Charts of Thai Fetal Biometries: 1. Methodology

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Abstract

A cross-sectional study was conducted in order to construct new reference charts for Thai fetal biometries that are commonly used in obstetric ultrasound practice. We discussed and illustrated a sound appropriate study design and statistical analysis which lead to more valid results. A total of 621 normal pregnant women between 12-41 weeks of gestation and their fetuses were recruited. Each fetus was measured once at a randomly assigned gestational age specifically for the purpose of this study only. Stepwise linear regression technique was used to model the mean and its standard deviation as functions of gestational age. Goodness of fit and normality of the data were checked before the final models were chosen. Reference centiles were derived, taking into account the increasing variation as pregnancy proceeds. We demonstrated the stated technique with humerus data from the same study. Reference charts for other fetal biometries have been derived and are presented in subsequent papers.

Key word : Fetal Biometries, Methodology, Reference Centiles

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Fetal size charts have been previously published by many authors(1,2). Unfortunately, many of these studies may have weaknesses in the study design, statistical analysis, or both. However, Altman et al(3,4) have suggested the design and analysis methods which are simple and considered appropriate for deriving fetal size charts. In our study, we adopted and discussed such design and analysis procedures to derive standard reference centiles for Thai fetal biometries. In this paper, we illustrate the analysis of fetal humerus length data and the reference centiles which were deve-

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loped using a similar approach. We also present Thai fetal size charts for commonly used fetal measurements in following papers, using the same study design and analysis methods.

Study design

Data collection procedures were designed specifically for the purpose of this study, in that each fetus was measured only once. We recruited pregnant women and their fetuses between 12-41 weeks of gestation, who attended the antenatal clinic at Siriraj Hospital, Mahidol University, Bangkok, Thailand. We identified pregnant women who had had a previous regular menstrual period for at least 3 months without contraception prior to current pregnancy, and uterine size at the time of examination was compatible with menstrual age. Exclusion criteria were as follows:

1. Uncertain date of last menstrual period.
2. Maternal conditions which may affect fetal growth (e.g., diabetes mellitus, hypertension, etc.).
3. Multiple pregnancies.
4. Fetal or neonatal malformation or abnormal karyotype.

A total of 621 pregnant women were recruited. The date of ultrasonographic measurement was randomly assigned to each woman at her first visit so that approximately equal numbers were measured at each week of gestation. As some of the women were delivered prior to the allocated date of measurement, further recruitment was performed from women between 37-41 weeks of gestation to get a sufficient number of measurements for the analysis.

We planned to measure all the variables in each fetus as shown in Table 1. However, not all measurements could be obtained from every fetus due to unfavorable fetal position in some cases. The number of fetuses that were measured at each week of gestation are shown in Table 2. They were measured by only one investigator, using a 5 MHz convex probe of the Acuson 128 XP4 model of ultrasound machine at the Maternal-Fetal Medicine Unit, Department of Obstetrics and Gynecology, Siriraj Hospital. All measurements were recorded on specifically designed paper forms, followed by computer forms. Computer entries were all checked against the paper records for any error and confirmation. Extreme values were rechecked again at the time of analysis, but they were not excluded.

Method of analysis

The mean of each measurement at each week of gestation was estimated using the stepwise linear regression technique. This was based on the assumption that the data in each gestational age were normally distributed. The standard deviation

Table 1. Fetal measurements made in the study.

Biparietal diameter	Humerus length
Fronto-occipital diameter	Ulna length
Head circumference	Radius length
Head area	Amniotic fluid index
Abdominal circumference	Umbilical artery waveform index
Abdominal area	- Systolic/diastolic index
Femur length	- Resistance index
Tibia length	- Pulsatility index
Fibula length	

Table 2. Number of fetuses measured at each week of gestation.

Gestational age (weeks)	Number of fetuses	Percentage
12	13	2.09
13	15	2.42
14	14	2.25
15	19	3.06
16	22	3.54
17	22	3.54
18	21	3.38
19	22	3.54
20	21	3.38
21	21	3.38
22	24	3.86
23	26	4.19
24	22	3.54
25	26	4.19
26	27	4.35
27	23	3.70
28	22	3.54
29	21	3.38
30	27	4.35
31	20	3.22
32	21	3.38
33	22	3.54
34	20	3.22
35	17	2.74
36	23	3.70
37	21	3.38
38	19	3.06
39	18	2.90
40	16	2.58
41	16	2.58
Total	621	100

(SD) was then modeled as a function of gestational age using the same method. All the final models chosen were the simplest ones which provided a good fit to the observed data.

To check for the goodness of fit of the model, in addition to R^2, a standard deviation score (SDS, which is also called standardized residual), was calculated for each observation. The scores were obtained from dividing the difference of the observed and fitted values (i.e., observed – fitted values) with the fitted SD. A plot of SDS and gestational age was examined for the existence of any pattern. Whether or not SDS are normally distributed can be determined either by using a normal plot or Shapiro-Wilk W test. The proportion of observations outside the specified centiles was checked to see if it was close to the expected values. Transformation of the data may be required if the models do not provide such a good fit.

Reference centiles for each gestational age were then derived from the combination of both fitted mean and SD. The 100αth centile was expressed as mean + Zα (SD), where Zα is the corresponding value from the standard normal distribution.

Construction of new fetal size chart

In this paper, we illustrate a step-by-step approach in deriving reference centiles for fetal humerus length from the same study sample, using the analysis method described above. Humerus length data were available in 482 out of 621 fetuses measured.

Step 1: Modeling the mean

Humerus length data was regressed against gestational age using the stepwise linear regression technique. This resulted in the following equation:

$$HL = -28.373 + 3.04\ W - 0.0005\ W^3$$

where HL = humerus length (mm), and W = gestational age (weeks)

Scatter plot of humerus length and gestational age with superimposed curve of fitted mean is shown in Fig. 1.

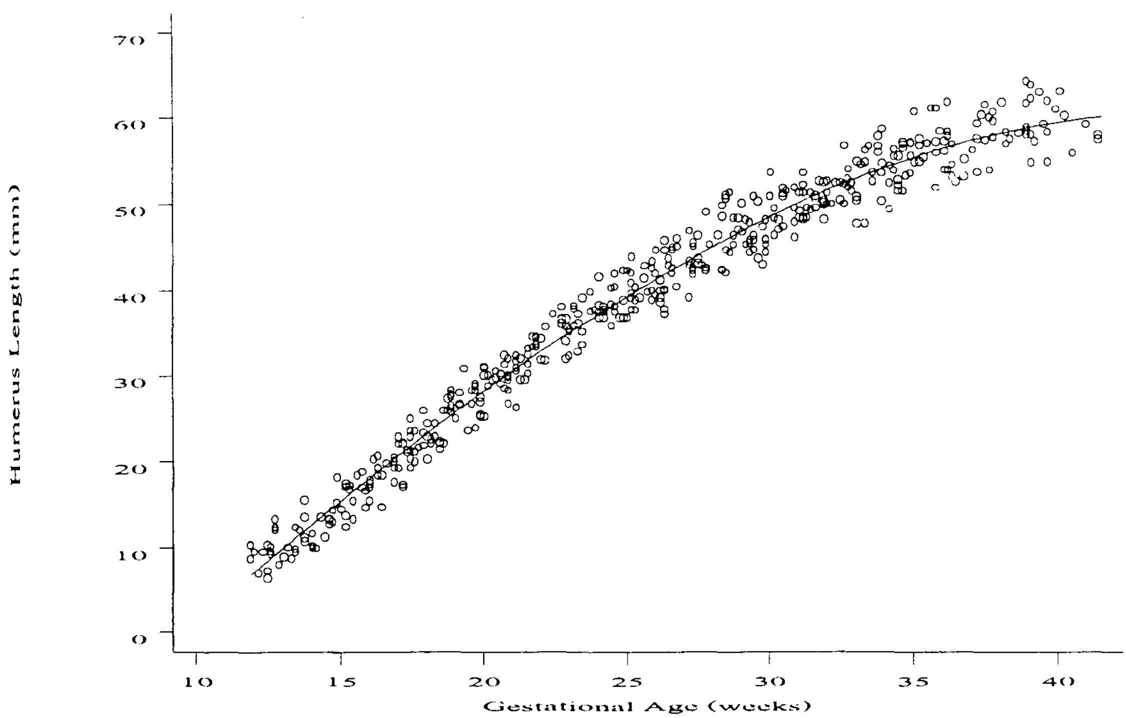

Fig. 1. Scatter plot of humerus length and gestational age with curve of the fitted mean.

Step 2: Modeling the variability

Residuals from the regression analysis were calculated and examined. As suggested by Altman et al,(3,4) the residuals were converted to absolute values and then regressed against gestational age to estimate gestational age-specific SD. The following equation for SD was obtained:

$$SD = 1.462 + 0.0047\ W^2$$

where SD = standard deviation (mm), and W = gestational age (weeks)

Step 3: Checking for the goodness of fit of the model

The above model for the mean gave R^2 of 0.98, which means that 98 per cent of the variability in the data can be explained by the model. SDS were calculated and plotted against gestational age, shown in Fig. 2, with superimposed lines of expected 10th and 90th centiles (i.e., ± 1.282). We found that 10.58 per cent (51 of 482) of the observations were above the 90th centile and 9.96 per cent (48 of 482) were below the 10th centile.

Normal plot of SDS is shown in Fig. 3, in which the values lie almost in a straight line. The associated Shapiro-Wilk W test gave a non-significant p value of 0.15. All the evidence suggested that the models provided a good fit to the data and normality assumption was achieved.

Step 4: Deriving the centiles

From the models, estimated mean and SD of humerus length for each gestational age were calculated. The 100αth centile can be derived from mean + Zα(SD), where Zα is the corresponding value from the standard normal distribution. The values of Zα are -1.88, -1.28, 0, 1.28, and 1.88 for the 3rd, 10th, 50th, 90th, and 97th centiles respectively. Centiles for fetal humerus length and estimated SD are shown in Table 3. A plot of humerus length data with the fitted centiles is shown in Fig. 4.

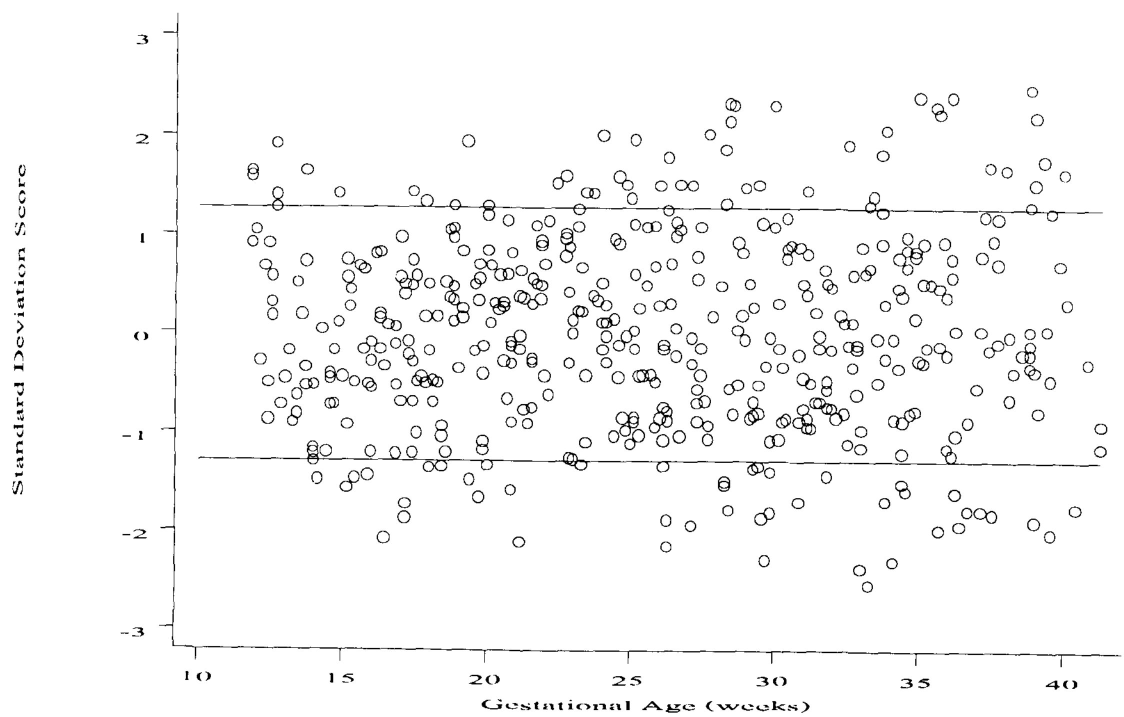

Fig. 2. Plot of SDS against gestational age, with the expected 10th and 90th centile lines.

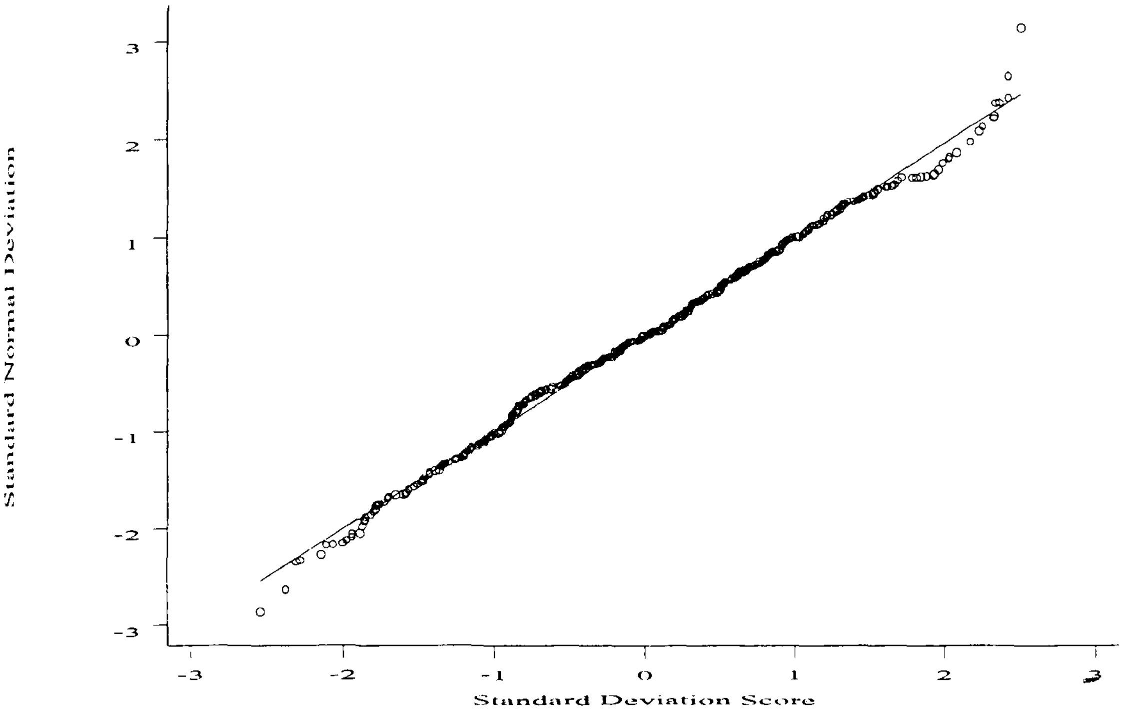

Fig. 3. Normal plot of SDS.

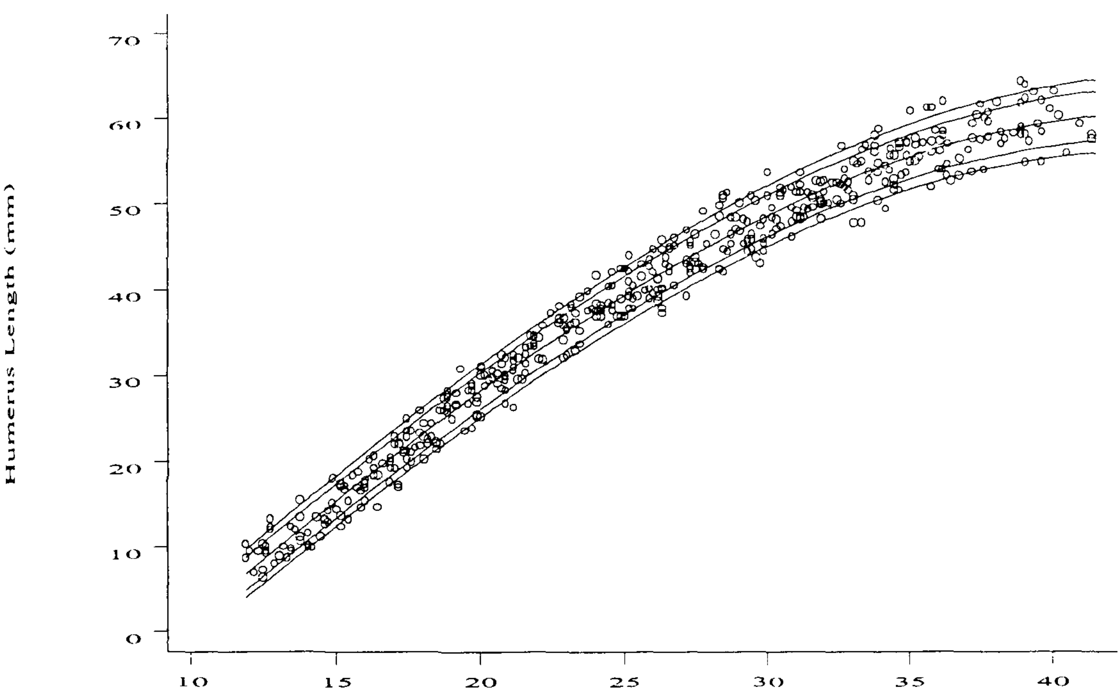

Fig. 4. Humerus length data with fitted 3rd, 10th, 50th, 90th, and 97th centile lines.

Table 3. Fitted centiles of Thai fetal humerus length.

GA (weeks)	Centile					SD
	3rd	10th	50th	90th	97th	
12	4.33	5.24	7.21	9.17	10.08	1.53
13	7.10	8.02	10.00	11.98	12.90	1.54
14	9.83	10.76	12.75	14.75	15.68	1.55
15	12.52	13.45	15.46	17.47	18.41	1.57
16	15.15	16.10	18.13	20.16	21.10	1.58
17	17.73	18.69	20.74	22.79	23.74	1.60
18	20.26	21.23	23.30	25.37	26.33	1.61
19	22.73	23.71	25.80	27.89	28.87	1.63
20	25.14	26.13	28.24	30.36	31.35	1.65
21	27.48	28.48	30.62	32.76	33.76	1.67
22	29.76	30.77	32.94	35.10	36.12	1.69
23	31.97	32.99	35.18	37.38	38.40	1.71
24	34.10	35.13	37.36	39.58	40.62	1.73
25	36.15	37.20	39.45	41.70	42.76	1.76
26	38.12	39.19	41.47	43.75	44.82	1.78
27	40.01	41.09	43.41	45.72	46.80	1.80
28	41.82	42.91	45.26	47.61	48.70	1.83
29	43.53	44.64	47.03	49.41	50.52	1.86
30	45.15	46.28	48.70	51.12	52.24	1.89
31	46.68	47.82	50.28	52.73	53.88	1.91
32	48.10	49.27	51.76	54.25	55.41	1.94
33	49.43	50.61	53.14	55.67	56.85	1.97
34	50.65	51.85	54.42	56.99	58.19	2.01
35	51.76	52.98	55.59	58.20	59.42	2.04
36	52.75	53.99	56.65	59.31	60.54	2.07
37	53.64	54.90	57.60	60.30	61.56	2.11
38	54.40	55.68	58.43	61.17	62.45	2.14
39	55.05	56.35	59.14	61.93	63.23	2.18
40	55.57	56.89	59.73	62.57	63.89	2.21
41	55.96	57.31	60.19	63.08	64.43	2.25

DISCUSSION

We have adopted and applied a new approach of deriving fetal size charts for Thai fetuses. This method has also been used by some investigators to develop reference centiles in other study populations[5-7]. As suggested by Altman et al,[3,4] this method differs from that used by others in many aspects. The data were collected in a cross-sectional fashion by measuring each fetus only once, specifically for the purpose of the study. The date of measurement was randomly assigned to each woman, so that approximately the same number of fetuses was measured at each week of gestation. Not only was linear regression analysis performed to estimate the mean of measurement, we also examined and modeled the variability (SD) as a function of gestational age. This takes into account the change in variability among fetuses with gestational age. All the final models were checked for the goodness of fit and whether they satisfied the assumption for normally distributed data.

Reference centiles charts should be based on data of normal fetuses. Therefore, we excluded the conditions during the antenatal period that may affect fetal size. However, fetuses that were found to be large or small for gestational age at birth were not excluded unless there was any congenital anomaly. All the measurements were made only for the purpose of this study. Data from ultrasonographic scans done for clinical indications, such as suspected growth retardation, were not included since they may bias the results.

Some investigators have suggested that the data should be collected prospectively from serial measurements of each fetus. This type of data may be more appropriate for deriving centiles for fetal growth, but may not be suitable for fetal size. Moreover, regression analysis done on such longitudinal data will remove some variability that will result in centiles that are too close together. This has been demonstrated by some investigators(8,9).

We used a parametric approach in this study to develop reference centiles. We modeled the mean using the stepwise linear regression analysis technique. The strong assumption that data are normally distributed was checked before the final model was chosen. Usually, cubic or quadratic models will be adequate for fetal size data. However, transformation of data may be needed if the normality assumption is not appropriate. In such cases, centiles were calculated from the fitted value in the transformed scale and then back-transformed to the original scale.

Non-parametric methods can also be used, such as calculating the observed centiles for each gestational age. The requirement of a large number of observations at each week of gestation to get precise estimates for extreme centiles will be the main drawback of this approach. Furthermore, the centile curves produced from non-parametric approach will not be as smooth as those from the parametric method.

Changes in the variability of measurement with gestational age are usually not taken into account or inadequately examined. This may result in an error that the centiles derived will be too far apart in early gestational age and too close later on. In this study, we allowed the variability to change with gestational age by modeling separately the residuals from the mean model. The centiles derived from combining the two models together will better explain the data and be more realistic.

There are some Thai studies that aimed to develop reference centiles for Thai fetal size (10-12). Nevertheless, none has used the described design and analysis methods especially in the issue of variability modeling. Some have used non-parametric approach which resulted in centiles that did not change smoothly with gestational age. Other possible weaknesses may include the sample selection method that was not specifically designed for the study and repeated measurements in some fetuses.

The described approach was also used to develop reference centiles for other measurements of Thai fetal biometries. We also compared the centiles produced by this method to those previously derived by others(5-7,10-12). This will be examined and discussed in the subsequent papers.

SUMMARY

In this study, we adopted and applied an approach to derive reference centiles for various measurements of Thai fetal biometries. A total of 621 pregnant women and their fetuses were recruited. Each fetus was measured only once at a randomly assigned gestational age. We used the linear regression analysis technique to model the mean of the measurements. Changes in the variability were assessed by examining the residuals and modeling them as a function of gestational age separately. Models were selected based on the goodness of fit with the observed data and whether or not they reached the assumption of normality. Combination of the estimated mean and SD were used to construct the centile chart. We demonstrated the use of this approach with fetal humerus data from the same study and a table of reference centiles was produced. We used the same analysis methods to develop centiles for other measurements of Thai fetuses as will be presented and discussed in following papers.

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ตารางอ้างอิงสำหรับขนาดทารกในครรภ์ : 1. ระเบียบวิธีวิจัย

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ได้ทำการศึกษาแบบตัดขวางเพื่อสร้างตารางอ้างอิง สำหรับขนาดของทารกในครรภ์ซึ่งวัดจากการตรวจด้วยเครื่องตรวจคลื่นเสียงความถี่สูง โดยได้ทำการปรับปรุงวิธีการดำเนินการวิจัยและการวิเคราะห์ข้อมูลทางสถิติให้เหมาะสมเพื่อให้ได้ผลที่แม่นยำและน่าเชื่อถือ

ทำการศึกษาสตรีตั้งครรภ์ปกติ จำนวน 621 ราย อายุครรภ์ระหว่าง 12–41 สัปดาห์ ทำการวัดขนาดของทารกในครรภ์แต่ละรายที่อายุครรภ์ต่าง ๆ กัน โดยการสุ่ม เพื่อการศึกษาครั้งนี้โดยเฉพาะ ทำการวิเคราะห์ข้อมูลโดยหาสมการถดถอยเชิงเส้น สำหรับค่าเฉลี่ยและส่วนเบี่ยงเบนมาตรฐานของขนาดทารกในช่วงอายุครรภ์ต่าง ๆ จากนั้นจึงทำการสร้างตารางอ้างอิงจากสมการทั้งสอง โดยคำนึงถึงการเปลี่ยนแปลงของส่วนเบี่ยงเบนมาตรฐานตามอายุครรภ์ที่เพิ่มขึ้น

ในรายงานนี้ได้ทำการวิจารณ์และแสดงตัวอย่างของวิธีการวิเคราะห์ข้อมูลดังกล่าว โดยใช้ข้อมูลของขนาดกระดูกต้นแขนทารกที่ได้จากการศึกษาเดียวกัน การวิเคราะห์และสร้างตารางอ้างอิงอื่น ๆ ของขนาดทารกในครรภ์นั้นจะนำเสนอในรายงานฉบับต่อไป

คำสำคัญ : ขนาดทารกในครรภ์, ระเบียบวิธีวิจัย, ตารางอ้างอิง

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