Nomogram of the Lungs Area by Tracing Method to Head Circumference Ratio in Normal Thai Fetuses at 20-40 Weeks of Gestation

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ABSTRACT

Objective: To establish the reference intervals with gestation for the area of the lungs to head circumference ratio (LHR) by tracing method in normal Thai fetuses at 20-40 weeks of gestation.

Methods: This was a prospective longitudinal descriptive study of 60 normal singleton pregnancies at 20-40 weeks of gestation. Right and left lung areas were obtained by manual tracing of the borders of the lungs technique at four-chamber view level. The examination was repeated every 4 weeks. Inter-observer and intra-observer reliabilities were assessed and the results showed very good correlation.

Results: The mean left lung area increased with gestational age from 246 mm^2 at 20 weeks to 646 mm^2 at 35 weeks and then slightly decreased to 622 mm^2 at 40 weeks. The mean right lung area increased from 354 mm^2 at 20 weeks to 938 mm^2 at 35 weeks and then slightly decreased to 795 mm^2 at 40 weeks. Accordingly, the left LHR increased with gestational age from 1.38 at 20 weeks to 2.02 at 34 weeks and slightly decreased to 1.80 at 40 weeks. The right LHR increased from 1.98 at 20 weeks to 2.93 at 34 weeks and slightly decreased to 2.30 at 40 weeks.

Conclusion: The reference intervals with gestation for the lungs' area to head circumference ratio (LHR) by tracing method in normal Thai fetuses at 20-40 weeks of gestation was established. The left and right LHR increased with gestational age from 20-34 weeks and then slightly decreased after that.

Keywords: Congenital diaphragmatic hernia, lungs' area, lung-to-head ratio, pulmonary hypoplasia, ultrasonography

Siriraj Med J 2014;66:75-78

E-journal: http://www.sirirajmedj.com

INTRODUCTION

Congenital diaphragmatic hernia (CDH) is a common cause of fetal and neonatal pulmonary hypoplasia and occurs sporadically with an incidence of 1/2,500 to 1/5,000 of newborns, depending on whether stillbirths are included.[1] The rate of prenatal detection has been increasing over time, and is now over 50%.[2-4] About 40% of cases have associated anomalies which are an independent predictor of neonatal death. The survival rate in this group is approximately 15% or less.[5,6] The majority that have an isolated defect have been reported with the survival rate of 60-80%.[7-11] Fetal lungs, either ipsilateral or contralateral or both, in CDH have severe developmental arrest of both airway and vessels, resulting in lung hypoplasia which is associated with high postnatal mortality.[12-14] Prenatal diagnosis and advancements in neonatal care have led to improved neonatal survival, but there remains a significant risk of morbidity in survivors, mainly due to lung hypoplasia and pulmonary hypertension.[14-16]

Prediction of severity of pulmonary hypoplasia and, thus, postnatal survival relies on imaging modalities that indirectly assess fetal lung volume. The most commonly used method is the measurement of lungs' area to head circumference ratio (LHR) using 2D ultrasound (US).[7,9,17-26] Many studies have reported improved neonatal survival with increasing LHR. However, the reported results on LHR performance lacked consistency, probably because of different criteria being used for patients' selection and different methodologies being used in the estimation of the lungs area.[21,27-30] Recently, it was reported that lungs' area derived by tracing method rather than diameter-derived method was more reliable.[31] Furthermore, the

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Received 23 May 2013
Revised 19 September 2013
Accepted 24 September 2013

LHR is a gestational age-dependent value that changes with fetal size. Using a certain value of LHR to predict fetal pulmonary hypoplasia at different gestational ages has been criticized to be less reliable.[24,32] Attempts to account for this variability have been made by adjusting the observed LHR against the expected value for gestational age, resulting in the observed to expected LHR ratio (O/E-LHR). Clinical studies suggest that O/E-LHR yields more accurate prediction of pulmonary hypoplasia.[33,34]

For Thai fetus, the construction of the reference intervals for lungs area by tracing method to head circumference ratio (LHR) with gestation has never been done before. Therefore, the aim of this study was to establish the reference intervals for the fetal lungs' area by tracing method to head circumference ratio (LHR) in normal Thai fetuses between 20-40 weeks of gestation.

MATERIALS AND METHODS

In this prospective longitudinal study, carried out in our center between January 2010 and January 2011, Thai women with singleton pregnancies at mid-gestation were invited to participate in the study. The institutional ethical committee approved the study (EC number 300/2553) and all the participants gave their written informed consents. The gestational age was confirmed by either correct menstrual history or ultrasound examination before 20 weeks. The fetal lungs area and head circumference were measured using two-dimensional (2D) ultrasound in 60 cases every 4 weeks. All examinations were performed transabdominally with a Voluson 730 Expert/ Voluson E8 scanner (GE Medical, systems, Milwaukee, WI, USA) equipped with a 2-7 MHz curve abdominal transducer. A transverse section of fetal chest, containing the four-chamber view of the heart, was obtained in fetal quiescent state. The areas of the right and the left lung were measured using manual tracing of the borders of the lungs technique (Fig 1). The head circumference (HC) was measured in the standard biparietal diameter view. The

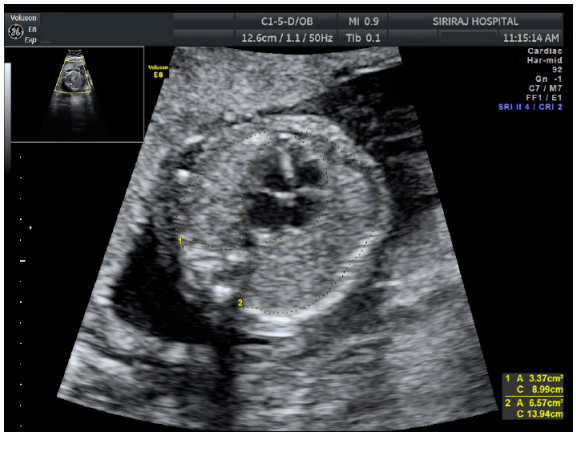

Fig 1. Demonstrates the measurement of lungs area by manual tracing technique. The picture is the cross section of fetal chest showing 4-chamber view of the fetal heart. Manual tracing of the borders of left (1) and right (2) lungs was made (yellow dotted lines) and the value of lungs area were achieved.

LHR was obtained by dividing the calculated area of each lung (mm^2) by the head circumference (mm). Neonatal outcomes were recorded and the cases with respiratory morbidities other than respiratory distress syndrome of prematurity, or unavailable data were excluded from the study. The cases that had abnormal fetal growth both larger and smaller than usual, either by the fetal factors or maternal medical/obstetrical disorders were also excluded.

Intra-observer and inter-observer agreement were assessed in 21 randomly selected cases. The retrieved pictures of fetal lungs were re-measured by the same operator (K.B.) and the results compared with the prior results and also with the results from the other experienced operator (P.W.).

Statistical analysis

The statistical software package SPSS version 13.0 (SPSS, Chicago, IL, USA) was used for descriptive analysis of mean and standard deviation (SD) of right and left lung areas and HC at each gestational week. The graphs of right and left LHR against gestational age were generated. Intra-class correlation coefficient (ICC) for inter- and intra-observer variation were also calculated using the same software.

RESULTS

The fetal lungs were successfully measured in all pregnancies and only 51 cases were included for analysis. The frequency of the examination was the highest at 28 and 32 weeks, 17 times, and lowest at 40 weeks, 1 time, totaling 217 times in all gestational ages.

The mean left lung area increased with gestational age from 246 mm^2 at 20 weeks to the maximum of 646 mm^2 at 35 weeks and then slightly decreased conversely with the gestational age to 622 mm^2 at 40 weeks (Table 1). The mean right lung area increased with gestational age from 354 mm^2 at 20 weeks to the maximum of 938 mm^2 at 35 weeks and then slightly decreased to 795 mm^2 at 40 weeks (Table 2).

The left LHR increased with gestational age from 1.38 at 20 weeks to 2.02 at 34 weeks and slightly decreased conversely with the gestational age to 1.80 at 40 weeks (Fig 2). The right LHR increased with gestational age from 1.98 at 20 weeks to 2.93 at 34 weeks and slightly decreased to 2.30 at 40 weeks (Fig 3).

Intra class correlation coefficients of intra-observer and inter-observer reliability were 0.999 and 0.998, respectively.

DISCUSSION

Our results showed that the left fetal lungs' areas were smaller than the right side at all gestational ages. This is the result of the fetal heart that occupies more in the left side of the thoracic cavity than the right side. Left and right lung areas increased with gestational age to 35 weeks and then slightly decreased afterwards. We believed that the fetal lungs did not decreased in size with time, but this possibly resulted from rapid growth of the

fetal heart especially at four-chamber level during the late gestational period. To confirm our belief, we measured the fetal thoracic cavity area and fetal cardiac area at four-chamber view and found the continuous increment throughout gestations (data not shown). Fetal lungs, occupy the thoracic cavity from below the clavicle to above the diaphragm, have irregular shape and may look smaller at four-chamber level after 35 weeks owing to the pressure effect of the fetal heart, which can still grow in other directions to maintain the growth of the fetal lungs. A nomogram of fetal lungs volume performed in 60 Thai fetuses in the year 2009 (unpublished data) also showed continuous increment of fetal lungs' volume throughout gestations and this confirms our explanation.

Decrement of fetal lungs' area after 35 weeks resulted in decrement of LHR in the same period. The unstable value of LHR throughout gestations seen in our study confirms previous suggestions that a certain cutoff of LHR was less reliable in predicting pulmonary hypoplasia at different gestational ages and should not be used. Using LHR as a percentage of normal mean for gestation (O/E LHR) can overcome this error and we believed that it can be used even after 35 weeks when LHR is decreased. Although the use of LHR or O/E LHR at late gestational ages is quite uncommon, because most cases of CDH are delivered when the lung maturity is confirmed, but the situation in Thailand is different. Many Thai women do not show up early for antenatal care and some cases of CDH may be diagnosed at very advanced gestational age. O/E LHR may be useful to predict postnatal survival and the parents can be prepared through the process of counseling.

The strength of this study was that it was a longitudinal study which could show better trend of a parameter

TABLE 1. Left lung area from 20 to 40 gestational weeks.

GA	N	Median	Minimum	Maximum	Mean	Std. Deviation
20	8	243.46	236.44	258.43	246.95	7.62
21	7	268.30	232.15	287.45	266.85	20.75
22	9	302.86	265.33	328.19	303.18	19.90
23	6	360.27	345.78	384.57	363.13	16.50
24	13	374.18	358.66	427.56	380.58	21.39
25	11	392.80	354.37	437.98	397.69	24.97
26	11	432.80	385.42	506.43	436.15	28.85
27	9	487.32	465.38	504.38	483.76	14.34
28	17	498.22	480.53	553.29	508.77	24.67
29	12	523.05	480.24	597.63	528.69	31.83
30	12	555.55	501.78	642.40	567.58	41.50
31	10	589.38	570.43	614.97	592.33	15.69
32	17	588.46	567.28	644.98	598.38	25.98
33	12	605.55	556.21	667.58	605.56	30.42
34	12	625.51	579.32	705.23	636.10	40.13
35	10	643.19	628.85	668.42	646.87	15.35
36	16	632.48	606.13	684.29	643.02	26.52
37	11	647.59	593.64	695.42	639.72	28.00
38	9	625.42	612.54	712.48	648.78	38.94
39	4	644.58	618.76	663.52	642.86	19.83
40	1	622.36	622.36	622.36	622.36	.
Total	217	558.32	232.15	712.48	520.05	126.99

TABLE 2. Right lung area from 20 to 40 gestational weeks.

GA	N	Median	Minimum	Maximum	Mean	Std. Deviation
20	8	356.35	340.57	364.13	354.26	7.71
21	7	398.46	364.87	408.62	390.80	16.99
22	9	452.93	418.96	478.32	454.35	19.46
23	6	522.54	512.23	544.26	526.57	14.51
24	13	568.39	543.76	620.34	573.25	22.42
25	11	598.69	556.63	643.36	600.11	25.06
26	11	653.76	605.23	712.49	656.66	26.60
27	9	724.88	706.84	758.32	726.45	16.61
28	17	748.95	734.67	804.27	761.07	23.11
29	12	787.64	744.24	857.44	791.86	30.57
30	12	838.68	781.49	934.68	851.89	42.39
31	10	869.52	854.43	903.66	875.84	16.95
32	17	875.42	854.03	931.78	881.86	25.48
33	12	897.47	846.73	957.43	898.15	29.90
34	12	913.99	872.16	995.34	925.25	40.13
35	10	936.09	915.43	958.43	938.40	15.70
36	16	924.27	905.72	975.32	934.72	25.42
37	11	897.45	843.12	945.74	893.22	27.55
38	9	859.85	845.18	943.63	881.14	40.22
39	4	863.53	819.76	875.89	855.68	24.71
40	1	795.26	795.26	795.26	795.26	.
Total	217	832.34	340.57	995.34	761.47	175.73

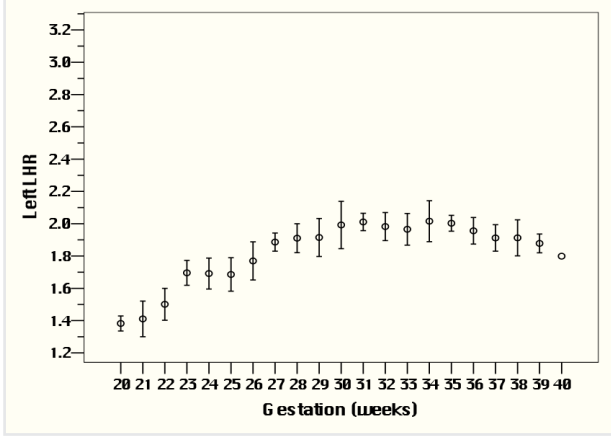

Fig 2. Left lung area to head circumference ratio (LHR) against gestational age (weeks).

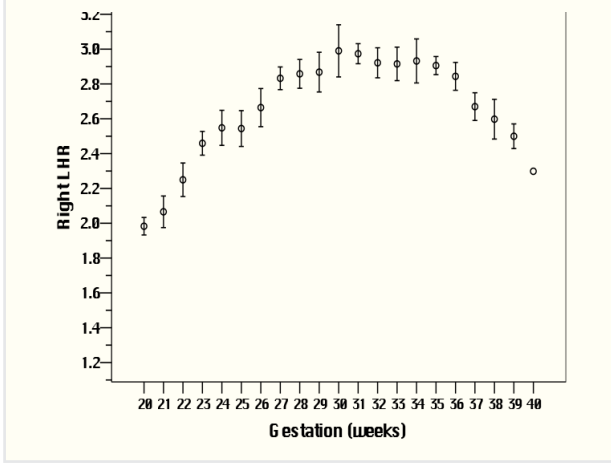

Fig 3. Right lung area to head circumference ratio (LHR) against gestational age (weeks).

provided that the distribution of samples at each time interval were not too different. Using coefficient of variation, we found that the difference of data at each gestational age in our study was less than 10% which made our results reliable. One limitation of the study was the accuracy of lungs area measurement may be less at later gestational age owing to the acoustic shadows from fetal ribs that obscure the border of the lungs. We believe that using the mean value of measurement from many cases can overcome this limitation. The other limitation was the small number of measurements at late gestational age e.g. after 37 weeks which could make the LHR values at these gestational ages less reliable and should be used with caution.

We believe that our study provides a useful reference interval with gestation, for the fetal lungs' area to head circumference ratio, in normal Thai fetus, for physicians who face a fetus at risk of pulmonary hypoplasia from various causes. Further studies should be conducted to confirm the usefulness and accuracy of O/E LHR by the tracing method forprediction of postnatal survival rate in Thai fetuses at risk of pulmonary hypoplasia.

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