Annals of Medicine and Surgery 72 (2021) 103050

Contents lists available at ScienceDirect

Annals of Medicine and Surgery

journal homepage: www.elsevier.com/locate/amsu

Cross-sectional Study

Maternal and fetal serum leptin levels and their association with maternal and fetal variables and labor: A cross-sectional study

Rawan A. Obeidat [a,*], Nour Abdo [b], Baraa Sakee [a], Shahed Alghazo [a], Omar F. Jbarah [c], Ethar A. Hazaimeh [d], Soha Albeitawi [e]

[a] Department of Obstetrics and Gynecology, Faculty of Medicine, Jordan University of Science and Technology, Irbid, Jordan
[b] Department of Public Health and Family Medicine, Faculty of Medicine, Jordan University of Science and Technology, Irbid, Jordan
[c] Department of Neuroscience, Neurosurgery Division, Faculty of Medicine, Jordan University of Science and Technology, Irbid, Jordan
[d] Department of Neuroscience, Neurology Division, Faculty of Medicine, Jordan University of Science and Technology, Irbid, Jordan
[e] Department of Obstetrics and Gynecology, Faculty of Medicine, Yarmouk University, Irbid, Jordan

ARTICLE INFO

Keywords:
Intrauterine growth restriction (IUGR)
Leptin
Macrosomia
Premature rupture of membranes

ABSTRACT

Background: Leptin is a polypeptide hormone that may be implicated in the pathogenesis of various disorders during pregnancy. We sought to determine serum leptin levels among pregnant women and their fetuses and to investigate their association with fetal and maternal variables.

Method: 452 pregnant women who attended to labor ward between January 2020 and August 2020 were included in the study. Serum leptin concentrations were measured using enzyme-linked immunosorbent assay method. Mann-Whitney *U* test and Spearman's correlation test were used for statistical analysis. A multivariate linear regression analysis was then performed. Significance level was considered at alpha <0.05.

Results: The median maternal and fetal serum leptin levels were 6.42 [4.16–8.51] ng/mL and 2.9 [1.03–5.36] ng/mL respectively. There was no significant correlation between maternal and fetal serum leptin levels ($p = 0.064$). Maternal serum leptin levels correlated positively with maternal body mass index (BMI) ($r = 0.117$, $p = 0.005$). Besides, maternal serum leptin levels were significantly higher in nulliparous women (7.57 [4.45–9.30] ng/mL vs. 6.22 [4.02–8.30] ng/mL, $p = 0.037$) and in women who were in active labor (6.83 [4.39–8.92] ng/mL vs. 6.25 [4.04–8.30] ng/mL, $p = 0.047$). Fetal serum leptin levels were significantly higher in large for gestational age (LGA) fetuses (4.81 [2.13–7.22] ng/mL vs. 2.80 [0.96–5.16] ng/mL, $p = 0.003$) and in fetuses with preterm premature ruptures of membranes (PPROM) (5.23 [2.42–8.07] ng/mL vs. 2.86 [1.00–5.23] ng/mL, $p = 0.021$).

Conclusion: Maternal serum leptin levels were influenced by maternal BMI, parity and labor. Fetal serum leptin levels were higher among LGA fetuses and in fetuses with PPROM.

1. Introduction

Leptin is a polypeptide hormone that plays an important role in modulating satiety and energy homeostasis and in regulating glucose metabolism [1,2]. Also, it is involved in the regulation of immune responses and inflammations and the control of reproductive functions particularly embryonic development [1,3,4]. Leptin is mainly synthesized and secreted by white adipose tissue [3–5]. Leptin acts mainly by binding to specific central and peripheral receptors in the hypothalamus, adipose tissue, liver and pancreas [4].

Maternal serum leptin levels increase 2–3 fold during pregnancy, particularly in the second trimester, and decline postpartum [1,2,6]. The role of leptin in pregnancy has not been fully elucidated but it is suggested to regulate trophoblast invasion, human chorionic gonadotrophin, pro-inflammatory cytokines and prostaglandins production, placental growth, amino acid uptake, and angiogenesis and mitogenesis [2,3]. Bedsides, compelling evidence suggests a role for leptin in fetal growth and development [1].

During pregnancy, leptin is produced in both maternal and fetal adipose tissues and the placenta [3]. It has been proposed that 95% of placental leptin production is secreted into maternal circulation and only 5% is delivered to the fetal circulation [1,7]. Fetal adipose tissue is the main source of fetal leptin and fetal leptin levels are strongly related to birth weight and fetal adiposity [4,7]. Cord blood leptin

* Corresponding author.
E-mail addresses: obeidat_rawan@yahoo.com, raobeidat3@just.edu.jo (R.A. Obeidat).

https://doi.org/10.1016/j.amsu.2021.103050
Received 20 September 2021; Received in revised form 6 November 2021; Accepted 9 November 2021

concentrations are lower than maternal serum leptin concentrations which are attributed to the role of the placenta in leptin production [6].

The research field has not yet generated enough conclusive evidence about the role of leptin in pathological states of pregnancy. The potential role of leptin has been suggested in various disorders during pregnancy such as recurrent miscarriages, gestational diabetes mellitus (GDM), intrauterine growth retardation (IUGR), and preeclampsia [1,4,5,8]. To date, it is not known whether maternal serum leptin concentrations could be used as a potential predictor for some complications of pregnancy. In the current study, we measured maternal and fetal leptin serum levels and studied their association with maternal and fetal characteristics, labor and some antenatal complications in an attempt to identify variables that affect leptin level and its possible use as a marker for maternal and/or fetal complications.

2. Material and methods

2.1. Study population

A cross-sectional study was conducted at the department of obstetrics and gynecology in King Abdullah University Hospital (KAUH) in Jordan. Pregnant women with singleton live fetuses who attended to labor ward between January 2020 and August 2020 were included in the study. All pregnant mothers gave written informed consent for participation in the study. The study was approved by the Institutional Review Board of the hospital (Approval no. 135/2019) and was performed in accordance with the Code of Ethics in the Declaration of Helsinki. Data has been reported in accordance with the Strengthening the Reporting of Cohort Studies in Surgery (STROCSS) guidelines [9]. This study was registered at the Research Registry as researchregistry7163.

Data were collected by registrars in labor ward. The data collected include maternal age, parity, weight, height, body mass index (BMI), the presence of medical illnesses, the presence of antenatal complications in the current pregnancy, gestational age of the fetus, delivery mode, whether the patient was in labor or not, neonatal weight, height and gender, Apgar score at 1 and 5 min and umbilical cord arterial pH. BMI was calculated as weight in kilograms divided by height in meters squared. Regarding antenatal complications, small for gestational age (SGA) was defined by birth weight below the 10th percentile for gestational age and large for gestational age (LGA) was birth weight greater than the 90th percentile for age. GDM was diagnosed at ≥24–28 weeks of gestation by 100 mg oral glucose tolerance test (OGTT) when one or more threshold values is exceeded (fasting ≥5.3 mmol/l, 1-h ≥10.0 mmol/l, 2-h ≥8.6 mmol/l, 3-h ≥7.8 mmol/l). Gestational hypertension (GHTN) was defined by the new onset of hypertension (systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg) at ≥20 weeks of gestation in the absence of proteinuria or new signs of end-organ dysfunction.

2.2. Sample collection and analysis

452 pregnant women were included in the study. Venous blood samples were obtained by qualified staff nurses from umbilical cord veins of the newborns immediately after their delivery. Maternal venous blood samples were obtained just before delivery in women who had vaginal deliveries and right before cesarean delivery in mothers who had elective or emergency cesareans. About 5 ml of venous blood was collected from each participant in a serum separator tube (SST) and samples were then centrifuged immediately. The samples were centrifuged for 10 min at 2000×*g* and the serums were then collected and divided into aliquots and stored at −80 °C until assay. The quantitative measurement of leptin in serum was performed by experienced personnel in a research laboratory using an enzyme-linked immunosorbent assay (ELISA) method. The assays were conducted according to the manufacturer's protocols (*ELISA for Leptin (LEP). Product No: SEA084Hu. Link:* https://www.cloud-clone.us/elisa/ELISA-Kit-for-Human-Leptin-LEP-2181.htm).

2.3. Statistical analysis

All analyses were conducted using the Statistical Package for Social Science (SPSS/version 26) software. Categorical variables were presented as frequency and percentages while continuous variables were presented as median and interquartile range (IQR). The normality of the distribution of data was examined by the Kolmogorov-Smirnov test. The differences between groups with regards to continuous variables were tested with Mann-Whitney *U* test. Spearman's correlation test was utilized to study the relation between two continuous variables. After that, multivariate analysis using linear regression model "Enter method" was performed. All variables with $p \leq 0.25$ on univariate analysis were included in the multivariate analysis. Statistical significance was set at $p < 0.05$.

3. Results

3.1. Descriptive characteristics of the study group

The demographic and clinical characteristics of the study population are summarized in Table 1. The median age of women was 31 [27–36] years and the median body mass index was 29.9 [27.3–33.2] kg/m^2. The reported medical illnesses and antenatal complications were 48 (10.6%) and 139 (30.8%) respectively. The most common medical problem among pregnant women was hypothyroidism (6%) and the most common antenatal complication was SGA (10%) followed by LGA (7.3%) and GDM (5.5%). The median gestational age of fetuses was 37.9 [37.1–38.9] weeks and the median birth weight was 3.1 [2.8–3.4] kg.

Table 1
Baseline demographic and clinical characteristics of the study group (N = 452).

Maternal Variables	Median [IQR]	Mean ± SE
	Frequency (%)	
Age (Calendar year)	31 [27–36]	31.53 ± 0.26
Weight on admission (kg)	77 [72–86]	79.06 ± 0.57
Height (cm)	160 [158–165]	161.24 ± 0.25
BMI on admission (kg/m^2)	29.91 [27.34–33.20]	30.41 ± 0.21
Parity		
Nulliparous	71 (15.7)	
Multiparous	381 (84.3)	
Reported medical illness		
Hypothyroidism	27 (6.0)	
Hypertension	11 (2.4)	
Diabetes mellitus (type I or II)	5 (1.1)	
Others	5 (1.1)	
Reported antenatal complications		
Small for gestational age	45 (10)	
Large for gestational age	33 (7.3)	
Gestational diabetes mellitus	25 (5.5)	
PPROM	13 (2.9)	
PROM	11 (2.4)	
Gestational hypertension	8 (1.8)	
Others	4 (0.9)	
Mode of delivery		
Vaginal delivery	289 (63.9)	
Cesarean section	163 (36.1)	
Gender		
Male	234 (51.8)	
Female	218 (48.2)	
Gestational age (weeks)	37.86 [37.14–38.86]	37.94 ± 0.07
Fetus weight (kg)	3.1 [2.8–3.4]	3.11 ± 0.02
Fetus height (cm)	50 [48–51]	49.81 ± 0.15
Apgar score at 1 min	8 [8–8]	7.98 ± 0.03
Apgar score at 5 min	9 [9–9]	9.04 ± 0.02
Arterial blood gases (N = 279)	7.31 [7.29–7.35]	7.31 ± 0.003

IQR: interquartile range, BMI: body mass index, PPROM: preterm premature rupture of membranes.
PROM: Premature rupture of membrane.

Apgar scores at 1 and 5 min were 8 [8–8] and 9 [9–9] respectively. Arterial cord blood pH was tested for 279 newborns and the median was 7.31 [7.29–7.35].

During the study period, 289 (63.9%) women had vaginal deliveries and 163 (36.1%) women had cesarean sections. The majority of cesarean sections were elective and the main indication for cesarean delivery was previous cesarean sections. 320 (70.8%) women were in established labor (had regular uterine contraction with a minimum of 4 cm cervical dilatation), 36 (8%) were in the latent phase (had irregular abdominal pain/tightness with cervical dilation ≤2 cm) and 96 (21.2%) were not in labor (had no uterine contractions).

3.2. Maternal leptin

The median maternal serum leptin level was 6.42 [4.16–8.51] ng/mL (Table 2). There was no significant correlation between maternal and fetal serum leptin levels ($p = 0.064$). Maternal serum leptin levels correlated positively with maternal BMI ($r = 0.117$, $p = 0.005$). Besides, maternal serum leptin levels were significantly higher in nulliparous women (7.57 [4.45–9.30] ng/mL vs. 6.22 [4.02–8.30] ng/mL, $p = 0.037$) and in women who were in established labor (6.83 [4.39–8.92] ng/mL vs. 6.25 [4.04–8.30] ng/mL, $p = 0.047$) (Tables 3 and 4). Other variables were not shown to be significantly associated with maternal serum leptin levels.

3.3. Fetal leptin

The median fetal serum leptin levels were 2.9 [1.03–5.36] ng/mL. Fetal serum leptin levels were significantly higher in LGA fetuses (4.81 [2.13–7.22] ng/mL vs. 2.80 [0.96–5.16] ng/mL, $p = 0.003$) and in fetuses with preterm premature ruptures of membranes (PPROM) (5.23 [2.42–8.07] ng/mL vs. 2.86 [1.00–5.23] ng/mL, $p = 0.021$) (Tables 3 and 4). Other variables were not shown to be significantly associated with fetal serum leptin levels.

4. Discussion

This study aimed to measure fetal and maternal serum leptin levels and to investigate their association with fetal and maternal characteristics, antenatal complications and labor. The present study showed that the mean maternal and fetal serum leptin levels were 6.22 ± 0.13 ng/mL and 3.46 ± 0.13 ng/mL respectively. Our study agrees with existing literature that fetal serum leptin levels were lower than those in paired maternal plasma [1,7,10]. Also in our study, there was no correlation between maternal and fetal serum leptin levels. The absence of correlation between maternal and cord serum leptin levels was reported in other studies and suggests a non-communicating, two-compartment model theory of fetoplacental regulation of leptin [1,4,10].

Data in the literature suggest that placental leptin production makes a substantial contribution to maternal circulating leptin levels during pregnancy [7]. However, maternal leptin is also produced by maternal adipose tissue and this is supported by the finding in our study and most of the studies in the literature that reported a positive correlation between maternal serum leptin levels and maternal BMI [6,11–14]. On the contrary, other studies reported no correlation between maternal serum leptin levels and maternal BMI [4,15]. In the current study, maternal serum leptin levels were significantly higher among nulliparous women compared with multiparous women. Similarly, Serapio et al. reported, among obese mothers, higher leptin levels in nulliparous women compared with multipara ($p = 0.035$) [16]. Also, Hedley et al. reported a significant negative association between maternal serum leptin levels and parity [17].

In the current study, there were no significant differences in maternal and fetal serum leptin levels among uncomplicated pregnancies and pregnancies complicated by SGA, GDM, GHN or premature rupture of membranes (PROM). Fetal, but not maternal, serum leptin levels were significantly higher among pregnancies complicated by PPROM. To our best knowledge, this is the first study that showed an association between fetal serum leptin levels and PPROM. The results of experimental studies on animals have shown that inflammatory cytokines including tumor necrosis factor-a (TNFa), interleukin-1 (IL-1) and bacterial lipopolysaccharide upregulate adipose tissue leptin production [18]. It could be that the subclinical infectious background in PPROM patients has led to an increase in leptin production in response to inflammatory cytokines. Regarding SGA/IUGR, data in the literature suggest that the association between maternal serum leptin levels and IUGR is controversial. Some studies reported a significant increase in maternal serum leptin levels in women with IUGR [7,15,19]. In contrast, other studies showed that maternal serum leptin levels did not differ significantly in IUGR compared to normal pregnancies [20,21]. Besides, other studies reported even lower maternal serum leptin levels among women with IUGR [22–24]. Similarly, research investigating fetal serum leptin levels in pregnancies complicated with IUGR is contradictory, with some studies reporting significantly lower cord leptin levels [15,21,23] in fetuses with IUGR while others reported no changes [20]. Also, Cetin et al. reported an increase in cord leptin concentration in severe IUGR fetuses [25]. Concerning GDM, maternal serum leptin levels were reported to be significantly elevated in pregnant women with GDM as opposed to those with uncomplicated pregnancies [26–29]. Moreover, abnormally high levels of maternal leptin in early pregnancy were shown to be predictive of an increased risk for GDM later in the pregnancy [30]. However, Festa et showed that gestational diabetics had lower maternal leptin levels than those of normal pregnant [31]. Fetal serum leptin levels were demonstrated to be significantly higher among fetuses of diabetic mothers [25,32]. However, Aghoozi et al. reported no association between fetal serum leptin levels and GDM [33].

Table 2
Reference values for maternal and fetal serum leptin concentrations.

Leptin level	Median [IQR]	Mean ± SE	Maternal leptin	Fetal leptin
			p-value[a]	
Fetal leptin (ng/ml)	2.9 [1.03–5.36]	3.46 ± 0.13	0.064	NA
Maternal leptin (ng/ml)	6.42 [4.16–8.51]	6.22 ± 0.13	NA	0.064

[a] Two-sided *p*-value based on univariate analysis –Spearman's correlation test.

Table 3
Univariate analysis - Fetal and maternal variables that are found to be significantly associated with fetal and/or maternal serum leptin levels (N = 452).

Maternal/Fetus Variables	Median [IQR]/Correlation Coefficient	*p*-value[a]
Maternal leptin		
Maternal BMI (kg/m^2)	$r = 0.117$	0.013
Parity		0.024
Nulliparous	7.57 [4.45–9.30]	
Multiparous	6.22 [4.02–8.30]	
Labor		0.036
Yes	6.83 [4.39–8.92]	
No	6.25 [4.04–8.30]	
Fetal leptin		
Maternal weight (kg)	$r = 0.103$	0.029
Maternal BMI (kg/m^2)	$r = 0.102$	0.031
Fetus weight (kg)	$r = 0.105$	0.025
Large for gestational age		0.005
Yes	4.81 [2.13–7.22]	
No	2.80 [0.96–5.16]	
PPROM		0.021
Yes	5.23 [2.42–8.07]	
No	2.86 [1.00–5.23]	

BMI: body mass index, PPROM: Preterm premature rupture of membranes.
[a] Two-sided *p*-value based on univariate analysis – Mann-Whitney test and Spearman's correlation test.

Table 4
Multivariate analysis - Fetal and maternal variables that are found to be significantly associated with fetal and/or maternal serum leptin levels (N = 452).

Predictor	Unstandardized Coefficients (β)	Standardized Coefficients (Beta)	Standard Error	*p*-value[a]	95% CI
Maternal Leptin					
Maternal BMI	0.085	0.133	0.030	0.005	0.026–0.144
Parity	−0.758	−0.098	0.363	0.037	−1.471–−0.044
Labor status	0.580	0.095	0.291	0.047	0.008–1.152
Fetal leptin					
LGA	1.498	0.137	0.510	0.003	0.496–2.50
PPROM	1.837	0.108	0.793	0.021	0.278–3.40

CI: confidence interval, BMI: body mass index, LGA: large for gestational age, PPROM: preterm premature rupture of membranes.
[a] Two-sided *p*-value based on multivariate analysis – linear regression.

The present study reported higher maternal, but not fetal, serum leptin levels among women who were in established labor. Similarly, Nuamah et al. measured maternal leptin levels at 3 points (before labor induction, during labor and in the early postpartum) in the same women and demonstrated a significant increase in maternal leptin concentrations during advanced labor and a decrease in the early postpartum period [34]. Furthermore, a study of 934 newborns showed that active labor delivery mode, as well as longer duration of labor, were associated with higher cord leptin concentrations [35]. Collectively, these findings led us to speculate that labor increases leptin production. This increase in leptin production during labor has been suggested to be caused by the increase in inflammatory factors and corticosteroids that accompanied active labour [18,33,34].

Our study showed no association between maternal serum leptin levels and maternal age, gestational age of the fetus, fetal weight and gender and mode of delivery. In agreement, different studies revealed no significant differences in maternal serum leptin concentrations in regard to fetal birth weight [4,6,15] and mode of delivery [6,33,36]. On the other hand, other studies reported a positive correlation between maternal serum leptin levels and fetal birth weight [11,37] and gestational age of the fetus [36]. Besides, higher maternal leptin levels have been reported in mothers with female fetuses as compared with mothers with male fetuses [36].

The current study reported significantly higher fetal serum leptin levels among LGA fetuses. Our findings are consistent with the literature and showed that fetal serum leptin levels are strongly related to birth weight and fetal adiposity [6,10,13]. Besides, the current study reported no association between fetal serum leptin levels and maternal age, gestational age of the fetus, fetal gender and mode of delivery. Similarly, other studies revealed no significant differences in fetal serum leptin concentrations in regard to fetal gender [6,10] and mode of delivery [6]. On the other hand, other studies reported a positive correlation between fetal serum leptin levels and the gestational age of the fetus [6,38]. Also, higher fetal plasma leptin concentrations were demonstrated in female fetuses as compared with male fetuses [1,39].

4.1. Study limitation

Our study has some limitations worthy of consideration. First, we have only measured maternal leptin serum levels in the 3rd trimester at the time of delivery and we have not explored the longitudinal changes in maternal leptin concentrations throughout pregnancy. Besides, the relatively small sample size of the subgroups (GDM, PPROM, etc.) limits the generalization of our findings and further studies with larger populations are needed to confirm our results. Finally, we did not investigate placental leptin expression as this will improve data interpretation.

5. Conclusion

Maternal serum leptin concentrations correlated positively with maternal BMI and were higher among nulliparous women and in women who were in established labor. Fetal serum leptin concentrations were higher among LGA fetuses and in fetuses with PPROM.

Further studies are required to clarify the definite role of leptin in the pathophysiology of high-risk pregnancies and explore its potential role as a biomarker for the detection of pregnancy complications.

Please state any conflicts of interest

All authors have approved the manuscript and support submission to this journal. There are no conflicts of interest to declare.

Please state any sources of funding for your research

This research has been funded by the Deanship of Research at Jordan University of Science and Technology, Irbid, Jordan. Research Grant No: [628/2020], the grant was awarded to Rawan Obeidat.

Consent

Written informed consents were obtained from the newborns' mother.

Registration of research studies

Name of the registry: Research Registry
Unique Identifying number or registration ID: researchregistry7163
Hyperlink to your specific registration (must be publicly accessible and will be checked): https://www.researchregistry.com/browse-the-registry#home/

Provenance and peer review

Not commissioned, externally peer-reviewed.

Research registration unique identifying number (UIN)

Name of the registry: Research Registry.

Research Registry Unique Identifying number: researchregistry7163

Hyperlink to our specific registration: https://www.researchregistry.com/browse-the-registry#home/registrationdetails/6147275ef092ea001e5ad133/

Ethics approval and patient consent

The study method and protocol were approved by the Institutional Review Board of KAUH. Written informed consents were obtained from the newborns' mothers.

Author's contributions

RO designed the study, carried out the statistical analysis, and wrote the manuscript. NA carried out the statistical analyses. SA, BS, OJ, and

EH collected the data. SoA participated in the study design and helped in drafting the manuscript. All authors have read and approved the final manuscript.

Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Funding

This research has been funded by the Deanship of Research at Jordan University of Science and Technology, Irbid, Jordan. Research Grant No: [628/2020], the grant was awarded to R Obeidat.

Guarantor

Rawan Ahmad Obeidat.

Declaration of competing interest

This article has not been published or presented elsewhere in part or entirety and is not under consideration by another journal. All authors have approved the manuscript and support submission to this journal. There are no conflicts of interest to declare.

Acknowledgement

This study was supported by the deanship of research at Jordan University of Science and Technology, Irbid, Jordan.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2021.103050.

References

[1] R. Bajoria, S.R. Sooranna, B.S. Ward, R. Chatterjee, Prospective function of placental leptin at maternal-fetal interface, Placenta 23 (2–3) (2002) 103–115, https://doi.org/10.1053/plac.2001.0769.
[2] N. Sagawa, S. Yura, H. Itoh, et al., Role of leptin in pregnancy–a review, Placenta 23 (Suppl A) (2002) S80–S86, https://doi.org/10.1053/plac.2002.0814.
[3] B.D. Taylor, R.B. Ness, J. Olsen, et al., Serum leptin measured in early pregnancy is higher in women with preeclampsia compared with normotensive pregnant women, Hypertension 65 (3) (2015) 594–599, https://doi.org/10.1161/HYPERTENSIONAHA.114.03979.
[4] M.A. Youssry, M.A. Gabreel, T.A. Patel, Changes in maternal serum leptin levels during pregnancy and after labor in preeclampsia, and its correlation to neonatal cord leptin, Open J. Obstet. Gynecol. 6 (10) (2016) 588–600, https://doi.org/10.4236/ojog.2016.610074.
[5] A. Pérez-Pérez, A. Toro, T. Vilariño-García, et al., Leptin action in normal and pathological pregnancies, J. Cell Mol. Med. 22 (2) (2018) 716–727, https://doi.org/10.1111/jcmm.13369.
[6] M. Stefaniak, E. Dmoch-Gajzlerska, B. Mazurkiewicz, W. Gajzlerska-Majewska, Maternal serum and cord blood leptin concentrations at delivery, PLoS One 14 (11) (2019), e0224863, https://doi.org/10.1371/journal.pone.0224863. Published 2019 Nov 7.
[7] J. Lepercq, J.C. Challier, M. Guerre-Millo, M. Cauzac, H. Vidal, S. Hauguel-de Mouzon, Prenatal leptin production: evidence that fetal adipose tissue produces leptin, J. Clin. Endocrinol. Metab. 86 (6) (2001) 2409–2413, https://doi.org/10.1210/jcem.86.6.7529.
[8] R.S. Baban, N.M. Ali, H.A. Al-Moayed, Serum leptin and insulin hormone level in recurrent pregnancy loss, Oman Med. J. 25 (3) (2010) 203–207, https://doi.org/10.5001/omj.2010.57.
[9] R. Agha, A. Abdall-Razak, E. Crossley, N. Dowlut, C. Iosifidis, G. Mathew, for the STROCSS Group, The STROCSS 2019 guideline: strengthening the reporting of cohort studies in Surgery, Int. J. Surg. 72 (2019) 156–165.
[10] T. Laml, B.W. Hartmann, E. Ruecklinger, O. Preyer, G. Soeregi, P. Wagenbichler, Maternal serum leptin concentrations do not correlate with cord blood leptin concentrations in normal pregnancy, J. Soc. Gynecol. Invest. 8 (1) (2001) 43–47.
[11] M.D. Fernandes, S. Daher, L.M. de Sousa, et al., Blood level of adipokines and nutritional status variables in adolescent pregnancy, Obstet. Gynecol. Sci. 63 (6) (2020) 683–689, https://doi.org/10.5468/ogs.20102.
[12] S. Salimi, F. Farajian-Mashhadi, A. Naghavi, et al., Different profile of serum leptin between early onset and late onset preeclampsia, Dis. Markers 2014 (2014) 628476, https://doi.org/10.1155/2014/628476.
[13] J.M. Walsh, J. Byrne, R.M. Mahony, M.E. Foley, F.M. McAuliffe, Leptin, fetal growth and insulin resistance in non-diabetic pregnancies, Early Hum. Dev. 90 (6) (2014) 271–274, https://doi.org/10.1016/j.earlhumdev.2014.03.007.
[14] S. Carlhäll, M. Bladh, J. Brynhildsen, et al., Maternal obesity (Class I-III), gestational weight gain and maternal leptin levels during and after pregnancy: a prospective cohort study, BMC Obes. 3 (2016) 28, https://doi.org/10.1186/s40608-016-0108-2. Published 2016 May 20.
[15] M. Pighetti, G.A. Tommaselli, A. D'Elia, et al., Maternal serum and umbilical cord blood leptin concentrations with fetal growth restriction, Obstet. Gynecol. 102 (3) (2003) 535–543, https://doi.org/10.1016/s0029-7844(03)00668-9.
[16] S. Serapio, F. Ahlsson, A. Larsson, T. Kunovac Kallak, Second trimester maternal leptin levels are associated with body mass index and gestational weight gain but not birth weight of the infant, Horm. Res. Paediatr. 92 (2) (2019) 106–114, https://doi.org/10.1159/000503422.
[17] P. Hedley, K. Pihl, L. Krebs, T. Larsen, M. Christiansen, Leptin in first trimester pregnancy serum: no reduction associated with small-for-gestational-age infants, Reprod. Biomed. Online 18 (6) (2009) 832–837, https://doi.org/10.1016/s1472-6483(10)60034-x.
[18] C.S. Mantzoros, S.J. Moschos, Leptin: in search of role(s) in human physiology and pathophysiology, Clin. Endocrinol. 49 (5) (1998) 551–567, https://doi.org/10.1046/j.1365-2265.1998.00571.x.
[19] H. Mise, S. Yura, H. Itoh, et al., The relationship between maternal plasma leptin levels and fetal growth restriction, Endocr. J. 54 (6) (2007) 945–951, https://doi.org/10.1507/endocrj.k06-225.
[20] H.I. Aydin, A. Eser, I. Kaygusuz, et al., Adipokine, adropin and endothelin-1 levels in intrauterine growth restricted neonates and their mothers, J. Perinat. Med. 44 (6) (2016) 669–676, https://doi.org/10.1515/jpm-2014-0353.
[21] M.A. Nezar, A.M. el-Baky, O.A. Soliman, H.A. Abdel-Hady, A.M. Hammad, M.S. Al-Haggar, Endothelin-1 and leptin as markers of intrauterine growth restriction, Indian J. Pediatr. 76 (5) (2009) 485–488, https://doi.org/10.1007/s12098-009-0079-0.
[22] J.M. Catov, T.E. Patrick, R.W. Powers, R.B. Ness, G. Harger, J.M. Roberts, Maternal leptin across pregnancy in women with small-for-gestational-age infants, Am. J. Obstet. Gynecol. 196 (6) (2007), https://doi.org/10.1016/j.ajog.2007.01.032, 558.e1-558.e5588.
[23] L. Yildiz, B. Avci, M. Ingeç, Umbilical cord and maternal blood leptin concentrations in intrauterine growth retardation, Clin. Chem. Lab. Med. 40 (11) (2002) 1114–1117, https://doi.org/10.1515/CCLM.2002.195.
[24] A. Karowicz-Bilińska, Analiza zachowania sie leptyny u kobiet z ciaza fizjologiczna oraz w hipotrofii wewnatrzmacicznej [Leptin concentration in women with normal pregnancy and intrauterine growth retardation], Ginekol. Pol. 75 (1) (2004) 10–14. Polish. PMID: 15112467.
[25] I. Cetin, P.S. Morpurgo, T. Radaelli, et al., Fetal plasma leptin concentrations: relationship with different intrauterine growth patterns from 19 weeks to term, Pediatr. Res. 48 (5) (2000) 646–651, https://doi.org/10.1203/00006450-200011000-00016.
[26] L. Bozkurt, C.S. Göbl, S. Baumgartner-Parzer, A. Luger, G. Pacini, A. Kautzky-Willer, Adiponectin and leptin at early pregnancy: association to actual glucose disposal and risk for GDM-A prospective cohort study, Internet J. Endocrinol. 2018 (2018) 5463762, https://doi.org/10.1155/2018/5463762. Published 2018 Jul 15.
[27] A. Kautzky-Willer, G. Pacini, A. Tura, et al., Increased plasma leptin in gestational diabetes, Diabetologia 44 (2) (2001) 164–172, https://doi.org/10.1007/s001250051595.
[28] N. Vitoratos, E. Salamalekis, D. Kassanos, et al., Maternal plasma leptin levels and their relationship to insulin and glucose in gestational-onset diabetes, Gynecol. Obstet. Invest. 51 (1) (2001) 17–21, https://doi.org/10.1159/000052884.
[29] W.Q. Xiao, J.R. He, S.Y. Shen, et al., Maternal circulating leptin profile during pregnancy and gestational diabetes mellitus, Diabetes Res. Clin. Pract. 161 (2020) 108041, https://doi.org/10.1016/j.diabres.2020.108041.
[30] C. Qiu, M.A. Williams, S. Vadachkoria, I.O. Frederick, D.A. Luthy, Increased maternal plasma leptin in early pregnancy and risk of gestational diabetes mellitus, Obstet. Gynecol. 103 (3) (2004) 519–525, https://doi.org/10.1097/01.AOG.0000113621.53602.7a.
[31] A. Festa, N. Shnawa, W. Krugluger, P. Hopmeier, G. Schernthaner, S.M. Haffner, Relative hypoleptinaemia in women with mild gestational diabetes mellitus, Diabet. Med. 16 (8) (1999) 656–662, https://doi.org/10.1046/j.1464-5491.1999.00122.x.
[32] B. Persson, M. Westgren, G. Celsi, E. Nord, E. Ortqvist, Leptin concentrations in cord blood in normal newborn infants and offspring of diabetic mothers, Horm. Metab. Res. 31 (8) (1999) 467–471, https://doi.org/10.1055/s-2007-978776.
[33] M. Faghani Aghoozi, N. Tehranian, M. Amerian, et al., The predictive role of serum leptin levels in pregnant mothers in relation to their delivery type, PCNM 8 (1) (2018) 28–35. URL: http://zums.ac.ir/nmcjournal/article-1-569-en.html.
[34] M.A. Nuamah, S. Yura, N. Sagawa, et al., Significant increase in maternal plasma leptin concentration in induced delivery: a possible contribution of pro-inflammatory cytokines to placental leptin secretion, Endocr. J. 51 (2) (2004) 177–187, https://doi.org/10.1507/endocrj.51.177.
[35] C.A. Logan, L. Thiel, R. Bornemann, et al., Delivery mode, duration of labor, and cord blood adiponectin, leptin, and C-reactive protein: results of the population-based ulm birth cohort studies, PLoS One 11 (2) (2016), e0149918, https://doi.org/10.1371/journal.pone.0149918. Published 2016 Feb 22.
[36] E. Domali, I.E. Messinis, Leptin in pregnancy, J. Matern. Fetal Neonatal Med. 12 (4) (2002) 222–230, https://doi.org/10.1080/jmf.12.4.222.230.

[37] S. Kharb, P. Panjeta, V.S. Ghalaut, J. Bala, S. Nanda, Maternal factors affecting serum leptin levels in preeclampsia and normotensive pregnant women and outcome of pregnancy, J. Pregnancy Child. Health 3 (1) (2016) 223, https://doi.org/10.4172/2376-127X.1000223.

[38] T. Hytinantti, H.A. Koistinen, V.A. Koivisto, S.L. Karonen, E.M. Rutanen, S. Andersson, Increased leptin concentration in preterm infants of pre-eclamptic mothers, Arch. Dis. Child. Fetal Neonatal Ed. 83 (1) (2000) F13–F16, https://doi.org/10.1136/fn.83.1.f13.

[39] J. Matsuda, I. Yokota, M. Iida, et al., Serum leptin concentration in cord blood: relationship to birth weight and gender, J. Clin. Endocrinol. Metab. 82 (5) (1997) 1642–1644, https://doi.org/10.1210/jcem.82.5.4063.