AN EXAMINATION OF GROSS AND HISTOLOGY OF THYMUS GLAND IN FOETUSES: A PROSPECTIVE STUDY

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ABSTRACT

Background: The thymus is the lymphoid organ of greatest importance. It is structurally separated lobules through the tissue of the connective septa. That lobule has a cortex and a medulla in it. Many studies of this organ related to the histology of early fetuses are focused on animals. The present study focuses on certain features relating to the histogenesis of the thymus and adolescent fetuses.

Materials and Methods: This is a prospective and observational study conducted in the Department of Anatomy, Ayaan Institute of Medical Sciences Teaching Hospital and Research Center has been undertaken on thymus specimens of 18 fetuses of different age corporations

starting from the crown - rump length (CRL) of these fetuses have been to challenge to morphometry and histometry. The acquired fetuses were set in formalin of 10 per cent. They have been exposed to dissection after correct fixation. The specimens acquired had been processed through a well-known paraffin block making process. Sections were taken with haematoxylin & eosin, and painted. The stained sections had been tested using 40x and 100x optical magnifications and pictures taken under light microscopy.

Results: The histometric analysis of parenchyma (cortex and medulla) and connective tissue indicates that there was no significant variation in their ratio. These corpuscles were frequently seen in thymuses of the early gestational period which were called as Solid Hassall Corpuscle (SHC) and were located at the periphery of the medulla within the age group of the present study. Their size ranged from 25-35 μ m with a mean of 27.156 μ m. This epithelial capsule was separated from the central mass by a subcapsular space that gave a cyst like an appearance hence named primary cystic Hassall's corpuscle (CHC I). Their size varied from 35-70 μ m with a mean of 48.153 μ m thickness Externally the whole structure was surrounded by an epithelial capsule as found in CHC I, hence named as secondary cystic corpuscles (CHC II). They were mainly observed in the central core of the medulla. Their size ranged from 50-100 μ m with a mean of 74.171 μ m thickness late stages were noticed.

Conclusion: Thymus gland involution, pondered in its anatomy and histology, will serve as a basis for becoming conscious of pathological conditions. Within the first 18 weeks of gestation, all structural changes viz. cortico-medullary differentiation, lobulation, and maturity of the hassall's corpuscles happened.

Keywords: Human Thymus Glands, Young Age, Old Age

INTRODUCTION

The thymus is a powerful lymphoid organ number one, and a main immune system regulator, and is responsible for the body's mobile immunity. The bilobed shape, divided into lobules via the septa connective tissue. Every lobule is composed of cortex and medulla. $_{[1,2]}$ This occurs due to accelerated circulating stage of sex hormones. $_{[3,4]}$ Intrauterine infection or stress, results in steroid mediated immune response and this involutes the fetuses thymus gland. Intraamniotic infection throughout pregnancy isn't always clinically obvious and calls for invasive assessments of amniotic fluid, but the easy measurement of fetuses thymic size to the gestational age can help in assessing the pathology. $_{[5-7]}$

Also in respiratory misery syndrome, the gland involutes in size in reaction to higher circulating glucocorticoid and as a consequence can function an important indicator of the disease. [8] The size of thymus depends on genetics and youth nutrition; specially the zinc stage and can turn out to be an oblique predictor of nutritional reputation of the developing fetuses. [9] The

measurement of fetuses thymus permits early prognosis of chorioamnionitis and this is beneficial in diagnosing premature rupture of membrane. [10]

The size of thymus gland in adults and in babies had been examined the use of computed tomography and ultrasonography images. [11] However the present observe specializes in direct visualization of the gland through fetuses autopsy. However, a fifteen years thymus gland in adolescents specializes in direct visualization of the gland by way of fetuses autopsy. Therefore, the simple morphological details and microscopic anatomy of fetuses thymus which predicts its adulthood can function an critical adjunct in diagnosing many diseases.

Materials and Methods

This is a prospective and observational study has been undertaken on thymus specimens of 18 fetuses of different age corporations starting from the crown - rump length (CRL) of these fetuses have been to challenge to morphometry and histometry. The fetuses have been obtained from the Department of Anatomy, Ayaan Institute of Medical Sciences Teaching Hospital and Research Center and one specimen of thymus gland.

The fetuses had been tested for their respective crown rump lengths, gestational a long time and frame weights were used for the study. They had been constant in 10% formalin for 10 days after which subjected to dissection. The volume of the gland, form and the number of lobes had been noted, photos taken and the gland was removed. The base width and maximum top of thymus gland had been measured using a measuring scale. The thymus gland's weight was measured using virtual weighing balance.

A complete anatomical examination in all specimens became accomplished to file routine anatomical growth. A well-known preformed was developed and used to establish a protocol to pick the usual fetuses as useful as possible.

The histological look at protected staining the thymus section the usage of hematoxylin and eosin, masson's trichrome stains. The connective tissue elements which include capsule, septae, and the parenchyma along with cortex, medulla, blood vessels and the cytology of lymphocytes, reticular epithelial cells, adipose cells and Hassall's corpuscle had been demonstrated. The fetuses were arranged as follows in four gestational age groups: between the 15 weeks gestation to 39 weeks gestation, the present study is done. Group I- 17-24 weeks; Group II- 25-30 weeks,; Group III- 31-35 weeks,; Group IV- 36-40 week of getational age.

RESULTS

Table 1 Gestational age based on CRL

15-18	61-100 mm	1
19-22	101-150 mm	2
23-26	151-200 mm	6
27-30	201-260 mm	3
31-34	261-320 mm	4
35-39	321-390 mm	2

Table 2 Grouping of fetuses

Phase	Groups	Gestational Age (Weeks)	Number of Fetuses
Early	Ι	17-24	6
	II	25-30	2
Late	III	31-35	6
	IV	36-40	4

Table 3 Analysis of weight and volume in fetal thymus

Group	Gestational Age	Weight (Grams)	Volume (mm3)
	(weeks)	Mean ± SD	Mean ± SD
Ι	17-24	0.65 ± 0.21	1321 ± 801.45
II	25-30	2.70 ± 0.76	2901 ± 991.31
III	31-35	6.54 ± 0.81	5301 ± 771.41
IV	36-40	13.121 ± 2.40	11366 ± 537.01
Kruskal-Wallis Test		18.343	18.456
p-value		0.001	0.001

Table 4 the weight of thymus and fetus was correlated during intrauterine life

S no	Weight of the fetus (in	Weight of the thymus (in
5.10	grams)	grams)
1	200	0.36
2	250	0.18
3	450	0.95
4	600	2.85
5	650	0.68
6	500	2.99
7	900	0.75
8	550	3.85
9	300	2.17
10	700	3.18

11	1000	0.79
12	1750	5.65
13	1700	4.55
14	1600	6.75
15	1200	5.98
16	900	6.99
17	2500	7.35
18	2900	10.13
19	2400	15.01
20	2600	14.96

Table 5 Ratio of cortex and medulla

	Gestational Age (Weeks)	Cortex (mm3)	Medulla (mm3)	Cortex/Medulla
Group		cortex (mms)	Wieduna (IIIIIS)	Ratio
		Mean ± SD	Mean ± SD	Mean ± SD
Ι	17-24	0.582 ± 0.65	0.485 ± 0.26	4.652 ± 1.75
II	25-30	0.592 ± 0.91	0.546 ± 0.23	5.014 ± 2.23
III	31-35	0.583 ± 0.201	0.452 ± 0.06	5.895 ± 4.51
IV	36-40	0.583 ± 0.028	0.494 ± 0.044	4.785 ± 0.815
Kruskal-Wallis Te	st	0.335	5.398	0.621
p-value		0.832	0.312	0.992

Table 6 Ratio of parenchyma and connective tissue

Group	Gestational Age (Weeks)	Connective Tissue (mm3)	Parenchyma (Cortex+Medulla)/ Connective Tissue
		Mean ± SD	Mean ± SD
Ι	17-24	0.263 ± 0.048	7.785 ± 3.845
II	25-30	0.235 ± 0.039	8.458 ± 3.584
III	31-35	0.258 ± 0.096	9.550 ± 3.298
IV	36-40	0.254 ± 0.017	7.862 ± 2.541
Kruskall Wallis Test		0.212	0.248
p-value		0.985	0.732

The histometric analysis of parenchyma (cortex and medulla) and connective tissue indicates that there was no significant variation in their ratio.

Gestational Age	Salid (SUC) um	Cynetic I (CHC I) um	Custic (CHC II) um
(Weeks)	5010 (SIC) μπ	Cysuc I (CHC I) µm	
17	29.01	57.33	72.00
19	37.74	70.00	66.00
20	36.88	72.48	71.00
22	32.00	67.00	98.00
24	30.34	48.98	82.00
26	33.12	57.75	72.00
27	34.75	40.85	67.57
28	29.75	40.85	67.00
28	34.75	72.05	97.00
29	32.87	52.75	103.84
30	29.75	49.75	78.00
31	28.00	48.36	82.00
32	27.00	42.00	71.25
32	28.00	48.50	64.00
33	24.30	44.75	75.00
34	29.30	54.75	77.00
36	24.30	51.61	71.00
37	24.30	35.21	84.00
38	36.75	39.75	60.85
39	29.60	39.75	52.75
Mean	29.159	50.163	72.171

Table 7 Diameter in different types of Hassall's corpuscles

These corpuscles were frequently seen in thymuses of the early gestational period which were called as Solid Hassall Corpuscle (SHC) and were located at the periphery of the medulla within the age group of the present study. Their size ranged from 25-35 μ m with a mean of 27.156 μ m. Certain corpuscles had a homogenous hyalinized eosinophilic mass in the center encircles by well defined, compactly packed concentric layers of epithelial cells which formed a capsule like structure. This epithelial capsule was separated from the central mass by a subcapsular space that gave a cyst like an appearance hence named primary cystic Hassall's corpuscle (CHC I). Their size varied from 35-70 μ m with a mean of 48.153 μ m thickness Externally the whole structure was surrounded by an epithelial capsule as found in CHC I, hence named as secondary cystic corpuscles (CHC II). They were mainly observed in the central core of the medulla. Their size ranged from 50-100 μ m with a mean of 74.171 μ m thickness late stages were noticed. They were identified especially in the central core of the medulla from late gestational age.

DISCUSSION

Histogenesis of thymus gland in general has been studied extensively by using various techniques starting with simple histological techniques with light microscope to recent immuno histochemical and computer analysis technique by the earlier workers, ^[12,13] to recent workers ^[14-16]. The differentiation of the thymic medulla and cortex occurs in embryos of about 40 mm C.R length. The former arises in the central part of the gland and in the deep portion of the lobules by hypertrophy of the cytoreticulum accompanied by degeneration or migration, of thymocytes. Later Hassall's corpuscles appear as differentiation of the cytoreticulum ^[17]. When sectioned, the thymus is seen to consist of an outer cortex of densely packed cells mainly of the T - lymphocyte lineage, the thymocytes, and an inner medulla rich in connective tissue but with fewer lymphoid cells.

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When sectioned, the thymus is seen to consist of an outer cortex of densely packed cells mainly of the T - lymphocyte lineage, the thymocytes, and an inner medulla rich in connective tissue but with fewer lymphoid cells. Both lobes have a loose fibrous connective tissue capsule, from which septa penetrate to the junction of cortex and medulla, to partially separate the irregular lobules each 0.5 to 2.0 μ m in diameter.

Their function is not clear, although in the past it has been suggested that they are graveyards for thymic cells or regions where immunoglobulins are concentrated. The present study demonstrated that, at 18 weeks - the section showing - the cortex and medulla are well demarcated. Capsule is well defined. The diameter of lobule is 0.4 μ m and diameter of H.C is 29 μ m the average number of H.C per lobule is 2 to 3. At 34 weeks, the section showed well defined capsule and cortex and medulla are well defined. The average diameter of lobule is 1.6 μ m and diameter of H.C is 61 μ m and the average number of H.C per lobule is 7 to 8.

At pubertal age, the section showed well defined capsule, cortex and medulla were well demarcated. Interlobular connective tissue is more with some adipose tissue. The average diameter of lobule is 2 μ m and average diameter of H.C is 94 μ m and average no of H.C per lobule is 8 to 9. The diameter of lobule is ranging from 0.4 to 2 μ m and diameter of H.C ranging from 29 to 94 μ m and there is gradual increase in thickness of interlobular connective tissue with some adipose cells observed at puberty.

CONCLUSION

There is clear demarcation of capsule and inter lobular septa with the advancement of age of fetuses. There is clear demarcation of lobules with the advancement of age of fetuses. Blood vessels in the interlobular septa became prominent with advancement of age of fetuses. Cortex and medulla are well demarcated at age of 18 weeks. Diameter of lobules is ranging from 0.4 to 2 μ m. Number of H.C is lobule increased with advancement of age. Inter lobular connective tissue increased with advancement of age. The diameter of H.C is ranging from 29 to 94 μ m. Demarcation of cortex and medulla is very clear with advancement of the age of fetuses.

REFERENCES

- **1.** Kapit wynn and Lawrence M. Elson. The Anatomy Coloring Book. 1st ed. New York; 1997.
- **2.** Guyton, Arthur, M.D. Text book of medical physiology'. 4th ed. Philadelphia: Saunders Company; 1971.
- **3.** Kendall MD. Functional anatomy of the thymic microenvironment. J Anat. 1991;117:1-29.
- **4.** Hamilton W.J., Boyd and Mossman H.W.. Human Embryology 4th ed ., The macmillan press Ltd. 1976:317,318,319.
- **5.** Carleton H.M., and Drury Rab. Histological Technique, 3rd ed. London : Oxford university press; 1957:216-217.
- **6.** A H. Hassall. The Microscopic anatomy of the human body in health and disease. Volume 2. London ;1849:9.
- 7. Gold stein G. Mackay IR . The Human Thymus. London: Heinemann printers; 1969.
- **8.** Blau JN . The dynamic behaviour of Hassall's corpuscles and the transport of particulate matter in the thymus of guinea pig : Immunol 1960;13:281- 292.
- **9.** Gui J, Mustachio LM, Su DM, Craig RW. Thymus size and agerelated thymic involution: early programming, sexual dimorphism, progenitors and stroma. Aging Dis. 2012;3(3):280.
- **10.** Baron RL, Lee JK, Sagel SS, Peterson RR. Computed tomography of the normal thymus. Radiol. 1982;142(1):121–5.
- **11.** Francis IR, Glazer GM, Bookstein FL, Gross BH. The thymus: reexamination of agerelated changes in size and shape. Am J Roentgenol. 1985;145(2):249–54.
- **12.** Baron RL, Lee JK, Sagel SS, Levitt RG. Computed tomography of the abnormal thymus. Radiol. 1982;142(1):127–34.
- **13.** Moore AV, Korobkin M, Olanow W, Heaston DK, Ram PC, Dunnick NR, et al. Agerelated changes in the thymus gland: CT-pathologic correlation. Am J Roentgenol. 1983;141(2):241–6.

- **14.** Hasselbalch H, Jeppesen DL, Ll AKE, Engelmann MD, Nielsen MB. Thymus size evaluated by sonography: a longitudinal study on infants during the first year of life. Acta Radiol. 1997;38(2):222–7.
- **15.** Ghali WM, Abdel-Rahman S, Nagib M, Mahran ZY. Intrinsic innervation and vasculature of pre- and post-natal human thymus. Cells Tissues Organs. 1980;108(1):115–23.
- **16.** Haar JL. Light and electron microscopy of the human fetal thymus. Anat Rec. 1974;179(4):463–75.
- **17.** Thymus size and age-related thymic involution: early programming, sexual dimorphism, progenitors and stromaAging Dis20123328090
- 18. Danielle Aw Alberto B. Silva Mandy Maddick Thomas von Zglinicki Donald B. Palmer Architectural changes in the thymus of aging miceAging Cell200872158671474-9718, 1474-9726Wiley
- **19.** Heather E. Lynch Gabrielle L. Goldberg Ann Chidgey Marcel R.M. Van den Brink Richard Boyd Gregory D. Sempowski Thymic involution and immune reconstitutionTrends Immunol2009307366731471-4906Elsevier BV
- **20.** Ira H. Gewolb Robert L. Lebowitz H. William Taeusch Thymus size and its relationship to the respiratory distress syndrome J Pediatr1979951108110022-3476Elsevier BV
- **21.** J Gui L M Mustachio D M Su R W Craig Thymus size and age-related thymic involution: early programming, sexual dimorphism, progenitors and stromaAging Dis201233280
- **22.** R L Baron J K Lee S S Sagel R R Peterson Computed tomography of the normal thymus.Radiol1982142112150033-8419, 1527-1315Radiological Society of North America (RSNA)
- 23. I R Francis G M Glazer F L Bookstein B H Gross The thymus: reexamination of agerelated changes in size and shapeAm J Roentgenol19851452249540361-803X, 1546-3141American Roentgen Ray Society