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COMPARISON BETWEEN RECOMMENDED DAILY DOSE AND MODIFIED REDUCED DOSES OF IRON PROPHYLAXIS IN NON-ANAEMIC PREGNANT WOMEN

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ABSTRACT

Background: Recommended prophylactic daily dose iron supplementation in non-anaemic pregnant mothers increases the body iron store that leads to unfavourable pregnancy outcome. So the present study was conducted on pregnant mothers with reduced dose of elementary iron and to investigate whether the reduce dose of iron supplementation can reduce the adverse effects. **Material and methods:** A prospective observational randomized hospital based clinical study was performed on 299 pregnant women with haemoglobin ≥ 10gm/dl and divided into three groups. One group received 100mg elementary iron daily, second group same dose but in alternate day and other received 200 mg elementary iron twice weekly. Blood ferritin concentration was measured at 28-32 weeks and was compared across the three study groups and also compared with the birth weight of their babies within a group. **Result:** There was significant increased concentration of blood ferritin level and this increased ferritin level were significantly associated with higher rates of intrauterine growth restricted baby in pregnant mothers receiving daily iron supplementation. Among the reduced and modified dose of iron supplementation alternate day 100 mg elementary iron prophylaxis strategy is much more subject friendly. **Conclusion:** The rationale of routine iron supplementation in non-anemic pregnant women needs to be re-examined.

KEYWORDS: Iron prophylaxis, intrauterine growth restriction, Ferritin, Non-anaemic pregnant mother.

1. INTRODUCTION

Iron is an essential element for both pregnant women and the growing foetus and so pregnant women are routinely recommended for iron supplementation [1-3] despite the fact that such prophylactic iron supplementation is still a matter of controversy. Indeed, animal studies suggest that the administration of iron daily at the current recommended dosages may be neither desirable nor innocuous[4] as elevated iron stores during pregnancy have been associated with increased risk of maternal and neonatal morbidity such as intrauterine growth restriction (IUGR).[5] So, the present study was conducted to evaluate the level of serum ferritin in pregnant mother between 28-32 weeks of gestation, which could point out whether the intermittent iron supplementation can reduce the incidence of this type of detrimental effect in pregnancy than daily dose and can stands for possible alternative strategy for giving supplementation in non-anemic subjects. As serum concentration of ferritin is in correlation with total iron reserve in the human and the decrease levels is in correlation with the decrease of iron reserves in the mother resulting from increased uptake (by the mother, placenta and foetus) as well as from hemodilution[6] therefore it was used as a reliable parameter for the estimation of iron status in body of study population.[7-9]

2. MATERIAL AND METHODS

2.1 Study area

The present study was conducted in the department of Biochemistry with the collaboration of department of Gynaecology and Obstetrics of Burdwan Medical College, Burdwan, West Bengal, India.

2.2 Selection of subjects

This prospective and observational study was performed between February 2011 and May 2013. One thousand pregnant mothers who attended first time in the antenatal clinic of Burdwan Medical College in first trimester after 20 weeks of gestation having blood haemoglobin level ≥ 10gm/dl were selected in this study. To exclude the subjects suffering from anemia we have chosen the study population that have haemoglobin ≥ 10gm/dl in blood (10). Subjects having any concomitant infection, history of smoking and chronic diseases such as nephropathy, hypertension, ischemic cardiopathy, malignant tumours and diabetes mellitus were not included in the study. Pregnant mother with pre-existing chronic anemia or other blood disorders and hemoglobinopathies, who might have very high ferritin concentration due to a problem with utilization, were also excluded. Then three hundred and

ten subjects were selected by a simple random method for this study after informed consent had been received. The proposal of this study was approved by the Ethics Committee of Burdwan Medical College, West Bengal.

2.3 Iron Supplementation

The mothers were divided into three groups. One group (n = 107) was received traditional prophylactic daily dose (100mg) of elementary iron, in second group (n = 119) given same dose of iron in alternate day and third group (n = 84) given 200mg elementary iron in twice weekly. All the groups were getting their respective way of supplementation with same compound of iron throughout the pregnancy. Complains of missing iron tables and gastrointestinal upsets such as nausea, vomiting, constipation, diarrhoea, epigastric pain was noted carefully.

2.4 Collection of samples

Peripheral venous blood from the entire pregnant mother under study were drawn at 28-32 weeks of gestation and allowed to coagulate at room temperature for 30–45 min, followed by centrifugation at 2500 rpm for 5 min. All serum samples were stored at -70^{0}C and kept under these conditions until chemical analysis was performed. The gestation of 28-32 weeks was chosen for the blood sampling because iron storage decreases with advancing gestation and the lowest of ferritin are recorded at this period after which the concentration stay on constant levels.[6] Furthermore, the demand for the power of the absorption of iron is greatest in the third trimester.[11]

2.5 Laboratory investigation

Serum ferritin estimation was done using micro-particle enzyme immunoassay, IMX system of Abbott Park, IL, USA. Intra-assay CV% and inter-assay CV% was 3.4 and 3.5 respectively.

2.6 Physical features at birth

After delivery, the data on infant characteristics for the presence of intrauterine growth restriction were retrieved from the records in our hospital for analysis.[12]

2.7 Statistical Analysis

The data for biochemical analysis was subjected to standard statistical analysis using the Statistical Package for Social Science (SPSS) 11.5 software for windows.

3. RESULT

Of the 310 pregnant women with a gestational age of 30–32 weeks included in the investigation, 11 were excluded during the investigation period for the following reasons: 3 pregnant women developed hypertension at 32 gestational weeks, 2 presented with gestational diabetes, 4 women delivered before the 37th completed week of gestation, whereas 2 blood sample was contaminated by the presence of fibrin and estimations of ferritin could not have been done.

3.1 Personal profile and clinical details of the pregnant mothers and their babies of Group I, II and III

Selected characteristics of the women at the beginning of the study as shown in the Table 1

Table 1: Personal profiles and clinical parameters of the pregnant mothers and their babies under the study.

Population characteristics	Group I	Group II	Group III	Group I vs Group II (p value)	Group I vs Group III (p value)	Group II vs Group III (p value)
n	105	111	83			
Mother's age (years)	26.34 ± 5.82	27.68 ± 6.36	28.12 ± 7.53	> 0.05	> 0.05	> 0.05
Gestational age (days)	272 ± 6.73	270 ± 6.17	271 ± 5.96	> 0.05	> 0.05	> 0.05
Singletons	47 (44.76)	53 (47.75)	39 (47)	>0.05	> 0.05	> 0.05
IUGR baby*	51 (48.57)	13 (11.71)	10 (12.5)	< 0.001	< 0.001	>0.05
Birth weight (gm)	2263 ± 159	2987 ± 336	2911 ± 225	< 0.001	< 0.001	>0.05
Hemoglobin (gm/dl)	11.4 ± 2.67	12.6 ± 1.59	12.1 ± 2.16	> 0.05	> 0.05	> 0.05
Complain of gastrointestinal upsets*	61 (58.09)	13 (11.71)	69 (83.13)	< 0.001	0.011	< 0.001
Missing iron tables*	2(1.9)	72 (64.86)	59 (71.08)	< 0.001	< 0.001	0.034

n = number of subject; p > 0.05 is considered statistically not significant; p < 0.05 is significant; Values are mean ± SD

*Data are expressed as numbers (group percentages in parentheses)

3.2 Comparison of the serum ferritin level between different groups

Comparison of the serum ferritin level between Group I, Group II and Group III in 28-32 weeks of gestation was performed and it was found that mean value of serum ferritin in Group I subjects (29.12µg/L) was significantly (p < 0.001) higher than Group II (13.27 µg/L)

and Group III (12.95 µg/L) but there was no significant difference between Group II and III as shown in the Table 2.

Table 2: **Comparison between concentrations of serum ferritin in Group I, Group II and III study population**

	Concentration of serum ferritin (µg/L)	Group I vs Group II (p value)	Group I vs Group III (p value)	Group II vs Group III (p value)
Group I	29.12 ± 19.44			
Group II	13.27 ± 2.65	**< 0.001**	**< 0.001**	>0.05
Group III	12.95 ± 2.32			

Values are mean ± SD; p value p < 0.05 considered statistically significant

3.3 Correlation of blood ferritin with birth weight of baby in the study groups

In case of traditional iron supplementation there was a more significant negative correlation between serum ferritin and birth weight (r = -0.773, p = 0.000) than in case of two modified types of iron supplementation (r = -0.199, p = 0.036; r = -0.235, p 0.032) as depicted in the Table 3 and Figure 1, 2 and 3. So it is clear that only in higher concentration of serum ferritin seriously affects in reduction of birth weight.

Table 3: Bivarient correlation between birth weight and serum ferritin in Group I, Group II and Group III study population

	Pearson's correlation	Significance
Group I	-0.773	0.000
Group II	-0.199	0.036
Group III	-0.235	0.032

p value p < 0.05 considered statistically significant

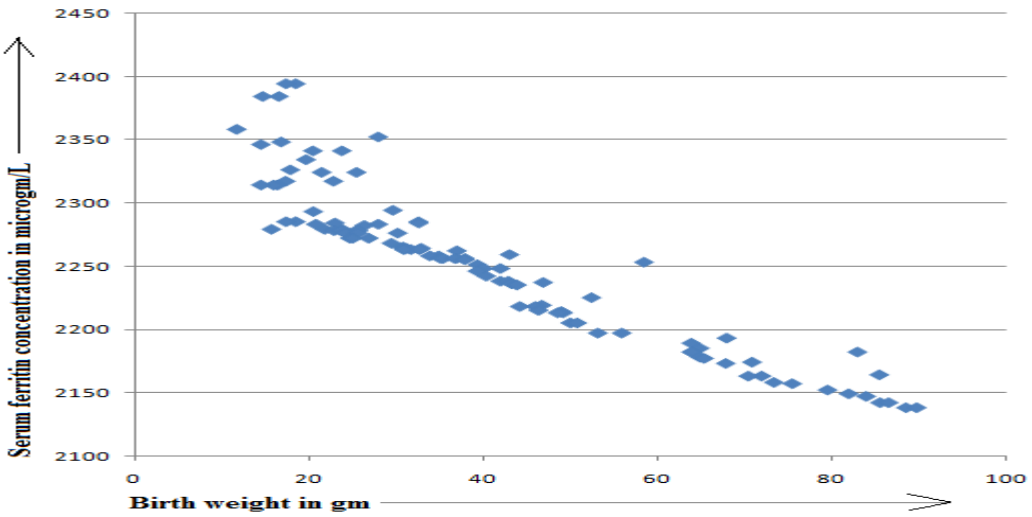

Figure 1: Correlation of birth weight (g) and blood ferritin levels (µg/L) in pregnant women between 30 and 32 weeks of gestation of Group I study population.

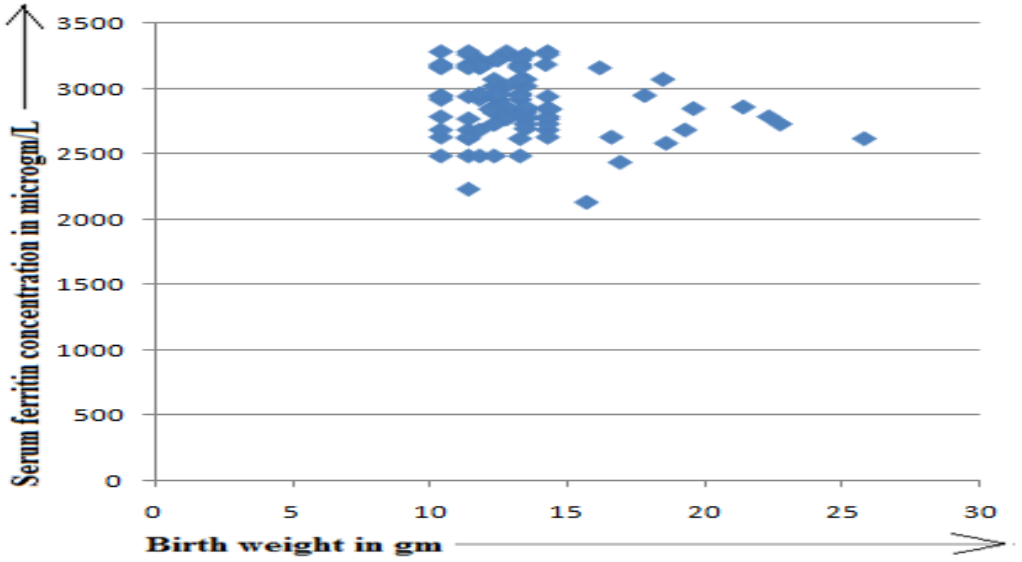

Figure 2: Correlation of birth weight (g) and blood ferritin levels (µg/L) in pregnant women between 30 and 32 weeks of gestation of Group II study population.

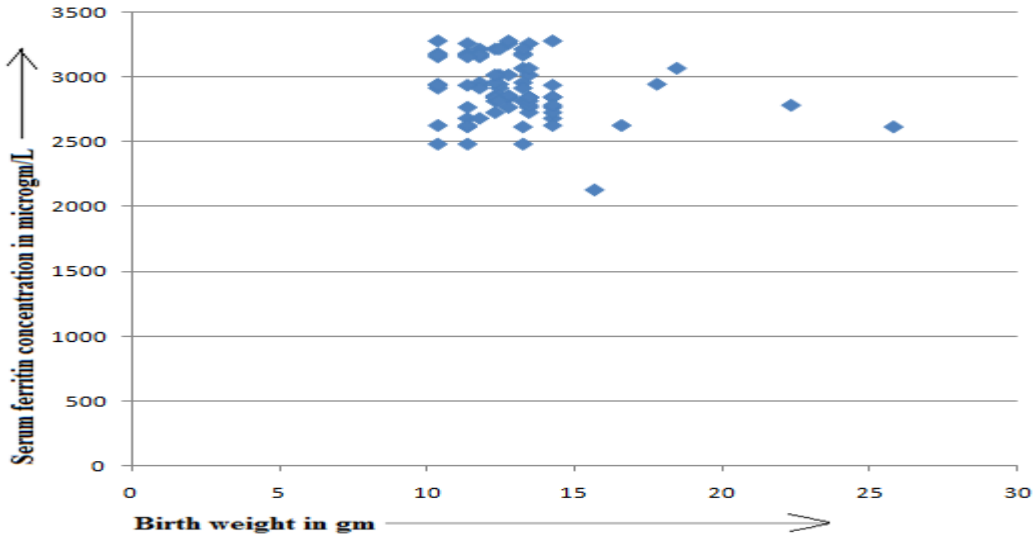

Figure 3: Correlation of birth weight (g) and blood ferritin levels (µg/L) in pregnant women between 30 and 32 weeks of gestation of Group III study population.

4. DISCUSSION

Iron and iron-containing compounds play vital roles in cellular function in all organ systems. The requirement for iron is greater in rapidly growing and differentiating cells[3] but excess iron causes several adverse pregnancy outcomes such as IUGR.[13] Traditional prophylactic iron supplementation is given in all pregnant mothers during antenatal period but who contain adequate red cell profiles such as haemoglobin there is an increase chance of delivery of small for gestational aged baby.[10] So, the concerns have led to studies looking at intermittent

versus daily iron dosing in an attempt to observed effect of pregnancy outcome and also identify the optimum supplementary protocol.

First of all, it was found that traditional iron supplementation causes elevated maternal serum ferritin level than other reduced dose of iron supplementation. Numerous recent studies have shown that iron supplementation in reduced dose in non-anemic pregnant women is an effective option for prophylaxis.[14]

Another important finding in the study was that elevated level of serum ferritin was associated with an increased risk of IUGR. Various previous studies have been shown that increased maternal iron store appear to have a negative impact on birth weight,[10,15] as raised serum ferritin level can point to impaired transfer of micronutrients from the mother to foetus.[6] In addition, there is the potential concern that some women who are not truly anemic may taking large doses of daily supplemental iron during pregnancy. Such a strategy has been suggested as a way to build up the mother's iron store and to increase blood viscosity to impair uteroplacental flow.[16-18] It is also possible that increased levels of plasma free iron as a result of daily iron supplementation at recommended dose also increase oxidative damage to DNA in the maternal-foetal unit.[1] But reduced dose iron supplementation has recently been associated with a reduced risk of low birth weight infants in pregnant women with no anemia.[19] Moreover Iron absorption is suppressed for at least 24 h after consumption of a high iron meal or iron supplement, principally by controlled suppression of intestinal mucosal cell uptake.[20-23] So, it has been suggested that less frequent supplementation may reduce the transient iron overload and may decrease the cost of routine daily supplementation[24] but there is a chance of missing table because mothers have to remember the particular date in a week when has to take.

Another important observation in this study was that though both the reduced modes of iron prophylaxis can effectively reduced the chance of IUGR baby but in respect to patient compliance alternate day 100mg elementary iron supplementation is far better than 200mg twice weekly supplementation.

5. CONCLUSION

Traditional daily dose of prophylactic 100 mg elementary iron supplementation to non-anemic pregnant mother causes elevation of maternal blood ferritin level and this increase has deleterious effect on pregnancy outcome. But when reduced dose supplementations were

applied they can effectively reduce the chance of development iron overload and consequently IUGR. But person compliance limits the use of 200 mg twice weekly supplementation. So, alternate day 100 mg supplementation as a possible alternative strategy that may enhance the effectiveness of operational programs.

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7. CONFLICT OF INTEREST

We do not have any conflict of interest.

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