



ORIGINAL ARTICLE

## The efficacy of oral iron treatment in Somalian nonpregnant female patients with mild/moderate iron deficiency anemia.

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**ABSTRACT... Objective:** To evaluate the efficacy of oral ferrous sulfate therapy in non-pregnant women with iron deficiency anemia in Somalia, which is one of the poorest and undeveloped countries in the world. **Study Design:** Cross Sectional. **Setting:** Turkey Recep Tayyip Erdogan Hospital, Mogadishu, Somalia. **Period:** December 2018 to June 2019. **Material & Methods:** The study included 117 ambulatory females between 18 and 41 years with iron deficiency anemia diagnosed with a hemoglobin level between 9 and 12g/dL and a serum ferritin level below of 15 ng/ml. The patients received ferrous sulfate 200 mg twice daily. Hemoglobin levels of the patients were measured at 2,4,8, and 12 weeks after the start of treatment, and ferritin levels were measured at 4,8 and 12 weeks. **Results:** The mean baseline hemoglobin and ferritin values were 9.71 ± 1.01 g/dl and 6.59 ± 3.63 ng/ml, respectively. After 2,4,8 and 12 weeks of treatment, the mean hemoglobin values were increased to 10.58 g/dl, 11.53g/dl, 12.24g/dl and 12.85 g/dl, respectively. At 12 weeks, 79% of participants had normalized hemoglobin concentrations. (>12 gr/dl). **Conclusion:** In conclusion, the present study also demonstrated that in patients with mild-moderate IDA oral ferrous sulfate is an effective and better-tolerated treatment. At the same time, oral ferrous sulfate treatment is cost-effective.

**Key words:** Anemia, Iron Deficiency, Iron Therapy, Somalia.

### INTRODUCTION

It is estimated that approximately a quarter of the world's population suffers from anemia, therefore, it is a severe public health problem.<sup>1</sup> According the World Health Organization (WHO) anemia, for non-pregnant women was defined as a hemoglobin concentration of less than 120 g/L. Anemia is classified as mild, moderate, or severe anemia according to the hemoglobin level in the blood 11.0-11.9 g/dl, 8.0-10,9 g/dl, and less than 8.0 g/dl respectively.<sup>2,3</sup>

As anemia is a global problem, the most common nutritional disorder worldwide is iron deficiency and it accounts for about half the world's anemia burden.<sup>1</sup> It is estimated that almost 1.24 billion people suffer from iron deficiency.<sup>4,5</sup> Iron deficiency is more prevalent in young children and women of reproductive age and it greatly impacts the lives of children, and premenopausal

women in developing countries.<sup>6</sup> From the time enter menarche until menopause, women are at high risk of iron deficiency, owing to menstrual blood losses, pregnancy, and childbirth.<sup>7</sup> Iron deficiency occurs following prolonged negative iron balance, the major causes of which include nutritional deficiencies, increased iron requirements (during periods of growth, repeated pregnancies), and chronic blood loss (parasitic diseases, menstrual bleeding, delivery).<sup>8</sup> The WHO threshold for diagnosis of iron deficiency in nonpregnant women is ferritin levels lower than 15 ng/mL.<sup>9</sup>

Regionally the highest prevalence of Iron deficiency anemia (IDA) is seen in Central and West Sub-Saharan Africa and South Asia. In these regions, anemia is a severe problem, approximately 35-40% of females have IDA.<sup>10-12</sup> According to the research of Wirth JP et al., 40%

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of women in Somalia, which is one of the poorest and undeveloped countries in the world were anemic and half of them were responsible for iron deficient.<sup>13</sup>

The standard treatment approach for IDA treatment is an oral iron replacement divided doses and is recommended to give as ferrous sulfate, ferrous fumarate, and ferrous gluconate. Yet the most frequently used preparation for IDA is iron sulfate, in line with The British Society of Gastroenterology (BSG) recommendation.<sup>14,15</sup> The standard recommended daily dose of iron replacement for adults is 100 to 200 mg of elemental iron. Doses are tailored depending on the clinical and laboratory findings of the patient as age, the severity of symptoms, ferritin level, and gastrointestinal tolerability of the iron replacement.<sup>16</sup> Nausea, vomiting, constipation, and diarrhea are the commonly reported side effects that may lead to loss of patient adherence to the treatment.<sup>17,18</sup> In this study, we aimed to evaluate the efficacy of oral ferrous sulfate therapy in non-pregnant Somali women with IDA.

## MATERIAL & METHODS

The present study was conducted from December 15, 2018, to 27 June 2019, at Turkey Recep Tayyip Erdogan Hospital, Mogadishu, Somalia. The study was done by the Declaration of Helsinki, the International Conference on Harmonization Good Clinical Practice, and local regulations. The Institutional Ethics Committee approved this study (No. MSTH/ 1333, dated December 15, 2018).

The study included 117 ambulatory females between 18 and 41 years with IDA, diagnosed with a hemoglobin level between 9 and 12 g/dL and a serum ferritin level below of 15 ng/ml.

The main exclusion criteria were as follows: pregnancy, menopause, severe anemia (Hb<8 g/dl), anemia is caused by nutritional factors other than iron deficiency such as vitamin A, folate and vitamin B12 deficiencies, acute and chronic inflammation, malignancies, chronic renal failure, any digestive disease which could modify iron absorption, parasitic infections, and

blood disorders.

The patients received ferrous sulfate 200 mg twice daily (total iron dose of 160 mg/day). The duration of the study was 12 weeks. Hemoglobin levels of the patients were measured at 2,4,8, and 12 weeks after the start of treatment, and ferritin levels were measured at 4.8 and 12 weeks.

The collected data were analysed by IBM SPSS Statistics Version 21 (IBM, Armonk, NY). The qualitative data were expressed in frequencies and percentages, and quantitative data were expressed as mean  $\pm$  standard deviation. The differences between baseline and post-treatment (at weeks 4,8, and weeks 12) hemoglobin and ferritin values within the study group were tested by the paired t-tests. The results were considered statistically significant if p value of less than 0.05.

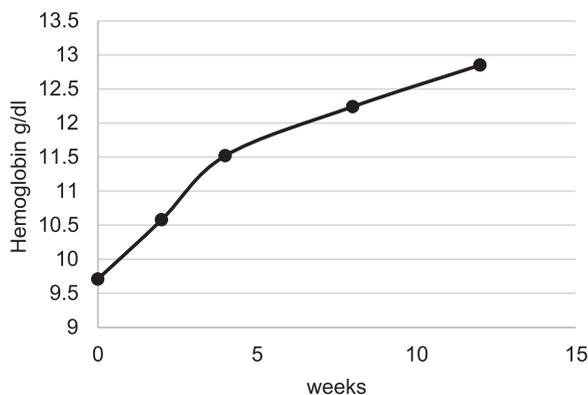
## RESULTS

The study population consisted of 117 patients. The patients included in the study were premenopausal and non-pregnant women, and their ages were between 18 and 41. The mean age of the patients was 29.58 $\pm$ 5.89 years. The hemoglobin values of the patients ranged from 11.9g/dl to 8g/dl. 13 of 117 patients (11.1%) were mild (Hb 11.9-11g/dl) and 104 (88.9%) moderate (Hb 10.9- 8 g/dl) IDA. No patient has severe anemia (Hb<8g/dl).

As can be seen from Table-I, the mean baseline hemoglobin and ferritin values were 9.71 $\pm$ 1.01 g/dl and 6.59 $\pm$ 3.63 ng/ml, respectively. After 2,4,8 and 12 weeks of treatment, the mean hemoglobin values were increased to 10.58 g/dl, 11.53g/dl, 12.24g/dl and 12.85 g/dl, respectively (Figure-1). The best improvement in hemoglobin level was seen at four weeks. The mean increase in hemoglobin from baseline was 1.81g/dl four weeks, 0.72 g/dl between 4 and 8 weeks, and 0.61 g/dl between 8 and 12 weeks. The mean hemoglobin increase rate between 0 and 4 weeks was 18.6% (p<0.001). The increase rates between the 4th and 8th weeks and the 8th and 12th weeks are 6.8% and 5.3%, respectively. (p<0.001 and p< 0.001, respectively)

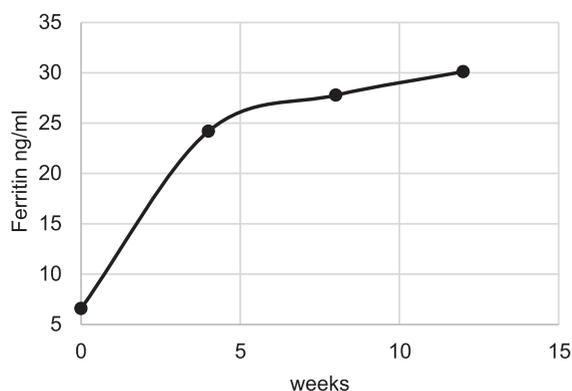
	0	Two weeks	Four weeks	Eight weeks	12 weeks
Hemoglobin g/dl	9.71±1.03	10.57±1.08	11.53±0.99	12.24±0.98	12.85±0.94
Ferritin ng/ml	6.59±3.63	-	24.20±10.07	27.78±12.14	30.11±11.86
Mean change Hemoglobin g/dl	-	0.86	1.81	2.53	3.14
Mean change Ferritin ng/ml	-	-	17.6	21.2	23.5

**Table-I. Hemoglobin and ferritin parameters changes assessed on visits**



**Figure-1. Mean Hb levels during treatment**

The ferritin values were at 4, 8, and 12 weeks, 24.18 ng/ml, 27.78ng/ml, and 30.11 ng/ml, respectively. Ferritin showed the most significant change at four weeks. The mean ferritin increase at four weeks was 17.6 ng/ml (Figure-2).



**Figure-2. Mean ferritin levels during treatment**

At four weeks, 43 (37%), at eight weeks, 77 (66 %), and 12 weeks, 93 (79%) of 117 patients had normalized hemoglobin concentrations. (>12 gr/dl). At twelve weeks 49 (42%) patients had a ferritin value above 30 ng/dl.

The vast majority of patients well-tolerated

treatment with oral ferrous sulfate. Gastrointestinal system-related side effects were reported in 34 (29%) patients. The most common gastrointestinal side effects were constipation, nausea, abdominal pain, and diarrhea. Treatment was not discontinued in any of the patients due to side effects.

## DISCUSSION

Iron salts such as iron sulfate, fumarate, and gluconate are the gold standard for treating IDA. 90% of cases of IDA in nonpregnant women in Somalia was being either mild or moderate anemia.<sup>13</sup> In the present study, we have evaluated the efficacy and side effect profile of oral ferrous sulfate in reproductive-aged Somalian women with mild-moderate IDA. The patient group in our study consisted mainly of patients with moderate levels, and patients with severe anemia (<8gr/dl) were not included in the study.

Patients with mild or moderate anemia showed a significant improvement in Hb and ferritin levels in the first four weeks with oral iron sulfate treatment. In the evaluations made in the following weeks, the increase in Hb and ferritin values slowed down considerably. The rate of increase was observed to be more pronounced, especially in ferritin levels. After 12 weeks of oral ferrous sulfate treatment, hemoglobin values normalized in 79% of the participants and exceeded 12 g/dl.

Serum ferritin was used as an indicator of iron storage in our study. After 12 weeks of oral iron therapy, only 49 (42%) patients had a ferritin value above 30 ng/dl. This showed us that oral iron therapy for 12 weeks is insufficient to replenish iron stores and that oral iron replacement therapy should be continued for at least 3 to 6 months after Hb the level returns to normal to replenish iron stores.

In our study, iron replacement with Ferrous sulfate was well tolerated by the patients, and they did not complain of any severe side effects. The most commonly reported side effects were constipation, nausea, abdominal pain, and diarrhea. As a parallel to the literature knowledge, 29% of our patients showed Gastrointestinal system-related side effects.<sup>19</sup> In all these patients, an iron replacement was continued with new dose adjustments, taking it every other day or after a meal.

Intravenous iron substitution is more expensive than oral iron, but in severe anemia patients, IV iron treatment improves anemia more effectively and increases hemoglobin levels faster than oral iron treatment. In addition, the IV iron treatment increases ferritin levels significantly quicker and more effectively when compared to oral treatment. Therefore, IV iron therapy should be considered in severe anemia (Hb <8 g/dL) and in patients with mild and moderate anemia where oral iron therapy is contraindicated, ineffective or intolerable, patients with malabsorption, and in cases where rapid correction of hemoglobin level is required.<sup>19,20</sup>

## CONCLUSION

In conclusion, the present study also demonstrated that in patients with mild-moderate IDA oral ferrous sulfate is an effective and better-tolerated treatment. At the same time, oral Ferrous sulfate treatment is cost-effective. Anemia is corrected in approximately 4/5 of the patients with this treatment in 12 weeks. The side effect profile is at an acceptable level. The present study revealed that ferrous sulfate treatment could be effectively used in patients who in low-income countries such as Somalia.

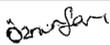
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### AUTHORSHIP AND CONTRIBUTION DECLARATION

No.	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Öznur Sarı	Study conception and design, Acquisition of data, Analysis and interpretation of data, Drafting of manuscript, Critical revision.	
2	Ümit Üre	Study conception and design, Data analysis, Drafting of manuscript, Critical revision.	