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Original Article

Morphological and Histological Features of Human Fetal Thymus Gland

M Mahima Sophia[1], R Kalpana[2]

[1]Associate Professor, Department of Anatomy, ACS Medical College and Hospital, Chennai, Tamil Nadu, India, [2]Professor, Department of Anatomy, Sri Muthukumaran Medical College & Research Institute, Chennai, Tamil Nadu, India

Abstract

Introduction: Thymus is a primary lymphoid organ and plays a very great role in strengthening of the immune system. The aim of this study is to observe the morphometric and histological changes of thymus gland at different weeks of gestational life of human fetuses.

Materials and Methods: Fifteen human fetuses ranging from 12th to 38th weeks were studied in the Department of Anatomy, Sri Muthukumaran Medical College and Research Institute, Mangadu, Chennai. The fetuses were examined for crown rump length and body weight to assess the gestational age (GA). The length and breadth of the lobes of fetal thymus were noted, and the tissue was processed for histological examination.

Results: The length of the right lobe of thymus gland was 0.2 cm at 12 weeks of gestation and 4 cm at 38 weeks of gestation. The breadth of the right lobe of thymus gland was 0.1 cm at 12th week of gestation and 2.1 cm at 38th week of gestation. The length of left lobe of thymus gland was 0.1 cm at 12 weeks of gestation and 4.5 cm by 38th week. The breadth of the left lobe of thymus gland measured 0.1 cm at 12th week of gestation whereas at 38 weeks it was around 2.1 cm. Formation of lobules were observed during the 12th week and differentiation of cortex and medulla was clearly evident during the 14th week. The presence of Hassall's corpuscles was observed from 15th week and found to be increased in size and number with an increase of GA.

Conclusion: Morphometry and histological observations of thymus gland show great variation at different weeks of gestation which can be considered during thymectomy and can also be used as reference value during imaging studies.

Key words: Fetal thymus, Histological differentiation, Histology of thymus, Morphometry

INTRODUCTION

The thymus gland is a primary central lymphoid organ and a key regulator of the immune system. It plays a significant role in cellular immunity of the body as T-lymphocytes develop in this organ and maturation takes place within it.[1] The name thymus is derived from the Latin derivative of the Greek word thymus meaning "warty excrescence" because of its resemblance to the flowers of the thyme plant.[2] The majority of the thymus is located in the middle mediastinum and it grows rapidly during the embryonic life and childhood and reaches its maximum size during the puberty. Thereafter, the growth stops and starts involuting gradually until the old age where the gland is often smaller than at birth.[3] The involution of the thymus gland is shown by decrease in the weight of the organ associated with atrophy of lymphoid tissue and replacement by adipose tissue.[4]

The thymus is a bilobed structure which is divided into lobules by connective tissue septa. Each lobule consists of cortex and medulla. At 8th week of gestational life, the two advancing lobes are united at midline and the basophilic stem cell and thymocytes come to lie between the epitheliocytes which can be easily differentiated. Thymus is covered with a connective tissue capsule which is composed of collagenous connective tissue fibers.[5] Hamilton and Mossman[6] reported that epithelial cells of developing thymus become loosely arranged to form a reticulum in which small lymphocytes appeared at around 9th week, and soon the vascular mesodermal tissue invaded the gland to produce lobulation.

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Corresponding Author: Dr. M Mahima Sophia, E33, Arihant Amara, Poonamallee High Road, Goprasanallur, Chennai - 600 077, Tamil Nadu, India. Phone: +91-9840319123. E-mail: mahimasophia1982@gmail.com

Lobulation of thymus gland was observed to occur at 10th week by Ghali *et al.*[7] and 12th week by Haar.[8] Differentiation of cortex and medulla observed at different timings by different workers - 11th week by Ghali *et al.*[7] and 14th week by Haar.[8] Hassall's corpuscles found to be observed ranging from 8th to 16th week at different gestational age (GA) groups.[9]

The thymic structures and the microarchitecture of thymus gland are mainly responsible for T-cell differentiation and development of cellular immunity. Hence a thorough understanding of the anatomical and histological features of the developing thymus gland is helpful for analyzing the pathology of the thymic neoplasia. Hence, the main aim of this study is to observe the morphometric and histological changes of thymus gland at different weeks of gestation in human fetuses.

MATERIALS AND METHODS

This study was conducted on 15 human fetuses of different GA groups ranging from 12th to 38th weeks in the Department of Anatomy, Sri Muthukumaran Medical College and Research Institute, Mangadu, Chennai. The fetuses were examined for crown rump length and body weight to assess the GA. The thorax of the fetus was opened by sternoclavicular disarticulation and resection of costal cartilage, and the lower part of the neck was also opened for complete exposure of the thymus gland in its natural location for proper recording.

The fetal specimens were categorized into three groups

- Group I - Up to 12 weeks
- Group II - 13-24 weeks
- Group III - 25-40 weeks.

The length and breadth of the thymus gland were measured, and the specimens were subjected to histological examination. After proper fixation, tissue was subjected to tissue processing and sections of 5 μ thickness were obtained and stained with hematoxylin and eosin. The tissues were examined under ×10 and ×40 magnifications using a binocular microscope. The results obtained were tabulated and analyzed.

RESULTS

Morphometry of Thymus Gland

The length and breadth of both right and left side lobes were measured (Figure 1) and tabulated for each group in Tables 1-3.

The morphometric measurements of thymus gland have been summarized in Tables 1-3. The length of the right lobe of thymus gland was 0.2 cm at 12 weeks of gestation and it is increased to a maximum of 4 cm at 38 weeks of gestation. The breadth of the right lobe of thymus gland increased gradually from 0.1 cm at 12th week of gestation to a maximum of 2.1 cm at 38th week of gestation. The length of left lobe of thymus gland was 0.1 cm at 12 weeks of gestation and increased up to 4.5 cm by 38th week. The

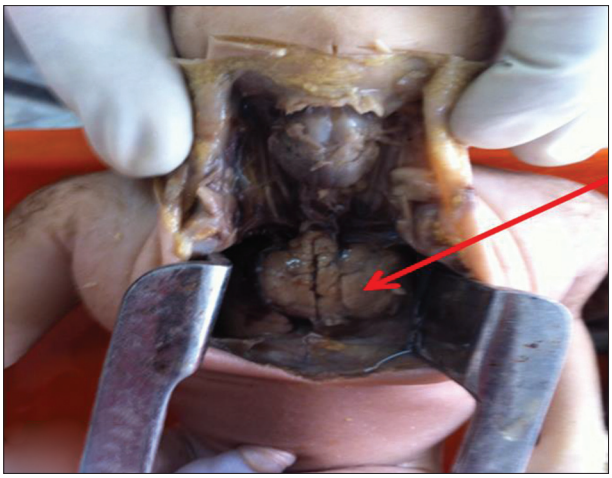

Figure 1: Right and left lobes of thymus (red arrow) at 34 weeks of gestation

Table 1: Group I (up to 12 weeks) – 1 fetus

GA (in weeks)	Right lobe		Left Lobe	
	Length (cm)	Breadth (cm)	Length (cm)	Breadth (cm)
12	0.2	0.1	0.1	0.1

GA: Gestational age

Table 2: Group II (13-24 weeks) – 7 fetuses

GA (in weeks)	Right lobe		Left lobe	
	Length (cm)	Breadth (cm)	Length (cm)	Breadth (cm)
14	0.1	0.1	0.3	0.1
16	0.7	0.2	0.5	0.2
17	0.9	0.4	0.5	0.4
18	0.9	0.4	0.8	0.4
20	0.8	0.3	0.7	0.2
24	1.1	0.4	1.1	0.3
24	1.7	1.6	0.8	0.9

GA: Gestational age

Table 3: Group III (25-40 weeks) – 7 fetuses

GA (in weeks)	Right lobe		Left lobe	
	Length (cm)	Breadth (cm)	Length (cm)	Breadth (cm)
29	2.1	1.5	3.0	1.5
30	2.2	1.5	3.6	1.8
32	2.3	1.4	2.9	1.6
32	2.5	0.9	2.8	1.7
34	2.8	1.3	3.0	2.0
34	2.8	1.4	2.3	1.6
38	4	2.1	4.5	2.1

GA: Gestational age

breadth of the left lobe of thymus gland measured 0.1 cm at 12th week of gestation whereas at 38 weeks it was around 2.1 cm. This shows that the both the right and left lobes shows a gradual increase in their morphological measurements.

Histological Observations

Under light microscope, the observation of the following groups at different gestational weeks was as follows:

Group I (up to 12 weeks)

The gland was seen to be made up of plenty of lymphocytes which are covered by a thin delicate capsule. Lobulation had just started with no distinct differentiation of cortex and medulla. Hassall's corpuscles were not seen at this stage. Trabeculae associated with blood vessels were recognizable (Figure 2).

Group II (13-24 weeks)

The gland was observed to be surrounded by a connective tissue capsule. The connective tissue trabeculae extended between the lobules, while the lobulation was still advancing at this stage. The number of lobules increased in number with the increase of GA. Cortex and medulla differentiation was observed from 14th week, and the peripheral part of the lobule which is darkly stained and heavily infiltrated with lymphocytes is its cortex while the central part of the lobule with few lymphocytes and lightly stained is its medulla. Hassall's corpuscles could not be seen until 14th week. Hassall's corpuscles were clearly visible in the medulla from 15th week and it also increased in size and number with an increase of GA. Blood vessels seen were extensive in between the lobules. Macrophages and monocytes were also observed at this stage (Figure 3).

Group III (25-40 weeks)

Each lobe seen to be surrounded by connective tissue capsule which extends into the lobe to form septa and divided the lobes into many lobules. Each lobule has an outer cortex and inner medulla. The trabeculae were seen extending into the cortex while the medulla remains undivided. The thymic tissue of each lobule is continuous with that of other lobules in the central part of each lobe. The blood vessels clearly evident at this stage.

The parenchyma of the cortex found to be made up of densely packed lymphocytes which occupy the spaces in the cytoreticulum. Lymphocytes were few in number in the medulla, and the cytoreticulum is clearly visible. The medulla of the adjoining lobules is seen to be continuous with each other. There is a clear demarcation between cortex and medulla forming a distinct corticomedullary junction.

Hasall's corpuscles were observed in various shapes and sizes as epithelial pearls and the majority of them were seen in the medulla (Figure 4). Hassall's corpuscles also found in other sites such as cortex, septa, and corticomedullary junction and also some of them seen close to blood vessels. Hassall's corpuscles in the formative stage were also noted.

DISCUSSION

Thymus gland develops as an epithelial outpouching from the ventral aspect of the third pharyngeal pouch. It starts to descend toward mediastinum and moves caudally forming what is known thymopharyngeal complex. Inferior parathyroid also develops from 3rd pharyngeal pouch. Ventral aspect of 4th pharyngeal pouch gives rise to very minor and rudimentary portion of thymic tissue.[10] Descent of heart and caudal migration of aortic sac helps in caudal migration of thymic rudiments.[11]

As reported by Hollinshead,[12] the upper pole of one or both lobes of the thymus extends upward into the neck or

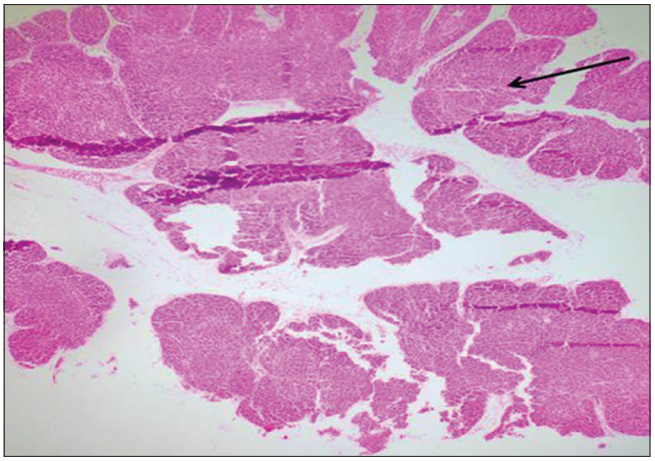

Figure 2: Human fetal thymus showing the lobulation (black arrow) at 12 weeks of gestation

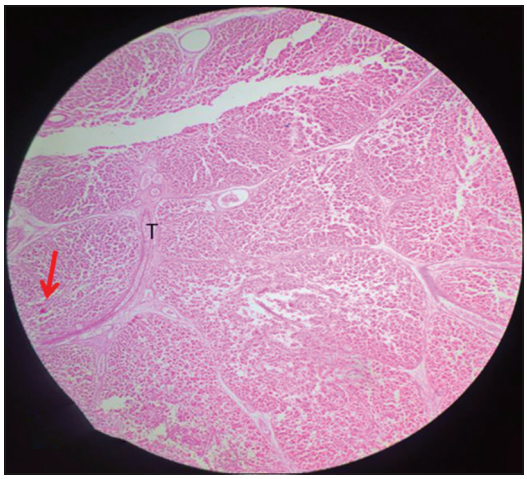

Figure 3: Human fetal thymus showing trabeculae (T), differentiation of cortex and medulla and Hassall's corpuscles (red arrow) at 24 weeks of gestation

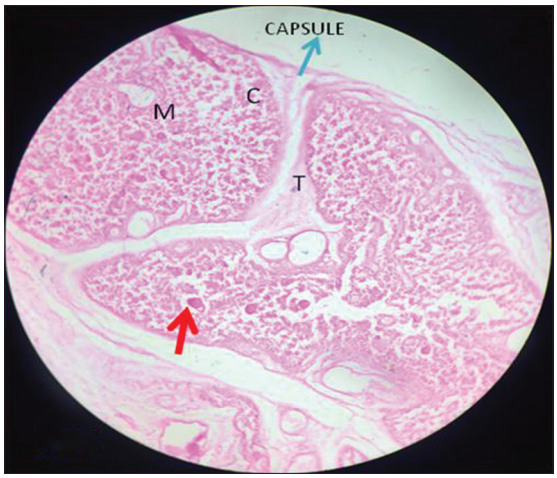

Figure 4: Human fetal thymus showing capsule (blue arrow), trabeculae (T), well-developed cortex (C) and medulla (M) with Hassall's corpuscles in it (red arrow)

to the level of the thyroid cartilage which is due to failure of the thymus to complete its migration into the thorax. Williams *et al.*[5] also reported that the upper pole of thymus can extend up to inferior pole of the thyroid gland. In the study conducted by Ajita *et al.*,[9] one of the specimen showed the extension of the upper pole of thymus into the lower pole of the thyroid gland. In this study, in all the specimens, the entire gland was seen to be soft, lobulated, and located in superior mediastinum behind the sternum. In a study conducted by Vijayalakshmi *et al.*,[10] rudiments of thymus was seen at 12 weeks of gestation with the right and left lobes weighing about 0.1 g. The length of the right and left lobe measured about 0.2 and 0.1 cm, respectively, and length of the gland reached a maximum of about 5.2 cm by 40 weeks of gestation. The breadth of the gland found to be 0.1 cm at 12 weeks of gestation and reached a maximum of 4.2 cm at 40 weeks of gestation. In this study, the length of the right and left lobe observed to be 0.2 and 0.1 cm showing dissimilarity in the lobulation of the thymus gland. The length of the gland reached a maximum of about 4.5 cm at and breadth of the gland reached a maximum of about 2.1 cm at 38 weeks of gestation which showed a gradual increase in the size of the thymus gland, whereas most of the authors reported a decline in the growth rate in the third trimester.

In the study conducted by Ajita *et al.*,[9] lobulation started at 9th week and completed by 12th week. Padmavathy[13] observed lobules had started formed during the 9th week and formation of lobules clearly evident after 12 weeks. In the study conducted by Vijayalaksmi *et al.*,[10] lobulation was reported to be observed at 16th week of gestation. In this study, lobulation was observed at 12th week of gestation but it can be clearly defined only after 14 weeks of gestation.

Differentiation of cortex and medulla was observed at 11th week of gestation by Ghali *et al.*,[7] 12th week of gestation by Hamilton and Mossman,[6] 14th week of gestation by Haar,[8] and 16th week of gestation by Vijayalakshmi *et al.*[10] In the study conducted by Padmavathy,[13] differentiation of cortex and medulla observed from 14th week onward. In this study, differentiation of cortex and medulla found to be observed at 14th week of gestation.

The appearance of Hassall's corpuscles was observed during the 8th week by Fawcett,[14] 9th week by Gilhus *et al.*,[15] 10th week by Williams *et al.*,[5] 11th week by Ghali *et al.*,[7] between 15-16th week of gestation by Lobach and Haynes.[16] In the study conducted by Padmavathy,[13] Hassall's corpuscles observed from 14th week of gestation. Vijayalakshmi *et al.*[10] observed the Hassall's corpuscles at 18 weeks of gestation. In this study, Hassall's corpuscles were found to be observed at 15th week of gestation and corpuscles increased in number, size, and maturity with an increase in GA.

Hayward[17] reported the appearance of epithelial cells from 10th week and von Gaudecker B, Müller-Hermelink[18] reported at 10th week and Ajita *et al.*[9] observed from 9th week onward. In this study, the epithelial cells observed from 12th week since fetus before 12th week were not examined in the study. Macrophages also found to be observed from 12th week onward.

Knowledge of morphometry of thymus gland is an important for clinicians to diagnose a variety of clinical (thymic hyperplasia) and congenital diseases of thymus. It is also an important for radiologists to differentiate thymus from other mediastinal structures, such as lymph nodes and superior sinus of the pericardium.

CONCLUSION

Morphometry and histological observations of thymus gland show great variation at different weeks of gestation which can be considered during thymectomy and can also be used as reference value during imaging studies in the prenatal stage. With the discovery of various intensive chemotherapy protocols and also infection with HIV leading to severe loss of T-lymphocytes has brought an importance to understand the role of human fetal thymus in building up the immune system in adults. Hence, the knowledge of embryology and anatomy of thymus is an important for clinicians to avoid unnecessary imaging and invasive procedures.

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