

ORIGINAL ARTICLE

Umbilical Cord Blood Leptin Concentration – What Does It Imply?

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ABSTRACT

Objective: The significance of the placental or umbilical cord leptin levels remains unresolved in spite of their well-documented function. In the current study we investigated, whether, leptin concentration that mirrors the fetal health is influenced by type of birth, placental weight, cord length, sex, weight, pO₂ and pH parameters. **Methods:** Umbilical cord blood samples were collected post placental delivery (n=40) from both normal and caesarian deliveries with all demographical information. Leptin concentration was determined from cord blood plasma, while fresh cord blood was used for blood gas analysis. **Results:** The average leptin concentrations of male and female fetal umbilical cord were 16.6 ± 1.6 and 18.2 ± 0.6 ng/ml respectively. The maximum threshold of the umbilical vein leptin concentrations were 15.3 ± 0.6 and 18.3 ± 1.2 ng/ml in male and females respectively. There was a direct relationship observed with the birthweight and leptin concentration. The mean pH 7.117 ± 0.02 and pO₂ 19.74 ± 2.01 mmHg did not significantly correlate with leptin levels. **Discussion:** Leptin concentration were significantly high in normal delivery than caesarian section. Placental weight or umbilical cord length did not affect the leptin concentration. We did not observe any significant alteration in pH or pO₂ levels influencing leptin. However, the most remarkable correlation was leptin with birth weight, which explains the best utilization of the maternal fuel resources in the development of the fetus. We did observe a level in female babies. **Conclusion:** Overall, the placental leptin concentration mirrors the health status of the fetus and weight metabolism.

Keywords: Leptin, Placental leptin, Cord blood leptin, Fetal obesity, Umbilical cord blood markers.

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INTRODUCTION

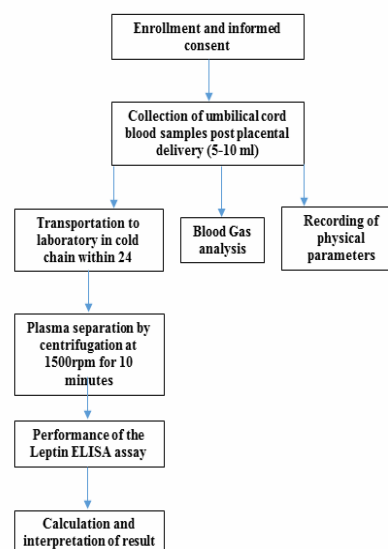
Leptin was discovered in the year 1994.¹ Leptin is a 16-kD protein encoded by the obese (*ob*) gene. Identifying the genes regulated by leptin will improve our understanding on regulation of weight and appetite.² It is known that during pregnancy, important changes occur in the body weight of the mother, which is caused by sodium and water retention and by an increase in body fat tissue, but the mechanisms that regulate maternal and fetal changes in fat mass are not clearly understood.³⁻⁴ Leptin is secreted in adipocytes as a regulatory hormone controlling food intake and energy expenditure. Any physiological imbalance in the production of leptin results in problems associated with obesity. Many genes at transcriptional levels control the leptin production and regulation.^{5,6} There are many functions attributed to the hormone leptin including regulation of ovarian function, oocyte maturation and embryo development, and in the implantation process. Further leptin is known to cross blood brain barrier and binds to specific receptors in the hypothalamus. These receptors produce a coordinated series of responses to match rates of energy utilization to regulate body weight causing a decrease in food intake and an increase in body temperature and energy expenditure. Hence, leptin resistance is a cardinal feature of human obesity.⁷⁻⁹ It represents a break down in the communication system between adipose tissue and the brain, which regulates stabilization of body weight on whole. Further leptin is known to be associated with functions associated with neuroendocrine function,¹⁰ angiogenesis,^{11,12} bone formation¹³ and reproduction¹⁴ in both adults and neonates. In pregnancy, leptin is known to regulate fetal growth, placental angiogenesis and mobilization of maternal fat.¹⁵ It may be noted that serum leptin levels in pregnant women are significantly higher than in non-pregnant women.¹⁶ The human placenta expresses high amounts of leptin mRNA and protein in early, mid, and late gestation^{17,18} though adipocytes have not been found in placental tissue.^{19,20} Leptin produced in the placenta deems increase in the maternal blood particularly in the second trimester and decline postpartum. Abnormally high levels of leptin have been observed in pregnancies complicated by conditions such as diabetes mellitus and pre-eclampsia.^{21,22} The role of leptin in fetal physiology is not clear, although cord blood values

correlate significantly with birth weight.

Therefore many areas of leptin physiology remain to be investigated. Especially the role of leptin in fetal metabolism, insulin sensitivity, and its involvement in endocrine function are active areas for research. While the future for leptin as a diagnostic, prognostic, or therapeutic agent is not clear, its involvement in many areas of physiology undoubtedly makes this a new hormone, which requires extensive study in the future to understand its physiology.

The main objective of this study is to explore the importance of cord blood leptin concentration as a marker of fetal health as reflected by fetal weight at birth.

OVERVIEW OF THE STUDY



MATERIALS AND METHODS

Umbilical cord blood samples (n=40) were collected from Abha maternity and children hospital after obtaining informed consent. The ethical clearance was obtained from the ethics committee at College of Medicine, King Khalid University (approval number REC # 2015-03-11). Cord blood serum was used to assess the leptin concentration at the stem cell unit, College of Medicine. Demographical data such as birth weight, sex, mode of delivery, placental weight and umbilical cord length were documented. Blood gas analysis were done immediately post cord blood collection at the

hospital premises by routine standard procedure.

Leptin ELISA

Leptin ELISA kit was purchased from Diagnostic Biochem Canada Inc. The assay was performed as per manufacturer instructions. Briefly the antibody coated microwell plate was incubated with known volume of cord blood serum, washed and re-incubated with sandwich antibody followed by substrate. The corrected readings were compared with standards and controls for calculating the concentration of Leptin in the cord blood samples.

Statistical Analysis

The leptin data are represented as the mean ± standard deviation. Statistical significance between the samples and controls, calculated by student t test as applicable. A p < 0.05 was considered statistically significant. Graph Pad Prism 5 used for the statistical assessment.

RESULTS

Among the variables examined, birth weight, but not the sex showed the highest degree of relationship with cord blood serum leptin concentration in newborns. Since we did not observe a significant difference in sex, though cord blood leptin from female babies were higher compared to the male, we merged male and female for the parameters like placental weight, umbilical cord length, pH and pO₂. Placental weight and leptin concentration showed a highly significant correlation (Table 1A), while umbilical cord length compared with leptin levels did not show significant correlation.

The average leptin concentration of male and female fetal umbilical cord were 16.6 ± 1.6 and 18.2 ± 0.6 ng/ml respectively (Fig1). We observed a higher concentration of the leptin for female babies and could not correlate to statistically significant observation in the current study. The maximum threshold of the umbilical vein leptin concentrations were 15.3 ± 0.6 and 18.3 ± 1.2 ng/ml in male and females respectively (Fig 2A, B). Though as mentioned above, female newborn umbilical cord had significantly higher plasma leptin concentration than males. None of the samples showed leptin concentration more than 15.4 and 18.5 ng/ml in cord blood serum collected from both male and female babies respectively (Fig 2A, B).

Figures and Tables

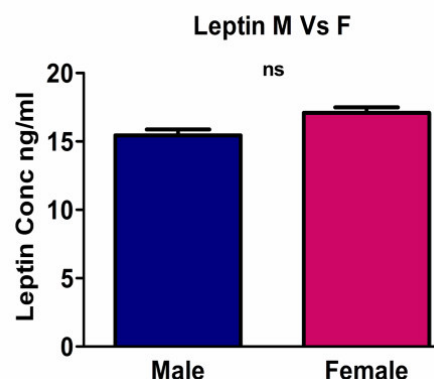


Fig 1. Umbilical cord leptin concentration; male and female

A				
Parameters (M&F)	Weight in Grams (g)			p-Value*
Placental Weight	400 -500	501-600	601 -700	0.0013
Leptin Conc ng/ml (Ave)	15.1	16.775	15.06	
Length in cms				
UC Length	40-45	46-50	51-55	0.3679
Leptin Conc ng/ml (Ave)	16.23	16.12	16.03	
* < 0.05				
B				
Parameters (M&F)	pH			p-Value*
pH	< 6.5	6.6-7.2	> 7.3	NA
Leptin Conc ng/ml (Ave)	0	16.65	0	
PO ₂ mm/Hg				
PO ₂	10 to 15	16 -20	> 21	0.145
Leptin Conc ng/ml (Ave)	16.33	15.98	16.06	
* < 0.05				

Table 1: A. Leptin Conc Vs Placental Weight and UC Length. B Leptin Conc Vs pH and P_O₂

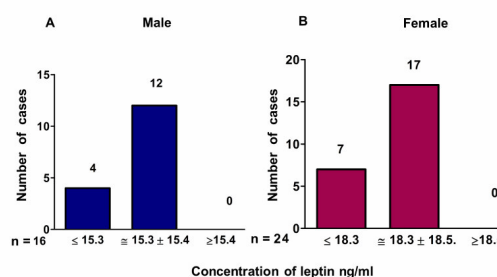


Fig 2. A. Leptin Threshold in Male (n = 16). B Leptin threshold in Female (n = 24)

The next parameter we measured was pH and pO₂ levels of the freshly collected cord blood (Table 1B). The mean pH 7.117 ± 0.02 and pO₂ 19.74 ± 2.01

mmHg did not significantly correlate with leptin levels. The pH of the cord blood irrespective of leptin concentration was within 6.5 to 7.2 and none showed less or above the depicted values (Table 1B). The most significant correlation was between the birth weight and leptin concentration. Cord blood leptin concentration was directly proportional to the birth weight of infants (Fig 3 A, B). An average age of 2.8 to 2.9 kg showed optimal leptin concentration compared to the low or obese in both male and female babies.

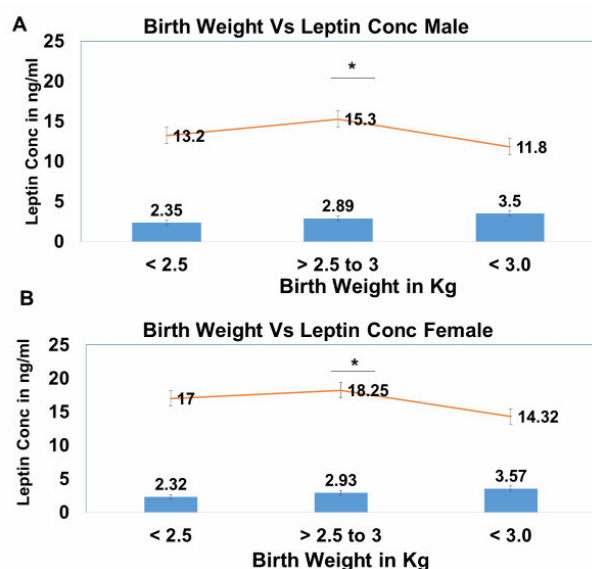


Fig 3. A. Male birth weight Vs Leptin (n = 16). B. Female birth weight Vs Leptin threshold (n = 24)

DISCUSSION

The significance of the current study is the use of the cord blood leptin as marker for fetal health. For instance, in the gynecologic surgery the serum leptin concentration is modified reflecting positive or negative impact on energy turnover. The same phenomenon is observed during caesarian²³⁻²⁵ reflecting the importance of the leptin concentration associated with women health. Our current study results did not show a statistical significant variation between male and female babies with slightly higher concentration of leptin observed in the female umbilical cord. These were consistent with range observed in various other studies. The significance of

umbilical cord leptin concentration is regarded as indicator of gynecobstetric diseases.²⁶ Since leptin has multiple functions such as gonadal regulation, regulation of fetal-placental metabolism, actions in the endometrium, mammary gland, the concentration of the placental and umbilical cord leptin is very important during pre and post pregnancy stages. Recently the importance of the leptin and the knowledge of serum leptin concentration in the oncological diseases is going-up. Though we do not know the correlation of the leptin levels with cancer incidence, there are various reports explaining the modified leptin levels in the choriocarcinoma, Meigs' syndrome and other tumors.²⁷

The relation between the fetal weight and leptin concentration is an indicator of the obesity at adulthood. A better understanding of regulatory mechanisms will have direct clinical significance, as leptin has been proposed to affect the causes of human perinatal morbidity and mortality that are associated with abnormalities of fetal maturity and development, general concept growth, trophoblast endocrinology, and placental sufficiency.²⁸ Further placental or cord leptin levels can be attributed to influence the physiology of female health issues pertaining to menstruation, pregnancy and lactation. There was a direct relationship observed with the birthweight and leptin concentration. These results were comparable with the published results of the studies done elsewhere.²⁹

The trend was so that, with increase in weight of the infant, the lower was the concentration of the cord blood leptin. This observation showed that increased fetal adipose tissue might decrease the leptin secretion at transcriptional level.³⁰ Overall, the variation in the concentration of leptin between individuals is mainly due to the environmental factors experienced by the mother during the course of gestation. This might be an influencing factor for higher weight babies or obese babies. Among the type of delivery, about 80% of the deliveries were normal and 20% were cesarean (data not shown). However, our data suggested that leptin levels were low in high weight babies, which is also reflected in some of the cesarean cases too, were due to eclampsia experienced by the women during delivery process. Hence, we could not determine any significance with the mode of the birth and leptin concentration. Further investigations in this area will

be necessary to improve new knowledge and a better understanding of the actions about this hormone related to fetal and mother health.

CONCLUSION

Higher concentration of the leptin with positive birth weight correlates the best utilization of the maternal fuel resources in the development of the fetus. We do not know the reason for the increased leptin levels in female cord blood samples. Overall the placental leptin concentration mirrors the health status of the fetus.

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