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Research Article

HISTO-MORPHOGENESIS OF THYMUS IN HUMAN FOETUSES

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ABSTRACT
The name thymus comes from the latin derivation of the Greek thymus, meaning "warty excrescence," due to its resemblance to the flowers of the thyme plant. The earliest known reference to the thymus is attributed to rufus of ephesus circa 100 a.d, a Greek anatomist renowned for his investigations of the heart and eye. Rufus attributed the discovery of the thymus to the Egyptians. 50 human foetal thymus were used for the present work . Thymus rudiment was found at 12 weeks of gestation in superior mediastinum. Lymphocyte infiltration in thymus of human fetuses is distinguished from 12th week of gestation onwards lobulation, cortex and medulla are seen by 16th week of gestation. Hassall's corpuscles were visible in medulla by 18th week of gestation.

Key Words: *Cortex, Hassall's Corpuscle, Lymphocytes, Thymus*

INTRODUCTION
The name thymus comes from the Latin derivation of the Greek thymos, meaning "warty excrescence," due to its resemblance to the flowers of the thyme plant. The earliest known reference to the thymus is attributed to Rufus of Ephesus circa 100 A.D, a Greek anatomist renowned for his investigations of the heart and eye. Rufus attributed the discovery of the thymus to the Egyptians. Hassall AH and Vanarsdale H (1846) used recent improvements in compound microscope lens quality to study the thymus more thoroughly. Hassall's famous corpuscles were thus named. They also described differences between the thymus and other lymphoid tissues.

Cooper (1833) noted that there was wide variability in thymic size and morphology and reconfirmed Galen's (1968) observations with regard to fetal and infant growth. The thymus is a primary central lymphoid organ and a key regulator of the immune system, and is responsible for cellular immunity of the body. It is a bilobed structure divided into lobules by the connective tissue septa. Each lobule consists of a cortex and medulla. At the 8th gestational week, the two advancing lobes were united at midline; and the basophilic stem cell and thymocytes came to lie between the epitheliocytes that were visibly differentiated Ajita *et al.,* (2006). Observations regarding morphology and histological changes of human foetal thymus at different gestational ages are recorded from 50 human foetusus

MATERIALS AND METHODS
The present work is the result of study of 50 human foetal thymus obtained from local government and private hospitals. Age of the fetuses ranged from 12-40 weeks. The age of fetuses is judged by CR lengths. 10 days after formalin fixation, fetal autopsy was done and thorax of the fetus is opened by sterno clavicular disarticulation and resection of costal cartilages for complete exposure of the thymus gland in its natural location for proper recording.

The human fetuses were categorized into 3 groups.

1st group - upto 12 weeks
2nd group - 13-24 weeks
3rd group - 25-40 weeks

The weight, and morphometry of the thymus were recorded and they were subjected to histological procedure as per protocol. Sections of 5microns thickness were stained with haematoxylin and eosin and examined under 10x and 40x magnifications using a trinocular microscope

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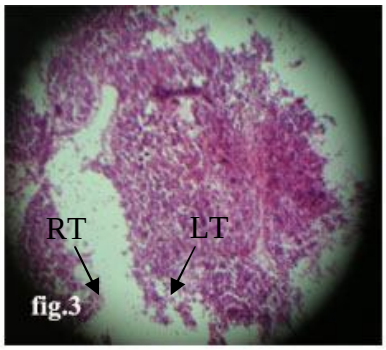
RESULTS

A rudiment of thymus was found at 12 weeks gestation, in superior mediastinum (Figure 1). The total weight of the thymus was 0.1 gms and the length is 0.2 cms. The weight of the thymus increased from fetuses of 12 weeks of gestation up to a maximum of 10 gms, by 38-40th week of gestation. The length of the right lobe of the thymus also increased gradually from 0.2 cms at 12th week of gestation to a maximum of 5.2 cms by 40th week.(Figure 2). Breadth of the right lobe at 12 weeks of gestation was 0.1 cms where as at 40 wks of gestation it was 4 cms. The left lobe of thymus measured a length of 0.1 cm at 12 wks of gestation and increased upto 4.8 cms by 40th week. The breadth of the left lobe was 0.1 cm at 12 weeks of gestation and it measured 4 cms by 40th week of gestation. [Table-1]



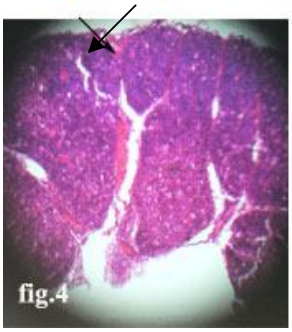


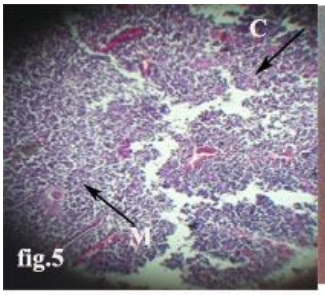
fig.1 showing thymus at 12 wks of gestation
fig.2 showing right and left lobes of thymus at 40 wks of gestation
fig.3 showing undifferentiated cortex at 12wks of gestation, H&E, 10X10
fig.4 showing lobulation and differentiationof cortex at 16 wks of gestation, H&E, 10X10

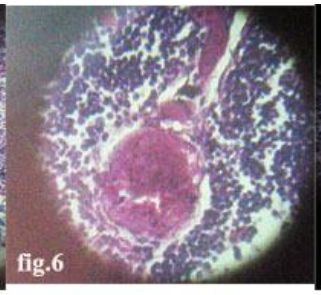
This shows that both right and left lobes of thymus showed a gradual increase and slightly dissimilarity in their morphological measurements. No abnormalities have been observed macroscopically. Both lobes of the thymus were covered by a very thin connective tissue capsule and the lobulation appeared by 16th week of gestation.

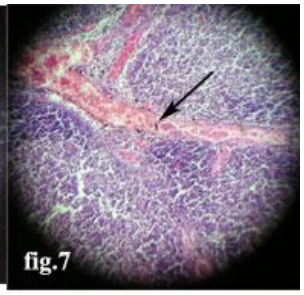
The lobulation and corticomedullary distinction was not observed at 12 wks gestation. The lymphocytes were seen dispersed all over the stroma (Figure 3) the capsule of the gland was modified to form septae separating the lobules with penetrating vessels (Figure 4). Differentiation of Cortex and Lymphocyte infiltration was noticed during 16th week of gestation. Medulla was recognized by its light stain containing R.B.C and epithelial cells.

Lobules were prominent and, differentiation of cortex and medulla became sharp. (Figure 5) Each lobule had a peripheral dark zone called cortex and a light central zone called medulla .Medulla was continuous from lobule to lobule throughout each lobe of thymus. Blood vessels , connective tissue of the capsule and trabeculae became more extensive. Hassall's corpuscles which are peculiar nest like bodies with a central mass consisting of more granular cells made their appearance in 18th week of gestation. (Figure 6) Very distinct trabecular frame work with vascularity was prominently noticed. Cortex with dense populated lymphocytes is observed. Medulla possessed Hassall's corpuscles of increasing maturity with few lymphocytes (Figure 7) in 20th week of gestation. Similar findings were observed in 24 weeks of gestation. The gland during 34th week of gestation showed internal architecture of lobulation, septation and cortical demarcation with increased density of lymphocytes and medulla

having Hassall's corpuscles. There is complete differentiation of epithelial cells into reticular cells. (Figure 8)







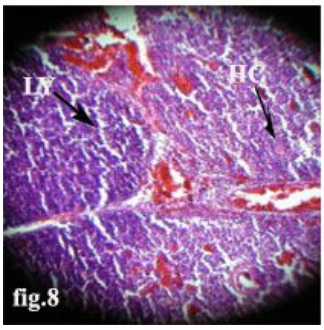


fig.5 showing differentiation of cortex and medulla at 18 wks of gestation, H&E, 10X10
fig.6 showing Hassall's corpuscle at 18 wks of gestation, H&E, 40X10
fig.7 showing trabecular frame work and vascularity at 20 wks of gestation, H&E, 10X10
fig.8 showing increased density of lymphocyes and Hassall's corpuscle at 34 wks of gestation, H&E, 10X10

Embryology

Thymus gland finds it's pathway of descent from 3rd branchial arch. During the 6th week of gestation, epithelial out pouching from the ventral aspect of 3rd branchial arch starts to develop and move caudally forming what is known as thymopharyngeal duct. Inferior parathyroid also develops from 3rd pharyngeal arch. There was a very minor and rudimentary portion of thymic tissue which develops from ventral aspect of 4th pouch.

Table 1: Showing Weight, Length and Breadth of Lobes of Thymus

S.NO	Foetus No	Age (weeks)	Weight (gms)	Length(cms) Right Lobe	Length(cms) Left Lobe	Breadth(cms) Right Lobe	Breadth(cms) Left Lobe
1.	10	12	0.1	0.2	0.1	0.1	0.1
2.	14	12	0.1	0.2	0.1	0.1	0.1
3.	31	13	-	-	-	-	-
4.	27	14	-	-	-	-	-
5.	08	16	0.2	0.2	0.5	0.2	0.1
6.	04	17	0.3	0.6	0.5	0.1	0.3
7.	05	17	0.4	0.8	0.4	0.4	0.1
8.	07	17	0.3	0.8	0.2	0.2	0.2
9.	06	18	0.5	0.8	0.4	0.3	0.5
10.	09	18	0.5	0.5	0.8	0.2	0.3
11.	19	18	0.5	0.8	0.6	0.3	0.3
12.	19	19	0.5	1.0	1.0	0.5	0.5
13.	32	20	1.0	1.5	1.5	0.5	0.8
14.	41	22	1.0	1.4	1.2	0.3	0.2
15.	42	22	1.5	1.5	1.5	0.3	0.3
16.	47	22	1.5	1.3	1.3	0.8	0.5
17.	44	23	2.0	1.0	1.5	0.3	0.5
18.	20	23	2.0	1.1	1.1	0.5	0.5

19.	21	24	2.0	1.5	1.3	0.3	0.5
20.	24	24	2.5	1.5	1.5	1.0	0.8
21.	02	25	2.5	1.5	2.0	0.7	0.7
22.	15	25	2.5	1.8	1.6	0.5	0.4
23.	22	25	2.0	1.5	1.5	0.5	0.3
24.	23	25	2.5	1.8	2.0	0.4	0.4
25.	49	25	2.0	2.0	2.5	0.5	0.5
26.	43	26	2.0	2.0	2.2	1.0	1.0
27.	12	27	3.5	2.2	2.5	1.0	1.0
28.	16	27	3.0	2.5	2.5	1.2	1.0
29.	50	27	3.0	2.0	2.5	1.2	1.2
30.	13	29	4.0	2.2	3.0	1.5	1.5
31.	37	29	3.0	1.5	2.3	2.2	2.0
32.	39	30	5.5	1.5	2.3	2.0	2.5
33.	33	31	4.0	2.2	2.2	2.2	2.4
34.	38	32	5.0	2.5	2.8	2.2	2.5
35.	26	33	5.3	3.5	3.8	2.6	2.6
36.	03	34	4.5	4.0	4.0	3.0	3.5
37.	17	34	6.0	3.5	4.0	2.5	3.5
38.	18	34	7.4	3.8	4.0	3.5	3.5
39.	25	35	6.0	3.0	3.0	3.5	3.2
40.	36	36	-	-	-	-	-
41.	45	37	7.0	3.5	3.8	3.4	3.6
42.	30	37	8.0	4.0	4.0	3.6	3.5
43.	11	38	10	4.2	4.0	3.2	3.8
44.	28	39	7.0	4.2	4.0	3.0	3.8
45.	01	39	8.0	4.0	4.6	3.8	3.5
46.	29	40	10	4.5	5.0	4.0	4.0
47.	34	40	8.5	5.5	4.5	4.2	4.0
48.	40	40	8.0	4.5	4.0	3.8	4.0
49.	46	40	10	5.2	4.8	4.0	4.0
50.	48	40	8.0	4.8	4.8	3.8	4.0

DISCUSSION

During 7th to 9th week of gestation primordium of parathyroid start to move to midline and eventually fuses and starts their descent towards mediastinum. The capsule around developing thymus maintains the gland in close association with parietal pericardium which is key in its descent to the mediastinum. In the present study, rudiment of thymus was observed at 12th week of gestation having both right and left lobes and weighing about 0.1 gm. The length of the right lobe showed 0.2 cms and left lobe 0.1 cms there by confirming the dissimilarity in the lobulation of the thymus as professed by Scott KJ (2002). The entire gland was soft, lobulated and is present in superior mediastinum behind the sternum, uncovered by origin of sternohyoideii and sternothyroideii. The length of the gland reached the maximum of 5.2 cms by 40th week of gestation whereas most of the authors describe a decline in the growth rate in the third trimester.

Even though, lobulation of thymus gland was reported to occur at 10th week of gestation by Ghali *et al.*, (1980) and 12th week of gestation by Haar (1974). In the present study, lobulation of the thymus was observed at 16th week of gestation. Differentiation of cortex and medulla at 11th week of gestation was reported by Ghali *et al.*, (1980) Hamilton and Mossman (1976) reported the differentiation of cortex and medulla at 12th week of gestation. Haar (1974), Lobach *et al.*, (1987) reported the differentiation by 14th

week of gestation. However, in the present study, the cortex and medulla were differentiated at 16th week of gestation.

Various workers reported the appearance of Hassall's corpuscles at different gestations ranging from 8th to 16th week. In the present study, Hassall's corpuscles were found at 18th week of gestation. Williams et al (1995), Hamilton and Mossman (1976) described, the presence of epithelial cells from 8th week of gestation. Hayward (1972) reported the component of thymus was recognized by the 10th week of gestation. Von Gaudecker and Muller-Hermelink (1980) reported that the primordium of thymus contained exclusively undifferentiated epithelial cells by 8th week of gestation and spindle shaped epithelial cells by 10th week of gestation. The present study, showed the presence of epithelial cells at 12th week of gestation. There were different observations by Williams *et al.,* (1995) that lymphocyte infiltration in the thymus took place as early as 8th week of gestation and at 9th week.

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