

**ESTIMATION OF THYMIC SIZE IN PRETERM AND TERM NEONATES BY ULTRASONOGRAPHY IN TERTIARY HEALTH CENTRE OF WESTERN MAHARASTRA**Sharanabasav Kirdi<sup>1</sup>, Rajkunvar Langade<sup>2</sup>, Sunil Rodagi<sup>3</sup>, Snehal Surana<sup>4</sup>, Amit Galgali<sup>5</sup>**HOW TO CITE THIS ARTICLE:**

Sharanabasav Kirdi, Rajkunvar Langade, Sunil Rodagi, Snehal Surana, Amit Galgali. "Estimation of Thymic Size in Preterm and Term Neonates by Ultrasonography in Tertiary Health Centre of Western Maharashtra". Journal of Evolution of Medical and Dental Sciences 2015; Vol. 4, Issue 37, May 07; Page: 6412-6419, DOI: 10.14260/jemds/2015/932

**ABSTRACT: OBJECTIVE:** To determine sonographically the thymic index of the neonates and present values for the thymic index for various gestational ages who are born by uncomplicated pregnancies between gestational ages of 28 to and 40 weeks and correlate thymic index with various parameters like gestational age, birth weight, birth length, sex of neonate and mode of delivery. **SETTING:** Neonatal intensive care unit, Department of pediatrics, Krishna Institute of Medical Sciences hospital and research centre Karad, Maharashtra India. **METHODS:** A prospective observational study was conducted. Eighty neonates were included of various gestational age between gestational age of 28 to 40 weeks and ultrasonography is performed on day five of post natal age by single radiologist. The neonates having antenatal, intranatal, postnatal complication and those having congenital malformations are exclude from the study. The size of thymus was measured by measuring transverse diameter, anterioposterior diameter and longitudinal diameter and thymic index is then calculated. **RESULTS:** Thymic index of various gestational age are calculated. The thymic index for gestational age group of 28 to 30 weeks is comparable to thymic index for gestational age 31 to 33 weeks ( $P>0.001$ ) while the thymic index for other gestational age groups statistically differ ( $P<.001$ ). Overall the mean thymic index is less when compared to north Indian population and western population. The mean thymic has highest positive correlation to birth weight ( $r=0.8428$ ). **CONCLUSION:** This study presents normative data for the ultrasound measurements of thymus of neonates of various gestational age. Thus thymic index can be considered as one of the parameter to assess the gestational age. Measuring the thymic size by estimating the thymic index also help in predicting the gestational age but large number of prospective studies are required to establish the standard values of thymic index for particular gestational age. Over all mean thymic index in our study is less as compared to north Indian population and western studies probably because of low nutritional status of population of this region.

**KEYWORDS:** Thymic index, preterm neonate, birth weight, ultrasonography.

**INTRODUCTION:** The thymus which is a central lymphoid organ which plays an important role for proliferation, differential and selection of T lymphocytes that are responsible for cellular immunity.<sup>1</sup> The thymus develops from the endoderm of the third pharyngeal pouch (which also gives rise to the inferior parathyroid glands). Early in development, this pouch is cut off, both from the pharyngeal wall and from the surface ectoderm.<sup>2</sup> The first lymphocytes appear in the thymus during ninth week of gestation (Jeppesen et al. 2003). The thymus grows and enlarges continuously between the prenatal period and puberty. Moreover, during its a prenatal development, the size of fetal thymus is in close relationship with T-cell output.

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The development and maturation of primary lymphoid organs and peripheral blood leukocytes occur throughout gestation but is not complete until after birth.

There are certain immunological peculiarities in preterm neonates like defective mucosal and skin barrier, low levels of secretory immunoglobulins, alkaline pH of stomach, low complement levels, defective phagocytocytosis, smaller number of CD4 and CD8 cells and decreased response to pathogens.<sup>3</sup>

Previous studies conducted by Ivana Musilova et al,<sup>4</sup> established a nomogram for the transverse diameter of the fetal thymus in uncomplicated singleton pregnancies between 19 and 38 weeks of gestation. The purpose of our study is to conduct a sonography study on thymus and establish values for thymic index in new born babies of gestational age ranging from 28 to 40 weeks gestational age and correlate thymic size with various birth parameters like birth weight, birth length, gestational age, sex of neonate and mode of delivery.

**MATERIALS AND METHODS:** This is a prospective observational study conducted in the Krishna Institute of Medical Sciences hospital, Karad. Eighty Consecutive asymptomatic neonates who had supervised antenatal period are included in the study. The gestational age is assessed from date of last menstrual period and ballard score. In a case of extremely preterm neonates only neonates are included in our study those who have received one course of antenatal steroids 24 hours prior to delivery, this is not to study the effect of antenatal steroids on thymic size. Neonates having maternal history of diabetes and hypertension, maternal history of HIV, TORCH, hepatitis, maternal history of pregnancy induced hypertension and eclampsia, maternal history of ante partum haemorrhage are excluded from the study, also preterm with birth asphyxia, meconium aspiration syndrome, preterm with congenital anomalies are excluded from the study.

The weight is measured on an electronic weighing scale. The length is measured using an infantometer. The measurement is taken on same equipment and by same observer. The ultrasonographic measurement of thymus is performed on day 4 to day 6 of postnatal age by the single radiologist. The thymic size is measured sonographically using Siemens Acuson x 300PE system and a 7.5MHZ probe. The thymus is examined in longitudinal and transverse planes by transsternal approach, parasternal and suprasternal approach as explained by Hasselbalch H.<sup>5</sup>

To obtain standardized thymic size values the measurement is performed during expiration when the thymus has the widest transverse diameter. By transsternal approach the maximum transverse diameter, right lobe anterioposterior dimension and left lobe anterioposterior dimension is measured. The longitudinal diameter of the largest lobe is measured by parasternal and suprasternal approach. The thymic index which measures thymic volume or thymic size is calculated by multiplying the transverse diameter, longitudinal diameter of largest lobe and anterioposterior diameter of largest lobe (sagittal area). The thymic index is measured in cubic centimeter. The correlation between thymic index and birth weight, birth length, gestational age and sex is assessed by using unpaired t test and pearson correlation coefficient.

**RESULTS:** Eighty neonates were included in the study. Among eighty neonates, sixty of them were preterm and twenty were terms. Preterm group further divided into three groups. Twenty of these were around gestational age 28 to 30 weeks, twenty of these were around gestational age 31 to 33 weeks, twenty of these around gestational age 34 to 37 week and twenty were term neonates.

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38 were males and 42 were females. Mean thymic index of male neonates is compared with mean thymic index of female neonates. Assuming the values are sampled from Gaussian distribution. The mean thymic index of these is compared by using unpaired t- test. The t value is 0.9110 and two tailed p value is 0.3644. In our study the gender of the neonate has no effect on the thymus volume (Table no. 1).

39 were born by normal delivery and 41 were born by cesarean section. Mean thymic index of neonates born by normal vaginal delivery is compared with mean thymic index of neonates born by caesarian section. Assuming the values are sampled from Gaussian distribution. The mean thymic index of these is compared by using unpaired t- test. The t value is 0.09564 and the two tailed p value is 0.9235, which is more than 0.005. In our study the mode of delivery has no impact on the thymus volume (Table no. 2).

The neonates were divided into four groups depending on their gestational age. The mean gestational age, mean birth weight, mean birth length, mean longitudinal diameter, mean transverse diameter and sagittal area of the largest lobe were calculated from which their thymic index was derived (Table No. 3).

Mean thymic index of these four groups of various gestational ages are calculated and compared by ANOVA (One-way Analysis of Variance) by using Tukey-Kramer multiple comparison test (Table No. 4).

The mean thymic index of group A (28 TO 30WK) is comparable to mean thymic index of group B (31 to 33wk) whereas mean thymic index of other groups differ significantly (Table No. 4).

Positive correlation between thymic index and gestational age (Figure 1), TI and Birth weight (Figure 2) and also the positive correlation between TI and Birth length was plotted (Figure 3).

In our study thymic index has highest positive correlation to birth weight followed by gestational age (Table No. 5).

**DISCUSSION:** The thymus which is a central lymphoid organ is located mainly in anterior superior mediastinum in front of the heart and behind the sternum sometimes it extends to inferior mediastinum. The unique feature of thymus is in its variation in size and shape. The thymus, a lymphoepithelial organ, is the main site of T-lymphocytes that orchestrate cell mediated immune function, which generally corresponds to its functional capacity and predicts early childhood survivorship.<sup>6</sup> Since thymus can be easily visualised on sonography in the infantile period it can be used to access its size.

Many authors conducted imaging studies to study the echogenicity of the thymus. Rajiv et al,<sup>7</sup> conducted sonographic study mainly to study the variation in the echogenicity of the thymus. The thymic appearance was described in terms of its echogenicity and echopattern, which were compared with that of the liver, spleen and the thyroid. Its echogenicity was measured quantitatively by the measurement of the echogenicity number.

Many ultrasonographic studies have attempted to establish standards for thymic size in infancy (Hasselbalch,<sup>5</sup> et al 1999, Kizilcan et al 1995, Varga et al,<sup>8</sup> 2011, Yekeler et al,<sup>9</sup> 2004). These studies tend to rely on healthy well-nourished infants in habitant sanitary, urban environment.

The thymus is susceptible to acute involution upon prenatal & postnatal malnutrition (Chandra 1992, Savino et al 2002), stress hormones (Savino & Dardene 2000), maternal smoking

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(Zeyrek et al 2008) so in our study the neonates having antenatal intranatal and postnatal risk factors are excluded from the study.

Ivana Musilova et al conducted sonographic study to determine the transverse diameter of the fetal thymus and in his study he presented nomogram for the transverse diameter of the 198 healthy foetal thymus in uncomplicated singleton pregnancies between 19 and 38 weeks of gestation. Similarly in our study instead of transverse diameter, thymic index which measures accurate dimensions of the thymus is calculated in neonates of various gestational ages from 28 to 40 weeks.

We calculated the mean value of thymic index for the particular gestational ages.

In the study conducted by Rajiv Azad<sup>7</sup> et al in 200 healthy term neonates found the overall thymic index dimensions and the thymic index in particular in the Indian neonates, are lower probably because of the lower birth weight, which correlated significantly with the thymic index. ( $r=0.29$ ,  $p<0.001$ ). In our study when compared to other studies conducted in north India and western countries the mean thymic index in all gestational age groups is less probably because of low nutritional status of parents when compared to north Indian and western country population.

In comparison of the mean thymus size between term and preterm neonates, we found that the term ( $5.642\pm 1.178\text{ cm}^3$ ) group had significantly greater values than the preterm ( $2.596\pm 0.984\text{ cm}^3$ ) group. Previous studies had similar results and considered that they were related closely to parameters such as health status, intrauterine growth, and birth weight.<sup>9</sup>

S. Magu et al,<sup>10</sup> and I. Varga,<sup>8</sup> et al found no difference in thymic dimensions when they compared the difference in the thymic size between the newborns born in two different ways (spontaneously and operatively). Some of authors like Rajiv et al included only those neonates that are born by normal vaginal delivery since according to him thymic size is known to be affected by stress. Similarly in our study mode of delivery had no impact on thymic dimensions.

The main goal of our study was to determine the thymic dimensions of neonates of various gestational ages in uncomplicated pregnancies with secondary aim to study the effect of gender and mode of delivery on thymic dimensions. The mean thymic index of group A (28 TO 30WK) was comparable to mean thymic index of group B (31 to 33wk) whereas mean thymic index of other groups differed significantly.

**CONCLUSION:** The thymus plays a pivot role in cell mediated immunity. It plays an important role in providing a suitable microenvironment for the proliferation, differentiation and selection of T lymphocytes. Functional assessment of thymus requires immunofluorescence, flow cytometry, immunohistological studies which are expensive and not easily available. Thymic size which generally corresponds to its functional capacity can be easily estimated by ultrasonography which can be alternative method for functional assessment of thymus. Measuring the thymic size by estimating the thymic index also help in predicting the gestational age but large number of prospective studies are required to establish the standard values of thymic index for particular gestational age. Over all mean thymic index in our study is less as compared to western studies probably because of low nutritional status of population of this region. The thymus size had highest positive correlation to birth weight.

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Sex	Sample Size	Mean Thymic Index in cm <sup>3</sup>
Male	38	3.548±1.312
Female	42	3.212±1.900

Table 1: Number of males, females and their respective mean thymic index

Mode of delivery	Sample Size	Mean Thymic Index in cm <sup>3</sup>
Normal	39	3.375±1.536
Caesarean section	41	3.410±1.725

Table 2: Mode of delivery & mean thymic index

Gestational Age	Mean Weight in kg	Mean Length in cm	Mean TD in mm	Mean APD of LL in mm	Mean LD of LL in mm	Mean SA of LL in cm <sup>2</sup>	Mean TI in cm <sup>3</sup>
27 to 30 wk	1.149±0.305	41.15±2.58	14.08±3.80	10.34±4.23	15.13±5.11	1.36±0.55	2.0016±0.50
31 to 33 wk	1.481±0.206	43.90±1.88	15.30±4.68	9.87±5.20	18.24±2.51	1.72±1.07	2.445±0.46
34 to 37 wk	1.823±0.130	47.35±1.61	16.80±4.67	13.35±4.20	17.18±3.10	2.27±0.98	3.352±1.05
>37 wk	3.048±0.366	49.6±0.59	19.82±1.70	12.46±1.22	22.72±260	2.81±0.49	5.642±1.17

Table 3: Mean gestational age, mean birth weight, mean birth length and their mean thymic index

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TD- Transverse Diameter; APD – Anteroposterior Diameter; LD – Longitudinal Diameter; SA – Sagittal Area; LL – Largest Lobe; TI – Thymic Index.

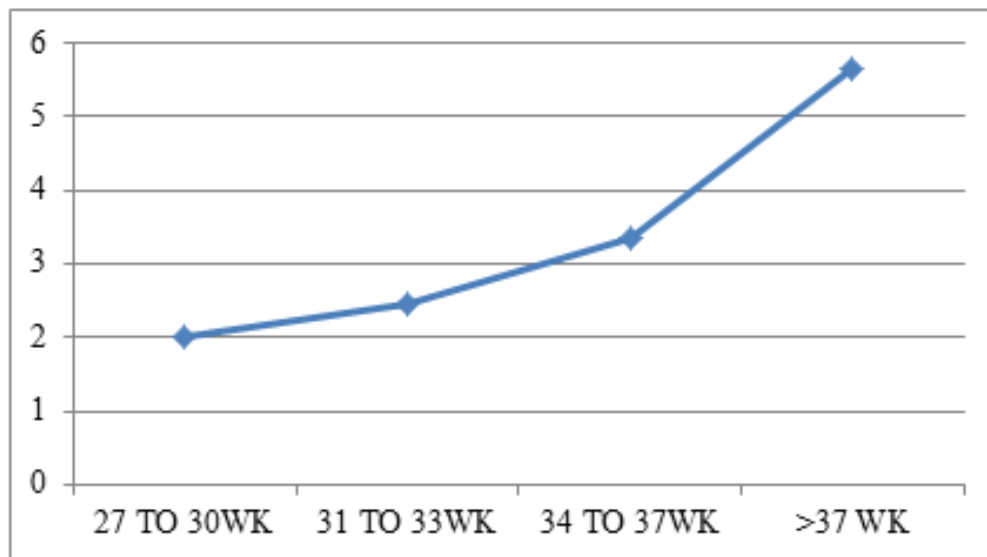
Comparison	Mean Difference of Thymic Index	P Value
Group A vs Group B	-0.4439	P>0.05
Group A vs Group C	-1.393	P<0.001
Group A vs Group D	-3.641	P<0.001
Group B vs Group C	-0.9494	P<0.01
Group B vs Group D	-3.197	P<0.001
Group C vs Group D	-2.247	P<0.001

**Table 4: Comparison of thymic index in various gestational age after application of anova test**

Correlation between	r value	P value
TI & BW	0.8438	P<0.0001
TI & BL	0.7390	P<0.0001
TI & GA	0.8257	P<0.0001

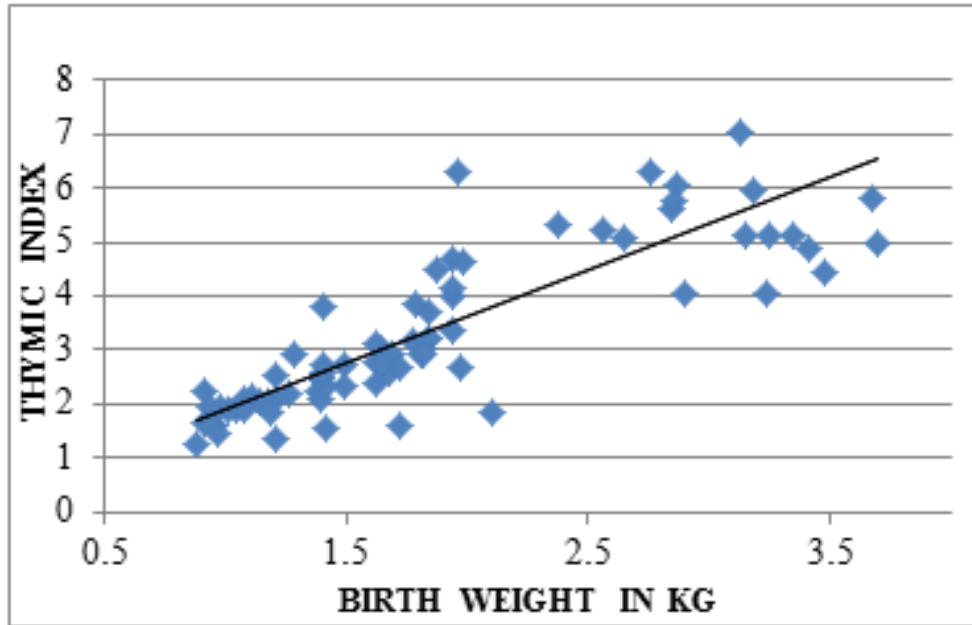
**Table 5: Positive correlation between thymic index, birth weight, birth length and gestation age**

TI – Thymic Index; BW – Birth Weight; GA - Gestational Age.

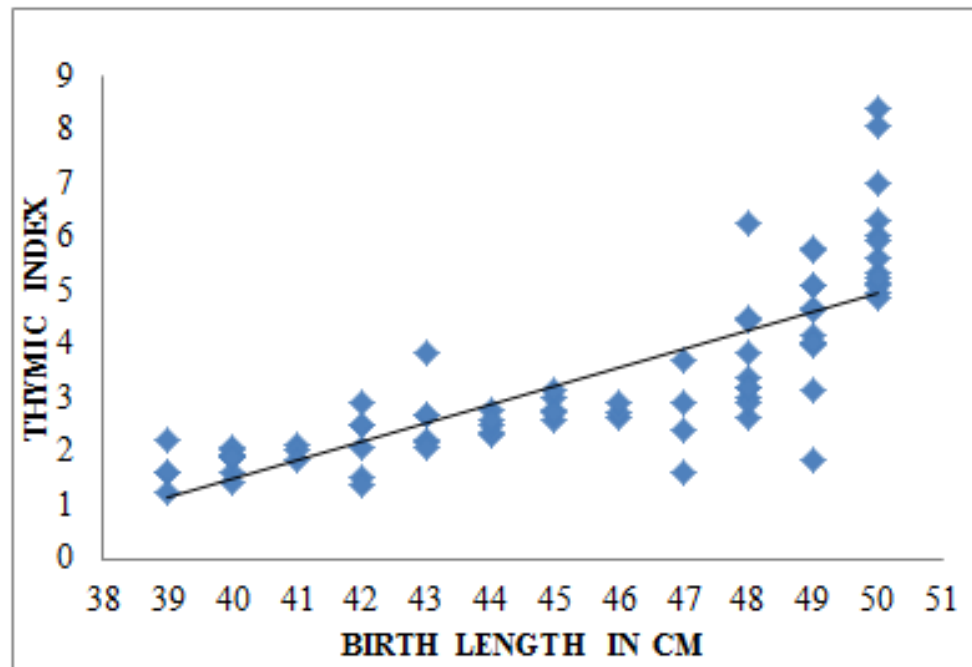


**Fig. 1: Positive Correlation between Thymic Index and Gestational Age**

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**Fig. 2: Positive Correlation between Thymic Index and Birth Weight**



**Fig. 3: Positive Correlation between Thymic Index and Birth Length**

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