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RESEARCH ARTICLE

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# Elevated Maternal Leptin Levels and Higher Birth Weight in Obese Mothers Compared with Normal-weight Mothers

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**Background:** Maternal obesity is associated with disrupted metabolic regulation, including elevated leptin levels that may affect fetal growth. Previous studies have reported mixed findings on maternal and cord blood leptin concentrations, with some showing higher leptin levels in infants born to obese mothers, while others found no significant differences. Associations between maternal obesity and neonatal outcomes have also been inconsistent. This study aims to generate new evidence from an Indonesian cohort by comparing maternal and cord blood leptin levels, as well as neonatal outcomes, between obese and normal-weight mothers.

**Materials and methods:** Analytical cross-sectional study enrolled 30 obese and 30 normal-weight mothers from two hospitals in Padang, Indonesia. Maternal and cord blood samples were collected at delivery, and leptin levels were measured using ELISA. Ethical approval and informed consent were obtained. Neonatal outcomes included birth weight, length, head circumference, and ponderal index. Data were analyzed using Independent Samples t-test or Mann–Whitney U test, with $p<0.05$ considered statistically significant.

**Results:** Maternal leptin levels were significantly higher in obese mothers than in normal-weight mothers (70.8±39.0 vs. 44.5±42.5 ng/mL; $p=0.002$). Cord blood leptin levels did not differ between groups (19.7±14.9 vs. 16.1±17.5 ng/mL; $p=0.394$). Neonates of obese mothers had higher birth weight ($p=0.003$), while other anthropometric measures were similar.

**Conclusion:** Maternal obesity was associated with elevated maternal leptin levels and increased neonatal birth weight, while cord blood leptin did not differ significantly between groups. These findings suggest that maternal leptin reflects maternal metabolic status rather than fetal growth.

**Keywords:** *maternal leptin, cord blood leptin, obesity, pregnancy, neonatal outcome*

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## Introduction

The increasing prevalence of obesity among women of reproductive age has become a major global health concern due to its association with reproductive disorders such as polycystic ovary syndrome (PCOS) and various adverse pregnancy outcomes.[1] Maternal obesity not only affects the mother but also the fetus and is linked to various complications such as gestational diabetes, insulin resistance, gestational hypertension, preeclampsia, fetal macrosomia, spontaneous abortion, cesarean delivery, neural tube defects, and stillbirth.[2-4] These conditions significantly increase maternal and neonatal morbidity and mortality, elevate healthcare costs, and pose a considerable public health burden.[5,6] These adverse outcomes are partly mediated by altered metabolic and hormonal regulation, particularly involving adipokines such as leptin.

One of the key molecular pathways linking maternal obesity to adverse pregnancy outcomes involves leptin, an adipokine that mediates energy homeostasis and placental function.[7] Among these adipokines, leptin plays a central role during pregnancy. Leptin is not only produced by adipose tissue but also synthesized by the placenta, where it regulates trophoblast proliferation, angiogenesis, cytokine secretion, and nutrient transport, all of which support fetal growth and development.[8] Maternal plasma leptin concentrations are significantly higher in obese pregnant women compared with normal-weight mothers, mainly due to increased adipose tissue deposition and placental contribution.[9]

Leptin enhances placental lipolysis, stimulates amino acid transport, and supports fetal development.[10,11] However, in obese mothers, placental expression of the leptin receptor (Ob-Rb) is reduced, leading to leptin resistance at the maternal fetal interface.[12] This mechanism suggests that although maternal leptin levels are elevated, their biological effects on fetal growth may be diminished, resulting in complex and sometimes paradoxical associations with neonatal outcomes.[7]

Evidence from previous human and animal studies has shown that maternal obesity alters placental nutrient transport and is correlated with increased birth weight, but does not always result in proportional changes in neonatal growth.[13,11] These findings suggest that leptin may serve more as a marker of maternal metabolic status than a direct predictor of neonatal size.[14,15]

Leptin's biological importance during pregnancy, its heightened levels in maternal obesity, and its potential influence on fetal development make it a key molecule to investigate in this context.[16] Prior research has reported inconsistent findings regarding maternal and cord blood leptin concentrations between obese and normal-weight mothers. Some studies have demonstrated significantly higher maternal and cord blood leptin levels in obese mothers, whereas others have found no notable differences.[10,14] In addition, associations between leptin and neonatal anthropometric outcomes have also varied. Certain studies reported positive relationships with birth weight and neonatal adiposity, while others observed weak or non-significant associations.[10,17-19] These discrepancies likely reflect differences in study populations, adiposity measurement methods, and maternal metabolic conditions, underscoring the need for further investigation.

Despite extensive evidence on the role of leptin in pregnancy, studies directly comparing maternal serum leptin, cord blood leptin, and neonatal outcomes in obese and normal-weight mothers remain limited, particularly in the Indonesian population. This study aimed to compare maternal and cord blood leptin levels, and to evaluate their associations with neonatal anthropometric outcomes including birth weight, length, head circumference, and ponderal index between obese and normal-weight mothers.

## Materials and methods

### *Study Design*

The study population included mothers who delivered at Dr. M. Djamil General Hospital and Hermina Hospital, Padang. The sample size of 60 participants (30 per group) was determined based on standard sample size calculations for comparing two independent means, using estimates of expected differences in maternal leptin concentrations from previous studies.[20,21] This sample size provides adequate statistical power (80%) to detect meaningful differences between obese and normal-weight pregnancies in both maternal and cord blood leptin levels, while accounting for potential biological variability. All procedures performed in this study were conducted in accordance with the ethical approval as stated in the ethical statement subsection.

### *Subject Selection*

Participants were selected based on the following inclusion criteria: singleton pregnancy, pregnant women

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at term gestation (≥37 weeks), possession of maternal and child health records (KIA book), pregnant women were categorized as obese (BMI>27 kg/m²) or normal-weight (BMI 18.5-24.9 kg/m²) according to Indonesian Ministry of Health guidelines.[22] Exclusion criteria included a history of diabetes mellitus, gestational hypertension, preeclampsia, intrauterine fetal death (IUFD), and congenital abnormalities based on hospital and national guidelines. Eligible subjects were provided with an explanation of the study's objectives and procedures before giving informed consent to participate.

Neonatal outcomes were assessed immediately after delivery. Birth weight was measured using a calibrated infant scale with the newborn undressed.[23] Body length was measured with an infantometer by two trained examiners. Head circumference was measured using a non-stretchable tape placed around the occipitofrontal circumference.12 The ponderal index was calculated as[17,24]:

$$PI = \text{weight (g)} \times 100 / \text{length (cm)}^3.$$

***Maternal and Umbilical Cord Blood Sampling***

Maternal blood samples (4-5 mL) were collected from the cubital vein during labor or prior to cesarean delivery, using plain serum separator tubes (BD Vacutainer SST, BD, USA). Blood was drawn simultaneously with routine hospital blood collection by trained medical staff.[15,25] Umbilical cord blood samples (4-5 mL) were collected immediately after delivery from the placental vein of the umbilical cord using sterile plain serum separator tubes.[26,14]

Both maternal and umbilical cord blood samples were allowed to clot at room temperature for 30 minutes. The samples were then centrifuged at 3000 rpm for 15 minutes to separate the serum. Serum aliquots were placed into labeled microtubes and transported in cool boxes maintained at 4°C. All serum samples were stored at −20°C until further analysis.

***Leptin Measurement***

Serum leptin concentrations were measured using a DBC Diagnostics ELISA Kit (No. CAN-LR-439-001, Diagnostic Biochem Canada Inc., Ontarion, Canada) according to the manufacturer's instructions. The assay employs monoclonal antibodies specific for human leptin. The calibrator/standard range is 0-100 ng/mL, with 0 ng/mL as the blank (zero standard) and 100 ng/mL as the highest standard, representing the upper limit of accurate detection. This corresponds to a limit of detection of 0.50 ng/mL. Samples exceeding the upper standard were diluted to fall within the assay range. All reagents were equilibrated to room temperature prior to use. Standards, controls, and serum samples were assayed in duplicate according to the manufacturer's instructions. Optical density was read at 450 nm using an xMark Microplate Reader (Bio-Rad Laboratories, Model XMark, Version 2.02.05, Serial 10108). Standard curves were generated using a four-parameter logistic (4-PL) regression fit.

***Statistical Analysis***

Statistical analyses were performed using IBM SPSS Statistics version 16.0 (IBM Corp., Armonk, NY, USA). Data distribution was assessed using the Shapiro–Wilk test. Variables that did not meet normality assumptions were log-transformed before further analysis. In the obese group, umbilical cord leptin and neonatal head circumference were log-transformed. However, head circumference remained non-normal. In the normal-weight group, maternal leptin, umbilical cord leptin, neonatal length, and ponderal index were log-transformed, with umbilical cord leptin and ponderal index achieving normality, whereas maternal leptin and neonatal length remained non-normal. Normally distributed variables (umbilical cord leptin, ponderal index, and birth weight) were analyzed using Independent Samples t-tests, with Levene's test performed to assess equality of variances. Non-normally distributed variables (maternal leptin, neonatal head circumference, and body length) were analyzed using the Mann–Whitney U test. All tests were two-tailed, with a significance level of $p<0.05$. Spearman's rank correlation was performed to examine the association between maternal serum leptin and umbilical cord leptin. No regression analysis was performed, as the primary objective was to compare group differences rather than develop a predictive mode.

## Results

***Maternal and Neonatal Characteristics***

In terms of demographic and obstetric characteristics, maternal age was slightly higher in the obese group (31.90±6.34 years, range 22.00-48.00) compared with the normal-weight group (29.03±5.71 years, range 16.00-40.00), although this difference did not reach statistical significance ($p=0.071$). As expected, pre-pregnancy BMI and maternal weight at delivery were significantly higher in the obese group (28.83±2.14 vs.21.59±1.99 kg/m², $p<0.001$,

and 81.16±8.45 vs. 64.98±9.31 kg, $p<0.001$, respectively). Interestingly, while systolic blood pressure was similar between groups ($p=0.200$), diastolic blood pressure and mean arterial pressure were significantly lower in obese women compared to normal-weight mother ($p=0.022$ and $p=0.030$) (Table 1). This finding may be explained by several factors the relatively young and healthy participants, allowing effective cardiovascular compensatory mechanisms; hemodynamic adaptations in the third trimester, including vasodilation that reduces systemic vascular resistance, individual variability in cardiovascular responses, and the influence of sample size, which may render small differences statistically significant. Additionally, all measurements were taken in a standardized manner during the third trimester, under resting conditions, which may have contributed to the observed blood pressure values. Random blood glucose levels tended to be higher among obese women, but the difference was not statistically significant (101.3±19.16 vs. 92.57±17.08 mg/dL, $p=0.067$). Among ultrasound parameters, only BPD approached statistical significance (9.22±0.28 vs. 9.15±0.40 cm; $p=0.050$). Regarding neonatal outcomes, birth weight was significantly higher in infants of obese mothers compared with controls (3238.37±346.97 vs. 2956.80±352.52 g; $p=0.003$), whereas birth length, head circumference, and ponderal index showed no significant differences ($p>0.05$).

***Maternal and Umbilical Cord Leptin Levels***

Maternal serum leptin was markedly higher in the obese group compared with the normal-weight group (70.79±39.01 vs. 44.47±42.52 ng/mL; $p=0.002$). Cord blood leptin levels were also higher in the obese group. However, the difference was not statistically significant ($p=0.394$) (Table 2).

## Discussion

Maternal characteristics in this study confirmed the significant difference in BMI between obese and normal-weight groups, consistent with global evidence demonstrating that maternal adiposity alters the intrauterine environment and influences fetal growth and metabolic programming.[12,27] Elevated BMI is associated with insulin resistance, increased circulating lipids, and a state of chronic low-grade inflammation, all of which contribute to altered nutrient transfer and fetal development.[28,29] In this study, fetal biometric measurements revealed consistently higher mean values in the obese group, particularly in biparietal diameter, head circumference, and abdominal circumference. These findings are consistent with evidence suggesting that maternal obesity creates a distinct intrauterine metabolic environment that promotes enhanced fetal growth.[13,30] Increased maternal adiposity leads to elevated circulating glucose, free fatty acids, and triglycerides, enhancing placental nutrient transport and stimulating fetal adipogenesis.[31,32]

Adiponectin is a hormone with important anti-inflammatory effects that enhances insulin sensitivity, but its levels decrease in obesity, thereby exacerbating inflammation caused by the expansion of adipose tissue. In contrast, leptin, a hormone predominantly secreted by adipose tissue, is elevated in obese pregnancies and plays a multifaceted role in fetal development, with abdominal circumference being particularly sensitive to maternal nutrient supply as leptin modulates placental nutrient transport and promotes fetal fat accumulation.[8,33] Leptin, a hormone secreted by adipose tissue, plays a crucial role in regulating fetal growth through placental nutrient transport and energy homeostasis. Maternal obesity alters leptin signaling, thereby impairing placental function and reducing nutrient flow to the fetus, which may contribute to the occurrence of intrauterine growth restriction (IUGR).[11,34] The increased abdominal circumference observed in obese pregnancies may therefore result from elevated maternal leptin combined with higher levels of circulating nutrients, supporting the concept of "fetal over-nutrition," in which maternal obesity drives disproportionate adipose deposition in the fetus.[32]

In contrast, head circumference and biparietal diameter are less affected by maternal metabolic alterations because their growth is primarily regulated by genetic factors and placental oxygenation rather than nutrient excess.[35,36] Neonatal outcomes in this study showed that neonates born to obese mothers had significantly higher mean birth weights than those born to normal-weight mothers ($p=0.003$). This finding aligns with established evidence linking maternal obesity with an increased risk of delivering large for gestational age infants.[37] The underlying mechanism involves maternal metabolic changes such as insulin resistance, hyperglycemia, and hyperlipidemia, which increase the availability of nutrients to the fetus and promote adipose tissue accumulation rather than proportional skeletal growth.[38] The absence of significant differences in birth length, head circumference, and ponderal index between groups suggests that maternal obesity predominantly affects fetal fat accretion rather than linear or

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**Table 1. Maternal and neonatal characteristics in obese and normal-weight groups.**

| Variable | Obese | Median (IQR) | Min–Max | Normal (Mean±SD) | Min–Max | Median (IQR) | *p*-value |
|---|---|---|---|---|---|---|---|
| **Demographic and Obstetric Characteristics** | | | | | | | |
| Maternal age (years) | 31.90±6.34 | 30.00 (27.00-35.00) | 22.00-48.00 | 29.03±5.71 | 16.00-40.00 | 28.50 (24.00-33.00) | 0.071 |
| Gestational age (weeks) | 37.87±1.01 | 38.00 (37.00-38.00) | 37.00-41.00 | 37.73±0.83 | 37.00-39.00 | 37.50 (37.00-38.00) | 0.719 |
| Parity | 1.43±1.28 | 1.00 (1.00-2.00) | 0.00-6.00 | 1.13±1.17 | 0.00-5.00 | 1.00 (0.00-1.00) | 0.248 |
| History of abortion | 0.20±0.48 | 0.00 (0.00-0.00) | 0.00-2.00 | 0.23±0.63 | 0.00-3.00 | 0.00 (0.00-0.00) | 0.991 |
| Weight gain during pregnancy (kg) | 12.03±5.49 | 11.00 (9.00-15.00) | 2.00-30.00 | 12.08±6.65 | 2.00-30.00 | 10.00 (8.00-15.00) | 0.973 |
| Pre-pregnancy BMI (kg/m²) | 28.83±2.14 | 28.38 (27.24-29.43) | 27.06-36.44 | 21.59±1.99 | 18.50-24.97 | 21.47 (19.71-23.44) | <0.001 |
| Maternal weight at delivery (kg) | 81.16±8.45 | 80.00 (75.00-85.00) | 68.00-108.00 | 64.98±9.31 | 49.50-90.00 | 63.00 (60.00-70.00) | <0.001 |
| Systolic blood pressure (mmHg) | 119.17±9.97 | 122.00 (114.00-125.00) | 90.00-139.00 | 123.23±13.99 | 93.00-144.00 | 123.50 (110.00- 133.00) | 0.200 |
| Diastolic blood pressure (mmHg) | 75.23±6.42 | 75.00 (70.00-80.00) | 63.00-89.00 | 80.10±9.32 | 62.00-105.00 | 80.00 (71.00-87.00) | 0.022 |
| MAP (mmHg) | 89.87±6.12 | 90.00 (86.70-93.00) | 72.00-105.70 | 94.82±10.52 | 73.00-117.00 | 93.70 (88.30-103.30) | 0.030 |
| Random blood glucose (mg/dL) | 101.30±19.16 | 96.00 (91.00–107.00) | 68.00-156.00 | 92.57±17.08 | 66.00-134.00 | 92.00 (77.00-106.00) | 0.067 |
| **Ultrasound Measurements** | | | | | | | |
| BPD (cm) | 9.22±0.28 | 9.19 (9.10-9.40) | 8.70-9.94 | 9.15±0.40 | 8.07-10.46 | 9.11 (8.90-9.30) | 0.050 |
| HC (cm) | 34.06±1.36 | 34.08 (32.80-34.84) | 31.74-38.41 | 33.43±1.53 | 29.92-35.50 | 33.85 (32.62-34.50) | 0.220 |
| AC (cm) | 33.29 ± 2.67 | 33.22 (32.18-34.50) | 29.98-35.66 | 32.42±2.10 | 25.94-35.10 | 33.05 (31.01-34.00) | 0.160 |
| **Comparison of Neonatal Outcomes between Obese and Normal Mothers** | | | | | | | |
| Birth weight (g) | 3238.37± 346.97 | 3159.00 (3000.00-3442.00) | 2636.00-4150.00 | 2956.80±352.52 | 2000.00-3700.00 | 3018.00 (2772.00-3186.00) | 0.003 |
| Birth length (cm) | 48.5±2.14 | 48.00 (47.00-50.00) | 45.00-53.00 | 47.60±2.30 | 40.00-52.00 | 48.00 (47.00-49.00) | 0.199 |
| Head circumference (cm) | 33.73±1.11 | 34.00 (33.00-34.00) | 32.00-37.00 | 33.03±1.47 | 30.00-36.00 | 33.00 (32.00-34.00) | 0.086 |
| Ponderal index (g/cm³) | 2.85±0.31 | 2.87 (2.71-2.98) | 2.06-3.70 | 2.75±0.32 | 2.35-3.75 | 2.72 (2.51-2.99) | 0.226 |

MAP: mean arterial pressure, BPD: biparietal diameter, HC: head circumference, AC: abdominal circumference

**Table 2. Comparison maternal leptin and cord blood leptin between obese and normal weight group.**

| Variable | Group | Mean | Std. Deviation | Minimum | Maximum | *p-value* | CI 95% |
|---|---|---|---|---|---|---|---|
| Maternal leptin (ng/ml) | Obese | 70.79 | 39.01 | 4.39 | 151.02 | 0.002 | 5.23-47.41 |
| | Normal | 44.47 | 42.52 | 4.85 | 206.04 | | |
| Cord blood leptin (ng/ml) | Obese | 19.71 | 14.89 | 1.76 | 67.56 | 0.394 | -4.80-12.00 |
| | Normal | 16.11 | 17.51 | 0.88 | 93.17 | | |

cranial growth, consistent with the concept of asymmetric fetal growth and the fetal overnutrition hypothesis.[39]

Maternal leptin levels were significantly elevated in obese mothers compared to the normal-weight counterparts, consistent with previous findings that leptin concentration correlates with maternal fat mass and reflects energy imbalance.[40] In this study, mean maternal serum leptin in the obese group was 70.79±39.01 ng/mL (range: 4.39-151.02 ng/mL), whereas in the normal-weight group it was 44.47±42.52 ng/mL (range: 4.85-206.04 ng/mL; $p$=0.002) (Table 2). Elevated maternal leptin contributes to leptin resistance and altered energy homeostasis, potentially influencing placental function and fetal metabolic regulation.[29]

Interestingly, although cord blood leptin was higher in the obese group, the difference was not statistically significant, suggesting that the placenta actively regulates fetal exposure to maternal leptin. This finding supports the hypothesis that placental leptin and leptin receptor (Ob-Rb) expression are modified in obesity, limiting leptin transfer to the fetus and maintaining metabolic equilibrium.[29] This regulatory mechanism may prevent excessive fetal fat accumulation despite elevated maternal leptin levels, indicating that fetal leptin production and placental transfer are influenced by complex interactions between maternal metabolic status, placental signaling pathways, and fetal growth demands, underscoring the placenta's protective role in obese pregnancies.[7]

Recent evidence consistently shows that maternal serum leptin rises in parallel with increasing adiposity and is markedly elevated in obese pregnancies, supporting its role as a marker of maternal metabolic dysregulation.[8,20] These findings align with the present study, in which obese mothers demonstrated significantly higher leptin levels than normal-weight mothers. Elevated maternal leptin has been linked to greater neonatal adiposity and higher birth weight through enhanced placental nutrient signaling and increased fetal fat deposition.[10] Recent studies also indicate that umbilical cord leptin does not always increase proportionally despite maternal hyperleptinemia, suggesting active placental regulation.[28,14] Altered expression or sensitivity of placental leptin receptors (Ob-Rb) in obese pregnancies may limit fetal exposure, thereby maintaining metabolic balance.[29,28] Collectively, these findings reinforce the concept that leptin regulation is compartment-specific, with maternal leptin reflecting maternal adiposity while fetal leptin is shaped predominantly by placental signaling.

Overall, these findings underscore the complexity of leptin biology during pregnancy and highlight the placenta's regulatory role in balancing maternal and fetal metabolic interactions. From a clinical perspective, this study emphasizes the need for effective preconception and antenatal management of obesity to reduce perinatal complications such as macrosomia and cesarean delivery, as well as to mitigate long-term metabolic risks in offspring. Future research should explore placental leptin signaling pathways, genetic polymorphisms in leptin receptors, and longitudinal effects on offspring metabolism. Larger studies incorporating placental histological and molecular analyses would provide deeper insights into the mechanisms underlying leptin regulation in obese pregnancies.

## Conclusion

Maternal obesity significantly alters the intrauterine environment, resulting in increased fetal adiposity and higher neonatal birth weight. Elevated maternal leptin levels were strongly associated with maternal adiposity, reflecting metabolic and hormonal adaptations during pregnancy. In contrast, the lack of significant differences in umbilical cord

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leptin concentrations between groups suggests a potential placental regulatory mechanism that limits direct fetal exposre to maternal leptin.

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## Authors' Contributions

RL, Y, and NS contributed to the conceptualization and design of the research. RL, and Y were responsible for data acquisition, data calculation, data analysis, drafting the manuscript, preparing and interpreting the results. All authors reviewed and critically revised the manuscript and approved the final version.

## Ethical Statement

The study was approved by the Ethics Committee of the Faculty of Medicine, Universitas Andalas (Approval No. 483/UN.16.2.KEP-FK/2025).

## Conflict of Interest

The authors declare that they have no conflicts of interest or competing interests related to the content of this manuscript.

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