

Histogenesis of Human Fetal Thyroid Gland

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Abstract: In human beings thyroid gland is one of the most important endocrine gland. It is differentiated at early embryonic life and has important role in human development. Thyroid gland regulates metabolic rate, psychological development and somatic development. It starts development as early as 24th day after fertilization. The various morphological and histological changes during development at different gestational age were identified during this study. The study was conducted with light microscopic study.

Materials & Methods: 25 intact fetus of different gestational age from 9th week to full term were obtained from department of gynecology, AMC, VSKP. The fetuses were stored in 10% formalin. Thyroid glands were removed with midline neck incision. Histological sections were taken and stained with haematoxylin and eosin stains. Histological changes were identified during different gestational ages.

Results: By the early of seventh week greater part of the glands including follicles and stroma and lobes appeared, there is gradual increases of architecture of gland with colloid material and cellular arrangements is associated with increase of crown rump length but the follicular appearances is not same in the entire lobular part. Gradual increase of colloid, follicular cell height ratio is found as age advances, connective tissue stroma and blood vessels formation structural maturity was completely observed at 18 weeks gestation.

Conclusion: Vascularity of the gland increases with age maximum maturity reached in the present study helps to understand the histological changes of the thyroid gland during embryonic life. It adds certain additional information to the already existing studies, it helps in understanding the thyroid disease of the patients.

Keywords: thyroid, gestational age, follicles, colloid.

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I. Introduction

Morphology : Histology of thyroid gland is important to understand the problems in human development. Studies had indicated that thyroid dysfunction is associated with psychological and developmental abnormalities, various immunoglobulin assays and histological examinations had been done in previous studies, but the anatomical study histological examinations has got very important role in understanding the disease pattern.

Aims & objectives: The present study is to study the histological changes of human thyroid gland during fetal life on spontaneously aborted fetuses from 10 weeks to 36 weeks collected from gynecology department at Andhra medical college, Visakhapatnam. The present study is an attempt to study the histogenesis of thyroid in intrauterine life.

II. Materials & Methods:

The present study was conducted on still born normal fetuses obtained from the department of obstetrics and gynecology, Andhra medical college, Visakhapatnam. Abnormal fetuses were eliminated from study. The fetuses were collected within 2-3 hours after abortion, all fetuses were fixed in 10% formalin by injection method at various sites and kept in formalin solution for 24 hours. Fetal thyroid glands were collected by dissection method and fixed in bouins solution serial sections were taken from different gestational fetuses and stained with haematoxylin and eosin stains the observations including the appearance of colloid in follicles, nuclear appearance and cell position, connective tissue formation were observed. The crown rump length and weight of the gland according to the gestational age were measured. Normal microscope high power or lower powers were used. The arrangement of cells, height, number of follicles were identified, with the help of micrometer and all the measurements were tabulated.

III. Results

The fundamental changes involved in the development are growth, differentiation of follicles, vascular changes, accumulation of colloid, shape of cells were noted. All the thyroid glands collected were grouped into A, B, C, D, E, F and their crown rump length, weight and gestational age were put into tabular form.

Table-1 Thyroid gland grouped in to A TO F

S.NO	Fetuses no	Crown rump length(mm)	Weight (grams)	Gestational age (in weeks)
1.	A			
2.	B	150 mm	119 gm	17-18 weeks II trimester
3.	C	170 mm	267 gm	20 weeks ii trimester
4.	D	185 mm	303 gm	22 weeks II trimester
5.	E	200 mm	368 gm	24 weeks II trimester
6.	F	310 mm	1617gm	32 weeks II trimester

By the early part of the seventh week the thyroid gland lies about the level of laryngeal primordium greater part of its bulk consists of lobes extending on either side of the mid line with only narrow isthmus.

During third month the epithelial cords break up to form cell nests surrounded by young vascular connective tissue more marked in 4th month the characteristic thyroid follicles established with its central mass of colloid surrounded by simple cuboidal or low columnar epithelium in the early part of 4th month, more relevant as gestational age advances.

The later changes involve the accumulation of greater amount of colloid with increasing number of follicles and gradual differentiation of embryonic connective tissue in to characteristic fibroblastic stroma of the adult gland. All the changes were grouped into I II & III as follows.

Group I (10-17 weeks) :

Capsule formation is seen, septa arising from the capsule divides the gland incompletely into lobules. And follicles are few and cords and clusters of epithelial cells were present .follicles seen at the periphery are of small size and irregular in shape during this period follicular cells were simple cuboidal and partly stained muscles fibers were found. In few follicles colloid was found as thin rim and in other follicles no colloid was found. Sinusoids are also seen.

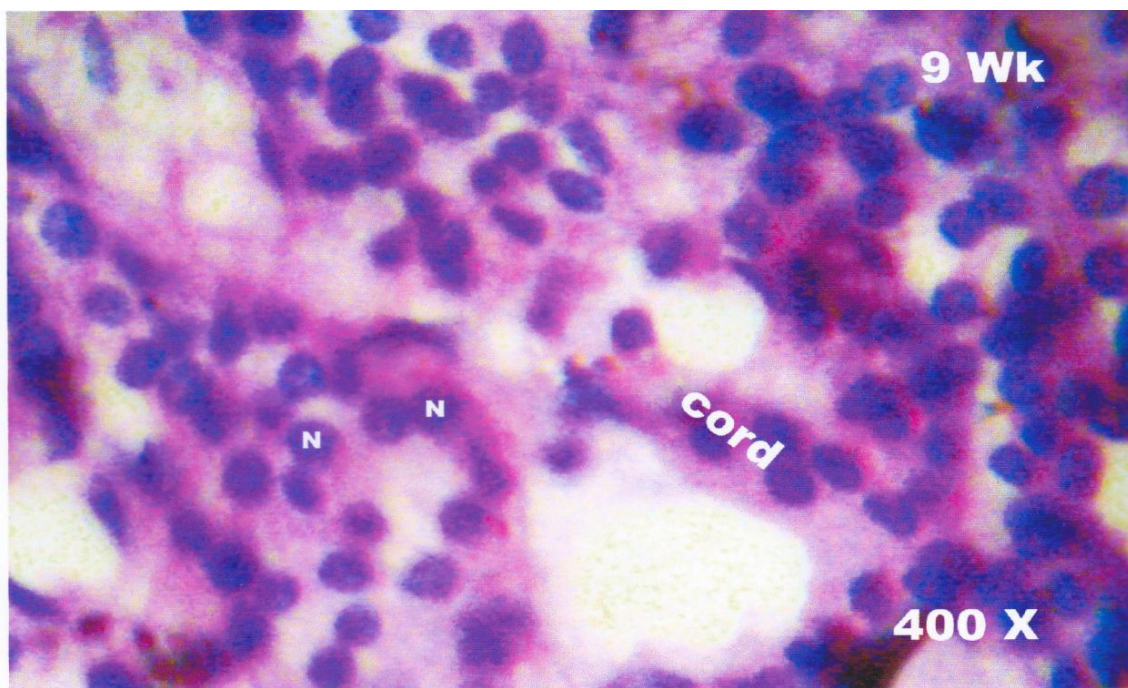


Photo No-1: Microscopic structure of thyroid gland of 9 weeks fetus (H&E 400X).

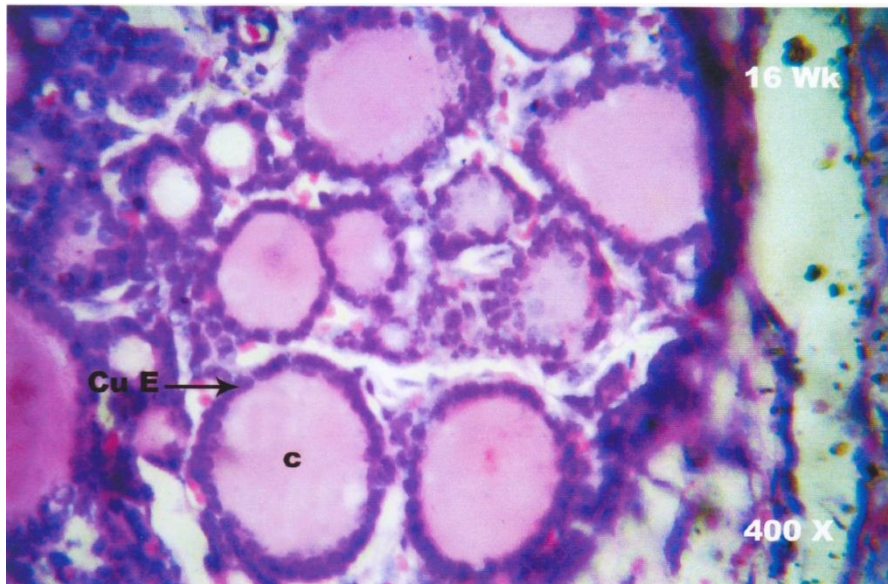


Photo No-2: Microscopic structure of thyroid gland of 16 weeks fetus (H&E 400X)

Group: II (18-22 WEEKS) :

In this stage capsule and septa is found, the number of follicles were increased at the peripheral and central portion of the gland when compared to group 1. The follicles present in the periphery were oval in shape with lumen having rim of colloid. Whereas the follicles present in the central part are small in size with or without lumen. Whereas sinusoids are abundant when compared with group I. This stage is folliculogenesis stage.

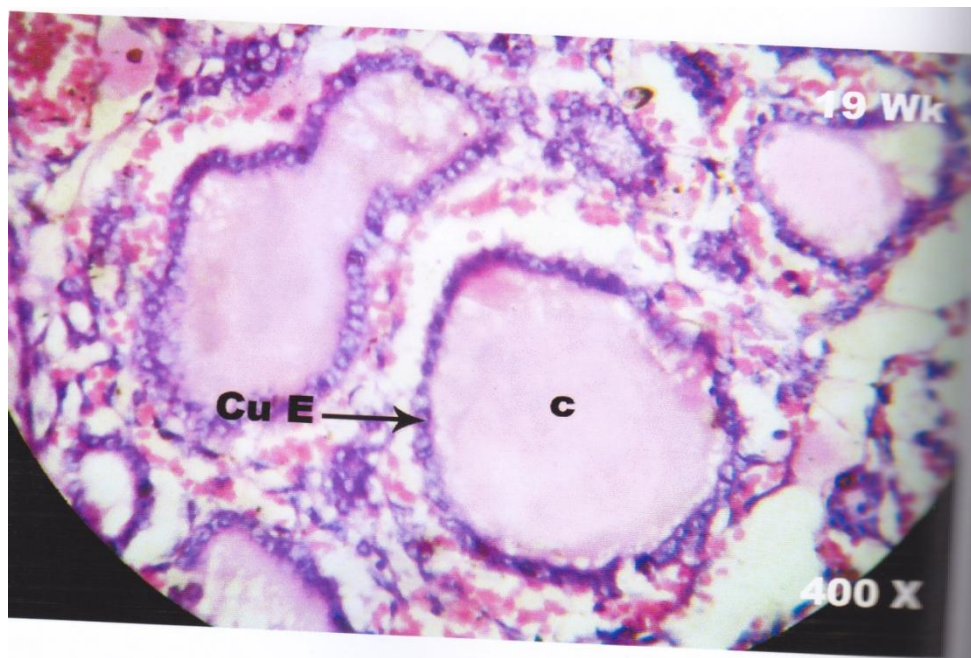


Photo No-3: Microscopic structure of thyroid gland of 19 weeks fetus (H&E 400X)

Group III (26-36 weeks) :

Group III is mature follicular stage, in this group capsule and septa are well defined, abundant blood vessels are also present in the connective tissue. Total number of follicles is increased and varying sizes of follicles were seen. Follicles show simple cuboidal epithelium with centrally placed nuclei, Colloid is present in good quantity and in vacuoles form.

As gestational age increases number and size of follicles increases. The follicles are lined by simple cuboidal epithelium and the connective tissue present between follicles decreases as gestational age is advancing and also associated with increased vascularity as similar to sheared et al studies.

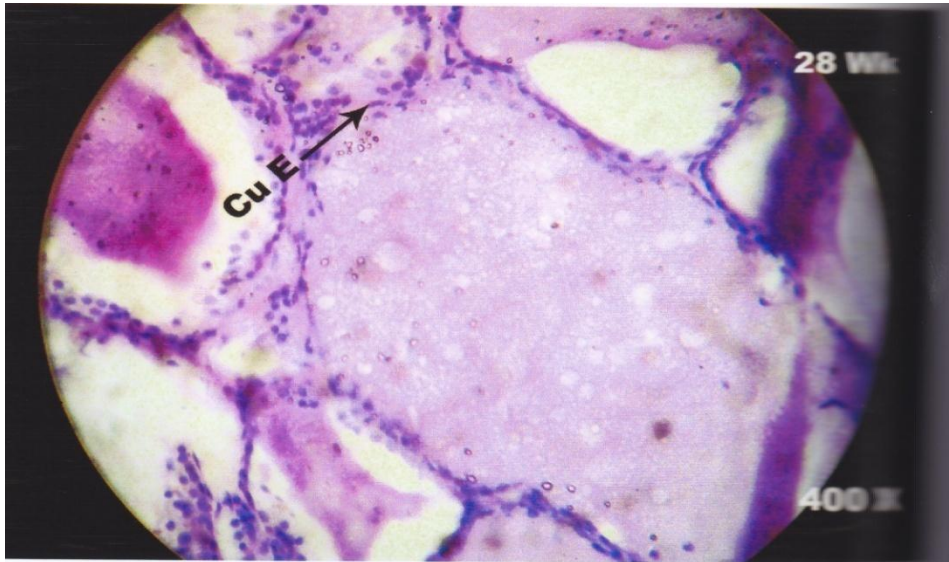


Photo No-4: Microscopic structure of thyroid gland of 28 weeks fetus (H&E 400X)

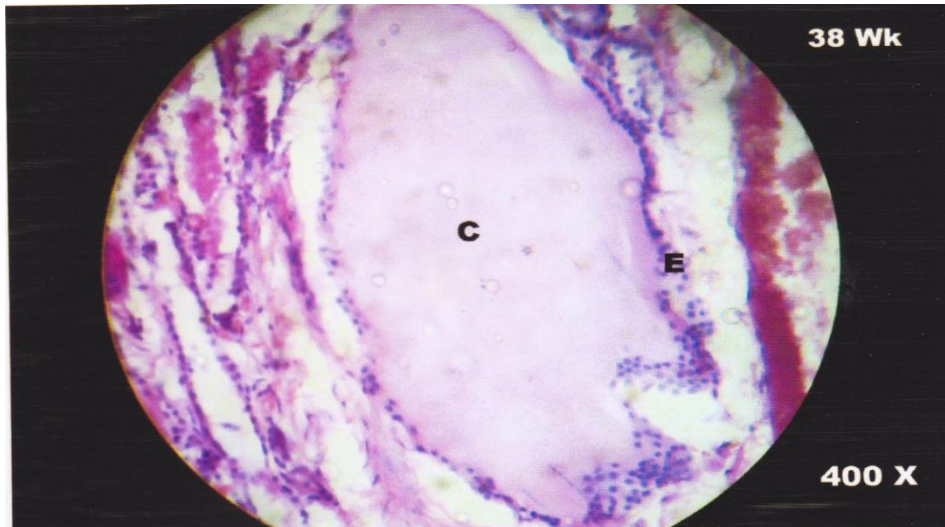


Photo No-5: Microscopic structure of thyroid gland of 38 weeks fetus (H&E 400X)

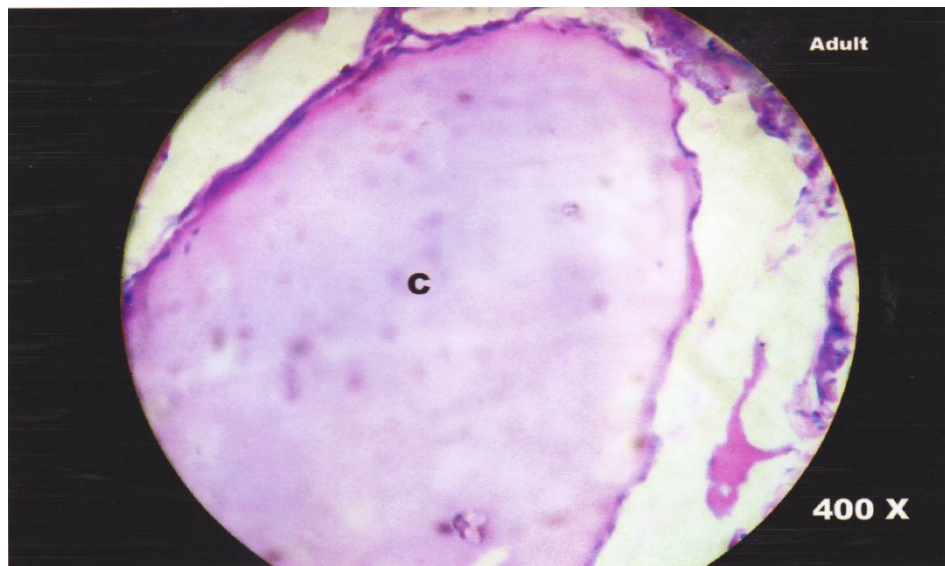


Photo No-6: Microscopic structure of Adult thyroid gland (H&E 400X)

IV. Discussion

Association between thyroid dysfunction and histological changes had been long recognized the association between crown rump length gestational age. According to J. Bocian et al studied on 27 fetuses of age ranging from 23rd to 40th week of intrauterine life, the volume of human fetuses increased proportionally with respect to their crown rump length (CRL). As per this study the number of thyroid follicles increased gradually from 77 in youngest fetus to 170 by the end of IUL. The volume (mm³) of thyroid epithelium, colloid and stroma increased gradually up to 31st week. (1)

Bheemshetty et al in 2015 was done histological study of thyroid gland among fetus in different age groups. In his study it was observed that the weight of thyroid gland showed gradual increase with the increase of gestational age of fetus. It was observed that presence of first colloid contain follicle occurred much earlier in the camel embryo. (2) In our study formation of colloid follicle appeared at 10 to 17 weeks.

A. Anupriya et al done study on 40 intact fetuses of different age ranging from 11 to 36wk, in their study it was observed that the thyroid gland was situated in its definitive location anterior to 1st to 6th tracheal ring in all fetuses and isthmus was related to 4th tracheal ring. The observation of the histological features revealed that development of thyroid gland has three stages as colloid formation, folliculogenesis, and mature follicular growth stage. (3) this study is simulating with present study.

Junguee Lee et al study revealed that as age increases there is variable sizing and enlargement of thyroid follicle, increased irregularity of follicle. Oncocytic changes in follicle, markedly dilated follicles empty of colloid and presence Tg globules. (4)

Though the development of thyroid gland and its maturation of the fetal thyroid function is relatively independent, transplacental passage from mother to fetus takes place, especially from mother iodine and T4 throughout gestation. Contribution of fetal thyroxin from the placenta is very important for normal maturation of the fetus and its neuronal development. (5, 6)

According to Taki.A et al three types of follicles appear in during development of gland those are primitive follicle with radial cells and central intracellular space, transitional type containing a distinct cavity but cells was still immature and definitive follicle. The primary follicle appeared first at 8wks of gestation which is favoring present study in which follicle present in first group. Follicles are very small in number at 8wk stage and increase in number gradually reaching to maximum by the age of 10 to 11 wk which is in favor of our study. (7) Definitive follicle made their appearance first in 13wks of gestational age. Large follicles appear at periphery and small follicles appear in centre. In our study we found the same.

The epithelial cells of the primitive follicle varied from primordial epithelium to follicle epithelium. In early stage 5wk of gestational age the epithelial cells are closely packed without any distinct cell borders, nucleus is vesicular, with a weak chromatic reticulum and eosinophilic nucleolus and varied in size and contour. (7) In our study by 13 wks epithelial cells became completely definitive follicular cell. Follicle cells were cubical to columnar. Those follicles placed peripherally it was tall columnar, while the follicles placed centrally were small and lined with cubical epithelium.

According to Thomas H. Shepard et al the human fetal thyroid between 65 to 80 mm crown rump attains maturity in terms of weight, appearance of colloid contain cavities and ability to produce iodinated organic products. Histogenesis of central colloid cavities is brought about by gradual enlargement and fusion of intracellular canaliculi. This mechanism is activated and controlled by the presence of increasing amount of specific cellular products. (8) Our study is similar to Shepard study.

Jyoti.R Gaikwad et al in their study mentioned about Histogenesis of developing human thyroid. According to the study at 12wks stage gland was covered with thin capsule containing large number of blood vessels, size of the follicle was 30 to 40 μ m with lining epithelium was cuboidal with dark stained nucleus. 13th wk capsule of gland show increased thickness, 15th & 16th Wk stage-At this stage the peripheral follicles were well developed with tall cuboidal epithelium & densely stained colloid, 18th wk capsule was well developed with increased vascularity, 20th to 22nd Wk stage-The thick connective tissue septa along with blood vessel were seen invading. The entire above mentioned feature were found in our study in the first and second group ranging from 18 to 22wk. 28th to 32nd Wk stage-The thyroid showed increase in number & size of follicles with darkly stained colloid in the follicles. Which is correlating with the present study? In present study we have tried to throw more light on histological aspect of fetal thyroid gland

V. Conclusion

The microscopic pattern of thyroid gland in the present study's similar to shepard etl, studies. In all cadavers thyroid gland is similar to previous studies by the present study histogenesis of developing thyroid can be divided in to three stages 10-17 weeks pre colloid stage in which capsule formation starts and the gland is like a small bulb. In 18-22 weeks follicular stage and colloid formation capsule and septa are better .

In 26-36 weeks thyroid gland is mature stage and structurally well differentiated. However the present study corresponds with previous studies and confirms the previous literature regarding thyroid development.

Learning more about the natural process of thyroid morphogenesis and histological features will help for better understanding of tumor cell differentiation and other diseases associated with thyroid gland.

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