
OBSTETRICS

Association of Fetal Growth Rate in First Trimester and Being Large or Small for Gestational Age

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ABSTRACT

Objective: To evaluate the association of fetal growth rate in first trimester and fetal birth weight.

Materials and Methods: The prospective cohort study was performed at the department of Obstetrics and Gynecology, Bhumibol Adulyadej Hospital, Bangkok, Thailand. Fetal growth rate was measured by ultrasound twice in first trimester. First Crown Rump Length (CRL) ultrasound was measured at first antenatal care (ANC) and second CRL ultrasound was at four weeks later. Delta CRLs was calculated and divided into 3 groups: larger than expected, smaller than expected and equal as expected. Patients were followed until delivery. Fetal birth weights were stratified and labeled as large for gestational age (LGA), small for gestational age (SGA) and appropriate for gestational age (AGA) by birth weight percentile at gestational age at delivery. Fetal growth rate in first trimester and fetal birth weight were analyzed.

Result: 114 pregnant women were recruited. 59 fetuses were equal as expected (51%), 43 fetuses were smaller than expected (38%) and 12 fetuses were larger than expected (11%). The delta CRLs were significantly associate to fetal birth weights ($p < 0.005$). Diabetic mellitus and hypertension were not significantly associated to fetal birth weights.

Conclusion: Fetal growth rate in first trimester was significantly associated to fetal birth weight.

Keywords: Delta Crown Rump Length (delta CRLs), large for gestational age (LGA), small for gestational age (SGA), crown-rump length (CRL), ultrasound scans, birth weight

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Introduction

Clinicians generally assume that the major variations in fetal size occur in the second half of

pregnancy, because variations in the first trimester are minimal. The gestational age (GA) can be accurately assessed during first trimester. However, several

studies have reported a correlation of first-trimester CRL with birth weight⁽¹⁻⁴⁾.

Smith GC suggested in 2004 from seminars in perinatology volume 28 that in some women complications of late pregnancy have their origins in the very earliest weeks of gestation⁽⁵⁾. Hackmon et al performed a case-control study in 2008 to (compare CRL measurements between 30 severely macrosomic neonates (birth weight > 97th percentile) born at term and a control group of 90 appropriate for GA neonates. The difference between the measured and expected CRLs (measured at 11–14 weeks) was significantly greater in the study group⁽⁴⁾. Many studies including Salomon LJ in 2011⁽⁶⁾, and Reljic M in 2001⁽¹⁾ suggested that fetal growth in early pregnancy affected fetal growth in later pregnancy, and was significantly independent predictor for both SGA, LGA and spontaneous or threatened abortion.

The newborn that was born with LGA or SGA often had many complications such as impaired thermoregulation, hypoglycemia, polycythemia, impaired immune function, impaired growth and neurodevelopment, birth injury, respiratory distress, increased neonatal mortality rate, sudden infant death syndrome. They may have long-term metabolic effects such as increased risk of obesity and insulin resistance⁽⁷⁻¹³⁾, thus, “how to predict the LGA & SGA earliest?” is very important. If we found the association between fetal growth rates in first trimester with fetal birth weight we can detect the problem earlier and have more time to solve and prevent LGA and SGA. Now with ultrasound measurements of CRL assessed GA are very accurate; especially in the first trimester.

The aim of this study was to assess association between fetal growth rate in the first trimester and fetal birth weight.

Materials and Methods

A prospective cohort design was used. Data were collected on pregnant women who visited ANC in the outpatient department of Obstetrics at Bhumibol Adulyadej Hospital in Bangkok, Thailand, from August 1, 2013 to March 30, 2014. The study was approved by the Institutional Review Board of Bhumibol Adulyadej

Hospital. The sample size was calculated. Thirty cases per group were needed for the study. The inclusion criteria included: 1) pregnant women who visited ANC in the Department of Obstetrics and Gynecology at Bhumibol Adulyadej Hospital with the GA of 14 weeks or earlier, 2) singleton pregnancy. The exclusion criteria included: 1) pregnant women who had abortions, ectopic pregnancies, or stillbirths, 2) CRL measurement could not be obtained on two occasions, 3) unable to obtain birth weight, 4) could not communicate in the Thai language.

To participate in the study, the patients had to give informed consent and entered ANC before 14 weeks of GA and was twice assessed fetal growth rate by measuring CRL. The fetal CRL was obtained from frozen sonographic images. The greatest length was measured by placing the calipers from the cephalus to the caudal pole, and the maximal straight line CRL values measured on 3 satisfactory images were averaged⁽¹⁴⁻¹⁵⁾. First CRL ultrasound scan and second CRL ultrasound scan was done four weeks apart. If second CRL ultrasound scan result more than 14 weeks was excluded from study. Only one trained obstetric sonographers performed the sonographic evaluations using a Voluson 730 system (GE Healthcare, Milwaukee, WI) equipped with vaginal and abdominal transducers of 5 to 9 and 2 to 7 MHz, respectively. Then converted CRL to the equivalent number of weeks and days of gestation according to the method of Tongsong T et al⁽¹⁶⁾. The expected GA calculated by first measured CRL plus four weeks. The difference between measurement and the expected fetal age (delta CRL) was expressed in weeks of gestation. The subjects were then categorized into three group: larger than expected (defined as positive difference at larger than 0.5 week)⁽¹⁵⁾, smaller than expected (defined as negative difference at larger than 0.5 week), and equal as expected (defined as difference between - 0.5 to 0.5 week). The fetal birth weight and GA at birth were collected then categorized into three groups according to Thaithamyanont P et al⁽¹⁷⁾: LGA (birth weight at or above the 90th percentile for gestational age), SGA (birth weight at or below the 10th percentile for gestational age), and AGA (birth weight between the 10th - 90th

percentile for gestational age⁽¹⁸⁻²⁰⁾. Association between fetal growth rate in first trimester and fetal birth weight were calculated.

Pilot study before the beginning of this research found incidence of SGA in delta CRL equal as expected group was 0.20 and incidence of SGA in delta CRL smaller than expected group was 0.45. This study used sample size formula to compare difference in proportion of SGA between group is $[(2(z\alpha + z\beta)^2 PQ)/(P1-P2)^2]$. when power of detection is 99% and alpha error at 0.05. The sample size is at least 30 patients per group. Data analysis were performed with SPSS version 17.0 for Windows software (SPSS Inc, Chicago IL) to calculated mean, standard deviation, analysis of variance (ANOVA) for continuous data and the X² test for categorical data.

Result

The study included 114 pregnant women. 59 fetuses were equal to the expected group (51%), 43 fetuses were smaller than expected group (38%) and 12 fetuses were larger than expected group (11%). The maternal age, maternal pre-pregnancy weight, total weight gain, GA at birth, GDM, PIH, nulliparity, multiparity was not significantly different among the groups (Table 1). Table 2 presents the delta CRL which divide the three groups into (larger than expected CRL, equal as expected CRL and smaller than expected CRL) were associated significantly with LGA, AGA and SGA, respectively ($p < 0.005$). The association of the maternal age, total weight gain, DM, PIH with birth weight was presented in Table 3. There was no significant association of the maternal age, total weight gain, DM, PIH with birth weight.

Table 1. Demographic characteristic data of pregnant women

	Delta Crown Rump Length			P
	Larger than expected (N = 12)	Equal as expected (N = 59)	Smaller than expected (N = 43)	
Maternal age	29 ± 6.01	30 ± 5.70	28 ± 5.91	0.205
Maternal pre-pregnancy weight	54 ± 14.72	58 ± 11.54	61 ± 11.48	0.143
Total weight gain	21 ± 17.98	17 ± 12.73	14 ± 5.27	0.177
Gestational age at birth	37 ± 2.62	38 ± 1.62	38 ± 1.18	0.134
GDM	0	9 (7.89%)	6 (5.26%)	0.362
PIH	0	2 (1.75%)	3 (2.63%)	0.509
Nulliparity	4 (33.33%)	22 (37.28%)	15 (34.88%)	0.951
Multiparity	8 (66.67%)	37 (62.72%)	28 (65.12%)	0.951

Table 2. Association between delta CRL group and birth weight group

Delta CRL	Birth weight			P
	AGA	SGA	LGA	
Equal as expected	52	1	6	< 0.005
Smaller than expected	23	6	14	
Larger than expected	5	1	6	
Total	80	8	26	

Table 3. Association of maternal age, total weight gain, DM, PIH with birth weight

	Birth weight			
	LGA	AGA	SGA	P
Maternal age	32.39 ± 5.321	29.37 ± 6.094	28.87 ± 4.389	0.095
Total weight gain	19.85 ± 16.169	16.46 ± 9.248	10.72 ± 4.158	0.230
DM	5	9	2	0.526
PIH	0	5	0	1.000

Discussion

This study was a prospective cohort design. The study included 114 pregnant women. The result of this study showed that delta CRL of fetuses in first trimester were significantly associated with birth weight ($p < 0.05$). There was no difference in demographic characteristic data between the three groups (larger than expected CRL, smaller than expected CRL and equal as expected CRL) regarding maternal age, maternal pre-pregnancy weight, total weight gain, GA at birth, GDM, PIH, nulliparity and multiparity. There was no association between birth weight and maternal age, total weight gain, DM, PIH with birth weight. These results, which studied the Thai population, support that growth rate of fetuses in the first trimester were associated with birth weight.

Several previous studies, such as Papastefanou I et al⁽²¹⁾, study in 2012 with 4702 pregnant women and El Daouk M et al⁽²²⁾, study in 2012 with 121 pregnant women, showed delta first-trimester CRL as a predictor of fetal LGA and SGA ($p < 0.0001$). Bukowski et al⁽²³⁾ also found that the size of the fetus in the first trimester of pregnancy was associated with the birth weight. The effect of first trimester fetal size on the duration of pregnancy accounted for about half of the association, and fetal growth in later pregnancy accounted for the other half. Those studies gave results similar to this study. But some studies, such as Mongelli M et al., study in 2012 with 107 pregnant women found that first-trimester CRL growth velocity did not correlate with birth weight and this may have been a result of the small sample size⁽²⁴⁾.

A limitation of this study was the small sample

size due to most pregnant women usually entering ANC after time limitations. This explained that why other factors such as DM, PIH, maternal age, and total weight gain were not show association with birth weight in this study. The proportion of complications was too small as well. Although the sample size was small but results of this study gave significant association between growth rates of fetuses in the first trimester with birth weight. All the cases studied were Thais, which may make these results specific for the Thai population.

As mentioned above, results of this study only showed significant association between growth rates of fetuses in first trimester with birth weight. There may some other first trimester of gestation factors that affect birth weight. Further study is required to improve knowledge in this field and should have a larger sample size than this study.

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ความสัมพันธ์ระหว่างการเจริญเติบโตของทารกในช่วงไตรมาสแรกของการตั้งครรภ์กับความเสี่ยงในการเกิดทารกน้ำหนักแรกเกิดมากกว่าอายุครรภ์ และทารกน้ำหนักแรกเกิดน้อยกว่าอายุครรภ์

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บทนำ: เพื่อหาความสัมพันธ์ระหว่างการเจริญเติบโตของทารกในช่วงไตรมาสแรกของการตั้งครรภ์กับน้ำหนักทารกแรกเกิด

วิธีการวิจัย: เป็นการศึกษาแบบไปข้างหน้าแบบ cohort ทำการศึกษาในสตรีตั้งครรภ์เดี่ยวที่มาฝากครรภ์ครั้งแรกในไตรมาสแรกของการตั้งครรภ์ การเจริญเติบโตของทารกทำโดยการอัลตราซาวด์ขนาด 2 ครั้ง ห่างกัน 1 เดือน ค่าความแตกต่างของความยาวของทารก (CRL) จะถูกนำมาคำนวณและแบ่งออกเป็น 3 กลุ่ม มากกว่าที่คาดไว้ น้อยกว่าที่คาดไว้ เท่ากับที่คาดไว้ หญิงตั้งครรภ์จะถูกติดตามจนคลอดบุตร น้ำหนักของทารกแรกเกิดจะถูกเก็บและแบ่งออกเป็น 3 กลุ่มตามอายุครรภ์ที่คลอด น้ำหนักแรกเกิดมากกว่าอายุครรภ์ น้ำหนักแรกเกิดน้อยกว่าอายุครรภ์ น้ำหนักแรกเกิดเท่ากับอายุครรภ์ วิเคราะห์หาความสัมพันธ์ระหว่างการเจริญเติบโตของทารกในช่วงไตรมาสแรกของการตั้งครรภ์กับน้ำหนักทารกแรกเกิดโดยใช้การทดสอบความเป็นอิสระต่อกัน (Chi-square test)

ผลการวิจัย: หญิงตั้งครรภ์ 114 คน แบ่งเป็น เท่ากับที่คาดไว้ 59 คน (51%), น้อยกว่าที่คาดไว้ 43 คน (38%) และมากกว่าที่คาดไว้ 12 คน (11%) ค่าความแตกต่างของความยาวของทารก (CRL) มีความสัมพันธ์กับน้ำหนักแรกเกิดอย่างมีนัยสำคัญทางสถิติ ($P < 0.005$) และไม่พบความสัมพันธ์กันระหว่างเบาหวานและความดันโลหิตสูงกับน้ำหนักทารกแรกเกิด

สรุป: การเจริญเติบโตของทารกในช่วงไตรมาสแรกของการตั้งครรภ์มีความสัมพันธ์กับน้ำหนักทารกแรกเกิดอย่างมีนัยสำคัญทางสถิติ
