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Iron Status of Paired Mother and Term Newborns in an Urban City in Nigeria

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Abstract

Objective This study aim at assessing the serum iron, ferritin, transferrin, transferrin receptor and Total Iron Binding Capacity (TIBC) in paired mother and newborns in the immediate neonatal period to establish the relationship between the pair, and the role of maternal iron status on that of the newborn.

Methods: The socio-demographic characteristics of the mothers were obtained using a structured questioner after informed consent was obtained from the parents of the baby. At delivery, paired mother and newborns had their serum iron, ferritin, transferrin, transferrin receptor and TIBC assayed, using cord blood in the newborn.

Result: One hundred and thirty-five mothers and their paired term newborns had their iron indices studied. The mean gestational age of the newborns was 39.0 ± 2.0 weeks whilst the mean age of the mothers was 29.2 ± 4.6 years, with 67% within the age bracket 21 to 30years.

The mean serum iron was significantly lower in the newborn (3.24 ± 1.77 µmol/L) than in the mothers (4.32 ± 1.39 µmol/L), p=0.001, with a feto-maternal ratio of 1 to 1.3. Ferritin was significantly higher in the newborns (217.19 ± 16.20ng/ml), than in the mothers (98.40 ± 10.83ng/ml) (p= 0.0011), with a maternal-fetal ratio of 2.2 to 1. Mean Transferrin Receptor levels were comparable in both groups p= 0.115.

Transferrin and TIBC levels were significantly higher in the mothers than their paired newborns, p= 0.001, with a maternal / newborn ratio of 1.3 to 1.

Conclusion: It is concluded that term newborns have higher serum ferritin and a lower serum iron, transferrin and TIBC levels than their maternal levels. Iron is distributed in favor of the newborn even in the face of iron deficiency in the mothers. Improving the iron intake of the mother through supplementation during pregnancy will benefit the newborn.

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Introduction

Pregnancy is associated with increased nutritional needs due to the physiologic changes of the woman and the metabolic demands of the embryo/fetus. Proper maternal nutrition during pregnancy is thus imperative for the health of both the woman and the offspring [1]. The nutritional requirements in pregnancy include calories, protein, lipids and micronutrients. Micronutrients are elements and vitamins required in trace amounts for normal growth and development, which influence the health of both the mother and foetus [2-4], of which iron is one. Multiple micronutrient deficiencies can result from poor quality diet, inadequate animal protein intake especially in developing countries [4].

Several factors contribute to iron deficiency such as insufficient dietary intake, malabsorption and infections [3]. Iron stores at birth were reduced when maternal stores were deficient, reflecting a limited fetal iron acquisition capacity [4]. Iron is required for the expansion of maternal red cell mass, placental and fetal growth in pregnancy. The requirement in pregnancy is increased to about 6-12 mg/ day to meet this need especially in the second half of pregnancy [5-7]. Because of the increased iron requirements during pregnancy, iron deficiency can lead to maternal anaemia and reduced newborn iron stores [2].

Coupled with the physiologic haemodilution in pregnancy, most women tend to become anaemic in pregnancy, especially in developing countries. With a normal average diet, the absorption of non-haem iron needs to increase to 50% in order to cover the increased needs. Absorption efficiency seems to increase during pregnancy but the studies vary considerably in estimates from 14.3% to 66% at 33 weeks' gestation [8].

Fetal requirement are however always met irrespective of the maternal iron status [9,10]. Despite the fact that fetal requirements are met even in a deficient stage of mothers, the fetus would still be faced with some consequences such low birth weight and prematurity among others [1,6]. Although foetal iron requirements are always met irrespective of maternal iron status, it is documented that neonatal iron stores can be compromised when the mother is iron deficient or anaemic [10,11]. Despite this fact, maternal iron deficiency has a number of adverse consequences on the fetus such as, preterm delivery and low-birth-weight [1,2,11]. There is however no correlation between the haematocrit of the fetus and that of the mother [10], as such there is no correlation between specific micronutrient support for haemoglobin formation such as iron in the mother and the fetus [9,12].

In Iron Deficiency Anaemia (IDA) in the first two trimesters of pregnancy is associated with a two-fold increased risk for preterm delivery and a three-fold increased risk for a low-birth-weight infant delivery [1,2,8,11,13]. Maternal morbidity, low birth weight and preterm labour are associated with Iron deficiency anaemia in pregnancy, yet little is known about the benefits of supplemental iron for the mother or her offspring during foetal and postnatal life [9,14]. The effects of a supplement are probably higher when the supplement is given in the first half or in early pregnancy [15]. Iron-deficiency present in pregnant anaemia can be diagnosed using soluble serum ferritin, serum iron as well as serum transferrin receptor assay [13].

Maternal iron status has not been correlated with that of the foetus which should form path of the basis for the present supplementation practiced in most part of the world. The provision of iron supplements during the prenatal period is a widely practiced preventive measure for anaemia in pregnancy. The pattern of iron status in the mother at the time of delivery as well as the immediate stores in the newborn will give a clear picture of what is expected at part for both mother and the child and further strengthen for the need or not for supplementation for both mother and the newborn knowing fully well the role of iron in cognitive development of the newborn and in prevention of anaemia and its consequences in the mother too.

Therefore, iron status of the mother and foetus/newborn has to be determined and correlated to prove or disapprove facts known before now. This would aid in decision making for the need for supplement not just for the mother and probably for the new born and would further enhance the prevention of iron deficiency anaemia and its attendant effects.

Methods

This is a prospective cross sectional study carried out over a one-year period (July 2015 to June 2016) where mothers with term pregnancy at the onset of labor and their respective newborn babies that were delivered in the labour room of the University of Ilorin Teaching Hospital (UITH) were studied. Ethical approval for this study was obtained from University of Ilorin Teaching Hospital Ethical Research Committee (registered with National Health Research Ethics: NHREC/02/05/2010). Informed consent was obtained from both the father and the mother of the newborns during the antenatal period/before delivery. The subjects were consecutive women presenting in labor and had completed labor at participation, at the labor ward of the hospital as well as their newborns when successfully delivered.

All consecutive admissions into the labor ward that fulfilled the inclusion criteria were enrolled into the study until the calculated minimum sample size of 120 mother and newborn pair is achieved. All the women recruited were assessed to be in good health and had experienced no medical complications during pregnancy. Mothers who received steroids (known to influence the level of many nutrients), micronutrient supplementation (except routine drugs), chronic diseases, and babies born with major congenital abnormalities were excluded from the study.

Five milliliters of blood was drawn under aseptic condition from the mother and five milliliters of cord blood was obtained for assay. The serum was separated immediately and sent to the laboratory and stored at -80^{o}C until assayed.

Serum iron was analyzed based on the principle of Transferrin-bound iron release at an acid pH reduction from ferric to ferrous ions which reacts with ferrozine to form a violet colored complex which is measured spectrophotometrically at 560 nm [16]. The absorbance measured at this wavelength is proportional to serum iron concentration. Total Iron-Binding Capacity (TIBC) was analyzed with a known amount of ferrous ions are added to serum at an alkaline pH, with ferrous ions binding with transferrin at unsaturated iron-binding sites. Unbound ferrous ions are measured using the ferrozine reaction. The TIBC is the sum of the serum iron concentration plus the Unsaturated Iron Binding Capacity (UIBC).

Serum ferritin was estimated using colorimetric enzyme immunoassay kit manufactured by Monobind and based on the principle of streptavidin biotin based sandwish assay. Serum total protein and albumin were analyzed using the biuret [17] and bromocresol green methods [18], respectively. Albumin was assayed using kits from Agappe Diagnostics, Kerala, India. Data analysis-SPSS statistical software package version 16 was used for data analysis. The variables were analyzed using a non-parametric test method, the two-sample Wilcoxon rank-sum Mann-Whitney test. Continuous variables were compared using paired student t-test. Pearson's correlation coefficient was also used to correlate categorical variables and p-value<0.05.

Results

One hundred and thirty-five mother/newborn pair completed the assessment process and wereanalyzed.

Table I shows that the mean age of the mothers was 29.2 ± 4.6 years with 67.4% within the age bracket 20 to 30 years, whilst the mean gestational age of the newborns was 39.0 ± 2.0 weeks. All the mothers attained some level of education with 74.1% attaining tertiary education and 22.9% with secondary education. Eighty-one percent of the mothers had some form of employment whilst 18.5% were unemployed.

Table 1: The socio-demographiccharacteristics of the mothers studied.

Variables	n= 135	Freq (%)
Age in years		
≤20		2 (0.7)
21-30		90 (67.4)
≥31		43 (31.8)
Mean Age	**29.2 ± 4.6**	
Educational Status		
Primary		4 (2.9)
Secondary		31 (22.9)
Tertiary		100 (74.1)
Tribe		
Yoruba		119 (88.1)
Hausa		3 (2.2)
Ibo		10 (7.5)
Others		3 (2.5)
Religion		
Christianity		40 (29.6)
Islam		91 (67.4)
Others		4 (2.9)
Occupation		
Unemployed		25 (18.5)
Self Employed		51 (37.8)
Employed		59 (43.7)
Place of Ante Natal Care		
UITH		108 (80.0)
Outside UITH		27 (20.0)
Booking Status		
Booked		113 (83.7)
Unbooked		22 (16.3)
Cigarette Use		
Yes		0 (0)
No		135 (100)
Alcohol Use		
Yes		0 (0)
No		135 (100)

Ninety-five percent of the mothers received antenatal care (80% within UITH). None of the mothers' drinks alcohol or smoke. All the mothers that provided the information took hematinic/multivitamins. Ninety-two percent of the babies were Appropriate for Gestational Age, whilst 5.1% were Large for Gestational Age, with the babies having a mean birth weight of 3.6 ± 1.2 kg, mean length of 49.1 ± 3.3 cm, and a mean head circumference of 34.2 ± 4.3 cm (Table II).

Table 2: Maternal and newborn anthropometric parameters of the total study population.

Variables	
Maternal	**Mean ± SD**
Mean Maternal Height (cm)	159.8 ± 19.7
Mean Booking Weight (kg)	73.5 ± 18.5
Mean Last Weight at ANC Visit (kg)	78.8 ± 17.4
Mean Weight at Presentation in Labour Ward	82.3 ± 20.5
BMI (kgm2)	29.9 ± 11.3
	Median (IQR)
Duration of Pregnancy at Booking (wks)	24.5 (17.8)
Duration of Pregnancy at Delivery (wks)	39.0 (2.0)
Newborn	
Growth Classification	Frequency (%)
SGA	3 (2.2)
AGA	125 (92.5)
LGA	7 (5.1)
Anthropometry	Mean ± SD
Mean Birth Weight (kg)	3.6 ± 4.2
Mean Length (cm)	49.1 ± 3.3
Mean Head Circumference (cm)	34.2 ± 4.3

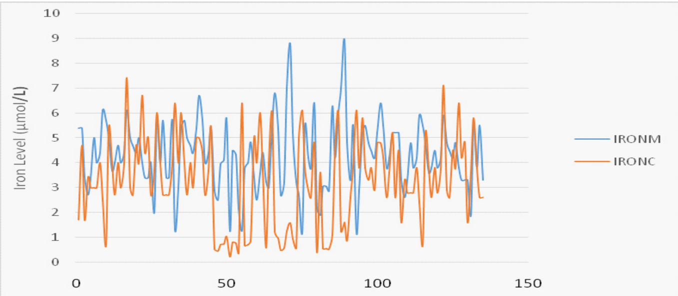
Table III shows that the mean iron levels were significantly higher in the mothers (4.32 ± 1.39 µmol/L) than in the newborn (3.24 ± 1.77 µmol/L) p= 0.001.

Figure 1 shows that the mothers have a higher iron levels that newborns at a ratio of 1.3:1.

Table 3: The mean serum iron, ferritin, transferrin receptor, transferrin and TIBC levels in paired mother and their term newborn.

Variable	n	Mean ± SD	95%CI	t test	p value
Total Protein (gm/L)					
Mother	135	70.78 ± 18.87	67.57 – 73.99		
Newborn	135	58.74 ± 12.29	51.62 – 55.85	8.75	0.001
Albumin (gm/L)					
Mother	135	44.35 ± 7.61	43.05 – 45.54		
Newborn	135	41.35 ± 7.21	40.10 – 42.59	3.30	0.001
Iron (µmol/L)					
Mother	135	4.32 1.39	4.08 – 4.56		
Newborn	135	3.24 1.77	2.94 – 3.54	5.57	0.001
Ferritin (ng/ml)					
Mother	135	98.40 ± 10.83	79.96 – 116.85		
Newborn	135	217.19 ± 16.20	189.00 – 229.50	-7.05	0.0011
Transferrin receptor (nmol/L					
Mother	135	29.70 ± 17.0	26.69 – 32.72		
Newborn	135	33.37 ± 20.29	29.92 – 36.83	-1.58	0.115
Transferrin (µmol/L)					
Mother	135	325.26 71.72	313.05 – 337.47		
Newborn	135	246.75 78.08	233.41 – 260.09	8.59	0.001
TIBC (µg/dL)					
Mother	135	468.49 ± 90.69	453.05 – 483.93		
Newborn	135	352.61 ± 108.75	333.88 – 371.3	9.46	0.001

Maternal: Newborn ratio	
@Total protein	1.2: 1
@Albumin	1.07: 1
@ Iron	1.3: 1
@ Ferritin	1: 2.2
@ Transferrin receptor	1: 1.12
@ Transferrin	1.3: 1
@TIBC	1.3: 1



→ Serial numbered mother and newborn pair Key:

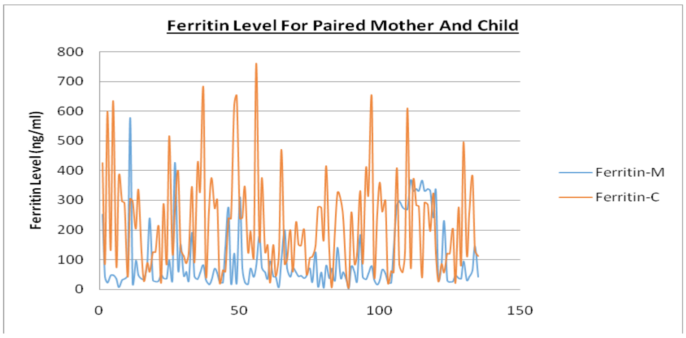
Newborn cord blood iron levels

Maternal iron levels

Figure 1: Serum Iron levels in paired mother and their term newborns.

Ferritin was significantly higher in the newborns (217.19 ± 16.20 ng/ml) than in their paired mothers (98.40 ± 10.83 ng/ml), p= 0.0011, with (Figure 2) showing that serum ferritin levels were lower in the mothers than their paired newborns at a ratio of

1 to 2.2 (Table III).

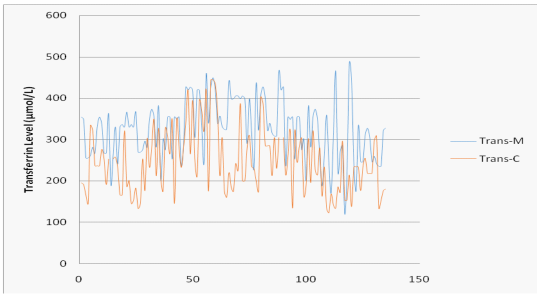


→ Serial numbered mother and newborn pair Key:

Newborn cord blood ferritin levels

Maternal ferritin levels

Figure 2: Serum Ferritin levels in paired mother and their term newborns. Transferin receptor was lower in the mothers (29.70 ± 17.0 µmol/L), than in the newborn (33.37 ± 20.29 nmol/L), though, the difference was not statistically significant p = 0.115, with the transferrin receptor levels being comparable in the mothers and their paired newborns at a ratio of 1 to 1.12 (Table III). The mean maternal serum transferrin levels of 325.26 ± 71.72 µmol/L was significantly higher than their paired newborn levels of 246.75 ± 78.08 µmol/L, p= 0.001 as shown in Table III, with a maternal fetal ratio of 1.3:1 (Figure 3).

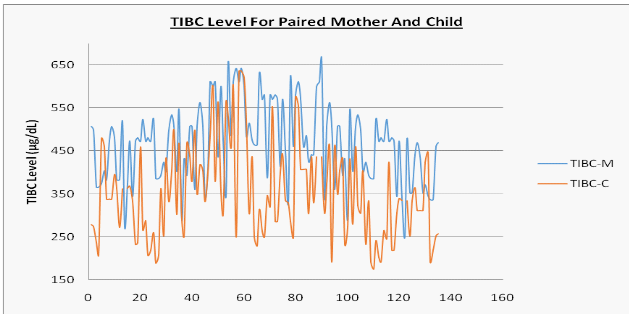


→ Serial numbered mother and newborn pair Key:

Newborn cord blood transferrin levels

Maternal transferrin levels

Figure 3: Serum Transferrin levels in paired mother and their term newborns.



→ Serial numbered mother and newborn pair Key:

Newborn cord blood Total Iron Binding Capacity levels

Maternal Total Iron Binding Capacity levels

Figure 4: Serum Total Iron Binding Capacity (TIBC) levels in paired mother and their term newborns.

The mean Total Iron Biding Capacity (TIBC) was significantly higher in mothers than their paired newborns (p= 0.001) (Table III), with a maternal -newborn ratio of 1.3:1 (Figure 4). Of the iron indices studied, there was a positive correlation between mother and their paired newborns in total protein (r= 0.32), albumin (r= 0.33), transferrin (r= 0.36) and TIBC (r= 0.32), p= 0.001, whilst there was no significant correlation between mother and newborn in iron, ferritin and transferrin receptor levels (p > 0.33) as shown in (Table IV).

Table 4: Correlation between mother and child for Iron, Ferritin, Transferin receptor, Transferin and TIBC.

Variable	n = 135	Pearson Correlation Coefficient	p value
Total protein		0.32	0.001
Albumin		0.33	0.001
Iron		0.04	0.64
Ferritin		0.09	0.33
Transferin receptor		0.02	0.79
Transferin		0.36	0.001
TIBC		0.032	0.001

Discussion

The serum protein, albumin, iron, transferrin and TIBC level are higher in the mothers than in their paired newborns, whereas, ferritin was significantly lower in the mothers than in the newborns in this study, a finding that establishes the relationship between the mother and their paired newborns in this locality. This finding is similar to that observed by other workers [16-19] , who reported some other micronutrients with a higher serum zinc in the cord blood than in the serum of the mothers ina ratio of 1.3 to 1.

The albumin levels are within normal limits in both the mothers and their paired newborns, though at a higher level in the mother, hence, the distribution of iron indices in the two groups in this study is a true reflection of the iron status of the subjects. This finding suggests that iron, transferrin and TIBC are distributed in favor of the mother whilst ferritin is distributed in favor of the newborn two folds, similar to reports from other workers [19-21].

Ferritin is a universal intracellular protein that stores iron and releases it in a controlled fashion. Ferritin reflects the total body iron, where it will be low in iron deficiency and high when there is an excess of iron in the body, hence, ferritin measures the body's ability to store iron. Serum ferritin is used as a standard measurement of iron stores in infants, children and adults [19-21], with 1μg/L of serum ferritin being equivalent to 8-10 mg of storage iron in adults [22].

We found that the ferritin levels are higher in the newborn than in their paired mothers, which is an indication of adequate iron store in favor of the newborn. This finding is in keeping with the notion that the foetus is favored when it comes to iron stores, even in the face of iron deficiency in the mother [19,20,23,24]. The low ferritin levels in the mothers is an indication of low iron stores in the mothers, yet the ferritin levels are within normal limits in the newborns in this study.

Factors that influence neonatal ferritin concentration at birth include duration of gestation, fetal sex, maternal iron status and conditions altering maternal-fetal iron exchange. The subjects in this study are term babies, hence, gestational age as a confounder is eliminated. Normal full term newborn infants had cord serum ferritin concentrations between 100 to 260 μg/L [25,26], which is in keeping with the findings in this study.

Transferrin is the transport protein for iron in the blood, hence, measures the level of iron carriage. The higher transferrin levels in the mothers in this study indicates that the mothers are more deficient in iron than their paired newborn, though, the transferrin levels in the paired subjects studied are within normal limits. An elevated transferrin level is an indication of iron deficiency anaemia. That the transferrin level is higher in the mothers is an indication of a higher iron storage in the newborn relative to that of the mothers. This observation is in consonance with other workers [22,23]. Total Iron Binding Capacity measures the transferrin capacity to bind iron. Transferin levels depends on the liver function where it is produced, and the kidney function where it is lost in the urine. Infections cause depression of transferrin levels, whilst its level is high in iron deficiency anaemia.

The lower transferrin levels in the newborns in relations to that of the mother shows that the newborns have near adequate iron levels, hence, a lower serum transferrin levels.

Transferrin Receptor (TfR) is the carrier protein for transferrin, and is required for the import of iron into the cell and is regulated in response to intracellular iron concentration [27]. It's a trans-membrane glycoprotein that enhances the entry of iron into cells through receptors on the surface of the cell membrane. TfR is highly expressed by the red blood cells, brain endothelial cells and tumor cells.

It imports iron by internalizing the transferrin iron complex through receptor mediated endocytosis. Low iron concentration promotes increased levels of transferrin receptor to increase iron intake into the cells. Serum Transferrin Receptor (sTfR) is a relatively new diagnostic tool for differentiating between Iron Deficiency Anaemia (IDA) and Anaemia of Chronic Disease (ACD) because it is not affected by inflammatory conditions unlike serum ferritin [25-28].

The lower iron levels in the newborn compared to that of the mothers with a corresponding elevated TfR levels above that of the mothers is expected, thus indicating more demand for iron.

The transferrin receptor levels are comparable in both mother and their paired newborns in this study, a finding that is similar to that of other workers [28,29], which tend to suggest that the requirement for transfer of iron in both groups equilibrate, thus indicating that the iron in newborns is a reflection of the maternal iron levels. As for TIBC, it measures the ability of transferrin to bind iron and transport it around the body. It is increased in pregnancy and iron deficiency anaemia. Low levels of TIBC is seen in malnutrition, inflammation, liver disease and nephrotic syndrome. The lower levels in the newborns compared to their paired mothers observed in this study is at variance with the findings of other workers in Brazil who found the levels of TIBC in both mother and newborn to be comparable [30]. This observation in this study suggests less binding of transferrin to iron, hence, iron is released more readily for use in the newborns.

Conclusion

We conclude that there is an established relationship between newborns and their paired mothers in terms of the serum levels of iron, ferritin, transferrin and TIBC at birth. Term babies have a lower serum albumin, iron, transferrin and TIBC levels, and a higher serum ferritin levels than their paired mothers. Mothers iron, transferrin and TIBC levels are 1.3 times that of their newborns whilst serum ferritin levels are higher two folds in newborns than in their mothers. The distribution of albumin, transferrin and TIBC correlates well in mothers and their newborn. This study corroborates the fact that the sharing of iron between mother and the fetus is in favor of the newborn even in the face of iron deficiency in the mother.

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