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STUDY OF ASSOCIATION BETWEEN SERUM FERRITIN LEVELS AT TERM PREGNANCY IN WOMEN WITH IRON DEFICIENCY ANAEMIA (IDA) AND NEW BORN SERUM FERRITIN LEVELS

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ABSTRACT

Background: In order to determine whether there is an association between the two, we compared the haemoglobin and serum ferritin levels of newborns delivered vaginally or by caesarean section to those of non-anaemic mothers and their newborns with iron deficiency anaemia.

Methods: The study involved recruiting 150 full-term mothers who were admitted through the OPD or labour room of Department of Obstetrics and Gynaecology, with age ranging from 18 to 40 years, who were in labour and had full-term new-borns without any prenatal or perinatal complications. The study was conducted at the Department of Obstetrics and Gynaecology, in a Tertiary care hospital of eastern India.

Results: During their pregnancy, 61% of patients did not take IFA (Iron Folic acid), compared to 28% of controls. The results of the analysis and computation of the p-value indicated that the data was statistically significant. The analysis revealed a strong link between the haemoglobin & serum ferritin levels of mothers and newborns. We applied the Spearman-Rho correlation test because the data was not normally distributed, and the results were significant. Because neonates delivered from Iron deficiency anaemia (IDA) women had considerably lower haemoglobin and ferritin concentrations than newborns delivered from non-anaemic (NA) mothers, maternal IDA has an impact on the iron reserve of newborns. To established relationship between the haemoglobin status of mothers and newborns in cases and controls, an independent t-test was used to
analyse the data, and statistical significance was observed.

Conclusion: Maternal IDA may have an impact on newborns' iron reserve. For foetal development to occur in utero and for storage of sufficient iron at birth to support growth in the early stages of infancy, there must be an ideal transfer of iron across the placenta. It appears that foetal iron requirements could be partially satisfied but not completely satisfied if maternal iron resources were exhausted. More research is needed to determine the association of the degree of lower cord serum Ferritin (SF) with the iron status and the developmental outcome of later part of infancy.

Keywords: Serum Ferritin Levels, Pregnancy, IDA, New-Born Serum Ferritin Levels.

INTRODUCTION

Worldwide, nutritional anaemia is a serious public health issue, especially for women of reproductive age in underdeveloped nations. The prevalence of anaemia among women throughout India who are of reproductive age is 57%. Slightly less than two-thirds of women (64%) in Odisha have anaemia, including 29 percent with mild anaemia, 33 percent with moderate anaemia, and 3 percent with severe anaemia. [1]

Anaemia among women has increased by 13 percentage points since NFHS-4."A condition in which the haemoglobin content of blood is lower than normal as a result of deficiency of one or more essential nutrients, regardless of the cause of such deficiency" is the definition of nutritional anaemia given by the WHO (World Health Organisation). WHO has defined anaemia in pregnancy as the haemoglobin (Hb) concentration of less than 11 g/dl.[2] In the newborn, low Hb was defined as cord blood Hb ≤130 g/L. This cutoff is ~2 SD below the mean for term births (153–156 ± 12–13g/L using modern machines). Low iron stores in cord blood was defined as SF<75 μg/L. Cord SF <35 μg/L was defined as severe ID, because this level indicates brain ID. Cord SF >370 μg/L and/or CRP >5 mg/L was considered suggestive of perinatal inflammation or infection. Women between the ages of 15 and 45 who are at high risk, along with young children and those who are pregnant or nursing, are the key target groups. High rates of low-birth-weight newborns, high perinatal death, high maternal mortality, and foetal wasting are all linked to nutritional anaemia. A vital micronutrient, iron is involved in many vital cellular processes in every organ system. As it promotes neuronal metabolism, myelination, and neurotransmitter production, it is essential for early brain development and function. An inability to obtain enough iron during the foetal or postnatal stages can cause long-term cognitive and motor disabilities that cannot be reversed by iron supplementation. It can also change brain shape, neurochemistry, and cognitive functioning. In addition, low iron stores at birth and iron deficiency anaemia during infancy can have negative effects on human cognition, motor, and neurophysiological development, with both immediate and long-term effects that cannot be remedied by iron replacement therapy. When they reach school age, newborns with cord ferritin concentrations in the lowest quartile (<76 μg/l) have compromised mental and psychomotor abilities.[3] Abnormal neurologic reflexes are present in pre-term newborns with low blood ferritin concentrations (<75 μg/l) at 37 weeks post-conception.[4] Normal body iron content in healthy term newborns is 75 mg/kg, with 1.35 mg of iron/kg/day accruing in the third trimester.[5] The most common nutritional deficiency during pregnancy is iron deficiency anaemia, which can affect the morbidity and mortality of both the mother and the foetus.

OBJECTIVES

To find a correlation between the serum ferritin and haemoglobin levels in newborns delivered vaginally or by caesarean section to mothers without iron deficiency anaemia with newborns of mothers with iron deficiency anaemia.

MATERIALS & METHODS

The study involved recruiting 150 full-term mothers who were admitted through the OPD or labour room, with age ranging from 18 to 40 years, who were in labour and newborns with birthweight >=2500grams without any prenatal or perinatal complications. Out of 150 full-term mothers, 75 were

selected as controls (non-anaemic, with Hg >11 gm/dl and serum ferritin >12 µg//L) and 75 as cases with IDA (Hg <11 gm/dl, serum ferritin <12 µg//L).
The umbilical cord clamping was done after one minute of delivery in all included cases.5 ml of maternal blood and 5 ml of cord blood were taken for analysis. Each sample was divided into 2 aliquots: one aliquot of whole blood was sent immediately for measurement of hemoglobin (Hb) to the hematology department, the remainder was left to clot at room temperature. The serum which was found in the 2nd aliquot was sent for study of serum ferritin concentration, Electrochemiluminescence immunoassay (ECLIA) for the in vitro quantitative determination of ferritin in human serum or plasma with testing time 18 min and Sandwich assay principle with 2 point calibration. The development of ECL immunoassays is based on the use of a ruthenium-complex and tripropylamine (TPA)).
This was an observational case control study conducted in the Department of Obstetrics and Gynaecology in a Tertiary care hospital of eastern India. The study was approved by the institutional ethics committee and written informed consent was obtained from participants.

Inclusion Criteria
Primigravida/multigravida, Women who were pregnant at term (>=37 weeks), women who were not anaemic (controls), women who were anaemic (cases), and newborns born to mothers without iron deficiency anaemia and with IDA (by vaginal delivery or caesarean section).

Exclusion Criteria
Preterm deliveries, women with multifetal gestation, eclampsia, antepartum haemorrhage, diabetes mellitus, cardiac, renal, respiratory, and hematologic illnesses were all excluded. Newborns with birth asphyxia or neonatal sepsis or any elevated marker of inflammation like C Reactive protein(>5mg/lit.) were excluded.

Statistical Methods
The SPSS 20 software was used for all of the analyses. A *p* value of < 0.05 was considered significance in tests. We examined the significance using a variety of statistical analysis techniques, including the independent t-test, Mann-Whitney U test, Pearson correlation coefficient test, Spearman rho correlation test, and chi-square test.

RESULTS

SES	**Case**	**Control**	**χ2 Value**	**P-Value**
Low	35	51	9.541	0.008
Middle	35	17		
High	5	7		
Total	75	75		
Socioeconomic Status Distribution				
Iron Intake during Pregnancy	**Cases (%)**	**Control (%)**	**χ2 Value**	**P-Value**
Yes	29 (38.7)	54 (72.0)	16.858	0.00004
No	46 (61.3)	21 (28.0)		
Total	75 (100)	75 (100)		
Distribution of Iron Intake during Pregnancy among Cases and Controls				
Table 1				

The chi-square test yielded a statistically significant p-value of 0.008 when the p-values of the two groups-the cases and the controls-were compared.

Hb Status(gm/dl)	**Mean**	**SD**	**Correlation Co-Efficient (r)**	**P-Value**
Maternal HB	10.629	2.0016	0.678	0.00001
Newborn HB	13.382	2.2406		

Correlation of Maternal and Newborn Haemoglobin				
Ferritin Levels(µg//L).	**MEAN**	**SD**	**Correlation Co-Efficient (r)**	**P-Value**
Maternal S. Ferritin	20.4982	14.1248	0.731	0.0001
Newborn S. Ferritin	104.9824	80.2754		
Correlation between Maternal and Newborn Serum Ferritin Levels				
Table 2				

Using Pearson's correlation test, the p-value of the aforementioned parameters was determined to be 0.00001, indicating a very significant statistical result.

Hb Status of Pregnant Women (gm/dl)	**Newborn Hb**		**P-Value**
	Mean	**SD**	
Cases (Hb <11)	11.656	0.813	0.0001
Controls (Hb >11)	15.1099	1.844	
Table 3: Association between Maternal and Newborn Haemoglobin Status in Cases and Controls			

The p-value was determined using the information in the above table, and the result was 0.0001, which indicates statistical significance.

Ferritin Status (µg//L) of Pregnant Women	**Newborn Ferritin**		**P-Value**
	Mean	**SD**	
Cases (S.Ferritin<12)	57.818	14.955	0.0001
Control (S.Ferritin>12)	152.146	90.789	
Table 4: Association between Maternal and Newborn Serum Ferritin Status in Cases and Controls			

We performed the Mann-Whitney U-Test to determine a correlation between them because of non parametric distributions of datas. Using the aforementioned information and parameters, the p-value was determined to be 0.0001, indicating a statistically significant link between the blood ferritin levels of mothers and newborns.

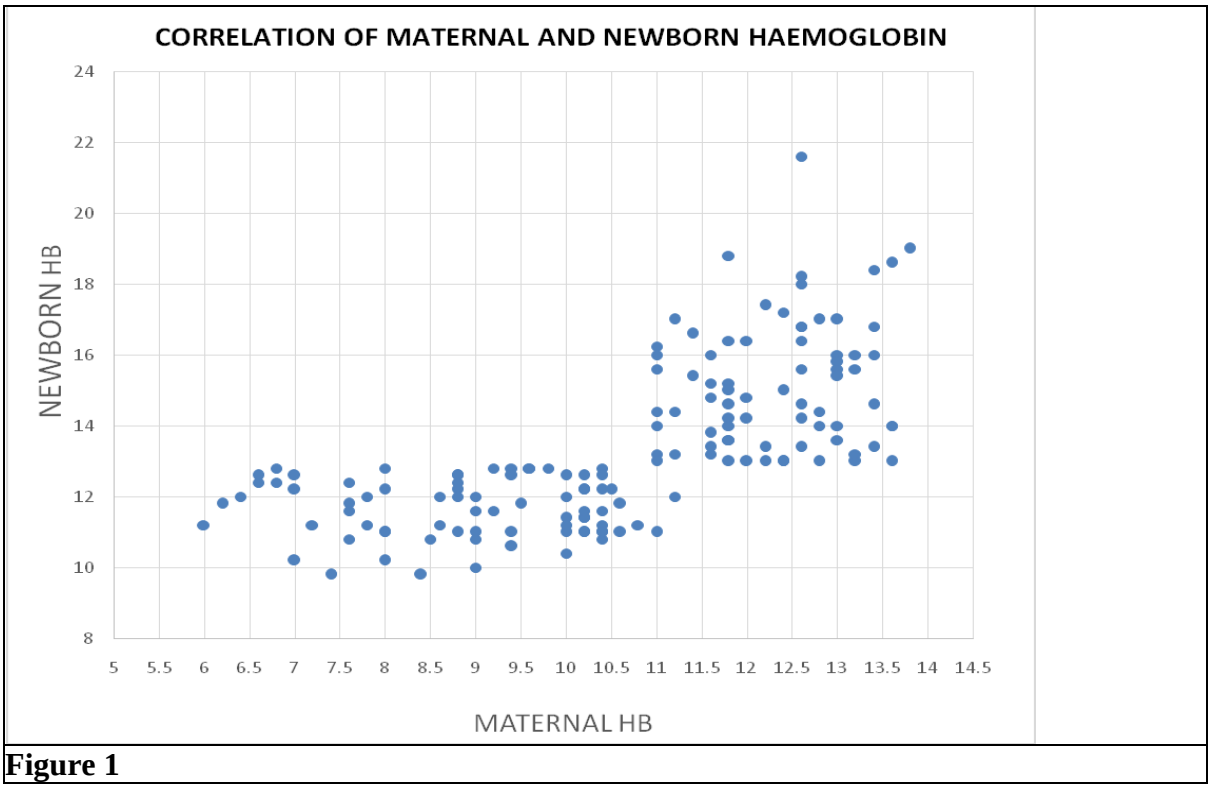

Figure 1

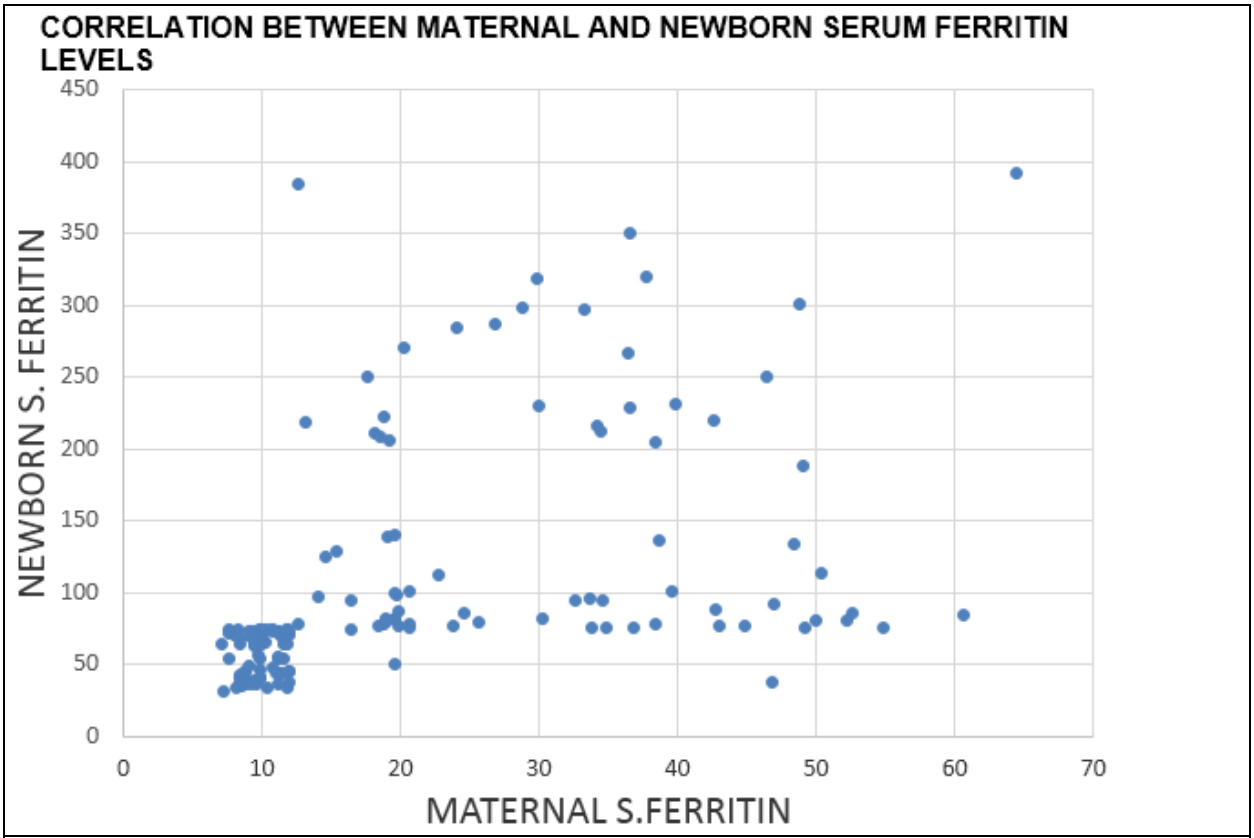

Figure 2

DISCUSSION

Out of the 150 participants, 75 were selected as controls (non-anaemic, with Hg >11 gm/dl and serum ferritin >12 µg//L) and 75 as cases with IDA (Hg <11 gm/dl, serum ferritin <12 µg//ml).

The age range of 23 to 32 years old accounts for the majority of cases (61.3%) and controls (73.3%), respectively. More than 60% of the women in the case and control groups are primigravidae. The majority of the women in both the case and control groups were found to be from low socioeconomic backgrounds.

During their pregnancy, 61% of patients did not take IFA, compared to 28% of controls. The data was found to be statistically significant.

Both the cases and the controls had different delivery modes, and it was found that the majority had been delivered vaginally. This result, however, does not significantly relate to our research.

The relationship between the haemoglobin of mothers and newborns was significantly (p-value 0.00001) correlated to one another. There was a correlation between a pregnant mother's and her newborn baby serum ferritin levels. We used the Spearman-Rho correlation test because the data is not normally distributed, and the results showed a strong positive correlation between the two research groups.

Haemoglobin ($p = 0.00001$) and serum ferritin levels ($p = 0.0001$) were significantly lower in newborns of IDA mothers than of non-anaemic mothers, suggesting that maternal IDA has an impact on the iron stores of neonates. These results were consistent with earlier studies from other sources. [6,7,8,9]

Table 2 shows relationship between the haemoglobin status of mothers and newborns in cases and controls. The results of the cord blood study showed that the likelihood of a newborn becoming anaemic is highest if the pregnant mother had low haemoglobin levels before delivery ($p = 0.0001$). The data was evaluated using an independent t-test.

Cord-blood SF was lower in infants of iron-depleted mothers than in the other group, as demonstrated by maternal SF below an empirically derived threshold. However, our results were in line with a

number of earlier investigations. [10,11] and lend credence to the idea that there was only a relationship between the iron status of the mother and the newborn if the mother's iron status was low.

The current study's findings, however, also demonstrated that the foetus's iron accretion was unaffected by the iron status of the mother.[12-14]

The disagreements may stem from variations in the low sensitivity cut-off value for serum ferritin (<12 μg//L); the omission of tests to exclude infection, which could conceal the true serum ferritin level; and variations in the study group's conditions, such as mothers receiving iron supplementation during pregnancy, which could have obscured the relationship between the iron status of the mother and the newborn.

Serum ferritin has been shown to be a reliable measure of the severity of iron reserve in the body.[15] Therefore, it is possible that the neonates of IDA women had fewer iron stores because of the noticeably lower ferritin levels in these babies as compared to those of NA mothers. Furthermore, the concentration of haemoglobin in the babies delivered by IDA mothers was significantly lower than that of the newborns delivered by NA mothers.

The lack of a statistically significant difference in the prevalence of anaemia among the babies of the two groups of mothers in this case is not surprising. This is due to the fact that noticeable differences, such as anaemia, are not anticipated at such a young age.

According to Hay et al.[16] the cord SF level is a good indicator of iron status in the first two years of life. Other research indicates that the effects of a mother's iron status on her infant's iron status become more noticeable later in infancy than during the newborn stage.[17-19]

Therefore, newborns of IDA women may be more susceptible to iron deficiency anaemia in their early years due to the significantly lower ferritin level and haemoglobin concentration in these babies as compared to newborns born to NA mothers. Cellular immunity and cognitive development may suffer significantly as a result.

The data from this study also shows that babies' ferritin and haematological markers were significantly greater than those of their mothers. Previous investigations also reported similar findings.[20-21] The fact that iron is actively transferred from the mother to the foetus through the placenta accounts for the higher ferritin levels seen in neonates.[22] Additionally, in cases of iron insufficiency, the placenta is able to more successfully compete with the erythroid marrow of pregnant mothers for circulating transferrin iron, thereby ensuring an adequate supply of iron for the developing foetus. This could be the result of an increase in transferrin receptor synthesis.[23] The relationship between the maternal and fetal iron status alters as ID gets more pronounced, which is explained by the present understanding of placental iron transport processes. Foetal requirement, which is primarily responsible for placental iron transport, is sent to the placenta through foetal transferrin binding and transferrin receptor saturation on the fetal-facing (basal) layer of the syncytiotrophoblast.[24-26] TfR mRNA concentrations and placental TfR expression are positively correlated with greater foetal iron demand or maternal iron deficiency. The latter facilitates increased placental iron uptake by delivering more iron to the apical (maternal-facing) surface.[27] The placenta responds to foetal cues by increasing the transfer of maternal iron when the mother's iron reserves are low, gradually depleting the mother of iron.[28] In the end, though, overexpression of placental TfR cannot produce sufficient iron transfer to return foetal iron pools to normal levels, and the mother as a whole develops iron deficiency. After that, the foetus will begin to have diminished SF and, eventually, decreased Hb or birth defects.

Given the prevalence of maternal ID throughout pregnancy, the specifics of iron absorption during pregnancy might also help to explain why a greater number of babies do not arrive noticeably anaemic or with ID. According to certain studies, iron is carried via the placenta regardless of the concentration gradient, and the placenta and foetus may have a particular affinity for iron in the mother's circulation.[29] Iron absorbed by the mother's gut appears to contribute proportionately more to the foetal iron than does iron stored in the mother.[30] After 30 weeks of gestation, when the mother's iron absorption efficiency peaks, the majority of the iron is transferred to the foetus.[31] Neonates born to mothers with low iron stores exhibited a considerably higher level of iron tracer from maternal oral

dosage compared to mother with sufficient stores, according to research by O'Brien et al.[28] When it comes to iron absorbed from the gut, the fetal needs appear to outweigh those of the mother.

According to this study, there was a noteworthy association between maternal and neonatal haemoglobin levels(r= +0.678).Also there is a positive correlation between maternal and neonatal ferritin levels(r= +0.731). Numerous researchers have established a relationship between the haemoglobin and ferritin levels of neonates and their mothers, yet the findings differ between these investigations. For instance, research by Kumar et al.[6] demonstrated a substantial link between maternal ferritin levels and cord blood ferritin ($r = +0.440$; $p < 0.001$) and Hgb levels ($r = +0.488$; $p < 0.001$). Additionally, Singla et al[8]. discovered a substantial correlation between cord blood Hgb ($rs = +0.390$, $p < 0.01$), cord serum ferritin ($rs = +0.523$, $p < 0.001$) and maternal serum ferritin.

We found that maternal IDA may have harmful effects even after pregnancy. This shows that a more robust approach is required to raise the iron status of mothers. Enhancing the nutritional condition of expectant mothers may benefit the maternal and neonatal iron levels as well. Delaying the cutting of the umbilical cord after delivery could be an alternative strategy to help improve the iron status of premature infants

Nevertheless, there is evidence in both humans and nonhuman primates that the iron status of the mother earlier in pregnancy or before conception has a greater influence on the iron status of the unborn child than it does at or near term.[32]

CONCLUSION

These results lead us to the conclusion that maternal IDA may have an impact on babies' iron reserves. A healthy placenta is necessary for foetal development in utero and for the creation of sufficient birth iron reserves to support growth during the early stages of infancy. It appears that foetal iron requirements could be partially satisfied but not entirely satisfied if maternal iron resources were exhausted. More research is needed to determine how the degree of lower cord SF detected affects iron status and the developmental outcome of later infancy.

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