

Association of Autoimmune Thyroiditis with Thyroid Dysgenesis

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Abstract

Introduction: The thyroid gland is bilobed, with isthmus bridging the two lobes. The thyroid gland develops from the thyroglossal duct, which arises from the foramen caecum as an endodermal thickening during 3th week of intrauterine life, which reaches its definitive position by the seventh week. The high division of the thyroglossal duct can lead to the creation of two distinct lateral thyroid lobes and the absence of the thyroid isthmus. Hence, agenesis of the thyroid gland can be linked to its early embryonic development. Thyroid dysgenesis is also clinically associated with autoimmune thyroiditis (e.g. Hashimoto's thyroiditis), dysorganogenesis, and ectopic thyroid tissue. **Aim:** To establish an association of Autoimmune thyroiditis with thyroid dysgenesis. **Settings and Design:** Descriptive observational study. **Methods and Material:** A study was conducted on 51 formalin-fixed cadaveric thyroid glands over twenty months. After carefully dissecting the anterior aspect of the neck, the thyroid glands with absent isthmus were identified and subjected to histological examination. **Statistical analysis used:** Statistical analysis and sample size calculation was done using formula for prevalence as per previous studies. **Results:** Out of 51 thyroid glands, five glands (9.8%) were found to have absent isthmus and were subjected to haematoxylin and eosin (H&E) staining. All glands demonstrated the presence of diffuse lymphocytic infiltration and atretic thyroid follicles. Three glands showed the presence of hurthle cells, empty thyroid follicles along with diffuse lymphocytic infiltration which are typical histological features of autoimmune thyroiditis. **Conclusions:** The present study of thyroid dysgenesis can be histologically correlated with Autoimmune thyroiditis due to the presence of specific features, such as hurthle cells, diffuse lymphocytic infiltrate, atretic and empty thyroid follicles as seen in 10X and 40X magnification in all five glands. All of the above histological findings are typically seen in auto-immune thyroiditis.

Key-words: Absent thyroid isthmus, Autoimmune thyroiditis, Diffuse lymphocytic infiltration, Hurthle Cells.

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Introduction

The thyroid gland is bilobed, located in the neck anteriorly clasping the trachea. The two lobes are joined in the front of the trachea by a connection of thyroid tissue known as isthmus[1]. The lateral lobes extend from the thyroid cartilage to the fifth tracheal ring. However, the thyroid isthmus extends from the second to fourth tracheal ring. The gland is encapsulated by the pre-tracheal fascia. (Figure 1)

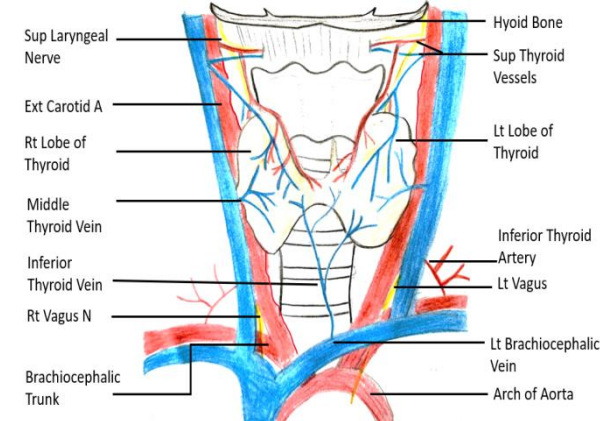


Figure 1: Normal Thyroid Gland

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The thyroid tissue is known to vary both in its structure and the level of hormone it produces during various physiological conditions as well as pathologies. The thyroid gland begins to develop from the foramen caecum as an endodermal thickening during the third week of IUL. The swelling soon proliferates below the foramen caecum to form the thyroglossal duct whose cranial end is connected to the tongue[14]. This duct grows downwards and descends in front of the neck and reaches its definitive position, below the hyoid bone with slight lateral propensity by seventh week, where its tip bifurcates and undergoes proliferation to form terminal bilateral swellings, which forms the thyroid gland. The high division of the duct may result in the formation of two distinct lateral lobes without isthmus. Hence, agenesis of the thyroid isthmus can be linked to its early embryonic development and also due to the persistence of the thyroglossal duct[15]. Thyroid dysgenesis is also clinically associated with autoimmune thyroiditis (Hashimoto's Thyroiditis), dysorganogenesis, and ectopic thyroid tissue[2,13]. Numerous other abnormalities such as aberrant thyroid, persistent pyramidal lobe, and thyroglossal duct are also associated with the thyroid gland[16].

Previous studies affirm that well-preserved thyroid glands in embalmed cadavers could be sectioned for histopathological diagnosis[3,4]. Hence, based on the aforesaid statement we in our study subjected the thyroid glands with absent isthmus for histological evaluation. Literature suggests that the absent thyroid isthmus has been rarely reported[5]. According to previous studies, the prevalence of the thyroid isthmus agenesis ranges between 5% and 10% as per Pastor et al[6].

Subjects and Methods

- To study the prevalence of thyroid dysgenesis

- To perform histological evaluation of thyroid tissue in cases of thyroid dysgenesis and correlate the findings to establish an association with autoimmune thyroiditis

Study Materials

51 embalmed formalin-fixed human cadaveric thyroid glands were studied. The present study is a descriptive cross-sectional study. Donated adult human cadavers both male and female were included in the study.

Exclusion Criteria

- Outside Indian ethnicity.
- Damaged and distorted neck region.
- Cadavers with a previous history of thyroid surgery, malignancy, and any growth that might distort the anatomy of the thyroid glands.

Sample size

Using the formula for prevalence, as per previous studies the sample size was calculated[6].
 Sample size (n) = $[Z^2 p (1-p)] / d^2$

Where, Z is Confidence Interval (CI),
 p is the proportion of cases with outcome of interest according to previous studies,
 d is the margin of error
 Considering Z = 1.64 (CI = 90%), p = 5% (0.05), d = 5% (0.05), the sample size is 51.

Methodology

Fifty-one formalin-fixed human cadaveric thyroid glands were studied after adequate dissection of the front of the neck. Skin with superficial fascia containing platysma muscle, the investing layer of deep fascia, and strap muscles were reflected. The gland was identified, and dissected and developmental anomalies were noted¹⁷. The thyroid gland with dysgenesis were subjected to histological examination. Ethical committee approval for the study was obtained on 20th February 2022

Results

Five cadavers (3 female and 2 male cadavers) out of forty-nine cadavers were found to have absent isthmus. (Table 1, Pie Chart 1)

Table 1: Incidence of Absent Thyroid Isthmus

Total thyroid glands dissected	No. of normal thyroid glands with isthmus	No. of the thyroid gland with absent isthmus
49	44	05
Percentage	89.8%	9.8%

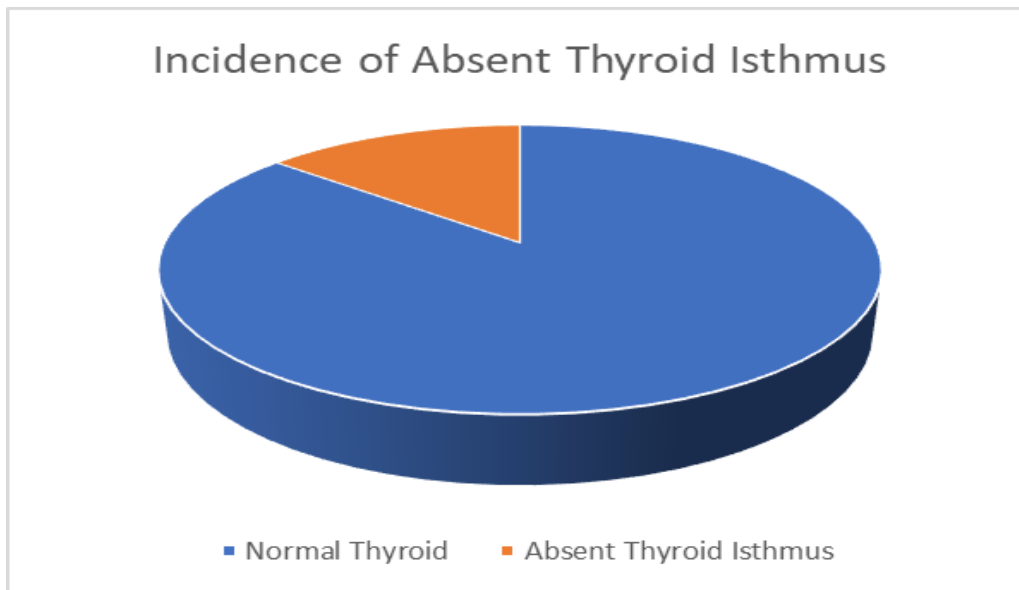


Fig. 1: Incidence of Absent Thyroid Isthmus

Gross Features

- The five lateral lobes were found to be devoid of midline thyroid tissue connection, suggestive of absent isthmus. (Figure 2 & 3)
- Arterial supply was usual and was provided by superior and inferior thyroid arteries.
- In the present study, due to the absent isthmus anastomosis between the anterior division of superior thyroid arteries was not seen.

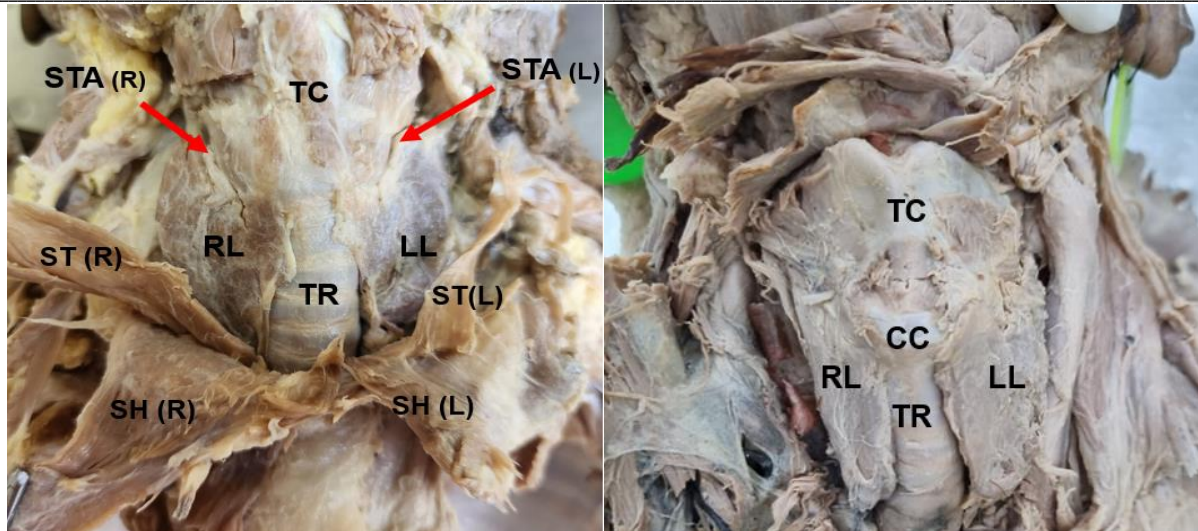


Figure 2: Dysgenic Thyroid gland with absent isthmus in cadaver 1
 Figure 3: Dysgenic Thyroid gland with absent isthmus in cadaver 2

RL- Right lateral lobe LL- Left lateral lobe
 TR- Tracheal rings TC- Thyroid cartilage
 STA (R) / (L) - Superior thyroid artery right /left
 ST (R)/(L)-Sternothyroid muscle (right/left)
 SH (R)/(L) - Sternohyoid muscle (right/left)

RL- Right lateral lobe
 LL- Left lateral lobe
 TR- Tracheal rings
 TC- Thyroid cartilage
 CC- Cricoid cartilage

Histological Features

All thyroid glands with absent isthmus were subjected to H&E staining. The description of the histology findings of all cadavers with absent isthmus is enumerated below. The comparative histological features of the thyroid glands in five cadavers are shown in Table 2.

Table 2: Comparison of Histological Features

Cadaver	Empty Thyroid follicles	Atreitic Thyroid follicles	Diffuse lymphocytic infiltration	Hurthle cells
1	Yes	Yes	Yes	Yes
2	Yes	Yes	Yes	Yes
3	No	Yes	Yes	No
4	Yes	Yes	Yes	Yes
5	No	Yes	Yes	No

Histological images under power 10x and 40x show features suggestive of Autoimmune thyroiditis which is enumerated in (Figures 4 and 5)

1. Diffuse lymphocytic infiltrate.
2. Hurthle cells.
3. Atretic thyroid follicles.
4. Empty thyroid follicles.

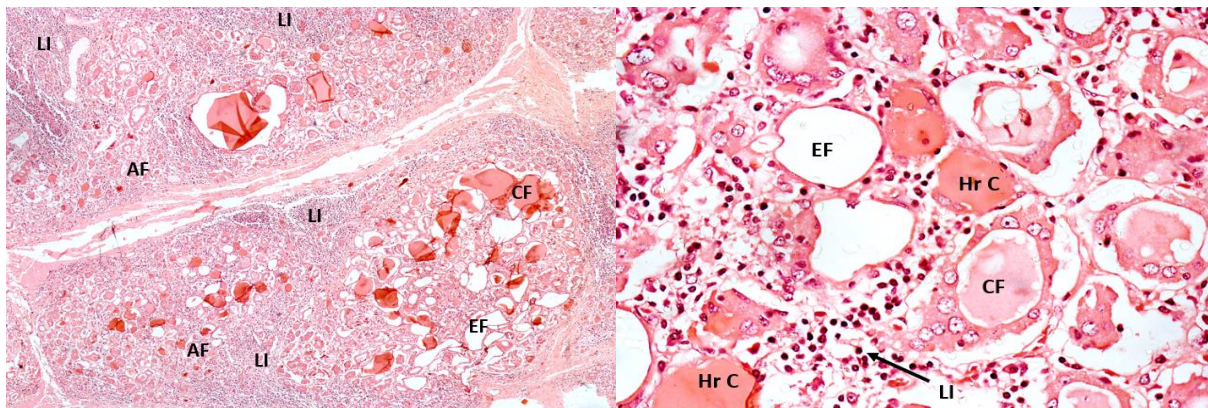


Figure 4: H&E of lateral lobes of the thyroid gland at 10 X magnification.

CF – Colloid filled thyroid follicle
AF- Atretic thyroid follicle
LI- Lymphocytic infiltrate
EF- Empty Thyroid Follicle

CF- Colloid filled thyroid follicle
LI- Lymphocytic Infiltrate
Hr C- Hurthle cell
EF – Empty thyroid follicle

Discussion

The term agenesis refers to the “total and congenital absence of thyroid isthmus” by Pastor et al[6]. According to Won and Chung et al, the thyroid isthmus was found to be absent in three percent of the patients[7]. The incidence of thyroid agenesis as per previous studies ranges from 5-10 % according to Pastor et al[6], 8-10% according to Marshal et al[8], 33% according to Ranade et al[9], 12.5% according to Hussein Muktyaz et al[18], and 10% according to Veena Kulkarni et al[19].

A defect in embryogenesis can account for the absence of the thyroid isthmus. The gland is composed of cells derived from endodermal cells and neural crest cells the former being the follicular cells and the latter being parafollicular cells.

Behind the tuberculum impar at foramen caecum endodermal swelling appears in the midline at the bottom of the pharynx. Afterward, due to the proliferation of endodermal cells, a median diverticulum appears

in the fourth week which grows downwards to form the thyroglossal duct. The lateral lobes and the isthmus are produced due to the division of the inferior end of the thyroglossal duct.

Due to developmental or embryonic failure, agenesis or hemigenesis of either the complete gland or a portion of the gland may occur, which may be unilateral or maybe an isolated absent isthmus in a normal position as elucidated by Kaplaw EL et al [1994][10].

Dysgenesis of the thyroid gland can be diagnosed radiologically, or it can be an incidental finding during surgery. During any finding of absent isthmus, a differential diagnosis of autoimmune thyroiditis, primary cancer, and neoplastic metastases should be considered[6].

Thyroid hemigenesis can be associated with Hashimoto’s thyroiditis or autoimmune thyroiditis as per Wang et al[11]. Comparative analysis of the incidence of absent thyroid isthmus from previous studies is described below. (Table 3, Graph 1)

Table 3: Comparative analysis of the incidence of absent thyroid isthmus as per previous studies

Author	Year	Percentage of Absent Isthmus
Marshal et al[8]	1895	8-10
Won HS et al[7]	2002	3
Pastor et al[6]	2006	5-10
Ranade et al[9]	2008	33
Present Study	2022-2024	9.8

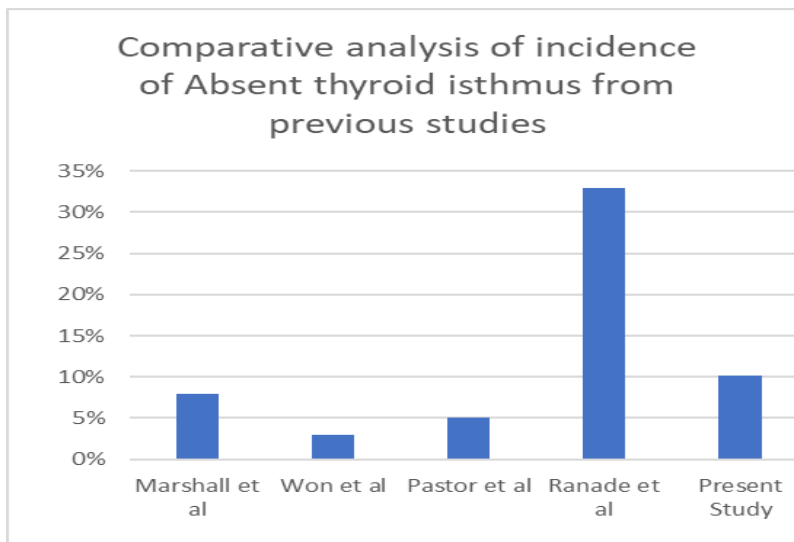


Fig. 5: Comparative analysis of the incidence of absent thyroid isthmus as per previous studies

In our study, lateral lobes of all five specimens with absent thyroid isthmus were subjected to histological examination and were observed under 10X & 40 X magnification, and all of the specimens exhibited typical features as seen in Autoimmune thyroiditis such as atretic, empty thyroid follicles, hurthle cells, diffuse lymphocytic infiltrate, and few colloid filled thyroid follicles.

Conclusion

The present study of thyroid dysgenesis can be histologically correlated with Hashimoto’s Thyroiditis /Autoimmune Thyroiditis in all five cadavers with absent thyroid isthmus where histological features of the gland were typical of autoimmune thyroiditis exhibiting specific features such as hurthle cell, diffuse lymphocytic

infiltrate, empty follicles, atretic thyroid follicle and few colloid filled thyroid follicles when viewed under 10X and 40X magnification.

Dysgenesis of the thyroid gland can be in the form of absent lateral lobes or isthmus or it can manifest congenitally as complete agenesis, the cause is mainly attributable to defective embryogenesis, therefore, its occurrence is significant and rare. As it is a developmental anomaly, it will be appropriate to investigate dysorganogenesis syndrome & ectopic thyroid tissue, as tracheostomy can be potentially dangerous in the latter²⁰.

Understanding the various abnormalities of the thyroid gland would aid surgeons in designing a more efficient and safe surgical procedure¹².

We propose that in cases of thyroid dysgenesis, the chances of autoimmune thyroiditis are high. However, no definite cause-effect

relationship can be attributed at this stage. We recommend further study to confirm the same.

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Disclosure of Interest

The Author and Co-Authors declare that they have no conflict of interest in the present study. All authors have declared that no financial support was received from any organization for the submitted work and authors have also declared that there are no other relationships or activities that could appear to have influenced the submitted work.

Author Contribution

All authors have approved the final version of the manuscript

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Data Curation: Dibendu Ghosh, Anandi S.

Methodology: Dibendu Ghosh, Anandi S.

Writing Original Draft: Dibendu Ghosh, Anandi S.

Validation: Debasis Bandyopadhyay and Dibendu Ghosh.

Review and Editing: Debasis Bandyopadhyay and Dibendu Ghosh.

Supervision: Debasis Bandyopadhyay.

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