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Original Article

Cord Blood Leptin In Neonates of Gestational Diabetic Mothers: Clinical Correlation with Birth Weight and Maternal Factors

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ABSTRACT

Background: Gestational diabetes mellitus (GDM) is a common metabolic complication of pregnancy associated with altered fetal growth, neonatal adiposity, and increased long-term risk of obesity and metabolic syndrome. Leptin, a placentally and adipose-derived hormone, plays a central role in energy homeostasis, appetite regulation, insulin sensitivity, and fat deposition. Cord blood leptin reflects fetal fat mass and may serve as an early biomarker of metabolic programming.
Objectives: To compare cord blood leptin levels in neonates born to mothers with GDM and those born to normoglycemic mothers, and to evaluate its association with neonatal anthropometric parameters and selected maternal factors.
Methods: A comparative cross-sectional study was conducted among 60 term neonates (30 born to GDM mothers and 30 to non-diabetic mothers). Cord blood leptin was measured using enzyme-linked immunosorbent assay (ELISA). Neonatal anthropometry (birth weight, length, head circumference) and maternal variables (BMI, duration of GDM) were recorded. Statistical analysis included group comparisons and correlation testing.
Results: Mean leptin levels were 11.8 ± 3.4 ng/mL in the GDM group and 11.2 ± 3.1 ng/mL in controls ($p = 0.42$). A significant positive correlation was observed with birth weight ($r = 0.46$, $p = 0.008$), but not with length, head circumference, maternal BMI, or duration of GDM. Conclusion: GDM did not independently influence cord blood leptin. Leptin closely reflected neonatal adiposity through its association with birth weight.
Conclusion: Maternal GDM did not independently influence cord blood leptin levels in this cohort. However, leptin demonstrated a strong association with neonatal birth weight, suggesting that it primarily reflects fetal adiposity rather than maternal glycemic status. Cord blood leptin may serve as a useful biomarker for identifying infants at potential risk for future obesity and metabolic disorders.

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

INTRODUCTION

Gestational diabetes mellitus (GDM) is one of the most prevalent metabolic disorders complicating pregnancy worldwide, with increasing incidence parallel to rising rates of obesity and sedentary lifestyles [1]. GDM is characterized by glucose intolerance of variable severity with onset or first recognition during pregnancy and is associated with both immediate and long-term adverse outcomes for mother and child [2]. Neonates born to mothers with GDM are at increased risk of macrosomia, shoulder dystocia, neonatal hypoglycemia, respiratory distress, and long-term metabolic derangements including obesity, insulin resistance, and type 2 diabetes mellitus [3,4].

Fetal growth and adiposity in pregnancies complicated by GDM are influenced not only by maternal hyperglycemia but also by complex endocrine, metabolic, and placental adaptations [5]. Hyperinsulinemia in the fetus in response to maternal hyperglycemia promotes increased fat deposition, altered body composition, and accelerated growth [6]. However, variability in neonatal size among infants of diabetic mothers suggests that additional regulatory factors beyond glucose and insulin contribute to fetal growth patterns [7].

Leptin is a 16-kDa adipokine predominantly secreted by adipose tissue and the placenta during pregnancy. It plays a pivotal role in appetite regulation, energy expenditure, lipid metabolism, insulin sensitivity, and neuroendocrine function [8]. In the intrauterine environment, leptin is thought to be involved in placental development, angiogenesis, and nutrient transport, thereby influencing fetal growth and fat accretion [9]. Cord blood leptin levels have been shown to correlate strongly with neonatal fat mass and birth weight, making leptin a potential marker of fetal adiposity [10].

Several studies have demonstrated elevated cord blood leptin concentrations in macrosomic infants and in offspring of obese mothers, reflecting increased adiposity at birth [11,12]. However, findings regarding the relationship between maternal GDM and neonatal leptin levels remain inconsistent. Some researchers have reported significantly higher cord blood leptin levels in infants born to GDM mothers compared to controls [13,14], while others have found no difference when glycemic control is adequate [15,16]. These discrepancies may be attributed to differences in maternal metabolic control, ethnicity, gestational age, degree of adiposity, and placental function [17].

The concept of fetal programming suggests that adverse intrauterine metabolic environments can permanently alter organ structure and function, predisposing offspring to chronic metabolic diseases later in life [18]. Leptin is increasingly recognized as a key mediator in this programming process. Elevated leptin exposure in utero may influence hypothalamic appetite regulation and adipocyte development, thereby shaping long-term energy balance and obesity risk [19].

In addition to maternal glycemic status, maternal body mass index (BMI), gestational weight gain, and placental function are important determinants of fetal leptin levels [20]. Some studies suggest that maternal obesity has a stronger influence on neonatal leptin than GDM itself [21]. Furthermore, the duration and severity of hyperglycemia during pregnancy may also modify fetal endocrine responses [22].

Given these considerations, understanding the clinical significance of cord blood leptin in pregnancies complicated by GDM is crucial. Identifying whether leptin levels are primarily influenced by maternal metabolic disease or by fetal growth parameters can help clarify its potential role as an early biomarker for metabolic risk.

MATERIALS AND METHODS

This was a hospital-based comparative cross-sectional study conducted in the Department of Biochemistry in collaboration with the Department of General Medicine and Department of Obstetrics and Neonatology at a tertiary care center.

Study Population

The study included 60 term neonates delivered during the study period:

- **GDM Group:** 30 neonates born to mothers diagnosed with gestational diabetes mellitus.
- **Control Group:** 30 neonates born to normoglycemic mothers.

Inclusion Criteria

1. Term neonates (gestational age 37–42 weeks).
2. Singleton pregnancy.
3. Mothers diagnosed with GDM based on standard oral glucose tolerance test (OGTT) criteria (for GDM group).
4. Mothers with normal glucose tolerance during pregnancy (for control group).
5. Informed consent obtained from the mother.

Exclusion Criteria

1. Pre-gestational diabetes mellitus.
2. Multiple pregnancies.
3. Preterm delivery (<37 weeks).
4. Congenital anomalies or chromosomal disorders in neonates.
5. Maternal chronic illnesses such as hypertension, thyroid disease, renal disease, or autoimmune disorders.
6. Intrauterine growth restriction (IUGR).
7. Neonates with birth asphyxia or severe perinatal complications.

Data Collection

Maternal variables recorded included age, body mass index (BMI), mode of delivery, and duration of GDM. Neonatal variables included sex, birth weight, birth length, and head circumference.

Cord Blood Sampling and Leptin Estimation

At delivery, umbilical cord blood was collected under aseptic conditions. Serum was separated and stored at appropriate temperature until analysis. Cord blood leptin levels were measured using a commercially available enzyme-linked immunosorbent assay (ELISA) kit following the manufacturer's protocol.

Statistical Analysis

Data were analyzed using standard statistical software. Continuous variables were expressed as mean ± standard deviation. Comparison between GDM and control groups was performed using Student's t-test. Correlation between cord blood leptin and neonatal/maternal variables was assessed using Pearson's correlation coefficient. A p-value <0.05 was considered statistically significant.

RESULTS

Table 1. Baseline Clinical Characteristics of Study Groups

Variable	GDM Group (n=30)	Control Group (n=30)	p-value
Maternal age (years)	27.8 ± 3.6	26.9 ± 3.4	0.34
Maternal BMI (kg/m²)	26.1 ± 2.9	25.4 ± 2.7	0.28
Mode of delivery (Vaginal/LSCS)	17 / 13	18 / 12	0.79
Neonatal sex (Male/Female)	16 / 14	15 / 15	0.80

There were no statistically significant differences in baseline maternal or neonatal characteristics between the GDM and control groups, indicating good comparability and minimal confounding.

Table 2. Comparison of Cord Blood Leptin Levels

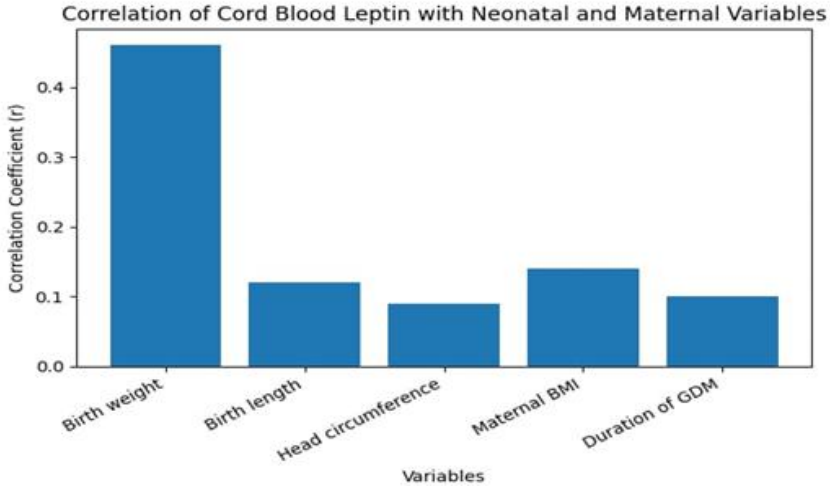
Parameter	GDM Group	Control Group	p-value
Cord blood leptin (ng/mL)	**11.8 ± 3.4**	**11.2 ± 3.1**	**0.42**

Mean cord blood leptin levels were slightly higher in neonates of GDM mothers; however, this difference was **not statistically significant (p = 0.42)**, indicating that gestational diabetes did not independently influence leptin concentrations at birth.

Table 3. Association of Cord Blood Leptin with Neonatal and Maternal Variables

Variable	Correlation with Leptin (r)	p-value	Clinical 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

Cord blood leptin showed a **moderate positive correlation with birth weight (r = 0.46, p = 0.008)**, confirming that higher leptin levels reflect increased neonatal adiposity. No significant correlations were observed with length, head circumference, maternal BMI, or duration of GDM.



Graph 1: . Association of Cord Blood Leptin with Neonatal and Maternal Variables

Table 4. Clinical Interpretation of Key Findings

Finding	Clinical Meaning
No significant difference in leptin between GDM and controls (11.8 ± 3.4 vs 11.2 ± 3.1 ng/mL; p = 0.42)	Suggests effective glycemic control and placental regulation may buffer fetal metabolic exposure
Significant correlation with birth weight (r = 0.46; p = 0.008)	Indicates leptin reflects neonatal fat mass and may predict future obesity risk
No association with maternal BMI or GDM duration	Fetal leptin appears more dependent on growth patterns than maternal metabolic severity

Baseline maternal and neonatal characteristics were comparable between the two groups. The mean maternal age in the GDM group was 27.8 ± 3.6 years compared to 26.9 ± 3.4 years in controls ($p = 0.34$). Maternal BMI was slightly higher in the GDM group (26.1 ± 2.9 kg/m²) than in controls (25.4 ± 2.7 kg/m²), but the difference was not statistically significant ($p = 0.28$). The distribution of mode of delivery (vaginal vs LSCS) and neonatal sex was also similar between groups ($p > 0.05$ for both).

Cord blood leptin levels were marginally higher in neonates born to GDM mothers (11.8 ± 3.4 ng/mL) compared with controls (11.2 ± 3.1 ng/mL); however, this difference was not statistically significant ($p = 0.42$). Correlation analysis demonstrated a significant positive relationship between cord blood leptin and neonatal birth weight ($r = 0.46$, $p = 0.008$), indicating that leptin levels increase with greater 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 ($r = 0.10$, $p = 0.44$).

DISCUSSION

This study evaluated cord blood leptin concentrations in neonates born to mothers with gestational diabetes mellitus and explored their relationship with neonatal anthropometry and maternal variables. The principal findings were: [1] no significant difference in cord blood leptin between GDM and control groups, and [2] a significant positive correlation between leptin levels and neonatal birth weight.

Leptin is widely recognized as a surrogate marker of adipose tissue mass in both adults and neonates. Previous studies have consistently demonstrated a strong association between cord blood leptin and neonatal fat mass [10,11]. Our finding of a positive correlation between leptin and birth weight aligns with the observations of Clapp and Kiess [12], who reported that leptin concentrations at birth closely reflect fetal adiposity. Similarly, Hauguel-de Mouzon et al. [13] demonstrated that cord blood leptin is proportional to neonatal fat mass and is influenced by placental synthesis.

The absence of a significant difference in leptin levels between neonates of GDM and non-diabetic mothers in our study is noteworthy. Some investigators have reported elevated cord blood leptin in infants of diabetic mothers [14,15], attributing this to increased fetal adiposity secondary to hyperinsulinemia. However, other studies have failed to demonstrate such differences when maternal glycemic control is optimal [16,17]. For instance, Schubring et al. [16] observed comparable leptin levels in well-controlled GDM pregnancies and normoglycemic pregnancies, suggesting that effective antenatal management may mitigate endocrine alterations in the fetus.

Our results support the latter view, indicating that GDM does not necessarily translate into altered fetal leptin levels, particularly when maternal metabolic status is adequately managed. This finding underscores the importance of antenatal care and glycemic control in preventing adverse fetal metabolic programming.

The lack of association between leptin and maternal BMI in our cohort contrasts with studies showing higher neonatal leptin levels in offspring of obese mothers [18,19]. Catalano et al. [18] demonstrated that maternal obesity exerts a stronger influence on fetal adiposity and leptin levels than GDM alone. The discrepancy in our findings may be due to the relatively narrow BMI range among participants and the exclusion of mothers with extreme obesity.

Similarly, no significant relationship was found between leptin levels and the duration of GDM. This suggests that the length of exposure to hyperglycemia during pregnancy may be less important than the overall pattern of fetal growth and fat deposition. Lindsay et al. [20] reported that fetal leptin concentrations are more closely related to placental function and fetal adipocyte development than to maternal metabolic indices alone.

From a pathophysiological perspective, leptin plays a central role in fetal energy homeostasis and adipogenesis. It is produced not only by fetal adipose tissue but also by the placenta, which acts as an endocrine organ modulating nutrient transfer and hormonal signaling [21]. Placental leptin expression has been shown to increase in response to hypoxia, inflammation, and insulin, further complicating the relationship between maternal metabolic status and fetal leptin levels [22].

The concept of fetal programming provides a framework for interpreting our findings. According to the Barker hypothesis, intrauterine environmental factors influence the long-term risk of metabolic disease [23]. Leptin exposure during critical periods of development may shape hypothalamic appetite regulation and adipocyte differentiation, thereby influencing future obesity risk [24]. Our observation that leptin correlates with birth weight supports its role as an early indicator of neonatal adiposity and potential metabolic vulnerability.

Clinically, the measurement of cord blood leptin may help identify neonates with increased fat mass who may be at higher risk for childhood obesity and metabolic syndrome, irrespective of maternal diabetic status. This could facilitate early lifestyle interventions and long-term follow-up in high-risk infants.

Nevertheless, our study has limitations. The sample size was modest, which may limit the detection of subtle differences between groups. Additionally, direct measures of neonatal body composition, such as skinfold thickness or dual-energy X-ray absorptiometry (DEXA), were not performed. Longitudinal follow-up of infants was also beyond the scope of this study, precluding assessment of long-term metabolic outcomes [25].

Despite these limitations, the study contributes to the growing body of evidence suggesting that neonatal leptin reflects fetal adiposity more than maternal glycemic status. This has important implications for understanding the mechanisms underlying metabolic programming and for developing early preventive strategies.

CONCLUSION

Cord blood leptin levels were not significantly different between neonates born to mothers with gestational diabetes mellitus and those born to normoglycemic mothers. However, leptin showed a significant positive correlation with neonatal birth weight, indicating that it primarily reflects fetal adiposity. These findings suggest that leptin may serve as a useful biomarker for identifying infants at risk of future obesity and metabolic disorders, independent of maternal diabetic status.

Limitations of the Study

1. Small sample size, limiting generalizability.
2. Lack of direct assessment of neonatal body fat composition.
3. Absence of long-term follow-up to correlate leptin levels with later metabolic outcomes.
4. Potential influence of unmeasured confounding factors such as maternal diet and physical activity.

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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