Pediatrics and Neonatology (2016) xx, 1–7

Available online at www.sciencedirect.com

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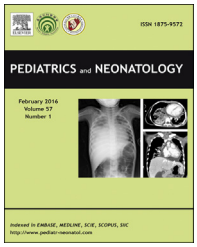

ORIGINAL ARTICLE

Maternal and Cord Blood Hepcidin Concentrations in Severe Iron Deficiency Anemia

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Received May 26, 2015; received in revised form Sep 7, 2015; accepted Sep 25, 2015
Available online ■ ■ ■

Key Words
cord blood;
ferritin;
hepcidin;
iron;
iron deficiency anemia;
maternal;
serum

Background: The present study was conducted to assess the maternal and cord blood hepcidin concentrations in severe iron deficiency anemia (IDA) and to find out its correlation with other iron status parameters.
Methods: This prospective observational study was carried out in 30 mothers with severe IDA (hemoglobin < 70 g/L and serum ferritin < 12 μg/L), and 15 healthy nonanemic (hemoglobin ≥ 110 g/L) mothers, who delivered live singleton neonates at term gestation. Mothers and neonates with infection/inflammatory conditions were excluded. Quantitative estimation of complete blood count, serum iron, ferritin, total iron binding capacity (TIBC), and transferrin saturation (Tfsat) was done in maternal and cord blood immediately after delivery by an auto analyzer. Serum hepcidin concentrations were measured by double-antibody sandwich enzyme-linked immunosorbent assay using a Human Hepcidin-25 kit. Data were analyzed by statistical software SPSS 16.0.
Results: The serum iron and ferritin concentrations in severe IDA were 6.7 ± 1.8 μmol/L and 4.1 ± 1.4 μg/L in maternal blood, and 9.5 ± 2.6 μmol/L and 55.4 ± 19.7 μg/L in cord blood, respectively, significantly lower than nonanemic controls ($p < 0.001$). The corresponding serum hepcidin concentrations were 76.6 ± 22.7 μg/L and 110.5 ± 11.8 μg/L, respectively ($p < 0.05$). The proportion of cord blood/maternal blood hepcidin concentration was similar in both anemic (1.4:1) and nonanemic (1.3:1) mothers. Significant correlation was observed among maternal and cord blood hepcidin concentrations and other iron status parameters.
Conclusion: Even in the presence of low serum iron and ferritin, maternal and cord blood

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http://dx.doi.org/10.1016/j.pedneo.2015.09.012

hepcidin concentrations remained high in severe anemia. Failure of this proportional suppression of hepcidin indicates poor systemic bioavailability of iron to the mother and poor placental transport.

1. Introduction

Iron is an essential micronutrient, necessary for oxygen transport and other vital biological processes of life. Worldwide, iron deficiency anemia (IDA) is the most common nutritional deficiency[1] and one of the major causes of anemia during pregnancy. As per the recent estimates, the worldwide prevalence of anemia in pregnant women is approximately 38%, and in $>$ 50% of them, the cause of anemia is iron deficiency.[2] The rate is even higher in developing countries, and India has the highest prevalence of maternal anemia in the world.[3]

Iron is necessary to support placental and fetal growth. Maternal IDA not only increases the incidence of maternal morbidity and mortality, but it also increases the risk of premature delivery, fetal growth restriction, and perinatal mortality and morbidity.[4–6] Moreover, maternal IDA precludes healthy neurodevelopment of the fetus, since iron is essential for proper neurogenesis, myelination, and neurocognitive maturity.[7,8] Impaired fetal iron transport may have lifelong, irreversible effects on future neurodevelopment.[9]

Iron requirement increases by nearly 10 times during pregnancy (0.8 mg/d in the 1st trimester to 7.5 mg/d in the 3rd trimester),[10] making iron accessibility critical throughout pregnancy. The developing fetus is entirely dependent on its mother for iron accretion, which takes place almost exclusively via the placenta. Placental iron homeostasis results from the tightly coordinated regulation of various proteins involved in iron uptake, transport, intracellular storage, and iron trafficking. The major regulator of systemic iron bioavailability in the human body is hepcidin, a small 25 amino acid amphipathic peptide hormone.[11] Hepcidin has also been documented recently to be one of the key determinants of placental transport of iron and the regulator of maternofetal iron transfer during pregnancy.[12] The fetal hepcidin-placental-ferroportin axis represents an important element in the fetus-dependent control of iron transport through the placenta.[13]

In a developing country like India, most pregnant women are iron-depleted and hardly receive any nutritional or iron supplementation during pregnancy. Although previous authors have shown a significant association among placental transport of iron and maternal hepcidin concentration,[11,12,14–17] no study has documented the state of maternal and fetal hepcidin concentration in the presence of severe maternal IDA. In the present study, we measured serum hepcidin and other iron status parameters, such as complete blood count, serum iron, ferritin, total iron binding capacity (TIBC), and transferrin saturation (Tfsat) in mothers with severe IDA and cord blood of their neonates. We also looked for any correlations among the parameters.

2. Methods

This study was carried out in the Neonatal Unit, Department of Pediatrics, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India, after obtaining approval from the Institute Ethics Committee.

2.1. Study participants

Consecutively admitted mothers with severe IDA, who delivered live singleton neonates at term gestation (37–41 weeks), formed the case group. Severe IDA was defined as a hemoglobin $<$ 70 g/L and serum ferritin $<$ 12 μg/L. Mothers with hemolytic anemias including thalassemia and sickle cell anemia, chronic infection/inflammatory diseases, hemochromatosis, chronic kidney disease, chorioamnionitis, infection with human immunodeficiency virus/ hepatitis B/syphilis, Toxoplasma, Rubella, Cytomegalovirus, Herpes (TORCH) infections, malaria, pregnancy induced hypertension, diabetes, and other obstetric complications were excluded from the study. Neonates with perinatal asphyxia, early-onset neonatal sepsis, isoimmune hemolytic anemias, and congenital malformations were also excluded.

Healthy nonanemic mothers with hemoglobin $\geq$ 110 g/L, delivering live singleton neonates at term gestation, served as controls. A written informed consent in the local language was taken from all parents before inclusion in the study.

2.2. Clinical work-up

Demographic details, as well as antenatal and perinatal history including iron and folic acid supplementation received by the mother during pregnancy, were noted. Nutritional status of the mother was determined by measuring weight, height, and body mass index after at least 48 hours of childbirth. Neonates were examined thoroughly after birth to exclude any congenital malformation or other systemic diseases. Birth weight was taken soon after birth. Gestational age was assessed from maternal history and antenatal ultrasound, and clinically corroborated after birth by the New Ballard Score.[18] Neonates were observed for development of any complications during the hospital stay and managed as per our unit protocol.

Please cite this article in press as: Basu S, et al., Maternal and Cord Blood Hepcidin Concentrations in Severe Iron Deficiency Anemia, Pediatrics and Neonatology (2016), http://dx.doi.org/10.1016/j.pedneo.2015.09.012