LOWERED ANTIOXIDANT STATUS IN PREGNANT WOMEN ON IRON SUPPLEMENTS: SIGNIFICANCE AND CANDIDACY OF IRON FOR THERAPEUTIC DRUG MONITORING IN PREGNANCY

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INTRODUCTION

IRON SUPPLEMENTS & ANTITOXIDANT STATUS IN PREGNANCY

Iron (Fe) remains a commonly prescribed supplement in pregnancy. But the pro-oxidant potential of Fe is often overlooked.

Fe supplement – associated oxidative stress may be unwittingly precipitated with risk of manifestations reminiscent of thalidomide toxicity in pregnancy.

Iron is one of the commonest over the counter (OTC) substances prescribed in pregnancy particularly in the developing countries. Micronutrient deficiency disorders (MDDs), especially those that play an important role in the antioxidant system are also more common in these countries (2,3, 4). We investigated the antioxidant status in pregnant women with and without Fe supplements.

METHODS

Fifty-eight pregnant women on Fe supplements were studied at the Teaching Hospital of the University of Ibadan (UCH), Nigeria. Fifty-five aged matched pregnant women attending Christ Apostolic Church (CAC), a non drug using sect in Ibadan, not on Fe, served as controls. Participants were classified according to their trimester of pregnancy.

POISONING IN PREGANCY & DEVELOPMENTAL DISORDERS

RESULTS

1. Fruit and vegetables consumption was higher in the supplement group than in controls (57.2 % vs. 37.3%). Serum Fe level was significantly higher in the supplement group than in controls (P< 0.001). Ascorbic acid, copper (Cu), zinc (Zn), and bilirubin were all significantly decreased (p<0.05, p<0.001, P<0.05 and p<0.05 respectively). There was relative stability of all antioxidants except uric acid in controls. The significantly higher Fe level in the second trimester was sustained in the third trimester (P<0.05); associated with significant decreases in ascorbic acid, bilirubin, Cu, and Zn (P<0.02, P<0.02, P<0.02, P<0.001 respectively) in the supplement group (Tables 2).

Table 1. Anthropometric indices, serum iron and antioxidant levels in the three trimesters of pregnancy in the supplement group
Values are mean ± SD. Negative (-) before figures indicate decreases

	First Trimester (n=10)	Second Trimester (n=23)	Third Trimester (n=25)	% Changes (bet. 1st & 3rd Tri.)
Age (Years)	28.40 ± 4.53	26.00 ± 4.25	26.81 ± 3.94	-
Gestation (Months)	2.10 ± 0.74	5.43 ± 0.73	8.08 ± 0.76	-
Height (m)	1.59 ± 0.26	1.59 ± 0.29	1.57 ± 0.23	-
Weight (Kg)	68.10 ± 6.02	65.57 ± 10.14	66.28 ± 13.2	-2.67
BMI (Kg/m²)	26.78 ± 5.45	26.07 ± 10.14	27.52 ± 1.51	2.76
Iron (µmol/l)	10.69 ± 4.15	21.30 ± 6.80	23.16 ± 10.14	116.65
Ascorbate (mmol/l)	19.71 ± 4.39	16.82 ± 5.91	14.98 ±2.23	-23.5
Bilirubin (µmol/l)	1.14 ± 0.83	0.70 ± 0. 57	0.60 ± 0.38	-47.36
Copper (µmol/l)	15.00 ± 6.12	15.93 ± 6.26	16.08 ± 10.93	7.2
Vitamin E (mmol/l)	11.96 ± 3.35	10.85 ± 4.24	9.90 ± 2.56	-17.22
Uric acid (µmol/l)	211 .00 ± 80.36	155.42 ± 84. 12	135.59 ± 42.8	-36.02
Zinc (µmol/l)	17. 68 ± 4.69	15. 49 ± 5.23	14.40 ± 4.09	-8.55

Table 2. Age, gestation, anthropometric indices, iron, ascorbate, copper, α-tocopherol, Bilirubin, zinc levels and fruit and vegetable consumption in supplement and non- supplement groups (1). Values are mean ± SD

	Test(n= 58)	Control(n= 55)	t- values	p- values
Age (Years)	26.81 ± 3.94	27.71 ± 4.78	1.09	>0.05
Gestation (Months)	6.0 ± 2.29	5.58 ± 2.50	0.929	>0.05
Height (M)	1.58 ± 0.61	1.60 ± 0.61	1.52	>0.05
Weight (Kg)	66.31± 12.43	71.45 ± 12.52	1. 89	>0.05
BMI (Kg/m²)	26.82 ± 5.75	27.85 ± 4.41	1.07	>0.05
Fe (µmol/l)	20.27 ± 9.29	13.81 ± 5.87	4.39	< 0.001
Ascorbate(mmol/l)	16.85 ± 7.70	20.59 ± 5.00	2.60	<0.05
Bilirubin(µmol/l)	0.84 ± 0.77	2.81 ± 2.0	4.66	<0.001
Cu (µmol/l)	16.12 ± 7.2	19.34 ± 5.9	2.59	<0.05
Vitamin E(µmol/l)	11.0 ± 3.67	11.07 ± 0.77	0.07	>0.05
Uric acid (µmol/l)	178 ± 78.3	205.53 ± 96.3	1.61	>0.05
Zn (µmol/l)	15.53 ± 5.3	18.43 ± 5.0	2.71	<0.01
Fruits &Vegetable Intake/24h (%)	57.17	37.13	-	-

Table 3. Anthropometric indices, serum iron and antioxidant levels in the three trimesters of pregnancy in non-supplement pregnant subjects (controls) Values are mean ± SD. Negative sign (-) before figures indicate decreases.

	First Trimester (n=12)	Second Trimester (n=20)	Third Trimester (n=23)	Percent (%) Changes (between 1st & 3rd Tri.)
Age (Years)	25.5 ± 4.53	29.20 ± 4.08	25.57 ± 4.88	-
Gestation (Months)	1.92 ± 0.79	5.0 ± 0.86	8.00 ± 0.80	-
Height (Meters)	1.59 ± 0.97	1.61 ± 0.90	1.60 ± 0.90	-
Weight (Kg)	67.33 ± 16.18	70.9 ± 11.63	74.09 ± 14.79	10.04
BMI (Kg/m²)	26.66 ± 3.24	27.29 ± 3.74	25.95 ± 5.47	-2.66
Fe (mmol/l)	11. 34 ± 3.37	11.89 ± 3.74	17.06 ± 6.98	50.44
Ascorbate (mmol/l)	17.21 ± 9.56	16.96 ± 7.74	16.58 ± 7.15	-3.66
Bilirubin (µmol/l)	2.46 ± 1.78	2.30 ± 1.81	1.23 ± 1.47	-50.00
Cu (µmol/l)	18. 91 ± 5.89	19.46 ± 5.92	19 .47 ± 3.27	2.96
Vitamin E (mmol/l)	11.55 ± 4.42	11.0 ± 5.31	10 .70 ± 3.27	-7.30
Uric acid (µmol/l)	233.87 ± 109.00	205.13 ± 84.59	150 .41 ± 60.47	-35.69
Zn (µmol/l)	18.90 ± 5.89	18.03 ± 4.96	16.09 ± 1.83	-14. 86

Table 4. Correlation of iron with antioxidant levels in supplement pregnant women

	r- values	p - values
Ascorbic acid (mmol/l)	-0.299	<0.05
Bilirubin (µmol/l)	-0.278	<0.05
Cu (µmol/l)	-0. 431	<0.01
Vitamin E (mmol/l)	-0. 120	>0.05
Uric acid (µmol/l)	-0. 383	<0.05
Zn (µmol/l)	-0.369	<0.05

3. Uric acid and bilirubin levels decreased by similar proportions during the period, while Zn decreased by 18.6% in the supplement group and by 14.9% in controls. All the antioxidants in supplement group except vitamin E, ascorbic acid, bilirubin, Cu, uric acid and Zn, were significantly inversely correlated with serum Fe (r -0.299, P<0.05, r-0.278, P<0.05, r-0.383, P<0.05 and r-0.036, P<0.05)

2. Percentage changes between the first and third trimesters revealed that serum Fe increased by 116% in the Fe group whilst it only increased by 50% in controls. This was associated with 23.5% decrease in ascorbate level (p<0.003) in the supplement group while decreasing by 3.7% in controls (p>0.05). Vitamin E decreased by 17.2% in the supplement group but decreased by 7.3% in controls during the period.

Table 5 Anthropometric indices, serum iron and antioxidant levels in the three trimesters of pregnancy in subjects on iron supplements. Taken together these data add and extend the growing mass of knowledge suggesting iron supplementation is associated with profound oxidative stress which may lead to teratogenic effects (birth defects), habitual abortions, retarded intrauterine growth, and low birth weight infants, pre-eclampsia and other complications of pregnancy (3).

	1st Trimester (n=10)	2nd Trimester (n=23)	3rd Trimester (n=25)	F - value	p
Age (Years)	28.40 ± 4.53	26.00 ± 4.25	26.81 ± 3.94	4.16	0.073
Gestation(Months)	2.10 ± 0.74	5.43 ± 0.73	8.08 ± 0.76	26.94	0.001
Height (Meters)	1.59 ± 0.26	1.59 ± 0.29	1.57 ± 0.23	5.109	0.051
Weight (Kg)	68.10 ± 6.02	65.57 ± 10.14	66.28 ± 13.2	5.11	0.051
BMI (Kg/m²)	26.78 ± 5.45	26.07 ± 3.36	27.52 ± 1.51	1.577	0.288
Iron (µmol/L)	10.69 ± 4.15	21.30 ± 6.80	23.16 ± 10.04	135.77	0.000
Ascorbic acid(mmo/L)	19.71 ± 4.39	16.82 ± 5.91	14.98 ± 2.23	17.055	0.003
Bilirubin(µmol/L)	1.135± 0.83	0.70 ± 0.97	0.60 ± 0.38	0.466	0.649
Copper (µmol/L)	15.00± 6.12	15.93±6.26	16.08±10.93	0.836	0.478
Vit. E (mmol/L)	11.96 ±3.35	10.85±4.24	9.90±2.56	3.189	0.114
Uric acid (µmol/L)	211±80.36	155.42±84.12	135.59±42.80	4597.6	0.000
Zinc (µmol/L)	17.68±4.69	15.49± 5.23	14.40±4.09	8.371	0.018

CONCLUSIONS

The markedly lowered antioxidant status in the Fe supplement group implies severe oxidative stress, with risk of adverse outcomes for mother and fetus. This may suggest need for monitoring of antioxidant and Fe status during Fe supplementation in pregnancy, and therapeutic drug monitoring (TDM) of Fe.

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