

## Original Article

## Correlation between the transverse diameter of the fetal thymus gland and gestational age of fetus in normal singleton pregnancy

Obstetric & Gynecology

Rehab M. Megahed<sup>1</sup>, Asmaa A. El-sheikh<sup>1</sup>, Hagar A. Magdy<sup>2</sup>

<sup>1</sup> Forensic Medicine and Clinical Toxicology Department, Faculty of Medicine for Girls, Cairo, Al-Azhar University, Egypt.

<sup>2</sup> Obstetrics and Gynecology Department, Faculty of Medicine for Girls, Cairo, Al-Azhar University, Egypt.

### ABSTRACT:

**Background:** The determination of gestational age has a critical role in clinical practice on a daily basis for optimal neonatal management. Measurement of the transverse diameter of fetal thymus (TL) can be utilized for estimating the gestational age (GA).

**Objective:** to determine the accuracy of TL in estimation of GA of the fetus and to correlate TL with conventional fetal parameters viz. head circumference (HC), bi-parietal diameter (BPD), abdominal circumference (AC), femur length (FL) and with the GA, also, to detect linear regression formulae for estimation of the GA from TL and the other conventional fetal parameters.

**Methodology:** This hospital based cross-sectional research was carried out on 282 pregnant women visited the outpatient obstetric clinic at Al-zahraa University hospital, from July to December 2022. Women with Singleton viable apparently normal fetus, GA between 17- 39 weeks were chosen to conduct the study. TL and the other conventional fetal parameters viz. BPD, HC, AC and FL were measured by ultrasound.

**Results:** There was an increase in the length of TL in relation to the increase of GA in weeks. There was a highly significant correlation (r) between the conventional fetal parameters viz. BPD, HC, AC, FL and TL also between the TL and GA. The linear regression formulae of TL and the other conventional fetal parameters had a statistically significant effect on estimating of the gestational age.

**Conclusion:** There was a highly positive correlation between TL, the conventional fetal parameters viz. BPD, HC, AC, FL and GA. The TL gland can be used for estimation of GA.

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**Key words:** Thymus gland, gestational age, ultrasound.

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**Corresponding author:** Rehab Mohamed Megahed, Forensic medicine and clinical toxicology department, faculty of medicine for girls, Cairo, Al-Azhar University, Egypt. **Tel:** 01120080162 **E-mail:** [rehabmegahed2015@gmail.com](mailto:rehabmegahed2015@gmail.com) - [rehabmohamed.medg@azhar.edu.eg](mailto:rehabmohamed.medg@azhar.edu.eg)

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## INTRODUCTION

Gestational age (GA) is the age of an unborn fetus. Several fetal parameters can be measured in ultrasound scan and serial ultrasound scan to assess GA during pregnancy to monitor fetal growth<sup>[1]</sup>. Estimation of the GA is crucial for the daily clinical practice and for providing the best neonatal management, preventing premature labor, and appropriately timing for chorionic villus sample<sup>[2]</sup>. Calculation of the GA is important in forensic medicine for number of reasons including vitality assessments, diagnosis of pathological conditions that may impair development, medical termination of pregnancy, and differentiating between aborted and stillborn fetuses, along with legal and illegal abortions. Sole biological profile element accurately achievable from fetal remains is the gestational age, which is helpful in forensic situations

to aid in the identification or assessment of the fetal viability<sup>[3]</sup><sup>[4]</sup>.

The fetal sonographic examinations also reveal details regarding fetal growth and the anticipated birth date, calculating fetal weight and identifying improper growth. A number of ultrasonic biometric parameters were provided by the real-time ultrasound scanner to determine GA. Most frequently, fetal measurements such as bi-parietal diameter (BPD), crown-rump length, head circumference, and femur length are employed to calculate GA<sup>[5]</sup>. The thymus gland is a bi-lobed essential organ of cellular branch of the immune system that performs crucial participation in selection, differentiation and development of T-cell lymphocytes<sup>[6]</sup>. The thymus organogenesis starts at third brachial

cleft and the first lymphocytes develops in the thymus in ninth week of pregnancy<sup>[7]</sup>.

Recent studies indicate the possibility of using measurement of transverse diameter of fetal thymus as ultrasound screening tool for estimating the GA. So that, the objective of this research was to determine accuracy of the transverse diameter of the fetal thymus (TL) in estimation of the GA of the fetus and to correlate TL with the other conventional fetal parameters viz. bi-parietal diameter (BPD), head circumference (HC), abdominal circumference (AC), and femur length (FL) and also with GA, and to detect linear regression formulae for estimation of the GA from TL and the other conventional fetal parameters.

## PATIENTS AND METHODS

This hospital based cross-sectional study included 282 pregnant women with age ranged from 19-37 years; all attended a routine antenatal care at outpatient obstetric clinic of Al-zahraa university hospital. The study was conducted at the period between July to December 2022. The research was done according to the ethics guidelines approved by the Research Ethics Committee at Al-Azhar University's Faculty of Medicine for Girls, Egypt. This follows the principles of the Helsinki Declaration.

### Inclusion criteria

Women with Singleton viable apparently normal fetus, Gestational age between 17- 39 weeks which is calculated from the last normal menstrual period and confirmed by ultrasound dating.

### Exclusion criteria

Women who were hesitant about her dates or those with abnormal fetus, multiple gestations, intrauterine fetal death, and subjects with medical disorders like diabetes mellitus and hypertension.

### All the included women after taking their informed consent either oral or written were subjected to:

Complete history taking which include Personal history (age, occupation, residence, special habits, ...etc), menstrual history mainly last menstrual period (LMP), obstetric history or operative complication and family history of (diabetes millets, hypertension, congenital anomalies, and consanguinity). General examination, abdominal examination, full routine investigation, and ultrasonic examination.

Ultrasonography examinations were carried using general electric (GE) ultrasound machine (2D trans-abdominal 3.5 MHz probe in the ultrasound unit in the obstetric clinic at Al-zahraa University Hospital). All women subjects were in a slightly slanted position with head of the bed raised 30 degrees and with a tiny pillow under the left lion.

Abdominal ultrasound examination were done mainly to determine the transverse diameter of the fetal thymus (TL), and the other conventional fetal parameters viz. bi-parietal diameter (BPD), head

circumference (HC), abdominal circumference (AC) and femur length (FL).

The fetal thymus was found between great heart vessel ("the three vessels" view) and the sternum in transverse section of the fetal chest. Maximum transverse diameter of the fetal thymus was measured positioning a line cursor upright to junction between the sternum and the spine. Each measurement was performed three times in each fetus. The average size was calculated and used for statistical analysis<sup>[8]</sup>.

The transverse diameter of fetal thymus was measured between 17- 39 weeks of gestational age routinely during the prenatal fetal ultrasound examination in the second and the third trimester of the pregnancy, as the first lymphocytes develops in the thymus in ninth week of pregnancy<sup>[7]</sup>. The thymus measurements did not perform before 17 weeks of gestation because at early age it is too small and there is no well-defined boundary between the thymus and the lungs<sup>[9]</sup>.

### Statistical analysis

Statistical analysis was done with IBM® SPSS® (Statistical Product and Service Solutions program), Version 20 for Windows. Descriptive statistics included the minimum, maximum, mean, and standard deviation ( $\pm$  SD) values. Pearson's correlation (r) was used to determine significant correlation between different fetal measurements and gestational age. Regression analysis (linear regression equations) has been computed to estimate gestational age from different fetal measurements.

## RESULTS

In the present study, 282 pregnant women with singleton uncomplicated pregnancies with no congenital anomalies were included. The mean age of women was (27.63 $\pm$ 5.45) years ranged between 19-37 years. The gestational age in weeks ranged from 17-39 weeks with Mean $\pm$  SD=28.34 $\pm$ 6.95 which was calculated by using the first day of last normal menstrual period (LMP) and corroborated with ultrasound dating (table 1).

The transverse diameter of the fetal thymus was measured using two-dimensional sonography at various gestational ages ranging from 17 to 39 weeks depending on (LMP). It was observed that there was an increase in the mean of TL in millimeter (mm) in relation to the increase of the GA in weeks (table 2).

Other conventional parameters viz. BPD, HC, AC and FL were also measured at the (17- 39) weeks of gestational age. The mean values of the BPD, HC, AC, F.L and TL were 71.44 $\pm$ 17.37, 253.73 $\pm$ 64.60, 239.01 $\pm$ 71.50, 53.42 $\pm$ 16.39 and 26.43 $\pm$ 8.66 respectively as shown in (table 3).

There was significant positive ( $p < 0.05$ ) correlation between the conventional fetal parameters viz. BPD ( $r=0.974$ ), HC ( $r=0.972$ ), AC ( $r=0.980$ ), FL ( $r=0.983$ ) and TL (table 4).

There was significant positive ( $P < 0.05$ ) correlation ( $r$ ) between the conventional fetal parameters viz. BPD

( $r=0.991$ ), HC ( $r=0.991$ ), AC ( $r=0.998$ ), FL ( $r=0.999$ ) as well as T.L ( $r=0.985$ ) and GA (table 5, and figure 1). The linear regression equations of the conventional fetal parameters and TL [ $GA = 7.462 + 0.790 \times T.L$  (mm)] ( $R = 0.985$ ), had statistically significant ( $P < 0.05$ ) effect on predicting the fetal gestational age (table 6).

**Table (1): Maternal and Gestational age of the studied fetuses**

Items	Pregnant women (n = 282)
<b>Maternal age (Years)</b>	
Range	19- 37
Mean± SD	27.63±5.45
<b>Gestational age (Weeks)</b>	
Range	17-39
Mean± SD	28.34±6.95

SD: Standard deviation

**Table (2): Mean of the transverse diameter of the fetal thymus at each gestational age**

GA (Weeks)	Number of Pregnant women	TL (mm)	
		Range	Mean ± SD
17	13	12 - 16	13.62 ± 1.39
18	11	11 - 18	14.64 ± 2.38
19	13	13 - 17	15.46 ± 1.13
20	12	14 - 19	16.00 ± 1.76
21	16	15 - 20	17.19 ± 1.83
22	15	15 - 21	18.27 ± 1.94
23	10	18 - 21	19.50 ± 1.08
24	11	18 - 21	19.64 ± 1.03
25	12	20 - 23	21.42 ± 0.79
26	8	20 - 24	22.25 ± 1.17
27	6	23 - 29	25.33 ± 2.50
28	8	24 - 29	25.63 ± 1.59
29	11	27 - 30	28.36 ± 1.36
30	13	27 - 31	28.69 ± 1.55
31	12	29 - 32	29.67 ± 0.89
32	15	27 - 34	30.67 ± 1.54
33	11	30 - 34	31.46 ± 1.21
34	15	31 - 35	33.20 ± 1.08
35	12	34 - 37	35.58 ± 0.90
36	16	35 - 38	36.25 ± 0.93
37	10	35 - 39	37.40 ± 1.51
38	15	36-41	38.60 ± 1.24
39	17	38 - 41	39.18 ± 1.02

GA: Gestational age, SD: Standard deviation, TL: Transverse diameter of the fetal thymus gland, mm: millimeter

**Table (3): Mean of different fetal biometry from (17- 39) weeks of gestational age**

Fetal biometry in (mm)	Range	Mean± SD
<b>BPD</b>	41-95	71.44±17.37
<b>HC</b>	135-341	253.73±64.60
<b>AC</b>	115-345	239.01±71.50
<b>FL</b>	25-80	53.42±16.39
<b>TL</b>	11-41	26.43±8.66

BPD: Bi-parietal diameter; HC: Head circumference; AC: Abdominal circumference; FL: Femur length; TL: Transverse diameter of the fetal thymus gland; mm: millimeter; SD: Standard deviation

**Table (4): Correlation between transverse diameter of the fetal thymus and the conventional fetal parameters**

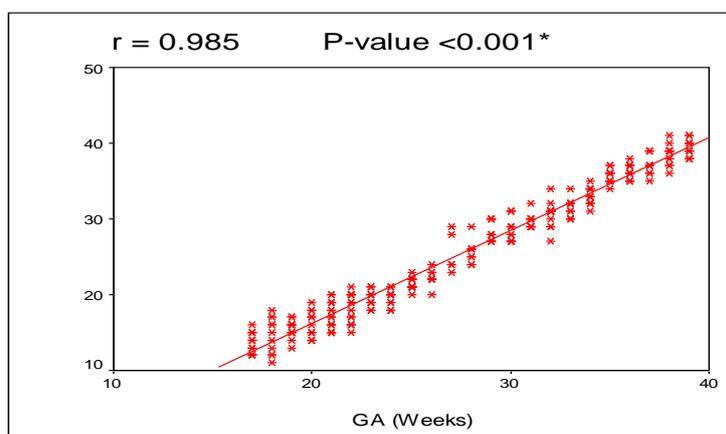
Fetal parameters in (mm)	TL (mm)	
	r	p-value
<b>BPD</b>	0.974	0.001*
<b>HC</b>	0.972	0.001*
<b>AC</b>	0.980	0.001*
<b>FL</b>	0.983	0.001*

r: Pearson’s correlation coefficient, TL: Transverse diameter of the fetal thymus gland, BPD: Bi-parietal diameter, HC: Head circumference, AC: Abdominal circumference, FL: Femur length; mm: millimeter; \*: Significant p value (<0.05).

**Table (5): Correlation between fetal gestational age in weeks and the different fetal biometry**

Fetal biometry in (mm)	Fetal GA (Weeks)	
	r	p-value
<b>BPD</b>	0.991	0.001*
<b>HC</b>	0.991	0.001*
<b>AC</b>	0.998	0.001*
<b>FL</b>	0.999	0.001*
<b>TL</b>	0.985	0.001*

r: Pearson’s correlation coefficient, GA: Gestational age, BPD: Bi-parietal diameter; HC: Head circumference, AC: Abdominal circumference, FL: Femur length, TL: Transverse diameter of the fetal thymus gland; mm: millimeter, \*: Significant p value (< 0.05).



**Figure 1: Scatter plot for correlation between the transverse diameter of the thymus gland (TL) in millimeter (mm) and the gestational age in weeks**

**Table (6): Linear regression equations for predicting the fetal gestational age from the conventional fetal parameters and the transverse diameter of the fetal thymus**

Fetal parameters in (mm)	Linear regression formulae	r	r <sup>2</sup>	SEE	t-value	p-value
<b>B.P.D</b>	<b>GA= 0.018 +0.397 × B.P.D (mm)</b>	0.991	0.983	0.910	126.82	0.001*
<b>H.C</b>	<b>GA= 1.306 +0.107 × H.C (mm)</b>	0.991	0.982	0.936	123.35	0.001*
<b>A.C</b>	<b>GA= 5.166 +0.097 × A.C (mm)</b>	0.998	0.996	0.426	272.75	0.001*
<b>F.L</b>	<b>GA= 5.716 +0.424 × F.L (mm)</b>	0.999	0.998	0.305	381.34	0.001*
<b>T.L</b>	<b>GA= 7.462 +0.790 × T.L (mm)</b>	0.985	0.969	1.216	94.29	0.001*

GA: Gestational age, SEE: Standard error of estimate, R: Correlation coefficient, R<sup>2</sup>: Coefficient of determination, BPD: Bi-parietal diameter, HC: Head circumference, AC: Abdominal circumference, FL: Femur length, TL: Transverse diameter of the fetal thymus gland, mm: millimeter, t: Student t-test, \*: Significant p value (< 0.05).

**DISCUSSION**

The transverse diameter of the thymus gland is easier to measure than the perimeter because of its relationship with lungs, which demarcates the lateral boundaries of the thymus [8]. This study was conducted to verify the relation between TL and GA, also with the conventional fetal parameters viz. BPD, HC, AC, and FL and for prediction of GA from TL measurements. The number of the pregnant women included in the study was in accordance with those of Tangshewinsirikul and Panburana [9], Cho et al. [10] and Asghar et al. [11].

Based on a statistical analysis, the present study revealed that TL increased in a linear manner with increase of the gestational age. There was significant positive correlation (r) between the conventional fetal parameters viz. BPD, HC, AC, FL and TL. Also, there was significant positive correlation (r) between the TL and GA. In accordance, Tangshewinsirikul and Panburana [9] conducted their study on 296 singleton pregnancies between 17 and 38 weeks of gestation and found that the maximal transverse diameter of thymus increased throughout pregnancy. Also, Cho et al. [10]

stated that the transverse diameter of the fetal thymus increased with increasing GA in a linear manner and detected a statistically significant correlation between the thymus diameter and GA, AC and FL. Similarly, Asghar et al. [11] who studied 89 fetuses between 12 and 40 weeks of gestational age and found that the Transverse diameter of thymus increased throughout pregnancy as GA advanced and it has strong relationship with GA.

Varol et al. [12] and Salomon et al. [13] stated that the ultrasonography was used to determine gestational age in pregnancy. The conventional fetal parameters viz. BPD, HC, AC, and FL are used widely for the gestational age assessment. The BPD and FL are the most accurate tools for estimating gestational age. As in the current work there was significant positive correlation ( $r$ ) between these conventional fetal parameters as well as TL ( $r=0.985$ ) and GA so TL can be utilized for estimation of fetal GA. Our findings were in accordance with those previously reported by Gamez et al. [14] concerning the sonographic changes in the fetal thymus transverse diameter during the second and third trimesters of an uncomplicated singleton pregnancy.

The results of the present study emphasized that the linear regression formulae of the conventional fetal parameters and TL [ $GA= 7.462 +0.790 \times T.L$  (mm)] ( $R= 0.985$ ) had statistically significant effect on estimating of the gestational age. In agreement, Musilova et al. [7] found that the regression equation of the transverse diameter of the fetal thymus as an indicator of gestational age to be highly statistically significant in estimating the gestational age with correlation coefficients,  $r=0.91$ . Also, in accordance with Tangshewinsirikul and Panburana [9] who stated that the regression equation for maximal transverse diameter of the thymus as a function of GA had statistically significant effect on estimating of gestational age ( $r = 0.915$ ;  $p < 0.001$ ). Asghar et al. [11] concluded that the regression equation for a transverse diameter of the thymus has strong relationship with GA.

## CONCLUSION

Thymus gland transverse diameter can be easily measured and could be a relevant measure for estimation of gestational age; the linear regression formulae of the conventional fetal parameters and the transverse diameter of the fetal thymus had a statistically significant effect on estimating of gestational age. This is a minor cross-sectional study so to do general equation a large scale study should be done.

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## الملخص العربي

الارتباط بين القطر المستعرض للغدة الصعترية الجنينية والعمر الحملي للجنين في حالات الحمل المنفرد الطبيعي

ريحاب محمد مجاهد<sup>1</sup>، أسماء عبده الشيخ<sup>1</sup>، هاجر عبد الجواد مجدي<sup>2</sup>

<sup>1</sup> قسم الطب الشرعي والسموم الاكلينيكية، كلية طب بنات، القاهرة، جامعة الازهر، جمهورية مصر العربية  
<sup>2</sup> قسم أمراض النساء والتوليد، كلية طب بنات، القاهرة، جامعة الازهر، جمهورية مصر العربية.

### ملخص البحث:

**الخلفية:** إن تحديد عمر الحمل له دور كبير في المتابعة الإكلينيكية بشكل يومي للمعالجة المثلى للمواليد. ويمكن استخدام قياسات القطر المستعرض للغدة الصعترية الجنينية في تحديد عمر الحمل للجنين.

**الهدف:** هو تقييم دقة قياسات القطر المستعرض للغدة الصعترية للجنين في تقدير العمر الحملي للجنين وربط قياسات القطر المستعرض للغدة الصعترية للجنين مع القياسات الجنينية المعتادة مثل محيط الرأس والقطر الثنائي للرأس ومحيط البطن وطول الفخذ وأيضاً مع عمر الحمل للجنين. وكذلك لصياغة معادلات الانحدار الخطي لتقدير العمر الحملي للجنين من قياسات القطر المستعرض للغدة الصعترية للجنين ومن القياسات الجنينية المعتادة الأخرى .

**الطرق:** اجري هذا البحث المقطعي على 282 من النساء الحوامل اللاتي قمن بزيارة العيادة الخارجية لقسم النساء والتوليد بمستشفى الزهراء الجامعي. في الفترة من يوليو إلى ديسمبر 2022. وقد تم اختيار النساء الحوامل اللاتي لديهن جنين منفرد وحى وطبيعي ، واللاتي تتراوح أعمار الحمل لديهن بين 17 و 39 أسبوعاً لإجراء هذه الدراسة. وقد تم قياس القطر المستعرض للغدة الصعترية للجنين، والقياسات المعتادة الأخرى مثل القطر الثنائي للرأس، ومحيط الرأس، ومحيط البطن، وطول الفخذ وذلك باستخدام الموجات فوق الصوتية.

**النتائج:** أوضحت نتائج هذه الدراسة انه كانت هناك زيادة في طول القطر المستعرض للغدة الصعترية الجنينية بزيادة عمر الحمل للجنين بالأسابيع. و كان هناك ارتباط معنوي ( $r$ ) بين القياسات الجنينية المعتادة مثل القطر الثنائي للرأس، ومحيط الرأس، ومحيط البطن، و طول الفخذ، و القطر المستعرض للغدة الصعترية للجنين وأيضاً بين القطر المستعرض للغدة الصعترية للجنين وعمر الحمل للجنين. وقد كان لمعادلات الانحدار الخطي للقطر المستعرض للغدة الصعترية للجنين تأثير ذو دلالة إحصائية على تقدير عمر الحمل للجنين.

**الاستنتاجات:** وقد خلصت هذه الدراسة الي انه كان هناك ارتباط إيجابي للغاية بين القطر المستعرض للغدة الصعترية للجنين والقياسات الجنينية المعتادة مثل القطر الثنائي للرأس، ومحيط الرأس، ومحيط البطن، و طول الفخذ، وعمر الحمل للجنين. كما اوضحت هذه الدراسة انه يمكن استخدام القطر المستعرض للغدة الصعترية للجنين لتقدير عمر الحمل للجنين.

**الكلمات المفتاحية:** الغدة الصعترية، عمر الحمل للجنين، الموجات فوق الصوتية.

الباحث الرئيسي

الاسم: ريحاب محمد مجاهد، قسم الطب الشرعي والسموم الاكلينيكية، كلية طب بنات، القاهرة، جامعة الازهر، جمهورية مصر العربية.

الهاتف: 01120080162

البريد الالكتروني : rehabmegahed2015@gmail.com / rehabmohamed.medg@azhar.edu.eg