

# Relationship between newborn leptin levels and selected growth parameters

Journal of International Medical Research

2019, Vol. 47(6) 2591–2597

© The Author(s) 2019

Article reuse guidelines:

[sagepub.com/journals-permissions](http://sagepub.com/journals-permissions)

DOI: 10.1177/0300060519848613

[journals.sagepub.com/home/imr](http://journals.sagepub.com/home/imr)



Amer Mahmoud Sindiani , Rawan Obeidat,  
Omar Jbarah and Ethar Hazaimh

## Abstract

**Objectives:** This study aimed to determine leptin levels in term newborns who were born in the north of Jordan. We also aimed to investigate the relationships of leptin levels with fetal growth parameters, and to assess the difference in leptin levels according to sex and gestational age.

**Methods:** A cross-sectional descriptive study that involved 170 term newborns was conducted. A working sheet for data collection was created for each newborn and included sex, weight, length, head circumference, gestational age, and Apgar score. Blood samples were obtained from the umbilical cord vein of newborns after delivery to measure serum leptin levels. Data are shown as frequency, percentages, means, and standard deviations.

**Results:** We found that the mean leptin level was  $1.17 \pm 0.48$  ng/mL. The independent t-test showed that the mean leptin level in boys ( $0.93 \pm 0.34$  ng/mL) was significantly lower than that in girls ( $1.38 \pm 0.47$  ng/mL). Pearson's correlations showed that leptin levels of newborns were positively and significantly correlated with weight, length, and head circumference.

**Conclusion:** In Jordanian healthy term newborns, leptin levels correlate with sex and intrauterine growth parameters.

## Keywords

Leptin, newborn, weight, length, Apgar score, head circumference

Date received: 2 October 2018; accepted: 15 April 2019

## Introduction

Leptin is considered an anorexigenic hormone that has an important function in regulating energy by lowering food intake and increasing consumption of energy.<sup>1–4</sup>

Department of Obstetrics and Gynecology, Faculty of Medicine, Jordan University of Science and Technology, Irbid, Jordan

### Corresponding author:

Amer Mahmoud Sindiani, Department of Obstetrics and Gynecology, Faculty of Medicine, Jordan University of Science and University, P.O. box 3030, Jordan Street, Irbid, 22110 Jordan.

Email: [amsindiani0@just.edu.jo](mailto:amsindiani0@just.edu.jo)



Adipose tissue is the main site of leptin production and to some extent it is produced by the placenta, stomach, and mammary epithelium.<sup>5-7</sup> Leptin plays an important role in development of a neonate's hypothalamic pathways and is involved in controlling energy and appetite.<sup>8</sup> Evidence from animal studies has suggested that leptin can act on the brain to improve formation of the neural circuits regulating future food intake and adiposity.<sup>9</sup> Many studies have focused on adult leptin levels and their correlation with body mass index, but limited studies have investigated newborn leptin levels and their correlation with intrauterine growth.<sup>10</sup>

In a cross-sectional study<sup>10</sup> on cord blood samples that were taken from 50 newborns, cord blood leptin levels were correlated with fetal growth. Recently, Ökdemir et al.<sup>11</sup> conducted a study on 84 mothers and their newborns to examine the relationships between leptin levels and maternal weight gain and newborn anthropometric measurements. These authors showed that in newborns, leptin levels significantly varied according to birth weight ( $P=0.013$ ). Furthermore, leptin levels were associated with fetal adiposity. Schuster et al.<sup>12</sup> conducted a prospective, longitudinal study to evaluate leptin levels in the blood of 23 healthy lactating mothers and in their breast milk, as well as in their neonates. These authors showed that serum leptin levels were much higher than those in breast milk.

A review of the relevant literature in Jordan showed some studies on leptin among adults, but no studies on leptin in newborns. Abu-Samak et al.<sup>13</sup> conducted a study to analyze the effect of hyperleptinemia on fasting lipid and hematological parameters in healthy young men in Jordan. These authors found that mean serum leptin levels were higher in those with hyperlipidemia than in those without hyperlipidemia.

The current study aimed to determine newborn leptin levels in the north of Jordan, to investigate the relationships between newborn leptin levels and selected growth parameters, such as weight, length, and head circumference, and to assess the differences in leptin levels according to sex and gestational age.

## **Methods**

### *Study design*

A descriptive-cross-sectional design was used to assess the relationship between newborn leptin levels and selected growth parameters, and to assess the differences in leptin levels according to sex and gestational age.

### *Samples and sampling technique*

A convenient sampling technique was used to recruit a convenience sample of 170 term newborns whose mothers agreed to participate in this study. Using a convenience sample may affect the external validity of the results because it is unlikely to be representative of the population under study. The eligibility criteria for the participants were as follows: term newborns of mothers who had no medical illnesses during their pregnancies, and mothers were aged older than 18 years old and agreed to include their newborns in the current study. Newborns of mothers with medical illness or those who were delivered preterm were excluded.

The sample size was calculated on the basis of parameters of G\* power software (free software).<sup>14</sup> The sample size required was 138 participants on the basis of the following statistical factors for Pearson's r: an alpha level of 0.05, a power level 0.95, and an effect size of 0.30. To overcome the problem of attrition or missing data, an extra 32 term newborns were included in

the final sample size to have at least 170 participants.

### *Site and setting of the study*

This study was conducted in the University Educational Hospital in Irbid Province, which has the second largest metropolitan population in Jordan after Amman. The total capacity of this hospital is more than 650 beds with an impressive occupancy rate of close to 99%. This hospital includes different specialties, such as internal medicine, cardiology, orthopedics, pediatric neurology, maternity, and dermatology.

### *Study procedure*

The study method and protocol were approved by the Institutional Review Board of the University Hospital. Written informed consent was obtained from the newborns' mothers, who agreed to include their newborns in the study. The confidentiality of the participants was protected by providing a code number for each participant during the data collection and analysis phases of the study. No physical, psychological, social, or economic harm or risk affected the newborn. There were no complications in the blood sample collection process for the newborns. No blood loss, infections, or complications developed during or after the procedure. A qualified competent staff nurse was responsible for obtaining blood samples from the umbilical cord of the newborns. This procedure was performed under a hospital policy of withdrawing blood under an aseptic technique. A blood sample was taken as a routine check for each newborn in the period immediately after delivery.

Files of the newborns and mothers were carefully checked to ensure their eligibility to participate in the study. The primary researcher collected data regarding sex, weight, length, gestational age, head

circumference, and Apgar score. To measure serum leptin levels, blood samples were obtained from the umbilical cord vein of the newborn after delivery.

### *Serum leptin measurement*

Approximately 5 mL of venous blood was collected from each newborn in a serum separator tube. The samples were allowed to clot for 2 hours at room temperature or overnight at 4°C before being centrifuged for 15 minutes at 1000 × g. The serum was then removed and assayed immediately or divided into aliquots, and the samples were stored at -80°C.

Quantitative measurement of serum leptin levels was performed using a leptin enzyme immunoassay or Human Leptin ELISA kit (MBS700713; MyBioSource, San Diego, CA, USA) according to the manufacturer's instructions. This assay uses the quantitative sandwich enzyme immunoassay technique. Antibody specific for leptin was pre-coated onto a microplate. Standards and samples were then pipetted into the wells and any leptin present was bound by the immobilized antibody. After removing any unbound substances, a biotin-conjugated antibody, specific for leptin, was added to the wells. After washing, avidin-conjugated horseradish peroxidase was added to the wells. Following a wash to remove any unbound avidin-enzyme reagent, a substrate solution was added to the wells and color developed in proportion to the amount of leptin that was bound in the initial step. Color development was stopped and the intensity of the color was then measured.

### *Statistical analysis*

Descriptive statistics, including frequency, percentage, mean, and standard deviation, are used to describe the data. The relationships between leptin levels and newborns'

growth parameters (weight, length, and head circumference) were tested using Pearson’s product-moment correlations. The independent t-test was also used to examine differences in leptin levels according to sex and gestational weeks. Significance was considered at  $P < 0.05$ .

**Results**

*General characteristics of newborns*

The newborns’ characteristics are shown in Table 1. The mean leptin level was  $1.17 \pm 0.48$  ng/mL, the mean birth weight was  $3.11 \pm 0.52$  kg., and the mean length was  $49.71 \pm 2.20$  cm. The mean gestational age was  $38.28 \pm 1.36$  weeks, and it ranged from 37 to 42 weeks. More than half of the newborns were girls ( $n = 92$ ).

*Effect of sex and gestational age on newborn leptin levels*

The mean leptin level in boys was significantly lower than that in girls ( $t[168] = 2.62$ ,  $P = 0.010$ , Table 2). Furthermore, the difference between the mean leptin level in newborns delivered at 37 to 38 weeks’ gestational age and the second group of

newborns delivered at  $>38$  to 42 weeks’ gestational age was not significant ( $t[168] = -0.39$ ).

*Relationship between newborn leptin levels and growth parameters*

There was a significant, but weak, positive correlation between leptin levels and newborn weight ( $r[168] = 0.16$ ,  $P = 0.044$ ). Furthermore, Pearson’s correlation also showed that there was a significant, but weak, positive correlation between leptin levels and newborn length ( $r[168] = 0.15$ ,  $P = 0.049$ ). Moreover, there was a significant, but weak, positive correlation between

**Table 2.** Effect of sex and gestational age on newborn leptin levels ( $n = 170$ ).

Variable	Standard		t(168)	P value
	Mean	deviation		
Boys	0.93	0.34	2.62	0.010
Girls	1.38	0.47		
37–38 gestational weeks	1.15	0.48	-0.39	0.69
>38–42 gestational weeks	1.22	0.52		

P was determined by the independent t-test

**Table 1.** Sample characteristics of the newborns ( $n = 170$ ).

Variable	Mean (SD)	Range	n (%)
Leptin levels (ng/mL)	1.17 (0.48)	0–4	
Birth weight (kg)	3.11 (0.52)	2–4	
Length (cm)	49.71 (2.20)	36–55	
Head circumference (cm)	35.15 (1.99)	29–53	
Apgar score at 1 minute	8.34 (1.00)	4–10	
Apgar score at 5 minutes	9.53 (0.74)	8–10	
Sex			
Boys			78 (45.9)
Girls			92 (54.1)
Gestational age categories			
37–38 gestational weeks			110 (64.7)
>38–42 gestational weeks			60 (35.3)

SD standard deviation.

**Table 3.** Pearson's correlations between newborn leptin levels and their growth parameters (n = 170).

Variable	Weight	Length	Head circumference	Apgar score at 1 minute	Apgar score at 5 minutes
Leptin	0.16 *	0.15*	0.16*	-0.02	-0.07

Values are shown as Pearson r. \*P < 0.05.

leptin levels and newborn head circumference ( $r[168]=0.16$ ,  $P=0.032$ ). However, there were no significant correlations between the Apgar score at 1 minute ( $r[168]=-0.02$ ) and the Apgar score at 5 minutes ( $r[168]=-0.07$ ) and leptin levels (Table 3).

## Discussion

The present study showed that the mean leptin level in Jordanian newborns was  $1.17 \pm 0.48$  ng/mL. In Ohkawa et al.'s study,<sup>15</sup> serum leptin levels of newborns were less (approximately 0.8 ng/mL) than those in our study. Our study showed that female newborns had higher leptin levels compared with male newborns. This finding is generally consistent with the results obtained by Torgerson et al.,<sup>16</sup> who reported that women had significantly higher levels of leptin than did men ( $P < 0.05$ ). Some studies reported differences in leptin levels between males and females that were attributed to differences in body composition, to variations in hormones, and to genes responsible for sex specifications.<sup>17</sup> Other studies have reported that sex hormones have different effects on leptin levels; testosterone has an inhibitory effect on leptin, whereas estrogen has a stimulatory effect.<sup>18</sup> However, a prospective cohort study<sup>19</sup> of 100 women who had full term newborns showed no significant difference in leptin levels between male and female newborns.

Our study showed positive correlations between newborn leptin levels and weight, length, and head circumference. These findings are consistent with the results of other studies as follows. Koistinen et al.<sup>10</sup> reported a positive correlation between leptin levels and fetal growth. Mantzoros et al.<sup>20</sup> found that leptin was a predictor of weight gain. Savino et al.<sup>21</sup> reported a relationship between serum leptin levels and body mass index ( $P=0.042$ ). However, Karakosta et al.<sup>22</sup> found a negative association of blood leptin levels with growth in early childhood. Additionally, another study conducted by Tung et al. (2009)<sup>23</sup> assessed the relationship between venous umbilical cord leptin levels and anthropometric measurements in term healthy Taiwanese newborns. These authors found that birth weight was the only predictor of leptin levels.

There was no association between newborn leptin levels and their Apgar scores in our study. This finding is not in agreement with that of Taghreed et al.<sup>24</sup> who reported a positive correlation between the Apgar score and leptin levels. However, these authors found growth-restricted fetuses had lower blood leptin levels compared with controls.

## Conclusions

We conclude that leptin is present *in utero* and it correlates with intrauterine growth parameters in newborns in Jordan. This finding confirms the results of other studies

about the possible role of leptin in fetal growth.

### Study recommendations and implications

A larger, randomly selected, and heterogeneous sample of participants from north, central, and south Jordan is required in the future to make our findings more widespread and applicable. This research can be considered a baseline for conducting other research projects that aim to assess changes in leptin levels in patients with comorbid diseases, such as diabetes and obesity. Furthermore, longitudinal research studies need to be conducted to assess the changes in leptin levels over time and their relationship with different physiological parameters.

This study provides better understanding of fetal growth and different factors that participate in growth. Future studies may implement multiple factors to predict newborns that are growth restricted rather than being small for gestational age.

### Study limitations

This study has some limitations. Restriction of the study to the north of Jordan and use of a convenience sample of newborns could pose a problem for its generalizability, and affect the external validity of the results. Therefore, we recommend that further studies be conducted, using a larger more heterogeneous sample, thereby enhancing the generalizability of the findings.

### Acknowledgements

The authors would like to thank the study participants and Jordan University of Science and Technology.


### Declaration of conflicting interest

The authors declare that there is no conflict of interest.

### Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

### ORCID iD

Amer Mahmoud Sindiani  <https://orcid.org/0000-0001-5115-7372>

### References

1. Olga M, Juana S, Andreu P, et al. A physiological role of breast milk leptin in body weight control in developing infants. *Obesity* 2006; 14: 1371–1377.
2. Perianes-Cachero A, Burgos-Ramos E, Puebla-Jiménez L, et al. Leptin-induced downregulation of the rat hippocampal somatostatinergic system may potentiate its anorexigenic effects. *Neurochem Int* 2012; 61: 1385–1396.
3. Sobrino Crespo C, Perianes Cachero A, Puebla Jiménez L, et al. Peptides and food intake. *Front Endocrinol (Lausanne)* 2014; 5: 58.
4. Deck CA, Honeycutt JL, Cheung E, et al. Assessing the functional role of leptin in energy homeostasis and the stress response in vertebrates. *Front Endocrinol (Lausanne)* 2017; 8: 63.
5. Galic S, Oakhill JS and Steinberg GR. Adipose tissue as an endocrine organ. *Mol Cell Endocrinol* 2010; 316: 129–139.
6. Itoh M, Suganami T, Hachiya R, et al. Adipose tissue remodeling as homeostatic inflammation. *Int J Inflam* 2011; 2011: 720926.
7. Coelho M, Oliveira T and Fernandes R. Biochemistry of adipose tissue: an endocrine organ. *Arch Med Sci* 2013; 9: 191–200.
8. Woods SC and D'Alessio DA. Central control of body weight and appetite. *J Clin Endocrinol Metab* 2008; 93: S37–S50.
9. Bouret SG and Simerly RB. Developmental programming of hypothalamic feeding circuits. *Clin Genet* 2006; 70: 295–301.
10. Koistinen HA, Koivisto VA, Andersson S, et al. Leptin concentration in cord blood correlates with intrauterine growth. *J Clin Endocrinol Metab* 1997; 82: 3328–3330.



11. Okdemir D, Hatipoglu N, Kurtoglu S, et al. The role of irisin, insulin and leptin in maternal and fetal interaction. *J Clin Res Pediatr Endocrinol* 2018; 10: 307–315.
12. Schuster S, Hechler C, Gebauer C, et al. Leptin in maternal serum and breast milk: association with infants' body weight gain in a longitudinal study over 6 months of lactation. *Pediatr Res* 2011; 70: 633.
13. Abu-Samak M, Yousef AM, Al-Jarie A, et al. Lipid and hematological parameters in hyperleptinemic healthy Arab male youth in Jordan. *Pak J Biol Sci* 2011; 14: 344–350.
14. Faul F, Erdfelder E, Lang AG, et al. G\*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behav Res Methods* 2007; 39: 175–191.
15. Ohkawa N, Shoji H, Ikeda N, et al. Relationship between insulin-like growth factor 1, leptin and ghrelin levels and catch-up growth in small for gestational age infants of 27–31 weeks during neonatal intensive care unit admission. *J Paediatr Child Health* 2017; 53: 62–67.
16. Torgerson JS, Carlsson B, Stenlöf K, et al. A low serum leptin level at baseline and a large early decline in leptin predict a large 1-year weight reduction in energy-restricted obese humans. *J Clin Endocrinol Metab* 1999; 84: 4197–4203.
17. Wilkin TJ and Murphy MJ. The gender insulin hypothesis: why girls are born lighter than boys, and the implications for insulin resistance. *Int J Obes (Lond)* 2006; 30: 1056.
18. Vázquez MJ, Romero-Ruiz A and Tena-Sempere M. Roles of leptin in reproduction, pregnancy and polycystic ovary syndrome: consensus knowledge and recent developments. *Metabolism* 2015; 64: 79–91.
19. Ali MA, Salman DA and Hallab HS. Neonatal and placental birth weight and its correlation with leptin level in maternal and cord blood. *Iraqi Med J* 2017; 63: 97–104.
20. Mantzoros CS, Rifas-Shiman SL, Williams CJ, et al. Cord blood leptin and adiponectin as predictors of adiposity in children at 3 years of age: a prospective cohort study. *Pediatrics* 2009; 123: 682–689.
21. Savino F, Liguori SA, Fissore MF, et al. Looking for a relation between serum leptin concentration and body composition parameters in healthy term infants in the first 6 months of life. *J Pediatr Gastroenterol Nutr* 2008; 46: 348–351.
22. Karakosta P, Roumeliotaki T, Chalkiadaki G, et al. Cord blood leptin levels in relation to child growth trajectories. *Metabolism* 2016; 65: 874–882.
23. Tung WK, Lin SJ, Hwang YS, et al. Association of cord plasma leptin with birth size in term newborns. *Pediatr Neonatol* 2009; 150: 255–260.
24. ALhaidari TK, Tuma WE and Jassim TK. The effect of leptin level in pregnancy complicated by intrauterine growth restriction on neonatal outcome, in an Iraqi center. *Al-Kindy Col Med J* 2012; 8: 1–13.