

The Characteristics of Non-Diabetic Mothers with Macrosomic Newborns

Makrozomik Bebek Doğuran Diyabeti Olmayan Annelerin Özellikleri

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Abstract

Introduction: Fetal macrosomia is a condition with heterogeneous etiologic factors and its' frequency is increasing in recent years. Many macrosomic infants are born without any risk factors and accurate prediction of macrosomia is not possible with only single risk factor. The aim of this study was to research the characteristics of healthy mothers without diabetes who gave birth to macrosomic infants.

Materials and Methods: This case-control study comprised 291 healthy pregnant women who were monitored and delivered at Mardin Women and Children's Hospital. Inclusion criteria were (a) no disease or conditions that may affect birth weight, (b) normal healthy pregnancy and (c) singleton live infants born between 37-42 weeks with no structural defects. A birth weight above 4.000 g was defined as macrosomic neonate. The study group was divided in two; group 1 had a birth weight less than 4.000 g and group 2 had a birth weight above 4.000 g. Characteristics of mother and newborn were analyzed to determine any association with macrosomia.

Results: The logistic regression analysis results indicated that the risk of macrosomic infant were male gender of the infant [odds ratio (OR): 3.39; 95% confidence interval (CI): 2.010-5.211; p<0.001], maternal age being above 35 years (OR: 2.25; 95% CI: 1.919-4.005; p=0.026) and duration of gestation being above 40 weeks (OR: 1.72; 95% CI: 1.103-2.949; p=0.009).

Conclusions: There are various factors behind having a macrosomic infant in the absence of glucose intolerance. These risk factors should be taken into consideration for possible complication of macrosomia and mothers with the risk factors should be informed.

Keywords

Newborn, birth weight, macrosomia, healthy pregnancy

Anahtar kelimeler

Yenidoğan, doğum ağırlığı, makrozomi, sağlıklı gebelik

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Öz

Giriş: Fetal makrozomi heterojen etiyolojik faktörlere sahip bir durumdur ve sıklığı son yıllarda giderek artmaktadır. Birçok makrozomik bebek belli bir risk faktörü olmaksızın doğar ve makrozominin doğru tahmini tek bir risk faktörü ile öngörülemez. Bu çalışmanın amacı makrozomik bebek doğuran diyabeti olmayan sağlıklı annelerin özelliklerini araştırmaktır.

Gereç ve Yöntem: Bu olgu-kontrol çalışması Mardin Kadın Doğum ve Çocuk Hastanesi'nde izlenmiş ve doğum yapmış 291 sağlıklı gebe kadından oluşmaktadır. Çalışmaya dahil edilme kriterleri (a) doğum ağırlığını etkileyecek hastalık veya

durum olmaması, (b) normal sağlıklı gebelik ve (c) 37-42 hafta arası yapısal defekti olmayan tekiz bebek doğurma idi. Dört bin gr üzeri doğum ağırlığı makrozomi olarak tanımlandı. Çalışma grubu ikiye ayrıldı; grup 1 4.000 gr altı doğum ağırlığı ve grup 2 4.000 gr üzeri doğum ağırlığı. Anne ve bebek özelliklerinin makrozomi ile ilişkisi olup olmadığı incelendi.

Bulgular: Lojistik regresyon analizi sonuçlarına göre makrozomik bebek sahibi olma riskleri erkek cinsiyet [odds oranı (OR) 3,39, %95 güven aralığı (GA): 2,010-5,211; $p < 0,001$], anne yaşının 35 üstü olması (OR 2,25, %95 GA: 1,919-4,005; $p = 0,026$) ve gestasyon haftasının 40 üstünde olması (OR 1,72, %95 GA: 1,103-2,949; $p = 0,009$) olarak bulundu.

Sonuç: Glikoz intoleransı olmadığı durumlarda makrozomik bebek sahibi olma ile ilişkili çeşitli faktörler bulunmaktadır. Makrozominin olası komplikasyonları açısından bu risk faktörleri bilinmelidir ve risk faktörlerine sahip anneler bilgilendirilmelidir.

Introduction

Fetal macrosomia is increasing in recent years and is a condition with heterogeneous etiologic factors (1). Zamorski and Biggs (2) reported the incidence of macrosomia in the general hospital population as 10%. Many macrosomic infants are born without any risk factors and accurate prediction of macrosomia is not possible with only single risk factor. In a study comprising 75.363 newborns, the incidence was 8% in non-diabetic pregnancies and 26% in diabetic pregnancies (3). It is important that macrosomia is diagnosed prenatally to decide on mode of delivery and reduce natal and perinatal morbidity. The aim of this study was to research the characteristics of healthy mothers without diabetes with macrosomic infants.

Materials and Methods

Study Design and Sample

A case-control study was carried out including 291 healthy pregnant women from September 2013 to February 2014 who were followed-up and delivered in Mardin Women and Children Hospital. The study population comprised singleton live infants born full-term between 37-42 weeks, by spontaneous vaginal delivery or cesarean section without structural defects. Estimated by the date of last menstrual period, gestational age was confirmed by ultrasonographic measurements of crown-rump length and recorded as completed weeks. Two groups were determined in the study group; Group 1; birth weight less than 4.000 g and Group 2; birth weight above 4.000 g. Data was collected by the same researcher who was trained in data collection. Data for newborns included gestational age at delivery, gender, weight, length, and head circumference. Pregnancy outcome data were extracted from the medical records. Characteristics of mothers that were recorded included maternal

age, gravida and parity, pre-pregnant weight, height, gestational weeks at delivery, delivery mode, having previous macrosomic newborn, birth interval of previous live born infants, weight and height of the fathers. Complete blood count level before delivery and oral glucose tolerance test (OGTT) with 50 g which was screened at 24-28 weeks of pregnancy were obtained from medical records. While abortions were excluded, birth interval was measured at range instead. Socioeconomic status (SES) was defined as one of these three levels: "good, moderate, or bad" according to the mothers' perception. Fathers who smoked more than five cigarettes a day in the house were considered to be smokers. University Ethical Committee approval and required legal permissions were obtained and parents provided written informed consent for participation of their infants.

Anthropometric Measurements and Body Mass Index

Measurements of newborn including weight, height and head circumference and mothers' height and weight were taken by the same researcher (NB). Fathers' height and weight were reported by mothers. Newborns were weighed naked on the same digital scale. Mothers were weighed in their underwear, without external clothing and weight was measured at 37 weeks' gestation and gestational weight gain (GWG) was calculated. Height was measured flat-lying in newborns and standing in mothers using the standard measurements. Pre-pregnancy weight was obtained from medical records. Pre-pregnancy body mass index (ppBMI) (kg/m^2) was calculated and categorized into underweight ($< 18.5 \text{ kg}/\text{m}^2$), normal weight ($18.5-24.9 \text{ kg}/\text{m}^2$), overweight ($25.0-29.9 \text{ kg}/\text{m}^2$), and obese ($\geq 30.0 \text{ kg}/\text{m}^2$). Macrosomic neonate was defined as an infant with a birth weight of more than $\geq 4.000 \text{ g}$.

Exclusion Criteria

Mothers with chronic diseases (including diabetes mellitus, hypertension, asthma, endocrine, metabolic, inflammatory diseases and hyperthyroidism), eclampsia, preeclampsia and oligo/polyhydramnios were excluded. Pregnant women who had an abnormal OGTT screening with 50 g glucose which was screened at 24-28 weeks of pregnancy -with serum glucose level >140 mg/dL in the first hour of the test- were excluded. Pregnant women who were admitted to the hospital after the first trimester as their first visit during pregnancy and women who had previous small for gestational age infants were excluded. Smokers (before or during pregnancy) and people who filled out the questionnaire incompletely were excluded.

Data Analysis

Statistical analysis was performed using SPSS software, version 19.0. The variables were investigated using visual (histograms, probability plots) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk's test) to determine whether or not they are normally distributed. Descriptive analyses are presented using mean, standard deviation, minimum, maximum values, frequency and percentage. Since the value of birth weight was normally distributed, the independent samples T test was conducted to compare the groups. The Chi-square test was used to compare categorical variables between the groups. A p-value of less than 0.05 was considered to show a statistically significant result. For the multivariate analysis, the possible factors identified by univariate analysis were further entered into the logistic regression analysis to determine independent predictors of birth weight. Hosmer-Lemeshow goodness of fit statistics was used to assess model fit. A 5% type-I error level was used to infer statistical significance. For logistic regression analysis the stepwise (Backward: LR) method was used. The goodness of fit of the logistic model was evaluated with the Hosmer and Lemeshow Test. This test identified a p value of 0.953, indicating high goodness of fit of the model. The Nagelkerke R Square value of the model was determined as 0.217 and Cox&Snell R Square value of the model was determined as 0.162.

Results

The characteristics of mothers and children are summarized in Tables 1, 2, 3.

A positive correlation was found between birth weight and gestational week at birth as shown in Figure 1 ($r=0.460$; $p<0.001$).

There was no correlation between birth weight of children and mothers' age in our study group ($r=0.107$; $p=0.068$). While 55.6% of patients were older than 35 years and had previous births to macrosomic infants, 44.4% had infants with birth weight below 4.000 g.

A positive correlation was found between ppBMI value and birth weight of the newborn in our study group ($r=0.152$; $p=0.010$) as shown in Figure 2.

The use of multivitamins, folic acid and iron supplements during pregnancy was shown not to be a statistically significant factor for birth weight between the groups ($p>0.05$).

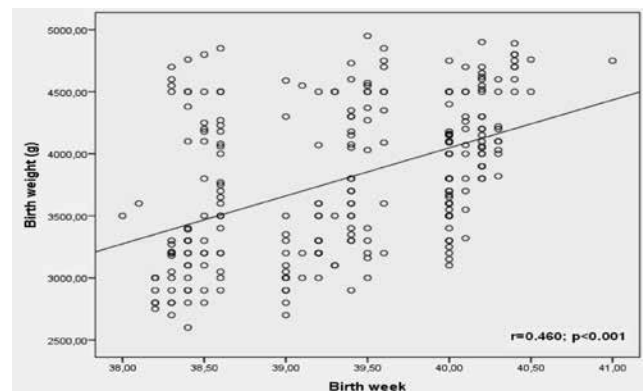


Figure 1. Correlation between birth weight and birth week of the children

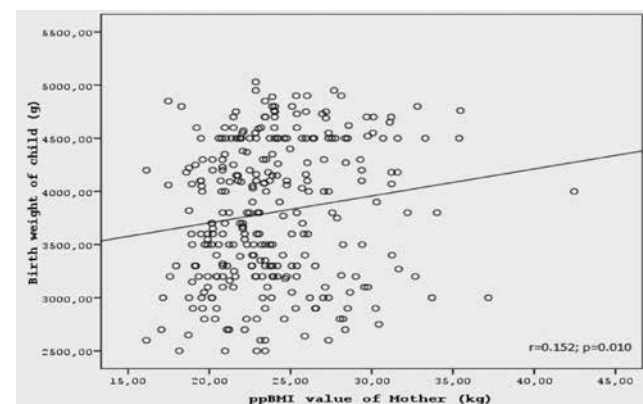


Figure 2. Correlation between birth weight and mother's pre-pregnancy body mass index value in our study group
ppBMI: Pre-pregnancy body mass index

Results of the Multivariate Analyses

According to univariate analysis results to calculate the OR values for dependent variables thought to be risk factors affecting birth weight, logistic regression

analysis was completed. For logistic regression analysis, the independent variables included were gestational age, gender, maternal age, ppBMI, weight gain during pregnancy, parity and SES.

Table 1. Characteristics of newborn in the groups

Variables	Group 1 (<4000 g)	Group 2 (≥4000 g)	p*
	(n=162)	(n=129)	
Gender			
Female	100 (61.7)	43 (33.3)	<0.001
Male	62 (38.3)	86 (66.7)	
Delivery type			
SVD	105 (64.8)	90 (69.8)	0.372
C/S	57 (35.2)	39 (30.2)	
Birth time (week)			
37-39	117 (72.2)	75 (58.1)	0.012
≥40	45 (27.8)	54 (41.9)	
	Mean±SD	Mean±SD	p**
Birth length (cm)	49.9±0.2	50.2±0.3	<0.001
HC at birth (cm)	35.0±0.2	35.3±0.2	<0.001

Group 1: Birth weight <4000 g (minimum: 2600 g-maximum: 3970 g), group 2: Birth weight ≥4000 g (minimum: 4000 g-maximum: 4950 g), *:Chi-square test; **: Student t test; SD: Standard deviation, C/S: Caesarean Section, SVD: Spontaneous vaginal delivery, HC: Head circumference

Table 2. Maternal characteristics of newborns in the groups

Variables	Group 1 (<4000 g)	Group 2 (≥4000 g)	p*
	(n=162)	(n=129)	
	n (%)	n (%)	
Maternal age (year)			
<20	25 (15.4)	14 (10.9)	0.286
20-35	125 (77.2)	100 (77.5)	
>35	12 (7.4)	15 (11.6)	
ppBMI (kg/m ²)			
<18.5	6 (3.7)	4 (3.1)	0.623
18.5-24.99	109 (67.3)	79 (61.2)	
25-30	36 (22.2)	33 (25.6)	
>30	11 (6.8)	13 (10.1)	
SES			
Good	86 (53.1)	43 (33.3)	0.043
Moderate	67 (41.4)	55 (42.6)	
Poor	9 (5.6)	31 (24.0)	
Maternal education			
Primary school	55 (34.0)	32 (24.8)	0.231
Elementary school	55 (34.0)	50 (38.8)	
High school	42 (25.9)	42 (32.6)	
University	10 (6.2)	5 (3.9)	

*:Chi-square test, SES: Socioeconomic status, ppBMI: Pre-pregnancy body mass index

According to logistic regression analysis, variables of gender, maternal age and gestational week of pregnancy were identified as risk factors affecting birth weight (Table 4).

The results of logistic regression analysis showed the risk of having a macrosomic infant was increased for; male infant [odds ratio (OR): 3.39; 95% confidence interval (CI): 2.010-5.211; p<0.001], maternal age above 35 years (OR: 2.25; 95% CI: 1.919-4.005; p=0.026) and gestational week more than 40 weeks (OR: 1.72; 95% CI: 1.103-2.949; p=0.009).

Gender is an important risk factor for macrosomia, using this parameter alone; the risk of macrosomia can be predicted with 61.7% sensitivity and 66.7% specificity. When maternal age and gestational week are included in the model with gender, the sensitivity and

specificity values were found to be 85.2% and 37.2%, respectively. It was observed that as other affecting factors are included in the logistic model with gender, the sensitivity increases but the specificity decreases.

When risk factors relating to the father are investigated in group 1, the rate of fathers who smoke was 59.3% while in the macrosomic group this rate was 50.4% (p=0.130). When all cases in the study groups were evaluated, there was no statistically significant difference between the birth weight of infants of fathers who were smokers or non-smokers (p=0.425).

Discussion

In the present study, macrosomia may be predicted with the presence of the following risk factors;

Table 3. Obstetrics characteristics of mothers in the groups

	Group 1 (<4000 g) (n=162)	Group 2 (≥4000 g) (n=129)	
	Mean±SD	Mean±SD	p*
Hgb	11.8±1.2	11.1±2.7	0.005
MCV	81.3±11.0	78.9±16.4	0.158
			p**
Having macrosomic infant before			
No	155 (95.7)	113 (87.6)	
1 time	6 (3.7)	12 (9.3)	
2 times	1 (0.6)	4 (3.1)	0.035
			p*
GWG (kg)	14.0±3.8	15.1±4.5	0.027
	n (%)	n (%)	p**
Gravida			
1	38 (23.5)	22 (17.1)	0.180
>1	124 (76.5)	107 (82.9)	
Parity			
1	40 (24.7)	23 (17.8)	0.158
>1	122 (75.3)	106 (82.2)	
	Mean±SD	Mean±SD	p*
Birth interval with the previous birth (mo)	33.7±29.2	27.5±25.4	0.072

*: Independent samples test, **: Chi-square test, SD: Standard deviation, Hgb: Hemoglobin, MCV: Mean corpuscular volume, GWG: Gestational weight gain, mo: Month

Table 4. Regression coefficients and odds ratios (95% CIs) for risk factors associated with birth weight*

Factor	β value	p value	Wald	Odds ratio (95% CI)
Malea	1.221	<0.001	20.954	3.39 (2.010-5.211)
Gestational weeks at birth (≥40)b	0.542	0.009	3.885	1.720 (1.103-2.949)
Mother age (≥35)c	0.983	0.026	8.601	2.25 (1.919-4.005)

*Multiple logistic regression (Stepwise Backward: LR) models, a: Male=1; Female=0, b: ≥40=1; <40=0, c: Other age (≥35=1, <35=0), CI: Confidence interval

previous delivery of an infant weighing ≥ 4.000 g, advanced gestational age, higher weight gain during pregnancy, gender of neonate and SES.

Maternal age above 35 years was found to be a risk factor for macrosomia at the level of 3 times (4). Kadanali et al. (5) also found association between newborn anthropometry and maternal age. In this study; although there was no correlation between birth weight of children and mothers' age; the mothers less than 20 years of age and above 35 years of age were more common in the macrosomic group.

Globally, especially in the west, the increasing rate of obesity is an important public health concern where 11% of pregnant women are obese and 28% are overweight (6). The risk of macrosomia has been shown to increase with ppBMI in previous studies (7). The current guidelines, recommended by the Institute of Medicine (IOM) to limit negative pregnancy outcomes, provide ranges of GWG based on ppBMI (8). The risk of having a weightier infant was strongly increased in women who exceeded the IOM 2009 GWG guidelines. A positive correlation was found between ppBMI value and birth weight of the newborn in our study group and GWG was higher in the macrosomic group. On the other hand, the effect of maternal underweight on obstetric performance is less clear. In this retrospective analysis, there was an insufficient number of underweight women or women with low GWG.

Mothers who previously gave birth to an infant weighing over 4.000 g were found to have a 5 to 10 times higher rate of having a subsequent infant above 4.500 g, compared to control group (9,10). In this study, women who had a macrosomic infant previously had a high rate of having macrosomic infant again.

The macrosomia rate was found to be 3-7 times higher in post-term infants compared to term infants (11). Spellacy et al. (11) found the macrosomia rate to be 10.8% in post-term infants and Berard et al. (12) found this rate to be 17%. Similarly; in this study a positive correlation was found between birth weight and gestational week at birth.

Previous studies showed that macrosomia resulted more in cesarean deliveries (13,14). Induction of labor may reduce the risk of cesarean delivery with known birth weight. The incidence of cesarean section was not increased in our study group. There was no birth weight above 5.000 grams in our study which may

explain low cesarean section needs. Additionally, this may also be due to higher rate of macrosomic newborn in lower-income families.

A range of good health outcomes are positively correlated with SES. There was no relationship found between high birth weight and SES in a report by Cesur and Kelly (15). The effects of factors relating to SES on the chances of having a macrosomic infant have been examined in a few studies (16). The present study showed that the macrosomia rate was higher in low-income families. However, GWG was also higher in this group. This may be the result of anxiety of possibly having a low-birth weight newborn that could lead to overfeeding. Hemoglobin value was also found to be lower in the macrosomic group which was thought to be linked to lack of variety of nutrition that may be due to lower SES.

The risk of macrosomia in multiparous women has been shown to be 2-3 times higher than that in control group in the majority of studies (2). The rate of macrosomia was 78% in multiparous women according to Berard et al. (12). Whether multiparity is an independent risk factor or is dependent on other factors such as age has not been determined. In this study in the macrosomic group, the number of multigravida and multiparity was higher though not statistically significant. In addition, 55.6% of patients were older than 35 years and 44.4% of those with a history of previous macrosomic infants had infants with birth weight below 4.000 g.

At any gestational age, male infants are heavier than female infants, and 60-70% of macrosomic infants are males (2,5). Similarly; in this study, in the macrosomic group, the number of male infants was significantly higher.

Approximately half of the variance in birth weight is explained by maternal factors, while no significant effect is found from paternal factors (17). It has been shown that paternal BMI can affect growth of the male newborn (18). Neither paternal BMI nor paternal smoking was found to have effect on macrosomia in this study.

Conclusion

In conclusion, the findings of this study advance our understanding of the factors behind having a macrosomic infant in the absence of glucose intolerance and confirm

the effects of previous delivery of an infant weighing ≥ 4.000 g, advanced gestational week at birth, higher weight gain during pregnancy, male gender of neonate and low SES. Studies examining eating attitudes of pregnant women are also needed to refine this topic.

Ethics

Ethics Committee Approval: Committee approval was obtained, Informed Consent: Consent form was filled out by all participants.

Peer-review: External and Internal peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Nazan Kaymaz, Sibel Cevizci, Şule Yıldırım, Concept: Nazan Kaymaz, Hakan Aylanç, Nurcan Bulur, Design: Nazan Kaymaz, Naci Topaloğlu, Meryem Gencer, Data collection or Processing: Nazan Kaymaz, Nurcan Bulur, Fatih Köksal Binnetoğlu, Mustafa Tekin, Analysis or Interpretation: Nazan Kaymaz, Sibel Cevizci, Fatih Battal, Literature Search: Nazan Kaymaz, Emine Coşar, Şule Yıldırım, Writing: Nazan Kaymaz, Şule Yıldırım.

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