Original Article

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Morphological and Histological Features of Human Fetal Thyroid Gland

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Abstract

Introduction: The thyroid gland regulates the basal metabolic rate, somatic growth, and psychic growth. Hence, the thyroid gland plays a major role for the normal growth of a fetus during the prenatal period. It is the first endocrine gland which starts to develop by 24 days after fertilization. The aim of our study is to study the morphological and histological features of the thyroid gland in various age group fetuses.

Materials and Methods: 40 intact fetuses of different gestational ages ranging from 11 to 36 weeks were studied in the Department of Anatomy, Sri Muthukumaran Medical College & Research Institute, Chennai. The fetuses were preserved in 10% formalin solution. Midline dissection of the neck was done to expose the thyroid gland. The situation, shape, and measurements of the gland were noted. Then, sections of the gland were taken for histological study. These sections which were preserved in 10% formalin was processed and stained with hematoxylin and eosin.

Results: It was observed that the thyroid gland was situated in its definitive location anterior to 1st-6th tracheal ring in all fetuses. The gland was horse-shoe shaped in all fetuses, except in one fetus (22 weeks), where isthmus was absent. The isthmus was related to 1-4th tracheal rings. The fetuses were categorized into three gestational age groups as: Group I: 10-17 weeks, Group II: 18-22 weeks, and Group III: 23-36 weeks. The mean and ranges of the length, breadth, and thickness of the right and left lateral lobes were measured in each group. The observation of the histological features revealed that development of thyroid gland has three stages as: Colloid formation stage, folliculogenesis stage, and mature follicular growth stage. These stages were correlated with gestational age.

Conclusion: The present study helps us to understand and correlate the morphological and histological changes during the development of thyroid gland. Such knowledge helps the clinicians to understand the anatomical and histo-pathological changes in certain thyroid gland disorders.

Key words: Fetal thyroid, Histogenesis of thyroid gland, Histological differentiation, Histology of thyroid, Thyroid gland

INTRODUCTION

The thyroid gland is the first endocrine glandular structure to be differentiated. It begins to form about 24 days after fertilization and by 7 weeks, thyroid gland assumes its definite shape and reaches its final site in the neck. By the 11th week, it starts its function of synthesis of thyroid hormones.[1,2] The thyroid gland is an unpaired derivative of the primitive pharyngeal floor, and most human embryologists are of the opinion that in man it follows the typical vertebrate pattern.[3] The morphology and histological structure of the thyroid gland were examined in fetuses to assess the peculiarities of thyroid differentiation before birth. The study of histological differentiation helps us to understand the morphological changes during the development of human thyroid. The thyroid gland regulates the basal metabolic rate, somatic growth, psychic growth, calcium metabolism, and circadian rhythm. Hence, thyroid gland plays a major role for the normal growth of the fetus during the prenatal period. Thyroid gland abnormalities both anatomical and functional are seen in approximately one in 2000-4000 new infants.[4] The main objective of our study is to study the morphological and histological features of the thyroid gland in various age group fetuses.

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MATERIALS AND METHODS

40 intact fetuses of varying gestational ages ranging from 11 to 36 weeks were studied in the Department of Anatomy, Sri Muthukumaran Medical College Hospital & Research Institute. The fetuses were preserved in 10% formalin solution. Following is the procedure followed for the exposure of the thyroid gland. Midline dissection of the neck was done. The situation and shape of the gland was noted. Measurements of the length, breadth, and thickness of the right and left lateral lobes and isthmus of the gland were noted for each fetus.

Processing was done for the histological study of sections taken from the thyroid gland of fetuses. These sections were preserved in 10% formalin. They were subjected to routine processing by dehydration in graded alcohols, clearing in xylol and were embedded in paraffin sections. Sections of 5 μm thickness were cut and stained with hematoxylin and eosin and mounted in Canada balsam. The histological features were observed using a light microscope and correlated with the gestational age.

Based on the histological differentiation and organization, the fetuses were grouped into three gestational age groups as: Group I: 10-17 weeks, Group II: 18-22 weeks, and Group III: 23-36 weeks. The histological features were same for all fetuses belonging to a particular group.

The mean and ranges of the length, breadth, and thickness of right and left lateral lobes and isthmus were calculated for the fetuses in each group.

RESULTS

In the present study, 40 intact fetuses of different gestational age and of both sexes were studied for morphological and histological features.

Morphological Features

Shape

The thyroid gland was "horse-shoe shaped" in all fetuses, except in one fetus where it was "irregular in shape" because isthmus was absent (2.5%).

Extent

The lateral lobes extended from middle or lower border of the thyroid cartilage to 3rd or 4th tracheal ring in all fetuses. The isthmus was related to 1st-4th tracheal rings. 2.5% (1 out of 40) specimens showed the absence of isthmus (Figure 1). Pyramidal lobe (PL) was seen in 30% (12 out of 40) specimens (Figure 2). Levator glandulae thyroidea was present in 15% (6 out of 40) specimens (Figure 3).

Figure 1: Absence of isthmus (shown by arrow) seen in a fetus

Figure 2: Pyramidal lobe (shown by arrow) seen in a fetus

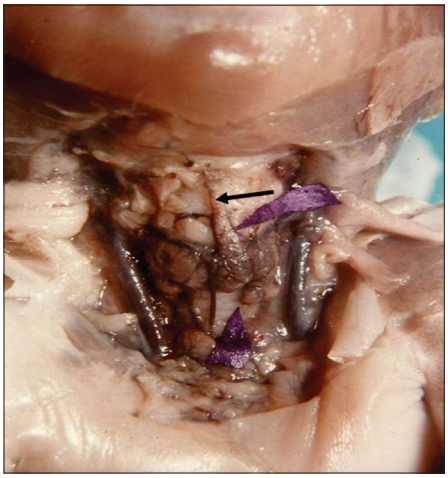

Figure 3: Levator glandulae thyroidea (shown by arrow) seen in a fetus

Dimensions

The mean and ranges of the length, breadth, and thickness of lateral lobes were measured and tabulated for each group as given in Table 1.

From the Table 1, it is observed that during the fetal life the mean of length, breadth, and thickness of lateral lobes for gestational ages 10-36 weeks ranged from 5.6 to 12.1 mm, 2.8 to 4.5 mm, and 1.8 to 2.9 mm, respectively.

The mean and ranges of the length and breadth of isthmus were measured and tabulated for each group as given in Table 2, after excluding one specimen in Group II as the isthmus was absent.

Hence, as noted from the Table 2, the mean of length and breadth of isthmus for gestational ages 10-36 weeks ranged from 4.07 to 10.6 mm and 2.2 to 5.6 mm, respectively, during the fetal life.

Histological Features

Group I (10-17 weeks): Colloid formation stage

In this stage, it was observed that the capsule was seen with septa dividing the gland into incomplete lobules. Cluster and cords of epithelial cells with very few follicles were seen in the central core of the glands. Follicles which were seen in the periphery were of small size and were irregular in shape. Follicular cells were simple cuboidal cells with darkly stained nuclei. Thin rim of colloid were present in few developing follicles. Colloid was absent in most of the follicles. Sinusoids were present between the follicles. Vascularity increased as gestational age increased. Hence, this stage is considered as "colloid formation stage" (Figure 4).

Table 1: The mean and ranges of the length, breadth, and thickness of lateral lobes

Groups (*n*=40)	Lateral lobes Mean and range (mm)					
	Length		Breadth		Thickness	
	Mean	Range	Mean	Range	Mean	Range
Group I (10-17 weeks) *n*=13	5.6	3-9	2.8	2-4	1.8	1-4
Group II (18-22 weeks) *n*=12	9.5	7-12	4.2	3-6	2.75	2-4
Group III (23-36 weeks) *n*=15	12.1	7-18	4.5	2-6	2.9	2-5

Table 2: The mean and ranges of length and breadth of isthmus

Groups (*n*=39)	Isthmus Mean and range (mm)			
	Length		Breadth	
	Mean	Range	Mean	Range
Group I (10-17 weeks) *n*=13	4.07	1-6	2.2	0.5-4
Group II (18-22 weeks) *n*=11	8.9	3-13	4.9	4-5
Group III (23-36 weeks) *n*=15	10.6	8-13	5.6	3-9

Group II (18-22 weeks): Folliculogenesis stage

In this stage, capsule and septae were present but were incomplete. The periphery and central core of the gland showed increase number of follicles. In the periphery of the gland, follicles were round to oval shape with lumen showing thin rim of colloid. In the central core of the gland, developing follicles were seen which were small in size with or without a lumen. Sinusoids were abundantly present. Hence, this stage is considered as "folliculogenesis stage" (Figure 5).

Group III (23-36 weeks): Mature follicular stage

It was observed in this stage that the capsule and septae were well-defined. Connective tissues between follicles

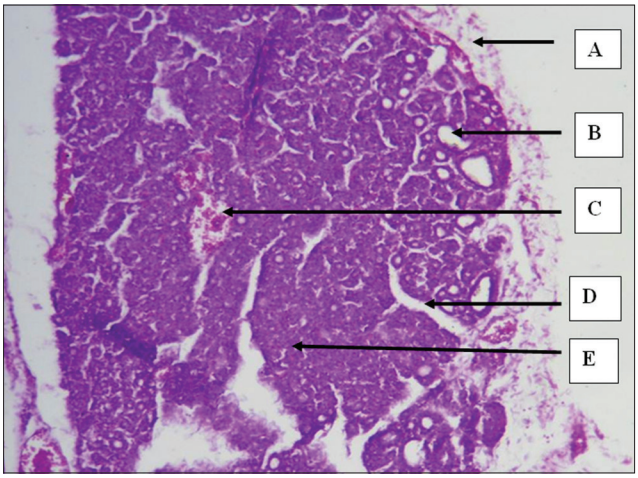

Figure 4: Colloid formation stage: (a) Capsule, (b) peripheral follicle, (c) sinusoids, (d) septa, (e) developing follicles as cluster of cells

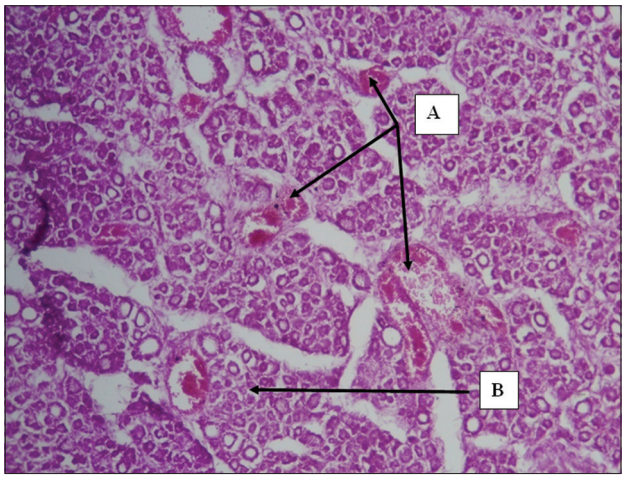

Figure 5: Folliculogenesis stage: (a) Abundant sinusoids, (b) developing follicles in central part of gland

showed abundant vessels. There was an increase in the number of follicles and follicles of varying sizes were also seen. More number of mature thyroid follicles was present in this group which showed simple cuboidal epithelium with centrally placed nucleus. Some follicles showed irregular eroded colloid with vacuoles in it. Hence, this stage is considered as "Mature follicular stage" (Figure 6).

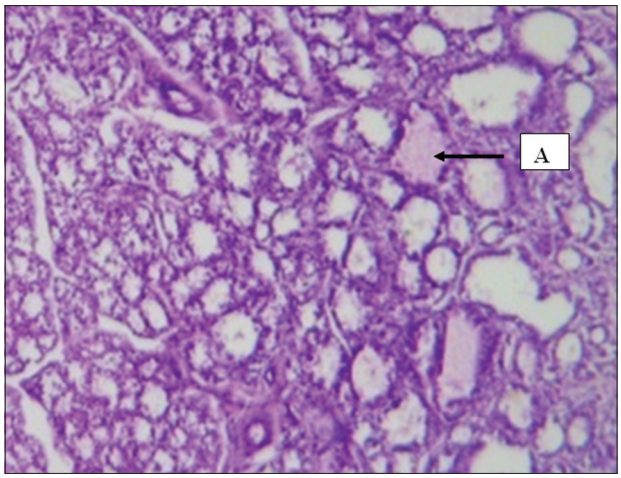

Figure 6: Mature follicular stage: (a) Follicle showing irregular eroded colloid with vacuoles in it

DISCUSSION

In the present study, it was observed that the thyroid gland was "horse-shoe shaped" in all fetuses, except in one fetus where it was "irregular shape" because isthmus was absent (2.5%). Harjeet *et al.*[5] observed different shapes of isthmus such as horse-shoe shaped (36.8%), irregular shape (5.1%), and glands with separate lobes (7.9%). The absence of isthmus was also observed by Lokanadham and Devi[6] in 6.6% specimens and Marshall *et al.*[7] in 10%. This agenesis can be due to an anomaly of embryological development, where there is a high division of thyroglossal duct leading to dysorganogenesis like the absence of isthmus or any one lobe.[8,9] The knowledge of the absence of isthmus is significant for surgeons when performing thyroidectomy as it causes difficulty in identifying vessels and hence leading to major complications.

The knowledge of the presence of PL is important because it causes hindrance during surgery. It also misleads diagnosis of scintigraphical images.[10] The incidence of PL in other studies conducted in different populations is shown in Table 3. In our study, PL was present in 12 out of 40 fetuses (30%).

Table 3: Incidence of pyramidal lobe in different populations

Authors	Presence of pyramidal lobe (%)	Populations
Braun *et al.*[10]	55	Austria
Gangbo *et al.*[11]	76.8	Korea
Lokanadham and Devi[6]	7	South India
Sadat[12]	41.6	Bangladesh
Present study	30	South India

In the present study, the dimensions of thyroid gland increased proportionately with the gestational age, as there is an increase in colloid formation and increase in number and size of the follicles in the gland.

According to the present study, based on the histological differentiation and organization, the fetuses were grouped into three gestational age groups:

1. Colloid formation stage: 10-17 weeks
2. Folliculogenesis stage: 18-22 weeks
3. Mature follicular stage: Above 22 weeks.

This staging differed from staging done by Jyothi *et al.*[13] where four stages were done as follows: Precolloid (upto 12 weeks), colloid formation (13 to maximum 20 weeks), folliculogenesis (14-20 weeks), and secretory stage (20-24 weeks).

In the present study, the capsule was observed from 11 weeks, and it became thick and vascularity increased as age advances. This was also observed by Arthur[14] and Jyothi *et al.*[13] reported that the capsule started to appear as a thin layer by 12 weeks and became thick as age advanced.

In the present study, thyroid follicles started to develop from the periphery of the gland as observed in Group I. According to Jyothi *et al.*,[13] differentiation of follicles started from the periphery as vascularity was more in the periphery than the central part of gland throughout the gestational age of the fetus. Potter[15] observed that epithelial cords are arranged to form small follicles which are solid at first then becomes hollow and filled with colloid. In our study, the epithelial cords formed small solid follicles then it matured to become colloid-filled follicles as age advanced. Hence, Group III fetuses showed few solid follicles in the center and many colloid-filled follicles in the periphery.

As was observed in our study, the number and size of follicles increased as gestational age increased. Follicles were lined by low cuboidal epithelium and appeared empty in sections. According to Shepard *et al.*,[16] connective tissues between follicles decreased as the vasculature increased, and there was a progressive increase in diameter of follicles as gestational age increased. Folliculogenesis is more prominent by 14-20 weeks[13] and 10-18 weeks,[17] and in our study, it was very well-established between 11 and 22 weeks.

Shepard *et al.*[16] observed that human thyroid follicles do not develop synchronously throughout, instead different stages of maturity was seen in fetuses belonging to same age group. Even in large fetuses, there were some areas in which follicles had not developed. Such immature follicles were also seen in Group III fetuses of our study.

In the present study, colloid appeared as a thin rim in the developing follicles of Group I fetuses and increased as gestational age advanced. Colloid in follicle is indicated by its affinity for acidic dyes. Clear vacuoles in colloid and apical position of epithelial cells indicate secretory activity of follicular cells.[18] In our study, it was seen in specimens belonging to Group III.

Junqueira *et al.*[19] observed an irregular outline of colloid in active follicles of fixed and stained histological preparation. Arthur[14] reported that colloid seems to have shrunken away from follicular epithelium in such a way as to present a serrated outline when the gland is active. In the present study, a colloid in the follicles appeared irregular and eroded at the periphery in Group III fetuses indicating secretory activity (Figure 6). According to Shepard *et al.*,[16] the scallop like vacuolization of the outer part of the colloid cavity is indicative of utilization of thyroid hormones. This stage corresponds with the time at which radioiodine has been found to accumulate as observed by authors such as Chapman *et al.*[20] and Hodges *et al.*[21]

This study helps us to correlate the morphological changes with histological changes during the development of fetal thyroid gland. Any delay between the stages of histological differentiation leads to hyperplasia of the gland as mentioned by Lokanadham and Devi.[6] The staging of histological differentiation helps us to understand the morphological and functional disorders of the thyroid glands which were also stated by Lokanadham and Devi.[6]

CONCLUSION

The present study helps us to understand and correlate the morphological and histological changes during the development of thyroid gland. Such knowledge helps the clinicians to understand the anatomical and histopathological changes in certain thyroid gland disorders.

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