

Morphometric Study of Isthmus of Thyroid Gland and Its Embryological and Clinical Corelation

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*Corresponding author: Dr. Rajashree Sheelawant Raut | Received: 28.12.2018 | Accepted: 07.01.2019 | Published: 18.01.2019
DOI: [10.21276/sijap.2019.2.1.4](https://doi.org/10.21276/sijap.2019.2.1.4)

Abstract

The thyroid gland is an important endocrine gland in human body. The organogenesis of thyroid gland is often disturbed leading to variety of morphological variations. The position, size of isthmus, posterior relations may vary greatly. Hence a descriptive cross sectional cadaveric study was conducted in western maharashtra population in india. The study was conducted on total of 60 thyroid glands (male-34, female-26) collected during routine dissection from adult cadavers in the anatomy department, B.J.Govt medical college, Pune. Presence or absence of isthmus, its dimentions, and posterior relations with tracheal rings were noted. Absence of isthmus was noted in total 5 cadavers, incidence is 8.33% , 3 in male cadavers (8.82%) and 2 in female cadavers (7.69%). Average length, breadth, thickness of isthmus was 16.1 mm, 16.53 mm, 3.24mm respectively. In maximum 13 out of 60 cadavers (21.66%) isthmus was anterior to tracheal rings 1,2,3 , in 10 cases (16.66%) - tracheal rings 1,2,3,4. About 8 cases (13.33%) anterior to 2nd, 3rd tracheal ring. A wide variation was seen in the position of isthmus, as high as cricoid cartilage to as low as 8th tracheal ring. The size of isthmus was also varying related to only 1st tracheal ring and related to 1st to 8th tracheal rings. From the study it is evident that detail knowledge of the thyroid isthmus anatomy and its variations is necessary for surgeons and physicians to avoid undue complications during tracheostomies and in evaluation of scintigraphy.

Keywords: Morphometry of isthmus, agenesis of isthmus, isthmus posterior relations.

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INTRODUCTION

The thyroid gland is an important endocrine gland in human body situated anteriorly in the lower part of neck extending from the level of 5th cervical to 1st thoracic vertebra. It consists of two symmetrical lobes connected by a median isthmus which lies against second, third, fourth tracheal rings. Each lobe is 5cm in length, 3cm in breadth, 2cm in thickness. The isthmus measures about 1.25cm both in vertical and transverse diameters. The condensation of the fibrous stroma of the gland forms the inner true capsule, while the splitting of pretracheal fascia forms the outer false capsule of the gland [1].The organogenesis of thyroid gland in human is often disturbed leading to a variety of morphological variations of thyroid such as hypoplasia, aplasia(agenesis of lobe or isthmus),ectopy etc. It is the most common site of endocrine tumours and most common endocrine gland that is surgically intervened. The position and size of isthmus may vary greatly in humans and sometimes absent. The relation of isthmus with tracheal rings also varies from cricoid cartilage to fourth tracheal ring (important in tracheostomy).Though many workers studied it worldwide; very less data is available in indian continent. Considering its clinical importance a study

was conducted on morphometry of isthmus, incidence of agenesis of isthmus, posterior relations of isthmus in western maharashtra population in India to see the variations and contribute additional data to literature.

AIM AND OBJECTIVES

To highlight the variation of thyroid gland isthmus from diagnostic and surgical approach. The aims of study are -

- To study the presence or absence of isthmus and its posterior relation with cricoid cartilage and tracheal rings.
- To study morphometric features of isthmus of thyroid gland.
- To compare the results of present study with previously available data.
- The data will be useful during tracheostomy and planning safe and effective surgery on thyroid.

MATERIALS AND METHODS

The cross sectional, descriptive study was conducted on total of 60 thyroid glands (male-34,female-26) collected during routine dissection from adult cadavers of both sexes age more than 18 yrs in the

department of anatomy , B.J.Govt medical college , Pune, Maharashtra, India in the duration from april 2013 to april 2015. The thyroid gland was examined for following parameters .

- Presence or absence of isthmus.
- Posterior relations of isthmus (with cricoid and tracheal rings).
- When present, isthmus dimentions - length, breadth, thickness.

The length of isthmus was measured between two horizontal planes, one passing along upper border and other passing along lower border of isthmus. The breadth of the isthmus was measured between two vertical points each passing along the medial surfaces of right and left lobes where the isthmus was connected with them. The thickness was measured by putting the two points of the calliper, one in front of isthmus and other behind the isthmus [2]. All the parameters were measured with sliding caliper. Then statistical analysis was done. The study is ethically approved by the ethical

committee of B.J.Govt medical college and S.G.H. Pune.

OBSERVATIONS AND RESULTS

Total study was conducted on total 60 cadavers -34 male, 26 female. The observations noted were as follows.

Absence of isthmus

Isthmus was absent in total 5 cadavers out of 60 cadavers, i.e. incidence in total was 8.33%. Isthmus was absent in 3 male cadavers i.e. 8.82%. And in 2 female cadavers i.e. 7.69%. The incidence of absence of isthmus was more in males. The chi square value and P value for absence of isthmus is 0.024 and 0.12 respectively. This variation absence of isthmus is not statistically significant. In present study, only one case of absence of isthmus in males is associated with levator glandulae thyroideae.

Morphometry of isthmus

Table-1: Isthmus Dimentions

	Total (60)			Males(34)			Females(26)		
	L(mm)	Br (mm)	Th(mm)	L(mm)	Br(mm)	Th(mm)	L(mm)	Br(mm)	Th(mm)
Min	5	5	1	5	9	1	9	5	1
Max	51	28	15	30	28	10	51	28	15
Mean	16.1	16.53	3.24	14.87	15.81	3.13	17.67	17.46	3.38
S.D.	7.42	5.17	2.49	6.02	5.10	2.20	8.81	5.23	2.86

Abbreviations - L – length, Br – breadth, Th- thickness

Isthmus length, breadth and thickness all parameters are more in females than males.

Posterior relations of isthmus with tracheal rings

Posterior relations of isthmus with cricoid and tracheal rings were noted as follows.

Table-2: Posterior relations of isthmus

Cricoid/Tracheal rings related posterior to isthmus	Frequency Actual Cases	Percentage (%) cases
Cricoid, 1	1	1.66
Cricoid, 1, 2	1	1.66
1	1	1.66
1, 2	8	13.33
1, 2, 3	13	21.66
1, 2, 3, 4	10	16.66
1,2,3,4,5	3	5
1,2,3,4,5,6	3	5
1,2,3,4,5,6,7,8	1	1.66
2,3	8	13.33
2,3,4	4	6.66
2,3,4,5	1	1.66
5,6	1	1.66

The relation of isthmus to tracheal rings was variable extending from cricoid cartilage to 8th tracheal ring. In maximum 13 out of 60 cadavers (21.66%) isthmus was related posteriorly to tracheal rings 1,2,3 and in 10 cases (16.66%) was related to tracheal rings

1,2,3,4. About 8 cases (13.33%) showed relation with 2nd and 3rd tracheal ring as stated in standard textbooks. A wide variation was seen in the position level of isthmus, as high as cricoid cartilage -1 case (1.66%) and as low as 8th tracheal ring -1 case (1.66%). The size of

isthmus was also variable, was so narrow that related to only 1st tracheal ring (1 case, 1.66%) and it was so big that related to 1st to 8th tracheal rings (1 case, 1.66%).

DISCUSSION

Agenesis of isthmus

Agenesis of thyroid isthmus is complete and congenital absence of isthmus as defined by Pastor *et al.* [3]. Basically it is a developmental anomaly. Absence of isthmus is quite rare in humans.

Table-3: Percentage of absence of isthmus compared with other previous studies

Sr. No.	Author and year of study	Sample size	% of absence of isthmus
1	Marshall C F (1895)[2,4]	60	10
2	Won and Chung (2002)[2,5]	--	3
3	Harjeet <i>et al.</i> (2004)[2,5]	--	7.9
4	Braun <i>et al.</i> (2007)[2,3,5]	58	6.9
5	Fakhrul A M H <i>et al.</i> (2007)[6]	54	5.56
6	Ranade <i>et al.</i> (2008)[2,4,5,7,8]	105	33
7	Nurunnabi A S M (2008)[4]	73	18.8
8	Daksha Dixit <i>et al.</i> (2009)[2,3]	41	14.6
9	Joshi S D <i>et al.</i> (2010)[8,9]	90	16.7
10	Prakash <i>et al.</i> (2011)[4]	70	8.57
11	O.Tanriover <i>et al.</i> (2011)[4]	90	2.22
12	Veena Kulkarni <i>et al.</i> (2012)[4,8,10]	20	10
13	Hussain Muktyaz <i>et al.</i> (2013)[4,11]	56	12.5
14	Veerahanumaiah S <i>et al.</i> (2014)[4,8]	89	9
15	Rathod S Mansingh <i>et al.</i> (2015)[8]	76	13
16	A J Rajkonwar <i>et al.</i> (2015)[8]	80	21.25
17	Arun Sharma <i>et al.</i> (2016)[2]	30	10
18	Shobha Gaikwad <i>et al.</i> (2016)[12]	100	29.78
19	R Sharda <i>et al.</i> (2017)[13]	37	16.2
20	S Z Sultana (2011) [15]	60	31.66
20	Present Study (2015)	60	8.33

The incidence of agenesis of isthmus is highly variable ranging from 3% to 33%. Hence the exact incidence is really difficult to determine. In present study, the incidence for absence of isthmus is more in males (8.82%) than females (7.69%). In Dixit *et al.* study the incidence was more in males than females with ratio of 5:1[3]. Rajkonwar found the incidence more in males than females [8]. According to Ranade *et al.* isthmus was more commonly absent in females (47.1%) than males (30.6%) [7] and according to Prakash it was more commonly absent in males (9.6%) than females (5.6%). In study by Lattupalli hema the incidence of absence was more in females (27.3%) than males (20.5%) [14]. According to S Z Sultana *et al.* the incidence was more in males (37.5%) than females (8.3%) [15].

According to available literature trisomy of chromosome 22 was supposed to be possible related factor, caused a syndrome (agenesis of thyroid isthmus with agenesis of gall bladder) [13]. Genetically developmental agenesis results from mutations in one of these genes (TITF1, PAX8, FOXE1/TITF2), especially TITF2 because these genes are essential for normal development of palate and thyroid gland [16]. Phylogenetically the isthmus may be missing in amphibians, birds and among mammals. In rhesus monkey (*Macacus rhesus*) the thyroid glands are normal

in position but there is no isthmus [4]. A high division of the thyroglossal duct can generate two independent thyroid lobes with absence of isthmus with or without pyramidal lobes [5]. Absence of isthmus may be associated with no anastomosis of superior and inferior thyroid arteries of both sides. The absence of isthmus can be associated with other types of dysorganogenesis, such as absence of a lobe or presence of ectopic thyroid tissue or familial syndromes and chromosomal aberrations. This type of variation is kept in mind during transthyroid tracheotomy procedures.

In human agenesis of isthmus is detected incidentally when patient is referred for other thyroid diseases. It can be diagnosed by scintigraphy, ultrasonography, CT, MRI or intraoperatively during a surgical procedure. When the condition is suspected it is necessary to enquire in depth for previous surgical procedures in the cervical region (isthmectomies due to neoplasms, decompressive techniques due to thyroiditis or due to transthyroid tracheotomies) [17]. Differential diagnosis can always be considered for pathological autonomous thyroid nodule, thyroiditis, primary carcinoma, neoplastic metastasis and infiltrative diseases such as amyloidosis [5]. This knowledge is important for surgeons in surgical intervention and for physicians while performing safe tracheostomies and

radiologists in scintigraphic evaluation of thyroid status of patients, the diagnostic and therapeutic approach.

Absence of isthmus may be associated with absence of whole or part of lobes and hence surgeons doing partial thyroidectomy for thyroid pathology

should confirm wheather that's the only functioning thyroid tissue in body otherwise patient may land up with hypothyroidism.

Isthmus morphometry

Table-4: Comparative study of Isthmus morphometry

Sr. No.	Author and year of study	Length (mm)	Breadth(mm)	Thickness(mm)
1	Berkowitz (2005) [18]	12	12	--
2	S.D. Joshi <i>et al.</i> (2009)[9]	11	18.5	--
3	Lattupalli Hema (2014)[14]	13	13	--
4	Fakhrul <i>et al.</i> (2016)[6]	14.6	17.2	5.3
5	Arun Sharma <i>et al.</i> (2017)[2]	28	19	--
6	Present Study [2015]	16.1	16.53	3.24

In present study all the parameters are more in females than males. According to Fakhrul *et al.* macroscopic difference was found with increasing age but not with sex [6]. Arun Sharma found all dimentions of isthmus greater [2]. Nurunnabi *et al.* found that there was no significant agewise and sexwise variation found in isthmus dimentions [18].

Posterior relations of isthmus

In present study, a wide variation was seen in the position, size, and posterior relations of isthmus. In maximum 13 out of 60 cadavers (21.66%) isthmus was anterior to tracheal rings 1,2,3 whereas about 8 cases (13.33%) showed relation with 2nd and 3rd tracheal ring as stated in standard textbooks. A wide variation was seen in isthmus position level, as high as cricoid cartilage-1 case (1.66%) and as low as 7th and 8th tracheal rings-1 case (1.66%). Isthmus was so narrow that related to only 1st tracheal ring and so big that related to 1st to 8th tracheal ring.

According to S D Joshi *et al.* out of 90 cadavers about 19 cases isthmus was related to 2nd - 3rd tracheal rings, in 14 cases isthmus was anterior to 1st - 2nd tracheal rings and in 12 cases , it was related to 1st , 2nd and 3rd tracheal rings. The isthmus was so narrow that related to only 1st tracheal ring and the broadest

isthmus related to 1st - 4th tracheal rings. The position was as high level as cricoid cartilage and as lower level as 5th tracheal ring [9].

According to S Z Sultana *et al.* the thyroid isthmus occupied variable position, extending from cricoid cartilage to 6th tracheal ring. The most frequent location of isthmus was found at 1st, 2nd, 3rd (18.3%) and 2nd , 3rd , 4th tracheal rings(18.3%) . Isthmus was as narrow as related to cricoid and 1st tracheal ring or 1st and 2nd tracheal ring and it was as broad as related to 1st to 5th tracheal rings. Enayetullah observed that in 72% cases isthmus was related posteriorly to 2nd to 4th rings of trachea. Begum found isthmus of thyroid gland anterior to 2nd, 3rd and 4th ring in 71.67% cases and against 2nd, 3rd, 4th and 5th rings in 26.77%cases [15].

According to Berkowitz (2005), the isthmus was usually placed anterior to 2nd and 3rd tracheal rings. Sultana (2011) found the most common location were 1st to 3rd and 2nd to 4th tracheal rings (18.3%) in both cases. Nurunnabi et al in 2013 reported isthmus to extend from 2nd to 4th tracheal ring in 91.7% cases and from 2nd to 5th ring in 8.3% cases [19]. This wide variability regarding position of isthmus may be explained by failure of descent or excessive descent of thyroid gland during its embryonic course.

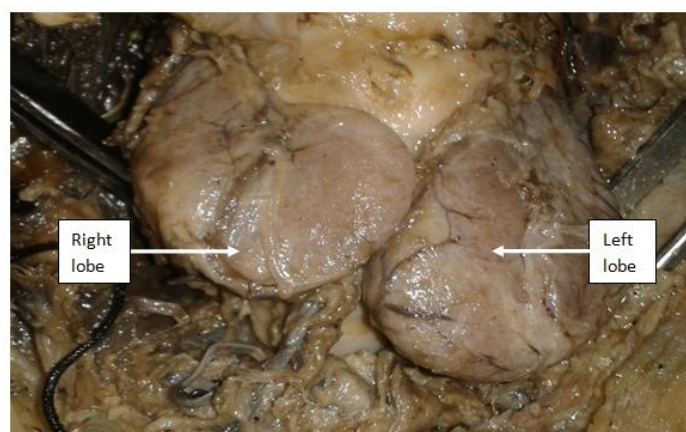


Fig-1: Absence of isthmus with large right and left lobes of thyroid gland

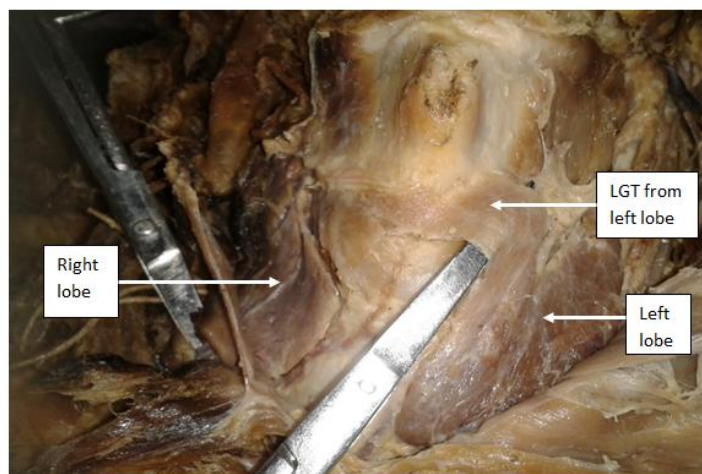


Fig-2: Absence of isthmus with levator glandulae thyroideae from left lobe thyroid gland to oblique line of thyroid cartilage on same side, muscular

CONCLUSION

From the study it is evident that agenesis of isthmus could be associated with dysorganogenesis or ectopic thyroid. Hence detail knowledge of the thyroid anatomy and its variations is necessary for surgeons and physicians to avoid undue complications pre operatively, in performing tracheostomies while securing difficult invasive airway and in evaluation of scintigraphy and other associated pathologies should not be overlooked in differential diagnosis. Thyroid gland isthmus position, size and tracheal ring relations are variable. This variation should be kept in mind during tracheostomy, tracheotomy, laryngotomy, cricothyroidotomy, coniotomy (opening the larynx) at the cricothyroid membrane, as it is necessary to divide the pretracheal layer in order to expose the isthmus of thyroid gland either to retract it up or down using isthmus hook or divide it after clamping followed by suturing the stump sometimes, the procedures are done above or below the isthmus. On the other hand, absence of thyroid isthmus may become God's gift for a patient needing emergency tracheostomy as it will save critical time of cutting and hooking isthmus [19].

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