RELATIONSHIP BETWEEN MATERNAL OBESITY, BIRTH WEIGHT AND FETAL ADIPONECTIN/LEPTIN RATIO: A POTENTIAL EARLY BIOMARKER OF CARDIOMETABOLIC RISK

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ABSTRACT

Adiponectin and leptin are key adipokines that play crucial roles in metabolic regulation and in fetal and neonatal growth. In adults, lower adiponectin/leptin ratio (AdipoQ/Lep) has been suggested as a potential biomarker for metabolic risk. This study aimed to investigate whether the AdipoQ/Lep ratio in fetal blood correlates with the maternal and neonatal phenotypes and whether it holds predictive value for the cardiometabolic risk of the offspring in early life. Umbilical cord blood (UBC) samples were collected at birth, and the concentrations of adiponectin and leptin levels were measured using ELISA kits. Infants were evaluated echocardiographically at 5±2 months-old (range: 1-12 months) and these parameters were correlated with the AdipoQ/Lep levels. Results show that fetal AdipoQ/Lep ratio was lower in infants born to mothers with prepregnancy obesity. Both prepregnancy weight and maternal weight at the end of the gestation correlated with the AdipoQ/Lep ratio in UBC, whereas gestational weight gain showed no such association. Additionally, birth weight, birth length and BMI-for-age Z-score were negatively correlated with the AdipoQ/Lep ratio. Notably, lower levels of this adipokine-based biomarker were associated with reduced Z-score of left ventricular end-diastolic diameter. However, multiple linear regression analysis showed that maternal obesity and somatometry at birth influence infants' cardiac function and structure, independent of UBC AdipoQ/Lep ratio, adiponectin or leptin alone. To our knowledge, this is the first investigation to explore the relationship between fetal AdipoQ/Lep levels, maternal-neonatal weight, and early cardiac alterations, highlighting the biomarker's potential predictive value for early-life cardiometabolic risk.

NEW & NOTEWORTHY: This study is the first to explore the association between fetal adiponectin/leptin (AdipoQ/Lep) ratio and maternal anf neonatal anthropometrics, and early alterations in cardiac structure. While maternal and neonatal weight metrics impact infant heart development, this occurs independently of the AdipoQ/Lep. However, lower levels of AdipoQ/Lep ratio were associated with reduced Z-score of left ventricular end-diastolic diameter, offering insights into fetal programming mechanisms linked to maternal metabolic status during

pregnancy.

KEYWORDS: adiponectin, leptin, umbilical cord blood, maternal obesity, birth weight, echocardiography

INTRODUCTION

Developmental Origins of Health and Disease (DOHaD) is aligned in "Barker's hypothesis" which relates malnutrition during pregnancy with low birthweight and increased risk of type 2 diabetes, obesity, hypertension, and other cardiometabolic disorders later in life(1, 2). In the past two decades, several mechanisms have been described to underlie infant programming in maternal obesity, including epigenetic changes (e.g., DNA methylation, histone modifications)(3); reduced mTOR/STAT3 activity, promoting gluconeogenesis, lipid oxidation, and fatty acid synthase activity(4), and altered adipokine signaling, which act as key mediators in the so-called "Adipokine Hypothesis"(5). Adiponectin and leptin are two adipokines that play crucial roles in the development of metabolic disorders(6), as well as in fetal and neonatal growth(7). Although umbilical cord blood (UBC) adiponectin appears to be a key biomarker in early life, potentially linking maternal metabolic status and gestational age(8), more research should clarify its role in long-term growth patterns and metabolic health. Conversely, UBC leptin is strongly associated with postnatal growth trajectories: lower levels predict faster weight gain in infancy, whereas higher levels are linked to slower growth, independent of birth weight(7). Maternal obesity and UBC hyperleptinemia appear to affect infant growth and may contribute to the intergenerational transmission of obesity and metabolic risk(7). The ratio between adiponectin and leptin (AdipoQ/Lep) is a promising biomarker of metabolic risk in adulthood(9). Recently, it was established sex- and age-specific percentiles for the AdipoQ/Lep ratio in healthy Danish children and adolescents (8–17y), providing a more differentiated interpretation(10). Still, the potential of this biomarker in early life was not explored. In this research, our goal was to determine whether the AdipoQ/Lep ratio in UCB – also referred to as fetal AdipoQ/Lep – is associated with the maternal and neonatal phenotype and holds predictive value for the cardiometabolic risk of the offspring in early life.

METHODOLOGY

Description of the study

The present study is a sub-study of the original PERIMYR birth cohort(11), which was approved by the Ethics Committee of Unidade Local de Saúde de São João, EPE (ULS São João), with the reference number ID201/18. Pregnant women in labor admitted to the delivery room were invited to participate in this study. After being informed about the project, the participants voluntarily signed the free and informed consent form, allowing the obstetric team to collect UBC at the time of birth. A transthoracic echocardiography (TTE) evaluation of the offspring was performed at 5±2 months (range: 1-12 months).

Clinical, anthropometric, and echocardiographic data collection

Demographic and clinical data of the mother [age, pregestational weight and body mass index (BMI), gestational weight gain, presence of pathologies before pregnancy, pathologies during pregnancy, use of medications, type of delivery] and the child (gestational age, weight and length at birth, complications after birth such as hypoglycemia, need for supplemental inhaled oxygen or positive pressure ventilation and phototherapy, age and weight, length at the time of TTE) were obtained through consultation of clinical files and the application of questionnaires. Weight-for-length Z-score and BMI-for-age Z-score were calculated using World Health Organization Anthro software available at https://www.who.int/tools/child-growth-standards/software.

The TTE was performed by the same operator according to the Guidelines and Standards for Performance of a Pediatric Echocardiogram of the American Society of Echocardiogram(12, 13) using the equipment Vivid^{TM} iq (GE Medical Systems, Norway), with a pediatric sectoral transducer appropriate to the child's age (6S 2.4-8.0 MHz) and continuous and simultaneous electrocardiographic recording. The echocardiographic variables were normalized to the Z-score using the Cardio-Z application (Apple version 3.0), developed by Evelina Children´s Hospital London, UK, in collaboration with the technology company UBQO, was employed to calculate Z-Score for various echocardiographic parameters and indices. These calculations accounted for age, sex, length and weight for each individual, enabling appropriate interpretation and statistical analysis within a pediatric sample. Z-score represents the number of standard deviations observed from the expected mean for a defined normal pediatric population (observed value – predicted value / standard deviation). Z-score below –1.64 (equivalent to the 5th percentile) or above +1.64 (equivalent to the 95th percentile) were considered outside the normal range(14).

Sample collection

Umbilical cord blood samples were collected in a sterile bag with CPDA-1 anticoagulant solution (Dermotek single blood bag - Demophorius Healthcare) by the obstetric team, at the time of delivery, after clamping the cord, following the collection protocol of the Portuguese Blood and Transplantation Institute. Samples were centrifuged for 15 minutes at 5,000 rpm at 4˚C. The plasma was then transferred to cryovials and stored at -80˚C until analysis.

Adiponectin and Leptin quantification

Levels of adipokine in UBC-derived plasma were quantified using Enzyme-linked Immunosorbent Assay (ELISA). Concentrations of adiponectin (Abcam, Cambridge, United Kingdom, Cat No: ab108786) and leptin (R&D Systems, Minneapolis, United States of America, Cat No: DY398-05) were measured following the manufacture instructions, using dilution factors of 1:2000 and 1:10, respectively.

Statistical analysis

After assessing data normality using the Kolmogorov-Smirnov test, continuous variables are presented as mean ± standard deviation. Categorical variables are expressed as absolute value and relative frequencies. Correlations between AdipoQ/Lep and maternal, infant, and echocardiographic outcomes were analyzed using either Pearson's or Spearman's correlation test, depending on data distribution. Since AdipoQ/Lep ratio levels are parametric, comparisons between different categories of echocardiographic Z-scores were performed using one-way ANOVA, followed by pairwise t-tests using the pairwise.t.test() function in R. This function applies Bonferroni correction across all possible group comparisons, with *p*-value adjusted for multiple testing. Multiple linear regression analysis was performed to assess whether the AdipoQ/Lep ratio mediated the relationship between maternal and neonatal factors and echocardiographic parameters. Statistical analyses, including graphical representations, were performed using RStudio version 4.3, with the ggplot2 package. Statistical tests were considered statistically significant when $p < 0.05$.

RESULTS

Description of participants

A total of 42 mother-neonate pairs were included according to the full availability of biological samples, clinical data, and echocardiography analysis. Clinical data are provided in Table 1.

Table 1. Clinical and anthropometric data of study mother-neonate' pairs

Maternal data		
Maternal age (years), mean±SD		34 ± 6
Pregestational BMI (kg.m^{-2}), mean±SD		27.8 ± 5.0
Pregestational BMI category, n(%)		
	Underweight	1 (2.4)
	Normal weight	11 (26.2)
	Overweight	17 (40.5)
	Obesity	13 (31.0)
Gestational weight gain (kg), mean±SD		9.47 ± 6.70
Gestational diabetes, n(%)		8 (19.0)
Gestational hypertension, n(%)		6 (14.3)
Peripartum/Neonate data		
Gestational age (weeks), mean±SD		39.0 ± 1.10
Delivery mode, n(%)	*Vaginal*	33 (78.6)
	C-section	9 (21.4)
Sex, n(%)	*Male*	23 (53.8)
	Female	19 (45.2)
Somatometry at birth, mean±SD		
	Weight at birth (g)	3161 ± 469
	Length at birth (cm)	49.0 ± 2.0
	Weight for length Z-score at birth	-0.45 ± 1.19
	BMI for age Z-score at birth	-0.51 ± 1.15
Infant data at echocardiographic evaluation		

Age (months), mean±SD		5 ± 2
Somatometry, mean±SD	*Weight (g)*	6352 ± 1540
	Length (cm)	62.7 ± 5.5

SD – Standard deviation, BMI – Body Mass Index

Umbilical cord blood AdipoQ/Lep ratio and its association with maternal and neonatal weight

As outlined in Figure 1, there were several significant correlations between AdipoQ/Lep and maternal neonatal and body somatometry. AdipoQ/Lep ratio and leptin were negatively correlated with pregestational BMI, pregestational weight and weight at the end of the pregnancy (Figure 1A, B and C). Significant correlations were also observed between levels of AdipoQ/Lep ratio, adiponectin and leptin, and neonate's BMI-for-age at birth and weight at birth (Figure 1D and E). Length at birth was only significantly correlated with AdipoQ/Lep ratio, but not with Z-score weight-for-length at birth ($r=-0.23$, $p=0.14$). No significant correlations were observed between the fetal AdipoQ/Lep and Z-score BMI-for-age ($r=-0.14$, $p=0.38$) and Z-score weight-for-age ($r=-0.13$, $p=0.41$) at the time of the echocardiogram assessment. However, correlations were found between Z-score weight-for-age and adiponectin ($r=0.380$, $p=0.013$) and leptin ($r=0.321$, $p=0.038$).

Figure 1. Plasma AdipoQ/Lep ratio, adiponectin and leptin in UBC and its association with maternal pregestational BMI (A), maternal pregestational weight (B), maternal body weight at the end of the pregnancy (C), neonatal Z-score BMI-for-age (D), weight at birth (E), and length at birth (F). Pearson's correlation coefficient (r) indicates the strength and direction of the linear relationship between the variables. Shaded areas represent 95% confidence intervals for the fitted regression line. AdipoQ/Lep, adiponectin/leptin ratio. BMI, body mass index.

Association between AdipoQ/Lep ratio and infant echocardiography

No correlations were found between AdipoQ/Lep ratio, adiponectin, and leptin levels and any echocardiographic parameter adjusted for Z-scores. After categorizing echocardiographic parameters into three Z-score-based groups, among the 14 cardiac structural and functional parameters analyzed, only AdipoQ/Lep ratio was significant lower in left ventricular end-diastolic diameter Z-score (LVIDd Z-score) <-1.64 in comparation a LVIDd Z-score of -1.64 to +1.64 (*p*=0.037) (Figure 2).

Figure 2. Violin plots illustrate the distribution of AdipoQ/Lep ratio according to categorized Z-scores for 14 cardiac structural and functional parameters.

Maternal and neonatal weight as determinants of cardiac outcomes independently of AdipoQ/Lep

Multiple linear regression analyses were performed to investigate whether the AdipoQ/Lep ratio, adiponectin, and leptin individually mediated the association between maternal or neonatal anthropometric measures and selected echocardiographic parameters (Table 2). In all models, the AdipoQ/Lep ratio, adiponectin and leptin were not a significant predictor, suggesting that this adipokine-based biomarker does not mediate the observed relationship between the anthropometric variables and cardiac measurements.

Table 2. Multiple linear regression analysis considering left ventricular end-systolic diameter Z-score (LVIDs Z-score), mitral valve A-wave velocity Z-score (MV-A-wave Z-score) and isovolumetric relaxation time Z-score (IVRT Z-score) as the dependent variables.

	Independent variables	B	Beta	P-value	Adjusted R^2	Model p-value
Pregestational BMI vs. *LVIDs Z-score*	Model unadjusted	0.114	0.396	**0.008***		
	Model 1	0.131	0.456	**0.006***	0.135	**0.022***
	Model 2	0.122	0.422	**0.013***	0.132	**0.039***
Pregestational BMI vs. *MV-A-wave Z-score*	Model unadjusted	0.109	0.324	**0.037***		
	Model 1	0.128	0.379	**0.025***	0.078	0.078
	Model 2	0.144	0.428	**0.013***	0.095	0.080

Z-score BMI-for-Age vs. *IVRT Z-score*	Model unadjusted	-0.391	-0.433	**0.004***		
	Model 1	-0.373	-0.413	**0.012***	0.148	**0.016***
	Model 2	-0.332	-0.368	**0.044***	0.134	**0.038***

** $p < 0.05$ indicates statistical significance.* ***Model 1****: adjusted for AdipoQ/Lep ratio.* ***Model 2****: adjusted for adiponectin and leptin levels. Adjusted R^2 values and associated p-values were obtained from a multiple linear regression. AdipoQ/Leptin: adiponectin/leptin ratio; B: unstandardized regression coefficient; Beta: standardized beta coefficient; BMI, body mass index.*

DISCUSSION

To the best of our knowledge, this study is the first to assess fetal AdipoQ/Lep ratio associated with maternal and infant anthropometry, and infant's echocardiographic parameters. The data collected showed that fetal AdipoQ/Lep levels were correlated with maternal obesity and neonate weight status, although no associations were found with cardiovascular parameters.

Several studies report strong associations between maternal obesity and infant overweight, as well as metabolic and cardiovascular diseases in both childhood and adulthood(15). A meta-analysis including 12,475 cases of obesity among 88,872 children reported a 264% increase in the odds of pediatric obesity when mothers have pregestational obesity(16). In addition, intrauterine exposure to maternal obesity or gestational diabetes predisposes approximately 50% increased risk of type 2 diabetes in young individuals aged 10-22 years(17). Recently, a population-based study of 5107 children described that obesity at 11 to 12 years old was silently associated with the development of cardiovascular dysfunction, assessed by pulse wave velocity(18). Identifying the metabolic pathways underlying the DOHaD and discovering early biomarkers could promote early preventive interventions. Adipokines are promising biomarkers and potential mediators of the DOHaD(7, 19). Unveiling the complex interplay between maternal metabolic signals, placental function, and fetal development is essential to better understand the intergenerational transmission of obesity and metabolic risk.

Adipose tissue is an essential organ for human health, and it is characterized by its amount, distribution, and function(20). In obesity, adipocyte hypertrophy transforms adipose tissue into an unhealthy metabolically active organ that secretes proinflammatory cytokines and a dysregulated hormonal profile, including altered levels of adiponectin and leptin. The AdipoQ/Lep ratio has been proposed as a hallmark of adipose tissue dysfunction(21). Since this ratio is negatively correlated with insulin resistance and BMI(9, 22), it may also serve as an early biomarker of cardiometabolic diseases.

To date, only one study assessed the AdipoQ/Lep ratio in umbilical cord plasma and maternal-infant outcomes(23), but it did not address cardiovascular outcomes. Therefore, this discussion relies on studies analyzing adiponectin and leptin separately. Thus, it is essential to note that a lower AdipoQ/Lep ratio reflects decreased adiponectin and increased leptin levels.

At present, it is impossible to determine whether fetal adiponectin and leptin derive exclusively from maternal or fetal adipose tissue. The origin of adiponectin in the fetus remains unclear, although it is believed to be produced by fetal adipose tissue(24). Leptin is produced mainly in the adipose tissue but also in the skeletal muscle, gastric mucosa, heart, mammary, salivary gland, and even placenta(25). However, only 5% or less of placental leptin is released into the fetal circulation, while the remainder enters the maternal circulation(26). Although several studies have linked maternal adiponectin and leptin levels to child outcomes(27), some evidence suggested that maternal concentrations do not significantly influence fetal adipokines levels(26). While it is widely established that UBC leptin levels are strongly associated with pregestational BMI(28, 29), no such association has been described yet for adiponectin(24, 28).

Samples of placentas from women with obesity showed downregulation of adiponectin and leptin systems (including both their synthesis and receptors)(30). The authors suggested that these epigenetic changes in placental adiponectin and leptin systems could program fetal growth and development later in life(30). Leptin upregulates placental GLUT1 expression and activity, enhancing glucose supply to the fetus, while adiponectin has been shown to modulate amino acid transporters (*e.g.*: SNAT2) and inhibit placental mTOR signaling via AMPK activation. This may lead to fetal overgrowth and increased cardiometabolic susceptibility later in life(31). Although, maternal plasma adiponectin and leptin levels were not measured in this cohort, maternal obesity – which is strongly associated with decreased circulating levels of maternal adiponectin and increased leptin(7) – was negatively correlated with fetal AdipoQ/Lep ratio and positively with fetal leptin.

We confirm previous data showing that adiponectin and leptin levels in UBC were related to weight at birth(32). The correlations we observed between the AdipoQ/Lep ratio, adiponectin and leptin and BMI-for-age Z-score and birth weight support the hypothesis that these adipokines are linked to infant absolute fat mass rather than relative adiposity, as weight-for-length is primarily a measure of body proportionality rather than fat content.

Adiponectin and leptin correlate positively with weight-for-length Z-score at a mean age of 5 months. Additionally, Mantzoros *et. al*., observed that lower levels of UBC adiponectin and leptin predict increased weight-to-length Z-score gain during the first 6 months of life(33). Similarly, in a prospective cohort study of 185 mother-infant pairs, higher levels of UBC leptin were associated with lower BMI in the first year of life(29). Despite the contradictory results and evidence showing that UBC adiponectin is not a predictor of adiposity at the age of 5 years(34), future research is needed to explore how the balance between these two adipokines may predict postnatal growth and body composition.

One of the main findings of this study was that the influence of maternal and neonatal weight on infant cardiac structure and function was not influenced by AdipoQ/Lep ratio, adiponectin or leptin. We observed that maternal obesity emerged as a significant predictor of changes in infant cardiac morphology, namely in the *LVIDs* and the *MV-A-wave Z-score*. Additionally, the neonatal BMI-for-age Z-score at birth was negatively associated with *IVRT* Z-score. Although this adipokine-based marker has been linked to maternal and neonatal weight status, it did not explain the observed variation in cardiac morphology, highlighting the multifactorial nature of intrauterine cardiovascular programming. Categorical analysis revealed that infants with lower ventricular diameter showed a significantly lower AdipoQ/Lep ratio, suggesting a possible link between the intrauterine metabolic environment and the early cardiac remodeling. Leptin has pro-hypertrophic effect on cardiomyocytes, contributing to ventricular remodeling and alteration in diastolic function, contributing to early myocardial changes even in asymptomatic neonates(35). In addition, a full cardiac system of adiponectin suggests a role in maintaining normal cardiac function(35). These findings underscore the importance of longitudinal cardiovascular monitoring in children exposed to maternal obesity, particularly those born with low birth weight, who are associated with an increased risk of coronary heart disease in adulthood(36). The limited associations observed between the AdipoQ/Lep ratio and most echocardiographic parameters underscore the intricate nature of fetal cardiovascular programming. This suggests that a singular hormonal ratio might not adequately reflect the complexity of multifactorial influences involved. As corroborated by previous research, cardiometabolic outcomes in infancy and childhood are shaped by the interplay of genetic, epigenetic, and environmental factors, including crucial elements suctiago costah as placenta adaptation, oxidative stress, and inflammatory signaling(37, 39). This complexity is further emphasized by the concurrent development and share developmental pathways of the placenta and fetal heart(38).

While our study provides valuable insights, it also presents limitations. The sample size limits our conclusions (n=42) regarding the potential biomarker value of AdipoQ/Lep to predict cardiac morphofunctional alterations. Studying fetal programming presents significant challenges, as establishing a clear cause-and-effect relationship between events during pregnancy and the development of diseases later in life, typically requiring 20 or more years of follow-up. Another limitation of this study is the lack of measurement of maternal adiponectin and leptin levels at the end of pregnancy. Although we recognize that our current results do not establish a direct connection between maternal concentration of these adipokines, fetal AdipoQ/Lep ratio, and infant anthropometry, we believe that this research represents an important first step toward identifying novel predictive biomarkers for future metabolic or growth-related risks.

In conclusion, our study provides preliminary evidence that maternal obesity predicts the AdipoQ/Lep ratio in UBC, and that a lower AdipoQ/Lep ratio is associated with neonatal somatometry at birth. Although no consistent associations were found between AdipoQ/Lep ratio and overall cardiac structure or function, infants with lower left ventricular end-diastolic diameter Z-scores exhibited significantly lower AdipoQ/Lep ratio, suggesting a potential link that warrants further investigation. More studies are needed to assess the predictive value of the AdipoQ/Lep ratio as an early biomarker of cardiometabolic health and growth throughout childhood. Such research is crucial to provide evidence for the potential utility of early-life biomarkers in identifying individuals at risk, to enable closer monitoring and intervention to prevent the onset of cardiometabolic diseases and promote long-term health.

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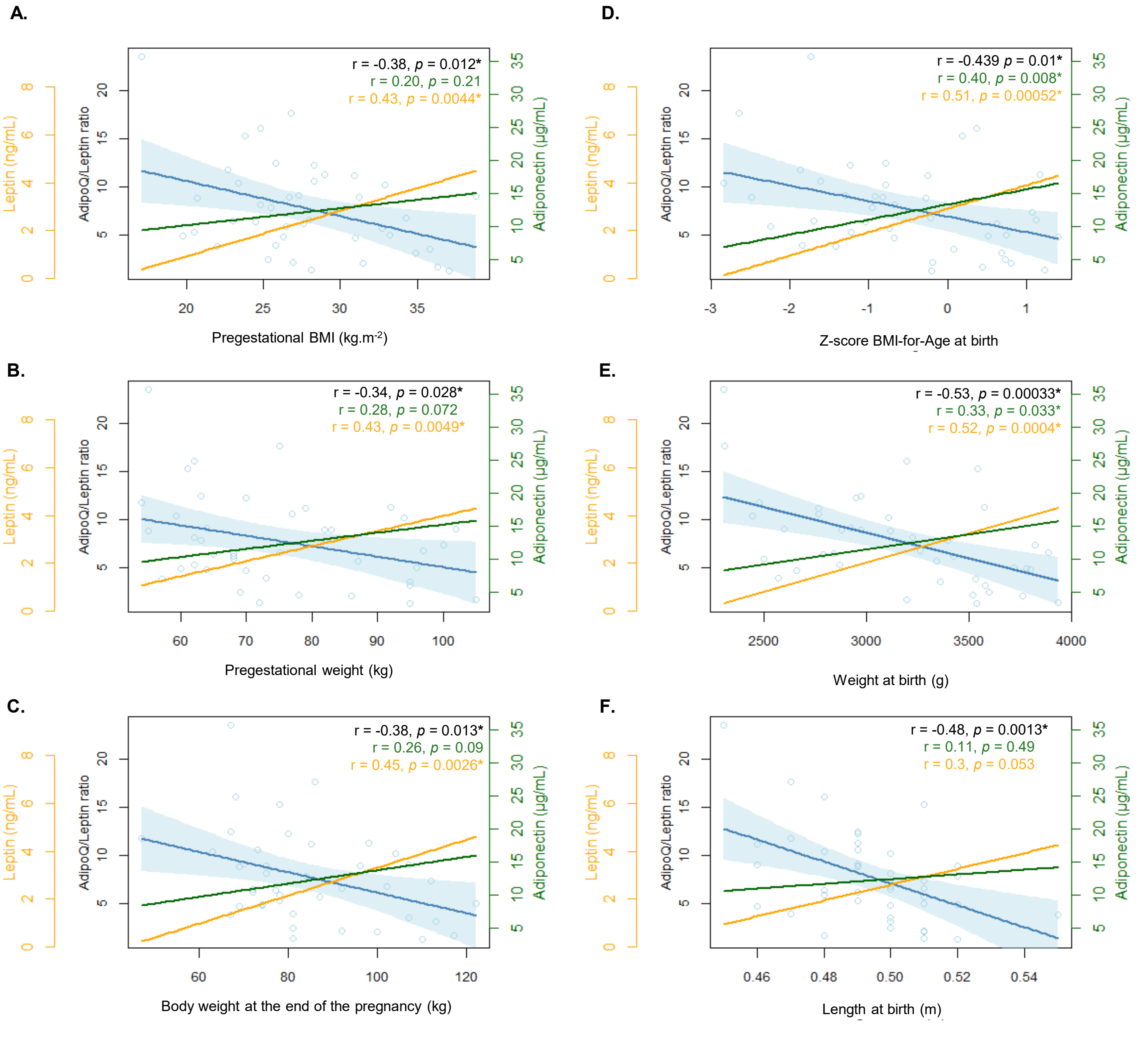
Relationship Between Maternal Obesity, Birth Weight And Fetal Adiponectin/Leptin Ratio: A Potential Early Biomarker Of Cardiometabolic

Figure 1.



Relationship Between Maternal Obesity, Birth Weight And Fetal Adiponectin/Leptin Ratio: A Potential Early Biomarker Of Cardiometabolic

Figure 2.

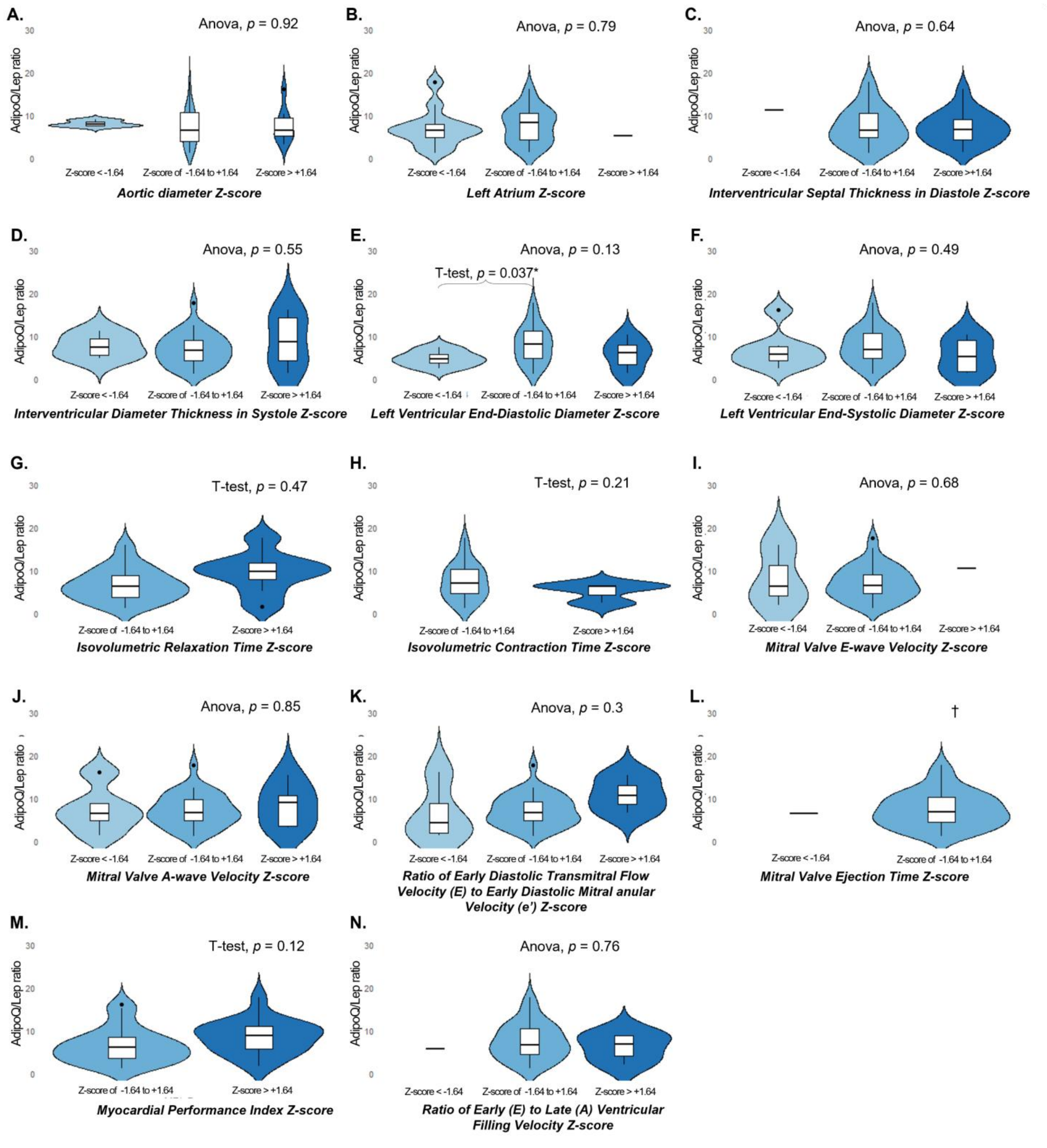


Table 1. Clinical and anthropometric data of study mother-neonate' pairs

Maternal data		
Maternal age (years), mean±SD		34 ± 6
Pregestational BMI (kg.m^{-2}), mean±SD		27.8 ± 5.0
Pregestational BMI category, n(%)		
	Underweight	1 (2.4)
	Normal weight	11 (26.2)
	Overweight	17 (40.5)
	Obesity	13 (31.0)
Gestational weight gain (kg), mean±SD		9.47 ± 6.70
Gestational diabetes, n(%)		8 (19.0)
Gestational hypertension, n(%)		6 (14.3)
Peripartum/Neonate data		
Gestational age (weeks), mean±SD		39.0 ± 1.10
Delivery mode, n(%)	*Vaginal*	33 (78.6)
	C-section	9 (21.4)
Sex, n(%)	*Male*	23 (53.8)
	Female	19 (45.2)
Somatometry at birth, mean±SD		
	Weight at birth (g)	3161 ± 469
	Length at birth (cm)	49.0 ± 2.0
	Weight for length Z-score at birth	-0.45 ± 1.19
	BMI for age Z-score at birth	-0.51 ± 1.15
Infant data at echocardiographic evaluation		
Age (months), mean±SD		5 ± 2
Somatometry, mean±SD	*Weight (g)*	6352 ± 1540
	Length (cm)	62.7 ± 5.5

SD – Standard deviation, BMI – Body Mass Index

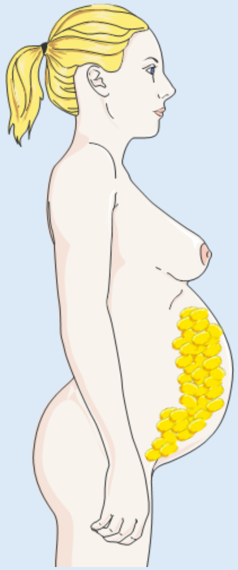
Table 2. Multiple linear regression analysis considering left ventricular end-systolic diameter Z-score (LVIDs Z-score), mitral valve A-wave velocity Z-score (MV-A-wave Z-score) and isovolumetric relaxation time Z-score (IVRT Z-score) as the dependent variables.

	Independent variables	B	Beta	P-value	Adjusted R^2	Model p-value
Pregestational BMI vs. *LVIDs Z-score*	Model unadjusted	0.114	0.396	**0.008***		
	Model 1	0.131	0.456	**0.006***	0.135	**0.022***
	Model 2	0.122	0.422	**0.013***	0.132	**0.039***
Pregestational BMI vs. *MV-A-wave Z-score*	Model unadjusted	0.109	0.324	**0.037***		
	Model 1	0.128	0.379	**0.025***	0.078	0.078
	Model 2	0.144	0.428	**0.013***	0.095	0.080
Z-score BMI-for-Age vs. *IVRT Z-score*	Model unadjusted	-0.391	-0.433	**0.004***		
	Model 1	-0.373	-0.413	**0.012***	0.148	**0.016***
	Model 2	-0.332	-0.368	**0.044***	0.134	**0.038***

** $p < 0.05$ indicates statistical significance. **Model 1**: adjusted for AdipoQ/Lep ratio. **Model 2**: adjusted for adiponectin and leptin levels. Adjusted R^2 values and associated p-values were obtained from a multiple linear regression. AdipoQ/Leptin: adiponectin/leptin ratio; B: unstandardized regression coefficient; Beta: standardized beta coefficient; BMI, body mass index.*

Fetal AdipoQ/Lep Ratio: a potential early biomarker of cardiometabolic risk

Maternal obesity



↑ Pregestational BMI

Pregestational weight

Body weight at the end of the pregnancy

Neonatal somatometry at birth

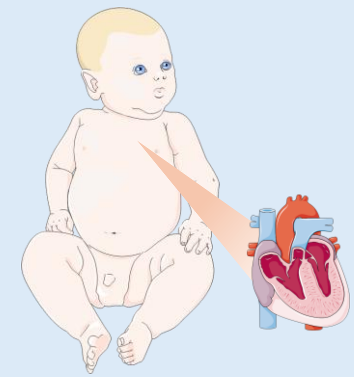
↑ Weight at birth

Length at birth

Z-score BMI-for-age at birth

↓ AdipoQ/Lep ratio in cord blood

Echocardiographic evaluation at 5 months old



↓ **Reduced diastolic function**

Z-score of left ventricular end-diastolic diameter < –1.64, suggesting a potential early sign of altered cardiac development

Conclusion | AdipoQ/Lep ratio in cord blood is linked to maternal obesity, greater birth size, and reduced left ventricular end-diastolic diameter, suggesting early cardiometabolic link.