Hb Mean  $\pm$ SD was  $9.6 \pm 0.6$  ranged from 8.3 to 10.6 and the change (after-before) in Hb Mean  $\pm$ SD  $0.5 \pm 0.2$  ranged from -0.5–0.8. However, they found that there was a significant difference in Ferrous Sulfate group before and after the treatment. There was non-significant difference between the two groups as regard Hb level at baseline despite, there was highly significant difference between the two groups as regard Hb level at follow up.

Also, Rezk et al., (22) they reported that in Group 1 (Lactoferrin group), Hb at enrolment was  $8.15 \pm 0.58$ , Hb after 1 month was  $9.33 \pm 0.37$ , Hb after 2 months was  $10.41 \pm 0.33$  and Total increase in Hb was  $2.26 \pm 0.51$ . while in Group 2 (Ferrous group), Hb at enrolment

was  $8.03 \pm 0.702$ , Hb after 1 month was  $8.65 \pm 0.718$ , Hb after 2 months was  $9.14 \pm 0.637$  and Total increase in Hb was  $1.11 \pm 0.22$ . There was no significant difference between the two groups Lactoferrin group and ferrous group as regard Hb at enrolment while there was highly significant difference between the two groups as regard Hb after treatment and in total increase in Hb.

As well, El-Nasr et al., (23) they revealed that in Group 1: Included 150 pregnant women received oral ferrous sulphate, Hb (g/dL) (Mean  $\pm$ SD) at Basal was  $8.79 \pm 0.86$ , after 1m was  $9.42 \pm 0.87$ , after 2M was  $10.02 \pm 0.91$  and Total increase of Hb level was  $2.25 \pm 0.80$ . In Group 2: Included 150 pregnant women received oral combined lactoferrin and ferrous sulphate, Hb (g/dL) (Mean  $\pm$ SD) at Basal was  $8.84 \pm 0.85$ , after 1m was  $9.82 \pm 0.84$ , after 2M was  $10.78 \pm 0.84$  and Total increase of Hb level was  $3.87 \pm 0.91$ . There was no significant difference between the two groups as regard Hb at basal measurement while there was highly significant difference between the two groups as regard Hb after treatment and in total increase in Hb.

Moreover, Balsha et al., (24) they demonstrated that in Lactoferrin (N=95) group, Hb (g/dL) (Mean  $\pm$ SD) at basal was  $9.4 \pm 0.9$  with range of 7.2–10.9, after treatment was  $10.9 \pm 1.0$  with range of 8.8–13.5 and the elevation in Hb was  $1.5 \pm 0.5$  with range of 0.3–2.7. While in Ferrous sulphate (N=93) group, Hb (g/dL) (Mean  $\pm$ SD) at basal was  $9.5 \pm 0.8$  with range of 7.1–10.8, after treatment was  $10.3 \pm 0.8$  with range of 7.9–12.3 and the elevation in Hb was  $0.8 \pm 0.4$  with range of 0.2–1.7. There was no significant difference in Hb level at basal measurement between the two groups while the change in hemoglobin level after treatment; there was a significant difference between the two groups, being higher in the lactoferrin group.

In our results, as regard the results of a mixed design ANOVA for hematocrit levels between the two groups of patients, there was no significant difference in hematocrit

levels between the two groups before or after the treatments, but group B had a significant increase in hematocrit from pre to post treatment.

In consistent with our results, Bayoumy et al., (21) they found that as regard basal laboratory findings in Lactoferrin (N=70) group, HCT (%); Mean  $\pm$ SD was  $28.5 \pm 2.2$  ranged from 22.6 to 34.0. While in Ferrous sulphate (N=70), HCT (%); Mean  $\pm$ SD was  $28.1 \pm 2.7$  ranged from 21.3 to 34.3 these values indicated that there was no significant difference as regard HCT (%) between the two groups.

Also, El-Nasr et al., (23) they revealed that in Group 1: Included 150 pregnant women received oral ferrous sulphate, HCT (Mean  $\pm$ SD) at basal was  $29.39 \pm 2.27$ , after 1m was  $31.42 \pm 2.40$ , after 2M was  $33.09 \pm 2.53$  and Total increase of HCT level was  $5.66 \pm 1.68$ . In Group 2: Included 150 pregnant women received oral combined lactoferrin and ferrous sulphate, HCT (Mean  $\pm$ SD) at basal was  $28.99 \pm 1.87$ , after 1m was  $32.23 \pm 1.85$ , after 2M was  $34.94 \pm 1.73$  and Total increase of HCT level was  $8.31 \pm 2.01$ . There was no significant difference between the two groups as regard HCT at basal measurement while there was highly significant difference between the two groups as regard HCT after treatment and in total increase in HCT.

In our findings, as regard the results of a mixed design ANOVA for mean corpuscular volume (MCV) levels between the two groups of patients, there was a significant difference in MCV levels between the two groups after the treatments, with group A having a higher MCV than group B. Our results also showed that both groups had a significant increase in MCV levels from pre to post treatment, indicating that the treatments affected the red blood cell size in both groups.

In supporting our results, Bayoumy et al., (21) they found that as regard basal laboratory findings in Lactoferrin (N=70) group, MCV; Mean  $\pm$ SD was  $72.1 \pm 6.5$  ranged from 54.6 to 88.6. While in Ferrous sulphate (N=70),



MCV; Mean  $\pm$ SD was  $71.1\pm 5.6$  ranged from 54.0 to 82.0. There was no significant difference as regard MCV between the two groups.

Also, El-Nasr et al., (23) they revealed that in Group 1: Included 150 pregnant women received oral ferrous sulphate, MCV (Mean  $\pm$ SD) at basal was  $69.36\pm 2.46$ , after 1m was  $71.78\pm 2.60$ , after 2M was  $73.59\pm 2.67$  and Total increase of MCV was  $6.34\pm 1.3$ . In Group 2: Included 150 pregnant women received oral combined lactoferrin and ferrous sulphate, MCV (Mean  $\pm$ SD) at basal was  $68.84\pm 2.095$ , after 1m was  $72.44\pm 2.05$ , after 2M was  $75.27\pm 2.09$  and Total increase of MCV was  $9.87\pm 2.03$ . There was no significant difference between the two groups as regard MCV at basal measurement while there was highly significant difference between the two groups as regard MCV after treatment and in total increase in MCV.

In our findings, as regard the results of a mixed design ANOVA for mean corpuscular hemoglobin (MCH) levels among the two groups of patients, there was a significant difference in MCH levels between the two groups after the treatments, with group A having higher MCH than group B. In addition, we revealed that both groups had significant changes in MCH levels from pre to post, with group A increasing and group B decreasing their MCH.

In agreement with our results, Bayoumy et al., (21) they found that as regard basal laboratory findings in Lactoferrin (N=70) group, MCHC; Mean  $\pm$ SD was  $23.3\pm 2.8$  ranged from 17.6 to 30.4. While in Ferrous sulphate (N=70), MCHC; Mean  $\pm$ SD was  $23.5\pm 2.8$  ranged from 18.0 to 32.1. There was no significant difference as regard MCHC between the two groups.

In the present study, as regard the results of a mixed design ANOVA for ferritin levels between the two groups of patients. We demonstrated that both groups had a significant increase in ferritin levels after

the treatments, but group B had a much higher increase than group A. We also found that there was no significant difference in ferritin levels between the two groups before the treatments, but there was a significant difference after the treatments, with group B having higher levels than group A.

In consistent with our results, Bayoumy et al., (21) they found that as regard basal laboratory findings in Lactoferrin (N=70) group, Serum ferritin; Mean  $\pm$ SD was  $10.8\pm 3.3$  ranged from 4.0 to 23.0. While in Ferrous sulphate (N=70), Serum ferritin; Mean  $\pm$ SD was  $10.7\pm 3.2$  ranged from 4.0 to 17.0. There was no significant difference as regard Serum ferritin between the two groups.

Also, El-Nasr et al., (23) they reported that in Group 1: Included 150 pregnant women received oral ferrous sulphate, Serum ferritin level (ng/mL) Mean  $\pm$ SD was  $136.65\pm 4.02$ . while in Group 2: Included 150 pregnant women received oral combined lactoferrin and ferrous sulphate, Serum ferritin level (ng/mL) Mean  $\pm$ SD was  $161.87\pm 30.34$ . Therefore serum ferritin level was significantly increased with combined ferrous sulphate and lactoferrin group than ferrous sulphate alone.

As well, Balsha et al., (24) they revealed that in Lactoferrin (N=95) group, Serum ferritin (ng/dL) (Mean  $\pm$ SD) at basal was  $9.2\pm 1.3$  with range of 6.5–11.9, after treatment was  $13.7\pm 1.4$  with range of 10.1–17.3 and the elevation in Serum ferritin was  $4.5\pm 0.5$  with range of 3.3–5.7. While in Ferrous sulphate (N=93) group, Serum ferritin (ng/dL) (Mean  $\pm$ SD) at basal was  $9.3\pm 1.2$  with range of 6.5–11.9, after treatment was  $10.6\pm 1.2$  with range of 7.6–14.0 and the elevation in Serum ferritin was  $1.3\pm 0.5$  with range of 0.6–2.4. There was no significant difference in Serum ferritin level at basal measurement between the two groups while the change in serum ferritin level after treatment; there was a significant difference between the two groups, being higher in the lactoferrin group.

## **CONCLUSION**

In our study we compared between lactoferrin with ferrous gluconate versus ferrous gluconate in treatment of iron deficiency anemia during pregnancy. Accordingly, we found that Oral lactoferrin with ferrous gluconate is better tolerated with higher increase in mean hemoglobin and lower side effects (nausea) when compared to oral iron therapy alone.

## **REFERENCES**

1. Zhao X, Zhang X, Xu T, Luo J, Luo Y, An P. Comparative effects between oral lactoferrin and ferrous sulfate supplementation on iron-deficiency anemia: A comprehensive review and meta-analysis of clinical trials. *Nutrients*. 2022;14(3): 543.
2. Kassebaum NJ, Jasrasaria R, Naghavi M, WulfSK, Johns N, Lozano R. A systematic analysis of global anemia burden from 1990 to 2010. *Blood, the Journal of the American Society of Hematology*. 2014; 123(5): 615-624.
3. Percy L, Mansour D, Fraser I . Iron deficiency and iron deficiency anaemia in women. *Best practice & research Clinical obstetrics & gynaecology*. 2017;(40): 55-67.
4. Pavord S, Myers B, Robinson S, Allard S, Strong J, Oppenheimer C. UK guidelines on the management of iron deficiency in pregnancy. *British journal of haematology*. 2012; 156(5): 588-600.
5. Kowalczyk K, Bartnik-Głaska M, Smyk M, Plaskota I, Bernaciak J, Kędzior M, et al. Comparative genomic hybridization to microarrays in fetuses with high-risk prenatal indications: Polish experience with 7400 pregnancies. *Genes*. 2022; 13(4): 690.
6. Soliman TW, Fawzy MM, Farrag IF. Lactoferrin versus Ferrous Sulphate for the Treatment of Iron Deficiency Anemia during Pregnancy (A Randomized Clinical Trial). *Al-Azhar Medical Journal*. 2020; 49(1): 271-282.
7. Abdelkarim M, Alashkar O, Abdeldayem T, Abdelfattah E, Donia H . Lactoferrin chelated iron versus ferrous fumarates for iron deficiency anemia during pregnancy. In *BJOG-AN International Journal of Obstetrics and Gynaecology*. 2021;128:162-162.
8. Bhadra P, Deb A. A review on nutritional anemia. *Indian Journal of Natural Sciences*. 2020; 10(59):18466-18474.
9. Kaur K. Anaemia ‘a silent killer’ among women in India: Present scenario. *European Journal of Zoological Research*. 2014; 3(1): 32-36.
10. Ogunbode O, Ogunbode O. Anaemia in pregnancy. *Contemporary obstetrics and gynecology for developing countries*. 2021;1: 321-330.
11. Eweis M, Farid EZ, El-Malky N, Abdel-Rasheed M, Salem S., Shawky S. Prevalence and determinants of anemia during the third trimester of pregnancy. *Clinical Nutrition ESPEN*. 2021; 44: 194-199.
12. Prasanth R . Prevalence of anemia in both developing and developed countries around the world. *World J Anemia* 2017; 1(2): 40-43.
13. Turawa E, Awotiwon O, Dhansay MA, Cois A, Labadarios D, Bradshaw D, et al. Prevalence of anaemia, iron deficiency, and iron deficiency anaemia in women of reproductive age and children under 5 years of age in south africa (1997–2021): A systematic review. *International Journal of Environmental Research and Public Health*. 2021; 18(23): 12799.
14. Helmy ME, Elkhoully NI, Ghalab RA . Maternal anemia with pregnancy and its adverse effects. *Menoufia Medical Journal*. 2018; 31(1): 7-8.

15. Lin L, Wei Y, Zhu W, Wang C, Su R, Feng H, et al. Prevalence, risk factors and associated adverse pregnancy outcomes of anaemia in Chinese pregnant women: a multicentre retrospective study. *BMC pregnancy and childbirth*. 2018;(18): 1-8.
16. Fisher AL, Nemeth E. Iron homeostasis during pregnancy. *The American journal of clinical nutrition*, 2017;106(6): 1567-1574.
17. Georgieff MK. Iron deficiency in pregnancy. *American journal of obstetrics and gynecology*.2020; 223(4): 516–524.
18. Richards T, Breymann C, Brookes MJ, Lindgren S, Macdougall IC, McMahon LP, et al. Questions and answers on iron deficiency treatment selection and the use of intravenous iron in routine clinical practice. *Annals of medicine*.2021; 53(1): 274-285.
19. Munim TF, Rashid S. The efficacy and safety of oral ferrous gluconate in premenopausal women with severe iron deficiency anaemia. *Annals of Abbasi Shaheed Hospital and Karachi Medical & Dental College*.2017; 22(1): 5-11.
20. Hemeda HM, Mohamed A, Islam B, Hasan A, Ewies A. Effectiveness of bovine lactoferrin versus ferrous fumarate in the management of iron deficiency anemia in pregnancy: Randomized clinical trial. *International Journal of Reproductive Medicine & Gynaecology*.2018; 4(1):6-11.
21. Gawai S, Fonseca M, Kapote D. A randomized controlled trial on lactoferrin versus ferrous sulphate for the treatment of mild to moderate iron deficiency anaemia in pregnancy. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*.2020; 9(2): 562-567.
22. Bayoumy KM, Ragab SG, Elghareeb NA. Compliance and Efficacy of Oral Lactoferrin versus Ferrous Sulfate in Treatment of Nutritional Iron Deficiency Anemia during Second Trimester among Egyptian Ladies. *The Egyptian Journal of Hospital Medicine*.2021; 83(1): 903-909.
23. Rezk M, Dawood R, Abo-Elnasr M, Al Halaby A, Marawan H. Lactoferrin versus ferrous sulphate for the treatment of iron deficiency anemia during pregnancy: a randomized clinical trial. *The Journal of Maternal-fetal & Neonatal Medicine: the Official Journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians*.2015; 29(9): 1387-1390.
24. El-Nasr IA, Mahmoud SA, Elnaddar EM, Ammar HA. Ferrous Sulphate Alone Versus Combination of Ferrous Sulphate and Lactoferrin for The Treatment of Iron Deficiency Anemia during Pregnancy and Their Effect on Neonatal Iron Store: A Randomized Clinical Trial. *The Egyptian Journal of Hospital Medicine*.2021; 84(1): 1955-1960.
25. Balsha KM, Rateb AM, Mamdouh AM . The effect of orally administered iron-saturated lactoferrin on systemic iron homeostasis in pregnant women suffering from iron deficiency and iron deficiency anaemia. *The Egyptian Jo*