International Journal of Clinical Obstetrics and Gynaecology

ISSN (P): 2522-6614
ISSN (E): 2522-6622

www.gynaecologyjournal.com
2021; 5(4): 23-27
Received: 19-04-2021
Accepted: 21-06-2021

Tawaqualit Abimbola Ottun
Department of Obstetrics & Gynaecology, Lagos State University College of Medicine/Lagos State University Teaching Hospital, Lagos, Nigeria

Fatai Oloyede
Department of Obstetrics & Gynaecology, Lagos State University Teaching Hospital, Lagos, Nigeria

Adeniyi Abiodun Adewunmi
Department of Obstetrics & Gynaecology, Lagos State University College of Medicine/Lagos State University Teaching Hospital, Lagos, Nigeria

Faosat Olayiwola Jinadu
Department of Radiology, Lagos State University Teaching Hospital, Lagos, Nigeria

Ayokunle Moses Olumodeji
Department of Obstetrics & Gynaecology, Lagos State University Teaching Hospital, Lagos, Nigeria

Corresponding Author:
Tawaqualit Abimbola Ottun
Department of Obstetrics & Gynaecology, Lagos State University College of Medicine/Lagos State University Teaching Hospital, Lagos, Nigeria

Daily versus intermittent iron supplementation in pregnancy: A randomized trial

Tawaqualit Abimbola Ottun, Fatai Oloyede, Adeniyi Abiodun Adewunmi, Faosat Olayiwola Jinadu and Ayokunle Moses Olumodeji

DOI: https://doi.org/10.33545/gynae.2021.v5.i4a.960

Abstract
WHO recommends daily oral iron supplementation for pregnant women to prevent maternal iron-deficiency anaemia however patients' adherence to daily oral iron regimens is poor. We compared the effect of daily and intermittent oral iron supplementation on hematologic and iron indices in pregnancy and fetal outcome. This was a prospective randomized clinical trial in which 300 healthy pregnant women without anemia, in their 20th week of pregnancy were randomly allocated to receive either 600mg-ferrous sulfate tablet daily or 600mg-ferrous sulfate tablet twice weekly. Hemoglobin and serum iron indices were measured before and after the supplementation and compared. There were no significant differences between the pre- and post-intervention hemoglobin levels when the two groups were compared. Birth weights and Apgar scores of babies born to mothers in both study arms were comparable. Therefore, twice weekly iron supplementation is equally effective as daily iron supplementation for healthy pregnant women with similar fetal outcomes.

Keywords: anaemia in pregnancy, hemoglobin concentration, iron supplementation, serum iron in pregnancy

Introduction
Maternal anaemia is a predominant problem in low-income and high-income countries with well-known adverse maternal and foetal implications [1]. This is mainly because the increased iron requirements in pregnancy, to meet increase demand of both mother and the fetus, is not met due to insufficient intake in many women in developing countries resulting in in anemia in pregnancy [2]. Because iron deficiency anaemia, the most common cause of maternal anaemia, is associated with adverse pregnancy outcomes, iron supplementation is recommended by the WHO [3, 4].

Despite widespread use of iron supplementation in pregnancy, iron-deficiency anaemia during pregnancy is still prevalent [5]. Poor compliance with iron supplementation protocols because of side-effects, especially gastrointestinal (GI) complications such as nausea, vomiting and constipation, is suggested as one of the main reasons for the inefficiency of daily iron supplementation regimens [6].

These GI side effects are probably caused by the challenges of coping with oxidative stress from large doses of iron [7]. The gut mucosal turnover rate is about 3 days. Some studies have suggested that continuous administration of oral iron impairs the absorption of a subsequent iron dose, [8] while others reported that intermittent iron supplementation may let the mucosa to heal, allow better iron absorption and reduce side effects [9, 10].

This study compared the effect of daily and twice weekly iron supplementation regimens, in non-anaemic pregnant women, on the following haematological indices: hemoglobin concentration (Hb), serum ferritin (SFT), serum iron (SFE) mean corpuscular volume (MCV) and mean corpuscular hemoglobin concentration (MCHC).

Materials and Methods
Participants
We assessed women at the antenatal clinic of Maternal and Child Centres of Isolo and Ifako General Hospitals, Lagos, Nigeria, both centres were at the time of the study run by the obstetrics and gynaecology department of the Lagos State University Teaching Hospital.

Between June 2014 and June 2015, pregnant women between 18-40 years of age at 20 weeks

gestational age, with parity ≤ 4, singleton pregnancy, body weight ≤ 90kg, haemoglobin concentration ≥ 10.0g/dl but ≤ 13g/dl were recruited for the study. A written informed consent was obtained from all participants.

Women were not eligible if they had high risk pregnancies, smoked cigarettes or if they were not willing or able to give informed consent. The ethics and research committee of the Lagos State University Teaching Hospital approved the study protocol.

Randomisation

Participants were randomly assigned (1:1) to a daily iron supplement of 200mg ferrous sulphate thrice daily (600mg daily) or 600mg ferrous sulphate twice weekly (taken on Mondays and Thursdays of the week). Both arms had the routine daily 5mg folic acid and 1 tablet of Vitamin B complex thrice daily. A 200mg-ferrous sulphate tab contained 60mg of elemental iron.

Procedures

The purpose and design of the study were explained by the research assistants to pregnant women and after obtaining written informed consent. Their sociodemographic and obstetric data were collected with the aid of a proforma designed for the study. Eligible women were randomly assigned to receive either daily iron supplementation or twice weekly iron supplementation from 20weeks gestational age until delivery. Without blinding, random allocation was done according to the day of week a pregnant woman attended the clinic: clients on even days were assigned to the daily group and attendees on odd days were allocated to the twice weekly group. Mothers of both groups received routine care and were followed up until delivery. Serum haemoglobin (Hb) and serum ferritin concentrations in the mothers were measured before commencement of iron supplementation and 4 weekly till delivery or 40 completed week. The birth weight and Apdgar scores of the babies were noted at delivery. The iron sulphate tabs were given free of charge to participants. Serum hemoglobin was measured with sysme x automated machine, Japan, serum ferritin (radioimmunoassay technique, Elber Europe).

Statistical analysis

The data obtained from the questionnaires were coded, imputed into the computer and analyzed using SPSS 19.0 statistical software. Percentage and proportions were determined for categorical variables. Pearson's Chi-square (test for association) was used to assess the significance of relationships between categorical variables. Students T test was used to compare the mean values of serum levels of hemoglobin, iron and ferritin among different groups and P – value less than 0.05 was considered to be statistically significant at confidence level 95%.

Results

A total of 300 non-anemic pregnant women were enrolled in the study. Out of these, 230 (76.7%) pregnant women completed the study, 110 (73.3%) pregnant women belong to the daily group, while 120 (80%) pregnant women belong to twice weekly group. A total of 70 pregnant women could not complete the study. There were no side effects of iron consumption such as nausea, vomiting and gastrointestinal disturbance among the study group. Out of the fallout, three women developed mild anemia at 32 weeks and 34 weeks gestational age. One is on daily iron supplementation while two were on twice weekly supplementation. Some of those lost to follow-up also had premature delivery, pre-eclampsia and migration from the location. (Figure 1)

The mean age, parity and hemoglobin concentration of pregnant women in both regimens were similar. (Table 1) There was significant increase in the mean hemoglobin concentration in both groups after iron supplementation. The mean serum iron for both groups were increased with iron supplementation but this was not statistically significant. The mean serum ferritin levels significantly decreased in both groups after iron supplementation. (Table 2)

The mean haemoglobin concentration, serum iron and ferritin levels, mean corpuscular volume (MCV) and mean corpuscular haemoglobin concentration (MCHC) were similar in women who had daily iron supplementation and women with twice weekly supplementation. (Table 3) The mean birth weight of babies born to mothers in the daily iron group and interemittent iron group were 3.06±0.49kg and 3.23±0.52kg respectively. The mean Apgar score at 1minute of birth of babies born to mothers in the daily iron group and interemittent iron group were 7.85±0.80 and 7.65±0.39 respectively. (Table 3)

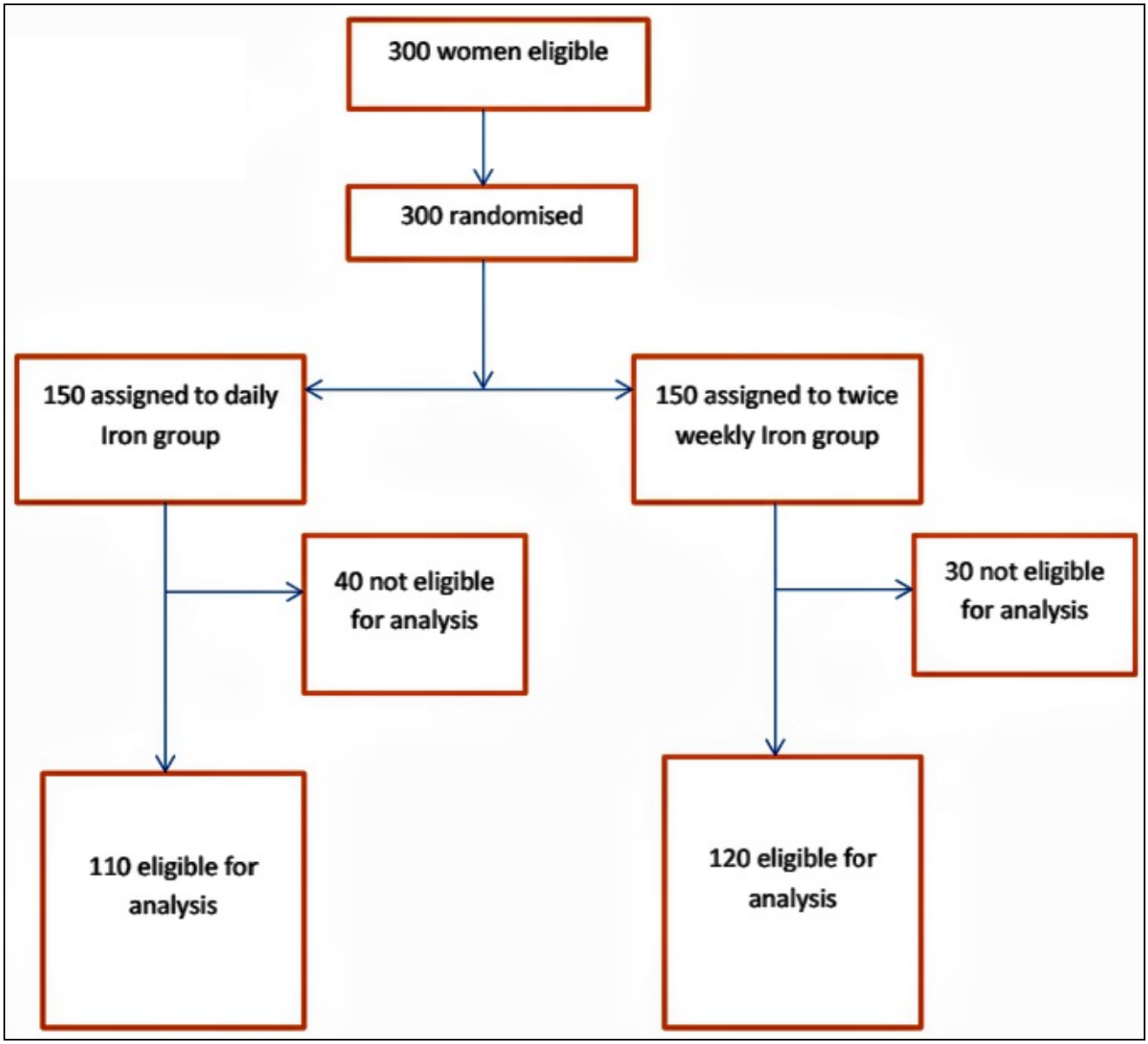

Table 1: Baseline Characteristics of Participants by Iron Supplementation Regimen

Variable	Daily Iron Regimen Group (n=110) Mean ± SD	Twice weekly Iron Regimen Group (n=120) Mean ± SD	p-value*
Age(years)	30.9 ± 0.94	30.1 ± 0.99	0.25
Parity	1.1 ± 1.4	1.0 ± 0.94	0.35
Haemoglobin(g/dL)	10.1 ± 0.51	10.2 ± 0.53	0.90
Serum Iron(ug/dl)	123.3 ±1.22	121.4±1.39	0.58
Serum Ferritin(ug/dl)	65.7 ± 0.95	68.5 ± 0.88	0.29

*Student t-test applied

Table 2: Mean Hematologic and Iron Indices Pre- and Post- Iron Supplementation

	Pre-supplementation	Post-supplementation	p-value*
Daily Iron Group			
Haemoglobin (g/dl)	10.1 ± 0.51	10.3 ± 0.59	0.00
Serum Iron (ug/dl)	123.3 ± 1.22	130.2 ± 0.97	0.19
Serum Ferritin (ug/l)	65.7 ± 0.97	60.2 ± 0.83	0.16
Twice weekly Iron Regimen Group			
Haemoglobin (g/dl)	10.2 ± 0.53	10.9 ± 0.50	0.02
Serum Iron (ug/dl)	121.4±1.35	127.9±1.11	0.36
Serum Ferritin (ug/l)	68.5 ± 0.88	57.5 ± 0.84	1.00

*Student t-test applied

Table 3: Comparing Pre- and Post- Supplementation Hematologic and Featal Indices in the Two Regimens

Variable	Daily Iron Regimen Group (n=110) Mean ± SD	Twice weekly Iron Regimen Group (n=120) Mean ± SD	p-value*
Hemoglobin (g/dl)			
Pre-supplementation	10.1 ± 0.51	10.2 ± 0.53	0.90
Post-supplementation	10.3 ± 0.59	10.9 ± 0.50	0.06
Serum iron (ug/dl)			
Pre-supplementation	123.3± 1.22	121.4 ± 1.39	0.58
Post-supplementation	130.2 ± 0.97	127.9 ± 1.4	0.32
Serum ferritin (ug/dl)			
Pre-supplementation	65.7 ± 0.95	68.5 ± 0.88	0.29
Post-supplementation	60.2 ± 0.83	57.5 ± 0.84	0.10
MCV (fl)			
Pre-supplementation	87.17 ± 0.83	84.1 ± 0.87	0.90
Post-supplementation	88.7 ± 0.88	85.17 ± 0.94	0.58
MCHC (g/l)			
Pre-supplementation	30.7 ± 0.36	31.4 ± 0.39	0.93
Post-supplementation	28.2 ± 0.40	31.4 ± 0.40	0.72
Fetal Outcome			
Birth Weight (kg)	3.06±0.49	3.23±0.52	0.96
Apgar Score†	7.85±0.80	7.65±0.39	0.95

* Student t-test applied, MCV – Mean Corpuscular Volume
† Apgar Score at 1 minute of life
MCHC – Mean Corpuscular Hemoglobin Concentration

Discussion

This study found that, in non-anaemic healthy pregnant women, haemoglobin concentration increased significantly in both women on daily iron supplementation (p=0.00) and twice weekly supplementation (p=0.02). Our study also found no difference in the serum iron, serum ferritin, MCV and MCHC when women on daily iron supplementation were compared with women on twice weekly iron supplementation. This suggests that the twice weekly regimen is as effective of daily iron supplementation in pregnant women. This is in keeping with findings in similar studies by Muslimatun and colleagues in Indonesia [12] and Casanueva *et al* in mexico [13]. However, Mukhopadhyay and colleagues [7] in India did not observe significant difference in hemoglobin levels after 17weeks of Iron supplementation. This may be due to the lower dose of 100mg elemental iron used in their study as against 180mg of elemental iron used in our study.

Serum ferritin decreased in both daily and intermittent iron supplementation in our study but this was not significant. This decrease may reflect the increased iron needs in pregnancy. This was also reported in a similar study by Zinatossadat *et al* in Iran [11], however Mumtaz *et al.* [14] in Pakistan noted elevated serum ferritin in women on daily iron supplementation. This difference may be explained by the difference in study population as Mumtaz *et al* studied women with anaemia in pregnancy while women with pre-existing anaemia were excluded from our study. Birth weight and Apgarscores were similar in both study arms.

For ethical reasons, financial constraint and larger sample size, blinding could not be done and the numbers of pills consumed could not be supervised directly in our study. However, because of appropriate education given to the participants and reinforcement calls between antenatal visit adherences to both protocol was high.

In conclusion, twice weekly iron supplementation is equally effective as daily iron supplementation and may be considered in healthy pregnant women who cannot tolerate daily dosing without associated adverse fetal outcome.

References

1. Stevens GA, Finucane MM, De-Regil LM *et al*. Nutrition Impact Model Study Group. Global, regional, and national trends in haemoglobin concentration and prevalence of total and severe anaemia in children and pregnant and non-pregnant women for 1995–2011: a systematic analysis of population-representative data. Lancet Glob Health 2013;1:e16-e25.
2. Puolakka J, Jänne O, Vihko R. Evaluation by serum ferritin assay of the influence of maternal iron stores on the iron status of newborns and infants. Acta Obstet. Gynecol. Scand 1980;95:53-56.
3. WHO. The Global Prevalence of Anaemia in 2011. Geneva: World Health Organization 2015.
4. Peña-Rosas JP, De-Regil LM, Garcia-Casal MN, Dowswell T. Daily oral iron supplementation during pregnancy. Cochrane Database Syst Rev 2015;7:CD004736
5. Rioux FM, LeBlanc CP. Iron supplementation during pregnancy: what are the risks and benefits of current practices? Applied Physiology, Nutrition, and Metabolism 2007;32:282-288.
6. Hyder SM. Do side-effects reduce compliance to iron supplementation? A study of daily- and weekly-dose regimens in pregnancy. Journal of Health, Population, and Nutrition 2002;20:175-179.
7. Mukhopadhyay A, Bhatla N, Kriplani A, Pandey RM, Saxena R. Daily versus intermittent iron supplementation in pregnant women. Hematological and pregnancy outcome. J Obstet Gynaecol Res 2004;30:409-417.
8. Bread JL. Effectiveness and strategies of iron supplementation during pregnancy. Am J Nutr 2000;71:1288-1294.
9. Frazer DM, Anderson GJ. The orchestration of body iron intake: How and where do enterocytes receive their cues?. Blood cells Mol Dis 2003;30:288-297. 10.1016/S1079-9796(03)00039-1
10. Solomens NM. Weekly versus daily oral iron administration. Nutr Rev 1995;53:326-327.
11. Bouzari Z, Basirat Z, Zeinal Zadeh M *et al*. Daily versus intermittent iron supplementation in pregnant women. BMC Res Notes 2011;4:444. https://doi.org/10.1186/1756-0500-4-444

12. Muslimatum S, Schmidt MK, Schultink W, West CE, Hautvast JA, Cross R, Muhilal. Weekly supplementation with iron and vitamin A during pregnancy increases hemoglobin concentration but decreases serum ferritin concentration in Indonesian pregnant women. J Nutr 2001;131:85-90.
13. Casanueva E, Viteri FE, Mares-Galindo M, Meza-camacho C, Loria A, Schnaas L *et al*. Weekly iron as a safe alternative to daily supplementation for noanemic pregnant women. Arch med Res 2006;37:674-820.
14. Mumtaz Z, Shahab S, Butt N, Rab MA, Demuynck A. Daily iron supplementation is more effective than twice weekly iron supplementation in pregnant women in Pakistan in a randomized double-blind clinical trial. J Nutr 2000;130:2697-2702.