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Original Article

Anatomy Section

Morphological Study of Foetal Thymus: A Cross-sectional Study

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ABSTRACT

Introduction: Thymus is a primary central lymphoid organ and a key regulator of the immune system. It develops from the ventral aspect of the 3rd pharyngeal pouch and also gets contribution from the 4th pharyngeal pouch. It migrates caudally into thorax due to its attachment to the pericardium and the aortic sac.

Aim: To determine the morphometry of thymus gland in human foetuses.

Materials and Methods: It was a cross-sectional study which included 33 human foetuses available in the Department of Anatomy, Sri Aurobindo Medical College and Postgraduate Institute (SAMC and PGI), Indore, Madhya Pradesh, India, over a period of three years. The samples were divided into four groups as per the Gestational Age (GA), (13-16, 17-20, 21-24, 25-29 weeks), based on measuring the Crown Rump (CR) length. After making a midline incision extending from the neck to the chest wall, the thoracic and cervical part of the thymus were displayed and its height and width were measured. For statistical analysis Statistical Package for the Social Sciences (SPSS), version 20.0 was used to analyse the association between the present findings in the given study groups.

Results: Cervical extension showed great variability in different groups. It was either bilateral (16), unilateral (9) or even absent (8) in some cases. Cervical extension showed variable appearances like, coiled, lobulated or cord-like. In four cases, it reached upto the lower pole of thyroid. The shape of the thoracic part of the thymus was either vertically elongated or curved, lobulated or retort shape.

Conclusion: The present findings of morphometry of foetal thymus are important for radiologists to differentiate thymus from other mediastinal structures and for surgeons during thymectomy. With increasing foetal age, there is regression in the cervical part of the thymus.

Keywords: Cervical extension, Crown rump length, Variation

INTRODUCTION

Thymus is one of the most mysterious organs of the human [1]. The name thymus is derived from the Greek word meaning 'warty excrescence'. It is the most important central lymphoid organ and a key regulator of the immune system [2]. Immunological function of thymus gland and its role in the maturation of T-lymphocytes is known. Thymus is also known to secrete proteins that act within it as paracrine mediators and function as growth factors to bring in stimulation and proliferation of T-lymphocytes [3]. During neonatal and early postnatal life, thymus is necessary for the regular development of lymphoid tissue [4]. It develops as an epithelial outpouching from the ventral aspect of the 3rd pharyngeal pouch. The ventral aspect of the forth pharyngeal pouch also contributes to the rudimentary portion of thymus [2,5-7]. An epithelial mesenchymal interaction between the third pharyngeal pouch endoderm and surrounding neural crest derived cells, ectomesenchyme is necessary for the proliferation and differentiation of thymic epithelial cells. Caudal migration of thymic rudiment occurs due to its attachment to the pericardium and the aortic sac when they descend into the thorax [5].

The final interrelationship between the cervical and the thoracic part of thymus continues to be enigmatic. The cranial extent, whether glandular or ligamentous, still needs to be evaluated. The shape and size of lobes are considered to be variable. Knowledge of morphometry of thymus gland is important for diagnosis of a variety of clinical and congenital diseases of thymus. It is also important for radiologists to differentiate thymus from other mediastinal structures e.g., lymph nodes. Morphometric observations of thymus gland can be helpful during thymectomy and imaging studies in the prenatal stage. Ectopic thymus, accessory nodules and cervical extensions are common variations [6,7]. Hence, the present study was conducted with an aim to determine the morphometry of thymus gland in human foetuses.

MATERIALS AND METHODS

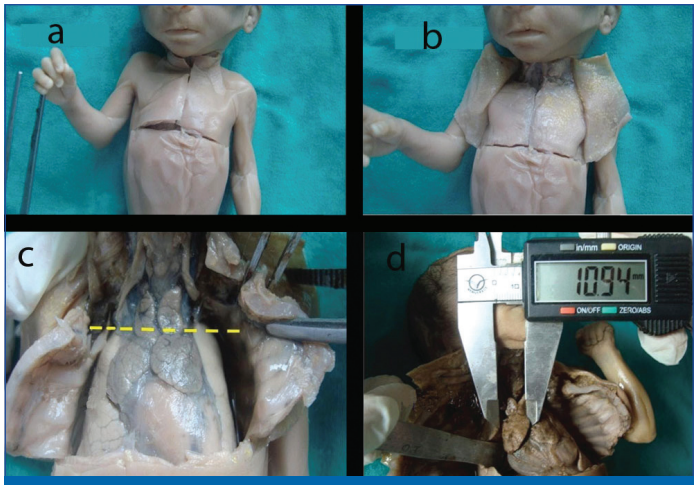
A cross-sectional study was conducted which included 33 human foetuses available in the Department of Anatomy, Sir Aurobindo Institute of Medical Sciences and PGI, Indore, MP, India, over a period of three years from (March 2018 to February 2021). Permission was obtained from the Institutional Ethical committee. Approval no: SAIMS/IEC/2021/17.

Inclusion and Exclusion criteria: The foetuses which appeared to be normal on external examination were included in the study; Those which were either haemorrhagic or discoloured after preservation or had any sign of congenital abnormality in appearance were excluded from the study.

On the basis of Crown rump (CR) length they were divided into four groups [Table/Fig-1] and their GA was calculated as per Boyd WJ et al., [8]. After making a midline incision extending from the front of the neck to the chest wall; median splitting of sternum was carried out and the anterior chest wall was retracted. The impression of the medial end of clavicle on the anterior surface of thymus and the level of the apex of the foetal lung demarcates the thoracic and cervical parts of thymus which were displayed and the thyroid was also visualised. With the help of vernier caliper, width and height of thoracic and cervical parts of thymus were measured and photographed [Table/Fig-2].

Groups	CRL (cm)	GA (weeks)	Number of foetuses
Group I	10-14	13-16	11
Group II	15-19	17-20	14
Group III	20-23	21-24	4
Group IV	24-27	25-28	4
Total			33

[Table/Fig-1]: Grouping of foetuses according to Crown Rump Length (CRL) and Gestational Age (GA).



[Table/Fig-2]: a,b) Showing steps of dissection to expose thymus; c) shows a yellow dotted line demarcating its cervical and thoracic part; d) shows the method to measure the thymic parameter with digital vernier callipers.

STATISTICAL ANALYSIS

For statistical analysis SPSS, version-20.0 was used to analyse the association between the present findings in the given study group ANOVA test was used.

RESULTS

Cervical extension [Table/Fig-3-5]

Group I: The cervical extension was bilateral in six cases; and was unilateral in four cases (three left and one right) and absent in one case. Cervical extension was absent on one case.

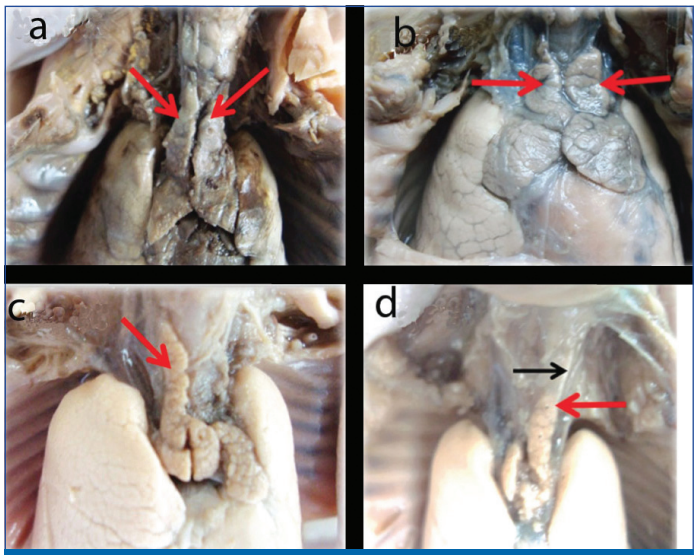
Group II: The cervical extension was bilateral in seven cases and unilateral in four (three left and one right), extension was absent in three cases.

Accessory thymus [Table/Fig-6]

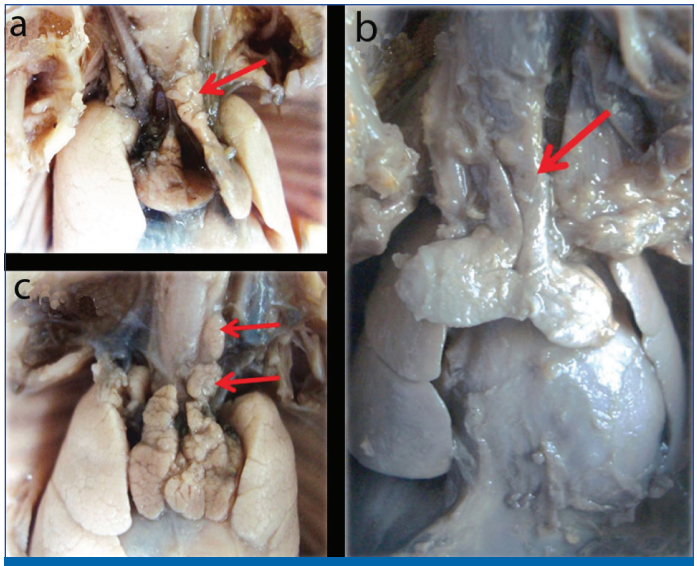
It was observed in three cases (9.09%). Of these in one case it was bilateral and in two cases it was on the left side.

Groups	Bilateral incidence n (%)	Unilateral incidence n (%)	Unilateral		Absent n (%)
			Right n (%)	Left n (%)	
Group I	6 (54.55%)	4 (36.36%)	1 (25%)	3 (75%)	1 (9.09%)
Group II	7 (50%)	4 (28.57%)	1 (25%)	3 (75%)	3 (21.43%)
Group III	2 (50%)	1 (25%)	----	1 (100%)	1 (25%)
Group IV	1 (25%)	----	----	----	3 (75%)

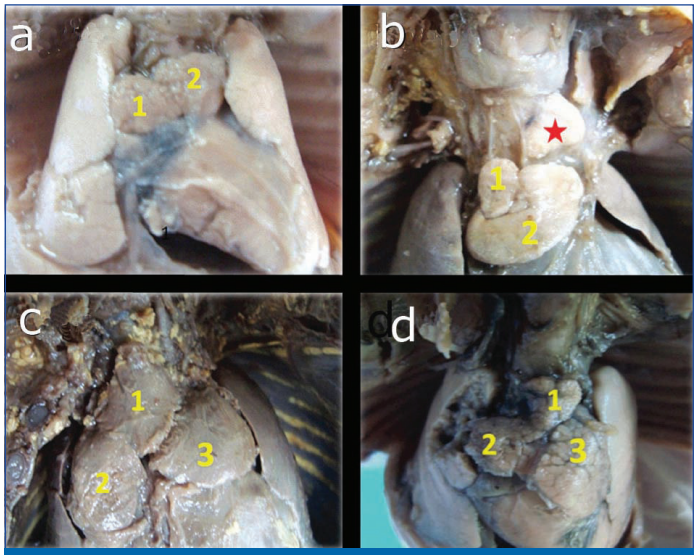
[Table/Fig-3]: Showing incidence of cervical extension (N=33).



[Table/Fig-4]: Types of cervical extension of thymus (red arrow): a,b) showing bilateral; c) unilateral right; d) unilateral left (black arrow) points at the thyrothymic ligament.



[Table/Fig-5]: Types of cervical extension marked by red arrow: a) coiled; b) cylindrical; c) Thymus in two parts on the left.



[Table/Fig-6]: Variable lobes of thoracic part of thymus indicated by numbers: a) bilobed; b) accessory lobe (red star); c,d) trilobed.

Shape of thoracic part of thymus [Table/Fig-7,8]

In five cases the thymus was observed to be vertically elongated with tapering ends. It was bilateral in three and unilateral in two cases (one right and one left) and in six foetuses the lobes of thymus were parallel [Table/Fig-7a,b]. In one case the medial border of right lobe was curved like the letter 'C' which was occupied by left lobe [Table/Fig-8a]; and in yet another case the concavity of left lobe was occupied by right lobe [Table/Fig-8b]. One case it was bilaterally lobulated and irregular [Table/Fig-7d], whereas in three cases only left lobe showed this feature [Table/Fig-5c]. one case both the lobes were retort shaped [Table/Fig-8c].

Comparision of height and width of lobes of thymus [Table/Fig-9]

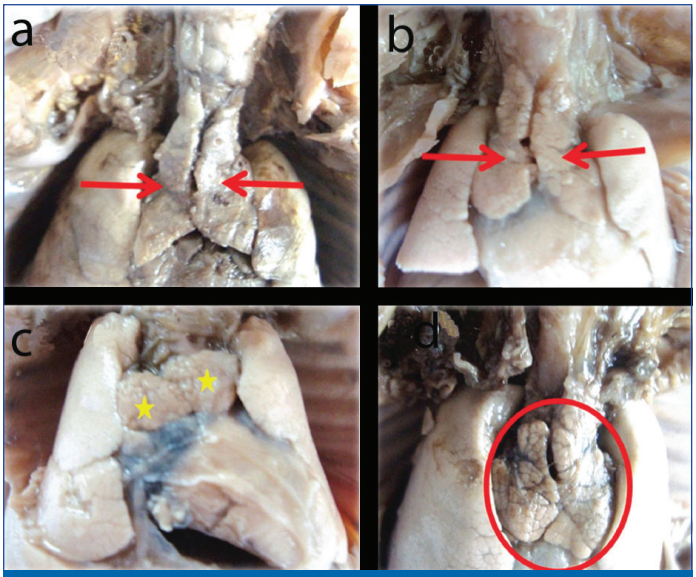
Group I: Left lobe was broader than right in seven cases and in two cases the right was broader. In one case, the left lobe was elongated and in yet another case the right was elongated.

Group II: Left lobe was broader in seven cases and right lobe was broader in five cases. In one case, the left lobe was elongated.

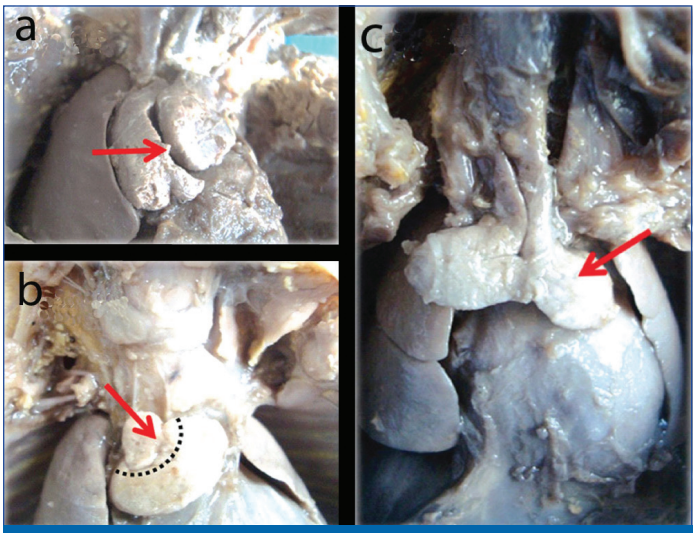
Group III: Left was broader in two case and right was broader in one case. In two cases the right lobe was elongated.

Group IV: Right was broader in three cases and in one case the right lobe is elongated.

The result of analysis by ANOVA revealed significant association between distribution of age group of study participants with thymic dimensions. The p-value was significant for Left Lobe



[Table/Fig-7]: Variable appearances of thoracic part of thymus: a,b) elongated and parallel with tapering ends; c) yellow asterisk showing right circular and left triangular lobes; d) Showing well defined lobulated appearance within the red circle.



[Table/Fig-8]: Various shapes of thymus. a) Right lobe is C-shaped and the left lodging in its concavity; b) C-shaped left lobe and the right lobe fitting in its concavity; c) Retort shaped left lobe.

Groups	Broader right lobe, n, (%)	Elongated right lobe, n, (%)	Broader left lobe, n, (%)	Elongated left lobe, n, (%)
Group I	2 (18.18%)	1 (9.09%)	7 (63.63%)	1 (9.09%)
Group II	5 (35.71%)	----	7 (50%)	1 (7.14%)
Group III	1 (25%)	2 (50%)	2 (25%)	----
Group IV	3 (75%)	1 (25%)	----	----

[Table/Fig-9]: Incidence of greater width of lobes of thymus in various groups.
In group II one foetuses did not fall in any of the categories mentioned above and in group III one foetus fall in both the category so number is more than 4

Thoracic Height (LLTH), Right Lobe Thoracic Height (RLTH), Left Lobe Thoracic Width (LLTW) which showed a strong association between these parameters and the foetal age [Table/Fig-10]. Mean value and the results of ANOVA in cervical region are represented in [Table/Fig-11].

Shape of the cervical extension

The cervical extensions, when present, showed variable appearance: (cord like, coiled and lobulated) [Table/Fig-5a-c].

Upper extent of thymus

Out of the 33 cases studied, in three cases the cervical extension reached upto the lower pole of thyroid out of which in two cases extended to the lower pole of both the lobes of thyroid and in one case the left lobe reached upto the lower pole of thyroid. In two cases the thyrothymic ligament [Table/Fig-4d] was observed.

Thymic parameters	Groups	Mean value (mm)	F-test, ANOVA	p-value
LLTH	I	8.019	3.398	0.031
	II	11.748		
	III	24.452		
	IV	12.917		
RLTH	I	7.720	5.245	0.005
	II	11.620		
	III	14.722		
	IV	18.125		
LLTW	I	5.862	3.895	0.019
	II	8.740		
	III	10.557		
	IV	12.852		
RLTW	I	5.659	2.092	0.124
	II	7.860		
	III	9.555		
	IV	9.182		

[Table/Fig-10]: Chart showing the mean values of thymic height and width (in right and left lobes) in different groups in thoracic region.
LLTH: Left lobe thymus height; RLTH: Right lobe thymus height; LLTW: Left lobe thymus width; RLTW: Right lobe thymus width, p-value <0.05 considered significant

Thymic or cervical parameters	Groups	Mean (mm)	F-test ANOVA	p-value
LLCH	I	6.092	0.270	0.846
	II	5.524		
	III	5.115		
	IV	3.807		
RLCH	I	4.660	0.170	0.916
	II	4.618		
	III	4.892		
	IV	2.897		
LLCW	I	2.136	1.322	0.287
	II	3.711		
	III	3.647		
	IV	1.675		
RLCW	I	1.490	0.467	0.708
	II	2.176		
	III	2.227		
	IV	0.875		

[Table/Fig-11]: Chart showing the mean values of thymic height and width (in right and left lobes) in different groups in cervical region and the result of ANOVA test.
p-value <0.05 is considered to be significant; LLCH: Left lobe cervical height; RLCH: Right lobe cervical height; LLCW: Left lobe cervical width; RLCW: Right lobe cervical width

Lower extent of thymus

Out of 33 cases, in two cases the lower pole of the left lobe was at a lower level and in four cases the right was at a lower level [Table/Fig-6c]. Out of all the cases, the descent of thymus was confined only upto the great vessels in one case. It extended upto the atria in three cases; and in the majority of the cases, it covered the ventricles upto a variable extent. In none of the cases studied the thymus extended upto the diaphragm.

Maximum average height and width of thoracic and cervical parts of thymus [Table/Fig-12,13]

The average thoracic height was found to be maximum in the left lobe in group III which was 24.45 mm. The average thoracic width of left lobe was maximum in group IV i.e., 12.85 mm. The average maximum cervical height of both the lobes was found in group IV (left lobe 15.23 mm and right lobe 11.59 mm).

Groups	Left lobe: thoracic height (mm)	Right lobe: thoracic height (mm)	Left lobe: thoracic width (mm)	Right lobe: thoracic width (mm)
Group I	8.01 (5.05-13.6)	15.08 (4.57-11.58)	5.84 (2.49-12.44)	5.65 (3.33-9.8)
Group II	11.9 (9.33-14.10)	11.62 (6.3-19.11)	8.72 (4.56-16.5)	7.89 (3.85-14.7)
Group III	24.45 (6.9-60.99)	14.72 (7.4-20.8)	10.55 (7.2-12.72)	9.55 (5.6-12.84)
Group IV	17.86 (10.4-22.76)	24.65 (18.2-29)	12.85 (1.9-17.35)	9.18 (1.4-16.2)

[Table/Fig-12]: Comparison between average height and width of thoracic part of right and left lobe of thymus.

Groups	Left lobe: cervical height (mm)	Right lobe: cervical height (mm)	Left lobe: cervical width (mm)	Right lobe: cervical width (mm)
Group I	7.44 (4.36-9.4)	7.32 (4.23-11.9)	3.36 (2.33-4.48)	2.68 (1.44-4.63)
Group II	7.18 (3.9-14.9)	7.49 (3.0-12.81)	4.88 (2.43-8.2)	3.54 (1.8-9.4)
Group III	6.82 (5.1-8.3)	9.78 (9.9-10.48)	4.86 (3.2-6.5)	4.45 (3.5-5.4)
Group IV	15.23 (15.23)	11.59 (11.59)	6.7 (6.7)	--

[Table/Fig-13]: Comparison between average height and width of cervical part of right and left lobes of thymus.

As the cervical extension in the group IV was present only in one case hence it has not been considered for the comparison between height and width of cervical part of right and left lobe of thymus.

In the present series, the two lobes of thoracic part of thymus were connected by a thin layer of connective tissue only.

DISCUSSION

In the present study, the incidence of cervical extension was found to be 90.9% in Group I, 78.57% in Group II; 75% in Group III and 25% in Group IV. It was found that there is a definite left predominance where the cervical extension was unilateral. The bilateral cervical extension was higher in incidence than unilateral. There was clearly a decrease in the cervical extension with an increase in the GA of the foetus studied. Hasini SH et al., in a detailed morphological and morphometric study of foetal thymus, gave an incidence of cervical extension as 60% [9]. They did not study the incidence and predominance in different GA group. Murthy KVJ and Velichety SD have found the cervical extension in 50%. In their study, which includes foetal and adult cadavers, they have described 11 types of cervical extension [4]. Sophia MM and Kalpana R have also described the caudal migration of thymic rudiment with the aortic sac, and have stated that the upper pole of one or both the lobes of thymus extends upwards into the neck, to the level of thyroid cartilage, due to the failure of thymus to complete its migration into the thorax [2].

In the present study, the cervical extension was reaching the lower pole of the thyroid gland in three cases. In two cases, the thyrothymic ligament was also seen. Keith A et al., described the pointed upper extremity of the lobes of thymus passing dorsal to the thyroid lobe reaching upto thyrohyoid membrane [7]. But in the present study, authors did not come across this extension upto the thyrohyoid membrane.

In the present study, the cervical extension was cord like, coiled and in two segments. This is in agreement with Boyd WJ et al., wherein it is stated that- "The cervical thymus shows much variation in its subsequent differentiation which is often asymmetrical [8]". Moore KL and Persaud TVN explained that the accessory thymic tissue may persist in the neck as it breaks free from the developing thymus while it shifts caudally in the neck [10].

All the cases in present study were multilobulated. Hasini SH et al., have also stated similar findings but in one case they have described it to be single lobed, which was not found in the present study [9]. They found bilobed in 84.5%, trilobed in 13.3%, single lobed in 2.2%. Murthy KVJ and Velichety SD reported that 74% of the thymus had two lobes, three lobes in 13% and four lobes in 13% [4]. In the present study, any thymus with four lobes was not seen.

In the present study, the various shapes of thoracic part of thymus observed were elongated and parallel, retort shaped, irregular, curved (C-shaped), elongated and tapering and circular. Boyd WJ et al., have stated that it may be broad and irregularly lobulated whereas Moore KL and Persaud TVN., have described the presence of flat glands with flask shaped lobes [8,11].

Hasini SH et al., described five shapes of thymus (oval, triangular, H-shaped, pyramidal and irregular) [9]. In present study authors did not come across any oval and H-shaped thymus gland. They have also described triangular, teardrop oval and sickle shaped thymic lobes, in the longitudinal scans of sonography and radiography. The sickle shape described by Hasini SH et al., seems to be similar to the C-shape thymus described in the present study. Felkar RE et al., have also described the various shapes viz., rounded, quadrilateral and pyramidal in their sonographic study [12].

The lower extent of thymus reached the great vessels in one case and in another three cases it covered the atria whereas in none of the cases studied, the thymus extended upto the diaphragm which is in agreement with Hasini SH et al., [9]. In the majority of the cases the left lobe reached ventricles upto a variable extent.

Findings of the present study regarding the maximum height and width of the thoracic part of thymus are in agreement with Sophia MM and Kalpana R, which shows that there is a gradual increase in the measurement with advancing foetal age and the measurement of cervical part of thymus decreases with the advancing GA [2]. Murthy KVJ and Velichety SD found an overlap between the two lobes of thymus in 20% cases whereas in the present series it was found in 3 cases only [4].

Limitation(s)

The number of foetuses in various age groups was small (specially group III and IV) and if it is carried out in a larger group it will provide more valid statistical values.

CONCLUSION(S)

There is a regression in the cervical part and an increase in the dimensions of the thoracic part with the advancing GA of the foetus. The present findings of morphometry of foetal thymus are important for radiologist to differentiate thymus from other mediastinal structures and for surgeons during thymectomy.

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