Original Article

Quantitative Assessment Of The Variations In Thyroid Dimensions In Relation To Increase In Serum TSH In Euthyroids

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ABSTRACT:

Background: Volumetric evaluation of thyroid gland volume (TGV) is one of the criteria determining the iodine status of a population. TGV is the product of 3 dimension of each lobe: Anterio-posterior (AP) x medio-lateral (ML) x and cranio-caudal (CC) x correction factor.

Objectives: To determine the effect of serum TSH on thyroid dimensions of each lobe and to measure the amount of effect of per unit increase in serum TSH on thyroid dimensions of each lobe in euthyroids.

Study Design: It was a cross-sectional study.

Setting: The study was conducted at Ziauddin University Hospital, Clifton, Karachi.

Methodology: Healthy participants aged 21 years and above were included through convenient sampling. Serum Thyroid stimulating hormone was evaluated and ultrasound of thyroid gland TG of 192 euthyroid participants was performed. Spearman correlation and regression analysis was applied to evaluate the relationship between TSH and TG dimensions

Results: Relationship of increase in serum TSH with decrease in light lobe AP dimension was most significant. (r= -0.142 P-Value=0.001) and CC dimension least significant (r= -0.0098 P-Value=0.001). Where as in the left lobe AP dimension decreases significantly with increase serum TSH (r= -0.147 P-value=0.001). 11.7% of total variation in AP dimension, 3.5% of total variation in ML dimension and 6.5% of total variation in CC dimension in right lobe thyroid are because of serum TSH. While 9.5% of the total variation in AP dimension in left lobe is also due to serum TSH.

Conclusion: Negative and significant correlation between serum TSH and thyroid dimensions was observed. Serum TSH inversely and significantly affects all the dimensions of the right lobe and only one dimension in the left lobe.

KeyWords: Thyroid Gland, Thyrotropin, Diagnostic imaging

INTRODUCTION:

After urinary iodine level assessment, volumetric evaluation of thyroid gland (TG) has also become critical for determining the iodine status of a population as World Health Organization (WHO) suggested that normal range of thyroid gland volume (TGV) is required for large scale iodine monitoring programmes in different populations[1,2]. Reference range of normal TG is important for diagnosing goiter, thyroiditis and other thyroid diseases. TGV is also required to calculate the dose of radioiodine and also to evaluate the response of suppression treatment. It is also important to assess the TGV of such patients who are regularly undergoing long term treatment of the drugs that deranged TGV[3]. Determination of TGV is also vital for minimally invasive thyroid surgery[4].

Ultrasonography of thyroid, due to its superficial location, is considered to be the best modality because it assures high sensitivity and specificity and good scanning speed[5,7]. Due to its cost effectiveness and noninvasive approach it is considered to be the first choice to measure TGV and its morphology[8]. American Thyroid Association in 2009 suggested ultrasonography of thyroid as the most common and beneficial modality to image TG and its pathologies.

According to WHO recommended criteria to evaluate TGV, is to calculate the volume of each lobe of TG by the formula: Volume (ml) = Length in cm (Cranio-caudal dimension) x Width in cm (Medio-lateral dimension) x Depth in cm (Anterio-posterior dimension) x 0.4790. (0.479 = correction factor)[1,2].Total TGV is the sum of the volume of right and left thyroid lobes. Isthmus dimensions were not included in the measurement of thyroid gland volume as recommended by W.H.O[1,2].

Among the numbers of genetic and environmental factors that are known to effect TGV[10-18], most extensively explored are the effect induced by iodine intake and thyroid stimulating

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hormone (TSH)[12,14,19]. TSH and along with its receptor is important in, organization of the follicular cells of the thyroid and controlling TGV. After the binding of TSH to its receptors on the follicular cells, it then stimulates the growth of the follicular cells. These follicular cells in turn increase the synthesis and secretion of thyroxine[20-22].

There are studies that reported significantly negative correlation between serum TSH and TGV[11-13]. Some of the studies also reported insignificant relationship between serum TSH and TGV[10,23] Volume of each lobe of thyroid gland is the product of its 3 dimension: Anterio-posterior(AP) x medio-lateral (ML) x cranio-caudal (CC) x correction factor[1,2]. To the best of our knowledge no study reported the effect of serum TSH on thyroid dimensions. Objectives of this study is to determine the effect of serum TSH on thyroid dimensions in each lobe and also to measure the amount of effect of per unit increase in serum TSH on thyroid dimensions in each lobe.

Methodology:

A cross-sectional study was carried out at Ziauddin University hospital Karachi. This study was approved by ethical committee of Ziauddin University and hospitals. Apparently healthy subjects aged 21 years and above were recruited in the study through convenient sampling. Every participant was asked questions related to demographic profile, personal history, past history, medical and drug history. Participants with known thyroid diseases, with history of thyroid surgery, or on medications that are known to derange TGV (especially lithium, carbamazepine, phenytoin and oral contraceptive) were excluded from the study. Females with pregnancy, lactation and those who had delivered in last 12 months were also excluded due to risk of deranged TGV during this period.

Signs and symptoms related with thyroid functions were then noted to rule out unidentified cases of thyroid diseases. Physical examination of thyroid gland was then performed. All participants with enlarged thyroid gland and palpable thyroid nodule were excluded from the study. In order to recruit euthyroid participants, serum TSH level of the participants was then evaluated by chemiluminescence method. Reference range of TSH was 0.23 – 4.0 µIU/ml as used by the laboratory of Ziauddin University Hospital.

Participants having Serum TSH between 0.23 – 4.0 µIU/ml underwent ultrasonography of thyroid. Ultrasound machine Toshiba model SSA-590A with a 7.5 MHz transducer and 4 to 6 cm linear probe was used in this study. To avoid the inter observer error ultrasound was performed by a single radiologist. For the performance of ultrasound accurately standard technique for ultrasonography was followed, participants were examined in supine position, with pillow under their shoulders and their neck hyperextended. Ultrasound gel was applied all over the thyroid area of the neck. The probe was placed directly on the skin over the thyroid gland. An image for each lobe of thyroid was obtained. Medio-lateral (ML) and antero-posterior (AP) dimensions of each lobe of thyroid were noted in transverse plane. Cranio-caudal (CC) dimension for each lobe of thyroid was noted in longitudinal plane[1,2].

Statistical Analysis:

Data was entered on Microsoft excel and analyzed on SPSS version 21. Mean with standard deviations were derived for serum TSH. Kolmogorov–Smirnov test was applied to check the normality. The data failed to follow the normality assumption therefore Log transformation was applied to normalize the data. Spearman correlation was applied for evaluating the correlation between thyroid dimensions and serum TSH level. Regression analysis was applied to evaluate the amount of variation in thyroid dimensions due to per unit increase in serum TSH. P-value < 0.05 was considered as significant.

RESULTS:

Mean serum TSH of 192 participants of the study was found to be 1.56µIU/ml ±0.78 µIU/ml with minimum and maximum 0.4µIU/ml to 3.74µIU/ml. Correlation Analysis between thyroid dimensions and serum TSH are shown in table 1. Change in thyroid dimension due to per unit increase in serum TSH shown in table 2. Graph1: Regression analysis determining the inverse linear relationship between serum TSH and Right Lobe Anterio-Posterior dimension of thyroid. (RT.AP LOG= Right lobe Anterio-Posterior Log transformation, TSHLOG=TSH Log transformation). Graph 2: Regression analysis determining the inverse linear relationship between serum TSH and Right Lobe Medio-Lateral dimension of thyroid. (RT.ML LOG= Right lobe Medio-Lateral Log transformation, TSHLOG=TSH Log transformation). Graph 3: Regression analysis determining the inverse linear relationship between serum TSH and Right Lobe Cranio-Caudal dimension of thyroid. (RT.CC LOG= Right lobe Cranio-Caudal Log transformation, TSHLOG=TSH Log transformation). Graph 4: Regression analysis determining the inverse linear relationship between serum TSH and Left Lobe Anterio-Posterior dimension of thyroid. (LT.AP LOG= Left lobe Anterio-Posterior Log transformation, TSHLOG=TSH Log transformation).

DISCUSSION:

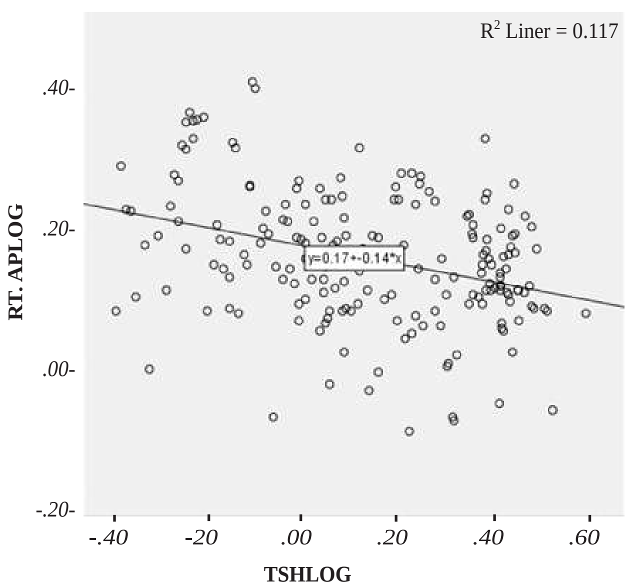
Volumetric evaluation of TGV is one of the criteria determining the iodine status of a population. Volume of each lobe of TG is the product of its 3 dimension: Anterio-posterior(AP) x medio-lateral (ML) x cranio-caudal (CC) x correction factor[1,2]. Previous studies reported either the inverse and significant relationship[11-13] or no relationship between serum TSH and TGV[10,23]. To the best of our knowledge no study reported the effect of serum TSH on thyroid dimensions. Objectives of this study were to determine the effect of serum TSH on thyroid dimensions of each lobe and also to measure the amount of effect of per

N=192	Right Lobe Dimensions			Left Lobe Dimensions		
	Anterio-posterior	Medio-lateral	Cranio-caudal	Anterio-posterior	Medio-lateral	Cranio-caudal
Correlation	-0.321	-0.177	-0.280	-0.271	-0.127	-0.122
P-Value	0.001	0.014	0.001	0.0001	0.080	0.092

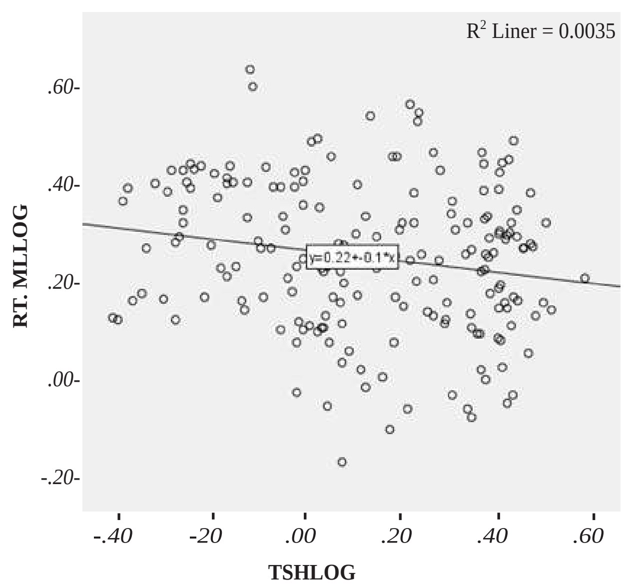
Table1: Correlation between serum TSH and Thyroid dimensions.
Correlation is significant at 0.05 level

N=192	Right Lobe Dimensions			Left Lobe Dimensions		
	Anterio-posterior	Medio-lateral	Cranio-caudal	Anterio-posterior	Medio-lateral	Cranio-caudal
Beta 1	-0.142	-0.1	-0.098	-0.147	-0.037	-0.039
B (constant)	0.174	0.223	0.449	0.158	0.200	0.434
R2	0.117	0.035	0.065	0.095	0.004	0.012
P-Value	0.001	0.009	0.001	0.001	0.397	0.132

Table2: Regression analysis between thyroid dimension and serum TSH,
Correlation is significant at 0.05 level (2-tailed)



Graph 1: Regression between serum TSH and Right Lobe Anterio-Posterior Dimension R^2 Liner = 0.117



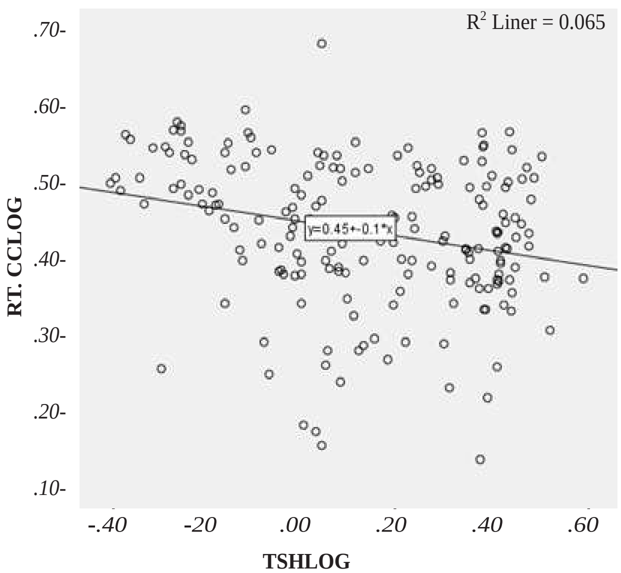
Graph 2: Regression between serum TSH and Right Lobe Medio-Lateral Dimension

unit increase in serum TSH on thyroid dimensions of each lobe.

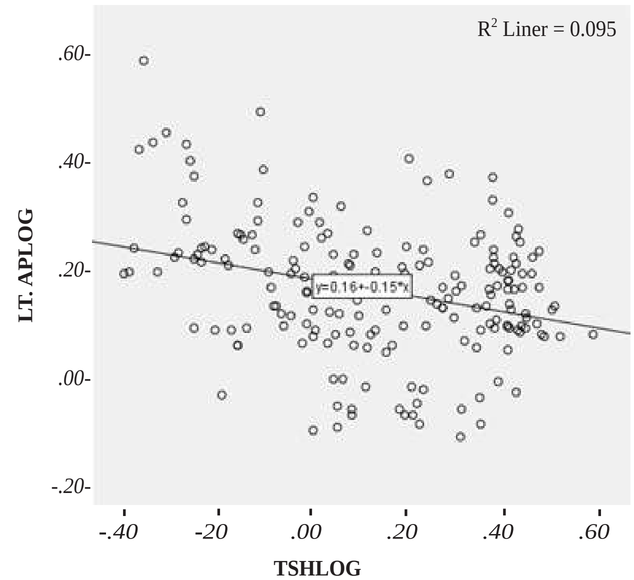
Just like the inverse effect of serum TSH on TGV as reported previously[11,13], this study reported negative correlation between serum TSH and thyroid dimensions. In the right lobe of TG, AP dimension (P-Value 0.001), ML dimension (P-Value 0.014) and CC dimension (P-Value 0.001) dimension was found to be negatively and significantly related to serum TSH. Among the three dimensions of right lobe, serum TSH demonstrated most negative correlation with AP dimension. Least negative correlation was observed between serum TSH and ML dimension of right lobe.

Regression analysis further demonstrated that with per unit increase with serum TSH, AP dimension decreases significantly by 0.142ml, ML dimension decreases significantly by 0.1ml and CC dimension decreases by 0.098ml in the right lobe of thyroid. 11.7% of total variation in AP dimension, 3.5% of total variation in ML dimension and 6.5% of total variation in CC dimension of right lobe thyroid are the result of serum TSH.

In the left lobe of thyroid, significantly negative correlation was found only between serum TSH and AP dimension. Correlation between serum TSH and left lobe ML and CC dimension was found to insignificant. This study further



Graph 3: Regression between serum TSH and Right Lobe Cranio-Caudal Dimension



Graph 4: Regression between serum TSH and Left Lobe Anterio-Posterior Dimension.

demonstrated that with per- unit increase in serum TSH only left lobe AP dimension decreased significantly by 0.147ml (P-Value=0.001). 9.5% of the total variation in AP dimension of left lobe was probably due to serum TSH. No correlation was reported between serum TSH and ML and CC dimension of left lobe of thyroid.

This study further demonstrated that if the effect of serum TSH was completely eliminated then in right lobe average of AP dimension would be 0.117cm, ML dimension would be 0.035 cm and CC dimension would be 0.06. In left lobe the average AP dimension would be 0.095 cm if the effect of serum TSH was removed.

Gomez et al., demonstrated negative and significant correlation between serum TSH and TGV in Spanish subjects (r=-0.26, P.value=0.001)[13]. Barrere et al also demonstrated inverse relationship between serum TSH and TGV among French subjects in both the genders[11]. Negative correlation between the two variables was also observed in the Karachi population (P-Value=0.03) and also between serum TSH and right lobe volume (P-Value=0.029)[12].

The overall results of this study were not in accordance to the study done by Berghout *et al in* 1987 in Amsterdam population[12] Ressmussan et al in 1989 in Danish subjects[23] and Adibi et al in 2008 in Iranian population where they failed to report any relation between serum TSH and TGV and concluded that there was a lack of significant correlation between serum TSH level and TGV[10,12,23].

Conclusion:

Previous studies reported significant relationship between serum TSH and TGV or no relationship between serum TSH and TGV. To the best of our knowledge no study reported that which thyroid dimension in each lobe was most and least likely responsible for this negative correlation. Negative and significant correlation between serum TSH and thyroid dimensions was observed in this study. Serum TSH inversely and significantly affected all the dimensions of the right lobe and only one dimension in the left lobe.

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Author Ship: This work was carried out in collaboration between all authors. Corresponding author Dr. Mahrukh Kamran designed the study, wrote the protocol, and wrote the first draft of the manuscript. Dr. Sahar Mubeen and Dr. Iffat Raza managed the literature search and critical analysis of the study. Author Dr. Sanober Bughio supported the study technically and clinically. Hira Waseem and Dr. Zainab Khaiq Ansari participated in study design, data analysis and interpretation. All authors read and approved the final manuscript.

Conflict of interest: There was no conflict of interest.

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