

# Normal range of intracranial translucency in healthy turkish pregnancies and its association with first trimester maternal serum biochemistry and ductus venosus Pulsatility Index

Prawidłowy zakres przezierności wewnątrzczaszkowej u zdrowych, ciężarnych Turczynek i jego powiązanie z wynikami badania krwi matki w pierwszym trymestrze i wskaźnikiem pulsacji w przewodzie tętniczym

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## Abstract

**Objective:** To measure the intracranial translucency (IT) by establishing reference ranges in uncomplicated singleton Turkish pregnancies and to evaluate the association of IT with maternal serum biochemistry, gestational week, crown-rump length (CRL) measurement, nuchal translucency (NT) and ductus venosus Doppler velocimetry.

**Materials and methods:** 190 uncomplicated singleton pregnancies were included in the study. IT, NT and CRL measurements between 11-14 gestational weeks were obtained with mid-sagittal plane. Two independent measurements were taken and averaged to obtain the final measurement used in the calculations. Statistical analysis was performed with SPSS for Windows 20.0 software package. Correlation analysis was used to determine the association between IT and NT, pregnancy-associated plasma protein-A (PAPP-A), free  $\beta$ -human chorionic gonadotropin ( $\beta$ -hCG) and CRL length. A p-value of  $<0.05$  was considered statistically significant.

**Results:** The assessment rate of IT was 167/190 (87.89%). The mean CRL length, gestational week, NT and IT measurements were  $63.63 \pm 10.05$  mm,  $12.28 \pm 0.75$  weeks,  $1.23 \pm 0.43$  mm (range: 0.20-2.68) and  $2.29 \pm 0.49$  mm (range: 0.18-3.80), respectively. There was no significant correlation between IT and maternal serum PAPP-A MoM ( $r = -0.34$ ,  $p = 0.698$ ) or maternal serum free  $\beta$ -hCG MoM ( $r = -0.79$ ,  $p = 0.363$ ), respectively.

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There was weak- but statistically significant correlation between IT with with maternal weight ( $r=0.172$ ,  $p=0.047$ ), CRL length ( $r =0.301$ ,  $p<0.001$ ), gestational week ( $r=0.286$ ,  $p=0.001$ ) and NT measurement ( $r=0.224$ ,  $p=0.007$ ), respectively. There was no significant association between IT with ductus venosus doppler pulsatility index ( $r=0.108$ ,  $p=0.213$ ).

**Conclusion:** IT can be easily measured while scanning for NT. This study shows normal range values in healthy Turkish pregnancies. Consistent with recent data, our results show positive correlation with gestational week and CRL length. Maternal serum biochemistry does not have any effect on IT. Besides, our study highlights that IT is correlated with NT and adds newly to the literature that there is no correlation of IT with ductus venosus pulsatility index.

Key words: **intracranial translucency (IT) / nuchal translucency (NT) / ductus venosus doppler velocimetry /**

## Streszczenie

**Cel:** Określenie wartości referencyjnych dla przejerności wewnątrzczaszkowej (IT) w niepowiktanej, pojedynczej ciąży u Turczynek i ocena jej związku z badaniem biochemicznym krwi matki, wiekiem ciążowym, pomiarem długości ciemieniowo-siedzeniowej (CRL), przejernością karkową (NT) i przepływem przez przewód żylny.

**Materiał i metoda:** Do badania włączono 190 zdrowych, pojedynczych ciąż. Pomiary IT, NT oraz CRL uzyskano w okresie między 11 a 14 tygodniem ciąży, w przekroju strzałkowym. Wykonano dwa niezależne pomiary, które po uśrednieniu wykorzystano do obliczeń. Analizę statystyczną wykonano przy pomocy pakietu SPSS dla Windows 20.0. Posłużono się analizą regresji celem określenia związku pomiędzy IT i NT, białkiem PAPP-A, wolną podjednostką beta-hCG i CRL. Za istotne statystycznie uznano  $p<0.05$ .

**Wyniki:** Wskaźnik oceny IT wynosił 167/190 (87,89%). Średnio CRL wynosiło  $63,63\pm 10,05$  mm, wiek ciążowy  $12,28\pm 0,75$  tygodni, NT  $1,23\pm 0,43$  mm (zakres: 0,20-2,68) i IT  $2,29\pm 0,49$  mm (zakres: 0,18-3,80). Nie znaleziono istotnego związku między IT a PAPP-A MoM w surowicy matki ( $r=-0,34$ ,  $p=0,698$ ) oraz IT a wolną podjednostką beta-hCG MoM w surowicy matki ( $r=-0,79$ ,  $p=0,363$ ). Znaleziono słabą lecz istotną statystycznie korelację pomiędzy IT a masą ciała ciężarnych ( $r=0,172$ ,  $p=0,047$ ), CRL ( $r=0,301$ ,  $p<0,001$ ), wiekiem ciążowym ( $r=0,286$ ,  $p=0,001$ ) oraz NT ( $r=0,224$ ,  $p=0,007$ ). Nie znaleziono istotnego związku między IT oraz indeksem pulsacji w przewodzie żylnym ( $r=0,108$ ,  $p=0,213$ ).

**Wnioski:** Przejerność wewnątrzczaszkowa może być z łatwością zmierzona w trakcie pomiaru NT. Nasze badanie przedstawia zakres prawidłowych wartości NT dla populacji zdrowych, ciężarnych Turczynek. Podobnie jak w poprzednich badaniach, również nasza analiza pokazuje związek IT z wiekiem ciążowym oraz CRL. Badanie biochemiczne krwi matki nie miało żadnego wpływu na IT. Nasza analiza podkreśla, że IT jest związany z NT i dodatkowo pokazuje brak związku między IT a indeksem pulsacji w przewodzie żylnym.

Słowa kluczowe: **przejerność wewnątrzczaszkowa / przejerność karkowa / przewód żylny / badanie dopplerowskie /**

## Introduction

Intracranial translucency (IT) is the translucent appearance of the 4<sup>th</sup> cerebral ventricle in normal fetuses [1, 2]. In case of neural tube defects (NTD), caudal displacement of the brain results in the compression of the 4<sup>th</sup> ventricle and loss of the IT image [3,4]. This finding was the key point for the earlier detection of the spina bifida [4, 5]. For the measurement of IT, the same plane of nuchal translucency (NT) is used: The true mid-sagittal plane should be obtained. The true mid-sagittal plane is seen with the nasal tip anteriorly and the NT posteriorly. The rectangular shape of the palate is seen with the the central translucent circle appearance of diencephalon. The appearance of the zygomatic bone is the sign of the rotation of the fetal head which ends up in false plane. The image should be magnified so that only fetal head and upper thorax were included in the image. IT is bordered with posterior line of the brain stem anteriorly and choroid plexus of the 4th ventricle posteriorly [6, 7].

In normal fetuses, IT is the third translucent space in mid-sagittal plane: the lowest part represents NT, the second one represents cisterna magna (CM) and the third one is IT (Figure-1).

The normal ranges of IT have been the topic of the recent few studies [8-10]. In this study, we aimed to evaluate the normal ranges of IT in a Turkish population and establish the association of the biochemical parameters of 11-14 week screening and also ductus venosus doppler indices with IT measurement.

## Material and Methods

Singleton uncomplicated pregnancies admitted to our perinatology outpatient department for 11+0 to 13+6 weeks screening were recruited into the study. This retrospective study was approved by the Institutional Ethics Committee and conducted for six month period. All examinations were carried out via transabdominal probe by two operators (B.A.U. and H.G.P.) accredited with the "Certificate of Competence" for the

11-14 week screening by the Fetal Medicine Foundation (FMF). The examinations were carried out by one of the operators, at that time the other operator was observing the fetal planes and measurements independently. A Voluson 730 Pro system with a RAB 3,5-MHz array probe (GE Medical Systems, Milwaukee, WI) was used. The true mid-sagittal plane was confirmed by assessing the presence of the tip of the nose anteriorly, the nuchal membrane posteriorly, the translucent diencephalon and midbrain in the middle, and by showing the rectangular shape of the palate [6]. IT was measured "in to in" at its widest part (Figure 1).



**Figure 1.** Ultrasonography imaging of intracranial translucency. NT – Nuchal translucency; IT – Intracranial translucency.

Two independent measurements were taken and averaged to obtain the final measurement used in the calculations. Statistical analysis was performed with SPSS for Windows 20.0 software package. Correlation analysis was used to determine the association between IT and NT, pregnancy-associated plasma protein-A (PAPP-A), free  $\beta$ -human chorionic gonadotropin ( $\beta$ -hCG) and CRL length. A p-value of  $<0.05$  was considered statistically significant.

## Results

One hundred and ninety 11-14 week scans were performed during the study period. The assessment of IT was not possible in 13 cases: resolution of the images was suboptimal, mainly due to abdominal obesity in 7 cases; appropriate fetal position and neutral mid-sagittal plane could not be provided for the remaining 6 cases. The assessment rate of IT was 167/190 (87.89%). The mean maternal age was  $29,71 \pm 5,43$ . The mean maternal weight was  $66.62 \pm 11.65$  (range: 48.0-105.0). The mean CRL length was  $63.63 \pm 10.05$  and mean gestational week was  $12.28 \pm 0.75$ . The mean NT and IT measurements were  $1.23 \pm 0.43$  (range: 0.20-2.68) and  $2,29 \pm 0,49$  (range: 0.18-3.80) respectively (Table I).

**Table I.** Descriptive data of the study population.

	Mean	Std. Deviation
<b>Maternal weight</b>	66,6222	11,65100
<b>PAPP-A MoM</b>	1,1167	,83361
<b><math>\beta</math>-hCG MoM</b>	1,3140	,98155
<b>CRL</b>	63,6323	10,05322
<b>Gestational week</b>	12,2857	,75356
<b>NT</b>	1,2341	,42973
<b>IT</b>	2,2983	,49074
<b>Ductus venozus PI</b>	1,1553	,57394

PAPP-A – Pregnancy-associated plasma protein-A; MoM – Multiple of Medians;  $\beta$ -hCG – free beta human chorionic gonadotropin; CRL – Crown-rump length; NT – Nuchal translucency; IT – Intracranial translucency; PI – Pulsatility Index

There was no significant correlation between IT with maternal serum PAPP-A MoM ( $r=-0.34$ ,  $p=0.698$ ) or maternal serum  $\beta$ -hCG MoM ( $r=-0.79$ ,  $p=0.363$ ), respectively. There was low- but statistically significant correlation between IT with CRL length ( $r=0.301$ ,  $p<0.001$ ), gestational week ( $r=0.286$ ,  $p=0.001$ ) and NT measurement ( $r=0.224$ ,  $p=0.007$ ), respectively. There was no significant association between IT with ductus venosus doppler pulsatility index ( $r=0.108$ ,  $p=0.213$ ) (Table II).

## Discussion

To the our best knowledge, this is the first study identifying the normal ranges of IT in a Turkish population and describing the association of IT with PAPP-A,  $\beta$ -hCG levels and ductus venosus doppler indices.

The identification of IT was possible in 167 cases in our study, with an assessment rate of 87.89% (167/190). Similarly, Fong et al announced an assessment rate of 79% (150 in 199 cases) [12]. Adiego et al. established 97% IT assessment rate [13]. Regarding normal fetuses, the main reasons for the non-visualisation of IT were technical problems to obtain the true fetal mid-sagittal planes or maternal obesity leading to improper resolution of the image [13]. However, non-visualisation of IT may also alarming for spina bifida, although there are also reported cases whose IT could be visualised, but had spina bifida [3, 14].

The normal size of IT in our study ranged from 0.18mm to 3.80mm with a mean value of  $2,29 \pm 0,49$  mm. Furthermore, our study showed that IT measurement was associated with gestational week and CRL measurements. The correlation was low, but statistically significant ( $r=0.286$ ,  $p=0.001$  and  $r=0.301$ ,  $p<0.001$  respectively). Similarly to our results, the study of Cahoui [3] and Adiego et al [13] showed a linear association of

**Table II.** Correlation analysis of IT with maternal weight, PAPP-A MoM,  $\beta$ -hCG MoM, CRL, NT and gestational week.

IT	Maternal weight	PAPP-A MoM	$\beta$ -hCG MoM	CRL	Gestational week	NT	Ductus Venosus PI
<b>r</b>	0.172	-0.34	-0.79	0.301	0.286	0.224	0.108
<b>p</b>	0.047 *	0.698	0.363	$<0.001$ *	0.001*	0.007*	0.213

PAPP-A – Pregnancy-associated plasma protein-A; MoM – Multiple of Medians;  $\beta$ -hCG – free beta human chorionic gonadotropin; CRL – Crown-rump length; NT – Nuchal translucency; IT – Intracranial translucency; PI – Pulsatility Index; \*significant,  $p<0.05$

IT with gestational week. Chen et al [9] evaluated 102 Chinese pregnancies and found that IT at first trimester ranged from 1.35 to 2.6mm. Cahoui et al [3] found that IT ranged from 1.5 to 2.5mm in correspondance with CRL measurement.

There was no significant correlation between IT with maternal serum PAPP-A MoM ( $r=-0.34$ ,  $p=0.698$ ) or maternal serum  $\beta$ -hCG MoM ( $r=-0.79$ ,  $p=0.363$ ), respectively. Similarly, Chen et al [9] established no association between maternal serum biochemistry and IT. They found also no association between NT and IT. However, in contrast to this study, our results showed a positive low, but statistically significant correlation of IT with NT measurement ( $r=0.224$ ,  $p=0.007$ ). Similarly to our results, Papastefanou et al. evaluated 465 fetuses and found no correlation of IT or CM with maternal demographic characteristics and biochemical indices. However, they suggested that IT showed a weak positive correlation with nuchal translucency [15].

To the our best knowledge, this is the first study evaluating the association between IT and fetal ductus venosus doppler velocity. We found no significant association between IT and ductus venosus doppler pulsatility index ( $r=0.108$ ,  $p=0.213$ ). Papastefanou et al. [14] proposed that IT was above the median value in chromosomal abnormal fetuses. From that point of view, regarding the IT values above the median value, we found no fetus with abnormal karyotyping and we found no associated abnormal ultrasonographic sign. Furthermore, biochemical screening markers and ductus venosus pulsatility were normal and showed no correlation with IT.

The main limitation of our study was that there was no fetus with spina bifida in our study. Therefore, we could not conclude the screening performance of IT for spina bifida. Larger prospective studies are needed to confirm the association between IT and spina bifida and chromosomal abnormalities.

## Conclusion

As a result, our findings showed that IT can be easily measured while scanning for NT. Consistent with recent data, our IT measurements show positive correlation with gestational week and CRL length. Maternal serum biochemistry does not have any effect on IT. Besides, our study highlights that IT is correlated with NT and adds newly to the literature that there is no correlation of IT with ductus venosus pulsatility index.

### Authors' Contribution:

1. Burcu Artunc-Ulkumenn – concept, assumptions, acquisition of data study design, analysis and interpretation of data, article draft.
2. Halil Gursoy Pala – study design, acquisition of data, analysis and interpretation of data, author corresponding.
3. Yildiz Uyar – analysis and interpretation of data.
4. Yesim Bulbul-Baytur – revised the article critically.
5. Faik Mumtaz Koyuncu - revised the article critically.

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