

ORIGINAL ARTICLE**Routine Iron Supplementation and Anaemia by Third Trimester in a Nigerian Hospital****Adanikin, Abiodun I¹, Awoleke, Jacob O¹, Olofinbiyi, Babatunde A¹, Adanikin, Pipeloluwa O², Ogundare, Omobolanle R³****ABSTRACT**

BACKGROUND: Anaemia in pregnancy is associated with adverse maternal and fetal outcome. Unfortunately, in developing countries its prevalence has continued to rise. To improve the situation, iron supplement is routinely prescribed during pregnancy. We therefore examine the impact of the intervention as being currently practised in our clinical setting.

METHODS: In total, 255 prenatal clinic attendees who had more than 8 weeks of prescribed iron supplements were sampled. Data was obtained on their socio-demographic features, haemoglobin concentration at booking, compliance with iron supplements and third trimester haemoglobin value.

RESULTS: Observed iron supplementation compliance rate was 184(72.2%). There was a significant drop in mean haemoglobin (Hb) concentration between the two time points (booking Hb: 32.56±2.99; third trimester Hb: 31.67±3.01; mean diff: 0.89±3.04; $t = 4.673$; 95% CI= 0.52-1.27; $p = <0.001$). Anaemia increased from 132(51.8%) to 150(58.8%) by the third trimester. Increase in anaemia occurred in both iron-compliant and non-compliant groups. Non-compliance however had higher odds of predicting anaemia by the third trimester (OR: 1.83; 95% CI: 1.03-3.26; $p = 0.04$).

CONCLUSION: Although iron supplementation is still a good intervention in developing countries, it is not sufficient to reduce overall prevalence of anaemia by the third trimester. There is a need to look beyond the approach and reinforce the importance of better feeding practices, food fortification and reduced frequency of pregnancies.

KEYWORDS: Anaemia, pregnancy, iron supplementation, outcome, food fortification

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INTRODUCTION

Combating high incidences of maternal morbidity and mortality that is characteristic of low-resource settings has been a daunting task. Ranging from the plague of obstetric haemorrhage, the devastating effects of unsafe abortions and the rampaging trend of unsupervised labour to the scourge of maternal under-nutrition and anaemia, maternal health researchers day-after-day have battled to wrest the woman from preventable deaths.

Anaemia in pregnancy, defined as haemoglobin concentration of less than 11 g/dL, is a major contributor to maternal morbidity and mortality in the developing world (1). For

example, it is estimated that close to 20% of maternal mortalities are directly linked to anaemia and another 50% of maternal deaths are associated with it (2). Sadly, more than half of gravid women in these areas have low haemoglobin concentrations and have to grapple with its consequences (3).

Iron deficiency is believed to be the most common cause of anaemia in pregnancy (4). Stemming from poor iron reserve right from birth, inadequate dietary intake of iron, defective iron absorption conferred by helminthic infestations and increased iron requirements due to and breastfeeding has made iron deficiency anaemia

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[IDA] to continue to soar (5).

Multiple control strategies aimed at combating IDA were indeed adopted. Notable ones were enrichment and fortification of food items, and educational interventions to promote dietary changes. Although these were met with some success in developed countries, it was not the same in developing world (2,6). Therapeutic approach in the form of iron supplementation was thus the promising option.

Advocacy for routine supplementation was hinged on the fact that physiological requirement for iron during pregnancy cannot be met by most diets and that even pre-pregnant iron replete women would be in need of iron supplements (7,8). It was therefore suggested that pregnant women should receive iron supplements ranging from 30-120mg daily depending on geographical prevalence of anemia, diagnosis of anaemia and/or available duration for the therapy (9).

However, the recommendation was not without scientific disagreement based on the possibility of excess iron causing polycythaemia, oxidative damage and triggering severe chronic diseases (6,10). Therefore, blanket administration of iron during pregnancy was not universally accepted though it is a popular practice in developing countries where it is most needed.

Again, emerging evidences on the effectiveness of the prescribed iron supplements have been inconclusive. While some reports found significant contribution of the approach to improving maternal haemoglobin concentration and pregnancy outcome (11,12), others have refuted the claim (13,14). Thus, considerable amount of information remains to be learnt about the influence of this approach on maternal anemia especially in African settings.

Therefore, this research sets out to examine the impact of routine iron supplementation on maternal anemia by third trimester in our environment.

METHODS AND PATIENTS

Study setting: This observational study was conducted at the department of Obstetrics and Gynaecology of Ekiti State University Teaching Hospital (EKSUTH), Ado-Ekiti, southwest Nigeria between February 1 and April 30, 2014. The hospital is a tertiary health facility that provides comprehensive maternity services,

accepts referral of high risk pregnancies and manages complicated labour cases from primary and secondary health centres within the geopolitical region. Its average delivery rate is 2,500 per year.

The obstetrics unit of EKSUTH operates a two firm system; one firm runs its prenatal clinic on Wednesday while the other does so on Friday. As largely practised in Nigeria, depending on when prenatal registration was done, our patients are usually seen every four weeks until twenty-eight weeks of gestation, then fortnightly until thirty-six weeks, and thereafter weekly until delivery. Some patients are, however, seen more frequently when clinically indicated.

Routinely at booking, screening and control/treatment of common ailments such as HIV infection, helminthic infestation, malaria, etc are done. In addition, the obstetrics unit administers malaria chemoprophylaxis (Intermittent Preventive Therapy) appropriately using Sulphadoxine/Pyrimethamine combination which is given at least twice with a minimum of 4-weeks interval between 16 weeks and 36 weeks gestational age. Aside these measures, in the course of prenatal care, overt development of features of malaria/helminthic infestation are promptly treated. Due to subsisting high prevalence of anaemia in pregnancy within the area, we practise blanket prescription of 120mg of elemental iron and 5mg of folic acid as daily supplements for all pregnant women.

Sampling procedure: Using a previous report of 20% prevalence of anaemia in the last trimester from Calabar, Nigeria (15), we calculated that a sample size of 246 women would be needed for an acceptable error margin of 5%, standard normal deviate of 1.96 and a confidence interval of 95%. Though unlikely, we decided to sample 255 participants to make allowance for attrition.

Eligible women were prenatal clinic attendees who registered at gestational age (GA) ≤ 26 weeks and whose pregnancies progressed to reach 35-36 weeks when recruited for the study. Those who did not meet the eligibility criteria and patients with multiple gestation, haemoglobinopathy or chronic medical illnesses were excluded. Eligible women were sequentially recruited after an informed written consent in the order on clinic attendance until the sample size was reached.

Recruitment was at GA of 35-36 weeks, and participants were administered a semi-structured questionnaire by trained resident doctors. The questionnaire was used to obtain information on patients' socio-demographic characteristics, compliance with prescribed iron supplementation, medication side effects (if any), possible reasons for non-compliance, etc. Venous blood specimen was then collected from them for estimation of their haemoglobin concentration at that GA. Information about the haemoglobin concentration of each participant at the time of prenatal care booking was obtained from the hospital files and respectively entered into the study proforma.

In this study, hemoglobin value of less than 11.0 g/dL was considered to be anaemia in pregnancy (1). The measurement of haemoglobin at booking and at third trimester (35-36 weeks) was made by spectrophotometer techniques (oxyhaemoglobin method). We defined compliance as the extent to which a patient acts in accordance with the prescribed dose and interval of the medication (16). Adherence of 80% or more was regarded as being compliant.

Statistical analysis: All relevant data was entered into Statistical Package for Social Sciences (SPSS) version 17. The computer software was used to generate the frequency table, and the results were tested for significance using paired *t* test, chi square test (χ^2) or logistic regression analysis as appropriate. Level of significance (α) was set at 0.05.

Ethical consideration: The research was conducted in accordance with prevailing ethical principles. The approval for the study was obtained from the Ekiti State University Teaching Hospital Ethics and Research Committee.

RESULT

Table 1 summarizes the socio-demographic characteristics of respondents. Fifteen (5.9%) were ≤ 24 years old, while 53(20.8%) were ≥ 35 years old; 187(73.3%) were between the ages of 25 and 34 years. Only 23(9.0%) were singles, while others were married. Thirty five (13.7%) respondents had primary education, 93(36.5%) had secondary education and 127(49.8%) attended tertiary schools.

Most of the women, 159(62.4%), were involved in semi-skilled jobs; less than a fifth had skilled jobs. Out of the studied population, 95(37.3%) were primigravida, and 160(62.7%) were multigravida. Thirtyseven (14.5%) had unplanned pregnancy.

Table 1: Demographic features of participants

Variables	Frequency (%)
Age (years)	
≤ 24	15(5.9)
25-34	187(73.3)
≥ 35	53(20.8)
Religion	
Christianity	237(92.9)
Islam	18(7.1)
Tribe	
Yoruba	222(87.1)
Igbo	30(11.8)
Hausa	3(1.2)
Marital status	
Single	23(9.0)
Married	232(91.0)
Educational level	
Primary	35(13.7)
Secondary	93(36.5)
Tertiary	127(49.8)
Occupation	
Unskilled	54(21.2)
Semi-skilled	159(62.4)
Skilled	42(16.5)
Gravidity	
Primigravida	95(37.3)
Multigravida	160(62.7)
Pregnancy Planned	
Yes	218(85.5)
No	37(14.5)

Table 2 shows that 132(51.8%) had anaemia at prenatal booking visit, but by third trimester, 150(58.8%) were anaemic. Compliance with iron supplementation was found in 184(72.2%) of the prenatal care attendees. Among the 71(27.8%) women who did not comply with the iron prescription, 32(45.1%) related reason to forgetfulness, 29(40.8%) did not use it because of side effects (gastrointestinal upsets, constipation and nausea), while others attributed non-usage to fear of harm to baby or negligence.

Table 2: Anaemia and iron supplementation compliance

Variable	Frequency (%)
<i>Anaemic at booking?; n=255</i>	
Yes	132(51.8)
No	123(48.2)
<i>Anaemic by third trimester?; n=255</i>	
Yes	150(58.8)
No	105(41.2)
<i>Compliant with iron prescription?; n=255</i>	
Yes	184(72.2)
No	71(27.8)
<i>Reasons for non-compliance, n=71</i>	
Forgetfulness	32(45.1)
Side effects	29(40.8)
Others	10(14.1)

Further analysis demonstrates that out of 132 respondents who were anaemic at the booking visit, 39(29.5%) did not comply with iron

supplementation regimen (Table 3). Among those who were non-anaemic at booking, 32(26.0%) were also non-compliant with the prescribed iron.

Table 3: Pattern of compliance with iron supplementation by anaemic status at booking

Variable	Iron compliant		Total
	Yes	No	
<i>Anaemic at booking?</i>			
Yes	93(70.5)	39(29.5)	132(100)
No	91(74.0)	32(26.0)	123(100)

By the third trimester, 101(76.5%) who had anaemia at booking were still anaemic while 49(39.8%) who were previously not anaemic

became anaemic (Table 4). Overall, an increase of 7% in prevalence of anaemia was observed.

Table 4: Relationship between anaemia at booking and at third trimester

Variable	Anaemic by third trimester		Total
	Yes	No	
<i>Anaemic at booking?</i>			
Yes	101(76.5)	31(23.5)	132(100)
No	49(39.8)	74(60.2)	123(100)

The mean haemoglobin concentration at booking was 32.56 ± 2.99 , and at third trimester it was 31.67 ± 3.01 . Paired t test analysis showed a significant drop in mean haemoglobin concentration between these two time points (mean diff: 0.89 ± 3.04 ; $t = 4.673$; 95% CI= 0.52-1.27; $p < 0.001$). Increased in prevalence of anaemia was observed in both iron compliant and non-compliant groups. Whereas 93(50.5%) of the

sampled subset who were compliant with iron had anaemia at booking, the number increased to 101(54.9%) by third trimester. Also, among the non-compliant subset, anaemia increased from 39(54.9%) at booking to 49(69.0%) by third trimester. Further analysis (Table 5), however, showed that the non-compliance had higher odds of predicting anaemia by the third trimester (OR: 1.83; 95% CI: 1.03-3.26; $p = 0.04$).

Table 5: Regression analysis of non-compliance with iron medication and anaemia by third trimester

Variable	Anaemia		Total	Odd ratio	95% CI	P value
	Yes	No				
<i>Non-compliant</i>						
Yes	49(69.0)	22(30.9)	71(100)	1.83	1.03-3.26	0.040*
No	101(54.9)	83(45.1)	184(100)	1.00		

*significant at p<0.05

Non-compliance with iron supplementation was more among respondents who were <24 years old, muslims, married, with secondary level of education, unskilled, multigravida and with

unplanned pregnancies. However, none of the socio-demographic features had statistical significance in predicting non-compliance with prenatal iron supplementation (Table 6).

Table 6: Predictor of non-compliance with iron supplementation

Variable	Non-compliant		Total	Adjusted odd ratio	95% CI	P value
	Yes	No				
Age (years)						
≤24	5(33.3)	10(66.7)	15(100)	1.00		
25-34	55(29.4)	132(70.6)	187(100)	1.25	0.41-3.55	0.749
≥35	11(20.8)	42(79.2)	53(100)	1.94	0.56-6.52	0.311
Religion						
Christianity	64(27.0)	173(73.0)	237(100)	1.75	0.66-4.51	0.278
Islam	7(38.9)	11(61.1)	18(100)	1.00		
Tribe						
Yoruba	59(26.6)	163(73.4)	222(100)	0.39	0.03-5.20	0.299
Igbo	12(40.0)	18(60.0)	30(100)	0.21	0.01-3.03	0.170
Hausa	0(0)	3(100)	3(100)	1.00		
Marital status						
Single	5(21.7)	18(78.3)	23(100)	1.00		
Married	66(28.4)	166(71.6)	232(100)	0.74	0.25-1.92	0.494
Educational level						
Primary	11(31.4)	24(68.6)	35(100)	1.00		
Secondary	32(34.4)	61(65.6)	93(100)	0.89	0.38-1.99	0.750
Tertiary	28(22.0)	99(78.0)	127(100)	1.64	0.72-3.67	0.250
Occupation						
Unskilled	16(29.6)	38(70.4)	54(100)	0.66	0.26-1.64	0.364
Semi-skilled	46(28.9)	113(71.1)	159(100)	0.69	0.30-1.50	0.332
Skilled	9(21.4)	33(78.6)	42(100)	1.00		
Gravidity						
Primigravida	24(25.3)	71(74.7)	95(100)	1.00		
Multigravida	47(29.4)	113(70.6)	160(100)	0.82	0.46-1.44	0.479
Pregnancy Planned						
Yes	58(26.6)	160(73.4)	218(100)	1.51	0.72-3.10	0.285
No	13(35.1)	24(64.9)	37(100)	1.00		

DISCUSSION

This study found out that after controlling malaria/helminthic infestation, a drop in mean haemoglobin concentration and 7% increase in prevalence of anaemia occurred among prenatal care attendees despite being on iron supplementation for more than 8 weeks with a compliance rate of 72.2%. Though statistical evidence shows that non-compliance with iron therapy would predict anaemia in the third trimester, compliance among three-quarter of the respondents was not sufficient to reduce the overall prevalence of anaemia. Surprisingly, increase in anaemia was observed in both compliant and non-compliant subsets of prenatal clinic attendees.

Some researchers have called to questioning the effectiveness of iron supplement in reducing prevalence of anaemia in all populations of pregnant women (14,17). Though others basically argued that its ineffectiveness may be attributable to low compliance (18), a reappraisal of this assertion may be necessary in that in our study iron supplements have failed to improve anaemia in the presence of good compliance.

Usually, due to poverty with attending inability to afford balanced diet and the problem of 'too frequent and too many pregnancies', women in low-resource areas tend to conceive with severely depleted iron store (5). Compounded by the habit of late prenatal care booking which allows less time for anemia correction (19), it is obvious that in resource-scarce settings we need to look beyond iron supplements as the only 'saviour'.

It could be that the supplementation can reduce the extent of iron depletion in the third trimester (20), but for women who became pregnant with very low or no iron stores, the approach may not be sufficient to prevent anemia by third trimester. Cogswell et al found that the effect of iron supplementation on anaemia by the third trimester is not significant (13).

Certainly, some research works have demonstrated positive influence of iron supplements on haemoglobin concentration by the last trimester (11,12). However, the complex interplay of clinical, cultural, societal and economic settings may not make that finding generalizable.

The World Health Organization recommends a 30mg daily dose of elemental iron in a setting where prevalence of anemia in pregnancy is <40% and 60mg daily in places with higher prevalence. Where anaemia is diagnosed or the available duration for supplements will be <6 months, a daily dose of 120mg of elemental iron is suggested (9). In our setting, because anemia is of severe public health importance and duration available for iron supplements is often <6 months, we routinely give 120mg of elemental iron to all prenatal care attendees.

In a submission by the Centers for Disease Control and Preventions (CDC), it noted that higher doses of iron do not necessarily provide greater benefit to pregnant women in correcting anaemia (21). This is possibly true in our observation because the high dose has not effectively reduced overall anemia prevalence. There may also be a need to exercise caution because of adverse effects that such dose may have (10).

Compliance rate among the gravid women was higher than 37.2% observed in Oyo state, Nigeria eight years ago (22). The variation can be attributed to passage of time, study location and the degree of enlightenment of participants. Whereas the aforementioned study was conducted at primary health care level, ours was done at a tertiary health facility which likely skewed participants towards more educated ones. It is therefore possible that reduced compliance and worse prevalence of anaemia at third trimester would be recorded at lower levels of care. Our compliance rate, however, is comparable with studies from India and Senegal where compliance was 65% and 69% respectively (23,24).

Forgetfulness and perceived side-effects accounts mostly for non-compliance; it is similar with what was found by Mithra et al (23). More provision of clear instruction on health benefits of the supplementation and tapering of the dose could enhance compliance.

This study is not without social desirability bias. There is a tendency that since compliance was self-reported, actual rate may be lower. Compliance is best measured by continuous direct observation that therapies are taken (25), a process that is impracticable in this circumstance. Although there is still a tendency of overestimation of adherence to therapy by pill

counts (25), for future studies, adjoining it as a measure of compliance will be suggested.

Predicting who will not comply with iron supplementation was difficult as none of the socio-demographic features was associated with non-compliance. Some studies, however, found that non-compliance was more among singles, teens and increasing maternal age (22,23).

It is uncertain if weekly iron supplementation will produce similar/better compliance and therapeutic effects in our environments as compared to daily regimen, but considering the stage of our socio-cultural evolvement, it may produce a lower compliance. However, it is worth investigating. Also, comparison of the impact of slow iron gastric-delivery system to high daily elemental iron doses in low-income settings can be researched into.

More needs to be learnt about how to safeguard pregnant women in resource-scarce settings from going into delivery process with sub-optimal hemoglobin concentration. It is evident that dependence on prenatal iron supplementation may not be the sole solution. There is a need to look beyond the approach and reinforce the importance of better feeding practices, food fortification and reduced frequency of pregnancies.

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