Risk Factors Associated with Large for Gestational Age Infants

GEBELİK YAŞINA GÖRE İRİ BEBEKLERLE İLİŞKİLİ RİSK FAKTÖRLERİ

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SUMMARY

Objective: *To investigate the risk factors associated with large for gestational age infants.*

Institution: *Department of Gynecology and Obstetrics, Osmangazi University, Eskisehir.*

Material and Method: *Five hundred and nine births took place In 15 months period. Four hundred twenty-six cases that were alive, single, without any anomaly and had sufficient data available were enrolled in this study. Forty-six large for gestational age infants and 380 appropriate for gestational age infants were investigated.*

Findings: *Univariate analyze showed that parity, body mass index and interbirth interval were significantly correlated with large for gestational age infant. However, the only factor having significant correlation with large for gestational age infant was maternal body mass index in the multiple logistic regression analyze. When the group which has body mass index of 18-22 was considered as reference, LGA risk was found to be 3.7 times higher in those who have BMI's of 22-28 (Old ratio=3.8).*

Results: *We found that the maternal body mass index is a major risk factor for LGA-infant birth in our population.*

Key Words: Body mass index, Fetal growth, Large for gestational age infant

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ÖZET

Amaç: *Gebelik yaşına göre iri bebek doğumu ile ilişkili risk faktörlerinin araştırılması.*

Çalışmanın yapıldığı yer: *Osmangazi Üniversitesi Tıp Fakültesi, Kadın Hastalıkları ve Doğum ABD, Eskişehir.*

Materyel ve Metod: *Kliniğimizde on beş aylık periyodda 509 doğum gerçekleşti. Bunlardan canlı doğan, anomalisi olmayan ve hakkında yeterli bilgi elde edilebilen 426 tekil gebelik çalışmaya alındı. Bu bebeklerin 46 tanesi gebelik haftasına göre iri (LGA), 380 tanesi gebelik haftasına göre uygundu (AGA).*

Bulgular: *Ünivariate analiz sonuçlarına göre, parite, maternal vücut kitle indeksi ve İki doğum arasında geçen süre gebelik haftasına göre iri bebek doğumu ile İlişkili bulundu. Multipl lojistik analiz yapıldığında gebelik haftasına göre iri bebek doğumu İle ilişkili tek faktörün maternal vücut kitle indeksi olduğu görüldü. Vücut kitle indeksi 18-22 olan grup referans olarak alındığında, vücut kitle indeksi 22-28 olan grupta gebelik haftasına göre iri bebek doğurma riskinin 3.7 kat arttığı saptandı.*

Sonuç: *Maternal vücut kitle indeksi, toplulumuzda gebelik haftasına göre iri bebek doğumu için majör risk faktörüdür.*

Anahtar Kelimeler: Fetal gelişme, LGA, Vücut kütle indeksi

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Pregnancies resulting in large for gestational age (LGA) infant birth are high risk pregnancies both for the fetus and the mother (1-3). Pregnancies resulting in LGA-infant births have higher risk for fetal and maternal injuries associated with difficult labor. Prevention of these problems depends on the identification of LGA-fetuses before delivery (4).

As reported in the literature, the predisposing factors for LGA infant birth include maternal diabetes mellitus, obesity, height, parity, age, previous history of LGA-infant birth and postterm pregnancy (5-7).

In this study, we aimed to find out the risk factors that can be effective in prediction of LGA infants in our obstetrics population.

MATERIALS AND METHODS

A total of 509 deliveries took place in our clinic in 15 months period. Forty-three cases were excluded from the study: 3 of them were born immaturely (less than 28 weeks), 13 were stillborn, 7 were multiple births, 8 had a fetal anomaly, and 9 did not have sufficient data available. That left 466 cases were included in the study.

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Maternal and paternal characteristics and antenatal follow-up data about all pregnant women enrolled in the study were obtained through personal inquiries and from patient records.

We used the nomogram that was prepared from our obstetrics population data (8). Infants born over the 90* percentile were classified as LGA and those born between the 10^{th} and 90^{th} percentiles as AGA (appropriate for the gestational age). The total number of pregnancies resulted in LGA infant births were 46 and those resulted in AGA infant births were 380.

The interbirth interval was calculated as the months elapsed between the date of birth for the previous pregnancy that resulted in a live birth and the date of birth for the current pregnancy. The birthweightforthe pregnancy that resulted in a live infant birth was determined by asking the woman or from patient records.

Body weight before pregnancy was subtracted from the weight at birth to calculate the weight gained during pregnancy (WGP).

Proteinuria was defined as the presence of at least one positive (+) result (0.3 g/dL or over) in urine analyses conducted with an Ames Multiple Reagent stick during antenatal visits.

When estimating the gestational age, the last menstruation date was taken as the basis. Gestational age calculated on the basis of last menstruation date was confirmed in 94.2% of the cases by ultrasonography. Whenever the last menstruation date was dubious, the earliest sonogram was used to estimate the gestational age.

The mothers body mass index (BMI) was calculated with a formula based on her weight before pregnancy and her height: BMI=body weight (kg)/height^2 (m^2).

Statistical analyses were conducted with chi-square test and multiple logistic regression analyses, using the BMDP and SYSTAT package programs. Statistical significance was defined as $p<0.05$,

RESULTS

Table 1 shows that, among the maternal sociodemographic features, only the parity had a significant relationship with LGA-infant birth. The incidence of LGA-infant birth was 7.4% in the primipara, and it rose to 18.8% in those with a parity of 2 or more ($p<0.05$).

Table 2 shows the characteristics of the previous delivery. Although the incidence of LGA-infant birth somewhat decreased as the duration of lactation increased, this correlation was not statistically significant ($p>0.05$). Similarly, the women with a previous history of LGA-infant birth had an incidence of as high as 20% versus 13.6%, but this difference was not statistically significant as well ($p>0.05$). In those women who had an interval of over 48 months between their previous delivery and the present pregnancy, the incidence of LGA-infant birth was found to be statistically significant (18.2% vs. 6.8%, $p<0.05$).

Table 1. Maternal sociodemographic characteristics

Characteristic	LGA (N=46)		AGA (N=380)	
	n	%	n	%
Age (x^2=1.90, p>0.05)				
<30	28	9.6	265	90.4
30-34	13	12.6	90	87.4
>34	5	16.7	25	83.3
Parity (x^2=6.40, p<0.05)				
0	16	7.4	199	92.6
1	21	12.9	142	87.1
>2	9	18.8	39	81.2
Abortion (x^2=0.71, p>0.05)				
0	32	10.4	276	89.6
1	9	10.6	76	89.4
>2	5	15.2	28	84.8
Education (x^2=3.76, p>0.05)				
Primary school	7	6.4	102	93.6
Secondary school	20	10.9	163	89.1
University	19	14.2	115	85.8
Working status (x^2=1.35, p>0.05)				
Yes	27	12.8	184	87.2
No	19	8.8	196	91.2

Table 2. Features of the previous delivery

Characteristic	LGA (N =30)		AGA (N== 181)	
	n	%	n	%
Lactation (x^2=0.43, p>0.05)				
1-6 months	18	15.7	97	84.3
7-11 months	5	12.8	34	87.2
>12 months	7	12.3	50	87.7
LGA infant birth (x^2=0.20, p>0.05)				
Yes	4	20.0	16	80.0
No	26	13.6	165	86.4
Interbirth interval (x^2=4.30, p<0.05)				
<48 months	5	6.8	69	93.2
>48 months	25	18.2	112	81.8

Evaluations of the weight before pregnancy and weight gained during pregnancy was given in Table 3. Although no significant relationship was established between WGP and the incidenee of LGA-infant birth, there was a significant relationship between weight before pregnancy, weight at birth, BMI and the incidence of LGA-infant birth. While the incidence of LGA-infant birth was 4.7% in those with a weight of less than 60 kg before pregnancy, it rose to 26.5% in those over 70 kg (**p**<0.001). Similarly, the incidence of LGA-infant birth was 4.2% in those women with a BMI of less than 22, whereas it rose to 16.7% in those with a BMI of over 28 ($p<0.001$).

No significant correlation was seen between antenatal and paternal characteristics and LGA-infant birth (Table 4).

Table 3. Maternal height and weight prior to and gained during pregnancy and body mass index

Characteristic	LGA (N=46)		AGA (N=380)	
	n	%	n	%
Height (x^2=3.88, p>0.05)				
<150	1	6.7	14	93.3
150-160	12	7.4	151	92.6
>160	33	13.3	215	86.7
Weight before pregnancy* (x^2=27.86, p<0.001)				
<60	12	4.7	244	95.3
60-70	24	19.4	100	80.6
>70	9	26.5	25	73.5
Weight at delivery (x^2=33.41, p<0.001)				
<70	6	2.9	203	97.1
70-80	22	14,8	127	85.2
>80	18	26.5	50	73.5
Weight gained during pregnancy (x^2=3.53, p<0.001)				
<7	5	13.2	33	86.8
8-17	30	9.4	289	90.6
>18	10	17.5	47	82.5
Body mass index (x^2-16.34, p<0.001)				
<22	8	4.2	183	95.8
22-28	33	16.6	166	83.4
>28	4	16.7	20	83.3

"There is 1 missing data in LGA, and 11 in AGA group

Table 4. Antenatal examination data

Characteristic	LGA (N=46)		AGA (N=380)	
	n	%	n	%
Antenatal visits (x^2=2.01, p<0.05)				
Yes	46	11.4	356	88.6
No	0	0	24	100
Week when visits began (x^2=0.25, p>0.05)				
<14	24	11.2	191	88.8
14-24	16	12.5	112	87.5
>25	6	10.2	53	89.8
No of visits (x^2=5.38, p>0.05)				
1-4	11	15.9	58	84.1
5-8	19	8.3	211	91.7
>9	16	15.5	87	84.5
Proteinuria* (x^2=3.50, p>0.05)				
Yes	1	6.2	15	93.8
No	45	11.3	354	88.8
3™ trimester hemoglobin (gr/dl)				
<9	0	0	16	100
9-12	16	9.6	150	90.4
>12	30	12.3	214	87.7

'There is 11 missing data in AGA group

In univariate analyze, parity over one, interbirth interval more than 48 months, weight over 60 kilograms before pregnancy and body mass index over 22 all seemed to increase the risk of SGA infant birth 2.9, 3.1, 4.9 and 3.8 times, respectively (Table 5).

Table 6 shows the results of a multiple logistic regression analysis. The results of the analysis indicated that the only factor significantly correlated with LGA-infant birth was the maternal BMI. When BMI values between 18 and 22 were taken as reference, women with a BMI of 22-28 had 3.7 times and BMI of over 28 had a 3.8 times increased risk for LGA-infant birth.

DISCUSSION

Although the rates reported in the literature for the incidence of LGA-infant birth range between 4.7% and 14%, there is general agreement on the rate of 10% (4,6,9). In our study, we calculated the incidence of LGA-infant birth as 9.9%.

It has been reported that the incidence of LGA-infant birth rises as maternal age increases (6,10,11). There are also some studies that failed to establish any correlation between age and LGA-infant birth (12,13). In univariate analyses, we found that the rate of LGA-infant birth was 9.6% in pregnant women under 30 years of age, and 16.7% in those older than 35 years of age. This difference is not statistically significant (p>0.05).

Many studies report that the possibility for giving birth to an LGA-infant increases with the parity (10,12). Larsen et al (11), reported an 1.5 times increased risk for LGA-infant birth in women with a parity of 2 or more. There are also studies that report no relationship between parity and LGA-infant birth (13,14). In our study, we found that the incidence of LGA-infant birth was 7.4% in primigravidae, compared with 18.8% in those with a parity of 2 or more (Table 1, p<0.05).

The LGA-infant rate increased as the woman's educational level rose; but the difference was not significant. This result may be confounded by the fact that the woman's economic status rises, her nutrition becomes better and the interval between her two pregnancies increases as her educational level becomes higher.

Though Alegre et al (15), reported that working during pregnancy reduce the mean fetal weight, we could not find any correlation between working status and LGA-infant birth.

In spite of the studies reporting an increased risk for LGA-infant birth in women with a history of LGA-infant (18,16,17), Boyd and colleagues (5) reported that they could not find such a correlation. We found that the possibility of LGA-infant birth for those women who had an LGA-infant in their previous pregnancy was 20.0% versus 13.6%, but this difference was not statistically significant. This result may be explained by the great number of diabetic cases in those studies reporting 10 to 13-times increased risk for LGA-infant birth in women who previously gave birth to an LGA-infant (12,16), but insufficient number of diabetic cases in our study.

Table 5. Results of the univariate analysis

Risk factor	LGA		AGA		OR	%95 CL	AR %
	n	%	n	%			
Parity							
0(R)	16	34.8	199	52.4	1.0		
1	21	45.6	142	37.4	1.8	0.9-3.7	5.4
>1	9	19.6	39	10.2	2.9	1.2-7.0	11.3
Interbirth interval							
<48 month							
>48 month	5	16.7	69	38.1	1.0		
	25	83.7	112	61.9	3.1	1.1-8.4	11.5
WBP (Kg)							
<60 (R)	12	26.7	244	66.1	1.0		
60-70	24	53.3	100	27.1	4.9	2.4-10.1	14.7
>70	9	20.0	25	6.8	7.3	2.8-19.1	21.8
Body Mass Index							
<22(R)*	8	17.8	183	49.6	1.0		
22-28	33	73.3	166	45.0	3.8	1.7-8.5	12.4
>28	4	8.9	20	5.4	3.8	1.1-13.9	12.5

WBP: Weight before pregnancy
OR: Odds ratio, CL: Confidence limits, AR: Attributable risk

Table 6. Results of the multiple logistic reggression analyse in LGA infants

Risk Factor	Coefficient	Standard Error (SE)	Coefficient/SE	Odd Ratio
Body Mass Index				
19-21 (R)				
<22	-12.3	365.3	-3353	0.5
22-28	1.3	0.4	3.2	3.7
>28	1.3	0.7	2.1	3.8

R: Reference group

For those women who had an interval of more than 48 months between their previous and current pregnancies, we found and LGA-infant birth incidence of as high as 18.2%, as compared with an incidence of 6.8 in those with a birth interval of 48 months or less (p<0.05). In the literature, we failed to find and studies investigating the relationship between lactation, birth interval and LGA-infant birth.

Another risk factor reported for LGA-infant birth is the height of mother (2,10,16). Klebanoff and colleagues (1), reported that mothers of LGA-infants were taller, but that this correlation was disappeared when they conducted a regression analysis together with other risk factors. Consistent with some other studies (7,13,18), we also failed to establish any significant correlation between LGA-infant birth and maternal height.

A number of studies specified maternal weight as an important risk factor for LGA-infant birth (6,12,18). In our study, univariate analyses have indicated that there is a significant relationship between weight before pregnancy and LGA-infant birth. It has been reported that the possibility for LGA-infant birth rises as the weight gain during pregnancy increases (1,14,18,19). Like Berk and colleagues (14), we did not find any relationship between WGP and LGA-infant birth. In recent years, BMI has been used in an effort to standardize maternal body size. It has been reported that BMI and LGA-infant birth have a linear relationship (11).In our study, we found that the incidence of LGA-infant birth was as high as 16.6% in women with a BMI of 22 to 28, and as high as 16.7% in those with a BMI of over 28, as compared to an LGA-infant birth rate of 4.2% in those with a BMI of less than 22 (p<0.001).

Insulin-dependent diabetes and gestational diabetes are important risk factors for LGA infant birth (5,6,12). In our study, we failed to establish any relationship between gestational diabetes and LGA-infant birth. Although the incidence of gestational diabetes has been reported to be 5% to 9% in the literature (4,6,7), the fact that gestational diabetes was observed in only 4 cases suggests that some gestational diabetes cases might have remained undetected.

As a result of the univariate analysis, the parameters significantly correlated with LGA-infant birth have been found to be parity, birth interval, weight before pregnancy and BMI. It may be noted that "time" is the common denominator for all these parameters. As the time passes, the parity, age, body weight and BMI of women increase. Does the birth interval act through this mechanisms as well? Or does this correlation result from the replenishment of depleted stores? Since parity, birth interval and body weight are interrelated, as the time being their common denominator, which of them does really interact with the possibility of LGA-infant birth? Some studies have reported a linear relationship between age, parity, body mass and gestational diabetes (17-20).

As a results of a multiple linear regression analysis, Wolfe and colleagues (21) have also reported that parity and body mass increase as maternal age progress. In the light of these views, we conducted a multiple logistic regression analysis in order to exclude any interactions between all of the characteristics that we investigated for their relationships with LGA-infant birth. As a result of this analysis, it was found that BMI was the only factor which had a significant relationship with LGA-infant birth. However, the parity and birth interval ceased to have any significant relationship (Table 6). When the BMI group of 19 to 21 was taken as a reference, BMI groups of 22 to 28 had 3.7 times and over 28 had a 3.8 times increased risk for LGA-infant birth. This results suggests that the reliance on univariate analyses alone cannot produce satisfactory results when investigating the risk factors for LGA-infant birth.

Inadequate statistical evaluation is one of the reasons for different and often contradictory results that have been reported. Another reason is the implementation of different criteria for describing LGA-infants. For the description of LGA-infants, studies used such different threshold values as 4.000 g (5), 4.500 g (6), 4.536 g (12), percentiles over 90 (14) or a standard deviation of + 2 (2). This makes it difficult to compare the results of studies. We believe that, population-specific cut-off values such as 90[th] percentile or two standard deviations should be used instead or random figures such as 4.000 9-

In conclusion, maternal BMI is the major risk factor for LGA-infant birth in our population. We think that many maternal and fetal injuries may be avoided if pregnant women with a BMI of over 22 are taken under close antenatal follow-up and if a iiberal cesarean section poiicy is followed.

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