Risk Analysis For The Birth Of A Small For Gestational Age (SGA) Infant

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Abstract

Objectives: To investigate the possibility of the births of small for gestational age (SGA) infant in patients with risk factors.Methods: This study enrolled 3046 babies born between 2005 and 2007. The cases were divided into the small for gestational age (SGA) group (312 cases) and the control group (2734 cases). A multivariable analysis was conducted to retrospectively analyze the factors associated with low fetal birth weight, which include abnormalities of the neonate, placenta and umbilical cord, and maternal complications.Results: The odds ratios (99% confidence interval) of SGA were 5.3 (3.4-8.3) for multiple pregnancy, 2.4 (1.2-4.7) for fetal malformation, 4.6 (2.0-10.5) for velamentous cord insertion, 2.0 (1.0-3.8) for marginal cord insertion, 3.7(2.0-6.9) for hypercoiled cord, 5.3 (3.2-9.0) for pregnancy induced hypertension, and 1.8 (1.2-2.6) for low maternal body mass index (BMI<18.5). Conclusion: A multivariable analysis was conducted to determine the odds ratios for the birth of an SGA infant -for various risk factors of fetal growth restriction. These data might improve the prognosis of infants through the intensive perinatal management.

INTRODUCTION

Low birth weight infants are at increased risk of perinatal death or mental retardation in comparison to normal or large infants. It is clinically and biologically important to identify the risk factors associated with the birth of such small infants.

Several authors[1-6] have recently reported that a low birth weight is associated with, maternal factors, such as fibroma, anomalies of uterus, intrauterine fertilization, drinking alcohol, smoking, pregnancy induced hypertension (PIH), malnutrition, low maternal body mass index (BMI). Other several authors[7-10] also have reported the relationship between SGA and umbilical cord or placental abnormalities. Tyson and Staat et al.[11] reported the relationship between SGA and fetal factors, such as multiple pregnancy, chromosomal abnormalities, fatal malformations, intrauterine virus infection.

Although these factors certainly affect fetal growth the individual contribution of each factor to the birth of SGA infants is unknown.

The purpose of this study was to analyze risk factors associated with fetal growth restriction using a multivariable logistic regression analysis.

MATERIALS AND METHODS

A retrospective study was conducted by a review of the medical records of pregnant women who delivered after 24 weeks. The study enrolled 3046 cases who delivered between April 2005 and February 2007 at Showa University Hospital.

The relationship between births of small for gestational age (SGA) infants and variables which may cause growth restriction were investigated.

The subjects were divided into two groups, depending on the birth weight. The SGA group included 312 cases in which the birth weights were less than -1.5 SD according to the Japanese reference value. Yoshida et al[12] has reported the Japanese reference value in 2000. The control group included the other 2734 cases. Factors that were thought to be associated with fetal growth were assessed. The fetal factors include multiple pregnancy, chromosomal abnormality and congenital anomalies, and placental and cord factors included placenta previa and velamentous cord

insertion (VCI), marginal cord insertion (MCI) and hypercoiled cord (HCC). The maternal factors included hyperemesis, smoking, pregnancy induced hypertension, and BMI less than 18.5.

Strong et al[13] has reported that HCC was diagnosed at delivery when the coiling index was more than 0.3. Single umbilical artery was pathologically diagnosed at delivery. Hyperemesis gravidarum was diagnosed when the body weight decreased more than 8 kg during pregnancy due to severe vomiting. Smoking patients were defined as those who smoked more than 5 cigarettes per day throughout pregnancy. Uterine malformation included uterus bicornis and uterus duplex. PIH was diagnosed when the systolic pressure of the patient was more than 140 mmHg, or diastolic pressure was more than 90 mmHg.

Data were entered into a computerized data analysis program (Stat View for Windows, SAS Institute, inc., Cary, NC, USA). A univariate analysis for quantitative and qualitative variables was then performed using Student's t-test and either Fisher's exact or the x^2test.

The magnitude of the univariate associations between potential risk factors and SGA was expressed by odds ratios. The multivariable analysis was based on logistic regression. Significant risk factors determined by the univariate analysis were used for the multivariable analysis. Statistical significance was defined as a p-value of <0.01.

RESULTS

The characteristic demographics of each group are shown in Table 1. Significant differences were found in all of the factors, except for maternal age. Less parity, shorter gestational age, lower birth weight, Apgar score, blood gas pH and base excess, and lighter placental weight were all observed in the SGA group in comparison to the control.

The results from the univariate analysis of each risk factor are shown in Table 2. Fetal malformations without chromosomal abnormalities included 5 cases of congenital heart disease, 3 gastrointestinal atresia, 2 cystic adenomatoid malformation (CCAM), 2 hypospadias, 2 holoprosencephaly, 2 polycystic kidney, 2 dysplasia of bone like achondroplasia, 2 cleft lip, 2 chylothorax, and 1 accessory ear. Chromosomal abnormalities included 2 cases of trisomy 18, 4 trisomy 21, 1 47,XXX and 1 chromosomal translocation. Multiple pregnancy and fetal malformations were significantly associated with SGA (p<0.01), while chromosomal abnormality was not. VCI, MCI, and HCC were significantly associated with SGA (p<0.01), while placenta previa, single umbilical artery and nucal cord were not significantly correlated with SGA. Fertility treatment, PIH and low BMI were significant for SGA (p<0.01), while hyperemesis, smoking, myoma uteri and uterine malformation were not significant. The factors significantly associated with SGA based on the univariate analyses were selected for the multivariable logistic analysis.

The results of the multivariable logistic analysis are shown in Table 3. The adjusted odds ratios(99% confidence interval) of SGA in the fetal factors were 5.3 (CI:3.4-8.1) and 2.7 (1.4-5.2) for multiple pregnancy and fetal malformation. Among the placental, cord and maternal factors, they were 4.5 (2.0-10.3), 1.9 (1.0-3.7), 3.7(2.0-6.8), 5.3 (3.1-8.9), 1.7 (1.2-2.5) for VCI, MCI, HCC, PIH, and low BMI, respectively.

Figure 1

Table 1 Maternal background

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Variables		SGA (312)	control (2734)	p-value
Maternal age at delivery (y)		32.4±0.3	32.3±0.1	0.62
Maternal weight (kg)		58.5±8.2	61.4±8.2	<0.01
Gestational age at delivery (w)		35.9±0.2	38.3±0.0	<0.01
Neonatal birth weight (g)		1902±515	2893±456	<0.01
Parity	median, range)	0, (0-4)	0, (0-7)	<0.01
AS 1 min	(median, range)	9, (1-10)	9, (1-10)	<0.01
5 min	(median, range)	10, (1-10)	10, (1-10)	<0.01
Blood gas pH		7.29±0.07	7.31±0.11	<0.05
Base excess	(mmol/l)	-4.6±0.2	-4.1±0.1	<0.05
Weight of placenta	(g)	524±260	592±142	<0.01

Data are presented as the means±standard deviations or median (range). Statistical analysis were performed between SGA and Control by t-test
SGA; Small for gestational age. AS; Apgar Score

Figure 2

Table 2 Univariate association of factors with SGA

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Variables	SGA		Control		unadjusted OR	99%CI	p-value
	N	%	N	%			
Fetal factor							
Multiple pregnancy	77	24.7	147	5.4	5.8	3.9-8.6	<0.01
Chromosomal abnormality	3	1.0	5	0.1	5.3	0.8-35.0	ns
Fetal malformation	22	7.1	92	3.4	2.2	1.2-4.1	<0.01
Placental and cord factor							
Placenta previa	6	1.9	22	0.8	2.4	0.7-8.0	ns
Velamentous cord insersion	24	7.7	108	4.0	5.5	2.6-11.7	<0.01
Marginal cord insersion	19	6.0	32	1.2	2.0	1.1-3.7	<0.01
Hypercoiled cord	30	9.6	79	2.9	3.6	2.0-6.4	<0.01
Single umbilical artery	3	1.0	10	0.4	2.6	0.48-14.5	ns
Nuchal cord	83	26.6	768	28.1	0.9	0.7-1.3	ns
Maternal factor							
Hyperemesis	3	1.0	6	0.2	4.4	0.7-27.5	ns
Smoking	33	10.6	202	7.4	1.5	0.9-2.1	ns
Fertility treatment	55	17.6	329	12.0	2,1	1.2-3.8	<0.01
Myoma or uterine anomaly	13	4.2	95	3.5	1.2	0.6-2.7	ns
Pregnancy induced hypetension	51	16.3	97	3.5	5.3	3.3-8.5	<0.01
BMI < 18.5	85	27.2	527	19.3	1.6	1.1-2.2	<0.01

X^2-test

SGA; Small for gestational age, OR; Odds Ratio, CI; Confidence Interval, BMI; Body mass index

Figure 3

Table 3 Results of the multivariate logistic regression analysis

Results of the multivariate logistic regression analysis		
Risk factor	Adjusted OR	99%CI
Fetal factor		
Multiple pregnancy	5.3	3.4-8.3
Fatal malformation	2.4	1.2-4.7
Placental and cord factor		
Velamentous cord insersion	4.6	2.0-10.5
Marginal cord insesion	2.0	1.0-3.8
Hypercoiled cord	3.7	2.0-6.9
Maternal factor		
Pregnancy induced hypertension	5.3	3.2-9.0
Maternal BMI < 18.5	1.8	1.2-2.6

SGA; small for gestational age, OR; odds ratio, CI; confidence interval, BMI; Body mass index

DISCUSSION

The multivariable logistic analysis showed the multiple pregnancy, fetal malformation, VCI, MCI, HCC, PIH and low BMI were significantly associated with SGA. Among them, the adjusted odds ratio was highest for PIH and multiple-gestation. Tyson et al.[11] has reported that multiple-gestation pregnancies are often associated with growth restriction of one or both babies. Therefore, multiple placentation might be lead to growth restriction by interference of unequal utero-placental circulation with each other, although minor placental or cord abnormalities might not cause growth restriction in singleton pregnancy.

Redman et al.[14] noted that preeclampsia appears to progress in two stages: preclinical and clinical. This variant arises from poor development of the early placenta and its maternal blood supply, called poor placental. In the second stage, an increasingly hypoxic placenta causes the maternal signs of the condition, including hypertension and proteinuria as well as clotting and liver dysfunction. In severe, particularly early onset disease, the fetus may suffer from increasing nutritional and respiratory insufficiency, asphyxia, or death. Furthermore, they reported that poor placentation did not always cause overt preeclampsia but associated with small size for gestational age fetuses, these cases might be affected by pathophysiological situation as same as preeclampsia. This mechanism may explain why the frequency of FGR increased in the PIH patient.

Tyson et al.[11] reported that chromosomal abnormality was not significantly different between the SGA and control groups. This result was contradictory to previous reports. Chromosomal abnormalities probably do affect fetal growth, however, the number of cases of chromosomal abnormality in this study was small and so the result could change if the number of cases was increased in further study. The growth restriction of the fetus may be genetic in origin compounded by abnormalities of the utero-placental circulation due to abnormal chorionic villus development. On the other hand, Hendrix et al.[5] reported that congenital malformations, in the absence of identifiable genetic defects, are responsible for 1 to 2 % of FGR. Khoury et al.[15] reported that the frequency of FGR increased the with increasing number of defects in the infant. Most of causes of SGA in fetal malformations were major abnormalities in the current study, and the majority of cases with malformation were complicated with severe pathologic conditions. However, there was no apparent association between the minor fetal abnormalities and SGA.

Umbilical cord abnormalities are associated with SGA due to chronic aggravation of umbilical blood flow. In of the findings of the current multivariable analysis, VCI, MCI and HCC were selected as risk factors for SGA. The odds ratio of VCI was particularly high (4.6, 99%CI: 2.0-10.5). As has been reported[7, 16, 17], potential complications associated with VCI include miscarriage, prematurity, low birth weight, fetal malformation, prenatal death, low Apgar scores and retained placenta. The cord of a fetus with MCI or VCI is easily obstructed due to torsion and the lack of Wharton's jelly, if these unprotected vessels become distorted by fetal movements before or during the course of labor. The previous study[18-20] reported that thin umbilical cords with decreased Wharton's jelly are associated with FGR and increased perinatal morbidity and mortality. Degani et al.[21] noted that a coiled umbilical cord with the support of Wharton's jelly is thought to be more resistant to torsion, stretch, and compression. However, several studies[9, 10, 13, 22] have noted that hyper-coiled cords (HCCs) are correlated with poor perinatal outcome such as low birth weight and meconium staining of amniotic fluid at birth, and fetal growth restriction. Recent study has reported HCCs are less flexible or more prone to kinking and torsion in labor, thus leading to hypoxia. Therefore HCC may have a similar harmful effect to that of cord insertion on fetal growth. Smoking is also associated with fetal growth. Cliver et al.[3] suggested there were many pathways by which cigarette smoking can lead to decreased fetal growth, because cigarette smoke contains over 2000 substances, many of which may be toxic to the developing fetus. The cessation of smoking by the end of the first trimester greatly reduces the

risk to the developing fetus. However, no strong association was identified between cigarette smoking throughout pregnancy and SGA by the multivariable analysis.

Ehrenberg et al.[6] has reported that pregravid BMI ≤19.8 is significantly associated with an increased risk of FGR. The current result was similar to that report, but there is insufficient evidence indicating the mechanism for this association.

In conclusion, a multivariate analysis showed that many factors affect fetal growth during pregnancy. Pregnant woman with these risk factors should receive precise perinatal care based on odds ratios for SGA. The results of this study will contribute to the improvement of prognosis of FGR through intensive managements during pregnancy.

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