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ORIGINAL ARTICLE
ORİJİNAL ARAŞTIRMA

Early Cardiometabolic Characteristics in Childhood Among Large-for-Gestational-Age Infants

Gebelik Haftasına Göre İri Doğan Çocuklarda Erken Dönem Kardiyometabolik Özellikler

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Abstract

Aim: To evaluate cardiometabolic characteristics in prepubertal children born large for gestational age (LGA) compared with those born appropriate for gestational age (AGA), with a focus on adiposity, insulin levels, and lipid parameters.

Material and Method: This study included 117 prepubertal children aged 6–9 years (59 LGA, 58 AGA). Anthropometric measurements, blood pressure, and fasting laboratory parameters were assessed. LGA was defined as birth weight ≥90th percentile for gestational age, and AGA as the 10th–90th percentile. Insulin levels and lipid profiles were evaluated. Statistical analyses included t-tests, Mann–Whitney U tests, and chi-square tests.

Results: Children born LGA had significantly higher weight, height, BMI, and waist and hip circumferences compared with AGA peers (p≤0.010). Obesity prevalence was higher in the LGA group (25.4% vs. 10.3%, p=0.030). Fasting glucose and insulin levels were similar between groups. Total cholesterol and LDL-C were significantly higher in LGA children (p=0.010 and p=0.030, respectively), while HDL-C was also higher (p=0.040) and triglyceride levels were lower (p=0.040).

Conclusion: Children born LGA showed greater adiposity and higher LDL cholesterol concentrations than AGA peers. Although insulin resistance and elevated blood pressure were not evident at this age, the cross-sectional design and the restriction to offspring of mothers without recognised metabolic disease mean that these findings represent associations rather than evidence of causation and require confirmation in longitudinal studies.

Keywords: Cardiometabolic characteristics, large for gestational age, lipid profile, obesity, prepuberty

Öz

Amaç: Bu çalışmada, gebelik haftasına göre iri doğan (GHİ) prepubertal çocukların kardiyometabolik özelliklerinin, gebelik haftasına göre uygun doğan (GHU) akranlarıyla karşılaştırılması ve özellikle adipozite, insülin düzeyleri ile lipid profili açısından değerlendirilmesi amaçlandı.

Gereç ve Yöntem: Çalışmaya 6–9 yaşları arasında toplam 117 prepubertal çocuk (59 GHİ, 58 GHU) dahil edildi. Katılımcıların antropometrik ölçümleri, kan basıncı değerleri ve açlık biyokimyasal parametreleri değerlendirildi. GHİ, doğum ağırlığının gebelik haftasına göre ≥90. persentilde; GHU ise 10.–90. persentiller arasında olması şeklinde tanımlandı. İnsülin düzeyleri ve lipid profilleri incelendi. İstatistiksel analizlerde Student t testi, Mann–Whitney U testi ve ki-kare testi kullanıldı.

Bulgular: GHİ grubundaki çocukların vücut ağırlığı, boy uzunluğu, beden kitle indeksi, bel çevresi ve kalça çevresi ölçümleri GHU grubuna göre anlamlı olarak daha yüksekti (tüm karşılaştırmalar için p≤0,010). Obezite sıklığı da GHİ grubunda anlamlı düzeyde daha yüksek bulundu (%25,4'e karşı %10,3; p=0,030). Açlık glukozu ve insülin düzeyleri açısından gruplar arasında anlamlı farklılık saptanmadı. Buna karşın, toplam kolesterol ve düşük yoğunluklu lipoprotein kolesterol düzeyleri GHİ grubunda daha yüksek bulundu (sırasıyla p=0,010 ve p=0,030). Ayrıca, yüksek yoğunluklu lipoprotein kolesterol düzeyleri daha yüksek (p=0,040), trigliserid düzeyleri ise daha düşük olarak saptandı (p=0,04).

Sonuç: Gebelik haftasına göre iri doğan çocuklarda, prepubertal dönemde artmış adipozite ve daha yüksek düşük yoğunluklu lipoprotein kolesterol düzeyleri saptanmıştır. Her ne kadar bu yaş grubunda insülin direnci ve yüksek kan basıncı açısından belirgin bir farklılık saptanmamış olsa da, çalışmanın kesitsel tasarımı ve metabolik hastalığı bulunmayan annelerin çocuklarından oluşan seçilmiş bir örneklemde yürütülmüş olması nedeniyle bulgular nedensellik değil ilişki olarak yorumlanmalı ve uzunlamasına çalışmalarla doğrulanmalıdır.

Anahtar Kelimeler: Kardiyometabolik özellikler, gebelik haftasına göre iri doğum, lipid profili, obezite, prepubertal dönem

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INTRODUCTION

Obesity and related metabolic perturbations emerging during critical periods of growth have implications not only for immediate child health but also for shaping cardiometabolic risk trajectories into adulthood. Early-onset disturbances such as insulin resistance, hypertension, dyslipidemia, and impaired glucose regulation may predispose individuals to long-term complications including type 2 diabetes and cardiovascular disease (1). Increasing evidence indicates that these risks may originate early in life, with fetal growth and the intrauterine environment implicated in later metabolic health (2).

Both small for gestational age (SGA) and large for gestational age (LGA) birth size have been associated with an increased risk of metabolic complications across the life course (3). LGA is typically defined as a birth weight above the 90th percentile for gestational age according to population-based reference standards (4). Infants born LGA are often exposed to an intrauterine environment characterized by maternal overnutrition or hyperglycemia, such as maternal obesity or gestational diabetes, which may lead to fetal hyperinsulinemia and excessive growth (5). These children are more likely to develop overweight or obesity during childhood and adolescence, and several studies suggest an increased risk of adverse cardiometabolic risk factors later in life (3,5). However, existing data on long-term metabolic outcomes remain limited and inconsistent, with some studies reporting adverse metabolic profiles in LGA children, while others indicate that birth weight alone may not predict later risk once postnatal growth and adiposity are considered (6,7).

Recent evidence demonstrates that cardiometabolic risk factors can be identified as early as the prepubertal period, supporting the concept that cardiometabolic programming begins in early childhood (8). Assessment during this period allows evaluation of early metabolic risk largely independent of pubertal hormonal influences. Identifying early alterations in cardiometabolic risk factors is therefore critical for timely preventive strategies. Accordingly, we aimed to evaluate cardiometabolic characteristics in prepubertal children born LGA compared with children born appropriate for gestational age (AGA), in order to determine whether LGA birth status is associated with early metabolic risk markers that may predispose to adverse cardiometabolic outcomes later in life.

MATERIAL AND METHOD

Study Design and Participants

This cross-sectional, comparative study was conducted at a single tertiary pediatric endocrinology center. The study was approved by the Gazi University Clinical Research Ethics Committee (Date: 15.06.2011, Decision No: 217). All participants and their parents received detailed information regarding the study procedures and provided written informed consent prior to enrollment.

Sample size calculation was based on previously reported obesity prevalence rates of 25% among children born large for gestational age (LGA) and 10% among those born appropriate for gestational age (AGA) (4,9). Using the standard formula for the comparison of two independent proportions, and assuming a two-sided alpha level of 0.05 and a statistical power of 80%, approximately 100 participants per group, corresponding to 200 participants in total, would be required. The target sample size could not be attained within the study period owing to the limited number of eligible children identified in the birth registry and the high rate of non-participation (**Figure 1**). A sensitivity analysis based on the achieved sample of 59 LGA and 58 AGA children indicated that the study had 80% power to detect an obesity prevalence of 30.6% or higher in the LGA group, corresponding to an absolute difference of approximately 21 percentage points.

Hospital records of 5,630 births at the study center were screened to identify eligible participants. The study group consisted of prepubertal children aged 6–9 years with a birth weight at or above the 90th percentile for gestational age (LGA) (4). The control group was selected from the same birth registry and individually matched to cases at the selection stage by age (±6 months) and sex, with birth weights between the 10th and 90th percentiles (AGA) (4); one matched control was subsequently excluded, resulting in 59 LGA and 58 AGA participants. To ensure comparability, both groups were evaluated at the same tertiary pediatric endocrinology outpatient clinic during the same study period.

Children born small for gestational age (SGA), preterm infants, and those with congenital anomalies or chronic conditions known to affect growth or metabolism were excluded from the study. All participants were confirmed to be prepubertal (Tanner stage 1).

To reduce maternal metabolic confounding, the study population was restricted to offspring of nonobese (prepregnancy body mass index (BMI) <30 kg/m^2), nondiabetic mothers without chronic hypertension or gestational diabetes mellitus (GDM) in the index pregnancy. This restriction was applied in order to examine LGA birth occurring in the absence of recognised maternal metabolic disease, and it consequently defines the population to which the present findings apply.Excessive gestational weight gain, defined according to the Institute of Medicine recommendations stratified by prepregnancy BMI categories (10), constituted an exclusion criterion to limit the influence of intrauterine overnutrition on offspring metabolic outcomes. All mothers underwent a 100-g oral glucose tolerance test between 24 and 28 weeks of gestation, and GDM was excluded based on standard clinical diagnostic criteria. Flow chart of the study is shown in **Figure 1**.

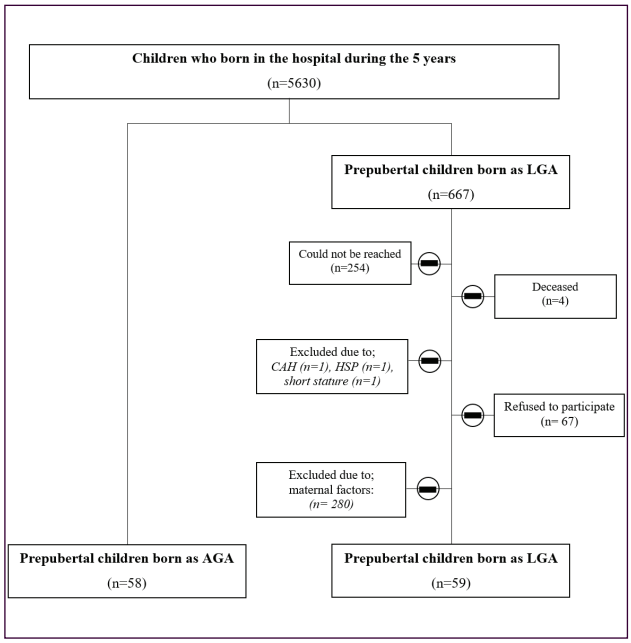

Figure 1. Flowchart of participants selection and group distribution.

AGA: appropriate for gestational age, CAH: congenital adrenal hyperplasia, HSP: Henoch schönlein purpura, LGA: large for gestational age

Postnatal factors, including breastfeeding duration, age at introduction of complementary foods, history of common childhood illnesses, and family history of metabolic diseases (obesity, type 2 diabetes, dyslipidemia, and hypertension), were recorded using standardized questionnaires.

Assessment of Cardiometabolic Characteristics

Individual cardiometabolic characteristics, including obesity, elevated blood pressure, dyslipidemia, impaired glucose metabolism, and insulin sensitivity as assessed by HOMA-IR, were evaluated (11).

Anthropometric and Clinical Assessments

Screening of the birth records and all anthropometric and clinical measurements were performed by the same investigator, who was therefore not blinded to the birth weight status of the participants. Measurements were obtained using standardised techniques and calibrated instruments in order to minimise measurement variability. BMI was calculated as weight divided by height squared (kg/m^2), and BMI percentiles were interpreted according to national growth charts for Turkish children (12). Overweight was defined as a BMI between the 85th and 94th percentiles, and obesity as a BMI at or above the 95th percentile.

Waist circumference was measured at the midpoint between the lowest rib and the iliac crest, and hip circumference at the level of the greater trochanters. Waist circumference percentiles were evaluated according to the reference values for Turkish children (13), and central obesity was defined as a waist circumference at or above the 90th percentile for age and sex.

Blood pressure was measured three times after a resting period, and the average of the measurements was used for analysis. Elevated blood pressure was defined as systolic and/or diastolic blood pressure at or above the 90th percentile for age, sex, and height (14). As blood pressure was assessed at a single visit, the term hypertension was not applied, since its diagnosis requires confirmation on separate occasions.

Laboratory Measurements

Fasting venous blood samples were obtained to measure plasma glucose, insulin, lipid profile (total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides), and liver enzymes. Dyslipidemia was defined according to the age- and sex-specific reference values reported in the IDEFICS study, with hypertriglyceridaemia defined as a triglyceride concentration at or above the 90th percentile and low HDL cholesterol as an HDL cholesterol concentration at or below the 10th percentile (11). Elevated LDL cholesterol was defined as an LDL cholesterol concentration at or above the 90th percentile according to the age- and sex-specific IDEFICS reference values for blood (15).

Insulin resistance was assessed using the homeostasis model assessment of insulin resistance (HOMA-IR), calculated as fasting insulin (μIU/mL) multiplied by fasting plasma glucose (mg/dL) and divided by 405.

HOMA-IR was analysed as a continuous variable, and no dichotomous threshold for insulin resistance was applied, as no single cut-off value is universally accepted for prepubertal children.

Statistical Analysis

All statistical analyses were performed using SPSS version 23.0 (IBM Corp., Armonk, NY, USA). Continuous variables were assessed for normality using the Shapiro-Wilk test. For consistency of presentation, all continuous variables are summarised as mean±standard deviation (SD) in the tables, irrespective of the test applied.

Comparisons between children born LGA and those born AGA were performed using the independent samples t-test for normally distributed continuous variables and the Mann–Whitney U test for skewed variables. Although controls were individually matched at the selection stage, the two groups were analysed as independent samples. This approach was adopted because matching was performed with respect to the exposure groups rather than to outcome status, a design in which analysing the groups as independent samples remains valid for hypothesis testing. Categorical variables were

compared using the chi-square test or Fisher's exact test, as appropriate. A two-tailed p-value <0.05 was considered statistically significant. No adjustment for multiple comparisons was applied. The comparisons were prespecified and hypothesis-driven rather than exploratory screening of a large number of unrelated variables, and given the limited sample size a correction would have substantially increased the probability of type II error. The findings are accordingly presented as exploratory. Multivariable analyses were not undertaken; the comparisons reported here are unadjusted, and the study is presented as a descriptive comparison of the two groups.

** The authors declare that artificial intelligence (AI) tools were used solely for language editing and grammar improvement. The authors take full responsibility for the content of the manuscript.

RESULTS

A total of 117 children (mean age 7.5±1.1 years; 53% male) were included, comprising 59 in the LGA group and 58 in the AGA group. The LGA group had a significantly higher mean birth weight than the AGA group (4150±400 g vs. 3300±450 g) (p<0.001) (**Table 1**). There were no significant differences between the groups in age, gestational age, or gender distribution (**Table 1**). More than 90% of children in each group had been breastfed for at least 6 months, with no between-group difference in breastfeeding duration.

Table 1. Demographic and birth characteristics of participants

Characteristics	LGA (n=59)	AGA (n=58)	p
Age (years) (mean±SD)	7.5±1.1	7.5±1.1	0.940
Gender, male (n (%))	32 (54)	30 (52)	0.850
Birth weight (g) (mean±SD)	4150±400	3300±450	<0.001
Gestational age (weeks) (mean±SD)	38.4±1.6	38.1±1.8	0.400

AGA: appropriate for gestational age, g: gram, LGA: large for gestational age, SD: standard deviation
Comparisons were performed using the independent samples t-test or the Mann-Whitney U test according to the distribution of each variable.

Children in the LGA group had higher anthropometric measurements compared with the AGA group. Mean body weight and height were greater in the LGA group (28±5 kg vs. 25±5 kg and 128±7 cm vs. 124±7 cm, respectively) (p=0.001 and p=0.002, respectively) (**Table 2**). Mean BMI was higher among LGA children than in the AGA group (17.5±2.8 vs. 16.0±2.4) (p=0.003) (**Table 2**). Waist and hip circumferences were greater in the LGA group (62±6 cm vs. 59±6 cm and 70±5 cm vs. 67±5 cm, respectively) (p=0.010 and p=0.005, respectively) (**Table 2**). No significant differences were observed between the groups in waist-to-hip ratio or blood pressure measurements.

Table 2. Anthropometric Measurements and Blood Pressure of LGA and AGA groups.

Measurements	LGA (n=59)	AGA (n=58)	p
Weight (kg) (mean±SD)	28±5	25±5	0.001
Height (cm) (mean±SD)	128±7	124±7	0.002
BMI (mean±SD)	17.5±2.8	16.0±2.4	0.003
Waist circumference (cm) (mean±SD)	62±6	59±6	0.010
Hip circumference (cm) (mean±SD)	70±5	67±5	0.005
Systolic BP (mean±SD)	101±8	100±7	0.650
Diastolic BP (mean±SD)	64±6	63±6	0.700

AGA: appropriate for gestational age, BMI: body mass index, BP: blood pressure, kg: kilogram, LGA: large for gestational age, SD: standard deviation
Comparisons were performed using the independent samples t-test or the Mann-Whitney U test according to the distribution of each variable.

Fasting glucose levels were within the normal range in both groups. There was no significant difference in fasting insulin concentrations between the LGA and AGA groups (p=0.400). Although the difference between the two groups was not statistically significant (p=0.117), HOMA-IR values (mean±SD) were higher in the LGA group (1.34±0.68) compared with the AGA group (1.11±0.63) (**Table 3**). In contrast, differences were observed in lipid profiles. The LGA group had higher mean total cholesterol and LDL cholesterol levels compared with the AGA group (165±25 vs. 150±30 mg/dL and 100±20 vs. 90±25 mg/dL, respectively) (p=0.010 and p=0.030, respectively) (**Table 3**). HDL cholesterol levels were higher in the LGA group (55±12 vs. 50±10 mg/dL) (p=0.040). Triglyceride levels were lower in the LGA group than in the AGA group (70±30 vs. 85±35 mg/dL, respectively) (p=0.040) (**Table 3**). Liver enzyme levels (AST, ALT) did not differ between the groups and were within normal ranges.

Table 3. The comparison of fasting biochemical and metabolic parameters between children born LGA and AGA.

Parameters	LGA (n=59)	AGA (n=58)	p
Fasting glucose (mg/dL) (mean±SD)	89±5	90±6	0.530
Fasting insulin (µIU/mL) (mean±SD)	8.0±5.0	7.0±4.0	0.400
HOMA-IR (mean±SD)	1.34±0.68	1.11±0.63	0.117
Total cholesterol (mg/dL) (mean±SD)	165±25	150±30	0.010
LDL cholesterol (mg/dL) (mean±SD)	100±20	90±25	0.030
HDL cholesterol (mg/dL) (mean±SD)	55±12	50±10	0.040
Triglycerides (mg/dL) (mean±SD)	70±30	85±35	0.040
AST (U/L) (mean±SD)	22±7	21±6	0.500
ALT (U/L) (mean±SD)	15±8	14±7	0.600

AGA: appropriate for gestational age; ALT: alanine aminotransferase; AST: aspartate aminotransferase; HDL: high-density lipoprotein; HOMA-IR: Homeostasis Model Assessment of Insulin Resistance; LDL: low-density lipoprotein; LGA: large for gestational age, SD: standard deviation.
Comparisons were performed using the independent samples t-test or the Mann-Whitney U test according to the distribution of each variable.

The prevalence of obesity was higher among children born LGA. In the LGA group, 25.4% (n=15) of children were classified as obese, compared with 10.3% (n=6) in the AGA group (p=0.030) (**Table 4**). The proportion of children who were overweight but not obese did

not differ between the LGA and AGA groups (15% vs. 21%) (p=0.470). When overweight and obesity were considered together, 40.7% of children in the LGA group and 31.0% in the AGA group had excess weight status (p=0.210). Central obesity, was present in 19/59 (32.2%) children in the LGA group and 11/58 (19.0%) children in the AGA group (p=0.100). Hypertriglyceridemia (≥90th percentile) was more frequent in the AGA group than in the LGA group (12.1% vs. 3.4%, respectively) (p=0.048) (Table 4). Low HDL cholesterol (≤10th) was observed in 10.3% of AGA children and 5.1% of LGA children, with no statistically significant difference between the groups (p=0.300) (**Table 4**).

Table 4. Comparison of cardiometabolic characteristics between the LGA and AGA groups.

	LGA (n=59)	AGA (n=58)	p
Overweight (n (%))	9 (15.3)	12 (20.7)	0.470
Obesity (n (%))	15 (25.4)	6 (10.3)	0.030
Central Obesity (n (%))	19 (32.2)	11 (19.0)	0.100
Elevated blood pressure (n (%))	2 (3.4)	1 (1.7)	0.610
Hypertriglyceridemia (n (%))	2 (3.4)	7 (12.1)	0.048
Low HDL (n (%))	3 (5.1)	6 (10.3)	0.300

AGA: appropriate for gestational age; HDL: high-density lipoprotein; LGA: large for gestational age.
*Overweight: BMI 85th–94th ; Obesity: BMI ≥95th ; Elevated blood pressure: BP ≥90th ; Hypertriglyceridemia: TG ≥90th percentile; Low HDL: HDL ≤10th percentile

DISCUSSION

In this study, prepubertal children born LGA had greater adiposity and higher obesity rates than those born AGA. By 7–8 years of age, about one-quarter of LGA children were obese versus roughly one-tenth of AGA peers. This aligns with research indicating that high birth weight is associated with an approximately twofold risk of early childhood obesity (3,4,9,16). Notably, this association was observed although mothers with obesity, diabetes, or excessive gestational weight gain were excluded by design, indicating that greater adiposity in childhood may accompany LGA birth even in the absence of recognised maternal metabolic disease (3,17). The cross-sectional design does not permit causal interpretation of this association.

Despite large differences in body size, we found no significant disparities in blood pressure or glycemic indices between LGA and AGA children at ~7 years of age. Fasting glucose and insulin were comparable between groups, indicating that LGA children did not have higher insulin levels than AGA peers at this stage. This finding contrasts with some reports describing higher insulin levels or reduced insulin sensitivity in LGA children during early childhood (18,19). Although the difference between groups did not reach statistical significance, HOMA-IR values were numerically higher in the LGA group compared with controls; this finding is consistent with the relatively higher prevalence of obesity among LGA children than AGA peers. Nevertheless, overall obesity rates in the study population were low, with only a limited number of obese LGA cases (18,19). The absence of differences in glycaemic indices and blood pressure may have several explanations. One is that the prepubertal period is too early for such differences to become apparent, and longitudinal data indicate that LGA-related differences in insulin metabolism become more pronounced with advancing age and increasing BMI (20). An equally plausible interpretation, however, is that current adiposity and maternal metabolic exposures are more important determinants of glucose regulation and blood pressure in childhood than birth size alone, particularly since mothers with diabetes, obesity and excessive gestational weight gain were excluded from the present study. Maternal gestational diabetes is a stronger predictor of offspring insulin resistance than birth weight alone (6), and LGA infants born to diabetic mothers carry a substantially higher risk of metabolic syndrome by adolescence (21). The cross-sectional design does not allow these possibilities to be distinguished, and the present findings should not be taken to indicate that metabolic abnormalities will necessarily emerge at a later stage.

The AGA group had a higher rate of hypertriglyceridemia and slightly lower HDL cholesterol despite having a lower prevalence of obesity. In contrast, the more obese LGA group showed lower triglyceride levels and slightly higher HDL cholesterol, a finding that appears counterintuitive given the established adverse effects of adiposity on lipid metabolism. One possible explanation is catch-up growth among a subset of AGA children who were at the lower end of the normal birth weight spectrum, as rapid postnatal weight gain in children born small has been associated with elevated triglyceride levels and adverse metabolic outcomes (19,22). This interpretation could be examined directly by stratifying the AGA group according to birth weight percentile, since children in the lower part of the appropriate-for-gestational-age range are those most likely to have undergone postnatal catch-up growth. Such a stratified comparison was not performed here, and we would encourage its use in future studies of this question. Beyond early growth patterns, triglyceride regulation in prepubertal children is known to be influenced by factors other than adiposity alone. Evidence indicates that triglyceride levels at this age are particularly sensitive to dietary carbohydrate quality, with high intake of refined carbohydrates and fructose promoting hepatic de novo lipogenesis and increased circulating triglycerides even in non-obese children (23). Physical activity levels and underlying genetic susceptibility have likewise been reported to modulate triglyceride concentrations (24). Dietary intake, physical activity and genetic factors were not assessed in the present study, and these considerations are therefore offered as possible explanations for the

pattern observed rather than as factors shown to account for it. Notably, LGA children did have significantly higher LDL cholesterol than AGA children. The increased adiposity and isolated LDL cholesterol elevation observed in children born LGA cannot be attributed to a specific mechanism on the basis of the present cross-sectional data. Experimental and human data suggest that variations in fetal nutrient exposure may influence adipocyte development and hypothalamic appetite regulation, predisposing to increased fat mass without immediate disturbances in glucose homeostasis (25). In parallel, variations in the intrauterine metabolic environment have been proposed to affect hepatic lipid metabolism, including altered cholesterol synthesis and LDL receptor activity, which may manifest as early LDL elevation independent of adiposity (26). These pathways were not assessed in the present study, and because mothers with diabetes, obesity, or excessive gestational weight gain were excluded by design, the present findings cannot be attributed to intrauterine overnutrition. Similarly, several pediatric studies report higher total and LDL cholesterol levels in individuals born LGA, even after accounting for current BMI (3,27). Metin girmek için buraya tıklayın veya dokunun. These findings suggest that isolated LDL elevation in LGA children may represent an early, subclinical cardiometabolic phenotype that could become more clinically relevant with advancing age or pubertal transition. The contrasting lipid patterns (higher LDL in LGA vs higher TG in AGA) suggest multiple pathways to pediatric dyslipidemia: one driven by increased adiposity and another influenced by early growth patterns or genetic predisposition. Any child with rapid early growth or excess weight gain, regardless of birth weight, should be monitored for lipid abnormalities. Moreover, as the children studied were relatively young (mean age 7.5 years), the absence of metabolic differences at this stage does not preclude their emergence during adolescence. In addition, the relatively small sample size may have limited the detection of subtle metabolic differences between groups.

A substantial proportion of LGA births occurs in the context of maternal obesity, gestational diabetes, or excessive gestational weight gain, and optimising maternal metabolic health before and during pregnancy therefore remains an important public health priority for reducing LGA birth and its long-term consequences (5,17). Mothers with these conditions were excluded from the present study by design, and the findings reported here neither address nor evaluate the impact of such interventions.

This study has some limitations that should be considered when interpreting the findings. First, the achieved sample size fell short of the number indicated by the a priori calculation, and the study was consequently underpowered. Although the difference in obesity prevalence between the groups reached statistical significance, the sensitivity analysis indicates that only relatively large effects could be reliably detected. This limitation is particularly relevant to the continuous metabolic parameters, for which the study was not specifically powered. HOMA-IR was consistently higher in children born LGA but did not reach statistical significance; a type II error therefore cannot be excluded for this parameter, and adequately powered studies with larger samples are required to determine whether this difference represents a genuine early divergence in insulin sensitivity. Second, the broad definition of the AGA group (10th–90th percentile) may have introduced heterogeneity, potentially including children with unrecognized fetal growth restriction followed by postnatal catch-up growth. Third, the lack of an SGA comparison group, which represents a well-recognized risk category for later metabolic disease, limits the ability to place the observed findings in a broader developmental risk context.

Important lifestyle-related determinants of cardiometabolic health such as dietary habits, physical activity, sedentary behavior, and fast-food consumption were not assessed, which may have introduced residual confounding. Anthropometric measurements and blood pressure are reported as absolute values rather than as age- and sex-standardised scores, and the descriptive statistics are presented with a limited number of decimal places, both of which restrict the precision with which the reported values can be interpreted and compared with other paediatric populations. Assessments were not performed under blinded conditions, as the investigator who screened the birth records also carried out the measurements; observer bias in the anthropometric and blood pressure measurements therefore cannot be excluded, although the laboratory parameters were determined by automated systems and are not subject to this limitation. Being a single-center, hospital-based study, selection bias cannot be excluded, and because mothers with obesity, diabetes, chronic hypertension, or excessive gestational weight gain were excluded, the study population represents a selected subgroup of LGA births to which the findings are confined.

Finally, the comparisons reported here are unadjusted. Multivariable analyses were not undertaken, and the associations observed therefore cannot be separated from the influence of potential confounders, including current adiposity and unmeasured factors such as socioeconomic status, diet, and physical activity. Whether LGA birth is independently associated with the observed cardiometabolic differences accordingly remains unresolved. The findings should be interpreted as descriptive, and causal inferences cannot be drawn from the present data.

CONCLUSION

In this cross-sectional study, children born LGA to mothers without recognised metabolic disease showed greater adiposity and higher LDL cholesterol concentrations than AGA peers. Although insulin level and blood pressure differences were not observed by age 7, the present design does not indicate whether such differences emerge later. Some AGA children also exhibited dyslipidemia, a pattern that may relate to early postnatal growth but that was not directly assessed. These associations support consideration of early, individualized metabolic screening in children with high birth weight or rapid weight gain. Longitudinal studies are required before causal or preventive implications can be drawn.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was approved by the Gazi University Clinical Research Ethics Committee (Date: 15.06.2011, Decision No: 217)

Informed Consent: All participants and their parents received detailed information regarding the study procedures and provided written informed consent prior to enrollment.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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