International Journal of Medical and Pharmaceutical Research

Online ISSN-2958-3683 | Print ISSN-2958-3675
Frequency: Bi-Monthly
Available online on: https://ijmpr.in/

Original Article

Serum Leptin in Umbilical Cord Blood of Infants Born to Gestational Diabetic and Non-Diabetic Mothers: A Comparative Biochemical Study

Dr Manju L John[1], Dr Renjith James[2]

[1]Assistant Professor, Department of Biochemistry, Government Medical College, Thiruvananthapuram, Kerala, India.
[2]Associate Professor, Department of General Medicine, Dr SMCSI Medical College, Karakonam, Thiruvananthapuram India.

Corresponding Author:

Dr Renjith James
Associate Professor, Department of General Medicine, Dr SMCSI Medical College, Karakonam, Thiruvananthapuram India.

Received: 21-12-2025
Accepted: 13-01-2026
Available online: 22-01-2026

ABSTRACT

Background: Leptin is a key adipokine involved in fetal growth, energy homeostasis, and long-term metabolic programming. Maternal hyperglycemia alters fetal insulin and fat accretion, potentially modifying cord blood leptin concentrations.
Objectives: To compare serum leptin levels in umbilical cord blood of infants born to gestational diabetic mothers (GDM) and non-diabetic mothers, and to evaluate correlations with neonatal anthropometric indices and maternal variables.
Methods: In this cross-sectional comparative study, 60 term neonates were enrolled (30 GDM, 30 controls). Cord venous blood was collected at delivery. Serum leptin was measured using a sandwich ELISA. Birth weight, length, head circumference, maternal BMI, and duration of GDM were recorded. Statistical analysis included independent t-test and Pearson correlation.
Results: Mean cord blood leptin levels did not differ significantly between infants of GDM and non-diabetic mothers. However, leptin showed a statistically significant positive correlation with neonatal birth weight. No significant correlation was observed with birth length, head circumference, maternal BMI, or duration of GDM.
Conclusion: Despite the metabolic alterations of GDM, cord blood leptin concentrations were comparable between groups. Leptin strongly reflects neonatal fat mass, evidenced by its association with birth weight, supporting its role as a biochemical marker of fetal adiposity rather than maternal glycemic status.

Keywords*: Leptin; Gestational diabetes mellitus; Cord blood; Fetal adiposity; Neonatal anthropometry; Placental hormones; Metabolic programming.*

INTRODUCTION

Leptin is a 167-amino-acid peptide hormone primarily secreted by adipocytes and encoded by the **ob** gene [1]. It plays a pivotal role in appetite regulation, energy expenditure, glucose metabolism, insulin sensitivity, and lipid homeostasis. Beyond its central hypothalamic actions, leptin exerts significant peripheral effects on pancreatic β-cells, hepatic glucose production, immune modulation, angiogenesis, and reproductive physiology. During pregnancy, leptin is synthesized not only by maternal adipose tissue but also by the placenta and fetal adipocytes, resulting in dynamic changes in circulating leptin levels in both maternal and fetal compartments [2,3].

Umbilical cord blood leptin is increasingly recognized as a biochemical surrogate marker of fetal adiposity and metabolic status. Several studies have demonstrated that cord blood leptin correlates strongly with neonatal fat mass, birth weight, and ponderal index, reflecting fetal energy storage and growth patterns. Leptin has also been implicated in fetal metabolic programming, influencing long-term risks of obesity, insulin resistance, and cardiovascular disease [4].

Gestational diabetes mellitus (GDM) is characterized by glucose intolerance of varying severity with onset or first recognition during pregnancy. GDM leads to maternal hyperglycemia, which crosses the placenta and induces fetal hyperinsulinemia. This metabolic milieu promotes increased nutrient uptake by the fetus, enhanced lipogenesis, and accelerated fat deposition, resulting in macrosomia and increased neonatal adiposity. Biochemically, these changes could modulate fetal adipokine secretion, including leptin [5-7].

Placental leptin production is regulated by insulin, glucose, inflammatory cytokines, and hypoxic conditions. In GDM, placental expression of leptin may be altered through insulin-mediated pathways and inflammatory signaling. Fetal adipocytes, stimulated by hyperinsulinemia, may further augment leptin synthesis. However, available literature presents conflicting results: some studies report higher cord blood leptin in infants of GDM mothers, while others demonstrate no significant difference or suggest that leptin levels are primarily determined by fetal fat mass rather than maternal glycemic status [8].

Understanding whether GDM independently alters fetal leptin concentrations is important for elucidating mechanisms of fetal metabolic programming and for identifying potential biochemical markers of intrauterine exposure to maternal metabolic disorders. If leptin primarily reflects fetal adiposity, it may serve as a marker of neonatal fat mass rather than a direct indicator of maternal glycemic control [9-13].

The present study was undertaken to biochemically evaluate cord blood leptin levels in neonates born to mothers with GDM and to compare them with those of non-diabetic mothers. Additionally, we examined the relationship between leptin and neonatal anthropometric indices as well as maternal metabolic parameters, including body mass index (BMI) and duration of GDM.

MATERIAL AND METHODS

Study Design and Setting

This cross-sectional comparative study was conducted at **SAT Hospital, Government Medical College, Thiruvananthapuram**, a tertiary care teaching hospital.

Sample Collection

Immediately after delivery, **cord venous blood** was collected under aseptic conditions. Samples were centrifuged at 3000 rpm for 10 minutes, and serum was separated and stored at **−20°C** until biochemical analysis.

Biochemical Assay

Serum leptin concentration was measured using a **commercial sandwich enzyme-linked immunosorbent assay (ELISA)** kit (Diagnostics Biochem Canada Inc.). Optical density was measured at **450 nm**, and leptin concentrations were calculated using a standard calibration curve.

Study Population

A total of **60 term neonates** were enrolled:

- **30 neonates born to mothers diagnosed with gestational diabetes mellitus (GDM group)**
- **30 neonates born to non-diabetic mothers (control group)**

Inclusion Criteria

1. Singleton term neonates (gestational age 37–42 weeks).
2. Mothers diagnosed with GDM based on standard oral glucose tolerance testing (for the study group).
3. Healthy neonates with **Apgar score ≥8 at 5 minutes**.
4. Written informed consent obtained from the mother.

Exclusion Criteria

1. Pre-gestational diabetes mellitus.
2. Maternal chronic systemic illness (hypertension, renal disease, thyroid disorders, autoimmune diseases).
3. Obstetric complications (pre-eclampsia, intrauterine growth restriction, polyhydramnios).
4. Multiple gestations.
5. Congenital anomalies or chromosomal abnormalities.

Sample Collection

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Biochemical Assay

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Variables Studied

- **Primary outcome:** Cord blood serum leptin (ng/mL)

- **Neonatal variables:** Birth weight, birth length, head circumference
- **Maternal variables:** Body mass index (BMI), duration of GDM

Statistical Analysis

Data were analyzed using **SPSS version 22**.

- Continuous variables were expressed as mean ± standard deviation.
- **Independent t-test** was used for comparison between groups.
- **Pearson correlation coefficient (r)** assessed associations between leptin and anthropometric/maternal variables.
- A **p-value <0.05** was considered statistically significant.

RESULTS

Mean serum leptin concentration in umbilical cord blood was 11.9 ± 3.5 ng/mL in infants born to mothers with gestational diabetes mellitus and 11.3 ± 3.2 ng/mL in infants of non-diabetic mothers. Although leptin levels were marginally higher in the GDM group, the difference was not statistically significant (t = 0.68, p = 0.50), indicating that maternal glycemic status did not independently influence fetal leptin secretion.

Table 1. Comparison of Cord Blood Leptin Between Study Groups

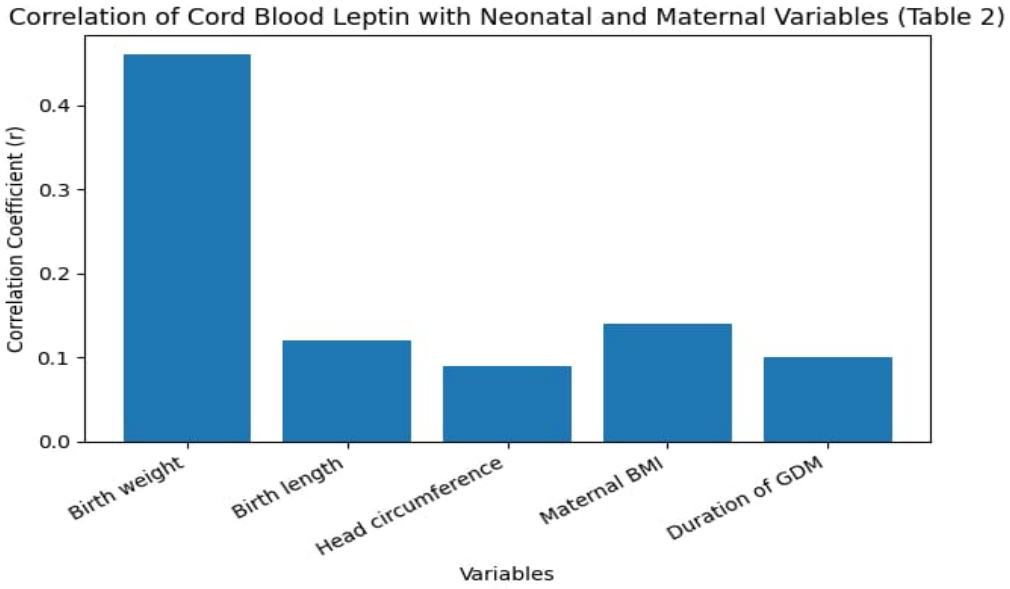
Group	N	Mean Leptin (ng/mL)	SD	t-value	p-value
Infants of GDM Mothers	30	**11.9**	**3.5**	**0.68**	**0.50**
Infants of Non-Diabetic Mothers	30	**11.3**	**3.2**	—	—

Interpretation: Mean serum leptin levels were slightly higher in infants born to GDM mothers (11.9 ± 3.5 ng/mL) compared to controls (11.3 ± 3.2 ng/mL); however, this difference was **not statistically significant (t = 0.68, p = 0.50)**, indicating that maternal hyperglycemia did not independently alter fetal leptin secretion.

Table 2. Correlation of Cord Blood Leptin with Neonatal Anthropometric and Maternal Variables

Variable	Pearson r	p-value	Significance
Birth weight	**0.46**	**0.008**	Significant
Birth length	0.12	0.38	Not significant
Head circumference	0.09	0.52	Not significant
Maternal BMI	0.14	0.31	Not significant
Duration of GDM	0.10	0.44	Not significant

Biochemical Explanation: Cord blood leptin demonstrated a **moderate positive correlation with birth weight (r = 0.46, p = 0.008)**, confirming its association with fetal adiposity. No significant correlations were observed with linear growth parameters, maternal BMI, or duration of gestational diabetes.



Graph 1: Correlation of Cord Blood Leptin with Neonatal Anthropometric and Maternal Variables

Table 3. Summary of Biochemical Findings

Parameter	Observation	Biochemical Inference
Cord blood leptin (GDM vs Control)	11.9 ± 3.5 vs 11.3 ± 3.2 ng/mL, p = 0.50	Fetal leptin production not directly influenced by maternal hyperglycemia
Leptin vs Birth Weight	r = 0.46, p = 0.008	Leptin reflects neonatal adiposity
Leptin vs Maternal BMI / GDM Duration	r = 0.14 / 0.10, p > 0.05	Neonatal leptin reflects fetal tissue status rather than maternal metabolic state

Correlation analysis demonstrated a significant positive relationship between cord blood leptin and neonatal birth weight ($r = 0.46$, $p = 0.008$), confirming that higher leptin levels reflect increased fetal adiposity. In contrast, no significant correlations were observed between leptin and birth length ($r = 0.12$, $p = 0.38$), head circumference ($r = 0.09$, $p = 0.52$), maternal BMI ($r = 0.14$, $p = 0.31$), or duration of gestational diabetes ($r = 0.10$, $p = 0.44$). These findings indicate that cord blood leptin is primarily determined by fetal fat mass rather than maternal metabolic variables.

No statistically significant correlations were observed between cord blood leptin and **birth length, head circumference, maternal BMI, or duration of GDM.** These findings indicate that neonatal leptin secretion is more closely associated with fetal tissue composition than with maternal metabolic characteristics.

DISCUSSION

Leptin is a pivotal adipokine regulating appetite, insulin sensitivity, lipid metabolism, and energy homeostasis [2]. During pregnancy, leptin is synthesized by maternal adipose tissue, placenta, and fetal adipocytes, and cord blood leptin is considered a biochemical indicator of fetal adiposity [3,4,14,15]. The present study demonstrates that cord blood leptin levels do not differ significantly between neonates born to gestational diabetic and non-diabetic mothers, but show a strong association with birth weight, highlighting leptin's role in reflecting fetal fat mass.

The comparison of mean cord blood leptin levels between neonates born to gestational diabetic mothers and those born to non-diabetic mothers showed **no statistically significant difference ($p > 0.05$).** This indicates that maternal hyperglycemia in gestational diabetes does not independently alter fetal leptin secretion. Similar findings have been reported by Kratzsch et al. [10] and Briana et al. [14], who demonstrated that cord blood leptin is not significantly influenced by maternal diabetic status when gestational age and birth weight are controlled. These observations suggest that fetal leptin production is tightly regulated and may be buffered from maternal metabolic fluctuations through placental mechanisms [16,17]. Therefore, despite the altered intrauterine glucose environment in GDM, fetal leptin levels remain comparable to those in normal pregnancies.

Several studies have suggested that gestational diabetes may increase fetal leptin levels due to fetal hyperinsulinemia and enhanced adipogenesis [7,11]. However, other investigations, including those by Kratzsch et al. [10] and Briana et al. [14], found no significant difference in leptin concentrations between GDM and control neonates, aligning with our findings. These discrepancies in literature may arise from variations in diagnostic criteria, glycemic control, ethnic background, and sample size.

Correlation analysis revealed a **significant positive association between cord blood leptin and neonatal birth weight ($p < 0.05$),** indicating that leptin concentration increases with increasing fetal mass and adiposity. This finding supports earlier studies by Ong et al. [6] and Schubring et al. [8], who demonstrated that cord blood leptin is proportional to neonatal fat mass and serves as a biochemical marker of fetal adiposity. In contrast, no statistically significant correlation was observed between leptin and birth length or head circumference, suggesting that leptin reflects **fat accumulation rather than linear growth or skeletal development,** as also described by Clapp et al. [5] and Cetin et al. [18].

Additionally, leptin showed **no significant correlation with maternal BMI or duration of GDM,** implying that fetal leptin production is more dependent on fetal adipose tissue activity than on maternal body composition or the chronicity of hyperglycemia. Similar conclusions were reported by Lepercq et al. [9] and Lindsay et al. [16], who noted that placental regulation limits the direct influence of maternal metabolic status on fetal leptin levels.

The summary table highlights the key biochemical interpretations of the study. First, the absence of significant difference in leptin levels between GDM and control groups suggests that **maternal glycemic exposure alone does not directly modify fetal leptin secretion,** consistent with previous findings by Briana et al. [14] and Hauguel-de Mouzon et al. [17]. Second, the significant positive correlation between leptin and birth weight reinforces leptin's established role as a **biochemical marker of neonatal adiposity,** as reported by Ong et al. [6] and Valsamakis et al. [15]. Finally, the lack of association with maternal BMI and duration of GDM confirms that fetal leptin reflects **fetal tissue status rather than maternal metabolic load,** supporting the concept of placental and fetal metabolic regulation described by Lindsay et al. [16] and Desoye and Nolan [19]. These findings collectively emphasize leptin's role in fetal metabolic programming rather than as a marker of maternal glycemic control.

The significant positive correlation between leptin and birth weight observed in our study confirms previous reports that leptin concentration increases with neonatal fat mass [6,8]. Since adipocytes are the primary source of leptin, increased adiposity leads to greater leptin secretion. This supports the hypothesis that leptin functions as a biochemical marker of fetal energy stores rather than merely a hormonal mediator of maternal-fetal glucose exchange [5,18].

The absence of correlation between leptin and birth length or head circumference suggests that leptin reflects adipose tissue accumulation rather than overall growth or skeletal development. Cetin et al. [18] emphasized that adipokines primarily represent metabolic tissue function, not structural growth parameters. Similarly, the lack of association with maternal BMI indicates that fetal leptin is not a direct reflection of maternal adiposity. Placental mechanisms regulate leptin transport and synthesis, ensuring fetal metabolic autonomy [16,17].

Moreover, the lack of correlation between leptin and duration of GDM suggests that prolonged exposure to hyperglycemia does not independently influence fetal leptin production. Desoye and Nolan [19] proposed that fetal metabolic programming in GDM is mediated through complex interactions between insulin, glucose, placental hormones, and inflammatory pathways rather than a single biochemical factor.

From a developmental perspective, leptin plays an important role in metabolic programming. Elevated leptin levels at birth have been associated with altered appetite regulation, insulin resistance, and increased risk of obesity later in life [12,13,15]. Thus, although GDM does not appear to independently modify cord blood leptin in our study, leptin remains a valuable biomarker for assessing fetal adiposity and potential long-term metabolic risk.

CONCLUSION

Cord blood leptin concentrations are not significantly different between neonates born to gestational diabetic and non-diabetic mothers. However, leptin demonstrates a significant positive correlation with birth weight, confirming its role as a biochemical marker of fetal adiposity. These findings indicate that fetal leptin reflects neonatal fat mass rather than maternal glycemic exposure and highlight its importance in understanding fetal metabolic programming.

Limitations

1. Small sample size limits external validity.
2. Cross-sectional design prevents causal inference.
3. Absence of direct measurement of neonatal body fat percentage.
4. Lack of long-term follow-up for metabolic outcomes

DECLARATIONS:

Conflicts of interest: There is no any conflict of interest associated with this study
Consent to participate: There is consent to participate.
Consent for publication: There is consent for the publication of this paper.
Authors' contributions: Author equally contributed the work.

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