The Association of Birth Weight with Cardiovascular Risk Factors in Early Childhood

Erken Çocukluk Döneminde Doğum Ağırlığının Kardiyovasküler Risk Faktörleri ile İlişkisi

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ABSTRACT

Objective: Our objective was to determine the effect of birth weight (BW) on risk factors of cardiovascular disease and body composition in early childhood.
Method: This descriptive and cross-sectional study included 66 early childhood aged between 2-5 years. The study population were stratified to three categories according to birth weight group: term appropriate for gestational age (AGA) children (n=22), term small for gestational age (SGA) children (n=22), term macrosomic children (n=22).
Results: There was no significant difference with regard to gender, mode of delivery. The height, head circumference, triceps skinfold thickness, chest and waist circumference in early childhood were similar in the three groups. Body mass index (BMI) were significantly higher in macrosomic group compared wtih SGA and AGA groups. The fasting glucose levels were significantly higher in SGA group and macrosomic group respectively than in AGA group. The children in SGA group had significantly higher insulin levels and Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) index when compared to the children in AGA and macrosomic groups. Total cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides, systolic and diastolic blood pressure were comparable among the study groups.
Coclusion: Our study shows that insulin levels and HOMA-IR indexes were higher at early childhood in SGA group when compared to the children in AGA and macrosomic groups. There were no differences between three groups in terms of anthropometric measurements, except BMI.

Keywords: anthropometric measurements; birth weight; cardiovascular risk; early childhood

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ÖZET

Amaç: Çalışmamızın amacı; erken çocukluk döneminde doğum ağırlığının kardiyovasküler risk faktörleri ve vücut kompozisyonu üzerindeki etkisini belirlemektir.
Yöntem: Tanımlayıcı ve kesitsel bu çalışmaya 2-5 yaş arasındaki 66 çocuk dahil edilmiştir. Çalışma popülasyonu doğum ağırlığına göre 3 kategoriye ayrıldı: Term gestasyonel haftasına göre uygun ağırlıkta doğan (AGA) çocuklar (n=22), term gestasyonel haftasına göre düşük doğum ağırlığında doğan (SGA) çocuklar (n=22), term makrozomik doğan çocuklar (n=22).
Bulgular: Cinsiyet ve doğum şekli açısından gruplar arasında önemli bir fark saptanmadı. Erken çocukluk döneminde boy, baş çevresi, triseps deri kıvrım kalınlığı, göğüs ve bel çevresi üç grupta benzerdi. Vücut kitle indeksi (VKİ), makrozomik grupta SGA ve AGA gruplarına göre anlamlı olarak daha yüksekti. Açlık glukoz seviyeleri sırasıyla SGA grubunda ve makrozomik grupta AGA grubuna göre anlamlı olarak daha yüksekti. SGA grubundaki çocuklarda; AGA ve makrozomik gruplardaki çocuklara göre anlamlı olarak daha yüksek insülin seviyelerine ve İnsülin Direncinin Homeostaz Modeli Değerlendirmesi (HOMA-IR) indeksi saptandı. Total kolesterol, yüksek yoğunluklu lipoprotein (HDL) kolesterol, trigliseridler, sistolik ve diyastolik kan basıncı çalışma grupları arasında önemli fark saptanmadı.
Sonuç: Çalışmamız, SGA grubunda erken çocukluk döneminde insülin düzeyleri ve HOMA-IR indekslerinin AGA ve makrozomik gruplardaki çocuklara göre daha yüksek olduğunu göstermektedir. VKİ dışında antropometrik ölçümler açısından üç grup arasında fark yoktu.

Anahtar Sözcükler: antropometrik ölçümler; doğum ağırlığı; kardiyovasküler risk; erken çocukluk

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INTRODUCTION

Cardiovascular disorders are one of the leading causes of mortality and morbidity in the modern world. It remains a significant public health problem because the prevalence increases progressively in the developed and developing countries (1). Since cardiovascular disorders are initially subclinical and it takes a long time for the symptoms of the disease to become apparent (2). Therefore it is important to point out the predisposing factors and early subclinical findings to improve the outcome. Birth weight (BW) abnormalities such as low and high birth weight are risk factors for metabolic syndrome during childhood when compared with appropriate for gestational age (AGA) children. In adult studies, mortality due to cardiovascular diseases was high in those with low birth weight (3). In these individuals, there is also evidence of peripheral insulin resistance, lower beta cell pancreatic function, central obesity, hypertension, multiple lipid abnormalities and diabetes (4, 5). Some investigators have reported that adults born as large for gestational age may have increased risk of cardiovascular disease (6). The underlying mechanisms for these effects are yet to be elucidated. Prevention of cardiovascular risks would be an ideal method for the future well-being of people (7). The aim of this study was to determine the effect of BW on risk factors of cardiovascular disease and body composition in early childhood.

MATERIALS and METHODS

Patient Population

This study was carried out prospectively in healthy children admitted to Pediatric Department of Cumhuriyet University in Sivas, Turkey, between January 2012 and January 2013. The study population comprised of early childhood aged 2-5 years, that is a term AGA children (n=22), term SGA children (n=22), term macrosomic children (n=22). All included children were born at term (≥ 37 weeks' completed gestation). Children were excluded if they had any of the following: (1) twin gestation, (2) type 1 or type 2 diabetes, (3) a condition known to influence body composition, insulin action, or insulin secretion (e.g. glucocorticoid therapy, hypothyroidism, Cushing's disease), (4) born to a woman with impaired glucose tolerance, gestational diabetes mellitus, chronic hypertension, obesity, or received drugs known to affect glucose metabolism throughout gestation.

All subjects were in good health. SGA, AGA, and macrosomia were defined by birth weight of <2500 g, ≥2500 <4000 g, and >4000 g, respectively. This study was approved by Human Research Ethics Committee of Cumhuriyet University. Parents of patients have given their informed consent for participation in this study.

Anthropometric Measurements

Following a thorough physical examination, anthropometric measurements including height, weight, skinfold thicknesses (subscapular and triceps), waist circumference, and head circumference were taken by standart methods. The body weight was determined to the nearest 0.1 kg, and the body length was measured to the nearest 0.1 cm. The head circumference was taken as the largest circumference of the skull using a flexible non stretchable tape to the nearest 0.1cm. The waist circumference was measured to the nearest 0.5 cm, during expiration when breathing normally, at the smallest diameter between the iliac crest and the lower rib. The skinfold thicknesses were measured to the nearest 0.1 mm, in duplicate, with Harpenden calipers. The duplicate measures were averaged. The body mass index (BMI) was calculated as the weight (kilograms) divided by the height (meters) squared. After 30 minutes in the supine position, systolic blood pressure and diastolic blood pressure were measured three times consecutively with an automatic blood pressure device (Dinamap; Critikon, Norderstedt, Germany) at the nondominant arm. The cuff size was adjusted to fit the arm length and circumference.

Blood samples

The venous blood samples were obtained to measure the plasma glucose and insulin levels in the morning at 08:00 a.m. by venipuncture after an overnight fasting. All blood samples were centrifuged at 3500 rpm (revolutions per minute) for 5 minutes, and the serum was separated and stored at -80°C until analysis. The plasma glucose level was determined by using the hexokinase methods (Roche Diagnostics using Cobas Integra kits, Basel, Switzerland), and the plasma insulin was measured with an Immulite 2000 analyzer (Siemens, Los Angeles, USA). The limit of detection was 2μU/mL with intraassay and interassay coefficients of variation of <7.3 % for quality control. The Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) was calculated with the formula: fasting insulin (μU/mL)x fasting glucose (mmol/L)/22.5. The serum total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglyceride concentrations were determined by the colorimetric enzymatic method (Cobas Integra 800; Roche).

Table 1: Characteristics of the participants by birth weight

	AGA infants (n:22)	SGA infants (n:22)	Macrosomic infants (n:22)	P
Gestational age, weeks, median (range)	39.2 (38.7-39.8)	38.2 (37.8-38.8)	39.8 (39.5-40.1)	0.9
Birth weight kg, median (range)	3.4 (3.2-3.5)	2.3 (2.3-2.4)	4.4 (4.2-4.6)	**0.001**
Lenght at birth, cm, median (range)	50.2 ±1.2	48.3 ± 2.4	52.2 ± 1.4	**0.04**
Head circumference at birth, cm, median (range)	34.8 ± 1.7	31.5 ±2.4	35.4 ± 1.8	**0.01**
Female gender, n (%)	15 (68.2)	11 (50)	7 (31.8)	0.06
Vaginal delivery, n (%)	9 (40.9)	11 (50)	5 (22.7)	0.2

Data collection

Data were prospectively collected by trained staff using a standart case report form, which included demographic characteristics; antenatal history; obstetrical history of mother; mode of delivery; health status and complications during birth; how was the baby fed in the first six months of life. All anthropometric measurements were taken by nurses who were blinded to the study. The weight, height, head circumference, skinfold thicknesses (subscapular and triceps), waist circumference were measured according to standart procedures.

Statistical Analysis

The results were analyzed using SPSS for Windows ver. 15.0 (SPSS, Chicago, IL). Continuous data were expressed as mean ± standard deviation if normally distributed, and as the median and range, otherwise. Rates were presented as percentages. The differences between groups were tested using student t-test and ANOVA with post-hoc Bonferroni correction for comparison of two or three groups, respectively. A p value <0.05 was considered statistically significant.

RESULTS

The demographic and clinical features of the study groups are summarized in Table 1. There was no significant difference with regard to gender, mode of delivery (p>0.05). The birth length and head circumference were significantly lower in SGA group when compared to the other two groups (p<0.05) (Table 1). There was no significant difference with birth lenght and head circumference between AGA ve macrosomic groups (p>0.05). The chronological age and anthropometric parameters of the study groups is presented in Table 2. There were no significant differences among the groups at 2-5 years of age with respect to the height, head circumference, triceps skinfold thickness, chest and waist circumference (p>0.05) (Table 2). At 2-5 years age, macrosomic group had significantly higher weight [median: 19 (18-20 kg)] and higher body mass index [17 (16-18)], (p<0.05), compared with those in AGA group [median 17 (16-18 kg)], (p<0.05); [median 16 (15-17)], (p<0.05), respectively and to those in SGA group [median: 16 (15-17 kg)], (p<0.05); [median: 15 (15-16)], (p<0.05), respectively).

There was no significant difference with body mass index between AGA ve macrosomic groups (p>0.05). The insulin levels and cardiovascular risk factors are shown in Table 3.

The fasting glucose levels were significantly higher in SGA group and macrosomic group [(median: 85 (80-91 mg/dl]; [87 (82-92 mg/dl)], respectively than in AGA group (p<0.05). There was no significant difference with fasting glucose levels between SGA ve macrosomic groups (p>0.05).

The children in SGA group had significantly higher insulin levels and HOMA-IR index when compared to the children in AGA and macrosomic groups (p<0.05). There was no significant difference with insulin levels and HOMA-IR index between AGA ve macrosomic groups (p>0.05). Total cholesterol, HDL cholesterol, triglycerides, systolic and diastolic blood pressure were comparable among the study groups (p>0.05).

Table 2: Body compositions of the SGA, AGA and macrosomic infants in early childhood

	AGA infants (n:22)	SGA infants (n:22)	Macrosomic infants (n:22)	P
Age, months, median (range)	49 (45-53)	50 (44-56)	49 (44-54)	0.9
Weight, kg, median (range)	17 816-18)	16 (15-17)	19 (18-20)	**0.01**
Height, cm, median (range)	106 (102-109)	102 (98-105)	106 (102-110)	0.1
Head circumference, cm, median (range)	50 (49-51)	50 (49-51)	50 (49-51)	0.6
BMI (kg/m2), median (range)	16 (15-17)	15 (15-16)	17 (16-18)	**0.04**
Triceps skinfold thickness, median (range)	11 (10-13)	11 (10-12)	11 (10-13)	0.9
Chest circumference, cm, median (range)	54 (53-56)	53 (51-54)	54 (53-56)	0.1
Waist circumference, cm, median (range)	52 (50-54)	51 (50-52)	53 (51-55)	0.4

Table 3: Cardiovascular risk factors of the SGA, AGA and macrosomic infants in early childhood

	AGA infants (n:22)	SGA infants (n:22)	Macrosomic infants (n:22)	P
Systolic blood pressure, mmHg, median (range)	92 (86-98)	89 (85-94)	91 (86.4-95.4)	0.8
Diastolic blood pressure, mmHg, median (range)	56 (51-61)	55 (52-58)	56 (53-59)	0.9
Fasting Glucose, mg/dL, median (range)	80 (75-85)	85 (80-91)	87 (82-92)	**0.04**
Insulin, mIU/ml, median (range)	5.3 (3.2-7.3)	7 (3.7-10.0)	4.5 (3.2-5.9)	**0.02**
Total cholesterol, mg/dL, median (range)	123 (106-140)	112 (99-125)	110 (94-124)	0.6
High-density lipoprotein cholesterol, mg/dL, median (range)	33 (29-38)	33.2 (29-38)	30 (23-36)	0.3
Trigliserdes, mg/dL, median (range)	82 (68-97)	80 (55-105)	94 (71-117)	0.4
HOMA-IR index, median (range)	1.02 (0.5-3.1)	1.5 (0.7-2.4)	1.01 (0.65-1.02)	**0.02**

DISCUSSION

The outcome of the study was to determine whether there was an association between the birth weight and insulin resistance and/or anthropometric measurements in early childhood.

There are limited data about the effects of birth weight on cardiovascular changes in early childhood. The concept of early life is an important period for determining future risk of cardiovascular disease and changes in body composition. When these important cardiovascular risk factors are present in childhood, they may also persist during adulthood (8). In our study, we found that the SGA children had significantly higher insulin levels and HOMA-IR index when compared to the children in AGA and macrosomic groups. We also found that the macrosomic children had significantly higher weight and BMI than AGA and SGA children in early childhood. However, other anthropometric measures were similar in the study groups.

In the evaluation of cardiovascular risks, HOMA-IR and fasting insulin levels were found to be significantly higher in SGA children. Accelerated early infant weight gain is associated with markers of the metabolic syndrome: increased basal insulin levels, HOMA-IR, adverse lipid profile and hypertension (9). Other studies have shown that in SGA groups early infant weight gain from birth to three months was positively associated with the fasting insulin concentration, HOMA-IR, basal lipid levels and systolic blood pressure (9,10). However, these studies were conducted in adolescence and young adulthood. We think that detection of high insulin levels and HOMA-IR index in the SGA group in early childhood will make a significant contribution to the literature. Adipose tissue plays a key role in developing insulin resistance. But, in our cohort, triceps skinfold thickness did not influence insulin levels or fasting glucose values.

The BW may be used as an indicator of child health in utero. A positive linear association has been identified between BW and subsequent childhood and adulthood obesity (11). The lowest and highest birth weights have revealed J- or U-shaped associations with a higher prevalence of obesity (12-14). The association between higher birth weight and higher adult BMI may be due to increased lean mass rather than an increase in fat tissue (15). The lower birth weight has been associated with lower lean body mass and greater central obesity, measured by the waist–hip ratio or skinfold thickness in adults (16). A cochrane metaanalysis revealed that high birth weight (>4000 g) was associated with increased risk of obesity compared with subjects with birth weight <4000 g (17). The subgroup analysis based on growth and developmental stage also revealed that high birth weight increased the risk of obesity from childhood to early adulthood (17). The results of our study do not support the existence of a relationship between birth weight and early child obesity because fat mass, lean mass and abdominal fat could not be assessed. Only BMI was found to be higher in macrosomic newborns when compared to the others (18). We definitely do not know whether birth weight is associated with obesity in early childhood (on the basis of BMI).

The metabolic syndrome refers to a combination of risk factors for cardiovascular disease and type 2 diabetes mellitus, which include central obesity, hypertension, dyslipidemia and altered glucose metabolism. There is still no standart definition of metabolic syndrome for use in the pediatric population. Recently, the International Diabetes Federation has proposed a new set of criteria to define metabolic syndrome in children and adolescents aged 6–16 years (19). In this study, a diagnosis of metabolic syndrome was thought to be unlikely for children around these ages because the clinical and laboratory findings of metabolic syndrome were not defined completely. The studies from Turkey have demonstrated that the prevalence of metabolic syndrome is 27.2-41.8 % in obese children and adolescents (20-22). However, challenges remain about the early identification of children at risk for metabolic syndrome and the determination of timing of insulin resistance. Therefore, our results should be used with caution in early childhood from other populations.

We sought to evaluate the association between birth weight and cardiovascular disease and body composition in early childhood. This study may result in early identification of children for risk of cardiovascular disease that may adversely affect their health. It allows health professionals to give appropriate advice to children who are likely to become cardiovascular disease before adult life. However, firstly, there were several limitations to this study such as the small sample size. Secondly, there has been a lack of reliable information on the growth and nutritional status in relation to cardiovascular disease of most patients who participated this study after birth.

In conclusion, our findings indicated that children in SGA group were shown to develop insulin resistance in early childhood. BMI was significantly higher for macrosomic children when compared to AGA and SGA children but other anthropometric measurements were not related to insulin resistance and metabolic syndrome. Further studies are needed in larger cohorts of children to confirm whether or not there is a relationship between birth weight and anthropometric measurements and the cardiovascular risk.

Conflict of interest

No conflict of interest was declared by the authors.

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