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Full Length Article

Maternal and cord blood hepcidin levels based on gestational weeks in term and preterm infants

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ABSTRACT

Background: The reliable assessment of iron deficiency (ID) and the iron parameters which contribute to anaemia in preterm and term infants are of vital importance.
Aim of the study: This study focuses on identifying maternal and cord blood hepcidin [Hep (CB)] levels based on gestational weeks (GW) and comparing them with other parameters in iron metabolism.
Patients & methods: This is a prospective and observational study including 102 pregnant women and their infants. Along with Hep(CB), iron, iron chelation capacity, ferritin, transferrin saturation, C-reactive protein level were recorded for mothers and infants.
Results: Maternal and cord blood hepcidin levels were 135.0 ng/ml (6.40–2846.0) and 286.30 ng/ml (90–1697) for those under 33 GW (n = 27), 66.4 ng/ml (11.0–3936.0) and 406.9 ng/ml (10.0–1867) for those between 33 and 37 GW (n = 33), 41.4 ng/ml (2.8–513.7) and 498.1 ng/ml (343.7–701.7) for those over 37 GW (n = 42), respectively. Hep(CB) [104.7 ng/ml (5.0–1022.0), n = 22] levels were lower for infants with ID compared to those without iron deficiency [463.3 ng/ml (131.3–2261.0), $p < 0.0001$, n = 80)]. While a strongly positive relationship was observed between Hep(CB) levels and cord blood ferritin levels (Rho = 0.76, $p < 0.0001$) in the correlation analysis, a weak relationship (Rho = 0.29, $p = 0.004$) was found for transferrin saturation. Additionally, it was observed that Hep(CB) levels were directly proportional to GW (Rho = 0.23, $p < 0.0001$) and birth weight (Rho = 0.21, $p = 0.03$). A decrease of 10 units in Hep(CB) level increases risk for ID anaemia by 5% [OR = 0.95 (0.9297–0.98099)].
Conclusions: This study, which compares Hep(CB) levels and iron parameters based on GWs, differs from similar studies in terms of assessment of both preterm and term groups along with maternal levels. It is evident that increase in hepcidin prevents ID anaemia.

1. Introduction

Hepcidin is a regulator of iron metabolism. It inhibits iron transport by binding to the iron export channel ferroportin located on the basolateral surface of gut enterocytes and the plasma membrane of macrophages. Hepcidin ultimately breaks down the transporter protein in the lysosome. Inhibiting ferroportin prevents iron from being exported, and the iron is sequestered in the cells [1,2]. It was reported that rat hepcidin level was the negative regulator of iron absorption in the intestines, iron transfer across placenta and iron emission from macrophages [3].

Hepcidin affects plasma iron concentration and tissue distribution of iron by inhibiting intestinal iron absorption, iron recycling

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by macrophages, and iron mobilization from hepatic reserves [4]. Increase in hepcidin levels during inflammation stimulates ferroportin intake and degradation in the cell in macrophages, hepatocyte and duodenal enterocytes, and leads to iron retention in these cells and decreases iron transmission to the plasma [5]. There is a total iron of 1 g in an infant's body during the birth, which is transmitted from the mother to the infant through the placenta [6]. It is created by a maternal diet of 600 mg and cessation of menstruation, and 400 mg is provided by maternal stores [6]. Several studies demonstrate that iron supplementation prevents prematurity and birth complication [7–9]. Decreases in iron levels lead to mental retardation and mental problems during adolescence [10,11].

Considerably high iron level, i.e. applying iron supplementation to a non-anaemic mother, may lead to negative results such as low birth weight and gestational diabetics [12]. Fetal iron levels are regulated by hepcidin synthesis in the liver, and hepcidin is produced as iron levels decrease. Hepcidin interacts with placenta through an unknown mechanism when it is transmitted to the circulatory system [13]. Therefore, hepcidin hormone, which influences iron metabolism, is of vital importance for mothers and newborns.

This study focuses on identifying levels of hepcidin hormone, which fulfils both iron and host defence and an anti-microbial function in the body, in mothers and newborns based on gestational weeks, and the relationship between iron metabolism and a mother-newborn.

2. Materials and methods

This study was approved by the decision of Erciyes University Faculty of Medicine Ethical Committee taken on 21.12.2010 and numbered 2010/22, and was supported by Erciyes University Faculty of Medicine Committee of Scientific Research Projects with the project number TSU-11-3485.

2.1. Study population

One hundred and two pregnant women, who were monitored between May 2011 and July 2011 at Gevher Nesibe Hospital Perinatology Department and whose GWs range from 27 + 0/7 to 41 + 0/7, and their infants were included in the study. The mothers' demographic features were identified based on the anamnesis and the existence of any early membrane rupture (EMR) and chorioamnionitis. Infants who were diagnosed with congenital anomaly in foetal ultrasonography (USG) or during birth and pregnant women with EMR or chorioamnionitis were not included in the study. Gestational complications were categorised as diabetes, hypertension, pre-eclampsia, liver dysfunction and other complications. Women who developed pregnancy complications were excluded from the study.

2.2. Maternal and cord blood measurements

Total blood volumes of 7 ml and 5 ml were taken from the mothers and cords, respectively. In addition to hepcidin values, the Human Hepcidin ELISA kit was used to measure hepcidin level in the samples taken from the mother 24-h prior to the birth and from the cord during the birth for complete blood count, iron, iron chelation capacity, transferrin saturation, ferritin and CRP as an infection marker. Hepcidin serum samples were stored at −80 °C for 3 months. The stored samples were later utilised for the measurement of hepcidin levels. Tests were performed with Hepcidin Prohormone ELISA (Solid Phase Enzyme-Linked Immunosorbent Assay) kits manufactured by USCN Life Science (USCN life Science, Inc., Wuhan, China) with the code number E 91979 Hu. Measurable ranges of hepcidin were 0–1000 ng/mL. The analytical sensitivity of hepcidin was found as <3.95 ng/mL, as given by the manufacturer.

2.3. Statistical analysis

Normal distribution suitability of the data was measured with the Shapiro–Wilk test. Data were expressed as mean ± standard deviation, median (25th percentile–75th percentile), frequency and percentages. Mann–Whitney U One-way variance analysis and the Kruskal–Wallis H test were used for the comparison of abnormally distributed data variables. The Spearman rank test was used for correlation analysis. $p < 0.05$ was considered as meaningful in the data analysis.

3. Results

A total of 102 infants and mothers were included in the study. Pregnant women were divided into three groups: 27 pregnant women under 33 weeks, 33 pregnant women between 33 and 37 weeks and 42 pregnant women over 37 weeks. The demographic features of the study population based on GW are given in Table 1, and the comparison of haematologic and biochemical parameters are given in Table 2 and Table 3, respectively.

Maternal and cord blood hepcidin levels were 135.0 ng/ml (6.40–2846.0) and 286.30 ng/ml (90–1697) for those under 33 GW (n = 27), 66.4 ng/ml (11.0–3936.0) and 406.9 ng/ml (10.0–1867) for those between 33 and 37 GW (n = 33), 41.4 ng/ml (2.8–513.7) and 498.1 ng/ml (343.7–701.7) for those over 37 GW (n = 42), respectively.

Hep(CB) [104.7 ng/ml (5.0–1022.0), n = 22] levels were lower for infants with ID (cord ferritin<60 μg/l) compared to those without iron deficiency (cord ferritin≥60 μg/l) [463.3 ng/ml (131.3–2261.0), $p < 0.0001$, n = 80)]. While a strongly positive relationship was observed between Hep(CB) levels and cord blood ferritin levels (Rho = 0.76, $p < 0.0001$) in the correlation analysis, a weak relationship (Rho = 0.29, $p = 0.004$) was found for transferrin saturation. Additionally, it was observed that Hep(CB) levels were directly proportional to GW (Rho = 0.23, $p < 0.0001$) and birth weight (Rho = 0.21, $p = 0.03$). Specific reference values based on GW are given in Table 4. A decrease of 10 units in Hep(CB) level increases risk for ID anaemia by 5% [OR = 0.95 (0.9297–0.98099)].

Furthermore, no correlation was observed among Hep(CB) levels and delivery method, mean corpuscular volume (MCV), cord blood iron and iron binding capacity. No statistically significant difference was observed in the hepcidin levels of infants delivered by mothers with ID [Maternal ferritin<30 μg/l]. In addition, no relationship was observed between mothers' iron and Hep(CB) levels.

Hep(M) and maternal ferritin levels decrease as GW increases, and these parameters are inversely proportional to Hep(CB). When hepcidin levels in maternal and cord blood were compared, it was found that the maternal hepcidin level was lower than the cord hepcidin level. No relationship was found between maternal and cord hepcidin levels.

4. Discussion

This study demonstrated that the increased levels of hepcidin prevented iron deficiency. There are many diseases in which inadequate iron absorption contributes to iron deficiency and anaemia. The treatment depends on the present hepcidin levels as oral treatment is unlikely to be effective when hepcidin blocks the enteral absorption. Parenteral iron treatment would be more appropriate for this treatment [2]. Our study found out that