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Umbilical cord asprosin and subfatin levels in relation to neonatal metabolic outcomes in gestational diabetes mellitus: a cross-sectional study

Figen Efe Camili^{1*} , Ozlem Kemer Aycan², Merve Akis Yilmaz³, Bayram Burak Ceviz¹, Selim Afsar¹, Gurhan Guney¹ and Mine Islimye Taskin¹

Abstract

Background Gestational diabetes mellitus (GDM) is a common pregnancy complication that may influence the intrauterine metabolic environment and neonatal glucose regulation. Novel adipokines such as asprosin and subfatin have been implicated in glucose homeostasis. This study aimed to evaluate umbilical cord blood levels of asprosin and subfatin in pregnancies complicated by GDM and to examine their associations with neonatal clinical and metabolic outcomes.

Methods This cross-sectional study included 40 women with GDM, 40 healthy pregnant women, and their newborns who delivered at Balikesir University Faculty of Medicine Hospital between August 2025 and October 2025. Maternal demographic characteristics, 75-g oral glucose tolerance test results, HbA1c levels and GDM treatment modality were recorded. Neonatal outcomes included Apgar scores, birth weight, early postnatal blood glucose levels, weight at one month and feeding mode. Umbilical cord blood asprosin and subfatin concentrations were measured using ELISA.

Results Mothers with GDM were older and had higher fasting glucose, 1- and 2-hour OGTT glucose levels, HbA1c and body mass index compared with controls (all $p < 0.01$). Infants born to mothers with GDM had higher birth weight ($p = 0.007$) and greater weight at one month ($p = 0.01$), while neonatal blood glucose levels were significantly lower during early postnatal follow-up ($p < 0.001$). In unadjusted analyses, umbilical cord asprosin (23.15 ± 10.21 vs. 35.63 ± 26.97 ng/mL, $p = 0.01$) and subfatin levels (2.85 ± 1.45 vs. 4.17 ± 3.11 ng/mL, $p = 0.03$) were lower in the GDM group. However, these differences were no longer statistically significant after multivariable adjustment (MANCOVA) for maternal age, body mass index, fetal sex and GDM treatment modality. In contrast, early neonatal blood glucose levels remained significantly lower in the GDM group after multivariable adjustment.

Conclusions Pregnancies complicated by GDM are associated with differences in neonatal growth and glucose regulation, while alterations in umbilical cord adipokine levels appear to be influenced by maternal and fetal characteristics rather than representing independent effects of GDM. These findings suggest that cord blood

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adipokines reflect the intrauterine metabolic environment but may have limited value as independent neonatal biomarkers.

Clinical trial number Not applicable.

Keywords Asprosin, Subfatin, Gestational diabetes mellitus, Umbilical cord blood, Adipokines, Neonatal outcomes

Introduction

Gestational Diabetes Mellitus (GDM) is a metabolic disorder characterized by glucose intolerance first recognized during pregnancy, posing health risks for both mother and fetus [1]. Its global prevalence varies depending on the diagnostic criteria and screening methods. According to the International Diabetes Federation (IDF) and recent meta-analyses, GDM affects about 14% of pregnancies worldwide based on IADPSG criteria with regional differences ranging from 7.8% in Europe to over 27% in the Middle East and North Africa [2–4]. These differences are influenced by diagnostic standards, screening strategies and demographic factors. Patients with GDM are at higher risk of preterm delivery, pre-eclampsia and assisted births [5–7]. In the long term, these women also carry a higher risk of developing type 2 diabetes and cardiovascular disease [8–10]. Infants of GDM mothers may experience high birth weight, shoulder dystocia, prolonged labor and postnatal hypoglycemia [11–13]. Moreover these children may be predisposed to obesity, glucose intolerance, early-onset diabetes and neurodevelopmental disorders later in life [14–16]. Early diagnosis and management of GDM are therefore crucial.

Adipokines, bioactive molecules secreted by adipose tissue, play an important role in metabolic regulation and inflammation. They have been increasingly studied for their role in GDM and its effects on maternal and fetal health [17–19]. Asprosin, a 140-amino-acid peptide encoded by the FBN1 gene, is secreted by white adipose tissue in response to fasting. It stimulates hepatic glucose release, increasing blood glucose levels, and crosses the blood–brain barrier to activate appetite-stimulating neurons, which can lead to weight gain [20, 21]. Asprosin has also been implicated in metabolic disorders such as NAFLD, obesity, metabolic syndrome, diabetes, PCOS and cardiovascular diseases [22–26].

Subfatin, also known as Metrnl (Meteorin-like protein) is a novel adipomyokine secreted by adipose tissue and skeletal muscle. It regulates energy metabolism, insulin sensitivity and inflammation [27]. Exercise and cold exposure increase subfatin levels, which enhance glucose uptake in peripheral tissues and reduce pro-inflammatory cytokines. It also promotes browning of white adipose tissue, increasing energy expenditure. Studies suggest that subfatin is associated with obesity, insulin resistance, type 2 diabetes and NAFLD through its effects on glucose metabolism and inflammation [28–32].

Although several studies have investigated the role of novel adipokines in gestational diabetes mellitus, existing evidence has predominantly focused on individual biomarkers. To date, asprosin and subfatin (Metrnl) have been evaluated separately in the context of GDM, and data regarding their simultaneous assessment in the same maternal–neonatal cohort are lacking. Given that both adipokines are involved in glucose homeostasis and energy metabolism, their concurrent evaluation may provide complementary insights into fetal metabolic adaptation in GDM pregnancies. Therefore, the present study aimed to simultaneously assess umbilical cord blood levels of asprosin and subfatin in neonates born to mothers with and without GDM and to examine their associations with neonatal clinical and metabolic outcomes.

Materials and methods

Study design and participants

This cross-sectional study included 40 healthy pregnant women and 40 women diagnosed with gestational diabetes mellitus (GDM), along with their newborns. The study was conducted at Balikesir University Faculty of Medicine Hospital between August and October 2025. Participants were consecutively selected from eligible postpartum women who provided written consent. Eligible participants were women aged 18–45 years with newborns at 37–41 weeks of gestation. The sample size was determined based on a power analysis using previously reported mean differences and standard deviations of plasma asprosin and visfatin levels [33, 34]. Visfatin was used as a reference adipokine due to the lack of prior studies reporting cord blood subfatin variability at the time of study planning. Using a two-sided independent samples t-test, with a significance level of 0.05 and 80% power, an effect size (Cohen's *d*) of 0.65 indicated that 40 participants per group would be sufficient to detect anticipated differences.

The GDM group ($n = 40$) consisted of women diagnosed according to the World Health Organization (WHO) 2013 criteria, using a 75 g oral glucose tolerance test OGTT performed between 24 and 28 weeks of gestation. Diagnosis was made if fasting plasma glucose was ≥ 5.1 mmol/L (92 mg/dL), 1-hour plasma glucose ≥ 10.0 mmol/L (180 mg/dL), or 2-hour plasma glucose ≥ 8.5 mmol/L (153 mg/dL) [35]. The healthy group ($n = 40$) included women without chronic diseases, whose gestational diabetes and other metabolic disorders were

excluded based on medical history and a normal OGTT. Women who experienced complications during delivery or whose newborns showed signs of fetal distress, were excluded. Women with type 1 diabetes mellitus were also not included.

Treatment modalities applied throughout pregnancy after the diagnosis of GDM were identified. Women with GDM were classified according to treatment approach as lifestyle and dietary modification or insulin therapy. Patients who maintained normal glucose levels without pharmacological treatment were included in the lifestyle and dietary modification group. Patients with insufficient follow-up data were classified as not followed-up.

Demographic data, including maternal age, gravidity, gestational age, body mass index (BMI) and gestational weight gain, were recorded for all participants. Laboratory parameters were collected by reviewing medical records, including fasting plasma glucose and HbA1c levels measured prior to delivery, as well as results from the 75 g OGTT performed between 24 and 28 weeks of gestation. Neonatal data, including birth weight, length, sex and APGAR scores at 1 and 5 min, were recorded. Early neonatal blood glucose measurements at 30 min after birth and, if available, hemoglobin (HB), white blood cell count (WBC) and C-reactive protein (CRP) values were also documented. Follow-up with the mothers was conducted to obtain information on the newborns' feeding method and weight at one month of age. Because some measurements were unavailable for certain participants, sample sizes varied across variables and the analyses were conducted based on the available number of participants for each parameter.

Asprosin and subfatin (Metrnl) measurement

Plasma levels of asprosin were measured using the Asprosin Sunred ELISA kit (Catalog No: 201-12-7691D, SunRed Biological Technology, Shanghai, China) with a sensitivity of 0.938 ng/mL and a detection range of 1.563–100 ng/mL. Plasma levels of subfatin (Metrnl) were measured using the Subfatin (Metrnl) Sunred ELISA kit (Catalog No: SRB-T-81862, SunRed Biological Technology, Shanghai, China) with a sensitivity of 0.042 ng/mL and a detection range of 0.05–15 ng/mL. The intra-assay CV was <10% and the inter-assay CV was <12% for both kits. Standards and samples were duplicated. The standard curves were plotted using a four-parameter logistic curve, and R^2 values were 0.997 and 0.999, respectively.

Statistical analysis

Statistical analyses were performed using Jamovi software (version 2.3.21). Normality of continuous variables was assessed using skewness, kurtosis, and the

Shapiro–Wilk test. Data are presented as mean \pm standard deviation or median, as appropriate.

Group comparisons were performed using independent samples t-tests or Mann–Whitney U tests for continuous variables and the Chi-square test for categorical variables.

Multivariate analysis of covariance (MANCOVA) was used to assess between group differences in umbilical cord asprosin, subfatin, neonatal birth weight and early neonatal blood glucose levels, adjusting for maternal age, body mass index (BMI), fetal sex and GDM treatment modality. Associations between cord blood adipokines and neonatal outcomes were analyzed using partial Pearson correlation analysis, controlling for maternal BMI.

A two-sided p -value < 0.05 was considered statistically significant. Analyses were conducted based on available data.

Due to missing data for some maternal and neonatal variables, statistical analyses were performed using available-case data for each parameter.

Results

Maternal demographic and metabolic characteristics are presented in Table 1. Women in the GDM(+) group were significantly older than those in the GDM(-) group ($p=0.02$). Pre-pregnancy body mass index (BMI) was also significantly higher in the GDM(+) group ($p=0.005$). As expected, fasting glucose ($p=0.001$), 1-hour OGTT glucose ($p<0.001$), 2-hour OGTT glucose ($p<0.001$), and HbA1c levels ($p=0.002$) were all significantly higher in the GDM(+) group. No significant differences were observed between groups with respect to gestational age at delivery ($p=0.94$) or gestational weight gain ($p=0.34$).

Among women diagnosed with GDM ($n=40$), 32 (80%) were managed with lifestyle and dietary modification alone, 5 (12.5%) required insulin therapy and 3 (7.5%) had incomplete follow-up data regarding treatment modality. Treatment approach was included as a covariate in the multivariable models to account for potential differences in glycemic management.

Baseline neonatal birth characteristics are summarized in Table 2A. Gestational age at birth and sex distribution did not differ significantly between groups. However, birth weight was significantly higher among infants born to mothers with GDM compared with controls ($p=0.007$). Birth length and Apgar scores at both 1 and 5 min were comparable between groups.

Postnatal neonatal biochemical measurements are shown in Table 2B. Early neonatal blood glucose levels were significantly lower in the GDM(+) group compared with the GDM(-) group ($p<0.001$). No significant differences were observed in neonatal white blood cell count ($p=0.34$) or C-reactive protein levels ($p=0.14$).

Table 1 Descriptive statistics of maternal demographic and clinical characteristics in groups

Variable	GDM (-) (n=40)	GDM (+) (n=40)	p value
Age (years)	27.15 ± 4.35	29.65 ± 5.06	0.02 ^a
Gestational age (weeks)	38.45 ± 1.03	38.48 ± 1.27	0.94 ^a
Pre-pregnancy BMI (kg/m ²)	28.18 ± 3.43 (n=40)	30.58 ± 3.94 (n=38)	0.005 ^a
Gestational weight gain (kg)	12.99 ± 5.35	11.88 ± 5.03	0.34 ^a
Fasting glucose (mg/dL)*	81.71 ± 4.28 (n=28)	92.47 ± 8.57 (n=36)	0.001 ^a
1-hour OGTT glucose (mg/dL)*	123.64 ± 14.75 (n=28)	159.53 ± 28.16 (n=36)	< 0.001 ^a
2-hour OGTT glucose (mg/dL)*	110.89 ± 17.98 (n=28)	128.50 ± 16.71 (n=36)	< 0.001 ^a
HbA1c (%)	4.95 ± 0.40	5.32 ± 0.61	0.002 ^b
GDM treatment modality, n (%)			
Lifestyle/diet only	-	32 (80%)	—
Insulin therapy	-	5 (12.5%)	—
Not followed-up	-	3 (7.5%)	—

Footnotes. Values are presented as mean ± standard deviation. p values indicate between-group comparisons. ^aIndependent samples t-test; ^bMann-Whitney U test. *OGTT-related measurements were available for a subset of participants due to incomplete test records; analyses were performed using available-case data. BMI: body mass index; OGTT: oral glucose tolerance test; GDM: gestational diabetes mellitus. Treatment modality is presented descriptively for the GDM group and was included as a covariate in multivariable analyses

Table 2A Baseline neonatal birth characteristics

Variable	GDM (-) (n=40)	GDM (+) (n=40)	p value
Gestational age (weeks)	38.45 ± 1.03	38.48 ± 1.27	0.94 ^a
Sex (male/female), n	18 / 22	23 / 17	0.35 ^b
Birth weight (g)	3080.13 ± 450.91	3363.13 ± 465.78	0.007 ^a
Birth length (cm)	49.00 ± 2.28	49.63 ± 3.18	0.32 ^a
APGAR score (1 min)	7.67 ± 1.02	7.80 ± 0.82	0.55 ^a
APGAR score (5 min)	8.78 ± 0.86	8.93 ± 0.57	0.36 ^a

Footnotes: Values are presented as mean ± SD or number. ^aIndependent samples t-test; ^bChi-square test. GDM: gestational diabetes mellitus

Table 2B Postnatal neonatal biochemical measurements

Variable	GDM (-)	GDM (+)	p value
Early neonatal blood glucose (mg/dL)*	66.52 ± 10.57 (n=27)	51.68 ± 8.12 (n=19)	< 0.001 ^a
WBC (10 ³ /μL)	15.72 ± 5.46 (n=27)	14.29 ± 4.37 (n=19)	0.34 ^a
CRP (mg/L)	3.55 ± 3.56 (n=27)	6.38 ± 9.00 (n=19)	0.14 ^a

Footnotes: Values are presented as mean ± SD. ^aIndependent samples t-test. *Early neonatal blood glucose was measured at 30 min after birth during routine clinical monitoring. WBC: white blood cell count; CRP: C-reactive protein

Table 2C Postnatal growth and feeding characteristics

Variable	GDM (-) (n=40)	GDM (+) (n=40)	p value
Weight at 1 month (g)	3902.13 ± 554.24	4241.25 ± 478.50	0.01 ^a
Feeding type, n (%)			0.74 ^b
— Exclusive breastfeeding	25 (62.5%)	23 (57.5%)	
— Formula feeding	3 (7.5%)	2 (5.0%)	
— Mixed feeding	12 (30.0%)	15 (37.5%)	

Footnotes: ^aIndependent samples t-test; ^bChi-square test

Postnatal growth and feeding characteristics are presented in Table 2C. Weight at one month of age was significantly higher in infants born to mothers with GDM ($p=0.01$). The distribution of feeding types (exclusive

breastfeeding, formula feeding, or mixed feeding), recorded descriptively at one month, did not differ significantly between groups ($p=0.74$).

Umbilical cord serum asprosin and subfatin concentrations, neonatal birth weight and early neonatal blood glucose levels were further evaluated using MANCOVA, adjusting for maternal age, body mass index (BMI), fetal sex and GDM treatment modality. Umbilical cord serum asprosin and subfatin levels in the GDM and control groups are illustrated in Fig. 1. In univariate analyses, early neonatal blood glucose levels remained significantly lower in the GDM group compared with controls after adjustment ($p<0.001$). In contrast, the previously observed between-group differences in birth weight (adjusted $p=0.25$), umbilical cord asprosin (adjusted $p=0.26$) and subfatin levels (adjusted $p=0.23$) were no longer statistically significant after controlling for confounding variables (Table 3).

Partial correlation analyses adjusted for maternal BMI were performed to explore associations between umbilical cord adipokines and neonatal outcomes (Table 4). A strong positive correlation was observed between asprosin and subfatin levels ($r=0.96$, $p<0.001$). In contrast, neither asprosin nor subfatin levels were significantly correlated with neonatal anthropometric measures, blood glucose levels, Apgar scores, or inflammatory markers (all $p>0.05$).

Discussion

In the present study, we investigated umbilical cord blood levels of asprosin and subfatin in pregnancies complicated by GDM and examined their relationships with neonatal metabolic outcomes. In unadjusted analyses, cord blood asprosin and subfatin levels were lower in the GDM group, and infants born to mothers with GDM had higher birth weight and greater weight at one month.

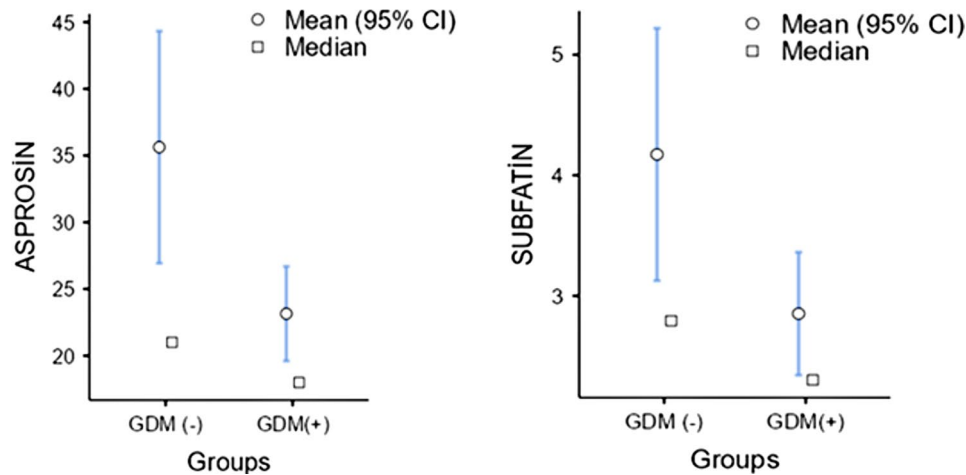


Fig. 1 Umbilical cord serum asprosin and subfatin levels in neonates born to mothers with and without gestational diabetes mellitus. Data are presented as box-and-whisker plots generated using jamovi software, showing the median (central line), interquartile range (box), and minimum–maximum values (whiskers). Concentrations are expressed in ng/mL

Table 3 Umbilical cord serum asprosin and subfatin concentrations: unadjusted and adjusted analyses

Parameter	Group	n	Mean ± SD	Unadjusted p value ^t	Adjusted p value ^m
Asprosin (ng/mL)	GDM (-)	37	35.63 ± 26.97	0.01	0.26
	GDM (+)	32	23.15 ± 10.21		
Subfatin (ng/mL)	GDM (-)	34	4.17 ± 3.11	0.03	0.23
	GDM (+)	31	2.85 ± 1.45		
Birth weight (g)	GDM (-)	40	3080.13 ± 450.91	0.007	0.25
	GDM (+)	40	3363.13 ± 465.78		
Early neonatal blood glucose (mg/dL)	GDM (-)	27	66.52 ± 10.57	<0.001	<0.001
	GDM (+)	19	51.68 ± 8.12		

Footnotes: Values are presented as mean ± standard deviation (SD).^tUnadjusted p values were calculated using Student's t-test.^mAdjusted p values were obtained from multivariate analysis of covariance (MANCOVA) controlling for maternal age, body mass index (BMI), fetal sex and GDM treatment modality. Sample sizes vary due to missing measurements. A p value < 0.05 was considered statistically significant. Abbreviations: GDM, gestational diabetes mellitus

However, the most consistent finding was that early neonatal blood glucose levels were lower in the GDM group during early postnatal follow-up. After adjustment for maternal age, body mass index, fetal sex and GDM treatment modality the differences in cord blood adipokine levels were no longer significant, suggesting that these differences may be related to underlying maternal and fetal characteristics rather than representing independent effects of GDM. In contrast, early neonatal blood glucose levels remained significantly different after multivariable adjustment, indicating an association with maternal glycemic status than with cord blood adipokine levels. Although early neonatal blood glucose levels remained statistically significant after multivariate adjustment, the effective sample size for this analysis was

Table 4 Partial correlations between umbilical cord adipokines and neonatal outcomes

Variable	Asprosin (r)	p value	Subfatin (r)	p value
Umbilical cord subfatin	0.96	<0.001	—	—
Birth weight (g)	-0.09	0.45	-0.18	0.16
Birth length (cm)	-0.19	0.13	-0.22	0.08
Weight at 1 month (g)	-0.13	0.31	-0.21	0.10
APGAR score (1 min)	0.07	0.57	0.04	0.75
APGAR score (5 min)	-0.02	0.90	-0.06	0.63
Early neonatal blood glucose (mg/dL)	0.20	0.24	0.17	0.32
Hemoglobin (g/dL)	-0.01	0.97	-0.09	0.60
White blood cell count (10 ³ /μL)	0.06	0.74	0.09	0.60
C-reactive protein (mg/L)	-0.17	0.32	-0.17	0.34

Footnotes: Values represent Pearson partial correlation coefficients adjusted for maternal body mass index (BMI). Analyses were performed using available-case data. p < 0.05 was considered statistically significant

reduced due to missing data. The missing data primarily resulted from the fact that early neonatal blood glucose measurements were obtained based on clinical indication during routine neonatal care, rather than being systematically performed in all participants. Given the number of covariates included in the adjusted model, the possibility of reduced model stability and overfitting cannot be entirely disregarded. Therefore, these findings should be interpreted with caution and validated in larger prospective cohorts.

To further explore the relationship between cord blood adipokines and neonatal outcomes, partial correlation analyses adjusted for maternal BMI were performed. Maternal BMI was selected as the primary covariate in partial correlation analyses due to its well-established association with adipokine secretion and fetal growth. Apart from a strong positive correlation between

asprosin and subfatin levels, no significant associations were observed between cord blood adipokines and neonatal anthropometric measures, early neonatal blood glucose levels or inflammatory markers. These findings suggest that while asprosin and subfatin may be closely interrelated, they are not independently associated with neonatal outcomes in this cohort. This lack of correlation further supports the interpretation that cord blood adipokine alterations reflect the intrauterine metabolic environment rather than serving as direct determinants of neonatal metabolic status.

Previous large-scale and cohort studies have consistently reported higher maternal age and BMI in pregnancies complicated by gestational diabetes mellitus, along with an increased risk of adverse neonatal outcomes such as macrosomia, neonatal hypoglycemia, neonatal infections, low Apgar scores and respiratory complications [36–38]. In line with these findings, our study also observed higher maternal age and BMI in the GDM group, while gestational weight gain did not differ between groups. Similarly, infants born to mothers with GDM had higher birth weights and lower early neonatal blood glucose levels.

However, unlike some previous reports, we did not observe significant differences in Apgar scores, inflammatory markers or indicators of neonatal distress between groups. These discrepancies may be related to differences in cohort size, prenatal care quality, maternal glycemic control, delivery practices and postnatal supportive care, which can substantially influence neonatal outcomes across studies.

By examining umbilical cord blood asprosin and subfatin levels alongside neonatal outcomes, our study adds to the limited data on fetal adipokine profiles in pregnancies complicated by GDM. While several previous studies have reported increased maternal and/or fetal asprosin levels in GDM, we observed lower umbilical cord asprosin concentrations. Specifically, Zhong et al. reported higher maternal and cord blood asprosin levels and demonstrated placental expression of asprosin, suggesting the placenta as a potential source, while Boz et al. and Hoffmann et al. also described elevated maternal and fetal asprosin levels in GDM pregnancies. In addition, Yalınbaş et al. reported higher neonatal serum asprosin levels in infants born to mothers with GDM [33, 39–41]. Based on these findings, asprosin has been proposed as a hormone associated with insulin-resistant states such as GDM.

However, the discrepancy between these reports and our observation of lower umbilical cord asprosin levels underscores the heterogeneity of asprosin regulation in the fetal compartment. Importantly, when maternal age, body mass index and fetal sex were accounted for in multivariable analyses, the differences in cord blood asprosin

were no longer statistically significant, indicating that this adipokine alterations may not represent independent effects of GDM. Differences in study design, population characteristics, maternal glycemic control and GDM treatment strategies may further contribute to this heterogeneity, suggesting that maternal, placental and fetal asprosin dynamics may vary across clinical contexts.

In a study evaluating maternal obesity and excessive gestational weight gain (EGWG), umbilical cord blood asprosin levels were reported to be higher in the EGWG group, while maternal asprosin concentrations did not differ between groups. Although neonatal Apgar scores were lower in the EGWG group, birth weight was similar between groups [42]. In our study, gestational weight gain did not differ between groups; however, umbilical cord asprosin levels were lower, whereas neonatal birth weight and weight at one month were higher in pregnancies complicated by GDM.

The lower asprosin levels observed in the GDM group were mainly evident in unadjusted analyses and were attenuated after adjustment for maternal and fetal characteristics. Accordingly, interpretations related to placental function or fetal glucose regulation remain speculative and should be approached with caution in this observational context. Chronic intrauterine exposure to maternal hyperglycemia and hyperinsulinemia has been associated with changes in fetal hormonal balance, which could influence adipokine profiles. Similar hormonal patterns, including reduced ghrelin and increased insulin or leptin levels, have been described in infants born to diabetic mothers [43–46]. In our study, the observation of lower neonatal blood glucose levels in the GDM group is consistent with these hormonal alterations, although causal relationships cannot be established. Moreover, the absence of measurements of key metabolic mediators such as insulin and leptin limits further mechanistic interpretation of these associations.

Consistent with our findings for asprosin, umbilical cord subfatin levels were lower in the GDM group in unadjusted analyses. The existing literature on subfatin in the context of GDM remains limited and studies specifically examining umbilical cord subfatin levels are rare. In this context, our findings add to the limited available evidence by reporting lower cord blood subfatin concentrations in infants born to mothers with GDM.

Ozturk et al. reported higher maternal and cord blood subfatin levels in pregnancies complicated by GDM [47]. In contrast, our study demonstrated significantly lower umbilical cord subfatin levels in the GDM group in the unadjusted analysis. This discrepancy highlights the heterogeneity of subfatin regulation in the fetal compartment. Lower subfatin levels in GDM-exposed fetuses may be related to alterations in fetal metabolic or inflammatory balance; however, these interpretations remain

speculative given the observational nature of the data. Supporting this variability, Lappas et al. reported that both maternal obesity and GDM were associated with lower adipokine concentrations in cord plasma [48]. Taken together, these findings suggest that fetal adipokine profiles may vary across different metabolic conditions, rather than indicating a uniform response to GDM. Importantly, in our study, the observed difference in cord blood subfatin levels was evident in univariate analyses but did not persist after multivariable adjustment, further underscoring the potential influence of confounding factors.

Although infants born to mothers with GDM tended to have higher weight at one month of age, the distribution of feeding types (exclusive breastfeeding, formula feeding and mixed feeding) did not differ significantly between groups. This suggests that postnatal feeding practices alone are unlikely to fully explain the observed differences in early weight gain. Instead, these findings raise the possibility that prenatal factors related to the intrauterine metabolic environment may contribute to early growth patterns in infants born to mothers with GDM. However, given the observational design and lack of adjustment for postnatal exposures, causal inferences cannot be drawn. These assessments should be interpreted as exploratory and hypothesis-generating inferences rather than confirmatory results.

Given the potential influence of treatment strategies in gestational diabetes mellitus, we also examined whether variability in GDM management affected neonatal outcomes and cord blood adipokine levels. In multivariate models including GDM treatment modality as a covariate, treatment type did not show a significant independent effect on umbilical cord asprosin or subfatin levels, nor on neonatal anthropometric outcomes. This finding indicates that differences in GDM treatment approaches may have a limited impact on the observed variations in adipokine levels. However, as treatment intensity and glycemic control may vary within treatment categories, residual confounding cannot be entirely excluded.

Our study has several limitations. First, our sample size is limited and there are missing data in some parameters, which may limit the generalizability of the results. Although sample size calculations were performed beforehand, these calculations were based on expected mean differences between groups and did not account for possible missing data or the need for multivariate adjustment models. Therefore, the study may be insufficient for certain secondary and adjusted analyses. This limitation should be considered when interpreting multivariate findings. Furthermore, as the study was conducted at a single center, its applicability to different geographic and socioeconomic populations is limited. Neonatal biochemical measurements were obtained as part of routine

clinical care; therefore, missing data were mostly due to clinical indications rather than study-related factors, but non-random missingness cannot be entirely ruled out.

The cross-sectional nature of the study limits the ability to draw causal inferences regarding early metabolic programming. Umbilical cord adipokine levels represent a single time-point measurement at birth and may reflect transient intrauterine metabolic conditions rather than long-term programming effects. In addition, the absence of longitudinal metabolic follow-up of the offspring precludes conclusions regarding future metabolic risk. Furthermore, key metabolic mediators such as insulin and leptin, which may play central roles in fetal metabolic regulation, were not measured. Therefore, our findings should be interpreted as associative rather than causal, and future longitudinal studies incorporating comprehensive hormonal profiling are warranted to clarify the role of adipokines in fetal metabolic programming.

Although intra- and inter-assay CV values provided by the manufacturer for ELISA kits were within acceptable ranges, no additional in-house assay verification was performed. In addition, formal batch-to-batch variability analyses were not conducted. These factors should be considered when interpreting the analytical variability of adipokine measurements.

Conclusion

In this cross-sectional study, gestational diabetes mellitus was associated with differences in neonatal growth and early postnatal glucose regulation. Although umbilical cord blood asprosin and subfatin levels were lower in unadjusted analyses, these differences were attenuated after multivariable adjustment, suggesting that cord blood adipokine levels are influenced by maternal and fetal characteristics rather than representing independent effects of GDM. In contrast, neonatal blood glucose levels remained robustly associated with maternal glycemic status. These findings indicate that umbilical cord adipokines reflect the intrauterine metabolic environment but have limited utility as independent neonatal biomarkers, warranting further investigation in larger longitudinal studies.

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Author contributions

Conceptualization, F.E.Ç., Ö.K.A.; Data curation, F.E.Ç., Ö.K.A. B.B.C.; Formal analysis, S.A., M.A.Y.; Methodology, F.E.Ç., Ö.K.A.; Supervision, S.A., G.G., M.İ.T.; Writing – original draft, F.E.Ç., Ö.K.A.; Writing – review & editing, F.E.Ç., S.A., Ö.K.A., G.G., M.İ.T. All authors have read and agreed to the published version of the manuscript.

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Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request and with permission. Access to the data requires approval from the corresponding author due to privacy and ethical considerations.

Declarations

Ethics approval and informed consent

This study was approved by the Ethics Committee of Balıkesir University Faculty of Health Sciences. (Decision No:2025/283). The study was conducted in accordance with the principles of the Declaration of Helsinki and adhered to the ethical standards of the country in which the research was carried out. Informed consent was obtained from all subjects involved in the study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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