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MORPHOLOGICAL VARIATIONS OF THE THYROID GLAND AND ITS RELATIONSHIP TO THE RECURRENT LARYNGEAL NERVE: A CADAVERIC STUDY.

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ABSTRACT

The thyroid gland is prone to variations due to its embryological origin and descent. These variations can cause distortion of its morphology and have been associated with thyroid disorders. This study aimed to provide evidence-based data on the morphological variations of the thyroid gland. In this study, the morphological variations of the thyroid gland pertained to the presence or absence of *pyramidal lobe (PL), levator glandulae thyroidae (LGT)* and *isthmus.* The main objective of this study was to assess the morphological variations of the thyroid gland and its relationship to the *recurrent laryngeal nerve* in cadavers. This was a cross-sectional descriptive study, conducted at the Pathology Department of the University Teaching Hospitals (UTH) in Lusaka, Zambia. In the study there were 46 cadavers; 36 males and 10 females aged between 20-64. The study involved dissection and removal of the hyoid bone, larynx, trachea, oesophagus, and thyroid gland en bloc. The thyroid gland was observed for the presence of the *PL* and *LGT,* and absence of *isthmus*. If present, the length, width and height were measured using a Vernier caliper. Location of the *isthmus* as well as the relationship of the thyroid gland to the *recurrent laryngeal nerves (RLNs)* were also observed. The most common variation was presence of *PL*, 32.61% (36% of males and 20% of females). The most common origin of the *PL* was both the *isthmus* (40%) and left lobe (40%). *Levator glandulae thyroideae* were commonly attached to the hyoid bone (72.7%). Statistically significant differences (<0.0001) were found in the mean length of *LGT* between males and females. Thickness of the *PL* was more in females than males and this difference was significant (< 0.015). The majority of the isthmi were found located on tracheal rings 1 and 2 (32.6%). The *RLNs* were mostly medial to the thyroid gland; *LRLN* (93.5%) and *RRLN* (91.3%). There was a high incidence of *RLNs* traversing the larynx posterior to the cricothyroid joint, 89.1% of *LRLN* and 93.5% of the *RRLN.* Knowledge of these variations, their measurements and the relationship of the thyroid gland to the *RLNs* may be of help to surgeons to perform safe and effective thyroid surgeries with reduced complications.

Keywords: Variations, thyroid gland, pyramidal lobe, levator glandulae thyroideae, isthmus, recurrent laryngeal nerve

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INTRODUCTION

The thyroid gland is an endocrine gland located anteriorly in the lower part of the neck (Drake *et al.*, 2015; Standring, 2016). It is the first endocrine gland to start developing in the embryo (Moore *et al.*, 2016). The thyroid gland has two (2) lobes connected by an isthmus. It is postulated that 50% of thyroid glands have a third lobe called the *pyramidal lobe* (Ranade *et al.,* 2008). The embryological origin and descent

of the thyroid gland predisposes it to multiple anatomical variations and congenital anomalies (Dessie, 2018). Some of these variations include, *pyramidal lobe* (*PL*), *levator glandulae thyroideae (LGT),* aberrant thyroid tissue and absence of isthmus. However, aberrant thyroid tissue is rare and occurs in 1 per 100 000-300 000 people (Noussios *et al*., 2011). Thyroid disorders are quite common and some have been linked to high incidence of variations such as the *pyramidal lobe* (Gurleyik, *et al*., 2015). Thyroid surgeries are one of the most common surgeries performed in the head and neck region (Raut *et al.,* 2018). Thus, knowledge of these variations is cardinal to surgeons to minimise iatrogenic injuries. The most common and serious complication that occurs after thyroid surgery is palsy of the recurrent laryngeal nerve due to its relation to the thyroid gland (Chaing, *et al*., 2010). Therefore, studying the relationship between *RLNs* and the thyroid gland and its variations, can help lower the risk of injuring these nerves. Several studies (Prakash *et al.,* 2012, Gaikwad and Joshi 2016, Diana *et al.,* 2019*,* Mitesh *et al.,* 2019, Al-Azzawi and Takahashi, 2021) have been done on the morphological variations of the thyroid gland. However, very little data was found in sub-Saharan Africa particularly, Zambia. In as much as studies agree that variations such as *PL*, *LGT* and absence of *isthmus* are common, their statistics vary. The studies also show differences in the morphometric measurements of the *PL, LGT* and *isthmi.* These differences are also seen when comparisons are made between gender. Therefore, it was important that evidence based data be obtained in a Zambian setting that would show if these variations were present, how common they occur and their measurements. Information on the point of entry of the *RLN* into the larynx and its relationship to the thyroid gland is scanty. Therefore, there also need to study this relationship as it has surgical implications.

MATERIALS AND METHODS

This was a cross sectional descriptive study conducted at the University Teaching Hospitals in Lusaka. The sample size was calculated using STATA. Assumptions using data from previous studies (Gurleyik *et al.,* 2015; Diana *et al.,* 2019; Mitesh *et al.,* 2019) were made. This data was imputed in STATA and an estimated sample size was calculated. Using systematic sampling, 46 non-embalmed cadavers, of which 36 were male and 10 were female, were selected. These were aged between 18-64 scheduled for post mortem examination. Due to age related changes that occur with age such as fibrosis and atrophy which leads to a reduction in volume (Ajish and Jayakumar, 2012, Lee *et al.,* 2016)) cadavers above the age of 70 were excluded from the study. Functional changes which result in increased risk of disorders of the thyroid gland which could affect morphology have been reported in individuals above the age of 60 (Gesing, 2015). The study also included cadavers that were collected within 48 hours of death to avoid the natural decay process which sets post-mortem. All cadavers were black and of Zambian origin. Excluded from the study were cadavers that had a history or evidence of neck surgery, trauma of neck region or had disease that distorted the morphology of the thyroid gland. This information was obtained from the files of the deceased, police reports and physical evidence obtained by forensic pathologists. The variations that were studied included presence of *PL, LGT* and absence of *isthmus.* A midline incision was made from the chin to the suprasternal notch. The infrahyoid and suprahyoid muscles were detached from there caudal attachments. The hyoid bone, larynx, trachea, oesophagus and thyroid gland were removed en bloc. Removal ensured that the inferior thyroid artery as well as the recurrent laryngeal nerve were

undisturbed. The thyroid was examined for absence or presence of the *levator glandulae thyroideae, pyramidal lobe* and *isthmus*. Location of *Isthmus* in relation to tracheal rings was also noted. The relation of the thyroid gland to the *RLN* at its point of entry into the larynx was also observed.

If *pyramidal lobe* was present, its origin was observed (right or left lobes or isthmus). Measurements in terms of length, width and thickness were done. The length of the *PL* was measured from the base to the apex, the width was taken as the transverse diameter of the base and thickness in the anteroposterior diameter of the base (Dessie, 2018). This was done using a Whitworth Vernier calliper. The vernier calliper was calibrated by Zambia Metrology Agency (ZMA), which is accredited by the Southern African Development Community Accreditation Service (SADCAS). To minimise intra-observer error, measurements were taken twice and an average was reported. The length of the *PL* was characterized as follows; short (≤15 mm), medium (16–30 mm), or long (≥31 mm) (Gurleyik, *et al*., 2015). If *levator glandulae thyroideae* was found, its origin as well as superior attachment and length were measured. The length, height and width of *isthmus* was also measured. Its location in relation to the tracheal rings was observed. The relationship of the *RLN*s in relation to the thyroid gland was also observed. Results were recorded in a data collection form. Data was analysed using STATA version 13 and all statistical analyses were significant if the P value was <0.05. To determine normality of the continuous variables, Shapiro-Wilk test was done which showed that data was normally distributed. Independent sample t-test was done to check for statistical significant differences in the morphometry of thyroid gland between males and females. This study was ethically approved by the Biomedical research ethics committee of the University of Zambia.

RESULTS

The number of cadavers with variations were 15 (32.6%) and those without variations were 31 (64.4%). Of the 15 cadavers with variations, 13 (86.7%) were male and 2 (13.3%) were females.

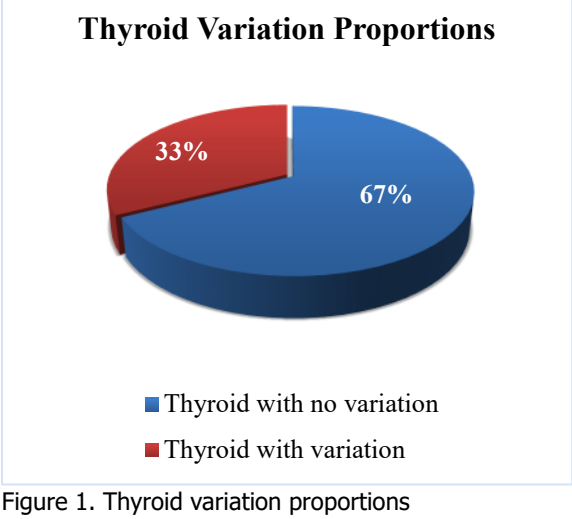

Figure 1. Thyroid variation proportions

Among the male cadavers (n=36) of the study, 23 (63.9%) had thyroid glands with no variations while 4 (11.1%) had a *PL* and 9 (25%) had both the *PL* and *LGT*. Thyroids without any variation were found in 8(80%) of female cadavers (n=10) of the study while 2(20%) had both *PL* and *LGT*. In this study, the presence of *PL* was associated with *LGT.* This is illustrated in the table below. Chi square test showed that there was no statistical significance (*p-value=0.474*) in the incidence of *PL* and *LGT* among males and females.

The common origin of the PL was both the left lobe (n=6, 40%) and the isthmus (n=6, 40%). The least common origin for PL was the right lobe. This is illustrated in figure 2. All the levator glandulae thyroideae were attached to the apex of the pyramidal lobe. The majority of the LGT were attached to the hyoid (n=8, 72.7%) superiorly and the rest

were attached to the thyroid cartilage (n=3, 27.3%) as shown in figure 3. The isthmus was commonly located in relation to tracheal rings 1 and 2 (n=15, 32.6%).

Table 1: Presence or absence of thyroid variations according to gender

Gender Cross tabulation						
				Gender		Total
	Male			Female		
	N	%	N	%	N	%
TG with no variation	23	63.9 %	8	80.0 %	31	67.4 %
Only *PL*	4	11.1 %	0	0.0%	4	8.7%
Both *PL* & LGT	9	25.0 %	2	20.0 %	11	23.9 %
Total	36	100.0 %	10	100.0 %	46	100.0 %

Key: TG=Thyroid gland; PL=pyramidal lobe; LGT=levator glandulae thyroideae

The pyramidal lobe (n=15, 32.61%) had a mean length of 15.29 mm, a width 8.75 mm and a thickness 2.34 mm. The thickness of the PL was more in females (3.85 mm) than males (1.97 mm) and this difference was significant with a p-value of 0.015. The mean length of the LGT was 22.26 mm, width 3.78 mm and thickness was 0.60 mm. The mean length of the LGT was more in males (23.86 mm) as compared to females (14.34 mm). This difference was statistically significant (p-value <0.0001). There was also a statistical difference in the mean of the width (p-value=0.033) and thickness (p-value=0.001) of the LGT. The isthmus was present in all the cadavers (n=46, 100%). It had a mean length of 9.85 mm, height was 10.99 mm and a thickness 2.32 mm. The mean thickness of the isthmus was more in females and this finding was statistically significant (p-value <0.001).

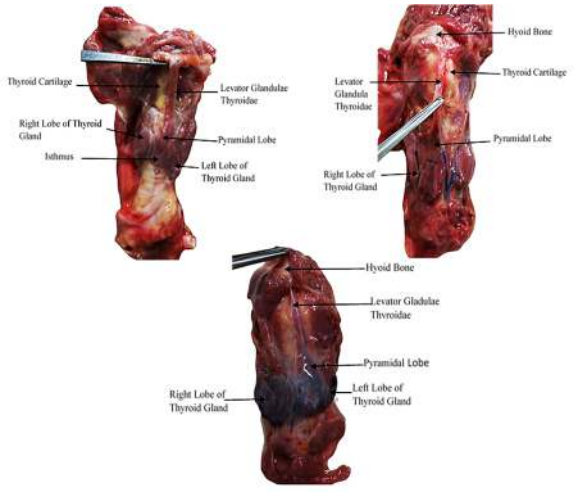

Figure 2: Anterior view showing origin of Pyramidal lobe; Isthmus (a), Right Lobe (B), Left Lobe (C)

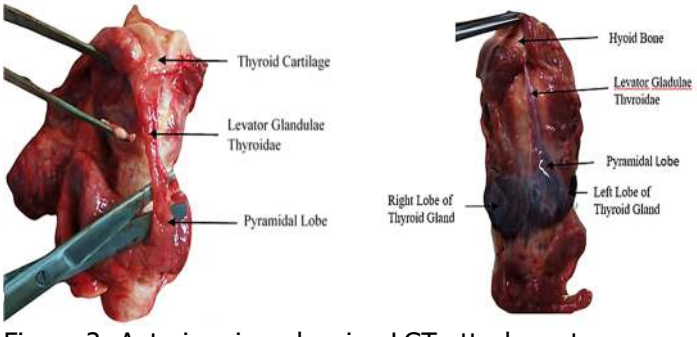

Figure 3: Anterior view showing LGT attachment to Thyroid cartilage (A) and Hyoid Bone (B)

Table 2: Descriptive Statistics of Morphometric Measurements in millimetres (mm)

	N	Minimum	Maximum	Mean	SD
PL Length	15	7.37	29.49	15.29	5.87
PL Width	15	5.11	15.77	8.75	3.19
PL Thickness	15	0.60	6.69	2.34	1.83
LGT Length	11	7.84	34.60	22.26	7.40
LGT Width	11	2.30	4.65	3.78	0.77
LGT Thickness	11	0.16	0.84	0.60	0.22
Isthmus Length	46	2.95	16.44	9.85	2.94
Isthmus Height	46	3.77	17.42	10.99	3.40
Isthmus Thickness	46	0.71	8.90	2.32	1.45

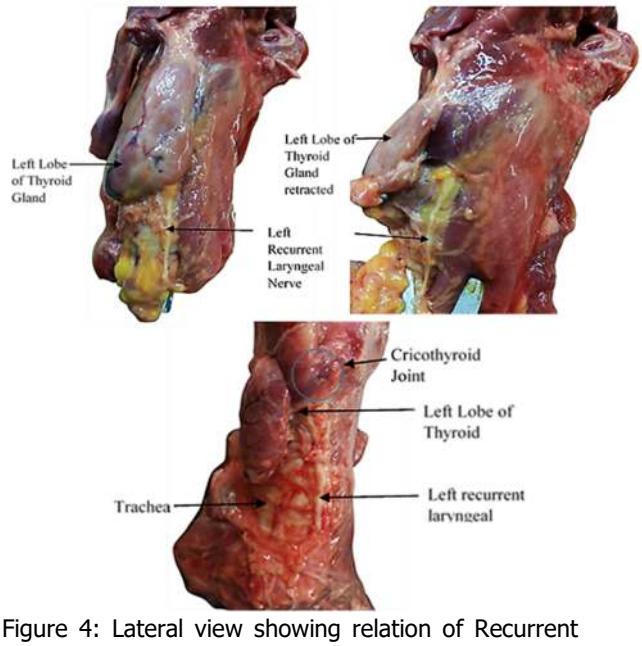

Figure 4: Lateral view showing relation of Recurrent laryngeal nerves to Thyroid Gland. Key: *LGT=Levator glandulae thyroideae*; *PL=Pyramidal lobe; N=Number*

The *recurrent laryngeal nerves* were commonly found medial to the thyroid gland, 43 (93.5%) for the *LRLN* and 42 (91.3%) for the *RRLN*. This is illustrated in *figure 4*. However, some of the nerves appeared as though they were posterior to the thyroid gland, 3 (6.5%) for the *LRLN* and 4 (8.7%) for the *RRLN*. However, this impression could have been spurious because the lobe appeared to be small (*figure 4C*).

The most common entry point into the larynx was posterior to the cricothyroid joint 41(89.1%) of *LRLN* and 43 (93.5%) of the *RRLN* (*figure* 4).

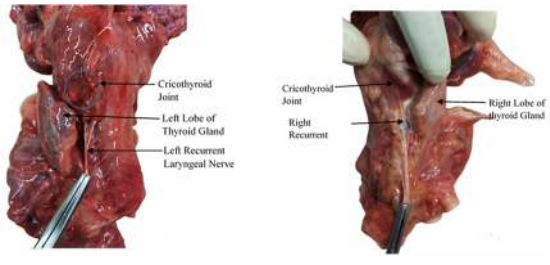

Figure 5: Lateral view showing recurrent laryngeal nerve; Branched (A) Not Branched (B); Point of entry

DISCUSSION

The thyroid gland is the first gland to develop approximately 24 days after fertilization (Maneenin *et al.,* 2019). It develops as a median endodermal thickening in the floor of the pharynx between tuberculum impar and copula. It descends in front of the pharyngeal gut as a bi-lobed diverticulum but remains attached to the tongue via the thyroglossal duct. As it descends the neck, it passes anterior to the developing hyoid and cartilages of the larynx. By week 7, the thyroid assumes its definitive shape and is located anteriorly on the lower part of the neck (Sadler, 2015; Moore *et al.,* 2016). Due to its origin and descent, the thyroid gland is prone to anatomical variations.

In the present study, there was a high incidence of the *pyramidal lobe* found in 15 (32.6%) of cadavers as compared to *LGT* found in 11(23.9%). A high incidence of *PL* than *LGT* was also found in studies done in 2018 by Dessie, (*PL* 52.5% and *LGT* 40 %) and Hemalatha *et al*., (*PL* 43.33% and *LGT* 36.66%). Another study conducted by Veerahanumaiah *et al., (2014),* found a higher incidence of *PL* (46%) than *LGT* (41%). However, a study done by Raut *et al.,* (2018) found a higher incidence of *LGT* (38.33%) than *PL* (25%). Geographical location and ethnicity could have contributed to differences in statistics (Gaikwad and Joshi, 2018).

In our study, there was a high incidence of *PL* in males (36.1%) than females (20%). That difference was not statistically significant. A similar study done by Gaikwad and Joshi *(2016),* found a high incidence of *PL* in male (37.77%) than female (16.66%) cadavers and this was also not statistically significant. In contrast, studies by Hemalatha and Subba-Rao (2018) and Mitesh *et al.,* (2019) found higher incidences of *PL* in females than males. The present study found a high incidence of *LGT* among males (81.8%) than females (18.2%) which was similar to a study by Prakash *et al.,* (2012).

However, a study by Mitesh *et al.,* (2019) found *LGT* more frequently in females than males. The *isthmus* was present in all cadavers and was commonly related to tracheal rings 1 and 2 in the present study.

Pyramidal lobe thickness was more in females than males and this was statistically significant (p-value=0.015). Mean length of *PL* was more in males but this was not significant. The mean length of the LGT was more in males than females and this was statistically significant (p-value <0.0001). Similar findings by Raut *et al.,* 2018. The findings were in contrast to others studies where the mean length of PL was 22.7mm and 23.1mm (Gurleyik *et al.,* 2015; Dessie, 2018 respectively). Differences in methodology when measuring the *PL* and *LGT* could contribute to the varying statistics.

The origin of the *pyramidal lobe* in this study were both the *isthmus* (40%) and left lobe (40%) with the least being the right lobe. Some other studies have found the most common origin was the *isthmus* (Raut *et al.,* 2018), others the left lobe (Prakash *et al.,* 2012; Rajkonwar and Kusre, 2016), and some the right lobe (Gurleyik *et al.,* 2015; Manneenin *et al.,* 2019). The results of the current study could have resulted from a small study sample. In males, the majority of the *LGT* were attached to the hyoid (n=7, 87.5%) while the rest were attached to the thyroid cartilage (n=2, 66.7%). In females, they were equally distributed. This is consistent with a study done by Raut *et al.,* (2018). In other studies, all cases of the *LGT* were found to be attached to the apex of the *PL* inferiorly and the hyoid superiorly (Begum *et al.,* 2009; Rajkonwar and Kusre, 2016).

In the current study, the majority of the *RLNs* were medial to the thyroid gland. Some of the observed *RLNs* branched before entering the larynx. However, despite the branching, the most common point of entry for the *RLNs* was posterior to the cricothyroid joint, 89.1% and 93.75% for *LRLNs* and *RRLNs* respectively. As a result of the *RLNs* branching, some of the nerves had branches that entered the larynx anterior and posterior to the cricothyroid joint, 8.7% for *LRLN* and 4.3% for *RRLN.*

Conclusion

The most common variation of the thyroid gland was the pyramidal lobe. Levator glandulae thyroideae were commonly found attached to the hyoid bone. All the cadavers had an isthmus and the majority were related to tracheal rings 1 and 2. The RLNs were mostly related to the thyroid gland medially.

Limitations of study

There were fewer post-mortem examinations done on females which explains the lower numbers.

With regard to the determination of relationship of thyroid gland to the *RLN* at its point of entry into the larynx, the anterior and posterior branching pattern was unexpected and requires further research

Recommendations

Surgeons, and radiologists to be conversant with the variations such as the *pyramidal lobe* for purposes of accurate diagnosis. We also recommend that during surgery, attention should be paid to the pre-laryngeal area for the presence of the *levator glandulae thyroideae.* Further research is required to determine if the risk of thyroid disorders has any relationship to morphological variations of the thyroid gland. Future studies to include the branching pattern of the *recurrent laryngeal nerve* at site of entry into the larynx.

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