Normal Fetal Lung Volume Determined by Three-Dimensional Ultrasonography using Virtual Organ Computer-Aided Analysis at 22-37 Weeks' Gestation

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ABSTRACT

Objective: To establish a reference of normal fetal lung volume using three-dimentional ultrasonography in the second half of pregnancy.
Methods: A prospective longitudinal study was conducted in 53 Thai healthy singleton pregnant women at 22-37 weeks of gestation. By using 3-D ultrasonography with Virtual Organ Computer-Aided Analysis (VOCAL), the whole fetal thorax was obtained as volume data and then calculated in each participant for 3-6 successions. Our method showed excellent intraclass correlation coefficients (ICC = 0.990-0.991) among three operators and validity ranged within 3% of the actual volume. Multivariate analysis was used to identify the relationship between lung volume and gestational age. This longitudinal data set was then analysed by mixed model regression analysis.
Results: A total of 260 fetal lung volumes were obtained. Average maternal age, gestational age and birth weight were 26.9 ± 4.7 years, 38.9 ± 1.3 weeks and 3,007.5 ± 349.3 grams. With mixed model of regression analysis, the relationship between lung volume and GA was demonstrated as follows: left lung volume (ml.) = (-12.19) + (0.22*GA) + (0.03*GA^2), right lung volume (ml.) = (-24.91) + (1.19*GA) + (0.02*GA^2), total lung volume (ml.) = (-37.32) + (1.43*GA) + (0.05*GA^2).
Conclusion: This is the normal fetal lung volume in the Thai population using the rotational technique (VOCAL). It could be considered as a reference for prenatal diagnosis of pulmonary hypoplasia.

Keywords: Fetal lung volume, three-dimentional ultrasonography, virtual organ computer-aided analysis (VOCAL), pulmonary hypoplasia

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INTRODUCTION

Pulmonary hypoplasia is characterized by incomplete development of lung tissue.[1-3] Mortality rates of 55-100% have been reported during the perinatal period in fetuses with this fatal condition.[3] The diagnostic criteria are mainly based on postnatal pathological evidence including reduced lung weight and volume,[3-5] which is not applicable to the prenatal period.

There are many published studies about evaluation of the actual size of fetal lungs using biometric parameters such as lung length, lung area, lung circumference and ratio of lung area to head circumference (LHR).[6-10] None of these is reliable enough to predict pulmonary hypoplasia with certainty, because of the irregular surface of fetal lungs. Alternatively, three-dimensional (3D) ultrasonography[11] and MRI[12] will help to precisely assess and correct this problem. Both are clinically applicable and reliable to predict the actual size of fetal lung volume[13,14] but three-dimensional ultrasonography has the advantage of cost effectiveness, less complicated and convenient for the patients.[1]

From previous studies about fetal lung volume estimation using 3D ultrasonography, the rotational

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measurement of volume with Virtual Organ Computer-Aided Analysis (VOCAL) has proved to be superior to the conventional multiplanar technique.[15,16] Despite numerous reported studies of VOCAL-developed nomograms of fetal lung volume,[16-18] most previous data in Asian population were acquired by using the conventional technique.[19,20] None has been studied in the Southeast Asian region. Furthermore, the Caucasian's biometric parameters are not applicable for Southeast Asian fetuses because of racial variation. For this reason, Southeast Asian's own data is necessary and should be developed. Therefore, the objective of this study was to create the reference of normal fetal lung volume in the Southeast Asian population.

MATERIALS AND METHODS

Between January and August 2008, this prospective longitudinal study was conducted at the Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital, Mahidol University. Sixty three Thai healthy singleton pregnant women at 22-37 weeks of gestation were enrolled into the study. All had known gestational age calculated by their last menstrual period and then confirmed by sonographic measurement of fetal biometric parameters at the time of recruitment (first half of pregnancy). Exclusion criteria were those with incomplete data (less than 3 times of ultrasonography), fetal lung volume inaccessibility, extreme fetal birth weight (outside percentile of 10 and 90) and any abnormalities resulting in pulmonary hypoplasia. All participants were scanned three to six times every one-four weeks. The protocol was approved by the Siriraj Institutional Review Board (Si. 129/2008).

Firstly, the validity of the volume measuring capacity of the system was tested on 20 lung models, scanned within a fluid-filled tank. Results confirmed an accuracy of measurement to within 3% of the actual volume. After that, this technique was then applied to the participants. All examinations were performed by three well-trained Maternal-Fetal Medicine specialists, using Voluson 730 Expert or Voluson E8 ultrasonographic machines (GE medical systems, Austria). The ultrasonography system used was a three dimensional (3D), 3.3-4.1 MHz annular array probe with a built-in electromechanical device for volume scanning. The routine data from ultrasonography scan such as number and position of the fetus, and biometric parameters were recorded. Fetal lungs were specifically scanned in three perpendicular planes: transverse, horizontal and longitudinal views, to retrieve 3D lung morphological data (Fig 1). The obtained data were integrated to calculate lung volumes using the rotational Virtual Organ Computer-Aided Analysis (VOCAL) technique (Fig 2).

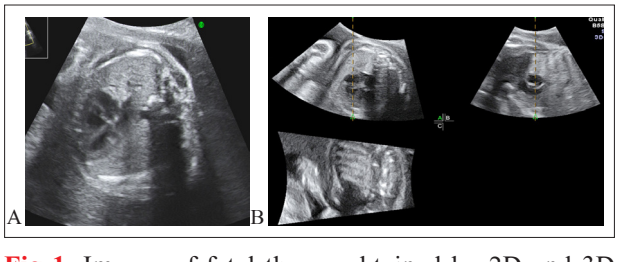

Fig 1. Images of fetal thorax obtained by 2D and 3D ultrasound machine. A) 2D transverse plane and B) 3D multiplanar perpendicular plane.

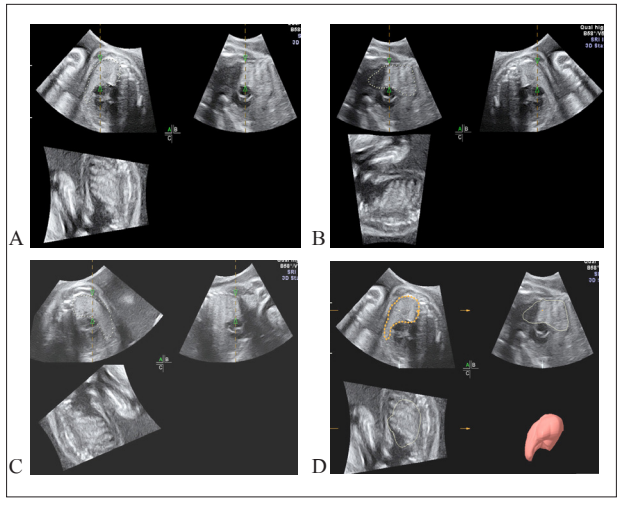

Fig 2. Assessment of the lung volume using the VOCAL technique. Measurements are performed on the transverse section by contouring the surface of lung, rotating the image 30 degrees, and contouring it again, which is repeated for 6 times until completing a rotation of 180 degrees, then the program automatically calculates the lung volume.

Sample size was calculated based on the anticipated correlation coefficient between fetal lung volume and gestational age. A sample of 51 pregnant women was required to test the Pearson's correlation coefficient of 0.8 against the null hypothesis of correlation of 0.6 at 2-sided type I error of 0.05 and 80% power. With the expected 20% drop-out, 62 pregnant women were studied.

As mentioned earlier, all fetal lung volumes, in this study, for each fetus, were measured by three operators. Inter-observer reliability was first assessed using scatter plot, intraclass correlation coefficient (ICC) and its 95% confidence interval (CI). Our method showed that the ICC were 0.990 (95% CI: 0.988, 0.992) and 0.991 (95% CI: 0.989, 0.993) for left and right lung volumes, respectively. Both average left and right volumes were then used to plot against gestational age to examine the correlation. To accurately determine the relationship between gestational age and lung volume, multivariate analysis was used to take into account the correlated nature of dependent variables. Since the dependent variables were quantitative data and there was variable number of measurements of lung volumes in each fetus, a mixed model was applied.

Statistical data analyses were performed using SAS 8.01 and SPSS 15.0. A 2-sided p-value of less than 0.05 was considered to be statistically significant.

RESULTS

There were 63 pregnant women recruited into the study and 10 were excluded on account of low birth weight fetus (n=1), incomplete data collection (n=2) and poor image quality (n=7). All participants were scanned

TABLE 1. Demographic characteristics (n= 53).

Characteristics	Mean (SD), or n (%)
Age (year)	26.9 (4.7)
GA at delivery (week)	38.9 (1.3)
Birth weight (gram)	3,007.5 (349.3)
Nulliparity	29 (54.7)
Cesarean delivery	11 (20.8)
Fetal male gender	28 (52.8)

3 to 6 times every 1-4 weeks, therefore a total of 260 fetal lung volumes were obtained. Of the remaining 53 pregnant women, the mean maternal age was 26.9 ± 4.7 years and 29 (54.7%) of these women were nulliparous. The average gestational age at delivery was 38.9 ± 1.3 weeks with spontaneous vaginal delivery in 42 women (79.2%). The mean birth weight was 3,007.5 ± 349.3 grams. All neonates had normal birth weight without any structural abnormalities, confirmed by postnatal examination. Demographic data were recorded, as shown in Table 1.

During the period of 22-37 weeks' gestation, left, right, and total lung volumes ranged from 7.53 to 34.07 ml., 12.42 to 43.87 ml., and 19.95 to 77.94 ml., respectively with the 5th, 50th and 95th percentile illustrated in Table 2. Significant increase in fetal lung volumes was established with advancing gestational age. With mixed model regression analysis, the relationship between each lung volume and GA was demonstrated as follows:

- Left lung volume (ml.) = (-12.19) + (0.22 * GA) + (0.03 * GA^2),
- Right lung volume (ml.) = (-24.91) + (1.19 * GA) + (0.02 * GA^2),
- Total lung volume (ml.) = (-37.32) + (1.43 * GA) + (0.05 * GA^2).

DISCUSSION

Volume measurement has become an important role in Obstetrics as abnormal volume often indicates abnormal function or pathology of various organs. Measurement of fetal lung volume may offer the possibility in management of pregnancies which are at increased risk of pulmonary hypoplasia, such as premature rupture of membranes or congenital diaphragmatic hernia.[21] To have fetal lung volume assessed precisely by using two dimensional (2D) ultrasonography, the fetal lung shape has to be an ideal geometric one.

Actually, fetal lungs have irregular contours with much error when evaluated by using 2D ultrasonography. Although both three dimensional (3D) ultrasonography and MRI are clinically reliable to predict the actual size of fetal lung volume,[11-14] in most countries, three dimensional (3D) ultrasonography is still more available and less expensive than MRI.

In this study, 53 from 63 pregnant women met the inclusion criteria. The volume of the left lung was less than the right lung due to the space taking intra-thoracic organ (fetal heart) on the left side. Overall, fair to good image quality was acquired in most cases (88.9%). Before 26 weeks' gestation and after 35 weeks' gestation, it is more difficult to measure lung volumes because of poor image quality. An unfavorable position of the fetus, increased ossification of the spine and ribs and motion artifacts which could affect visualization of the lungs. Most previous studies had success rates of 85-90%.[16-21] In this study, not only the feasibility of fetal lung volume measurements, but the reliability was also good as shown by its high validity and intraclass correlation coefficients. The accuracy of the method of evaluation of gestational age is a limiting factor of this study including the fact that most pregnant women in Thailand first attend antenatal care in the second trimester. Ultrasonography to confirm gestational age in the second trimester is actually not as precise as that in the first trimester.

Until now, nomograms of fetal lung volumes have been created mostly using multiplanar technique.[19,20,22,23] This study has presented normal fetal lung volume in Thai population from 22-37 weeks of gestation, longitu-

TABLE 2. Percentiles of left, right and total fetal lung volumes against gestational age.

GA (wk)	n	Left lung volume percentile			Right lung volume percentile			Total lung volume percentile		
		5	50	95	5	50	95	5	50	95
22	13	6.71	7.5	10.47	8.37	12.42	15.02	15.08	19.95	25.49
23	13	7.25	8.34	11.69	10.14	14.21	16.25	17.39	22.55	27.94
24	11	7.59	8.43	12.55	11.61	15.74	17.42	19.20	24.17	29.97
25	16	8.77	9.96	13.23	12.71	16.52	21.74	21.48	26.48	34.97
26	10	10.60	12.71	17.29	14.09	18.51	22.09	24.69	31.22	39.38
27	13	11.92	13.57	20.84	15.37	20.22	25.73	27.29	33.79	46.57
28	13	12.87	15.04	22.96	17.65	24.98	28.84	30.52	40.02	51.80
29	13	13.63	16.50	27.28	20.73	26.00	30.28	34.36	42.50	57.56
30	13	15.77	19.20	29.45	22.00	28.75	34.01	37.77	47.95	63.46
31	17	18.32	22.88	32.84	23.85	31.61	38.39	42.17	54.49	71.23
32	24	20.23	23.21	34.11	25.17	34.81	44.36	45.40	58.02	78.47
33	15	23.39	26.18	38.49	26.66	36.79	46.66	50.05	62.97	85.15
34	30	25.20	28.85	39.53	29.85	37.92	53.42	55.05	66.77	92.95
35	12	28.42	32.94	42.0	32.56	40.33	54.02	60.98	73.27	96.05
36	31	29.99	33.36	43.53	34.38	42.50	55.51	64.37	75.86	99.04
37	16	30.88	34.07	46.43	35.78	43.87	59.32	66.66	77.94	105.75
Total	260									

dinally measured by using VOCAL technique. Further studies are needed to calculate precise estimation of this reference interval of the fetal lung volume for pulmonary hypoplasia diagnosis.

In conclusion, this is the normal fetal lung volume in Thai population using the rotational technique (VOCAL). It could be considered as a reference for prenatal diagnosis of pulmonary hypoplasia after testing its utilization.

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