Nomogram of Intracranial Translucency in the First Trimester Ultrasound of Pregnant Women at Thammasat University Hospital

Tongta Nanthakomon MD*, Densak Pongrojpaw MD*,
Athita Chanthasenannont MD*, Charintip Somprasit MD*,
Chamnan Tanprasertkul MD*, Komsun Suwannarurk MD*

** Department of Obstetrics and Gynaecology, Faculty of Medicine, Thammasat University, Pathumthani, Thailand*

Objective: *The aim of the study was to determine normative values of intracranial translucency (IT) by ultrasonography in singleton pregnant women patient at Thammasat University Hospital during the first trimester.*
Material and Method: *The first trimester singleton pregnant women (11-13 weeks) underwent routine ultrasonography screening. The gestational age was calculated by measuring the length of the embryo or fetus from the top of its head to bottom of the buttocks (crown-rump length; CRL) and IT of the brain region in the mid-sagittal planefetal face position. Repeated ultrasonography was performed in the second trimester period as well as after birth infant check-up for disability.*
Results: *One hundred and ninety one singleton pregnant women were examined by an ultrasonography to measure CRL, GA and IT. The average age was 29.71±5.09 years (16-39 years). All participants were healthy without a history of anomaly in previous pregnancies. Half of cases were nulliparity. Participants were followed until birth. There was no open neural tube defect baby in this study. Median GA, CRL and IT in this study were 12.6±0.7 weeks, 64.0±10.2 (40.0-80.9) and 1.3±0.3 (0.5-2.5) mm, respectively. IT measurement value increased in correlation with increasing CRL and advancing GA ($p<0.05$).*
Conclusion: *IT values increased significantly with CRL and GA increasing.*

Keywords: *First trimester, Intracranial translucency, Ultrasound*

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Ultrasonography was a very helpful study for pregnant women. The first trimester ultrasonography played a significant role as it could be used to calculate an accurate gestation date and also create maternal fetal interaction. Important of early recognizable ultrasonography marker reminded the physicians to repeat early second trimester scan. Since termination of pregnancy during the first trimester is known to present fewer complications and less effect on mother's feeling compared to the older gestational age.

In previous literatures[1], values or markers of the first trimester ultrasonography was a tool for prenatal diagnosis. For example, nuchal translucency (NT) was extensively studied and used for Down's syndrome diagnosis. The normative values was well accepted and commonly used. Intracranial translucency (IT) could be used in prenatal diagnosis/early detection of open neural tube defects (NTD), for example spina bifida. IT was the measurement of the fourth ventricle at 11-14 week by measuring at anechoic under the brain stem in mid-sagittal plane, which was the same position used for nuchal translucency assessment and nasal bone measurement. If IT could not be found or is very small, there is a risk of spina bifida caused by an obstruction of the cerebrospinal fluid flow. It was important earlier recognizable sonographic marker, which has been suggested for detection of spina bifida. IT value has a direct variation with advancing gestation or increasing CRL baby's length. There are normative values of IT in some countries. However, there is no standard value in Thai population. Thus, the background of this study is to determine the normative value of IT that can be used as a reference for Thai pregnant women in Thammasat University Hospital.

Correspondence to:
Nanthakomon T, Department of Obstetrics and Gynecology, Faculty of Medicine, Thammasat University, Pathumthani 12120, Thailand.
Phone: +66-2-9269343
E-mail: ntongta@gmail.com

Material and Method

This study was approved by Ethical Committee. Data collection was obtained during October 2012 to September 2013. Participants were the singleton pregnant women who came to Thammasat University

Hospital for routine prenatal care. They underwent ultrasonography during their first trimester of pregnancy. Participants were explained and counseled to participate in this study. Then, they signed the written informed consent after thoroughly understood this study. They were examined with ultrasonography to measure IT (intracranial translucency) and CRL (crown-rump length) for exactly gestational age calculation. All ultrasound parameters were measured in millimeter unit scale. All collected data were processed to determine the normative value of IT.

Demographic data were collected including maternal age, parity, miscarriage, birth defects in a previous baby or fetus and confirmed gestational age by ultrasonography. Results of the second trimester ultrasound detected neural tube defect (NTD) was collected from the patient's records. Infantile disabilities after birth has been followed-up from patient records or a phone call inquiry in case of delivering outside the hospital.

Sonographic screening was performed at 11-13 weeks gestation by only one certificated staff in Maternal Fetal Medicine using only Voluson E8 machine (GE Medical Systems, Zipf, Austria). Standard IT measurement in this study had been reported after appropriately measured following these steps[1-3]: 1) visualization of the lateral upper fetal chest, 2) identify the exact mid-sagittal plane of fetal face as properly identified by the echogenic tip of the nose, rectangular shape of the palate anteriorly, the translucent thalamus in the center and the nuchal membrane posteriorly, 3) visualize the position in which the fluid in the third ventricle between the right and left of thalamus could be seen and presence of cerebral aqueduct of Sylvius between brain tissue of both sides can be seen, and 4) IT measurement of the posterior border of the brain stem anteriorly and the choroid plexus of the fourth ventricle posteriorly then the widest hypoechoicpart was measured for 3 times and used average values.

Statistical analysis was performed by using Statistical Package for the Social Sciences (SPSS) version 14.0 (SPSS, Chicago, IL, USA). Mean, standard deviation, median and percentile values were represented for IT characteristics. IT length, gestational age and CRL were calculated for the linear regression analysis. A *p*-value less than 0.05 were classified as statistical significant.

Results

One hundred ninety-four pregnant women attended the sonographic features and IT measurement at Maternal Fetal Medicine Unit, Thammasat University Hospital. Three cases were unable to visualize IT position and therefore excluded from the study. There was no abnormality detection in the excluded three cases in their second ultrasonographic follow-up. The total number of cases reduced to 191 pregnant women in the present study. Participants were all walk-in patients who attended for antenatal clinic. Forty-eight cases were measured at 11 weeks (11^{+0}-11^{+6} weeks), 69 cases at 12 weeks (12^{+0}-12^{+6} weeks) and 74 cases at 13 weeks (13^{+0}-13^{+6} weeks). Their ages ranged from 16 to 39 years, with average age of 29.7$\pm$5.1 years as shown in Table 1. Pregnant women had neither underlying diseases nor fetal abnormality histories in previous pregnancies. Half of cases (98/191) were nulliparous. Miscarriage history in their previous pregnancies was

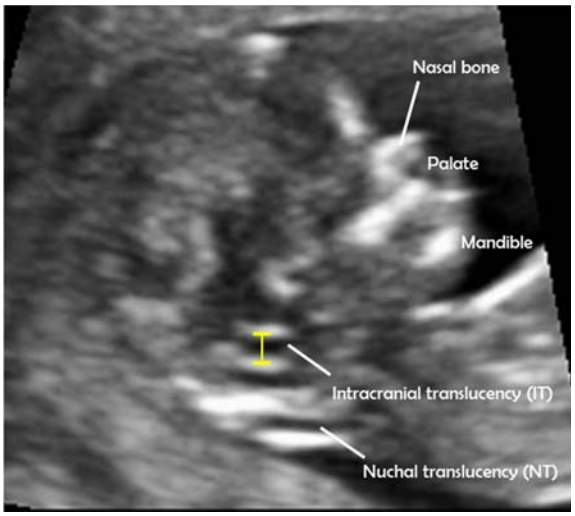

Fig. 1 The measurement of intracranial translucency.

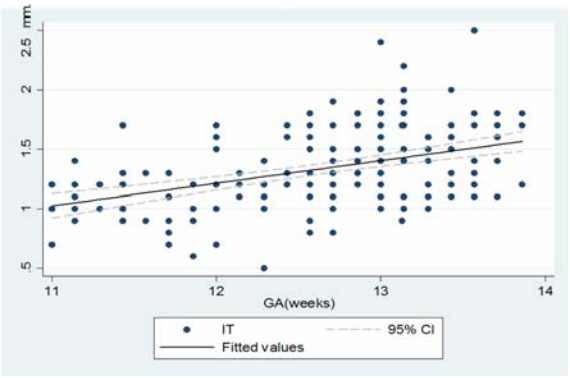

Fig. 2 Intracranial translucency (IT) measurement according to gestational age (GA).

Table 1. Demographic characteristics and IT in the first trimester ultrasonography at Thammasat University Hospital, Thailand

Characteristics	Mean ± SD
Age (years)	29.7±5.1
Gestational age (week)	12.6±0.8
IT (mm)	1.3±0.3
Nulliparity, n (%)	51.3 (98)
Previous miscarriage, n (%)	15.2 (29)

IT = intracranial translucency

Table 2. Proportion of IT and CRL

CRL (mm)	IT (mm)		
	n (%)	Mean	SD
40-44	10 (5.2)	1.09	0.20
45-54	31 (16.2)	1.10	0.27
55-64	52 (27.2)	1.27	0.29
65-74	72 (37.7)	1.43	0.33
75-84	26 (13.6)	1.52	0.31
Total	191 (100)	1.33	0.33

IT = intracranial translucency; CRL = crown-rump length

found in 29 cases.

There was no case of NTD from the second trimester ultrasonography follow-up. Neither "lemon-shape" head nor "banana shape" cerebellum was found from sonographic study. There was no NTD or any abnormal baby in postpartum period.

The average CRL, GA and IT were also shown in Table 1. The percentile values of IT at 5th, 5th, 50th, 75th and 95th were 0.9, 1.1, 1.3, 1.6 and 1.9 mm, respectively. IT length increased proportional CRL as presented in Table 2 (p<0.05).

Discussion

It is a well-known fact that the majority of severe fetal abnormalities can be early detected by ultrasound during pregnancy. Early detection practices allow planning for proper prognosis that will benefit both patient and obstetrician. Nuchal translucency (NT)" is a common protocol use to screen chromosomal abnormalities in the first trimester. In the second trimester, "high frequency ultrasound" of fetal brain and spine was used to diagnose "Arnold-Chiari" malformation. Detection of abnormal brain tissue such as "lemon sign" or "banana sign" which resulted from neural tube defect (caused the displacement of cerebellum). During the first trimester, IT measurement protocol assisted obstetrician to diagnose a suspected case of spina bifida. Early detection gave valuable information for physicians and both parents for extensive counseling for termination of pregnancy in severe malformation cases. It also helped patients in obtaining earlier proper care from specialist in the early stage of pregnancy. There was no spina bifida case in this study. Since spidia bifida is a statistically 1/1,000 encounter, additional research is needed in order to have sufficient number of samples. Evaluation of nomogram in this study yielded similar result with previous studies[1,4-6]: IT score is directly proportional to gestation age and CRL. Appropriate IT measurement should be done at gestation age during 11+0 to 13+6 weeks[2]. Several reasons supported these findings for example; an ultrasonography study was difficult during 10 weeks gestation age because of small fetus size and difficulties to determine the exact fetal mid-sagittal plane[7]. Experience gained from this study was the same way with previous literatures. Gestational age less or equal 10 weeks old demonstrated imperfect fetal visualization leading to inconsistency of measurement. If gestation age was 14 weeks or more, the study found that there were several problems associated to this gestation; changes in chromosome abnormal fetal accumulation cerebrospinal fluid, difficulties of measurement when fetus is in true sagittal position, which can make NT and IT test result inaccurate[7]. Factors that encouraged IT test were larger CRL, older gestation age, smaller maternal weight and supine position[7]. Moreover, previous study also found that if the gestation age was older than 11 weeks or any abnormality was detected, obstetrician could perform "chorionic villi" sampling with decreasing chance of "limb reduction defect". In our opinion, previous literatures indicated that spina bifida defect was suspected in absent IT findings[1,8]. Although spida bifida is clearly related to the absent IT; pregnancies with normal IT can, however, be a spida bifida as reported in many cases[8]. This reflects the fact that the first trimester testing protocol alone cannot replace additional abnormality scan in the second trimester. The strength of this study was present, absent IT or IT used in normogram that were less than the 5th percentile, guided obstetricians to demonstrate fetal abnormality, thoroughly. High frequency spinal ultrasonography was necessary to do or refer to the other expert sonographers. Another advantage of IT in the first

trimester was similar to nuchal translucency (NT). Both IT and NT needed the same obstetrician's skills to identify gestational age and visualizing plane. Obstetricians who had been already well trained in NT measurement could retrieve the information from NT and IT at the same time. Prospective large study sizes are necessary to define respectable nomograms.

Conclusion

At this moment, obstetricians regard the practice to screen physical and chromosomal-abnormality as a necessary means for prognosis. Nomogram study in pregnancy at Thammasat University Hospital found IT increased proportional to gestational age and CRL. These findings complied with previous literatures and valuable for references in further studies.

What is already known on this topic?

IT value has a direct variation with advancing gestation or increasing CRL baby's length.

What this study adds?

Nomogram study in pregnancy at Thammasat University Hospital found IT increased proportional to gestational age and CRL and spida bifida is clearly related to the absent IT but in the fact the first trimester testing protocal alone cannot replace additional abnormality scan in the second trimester.

Potential conflicts of interest

None.

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ค่าปกติของ Intracranial translucency จากการตรวจคลื่นเสียงความถี่สูงไตรมาสแรกในหญิงตั้งครรภ์ในโรงพยาบาลธรรมศาสตร์เฉลิมพระเกียรติ

ต้องตา นันทโกมล

วัตถุประสงค์: เพื่อให้ทราบค่าปกติ (Nomogram) ของ intracranial translucency (IT) ทารกในครรภ์จากการตรวจคลื่นเสียงความถี่สูงไตรมาสแรกในหญิงตั้งครรภ์โรงพยาบาลธรรมศาสตร์เฉลิมพระเกียรติ

วัสดุและวิธีการ: สตรีตั้งครรภ์เดี่ยวที่ส่งมารับการตรวจในคลินิกไตรมาสแรก (early clinic) อายุครรภ์ 11-13 สัปดาห์ อายุครรภ์ (gestation age; GA) ทารกถูกคำนวณจากความยาวทารกจากศีรษะจนถึงส่วนท้ายหรือก้นทารก (crown lump length; CRL) และ วัด intracranial translucency (IT) บริเวณสมองทารกในท่า mid-sagittal planefetal face จากนั้นติดตามผลการตรวจคลื่นเสียงความถี่สูงในไตรมาสที่ 2 เพื่อคัดกรองความพิการและติดตามความพิการของทารกหลังคลอด

ผลการศึกษา: สตรีตั้งครรภ์เดี่ยวจำนวน 191 คนได้รับการตรวจด้วยคลื่นเสียงความถี่วัดค่า CRL GA และ ค่า IT พบว่ากลุ่มตัวอย่างมีอายุเฉลี่ย 29.71±5.09 ปี (16-39 ปี) ผู้ป่วยทั้งหมดไม่มีโรคประจำตัวและไม่มีประวัติความพิการของทารกในครรภ์ก่อน เป็นครรภ์แรกร้อยละ 51.30 ติดตามผลการตรวจคลื่นเสียงความถี่สูงในไตรมาสที่ 2 และเมื่อติดตามหลังคลอดไม่พบมีหญิงตั้งครรภ์รายใดที่มีทารกพิการจากภาวะ open neural tube defect จากการศึกษาพบว่าความยาวทารกเฉลี่ย 64.05±10.23 มิลลิเมตร (40.0-80.9 มิลลิเมตรอายุครรภ์เฉลี่ยที่ทำการตรวจคลื่นเสียงความถี่สูงคือ 12.62±0.75 โดยค่า IT เฉลี่ย 1.33±0.33 มิลลิเมตร (0.5-2.5 มิลลิเมตร) และค่าของ IT เพิ่มขึ้นสัมพันธ์กับการเพิ่มขึ้นของอายุครรภ์และความยาวทารก ($p<0.05$)

สรุป: ค่าปกติของ IT (normogram) ในหญิงตั้งครรภ์เดี่ยวโรงพยาบาลธรรมศาสตร์เฉลิมพระเกียรติเพิ่มขึ้นตามอายุครรภ์ และความยาวทารก