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CONSEQUENCES OF DIETARY IRON DEFICIENCY ON PREGNANCY OUTCOME AND MATERNAL HEALTH

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***Abstract*— Iron deficiency anemia is widely prevalent in India. It is the most pervasive of all nutritional deficiencies, particularly affecting pregnant women. Iron deficiency during pregnancy is one of the leading causes of anemia in infants and young children. Many women go through the entire pregnancy without attaining the minimum required intake of iron. This may affect the maternal health adversely. Iron deficiency may lead to abnormal functioning of thyroid gland as it plays an important role in synthesis as well as metabolism of thyroid hormones. Iron is an important component of many enzymes including thyroid peroxidase (TPO). It is very important to note the changes in the thyroid activity by severe anemia during peripartum period. The present study aims to determine the impact of iron deficiency and iron deficiency anemia on the mothers and the neonates and thyroid functioning of mothers. The female albino rats of Wister strain were fed on iron deficient diets (30, 15, 7, 2 mgFe/kg of diet) and control diets (50 mgFe/kg of diet). Prior to one month of mating the females were anaesthetized by ether and the tail blood was collected for the evaluation of blood hemoglobin, hematocrit and estimation of thyroid stimulating hormone (TSH) hormone. The rats were then kept for mating. The tail blood was again collected during 18th–20th day of gestation and after ten days of delivery by anaesthetizing the females by ether. They were kept on the same diet throughout gestation and also after the deliveries. The hemoglobin, hematocrit, thyroid stimulating hormone (TSH) hormone and body weights of mothers were compared in all the three stages (before pregnancy, during pregnancy and after delivery) with decreasing levels of dietary iron, within the groups and between the groups by one way ANOVA. Significant ($P<0.05$) differences in the levels of the three parameters were observed. The two-way ANOVA (between iron diets and stages i.e., before pregnancy, during pregnancy and after delivery) also showed a significant ($P<0.05$) rise in the levels of TSH. The severely iron deficient mothers showed postpartum hypothyroidism. The two-way ANOVA (between iron diets and stages i.e., before pregnancy, during pregnancy and after delivery) also showed a significant ($P<0.05$) decline in the weights of mothers. The preterm delivery (between 12th to 15th days) was also observed in severely iron deficient mothers (7 and 2 mgFe/kg of diet). The weight of neonates was also taken. The females with severe iron deficiency anemia (7, 2 mgFe/kg of diet) could not lactate and failed to conceive months after their first premature deliveries and were very feeble and underactive. The possible reason of postpartum rise in the TSH and hypothyroidism in the severe iron deficiency anemic mothers may be the hypo function of pituitary and changes in the TSH secreting cells of the pituitary which led to the dysfunction of the thyroid gland after delivery. Due to severe iron deficiency low thyroid peroxidase activity possibly decreased the synthesis of thyroid hormones which in turn had affected the pituitary and resulted in hypothyroidism. No lactation and infertility also reflect the hypo function of pituitary.**

***Keywords*— Deficiency, Gestation, Hemoglobin, Preterm, Thyroid Stimulating Hormone**

I. INTRODUCTION

Iron deficiency anemia is extremely common, particularly in the developing world, reaching a state of global epidemic. The deficiency of iron continues to be a widespread condition affecting millions of people throughout the world. Although poor populations suffer from it most, lack of iron is one of the few nutrition pathologies present in affluent societies with pre-school age children and women of childbearing ages being the most vulnerable groups. Iron deficiency is the most common nutritional deficiency encountered in surveys of diverse populations in industrialized countries (1) and it is said to be the most common cause of anemia in the world. The world health organization estimates that 66-80% of the population is suffering from Fe deficiency (2). A UN report in 1980 on world nutrition quotes a figure of 43% of children between birth and four years, as being anemic,20% of adult men and 35% of adult women are anemic with iron deficiency accounting for more than half of the cases. Iron deficiency anemia is widely prevalent especially amongst women in India (3, 4, 5). Iron deficiency anemia is considered very serious during pregnancy, with deleterious consequences for both the mother and developing fetus. In most species, maternal blood volume increases and hematocrit and hemoglobin concentration fall during pregnancy; this is known as the anemia of pregnancy Anemia is generally defined according to hemoglobin levels, which may vary according to many factors most importantly age, gender, and ethnicity. Any level below 13 g/dL for males, and below 12 g/dL for females is considered abnormal (6). Hemoglobin levels of less than 11 g/dL at any time during pregnancy are considered abnormal. Once anemia is recognized, the possibility of iron deficiency should be considered (7). Chronic iron deficiency anemia lowers work tolerance, productivity, and the quality of life. This leads to further socio-economic difficulties. Dysfunction in the immune system results in increased risks for infections (8). Some studies have shown that ID can negatively impact thyroid function by interfering with oxygen transport or affecting thyroid peroxidase activity (9,10). IDA could impair thyroid metabolism through anemia and lowered oxygen transport (11). Malfunction of the thyroid gland is the second most common endocrine disorder encountered during pregnancy. It is well known that overt disease of the thyroid gland, either hyper or hypo can adversely affect pregnancy outcome (12). The present study was aimed to observe whether the dietary iron deficiency anemia impairs the thyroid functioning during peripartum period effecting maternal thyroid functioning and the pregnancy outcome.

II. MATERIALS AND METHODS

A. Experimental animals

Female rats of Wister strain were bred under laboratory conditions from the stock colonies for the constant availability throughout the period of study. The experimental animals were of similar body weight (170-200gms), size and age and were group- housed in cages under constant temperature and humidity. Controlled illumination with a 12hrs light and 12hrs dark photoperiod was maintained to ensure regular estrous cycles. All animals were fed ad libitum and provided with distill water. Thirty female rats were fed control diet for two weeks to adapt to the new conditions, before being randomized into five groups. The first group of rats (n=6) remained on the control diet (50mg/kg), whereas the remaining four groups (n=6each) were placed on experimental diets of reduced Fe content (30, 15, 7, 2mg/kg). All diets were freely available, and body weights were recorded three times per week throughout the experiment. All groups were fed these diets for four weeks before mating. To prepare the rats and reduce the stress response at the time of blood collection, all were picked up and handled daily. The tail blood from the rats (in proesterus) of each group was collected into heparinized collection tubes to determine baseline hemoglobin and hematocrit values. Serum was collected for the estimations of thyroid stimulating hormone. The rats were then mated and the mating was confirmed by detection of a vaginal plug, and this day was denoted as day 0. The female rats were maintained on the same experimental diet throughout the pregnancy and one week after that. The day of delivery was

noted down to find out the duration of gestation. Maternal blood was collected at the starting of the experiment, during pregnancy, at the time of delivery and after one month for the measurement of Hemoglobin, hematocrit and estimation of TSH. After delivery the mothers were weighed and the activity of the mothers and the neonates was noted.

B. Diet

The experimental diets used were based on casein (as a source of protein 20%), starch (as a source of carbohydrate 70%) and vegetable oil (as a source of fat 5%). Vitamin mixture (1%) and chemically pure inorganic salt mixture (4%) (Except iron) were added. Iron (crystalline ferrous sulfate, FeSO4.7H20) was finely ground by mortar and pestle and then added to achieve dietary levels of added Fe of 50 (control diet), 30, 15, 7 and 2mg/kg. (National Institute of Nutrition, ICMR, Hyderabad). Non-nutritive cellulose was deleted from diets because of its variable iron contents. Rats were given free access of food and water. (Dietary ingredients were purchased from scientific and general agency, Jaipur) TABLE 1

C. Hematological Measurements

Maternal blood was collected at the starting of the experiment. during pregnancy, at the time of delivery and after one month. Hemoglobin was measured in hemoglobinometer, and hematocrit Estimation was done by centrifugation method. Estimation of TSH hormones were done. The hormone analyses were performed on fully automated Chemiluminescent Immuno Assay based instrument (ADVIA centaur, immunoassay system, USA) The mothers were weighed in the time intervals. After delivery the neonates were weighed.

D. Statistical Analysis

All the values are expressed as means ± SEM. To find out the significance of difference between maternal hemoglobin, hematocrit, TSH hormones, maternal and neonatal body weight. The mean values were calculated and compared with that of controls by the student's t-test with accepted level of significance of 0.001. Table 1.

Table 1. Diet (Composition of Mineral Mixtuire)

Composition of mineral mixture (g/100g of salt mixture)	
Calcium carbonates	38.1400
Cobalt chloride	0.0023
Cupric sulfate	0.0477
Magnesium sulfate	5.7300
Potassium iodide	0.0790
Potassium phosphate monobasic	38.9000
Sodium chloride	13.93
Zinc sulfate	0.0548
Composition of vitamin mixture	
Vitamin A+	2000 IU
Vitamin D+	200 IU
Vitamin E	10 IU
Vitamin K (Menadione)	0.5mg
Thiamine	0.5mg
Riboflavin	0.8mg
Pyridoxin	0.5mg
Calcium pantothenate	4.0mg
Niacin	4.0mg
Inositol	10.0mg
Para aminobenzoic acid	10.0mg
Biotin	40.0 µg
Folic acid	0.2mg
Vitamin B12	3.0µg
Ccholin chloride	200.0mg

All the above ingredients were mixed and sufficient amount of starch was added to make up to one gram.

III. RESULTS

The hemoglobin and hematocrit decrease appreciably (P< zero.05) in all the tiers (before being pregnant, all through being pregnant and after transport) with decrease inside the nutritional iron contents (30, 15, 7 and 2 mg Fe/kg of weight-reduction plan). Decrease inside the hemoglobin of the iron poor organizations (Groups C, D and E) had been observed great (P< zero.05) in all the stages while as compared with the iron sufficient control organization (Group A) and this decline within the hemoglobin and hematocrit turned into again found tremendous inside the businesses D and E on evaluating them with the institution C. During being pregnant the extensive (P< zero.05) decline within the hemoglobin contents within the agencies A, B and

C, and in all of the agencies after delivery, have been determined while had been compared with the before pregnancy degree (Table 2).

Body weight: In the manipulate organization A and institution B, a widespread (P< 0.05) rise in the frame weight grow to be determined during pregnancy and after transport. Whereas maternal body weight end up discovered notably (P< 0.05) decreased after shipping in assessment to before being pregnant diploma, inside the agencies C, D and E.

The decrease inside the maternal frame weight become huge (P< zero.05) inside the iron deficient groups (institution C, D and E) in comparison to group A, within the levels throughout pregnancy and after delivery. The decline in the body weights of neonate of severe anemic moms become discovered great.

(Table 3).

Thyroid stimulating hormone (TSH): TSH modifications Significantly (p<0.05) in all the tiers with the reducing iron contents of the maternal weight loss plan. Before pregnancy and in the course of pregnancy the hormone rises Significantly (p<zero.05) in all of the iron deficient organizations as compared to the control group A and further within the severe iron poor corporations (D and E) the upward thrust turned into determined widespread while compared with the group C. After transport the groups B and C confirmed a rise compared to govern institution A and the severe iron deficient companies D and E confirmed a Significant (p<0.05) decline within the hormone when in comparison with the companies A and C.

The postpartum decline inside the hormone of the excessive iron deficient groups D and E became additionally discovered massive (p<zero.05) compared to pre-pregnancy stagess (Table 3).

Table 2. Effect of different levels of dietary iron contents on the maternal Hemoglobin and Hematocrit values before pregnancy, during pregnancy and after delivery

	HEMOGLOBIN (g%)			HEMATOCRIT (%)		
Groups	Before Pregnancy (bp)	During Pregnancy (dp) (18-20 day of gestation)	After Delivery (ad) (Eight weeks postpartum)	Before Pregnancy (bp)	During Pregnancy (dp) (18-20 day of gestation)	After Delivery (ad) (Eight weeks postpartum
GROUP-A 50mg Fe/kg of diet (Control)	14.165±0.300	$12.22^{\#}$±0.245	11.72* ±0.439	42.05±0.213	$34.36^{\#}$ ±0.131	32.74*±0.084
GROUP-B 30 mg Fe/kg of diet	13.857±0.279	$11.51^{\#}$±0.335	11.39* ±0.420	40.20^{a}±0.145	$32.26^{a\#}$±0.116	32.59*±0.157
GROUP-C 15mg Fe/kg of diet	12.463^{a}±0.229	$10.43^{a\#}$±0.220	9.092^{a}*±1.072	29.95^{a}±0.331	$27.84^{a\#}$±0.106	$26.18^{\mathbf{a}}$*± 0.186
GROUP-D 7mgFe/kg of diet	8.394^{ab}±0.254	7.723^{ab}±0.185	6.110^{ab}*±0.176	27.30^{ab}±0.154	$25.71^{ab\#}$±0.135	$23.41^{\mathbf{ab}}$*±0.120

GROUP-E 2 mg Fe/kg of diet	6.285 [ab]±0.309	5.191[ab]±0.439	3.840[ab]*±0.307	24.03[ab]±0.062	20.10[ab#]±0.060	17.85[ab]*±0.184

Values Mean ± S.E.M. (n=6)

[a]P<0.05 groups B, C, D and E compared with group A

[b]P<0.05 groups D and E compared with group C

***P<0.05 stage after delivery compared with before pregnancy (bp)**

[#]P<0.05 stage during pregnancy compared with before pregnancy

Table 3. Effect of different levels of dietary iron contents on the maternal body weights and the levels of maternal Thyroid Stimulating Hormone (TSH), values before pregnancy, during pregnancy and after delivery

	BODY WEIGHT(g)			TSH (mIU/L)		
Groups	Before Pregnancy (bp)	During Pregnancy (dp) (18-20 day of gestation)	After Delivery (ad) (Eight weeks postpartum)	Before Pregnancy (bp)	During Pregnancy (dp) (18-20 day of gestation)	After Delivery (ad) (Eight weeks postpartum
GROUP-A 50mg Fe/kg of diet (Control)	208.5±4.318	230.26[#]±5.016	226.66*±2.108	1.89±0.208	1.12±0.084	1.88±0.220
GROUP-B 30 mg Fe/kg of diet	204.16±6.379	228.26[#] ±4.23	225 *±1.825	2.418[a] ±0.014	2.452[a]±0.017	2.430[a]±0.143
GROUP-C 15mg Fe/kg of diet	207.5±5.737	212.15 [a]±2.361	167.5[a*] ±2.140	2.461[a]±0.0210	2.462 [a]±0.019	2.313 [a]±0.123
GROUP-D 7mgFe/kg of diet	204.66±4.558	198.42[ab]±5.434	162.5 [a*] ±2.140	3.367 [ab]±0.027	3.362[ab]±0.019	0.180[ab*]±0.061
GROUP-E 2 mg Fe/kg of diet	204.16 ±6.88	196.68[ab]±4.234	148.33[ab]*±2.108	3.440[ab]±0.148	3.333[ab]±0.155	0.125[ab*]±0.042

Values Mean ± S.E.M. (n=6)

[a]P<0.05 groups B, C, D and E compared with group A

[b]P<0.05 groups D and E compared with group C

***P<0.05 stage after delivery compared with before pregnancy (bp)**

[#]P<0.05 stage during pregnancy compared with before pregnancy (bp)

Table 3. Effect of different levels of dietary iron contents on the weights of the neonates.

	NEONATAL BODY WEIGHT (g)
Groups	
GROUP-A 50mg Fe/kg of diet (Control)	5.4±0.0527
GROUP-B 30 mg Fe/kg of diet	5.1±0.0333
GROUP-C 15mg Fe/kg of diet	4.8[a]±0.0111
GROUP-D 7mgFe/kg of diet	3.6[a]±0.0410'
GROUP-E 2 mg Fe/kg of diet	3.3[a]±0.0666

Iron is the most abundant transition metal in the human body because it is essential to the proper structure and function of myoglobin, haemoglobin, cytochromes, hemerythrins, and various enzymes involved in the manufacture of porphyrins, oxygen control, and immunity (thirteen). At least 1.32 billion people worldwide suffer from iron deficiency anaemia, which is the most common kind of nutritional anaemia worldwide, according to the World Health Organisation (WHO)(14). Girls of childbearing age are the maximum prone organizations stricken by iron deficiency anemia. Iron (Fe) deficiency in being pregnant has severe effects for both the mom and her infant. In the immediate postnatal period, those encompass extended chance of low start-weight, elevated morbidity and mortality (15,sixteen,17). In the neonatal period, there may be an increased hazard of impaired motor improvement and coordination. In children, language development and scholastic success may be affected and there are enormous mental and behavioral effects, decreased physical activity (18, 19) and impaired ability for work (20). In the existing take a look at it's been located that nutritional iron deficiency reasons many hematological alterations and behavioral disturbances inside the woman rats at some point of the peripartum period.

The women of low iron companies (15, 7 and a pair of mgFe/kg of eating regimen) confirmed marked reduction in the body weight eight weeks after transport. The degree of iron deficiency produced by our iron-restricted diets became severe enough to impair weight gain and to reduce very last frame weight. Iron deficiency consequences no longer simplest in reduced meals intake but additionally in decreased feed efficiency (21,22,23). The huge decline inside the body weights of neonate of excessive anemic moms turned into discovered. The hemoglobin concentrations alternate because of the adjustments in plasma quantity. The lack of competent extension of plasma amount might lead to a constrained foetal growth. Our results suggest that iron-deficient moms are unable to meet the growing needs of the developing foetus. Being a necessary mineral, non-haem tissue, including skeletal muscle, the heart, and the mind, will become iron deficient when iron delivery is insufficient to fulfil foetal need (24). Reduced levels of dietary iron in the women can increase the risk of preterm delivery in addition to low birth weight. Severe anaemia, particularly in the first trimester, is strongly associated with unfavourable pregnancy outcomes. Preterm delivery and start weight are impacted by

maternal anaemia; nevertheless, among their group, adverse perinatal outcomes are not linked to it (25).Although oxidative load is the main factor, infections and hypoxia brought on by iron deficiency can also play a role in the premature delivery process. The increased metabolism occurring inside the baby during pregnancy results in higher oxygen requirements. Mothers with low iron levels have reduced oxygen delivery to the foetus (26).

IV. CONCLUSION

Based on the current research, it can be said that iron deficiency anaemia (IDA) is harmful to the mother's and her newborns' health. Anaemia and reduced oxygen delivery are two ways that iron deficient anaemia may try to hinder thyroid metabolism (27, 28). This may also govern nuclear T3 binding (30) and thyroid metabolism (29) through crucial apprehensive devices. Thyroid peroxidase (TPO) activity impairment is another possible cause.

TPO is a 103-kDa Fe-based enzyme that is found on the thyrocyte's apical membrane (31). Iodination of thyroglobulin and coupling of the iodotyrosine residues are the initial two stages in the manufacture of thyroid hormones, which are catalysed by TPO. A heme protein linked to ferriprotoporphyrin IX or an intently related porphyrin is required for TPO hobby (32). IDA decreases the activities of other heme-containing enzymes, such as succinate-ubiquinone oxidoreductases, myeloperoxidase, and cytochrome oxidase, all of which are susceptible to depletion during Fe deficiency (33). Similar to this, IDA decreases TPO production, which interferes with the thyroid's ability to metabolise iodine (34) and causes a rise in TSH. Furthermore, pregnancy may significantly affect thyroid homeostasis (35) and make the prognosis of hypothyroidism more difficult.

Iron deficiency affects hormone functioning, metabolic processes, and painting performance overall. Poor iron levels in the mother's diet lead to preterm births and extremely fragile newborns. Extremely low iron in the mother weight-reduction strategy can also result in postpartum pituitary hormone shortages, which can potentially terminate nursing and weaken the newborns of severely anaemic mothers. As a result, by raising the dietary iron contents to a level that appropriately satisfies the needs of both the mother and the foetus, it is possible to improve pregnancy outcomes while simultaneously protecting mothers from the difficult circumstances of endocrine disorders and biological and physiological disturbances following delivery.

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