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To study the correlation between maternal serum iron and ferritin levels with cord blood iron and ferritin levels

Bussa Sandeep[1], Gandhari Srinivas[2], Sandhya Jalagam[3], Farah Naaz[4]
[1]*Assistant Professor, Department of Pediatrics, Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar, Telangana, India.*
[2]*Assistant Professor, Department of Pediatrics, Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar, Telangana, India.*
[3]*Assistant Professor, Department of Pediatrics, Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar, Telangana, India.*
[4]*2nd Year Postgraduate, Department of Pediatrics, Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar, Telangana, India.*
CORRESPONDING AUTHOR: Dr. Bussa Sandeep MBBS, DNB Pediatrics, Assistant Professor, Department of Pediatrics, Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar, Telangana, India.

Abstract
Introduction: *Iron deficiency anaemia is one of the most important causes of nutritional anaemia and is the most common micronutrient deficiency worldwide especially in developing countries. Anaemia affects nearly half of all pregnant women in the world 52% in developing countries compared with 23% in developed countries. Pregnant women are vulnerable to iron deficiency because of the increased metabolic demands imposed by pregnancy involving a growing placenta, fetus, and maternal issues, coupled with dietary risks.*
Aims and Objectives: *To study the correlation between maternal serum iron and ferritin levels with cord blood iron and ferritin levels.*
Materials and Methods: *This was a Prospective observational study conducted at Janardani hospital, a tertiary care centre in Guntur. The study was approved by the institute ethical committee. A detailed informed and written consent from the parents was taken prior to the study. All pregnant women admitted for delivery in Janardani Hospital were included. Informed consent was taken prior to the study. After a detail medical history and thorough physical examination of newborn, laboratory tests were done in a step wise manner.*
Results: *Mean age of mothers in this study was 25.44 ± 3.72 years. Majority (51.00%) of the mothers belonged to age group >25 years followed by 42.00% of age group 21-25 years. Mean gestational age was 38.08 ± 1.66 weeks. Mean Maternal PCV (%) was 33.54 ± 4.65. Mean maternal platelets was 186960/cumm. Mean Maternal TLC was 11290. Number of term babies were 95% and preterm were 5%. Mean Maternal iron was 79.97 µg/dL; Mean Maternal ferritin was 44.74 µg/L; Mean Maternal haemoglobin was 11.18 gm%. Mode of delivery in most of the women (84.00%) was LSCS; followed by NVD in 16.00%. 50% of women were multipara and 50% primipara. All the pregnancies in the study were singleton. Gestational diabetes was present in 2% women. In 98% women, cephalic presentation was present.*
Conclusion: *We found a statistically significant negative correlation of baby iron with maternal ferritin. The median maternal ferritin levels were significantly higher for the new-borns who required oxygen, or had NICU admission or any respiratory problems as compared to the new-borns who did not have them.*

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I. Introduction

Iron deficiency anaemia is one of the most important cause of nutritional anaemia and is the most common micronutrient deficiency worldwide especially in developing countries.(1) Anaemia affects nearly half of all pregnant women in the world.52% in developing countries compared with 23% in developed countries.(2) Pregnant women are vulnerable to iron deficiency because of the increased metabolic demands imposed by pregnancy involving a growing placenta, fetus, and maternal issues, coupled with dietary risks.

Causes of anaemia during pregnancy in developing countries are multi-factorial. This include nutritional deficiencies (iron, folate and vitamin B12), and parasitic diseases such as malaria and hookworm infestation.(3) However, micronutrient deficiency, especially iron deficiency is believed to be the main underlying cause for anaemia in pregnancy.(4)

The outcome of severe anaemia in pregnancy has been associated with increased incidence of premature births , fetal distress, increased perinatal mortality and higher frequency of maternal deaths.[5]

WHO has accepted up to 11 gm percent as the normal hemoglobin level. Below 11gm percent in pregnancy should be considered as anaemia. As iron is depleted, changes are seen first in ferritin levels and bone marrow iron, which reflect storage iron available for mean corpuscular volume.

Understanding relationships between maternal and neonatal iron indices help in formulating the protocols to improve the maternal and neonatal outcome. Therefore, this study was planned to evaluate the relationship between maternal and neonatal iron stores at birth .

The transfer of iron from the mother to the fetus is regulated by the placenta. The placental iron transfer system involves placental structure, iron transporters [e.g., transferrin receptor (TfR)-1,[6,7] divalent metal transporter-1 (DMT-1), ferroportin], and regulation of placental expression of these proteins.[8] The regulatory system is intact beginning at ∼24 wk of gestation.[9] Iron transfer from mother to foetus occurs against the concentration gradient.

The placental transfer of iron from maternal plasma to the foetal circulation during pregnancy is controlled by hepcidin. When hepcidin concentrations are low, iron enters blood plasma at a high rate; when hepcidin concentrations are high, ferroportin is internalised, and iron is trapped in enterocytes, macrophages and hepatocytes.[10] Though falsely high values may be found in acute and chronic inflammatory conditions, measurement of serum ferritin concentrations has been shown to be a good index of iron store.[11] This is preferred to examination of bone marrow aspirates for hemosiderin, which is a gold standard for iron store.[12]

AIMS AND OBJECTIVES:

1. To study the correlation between maternal serum iron levels with cord blood iron and ferritin levels.
2. To study the correlation between maternal serum ferritin levels with cord blood iron and ferritin levels.

II. Materials And Methods

Study design: Prospective Observational study
Study place: Janardani Hospital, Guntur
Study period: 1st November 2017 - 31st October 2019
Study sampling: Systematic sampling was done where every 3rd delivery at the hospital fulfilling the inclusion and the exclusion criteria was included in the study.

Inclusion Criteria:

1. All pregnant women and their babies delivered in Janardani Hospital, Guntur, Andhra Pradesh.
2. Pregnant women who gave consent for the study.

Exclusion Criteria:

1. Pregnant women who had any chronic medical conditions like liver disease, renal failure and malignancy or
2. Pregnant women who had features of sepsis or infection which could alter ferritin levels.

Sample Size: The minimum required sample size with 95% power of study and 5% level of significance is 66 patients. To reduce margin of error, total sample size taken is 100.

Study Method

This was a Prospective observational study conducted at Janardani hospital, a tertiary care centre in Guntur. The study was approved by the institute ethical committee. A detailed informed and written consent from the parents was taken prior to the study. All pregnant women admitted for delivery in Janardani Hospital were included.

Informed consent was taken prior to the study. After a detail medical history and thorough physical examination of new born , laboratory tests were done in a step wise manner.

Procedure, Timing, collection, Transport and Analysis of sample.

Mothers blood(3ml) was collected between six hours prior to delivery and time of birth and cord blood(3ml) from the newborns after delivery. The pediatrician who attended the delivery collected the sample from mother and baby and 3ml was collected in plain tubes for estimation of serum iron and ferritin levels . The collected samples was sent to Thyrocare service centre, Guntur from which the sample was sent for processing at Thyrocare Technnologies limited, Mumbai. Iron levels were estimated by Ferrozine without deproteinization

technology,Olympus machine and photometry method. Ferritin levels were estimated by fully automated bidirectionally interphased chemiluminiscent immunoassay technology, Centaur machine and CLIA method. In all cases, relevant information was collected in a predesigned proforma including antenatal history, birth history, feeding details,NICU admission etc.

ETHICAL APPROVAL: Approved by institute approval committee.

STATISTICAL ANALYSIS

Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean ± SD and median. Normality of data was tested by Kolmogorov-Smirnov test. If the normality was rejected then non parametric test was used.

Statistical tests were applied as follows-

1. Quantitative variables were compared using Independent t test/Mann-Whitney Test (when the data sets were not normally distributed) between the two groups and Kruskal Wallis test was used for comparison between three groups.
2. Qualitative variables were correlated using Chi-Square test/Fisher's Exact test.
3. Spearman rank correlation coefficient was used to assess the correlation of baby ferritin, haemoglobin, iron with maternal baby ferritin, haemoglobin and iron.

A p value of <0.05 was considered statistically significant.

The data was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0.

III. Results And Observation

This was a Prospective Observational study conducted at Janardani Hospital, Guntur, Andhra Pradesh from 1st November 2017 to 31st October 2019. After taking informed consent, 100 pregnant women and their babies delivered in hospital were included in the study by systematic sampling as described in the methodology. Detail medical history and thorough physical examination of newborn was done, and laboratory tests were also done. Following were the results pertaining to the study.

Table 1:-Distribution of maternal parameters of study subjects.

Maternal parameters	Frequency	Percentage
Age distribution in years		
18-20	7	7.00%
21-25	42	42.00%
>25	51	51.00%
Mean ± SD	25.44 ± 3.72	
Median(IQR)	26(22 - 28)	
Gestational age (weeks)		
Mean ± SD	38.08 ± 1.66	
Median(IQR)	38(38 - 39)	
Maternal PCV (%)		
Mean ± SD	33.54 ± 4.65	
Median(IQR)	34.8(31.050 - 36.400)	
Maternal platelets(/cumm)		
Mean ± SD	186960 ± 55382.22	
Median(IQR)	179000(141000 - 226500)	
Maternal TLC		
Mean ± SD	11290 ± 2880.08	
Median(IQR)	11050(9000 - 13350)	

Term/Preterm		
Preterm	5	5.00%
Term	95	95.00%
Maternal iron(µg/dL)		
Mean ± SD	79.97 ± 45.03	
Median(IQR)	75.5(55 - 96.500)	
Maternal ferritin(µg/L)		
Mean ± SD	44.74 ± 40.77	
Median(IQR)	31.8(18.600 - 53.750)	
Maternal haemoglobin (gm %)		
Mean ± SD	11.18 ± 1.55	
Median(IQR)	11.6(10.350 - 12.150)	
Mode of delivery		
LSCS	84	84.00%
NVD	16	16.00%
Gravida parity		
Multi	50	50.00%
Primi	50	50.00%
Single ton/multiple		
Single ton	100	100.00%
APH	0	0.00%
PROM	0	0.00%
Infection	0	0.00%
Gestational diabetes	2	2.00%
Antenatal cortico steroid given	1	1.00%
Presentation		
Breech	1	1.00%
Cephalic	98	98.00%
Transverse	1	1.00%

TABLE:2 CORRELATION OF MATERNAL PARAMETERS WITH MATERNAL FERRITIN

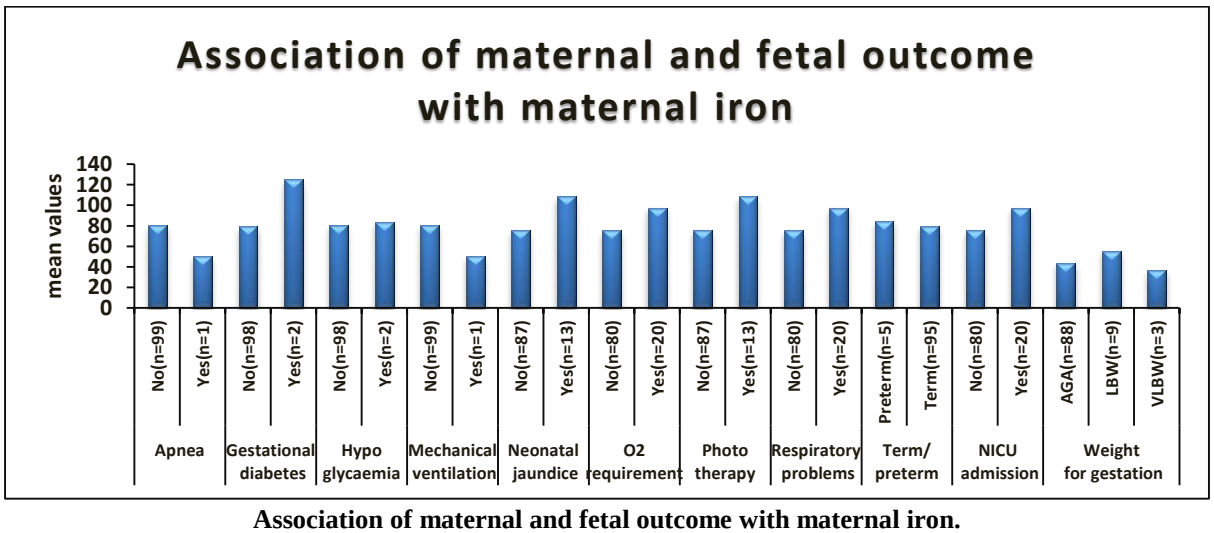
Group Statistics						
	MATERNAL FERRITIN(ngs/ml)	N	Mean	Std. Deviation	Std. Error Mean	P-VALUE
HB	1 (<20)*	29	10.262	1.4644	.2719	0.01
	2 (>20)*	71	11.559	1.4315	.1699	
PCV	1	29	30.786	4.3933	.8158	0.01
	2	71	34.672	4.2919	.5094	
IRON	1	29	60.76	28.756	5.340	0.006
	2	71	87.82	48.179	5.718	
FERRITIN	1	29	13.752	4.1327	.7674	0.01
	2	71	57.390	42.2310	5.0119	

*1=maternal ferritin <20 ng/ml; 2= maternal ferritin >20 ng/ml

Table 3:-Association of maternal and fetal outcome with maternal iron.

Maternal iron(µg/dL)		Mean ± Stdev	Median(IQR)	P value
Apnea	No(n=99)	80.27 ± 45.15	76(56 - 96.750)	0.299*
	Yes(n=1)	50 ± 0	50(50 - 50)	
Gestational diabetes	No(n=98)	79.05 ± 44.19	75.5(54 - 96)	0.375*
	Yes(n=2)	125 ± 84.85	125(65 - 185)	
Hypoglycaemia	No(n=98)	79.9 ± 45.41	75.5(54 - 96)	0.631*
	Yes(n=2)	83.5 ± 26.16	83.5(65 - 102)	
Mechanical ventilation	No(n=99)	80.27 ± 45.15	76(56 - 96.750)	0.299*
	Yes(n=1)	50 ± 0	50(50 - 50)	
Neonatal jaundice	No(n=87)	75.7 ± 30.92	75(54.500 - 95)	0.354*
	Yes(n=13)	108.54 ± 94.13	84(56 - 113)	
O_2 requirement	No(n=80)	75.62 ± 31.2	74.5(55 - 94)	0.348*
	Yes(n=20)	97.35 ± 78.23	85.5(54 - 101.500)	
Phototherapy	No(n=87)	75.7 ± 30.92	75(54.500 - 95)	0.354*
	Yes(n=13)	108.54 ± 94.13	84(56 - 113)	
Respiratory problems	No(n=80)	75.62 ± 31.2	74.5(55 - 94)	0.348*
	Yes(n=20)	97.35 ± 78.23	85.5(54 - 101.500)	
Term/preterm	Preterm(n=5)	84.4 ± 48.71	65(48.500 - 116.250)	0.994*
	Term(n=95)	79.74 ± 45.09	76(56 - 95.750)	
NICU admission	No(n=80)	75.62 ± 31.2	74.5(55 - 94)	0.348*
	Yes(n=20)	97.35 ± 78.23	85.5(54 - 101.500)	
Weight for gestation	AGA(n=88)	43.91 ± 42.6	28.15(17.350 - 51.950)	0.776#
	LBW(n=9)	55.4 ± 25.78	49.3(38.900 - 78.175)	
	VLBW(n=3)	36.93 ± 6.87	33.9(32.550 - 42.075)	

*-Mann Whitney test #-Kruskal Wallis test

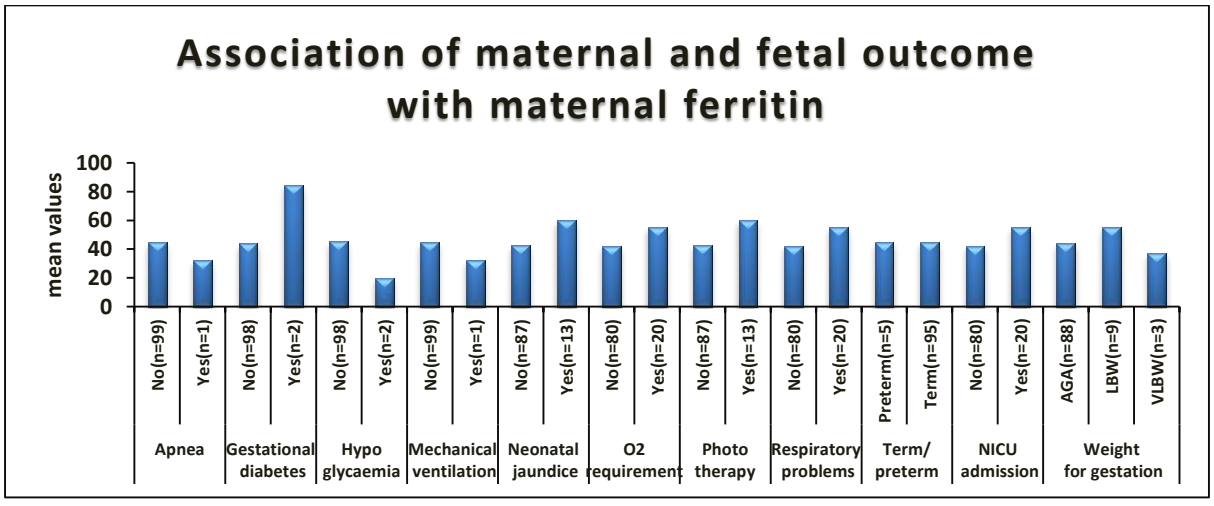


Association of maternal and fetal outcome with maternal iron.

Table 4:-Association of maternal and fetal outcome with maternal ferritin.

Maternal ferritin(µg/L)		Mean ± Stdev	Median(IQR)	P value
Apnea	No(n=99)	44.86 ± 40.95	31.8(18.250 - 54.175)	0.959*
	Yes(n=1)	32.1 ± 0	32.1(32.100 - 32.100)	
Gestational diabetes	No(n=98)	43.92 ± 39.35	31.8(19.300 - 52.900)	0.922*
	Yes(n=2)	84.85 ± 105.29	84.85(10.400 - 159.300)	
Hypoglycaemia	No(n=98)	45.24 ± 41	31.95(19.300 - 54.600)	0.268*
	Yes(n=2)	19.8 ± 13.29	19.8(10.400 - 29.200)	
Mechanical ventilation	No(n=99)	44.86 ± 40.95	31.8(18.250 - 54.175)	0.959*
	Yes(n=1)	32.1 ± 0	32.1(32.100 - 32.100)	
Neonatal jaundice	No(n=87)	42.44 ± 39.96	27.4(17.675 - 50.575)	0.068*
	Yes(n=13)	60.08 ± 44.41	44.8(31.300 - 88)	
O_2 requirement	No(n=80)	42.18 ± 40.65	27.3(17.500 - 48.300)	**0.09***
	Yes(n=20)	54.94 ± 40.63	44.1(25.300 - 79.150)	
Phototherapy	No(n=87)	42.44 ± 39.96	27.4(17.675 - 50.575)	0.068*
	Yes(n=13)	60.08 ± 44.41	44.8(31.300 - 88)	
Respiratory problems	No(n=80)	42.18 ± 40.65	27.3(17.500 - 48.300)	**0.09***
	Yes(n=20)	54.94 ± 40.63	44.1(25.300 - 79.150)	
Term/preterm	Preterm(n=5)	44.38 ± 23.97	33.9(29.125 - 61.225)	0.452*
	Term(n=95)	44.75 ± 41.54	30.4(17.675 - 52.425)	
NICU admission	No(n=80)	42.18 ± 40.65	27.3(17.500 - 48.300)	**0.09***
	Yes(n=20)	54.94 ± 40.63	44.1(25.300 - 79.150)	
Weight for gestation	AGA(n=88)	43.91 ± 42.6	28.15(17.350 - 51.950)	0.111#
	LBW(n=9)	55.4 ± 25.78	49.3(38.900 - 78.175)	
	VLBW(n=3)	36.93 ± 6.87	33.9(32.550 - 42.075)	

*-Mann Whitney test
#-Kruskal Wallis test



Association of maternal and fetal outcome with maternal ferritin.

We found that the median maternal ferritin levels were higher for the newborns who required oxygen, or had NICU admission or any respiratory problems as compared to the newborns who did not have them. ($P<0.05$)

IV. Discussion

It is not certain whether the amount of iron transferred across the placenta is proportional to iron available in the mother or the whether the fetus receives the iron preferentially as per its requirements. Whether a maternal dietary iron transfer to the fetus is related to maternal iron status is still debated. Previous studies on the relationship between maternal and neonatal iron status using multiple parameters showed contrasting results.[(12)]

Thus, we did this prospective observational study at Janardani Hospital, Guntur, Andhra Pradesh from 1st November 2017 to 31st October 2019. We aimed to study the correlation between maternal serum iron and ferritin levels and cord blood iron and ferritin levels. We also assessed the correlation between iron and ferritin levels in mother with Newborn outcomes like premature births, birth weight, Apgar score, respiratory distress.

We found that there was no significant correlation of baby ferritin, baby haemoglobin and baby iron with maternal iron. We observed that there was no significant correlation of baby ferritin, or baby haemoglobin with maternal ferritin but a significant negative correlation of baby iron with maternal ferritin. Among the feto-maternal outcomes, we found that the median maternal ferritin levels were higher for the new-borns who required oxygen, or had NICU admission or any respiratory problems as compared to the newborns who did not have them. ($P<0.05$). Otherwise, there was no significant association of the fetomaternal outcomes with maternal iron and maternal ferritin.

V. Conclusion

We found a statistically significant negative correlation of baby iron with maternal ferritin. The median maternal ferritin levels were significantly higher for the new-borns who required oxygen, or had NICU admission or any respiratory problems as compared to the new-borns who did not have them. Such association portray the intricate mechanism linked between the fetal iron demand and the maternal iron absorption and increase in the subsequent iron stores.

It can be concluded that the improvement in the nutritional status and iron status of pregnant women and new born will stabilise the demand and supply balance. As the deleterious effects of maternal anemia extend far beyond pregnancy as well as early infancy, in the developing world, it is recommended to adopt effective strategies for controlling maternal anemia.

We also recommend to conduct more studies on chronic anemia mothers to know its impact on newborn parameters. Future long-term studies are recommended so that it gives an idea about iron supplementation in infancy also.

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