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Relation of Maternal Blood Iron, Total Iron Binding Capacity and Ferritin Levels with Fetal Values

NILÜFER IMAMOGLU†, ISMET ALKIS*, SAFIYE SAYLIK§, VOLKAN TUNA‡, NEBAHAT BAYRAM¶, AHMET GULKILIK†† and HALIT DEMIR‡‡
Medical Park Hospital, Department of Obstetric and Gynaecology, 65100 Van, Turkey
Tel: (90)(432)2173252/1625; E-mail: ismetalkis@hotmail.com

In this study, 74 prospective mothers proposed delivery during the period of 01.11.2003-31.08.2004 in Bakirkoy Maternity and Woman's and Children's Diseases Education Hospital, Turkey were included. They were divided into two groups based on hemoglobin levels of mothers as group I (hemoglobin = 11 g/dl, n = 42) and group II (hemoglobin < 11 g/dl, n = 32). Hemoglobin (Hb), hematocrit (Htc), mean erythrocyte corpuscular volume (MCV), mean erythrocyte corpuscular hemoglobin concentration (MCHC), serum iron, total iron binding capacity (TIBC), serum ferritin levels and the percentage of transferrin saturation were determined in mothers and umbilical cord blood of their newborns. Additionally, birth weight of all babies were recorded. Mean ferritin level in umbilical cord blood was found higher than that in mother's blood. A significant correlation was found between serum ferritin levels of mothers and infants and between serum ferritin levels of babies of anemic and non-anemic mothers. No difference was found in terms of baby weight between two groups. In this study, it was concluded that iron deficiency of mother affected ferritin level of infant and that serum ferritin level should be increased in pregnant women for diminishing the risk of iron deficiency anemia in newborn infants.

Key Words: Pregnancy, Newborn, Anemia, Ferritin, Iron.

INTRODUCTION

The iron deficiency anemia is the most frequent form of anemia worldwide today, as well as in the past. Though it occurs at every age and in all socioeconomic groups, it is more frequent in children and young people, persons nourished with poor diet and in fertile-age women[1-3].

†Department of Obstetric and Gynaecology, Hayat Hospital, Malatya, Turkey.
‡Department of Obstetric and Gynecology, Nizip Government Hospital, Nizip, Turkey.
§Department of Obstetric and Gynecology, Guven Hospital, Van, Turkey.
¶Trabzon Maternity and Woman's and Children's Diseases Hospital, Trabzon, Turkey.
††Bakirköy Maternity and Woman's and Children's Diseases Education Hospital, Istanbul, Turkey.
‡‡Department of Chemistry (Biochemistry), Art and Science of Faculty, Yuzuncu Yil University, Van, Turkey.

According to the data of World Health Organization (WHO), iron deficiency anemia affects about 30 % of worldwide population namely 1.3 billion persons. Of pregnant women 51 and 43 % of pre-school children and 37 % of school age children are anemic[2]. Even though anemia is not apparent, in 50 % of women and in 90 % of pregnant women it has been determined that iron stores are extremely lessened. Because iron need increases in pregnancy, anemia can easily develop and iron stores can be insufficient[4].

Iron deficiency anemia causes impaired performance at work in adults, low birth weight, prematured delivery, high perinatal morbidity and mortality in pregnant women. Iron deficiency in growing period affects growth and functions of multiple organ systems including hematopoietic, cardiac muscle and gastrointestinal systems. Probably the most affected organ in childhood from iron deficiency is the developing brain. Neurophysiological studies report that early iron deficiency worsens cognitive functions of infant and that the consequences can become apparent after a long time[5,6].

Because the fetus obtains all of his/her needs from mother *via* placenta, he/she is influenced by most of the changes of maternal metabolism.

In present study, comparing hematological parameters of mothers (anemic and non-anemic) and their newborn infants umbilical cord blood it is aimed to see whether iron stores of mother affected newborn. For this purpose, we analyzed Hb, Htc, MCV, MCHC, serum iron, total iron binding capacity and serum ferritin levels in mothers giving birth and in umbilical cord blood of their newborn infants and we investigated the relationship between these values. In addition, it is also investigated if there was an association between anemia of mother and birth weight of newborn.

EXPERIMENTAL

After ethics committee decision obtained, 74 random cases from full-term pregnant women at delivery admitted to Bakirkoy Maternity and Woman's and Children's Diseases Education Hospital, Turkey between 2003-2004 were included in the study. Based on mother's hemoglobin level, they were divided into two groups as follows: 42 non-anemic mother with hemoglobin 11 g/dl and above (group I) and 32 anemic mother with hemoglobin 11 g/dl and lower (group II). Pregnant women had anemia due to any reason other than iron deficiency, multiple pregnancy, smoking, preeclampsia, abruptio placenta and placenta previa with hemorrhage, history of splenectomy, early membrane rupture, gastrointestinal system or urinary tract bleeding during pregnancy were excluded. For every patient, age, weight, education level, gravidity, parity, gestational age, iron consumption during pregnancy were recorded. From prospective mothers blood samples (2 mL blood put in ethylene diamine tetraacetic acid (EDTA) tube for hemogram and 6-8 mL blood put in dry tube purified from iron for serum iron, total iron-binding capacity and serum ferritin level analyzing) were collected within one hour preceding delivery. From the same cases, immediately after clamping umbilical cord following birth a blood sample was obtained from placental site of umbilical cord. For hemogram 2 mL blood

sample was put in EDTA tube and 6-8 mL blood sample was put in a dry, iron-free tube for serum iron, iron-binding capacity and serum ferritin level analyzing. Gender, birth weight and form of delivery were recorded for all newborns. Blood samples of mother and umbilical cord for hemogram were analyzed within 2 h. For serum iron, iron-binding capacity and serum ferritin level analyzing, serum was separated from blood obtained from mother and umbilical cord. Serum iron and iron-binding capacity tests were performed by Modular P+ISE 900 Kinetic-End Point device. Serum ferritin was tested by Modular E-70 Electro Chemi Lumineconse device. For each mother and newborn serum transferrin saturation was calculated as follows: (serum iron/total iron binding capacity) × 100.

For statistical analysis, SPSS 11.5 program was used. Paired Sample T-test was used for comparing in-group values, Independent Sample T-test was used for evaluation between groups. Non numeric data was evaluated with Chi-square test. The results were given as mean ± standard deviation. For all evaluations $p < 0.05$ was accepted as significant.

RESULTS AND DISCUSSION

While mean age was 25.80 ± 5.08 in group I, it was 25.31 ± 5.37 in group II. No statistically significant difference was found between groups ($p > 0.05$) (Table-1). Mean gestational age was found as 39.27 ± 1.46, in group I 39.72 ± 1.51 and in group II 38.67 ± 1.16. There was no statistically significant difference between groups ($p > 0.05$) (Table-2).

TABLE-1
AGE, WEIGHT

	Mean	Group I	Group II	p
Age	25.59±5.18	25.80±5.08	25.31±5.37	>0.05
Weight	71.56±10.22	70.45±10.09	73.03±10.37	>0.05

TABLE-2
EDUCATION

	Group I (%)	Group II (%)	p
No education	7.1	12.5	>0.05
Elementary school	69.0	62.5	>0.05
Junior high school	11.9	25.0	>0.05
High school	9.5	–	>0.05
College	2.4	–	>0.05

Evaluation of parity and gravidity numbers between groups was resulted as no statistically significant difference (Tables 3 and 4). In group II iron consumption less than a month was frequent; while iron consumption more than one month was frequent in group I. There was no statistically significant difference between two groups (Table-5).

TABLE-3
PARITY

	Group I (%)	Group II (%)	p
0	45.2	31.3	>0.05
1	38.1	43.8	>0.05
2	14.3	18.8	>0.05
3 and above	2.4	6.3	>0.05

TABLE-4
GRAVIDITY

	Group I (%)	Group II (%)	p
1	45.2	31.3	>0.05
2	26.2	43.8	>0.05
3	26.2	9.4	>0.05
4 and above	2.4	15.6	>0.05

TABLE-5
IRON CONSUMPTION

	Group I (%)	Group II (%)	p
Consuming less than a month	40.5	65.6	>0.05
Consuming more than a month	59.5	34.4	>0.05

Comparison of mothers blood yielded statistically significant differences for all parameters (Hb, Htc, serum iron, serum ferritin, total iron binding capacity, MCV, MCHC) evaluated in both groups (Table-6).

TABLE-6
MOTHER BLOOD VALUES

	Mean	Group I	Group II	p
Hct	34.34±4.56	37.30±2.93	30.46±3.19	<0.001
Hb	11.22±1.75	12.42±0.96	9.63±1.19	<0.001
RBC	4.02±0.38	4.16±0.30	3.84±0.40	<0.001
Serum iron	63.59±35.89	81.11±35.52	40.59±20.08	<0.001
TIBC	513.00±55.75	495.69±59.26	535.71±41.68	<0.001
SerumFerritin	13.56±10.26	18.02±11.25	7.69±4.25	<0.001
MCV	84.94±10.56	89.89±3.71	78.46±12.95	<0.001
MCHC	32.55±1.62	33.31±1.11	31.51±1.65	<0.001

Comparison of umbilical cord blood yielded no statistically significant difference for any parameters of Hb, Htc, serum iron, total iron binding capacity, MCV, MCHC evaluated in both groups ($p > 0.05$). But, a statistically significant difference was found between serum ferritin levels ($p < 0.01$) (Table-7).

TABLE-7
UMBILICAL CORD BLOOD VALUES

	Mean	Group I	Group II	p
Hct	45.27±4.66	45.90±4.35	44.43±4.97	> 0.05
Hb	15.00±1.58	15.13±1.31	14.83±1.88	> 0.05
RBC	4.23±0.42	4.29±0.41	4.15±0.42	> 0.05
Serum iron	157.05±40.24	153.52±33.98	161.68±47.40	> 0.05
TIBC	245.18±38.26	241.30±34.14	250.28±43.10	> 0.05
Serum ferritin	163.80±91.98	185.64±83.72	135.13±95.70	> 0.05
MCV	107.09±4.62	107.21±4.22	106.93±5.18	> 0.05
MCHC	32.92±1.11	33.00±1.15	32.80±1.07	> 0.05

Mean transferrin saturation of mothers was 16.63 ± 7.75 in group I, it was determined as 7.68 ± 3.98 in group II. There was a statistically considerable difference between groups ($p < 0.001$). Mean transferrin saturation of babies was 65.51 ± 18.84 in group I, it was 66.91 ± 21.88 in group II. No statistically significant difference was found ($p > 0.05$).

According to the WHO data, iron deficiency anemia affecting 30 % of world population influences 43 % of pre-school children and 51 % of pregnant women[5]. Especially in third world countries, degree of anemia is more severe and anemia is more common. In a study of Malhotra *et al.*[7] anemia in pregnancy has been detected as 72.5 % in India in 2002. Choi *et al.*[8] has found the rate of anemia in pregnancy as 35.3 % in their study conducted in Korea in 2000. In present study 43 % of pregnant women were found anemic.

Anemia in pregnancy has been described as Hb = 11 g/dl according to WHO criteria[9]. Malhotra *et al.*[7], Choi *et al.*[8,9] and many authors have used this value in their studies. In present study anemic and non-anemic pregnant women groups also were constituted based on that value.

Mean Hb level in mothers has been reported by Tekinalp *et al.*[10] as 12 ± 3.7 g/dl, by Milman *et al.*[11] as 13.2 ± 1.1 g/dl in Denmark and by Thavaraj *et al.*[12] as 11.5 ± 0.3 g/dl in pregnant women.

Mean serum iron in mothers has been found as 76.76 ± 32 µg/dl by Choi *et al.*[8,9], as 58.8 ± 26.2 µg/dl by Okuyama *et al.*[13], as 128.4 ± 67 µg/dl by Milman *et al.*[11] Mean iron-binding capacity has been reported by Choi *et al.*[8,9] as 473.86 ± 74.15 µg/dl, by Okuyama *et al.*[13] as 495 ± 100.3 µg/dl. In present study, it is found that the mean of serum iron values of group as 63.59 ± 35.89 µg/dl and the mean of total iron-binding capacity values of group as 513 ± 55.75 µg/dl. Mean serum ferritin level in mothers has been reported by Choi *et al.*[13] as 19.08 ± 8.43 µg/dl, Okuyama *et al.*[13] as 9.6 ± 7.2 µg/dl, Tekinalp *et al.*[14] as 26.7 ± 3.7 µg/dl. In this study, mean serum ferritin level in mothers was determined as 13.56 ± 10.26 µg/dl. These results obtained correspond with literature.

Mean transferrin saturation in mothers has been reported as 16.21 ± 7.91 by Choi *et al.*[14]. In present study transferrin saturation of mothers was found as 12.76 ± 7.77.

Haematologic results correlate with socioeconomic situation of the countries. On comparing the present findings belonging to the group of mothers with literature data, we determined that there was a relevance.

Mean Hb in newborn umbilical cord blood has been found by Tekinalp *et al.*[10] as 19.6 ± 4 g/dl, by Harthoorn-Lasthuizen *et al.*[15] as 16 g/dl. In present study it was found as 15 ± 1.58 g/dl. Mean iron and total iron binding capacity in umbilical cord blood have been found by Choi *et al.*[8] as 196.92 µg/dl and 307.71±71 µg/dl, respectively; and by Okuyama *et al.*[13] as 161.5±43.5 µg/dl and 177.7±33.9 µg/dl, respectively. In present study, these values were found as 157.05 ± 40.24 µg/dl and 245.18 ± 38.26 µg/dl, respectively. In two studies of Choi *et al.*[8,14] umbilical cord blood transferrin saturation has been reported as 63.92 ± 13.82 and 69.2 ± 15.3. In this study, umbilical cord transferrin saturation was determined as 66.11 ± 20.08. Newborn serum ferritin level was reported by Choi *et al.*[8] as 183.27 ± 54 µg/L, by Okuyama *et al.*[13] as 160.5 ± 67.2 µg/L, by Tekinalp *et al.*[10] as 303.8 ± 60.8 µg/L. In present study, mean serum ferritin level in newborn was found as 163.80 ± 91.98 µg/L.

In comparison to newborn mean haematological values in literature, it was seen that present findings were in parallel with literature values.

In present study, we classified non-anemic mothers as group I and anemic mothers as group II. We determined a positive correlation between haematological values of group I and group II ($p < 0.001$). In non-anemic and anemic mothers Hb levels have been found by Kilbride *et al.*[16] as 12.2 ± 0.9 mg/dl and 9.9 ± 0.7 mg/dl, respectively and by Okuyama *et al.*[13] as 11.7 ± 0.8 mg/dl and 9.8 ± 1.1 mg/dl, respectively. In this study, group I and group II values were determined as 12.47 ± 0.96 and 9.63 ± 1.19 mg/dl, respectively. Serum ferritin levels, a marker of body iron stores, were found by Kilbride *et al.*[16] as 21.9 ± 21.4 µg/L and 7.6 ± 5.5 µg/L, by Okuyama *et al.*[13] as 19.4 ± 11.7 µg/L and 5.2 ± 2.2 µg/L, in non-anemic and anemic mothers, respectively. It is found that these values as 18.2 ± 11.25 µg/L and 7.69 ± 4.25 µg/L, respectively. Since serum ferritin level < 12 µg/L indicates insufficient iron stores[17], current findings point out that iron stores of anemic mothers are very insufficient. Serum transferrin saturation under 16 % indicates insufficient iron for erythropoiesis and serum transferrin saturation under 10 % means certain diagnosis of iron deficiency anemia[17]. In this study, transferrin saturation is determined as 7.68 ± 3.98.

For umbilical cord values, we made two groups. Group I consists of newborns of non-anemic mothers and group II consists of newborns of anemic mothers.

Umbilical cord Hb level has been found as 16.8 g/dl in non-anemic mothers and 15.6 g/dl in anemic mothers by Sweet *et al.*[18]. We found umbilical cord blood Hb level as 15.13 ± 1.31 g/dl in non-anemic and as 14.83 ± 1.88 g/dl in anemic ones. Umbilical cord Htc value has been found as 46.1 ± 4.4 in non-anemic and as 46.8 ± 4.7 in anemic women by Kilbride *et al.*[16]. In present study, it is found Htc as 45.90 ± 4.35 in non-anemic women and as 44.43 ± 4.97 in anemic ones. Serum iron level has been found in non-anemic as 221.24 ± 51.43 and in anemic women as 172.12 ± 57.16 by Choi *et al.*[8]. We found it as 161.68 ± 47.40 and 153.52 ± 33.98,

respectively. Transferrin saturation percentage has been found as 76.47 ± 16.01 and 51.86 ± 17.75 by Choi *et al.*[8]. We calculated transferrin saturation percentage as 65.51 ± 18.84 in non-anemic and as 66.91 ± 21.88 in anemic ones.

In many studies conducted, it has been determined that umbilical cord blood serum ferritin level was influenced by anemia of mother. Umbilical cord serum ferritin levels of non-anemic and anemic mothers have been reported as 320.6 ± 71.4 µg/L and 262.0 ± 170.4 µg/L, respectively, by Tekinalp *et al.*[10], as 215 ± 47.35 µg/L and 161.62 ± 56.38 µg/L by Choi *et al.*[8], as 200 ± 124 µ/L and 95 ± 149 µg/L, respectively, by Kilbride *et al.*[16]. In present study, it is found that these values as 185.64 ± 83.72 µg/L and 135.13 ± 95.70 µg/L, respectively and it has been seen that this result was statistically significant ($p < 0.01$). Therefore, it can say that these newborns require careful attention to anemia in nursling period since anemia influences iron stores of newborn and these mother would also be anemic during breast-feeding period and iron deficiency in infant age worsens neurological development.

Erdem *et al.*[19] in a study about the effect of iron deficiency on fetal erythropoiesis, comparing serum erythropoietin, Hb and serum ferritin levels in mother and newborn, has determined that maternal erritin levels correlated with fetal ferritin levels ($p=0.002$).

Harthoorn-Lasthuizen *et al.*[15] has analyzed Hb, zinc, protoporphyrin and serum ferritin levels of mothers and newborns in a study in Amsterdam and has demonstrated no difference between newborns of mothers with iron deficiency and newborns of mothers with sufficient iron.

Diverse results have been reported about the correlation between anemia of mother and birth weight of newborn. Malhotra *et al.*[7] in a study dividing anemic mothers into three categories (slight = Hb: 9-10.9 g/dl, mild = Hb: 7-8.9 g/dl, severe = Hb<7 g/dl) has determined that severe anemia was related to low birth weight babies. Milman *et al.*[20] has determined decreased birth weight of newborn in case of MCV < 86 g/L and > 145 g/L in mother. Steer[21] has reported that severe anemia (MCV< 80 g/L) caused low birth weight. Singla *et al.*[22] in a study has reported that maternal anemia influenced fetal birth weight. Allen[23] in a review in 2000 has determined that there was a U-shape correlation between maternal Hb level and birth weight.

Georgieff *et al.*[24], in a study comparing serum ferritin levels in umbilical cord blood of newborns, has determined no scant difference between the group of low serum ferritin level (< 5 percentile) and the group of normal serum ferritin level in terms of birth weight. Singla *et al.*[22] has determined birth weight as 3374 g in babies of non-anemic mother and as 3287 g in babies of anemic mother and has found no significant difference between them. In present study, it is found birth weight as 3402.38 ± 419.56 gr in babies of non-anemic mother and as 3306.87 ± 453.21 g in babies of anemic mother. No statistically significant difference was determined between them ($p > 0.05$).

In Turkey, considering educational situation of mothers and insufficient consumption of iron products, iron deficiency anemia emerge as an important problem of pregnant women and mothers. That iron deficiency anemia was determined 43 % of full term pregnant women in our study supports this opinion.

Fetus uptakes iron *via* placenta by active transport. Thus, anemia doesn't occur in newborn. But anemia in mother influences iron stores of newborn as is seen in many studies performed. Between babies of anemic mothers and babies of non-anemic mothers, there is a significant difference ($p < 0.01$) in ferritin levels which is a marker of iron stores. Considering that anemia will continue during breast feeding period and that iron demand of newborn will increase further and that iron deficiency in infancy worsens neurological development it is necessary to pay attention to these newborns for developing anemia in nursing period.

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