Zagazig University Medical Journal
www.zumj.journals.ekb.eg
https://doi.org/10.21608/zumj.2024.328414.3641 Volume 31, Issue 1.1, JAN. 2025, Supplement Issue
Manuscript ID: ZUMJ-2410-3641
DOI: 10.21608/zumj.2024.328414.3641

ORIGINAL ARTICLE

Cord Blood Metabolic Markers as Mediators of the Effect of Maternal Adiposity on Fetal Growth in Diabetic and Non-diabetic Mothers

Hytham Reda Badr[1]*, Alaa Abdel Sallam Dawoud[1], Mahy Nabil Egiz[2], Dina Ahmed Abdelaziz Attia[1], Moustafa Bakrey Hamed Ata[1]

[1] Internal Medicine Department, Faculty of Medicine, Menoufia University, Menoufia, Egypt
[2] Obstetrics and Gynecology Department, Faculty of Medicine, Menoufia University, Menoufia, Egypt

***Corresponding author:**
Hytham Reda Badr.

Email:

hythambadr87@med.menofia.edu.eg,
hythambadr87@yahoo.com

Submit Date: 21-10-2024
Revise Date: 05-11-2024
Accept Date: 10-11-2024

ABSTRACT

BACKGROUND: Obesity and Type2 diabetes (T2DM) have multiple complications may be related to insulin resistance (IR). T2DM is widely spreading disease among pregnant women. Unfavorable perinatal outcomes have to occur in obese diabetic mothers. The aim of this work was to analyze the link between maternal obesity and neonatal anthropometric results, as well as the link between cord blood metabolic indicators and the fetal overgrowth.

METHODS: 140 pregnant women were included at Menoufia University Hospital in prenatal and postpartum phases. All participants were divided into four equal groups: group (1) obese, diabetic, group (2) obese non diabetic, group (3) non obese diabetic and group (4) was non obese non diabetic. All patients subjected to full history taking, anthropometric measures (weight and height), clinical assessment and laboratory investigations including (C-peptide, triglycerides, HDL, Random blood sugar).

RESULTS: Obese patients had higher significant mean serum c-peptide level. It was shown to be responsible for 18% (95 percent) confidence interval of the link between maternal body mass index (BMI) and large for Gestational age (LGA). Regarding fetal outcomes, diabetic patients have a higher significant LGA.

Diabetic patient has higher statistically significant difference of CRP *P*=(0.001) rather than non-diabetic.

Regarding HDL obese patient have higher significant differences than other groups.

CONCLUSIONS: Pregnant women with Gestational Diabetes Mellitus, and T2DM all had higher C-peptide levels in their baby's blood than women with normal glucose tolerance.

KEYWORDS; Perinatal Outcomes ; Maternal Obesity ;Gestational Diabetes ;Metabolic Markers ,Fetal Growth.

INTRODUCTION

Overweight is a condition of excessive fat deposits. Obesity is a chronic condition in which excessive fat deposits can impair health. There has been a rise in the prevalence of overweight and obesity worldwide, as it has more than doubled since 1990 also among reproductive-age women in both low- and high-income nations [1].

Obesity among pregnant women is becoming one of the most important women's health issues as it is associated with increased risk of almost all pregnancy complications like: gestational HTN, preeclampsia, gestational DM, delivery of large for gestational age (LGA) infants and higher incidence of congenital defects. It is evident that obese pregnant women are at increased risk of maternal death and complications during pregnancy and labor. The confidential Enquiry into Maternal and Child Health (CEMACH) reported that more than half of the deaths during late pregnancy or labor were in overweight or obese women [2].

Triglyceride (TG) and cholesterol levels in lipoproteins often fluctuate in the presence of metabolic problems. Overweight and obesity are linked to metabolic problems, such as hepatic steatosis, yet obesity under the skin has the

opposite effect. Because of the buildup of pro-inflammatory macrophages in adipose tissue, obese persons experience continuous low-grade inflammation, which contributes to the development of systemic insulin resistance [1].

High-calorie diets consumed by women during pregnancy, childbirth, and nursing have a long-term effect on the body composition, cardiovascular system, and metabolic health of the child or children. IR, decreased glucose tolerance, an increase in offspring fat mass, and other pathophysiological implications, such as low-grade inflammation, have all been related to maternal obesity (MO) [3].

Studying whether cord blood metabolic parameters are associated with fetal overgrowth and whether or not they are a mediator of the influence of MO on newborn anthropometric outcomes was the goal of this investigation.

The current study is essential due to the rising prevalence of gestational diabetes mellitus (GDM) and its associated risks for mothers and infants. Understanding the effects of maternal glycemic control and body composition on pregnancy outcomes is crucial, yet gaps remain in knowledge about pre-gestational glycemic status and insulin management. This study aims to address these gaps, providing insights that can enhance clinical practices and improve health outcomes for high-risk populations.

METHODS

This study was performed in the Gynecology and Internal Medicine department, Faculty of Medicine, Menoufia University during period from May 2022 to May 2024. The Ethics Committee (Institutional Review Board, Faculty of Medicine, Menoufia University) gave their approval to the research (approval number: 5/2021 INTM 27). A total of 140 pregnant women at Menoufia University Hospital in the prenatal and postpartum phases. All participants were divided into four equal groups: obese diabetic, obese non diabetic, non obese diabetic and the last was non obese non diabetic.

All pregnant females, provided their informed consent. The study has been carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

Pre-gestational glycemic status was evaluated by collecting fasting glucose and HbA1c measurements prior to conception. Participants were categorized based on their glycemic levels to analyze its impact on gestational outcomes. Additionally, we documented the glycemic control measures of participants with pre-existing diabetes during pregnancy to understand the relationship between pre-gestational glycemic status and birth outcomes.

We implemented a structured approach to glycemic control and insulin dosing for pregnant women with diabetes. Blood glucose levels were monitored at least four times daily, targeting fasting levels of 60-95 mg/d L and postprandial levels under 140 mg/dL. Insulin therapy was initiated for those unable to achieve targets through diet and exercise, starting at 0.5 to 1.0 units per kilogram of body weight per day. Dosing was adjusted throughout pregnancy, particularly in the second and third trimesters, to accommodate increased insulin requirements, with individualized treatment plans developed for optimal maternal and fetal outcomes.

T2DM was diagnosed according to American Diabetes Association (ADA) guidelines with fasting blood glucose (FBG) more than 126mg/dl, 2 hour postprandial glucose (2hppBG) more than 200 and/or HbA1c more than 6.5 mg%

Pregnant females with type 1DM or having twins, others with chronic liver disease, chronic renal failure, and heart failure were excluded.

Samples were collected from cord blood at fetal side of the operating room at the time of delivery under the complete aseptic condition then sample put in chemistry tube labeled by patient data. All samples were immediately centrifuged after being collected and serum absorbed by special absorbent and put in another chemistry tube then frozen until the time of analysis. Samples were analyzed for C-peptide, HDL, Triglycerides and Random blood sugar. Fetal weight was documented after delivery. All results are documented and statistically analyzed.

Statistical analysis

The IBM SPSS 20.0 software suite was used to analyze the data (IBM Corporation, Armonk, New York.) .Numbers and percentages were used to describe qualitative data. The distributions were determined using the Kolmogorov-Smirnov test. The range (minimum and maximum), mean, standard deviation, median, and interquartile range were used to characterize quantitative data (IQR). Multivariate analysis was also conducted. The significance of the findings was determined at a 5% level of significance.

RESULTS

One hundred and forty pregnant women were included, and according to BMI and presence or absence of type 2 diabetes were divided into four equal groups. Between all groups studied there were 70 (50.0%) had a history of diabetes (gestational or T2DM) with mean duration of

diabetes 3.86 (± 1.20) SD. Regarding BMI there were 70 (50%) non and 70 (50%) obese with mean BMI 28.04 (± 5.65) SD. There was a highly statistically significant difference between the studied groups regarding mean gestational age at birth (weeks), higher significant difference in group IV than it was in the other examined groups **(Table 1).**

There was a highly statistically significant difference between the studied groups regarding mean birth weight (grams), higher significant difference in group III than it was in the other examined groups.(**Table 2**)

There was a statistically significant difference between the studied groups regarding mean C-PEPTIDE (nmol/l), higher significant difference in group I than it was in the other examined groups. There was a highly statistically significant difference between the studied groups regarding mean HDL mmol/l, higher significant difference in group III than it was in the other examined groups. **(Table 3)**

There was no statistically significant difference between the studied groups regarding mean Glucose (mmol/l) and mean Triglycerides (mmol/l). (**Table 4)**

There was a statistically significant difference in CRP levels between the groups studied. (**Table 5)**

A multiple linear regression analysis was conducted to assess the impact of maternal and neonatal factors on birth weight (grams). Significant predictors included maternal age, C-peptide levels, BMI, gestational weight gain (GWG), duration and history of diabetes, and CRP (>0.3). Standardized beta coefficients (β), p-values, and 95% confidence intervals (CIs) were reported.

Maternal age was positively associated with birth weight (β = 0.181, p = 0.009, 95% CI [3.468, 23.431]). Similarly, BMI showed a positive effect on birth weight (β = 0.205, p = 0.005, 95% CI [3.211, 17.406]). C-peptide had a strong positive association (β = 0.456, p < 0.001, 95% CI [679.563, 1662.154]), as did GWG (β = 0.296, p < 0.001, 95% CI [15.852, 39.613]). Duration of diabetes (β = 0.547, p < 0.001, 95% CI [49.258, 83.526]) and history of diabetes (β = 0.630, p < 0.001, 95% CI [149.877, 492.739]) were also significant positive predictors. Conversely, CRP > 0.3 was associated with a decrease in birth weight (β = -0.267, p < 0.001, 95% CI [-217.635, -66.582]).

Other factors, including glucose, HDL, triacylglycerol, smoking, and the neonate's sex, were not significantly associated with birth weight **(Table 6).**

Table (1): Distribution of the studied cases according to history, duration of diabetes and BMI (n = 140)

		No.	%
History of diabetes			
No		70	50.0
Yes	T2DM	50	50.0
	Gestational	20	
Duration of diabetes (months)		(n = 70)	
Min. – Max.		1.0 – 5.0	
Mean ± SD.		3.86 ± 1.20	
Median (IQR)		4.0 (3.0 – 5.0)	
BMI			
Non-obese (<30)		70	50.0
Obese (≥30)		70	50.0
Min. – Max.		19.00 – 37.60	
Mean ± SD.		28.04 ± 5.65	
Median (IQR)		29.80 (22.45 – 33.50)	

IQR: Inter quartile range SD: Standard deviation

Table (2): Comparison between the studied different groups according to demographic of neonate

	Diabetic obese (n =35)		Diabetic non-obese (n =35)		Obese non-diabetic (n =35)		Non-obese non-diabetic (n =35)		Test of Sig.	p
	No.	%	No.	%	No.	%	No.	%		
Sex of the neonate										
Male	16	45.7	20	57.1	21	60.0	19	54.3	χ^2= 1.612	0.657
Female	19	54.3	15	42.9	14	40.0	16	45.7		
Gestational age at birth (weeks)										
Min. – Max.	38.70 – 40.40		38.20 – 40.50		28.10 – 39.50		38.0 – 39.10		F= 10.111*	<0.001*
Mean ± SD.	39.54 ± 0.51		39.42 ± 0.62		38.48 ± 1.86		38.57 ± 0.36			
Median (IQR)	39.5(39.2–40.0)		39.2(39.1–39.9)		38.7(38.4–39.2)		38.5(38.3–38.9)			
Sig. Bet. groups	p_1=0.964,p_2<0.001*,p_3=0.001*,p_4=0.001*,p_5=0.004*,p_6=0.982									
Birth weight (grams)										
Min. – Max.	3500.0 – 4200.0		3500.0 – 4200.0		3000.0 – 3800.0		3000.0 – 3800.0		F= 49.988*	<0.001*
Mean ± SD.	3730.14 ± 161.81		3721.29 ± 142.38		3579.71 ± 170.54		3273.17 ± 227.98			
Median (IQR)	3700.0(3600–3850)		3700.0(3625–3800)		3600.0(3450–3725)		3200.0(3100–3453)			
Sig. Bet. groups	p_1=0.997,p_2=0.003*,p_3<0.001*,p_4=0.006*,p_5<0.001*,p_6<0.001*									
Large for gestational age										
No	26	74.3	25	71.4	30	85.7	32	91.4	χ^2= 6.011	0.111
Yes	9	25.7	10	28.6	5	14.3	3	8.6		

*: Statistically significant at p ≤ 0.05

P1: Diabetic obese *vs* Diabetic non-obese , P2: Diabetic obese *vs* Obese non-diabetic,

P3: Diabetic obese *vs* Non-obese non-diabetic, P4: Diabetic non-obese vs Obese non-diabetic

P5: Diabetic non-obese vs Non-obese non-diabetic

P6: Obese non-diabetic *vs* Non-obese non-diabetic

Table (3): Comparison between the studied different groups according to different parameters

	Diabetic obese (n =35)	Diabetic non-obese (n =35)	Obese non-diabetic (n =35)	Non-obese non-diabetic (n =35)	F	p
Fasting Glucose (mg)						
Min. – Max.	46.8– 102.6	50.4– 102.6	52.2– 100.8	52.2– 106.2	0.889	0.448
Mean ± SD.	75.42± **19.26**	79.74± 17.46	73.62± 16.74	78.3± 14.04		
Median (IQR)	73.8 (73.8– 99)	79.2 (66.6– 100.8)	75.6 (57.6– 86.4)	79.2 (66.6– 86.4)		
C-PEPTIDE (nmol/l)						
Min. – Max.	0.27 – 0.63	0.27 – 0.63	0.25 – 0.49	0.29 – 0.53	5.958*	0.001*
Mean ± SD.	0.43 ± 0.12	0.41 ± 0.10	0.34 ± 0.08	0.36 ± 0.07		
Median (IQR)	0.39 (0.3 – 0.5)	0.37 (0.3 – 0.5)	0.32 (0.3 – 0.4)	0.35 (0.3 – 0.4)		
Sig. Bet. groups	p_1=0.773,p_2=0.001*,p_3=0.024*,p_4=0.029*,p_5=0.226,p_6=0.808					
HDL mg						
Min. – Max.	7.56– 32.94	7.92– 15.66	7.38– 21.6	7.74– 16.02	8.887*	<0.001*
Mean ± SD.	11.7± 4.32	11.7± 2.16	14.4± 3.96	10.44± 2.16		
Median (IQR)	11.16 (9– 12.6)	11.52 (10.8– 12.6)	14.4 (10.8– 18)	9.9 (9– 10.8)		
Sig. Bet. groups	p_1=1.000,p_2=0.004*,p_3=0.424,p_4=0.003*,p_5=0.467,p_6<0.001*					
Triglycerides(mg)						
Min. – Max.	4.68– 9.18	4.68– 9.18	5.04– 10.26	5.58– 10.8	2.383	0.072
Mean ± SD.	6.84 ± 1.62	6.48± 1.62	6.84± 1.62	7.38± 1.44		
Median (IQR)	6.84 (5.4– 7.2)	5.94 (5.4– 9)	6.66 (5.4– 7.2)	7.38 (5.4– 9)		

*: Statistically significant at p ≤ 0.05

P1: Diabetic obese *vs* Diabetic non-obese , P2: Diabetic obese *vs* Obese non-diabetic,

P3: Diabetic obese *vs* Non-obese non-diabetic, P4: Diabetic non-obese vs Obese non-diabetic
P5: Diabetic non-obese vs Non-obese non-diabetic
P6: Obese non-diabetic *vs* Non-obese non-diabetic

Table (4): Comparison between the studied groups according to CRP

CRP	Diabetic obese (n =35)		Diabetic non-obese (n =35)		Obese non-diabetic (n =35)		Non-obese non-diabetic (n =35)		χ^2	p
	No.	%	No.	%	No.	%	No.	%		
No	14	40.0	19	54.3	32	91.4	25	71.4	22.524*	<0.001*
Yes	21	60.0	16	45.7	3	8.6	10	28.6		

χ^2: Chi square test **p:** p value for comparing between the studied groups
*: Statistically significant at p ≤ 0.05

Table (5): Correlation between different parameters in each group

	Gestational age at birth (weeks)		Birth weight (grams)	
	r	p	r	p
BMI (kg/m²)				
Diabetic obese (n =35)	–0.088	0.614	–0.075	0.667
Diabetic obese (n =35)	0.217	0.211	0.285	0.097
Diabetic obese (n =35)	–0.048	0.785	0.042	0.811
Diabetic obese (n =35)	–0.179	0.304	–0.112	0.523
C-PEPTIDE (nmol/l)				
Diabetic obese (n =35)	0.077	0.660	0.805*	<0.001*
Diabetic obese (n =35)	–0.222	0.199	0.722*	<0.001*
Diabetic obese (n =35)	–0.395*	0.019*	0.424*	0.011*
Diabetic obese (n =35)	–0.266	0.122	0.550*	0.001*
HDL (mg)				
Diabetic obese (n =35)	0.015	0.934	–0.133	0.447
Diabetic obese (n =35)	0.064	0.715	0.007	0.966
Diabetic obese (n =35)	0.235	0.174	–0.105	0.550
Diabetic obese (n =35)	–0.074	0.674	0.179	0.305
Triglycerides(mg)				
Diabetic obese (n =35)	0.052	0.766	0.752*	<0.001*
Diabetic obese (n =35)	–0.295	0.085	0.708*	<0.001*
Diabetic obese (n =35)	–0.461*	0.005*	0.377*	0.025*
Diabetic obese (n =35)	0.046	0.792	0.509*	0.002*

r: Pearson coefficient *: Statistically significant at p ≤ 0.05

Table 6. Regression Analysis of Predictive Factors Affecting Birth Weight Outcomes

Variable	Standardized β	P	95% CI Lower Bound	95% CI Upper Bound
Age (years)	0.181	0.009	3.468	23.431
Glucose (mmol/l)	0.153	0.066	-2.759	86.130
C-Peptide (nmol/l)	0.456	<0.001	679.563	1662.154
BMI	0.205	0.005	3.211	17.406
HDL (mmol/l)	0.022	0.724	-131.073	188.275
Triacylglycerol (mmol/l)	-0.123	0.175	-860.618	157.855
GWG (kg)	0.296	<0.001	15.852	39.613
Duration of Diabetes (months)	0.547	<0.001	49.258	83.526
History of Diabetes	0.630	<0.001	149.877	492.739

Variable	Standardized β	P	95% CI Lower Bound	95% CI Upper Bound
CRP > 0.3	-0.267	<0.001	-217.635	-66.582
Smoking	-0.071	0.295	-314.178	95.959
Sex of the Neonate	0.006	0.929	-66.012	72.264
Duration of Diabetes (months)	0.057	0.735	-33.143	46.888

The standardized β coefficient indicates the strength and direction of each predictor's relationship with birth weight. A p-value (P) below 0.05 signifies statistical significance, while the 95% confidence interval (CI) estimates the range for the true effect size. Here, GWG stands for Gestational Weight Gain, and CRP refers to C-Reactive Protein, both of which may impact birth weight.

DISCUSSION

The global surge in T2DM, especially among younger individuals, has been increased its occurrence in pregnancy, linked to poor perinatal outcomes. Despite improved management, challenges persist in addressing neonatal complications. Maternal metabolic health during pregnancy significantly influences fetal growth and neonatal outcomes [3].

This study revealed that (MO) and gestational diabetes (GDM) were associated with higher gestational age at birth and higher birth weight compared to non-obese, non-diabetic mothers. In diabetic obese and non-obese mothers, there was a significant positive correlation between birth weight and cord blood levels of C-peptide and triglycerides. Similarly, in obese non-diabetic mothers, birth weight positively correlated with triglyceride levels. Notably, high cord blood C-peptide emerged as a strong mediator of the effect of maternal body size on fetal growth across the glucose tolerance spectrum.

There were significant differences in gestational weight gain GWG, with Groups I and II gaining more weight compared to Groups III and IV. High GWG has been associated with an increased risk of gestational diabetes, preeclampsia, and neonatal complications such as LGA [4]. Conversely, insufficient GWG can lead to low birth weight and preterm birth. The observed lower GWG in Groups III and IV might be associated with the shorter gestational age and lower birth weights reported, aligning with findings from other studies.

The observed shorter gestational age at birth in Group IV (non-obese and non-diabetic) may be attributed to factors such as undiagnosed pregnancy complications, variations in maternal health, or environmental influences.

The prevalence of smoking and maternal complications like hypertension and pre-eclampsia was low across all groups, which is positive as these factors are well-known risk factors for adverse pregnancy outcomes [5]. The minimal differences observed here might indicate that these were not major contributing factors to differences in neonatal outcomes across the groups.

Our study found no significant differences in the distribution of male and female neonates across the groups, which aligns with existing literature indicating that sex distribution is generally balanced and not influenced by maternal factors such as adiposity or diabetes status [6]. This finding suggests that maternal metabolic status may not directly impact the sex of the offspring, emphasizing the importance of genetic and other environmental factors in determining neonatal sex.

In a study conducted by Dieberger et al. [7] researchers found significant correlations between maternal adiposity, cord blood C-peptide levels, and neonatal adiposity, suggesting that maternal body composition influences fetal insulin resistance and subsequent fat deposition, which aligns with the significant findings of varied C-peptide levels across different maternal adiposity groups in our study.

This study suggests that the variation in maternal adiposity and diabetes status may not directly affect cord blood glucose levels. This finding is consistent with studies by Lee et al. [8] who reported no significant changes in fetal glucose levels with varying maternal glucose levels in non-diabetic pregnancies. However, it contrasts with Gojnic et al. [9] who observed elevated fetal glucose levels correlated with increased maternal glycaemia in diabetic pregnancies.

There were statistically significant differences in C-peptide levels among the groups (p=0.001), particularly low in Group III (non-diabetic, higher adiposity) in which fetal insulin resistance or beta-cell activity is affected. Our results support the findings of Lee et al. [8], who suggested that increased maternal adiposity is associated with lower fetal insulin sensitivity. In contrast with Josefson et al. [10] who found no impact of maternal adiposity on cord C-peptide levels in non-diabetic mothers. The discrepancy might be attributed to different study populations or methods of measuring adiposity.

Maternal metabolic status may increase fetal lipid metabolism, potentially impacting long-term cardiovascular health. This could be proved by a significant variance in HDL cholesterol levels across the groups ($p<0.001$), with Group III having higher median levels. This supports the findings by Chen et al. [11], indicating higher fetal HDL in pregnancies associated with higher maternal BMI. This differs from Wang et al. [12] who reported no statistically significant differences in fetal HDL levels by ma ternal diabetes status. The variation could be due to differences in maternal diet, genetic factors, or the timing of sample collection.

The correlations between HDL cholesterol levels and both gestational age and birth weight in our study were generally weak across all groups. This finding could suggest that fetal HDL levels are not a major determinant of these outcomes, or that their influence might be obscured by other stronger determinants such as genetic factors or overall maternal-fetal health. This aligns with literature suggesting that maternal lipid profiles may not directly impact fetal growth but could have long-term effects on child health [13].

Our findings are consistent with Eppel et al. [14] in finding triglycerides levels being stable across different maternal metabolic conditions. It might indicate that fetal TG levels are more influenced by factors other than immediate maternal metabolic status, such as genetic predispositions or placental function.

Strong correlations between TG levels and birth weight were noted, especially in Groups I, II, and IV. This suggests that higher levels of triglycerides in cord blood are associated with increased birth weight, supporting findings from [15], who noted similar associations. The negative correlation with gestational age in Group III might suggest that elevated triglyceride levels could be associated with shorter gestation, which is consistent with research indicating metabolic stress in the fetus [15].

The differences in CRP levels among the groups were statistically significant ($p<0.001$), particularly higher in groups with diabetic mothers, suggesting an inflammatory response possibly linked to maternal glycemic control. This is in line with literature suggesting that maternal diabetes can increase fetal inflammation, which could have implications for neonatal outcomes and long-term health Farghaly et al. [16].

This study investigated the correlations between BMI of mother and both gestational age at birth and birth weight across the four groups which were generally weak and non-significant. This lack of strong correlation is consistent with findings from Antoniou et al. [1] who reported that maternal BMI might not have a direct impact on these outcomes. However, some studies Patnaik et al. have suggested a more pronounced impact of high BMI on birth outcomes, particularly in causing macrosomia or preterm birth [17].

This study shows no significant correlation between the duration of diabetes and BMI among diabetic mothers. This lack of correlation might suggest that the duration of diagnosed diabetes does not necessarily affect BMI, possibly due to varying levels of glycemic control, lifestyle changes, or treatment adherence among individuals. This is an area where existing literature provides mixed results, with some studies suggesting a potential link [15].

A statistically significant correlations between C-peptide levels and birth weight in all groups except Group I are observed in this study, indicating that higher C-peptide levels are associated with higher birth weight. This relationship supports the hypothesis that fetal insulin levels, can influence fetal growth a phenomenon well-documented in diabetic pregnancies [18]. The negative correlation in Group III between C-peptide and gestational age might indicate that higher insulin levels are associated with earlier delivery, which aligns with studies suggesting that IR might lead to earlier onset of labor.

Our study shows significant variations in maternal age across the groups, particularly between Group IV and the other groups, where the younger age profile in Group IV is notable. This could have implications for both maternal and neonatal outcomes. Literature indicates that younger maternal age is often associated with a higher risk of adverse pregnancy outcomes, including preterm birth and low birth weight [19]. However, our findings do not directly correlate younger maternal age with poorer outcomes, possibly reflecting effective prenatal care or differences in health status among the groups.

Significant differences were observed in both gestational age at birth and birth weight across the groups. Groups III and IV had significantly lower mean gestational ages and birth weights compared to Groups I and II. These findings are consistent with previous research linking maternal metabolic conditions, such as diabetes and adiposity, with adverse neonatal outcomes, including preterm birth and low birth weight [9]. The lower birth weights observed in Groups III and IV may reflect the metabolic challenges faced by mothers in these groups, highlighting the importance of targeted interventions to improve maternal metabolic health during pregnancy.

Although not statistically significant, there was a trend towards higher rates of LGA infants in

Groups I and II compared to Groups III and IV. This finding is consistent with studies suggesting that excessive maternal weight gain during pregnancy is associated with an increased risk of delivering LGA infants [20]. However, the lack of statistical significance may be attributed to sample size limitations or other confounding factors not accounted for in this study.

Our multiple linear regression analysis identified key predictors of birth weight, including maternal age, C-peptide levels, BMI, gestational weight gain (GWG), duration of diabetes, and history of diabetes. C-peptide levels showed a strong positive association with birth weight ($\beta = 0.456$, $p < 0.001$), while maternal age ($\beta = 0.181$, $p = 0.009$) and BMI ($\beta = 0.205$, $p = 0.005$) also contributed positively. In contrast, elevated CRP levels (>0.3) negatively affected birth weight ($\beta = -0.267$, $p < 0.001$). These results underscore the importance of maternal metabolic factors on neonatal outcomes.

Lee et al. [8] similarly found that elevated cord C-peptide was significantly associated with increased birth weight z-scores ($\beta = 0.57$), as well as measures like subscapular skinfold thickness (SSF) and percentage of body fat. Conversely, no significant associations were observed for cord glucose, HDL cholesterol, or CRP levels with neonatal outcomes. These consistent findings highlight C-peptide's critical role in influencing neonatal growth and the risk for LGA.

This study has several strengths, including a robust sample size and a comprehensive approach to assessing glycemic control and pregnancy outcomes. However, it is limited by its observational design, which may introduce confounding factors not accounted for. Future studies should consider longitudinal designs with diverse populations to validate our findings and explore the long-term effects of maternal glycemic status on child health. Additionally, incorporating more detailed assessments of dietary and lifestyle factors could enhance the understanding of their impact on pregnancy outcomes.

Conclusions

Pregnant women with normal glucose tolerance (NGT), gestational diabetes mellitus (GDM), or type 2 diabetes mellitus (T2DM) exhibited elevated cord blood C-peptide levels, indicating its significant role as a mediator in how maternal body size affects fetal development. Our findings suggest that long-term follow-up of this high-risk group will provide deeper insights into the impact of the intrauterine metabolic environment on the child's future cardiometabolic risk.

Conflict of Interest :None

Financial Disclosures: None

REFERENCES

1- Antoniou MC, Quansah DY, Mühlberg S, Gilbert L, Arhab A, Schenk S, et al. Maternal and fetal predictors of anthropometry in the first year of life in offspring of women with GDM. Frontiers in Endocrinology. 2023 Mar 28;14:1144195.

2- Heslehurst N, Simpson H, Ells LJ, Rankin J, Wilkinson J, Lang R, et al. The impact of maternal BMI status on pregnancy outcomes with immediate short-term obstetric resource implications: a meta-analysis. Obesity reviews. 2008;9(6):635-83.

3- Sweeting A, Wong J, Murphy HR, Ross GP. A clinical update on gestational diabetes mellitus. Endocr Rev.2022;43(5):763-93.

4- Mackeen AD, Young AJ, Lutcher S, Evers C, Kim K. Encouraging appropriate gestational weight gain in high-risk gravida: A randomized controlled trial. Obes Sci Pract.2022;8(3):261-71.

5- Wei J, Liu CX, Gong TT, Wu QJ, Wu L. Cigarette smoking during pregnancy and preeclampsia risk: a systematic review and meta-analysis of prospective studies. Oncotarget. 2015;6(41):43667.

6- Inkster AM, Fernández-Boyano I, Robinson WP. Sex differences are here to stay: relevance to prenatal care. J Clin Med. 2021;10(13):3000.

7- Dieberger AM, Obermayer-Pietsch B, Harreiter J, Desoye G, van Poppel MN. Physical activity and sedentary time across pregnancy and associations with neonatal weight, adiposity and cord blood parameters: a secondary analysis of the DALI study. Int J Obes (Lond). 2023 Sep;47(9):873-81.

8- Lee IL, Barr EL, Longmore D, Barzi F, Brown AD, Connors C,et al. Cord blood metabolic markers are strong mediators of the effect of maternal adiposity on fetal growth in pregnancies across the glucose tolerance spectrum: the PANDORA study. Diabetologia.2020;63(3):497-507

9- Gojnic M, Todorovic J, Stanisavljevic D, Jotic A, Lukic L, Milicic T, Lalic N, et al. Maternal and fetal outcomes among pregnant women with diabetes. *Int J Environ Res Public Health.* 2022 Mar 20;19(6):3684.

10- Josefson JL, Scholtens DM, Kuang A, Catalano PM, Lowe LP, Dyer AR, et al. Newborn adiposity and cord blood C-peptide as mediators of the maternal metabolic environment and childhood adiposity. Diabetes Care. 2021;44(5):1194-202.

11- Chen Q, Chen H, Xi F, Sagnelli M, Zhao B, Chen Y, et al. Association between maternal blood lipids levels during pregnancy and risk of small-

for-gestational-age infants.Sci Rep. 2020;10(1):19865.
12- Wang J, Li Z, Lin L. Maternal lipid profiles in women with and without gestational diabetes mellitus. Medicine. 2019 Apr 1;98(16).
13- Wild R, Feingold KR. Effect of pregnancy on lipid metabolism and lipoprotein levels. Endotext [Internet]. 2023 Mar 3.
14- Eppel D, Feichtinger M, Lindner T, Kotzaeridi G, Rosicky I, Yerlikaya-Schatten G, Eppel W, et al. Association between maternal triglycerides and disturbed glucose metabolism in pregnancy. Acta Diabetologica. 2021;58(4):459-65.
15- Medhi GK, Dutta G, Borah P, Lyngdoh M, Sarma A. Prevalence of diabetes and its relationship with body mass index among elderly people in a rural area of Northeastern state of India. Cureus. 2021 Jan;13(1).
16- Farghaly TA, Helmy NA, Abbas AM, Ahmed AG. C-reactive protein as a screening test for gestational diabetes mellitus in first-trimester of pregnancy: a prospective cohort study. Int J Reprod Contracept Obstet Gynecol. 2018 Dec 1;7(12):4798-803.
17- Patnaik N. Study the effect of increased maternal BMI on fetal outcome: A prospective observational study. *J Family Med Prim Care*. 2020;9(12):5906-8.
18- Morigny P, Houssier M, Mouisel E, Langin D. Adipocyte lipolysis and insulin resistance. Biochimie. 2016 Jun 1;125:259-66.
19- Londero AP, Rossetti E, Pittini C, Cagnacci A, Driul L. Maternal age and the risk of adverse pregnancy outcomes: a retrospective cohort study. BMC Pregnancy and childbirth. 2019;19(1):261
20- Gaillard R, Durmuş B, Hofman A, Mackenbach JP, Steegers EA, Jaddoe VW. Risk factors and outcomes of maternal obesity and excessive weight gain during pregnancy. Obesity 2013;21(5):1046-55.

Citation

Badr, H., Dawoud, A., Egiz, M., Attia, D., Hamed, M. Cord Blood Metabolic Markers as Mediators of the Effect of Maternal Adiposity on Fetal Growth in Diabetic and Non-diabetic Mothers. *Zagazig University Medical Journal*, 2025; (62-70): -. doi: 10.21608/zumj.2024.328414.3641