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Normative data of thyroid volume-ultrasonographic evaluation in clinically asymptomatic Nigerian adults at Benue state university teaching hospital, Makurdi

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ABSTRACT

Background: Thyroid gland volume is highly variable among communities. Current study was aimed to determine the local normative data on thyroid volume, assessed by ultrasonography in asymptomatic Nigerian adults.

Methods: A prospective cross-sectional study conducted at a tertiary hospital between February 2020 to February 2021, which included 500 clinically asymptomatic adults in Makurdi, North-Central Nigeria. Age specific reference values for thyroid volume were obtained. Structured questionnaire was used to obtain information on other variables that could influence thyroid gland volume. The data obtained, including that from blood tests of thyroid function was collated and analysed using SPSS 23, with p=0.05.

Results: The mean total thyroid gland volume for both lobes in the entire population of the study was 6.91 ± 2.41 cm³. The mean thyroid volume for both lobes in males 7.09 ± 2.60 cm³ was higher than that of females 6.73 ± 2.38 cm³. The mean right and left lobe volumes were 3.56 ± 1.14 cm³ and 3.35 ± 1.10 cm³ respectively. The right lobe volume was significantly greater than the left lobe (p=0.000). There was a consistent steady increase in thyroid gland volume with increasing age for the general, male and female population until at least the 5th or 6th decade. The total thyroid gland volume significantly correlated with the individual's body parameters. Highest correlation was found with height (r=0.256, p<0.05)).

Conclusions: Ultrasonography was valuable in the determination of thyroid gland volume and normal values were different in various communities.

Keywords: Asymptomatic, Normative data, Nigerian adults, Thyroid gland volume, Ultrasonography

INTRODUCTION

The thyroid gland is the largest and most prominent of all the endocrine glands, weighing about 15-25 grams. It makes proteins, controls how quickly the body uses energy and how sensitive the body should be to other hormones. It does this by secreting thyroid hormones, principally thyroxine (T4) and triiodothyronine (T3).¹⁻³

The limits of normal thyroid gland volume are highly variable as they are greatly influenced by age, gender, iodine status of the population as well as geographic and another regional factors.³⁻⁶ However, recent advances with other increasing use of iodine supplementation by countries is bound to lower the total thyroid gland volume, thus providing more accurate facts and figures regarding the size of this organ.⁷

The most common endocrine abnormalities seen worldwide are thyroid disorders, which were once overlooked and thought to be uncommon in Africa and Nigeria, in particular. However, current evidence has since proven this to be the contrary, and has further demonstrated the role environmental (iodine deficiency) and nutritional factors (goitrogens) play in the emergence of some of these thyroid disorders, which unfortunately are the second most common endocrinopathies seen at endocrinology clinics, after diabetes mellitus.8-10 The accurate estimation of the thyroid size is therefore not only very important for the diagnosis and treatment of these disorders but also invaluable in the general management of disorders arising from iodine deficiency.11

The estimation of thyroid gland size and volume can be achieved by numerous methods like palpation, ultrasonography, radionuclide study, computed tomography (CT), and magnetic resonance imaging (MRI). Palpation of this gland is easily done, since it is located superficially in the neck. Nevertheless, currently, it is really difficult to propose the use of any one single method over another, due to dearth of sufficient data to comparethe different methods of thyroid gland examination or size determination.^{12,13}

However, ultrasonographic estimation of thyroid gland volume is highly recommended as it overcomes the problems of marked interobserver variability and overestimation of goiter prevalence associated with the palpation estimates.¹²⁻¹⁴ Besides, ultrasonography is universally available, cost-effective, painless, noninvasive, does not use ionizing radiation, and is easier to use compared to the other imaging modalities.¹⁵ Computed tomography (CT) and magnetic resonance imaging (MRI); on the other hand, provide structural information of the thyroid gland just like ultrasound, but are very expensive and not readily available. Computed tomography (CT) in addition uses ionizing radiation. Radionuclide studies provide functional rather than structural information.^{16,17} Thyroid gland volume estimation using ultrasound, therefore is better suited in our resource-poor environment, where more sophisticated modern imaging techniques are not readily easy to find or simply beyond the rich of the common man.¹⁷⁻¹⁹

Normative data of thyroid volume-ultrasonographic evaluation has not been carried out in our center. Reports, however exists of investigators who have contributed substantial knowledge to this subject matter in other parts of our country.^{3,8,15-17,20,21,30}

The study seeks to establish normal thyroid gland volume in adult Nigerians in Makurdi and to compare this value with those already existing in the literature. The study will also examine if other determinants, such as age, sex, weight, and height of participants have any relationship with thyroid gland volume.

METHODS

This was a prospective study, carried out at the department of radiology, Benue state university teaching hospital (BSUTH), Makurdi, from February 2020 to February 2021. The department offers ultrasound services with a large turnout of clients drawn from within and outside the state.

Sample size was determined based on the Fisher's formula mentioned below for a population greater than 10,000.^{3,4,21}

$$n = z^2 p q/d^2$$

Where: n=desired sample size, z=standard deviation, using set at 1.96, which correspond to 95% confidence level, p=proportion in target population estimated to have a particular characteristic. If no reasonable estimate, 50% (0.5) is used, q=1– p and d=degree of accuracy desired, usually set at 0.05. Sample size was calculated as 384. However, a sample size of 500 was used to increase the statistical power of the study.

Inclusion criteria

The inclusion criteria for this study were males or females above the age of 18 years; patients referred for ultrasound assessment other than thyroid ultrasound scan with no known clinical, pathological or radiological evidence of thyroid/endocrine disorder; those who voluntarily consented to participate in both the study and in the laboratory assessment of their thyroid function; as well as patients with normal laboratory values of TSH (0.4-4.8 mIU/l), T4 (5.1-12.0µg/dl), and T3 (0.7-2.0ng/ml).

Exclusion criteria

The exclusion criteria were applicable to individuals on drugs that cause thyroid dysfunction like lithium, amiodarone, immunomodulating drugs such as interferon alpha; females during menstruation, pregnancy or who have delivered within the last twelve (12) months; patients with anterior neck swelling or those with clinical, and/or radiological pathologic evidence of thyroid/endocrine disorder manifested on ultrasonography as among other findings, heterogeneous thyroid parenchyma and/or nodule; patient with previous thyroid surgery, wasting or chronic illness like chronic renal/liver disease, malignancy as well as those who declined participation in the study and/or had abnormal laboratory values of TSH, T4 and T3.

Procedure

Informed consent was obtained and a questionnaire administered on all the participants, after the procedure was explained to all of them. Their weights and heights were measured respectively, by having them climb a weighing scale and by positioning them erect against a wall that was marked in meters.

Sonographic examination was done for those who met the inclusion criteria, using Siemens Sonoline G-50 machine fitted with a linear 5-10 MHZ transducer, held at a 90degree angle to skin, using only minimal pressure so as not to distort the gland anatomy. The subjects were examined in supine position, with pillow placed under their shoulders to hyperextend the neck. Ultrasound gel was applied over the thyroid region. To provide accurate results, multiple measurements (at least thrice) were done and an average obtained for the thyroid gland volume. The transducer was directly placed on the skin over the thyroid gland, and an image of each lobe was obtained in transverse and longitudinal planes. The transverse scan (Figure 1) measures the maximal width (mediolateral) and depth (anteroposterior) of the transverse section of each lobe, with the depth measurement at 90 degrees to the skin surface and the width measurement at 90 degrees to the depth measurement. Reference anatomical landmarks for the transverse scan included the trachea with its echogenic cartilage rings and air shadows in the midline; the echo-free lumina of the carotid arteries (pulsation) and jugular veins (distension on Valsalva) delineated the lateral aspect. The longitudinal study (Figure 2) measures the maximal length of the longitudinal section of the lobe, and the reference anatomical landmarks for the longitudinal scan includes the strap muscles which appeared anteriorly as hypoechoic structures relative to the thyroid gland. Posterior to the medial portion of the thyroid, the trachea with its echogenic cartilage and air shadows was often seen. Posterior to the lateral portion of the thyroid, venous structures and the common carotid artery are visualized as echo-free tubular structures.22



Figure 1: The transverse thyroid scan showing both lobes and the Isthmus as well as measurement of the maximal width (AB) and depth (CD) of the transverse section of the right lobe.

With the ellipsoid model, the length, the width, and the depth of each lobe were measured and multiplied. The obtained result was then multiplied by a correction factor, which is 0.479.^{4,22} The volume of each thyroid lobe was calculated with ellipsoid formula: (volume in ml = length in cm × width in cm × depth in cm × 0.479. Total volume

is obtained as the sum of two thyroid lobes. The isthmus was not included into the sum.



Figure 2: The longitudinal thyroid scan showing measurement of the maximal length of the longitudinal section of each thyroid lobe (EF) in between the white cursors.

Body mass index (BMI) (kg/m²) was calculated as= weight/height.^{2,3,5,14,21} According to BMI <20 kg/m² was considered as underweight 20-25 kg/m² as normal weight and >25 kg/m² was considered as overweight. The body surface area was calculated using the formula of Dubois and Dubois.²² Body surface area BSA (m²) =weight $^{0.425} \times$ height $^{0.725} \times 71.84 \times 10^{-4}$.

BSA categories.^{3,21}

In males BSA 1.91 m² and in females BSA 1.6 m² was considered as normal. BSA >1.91 m² in males and >1.71 m² in females was considered as abnormal. The participants` blood samples were taken for thyroid function tests (TSH, T4 and T3). Results that were not within the normal range TSH (0.4-4.8 mIU/l), T4 (5.1-12.0µg/dl) and T3 (0.7-2.0ng/ml) were excluded.

Other information including age and socio-demographic biodata, were entered into statistical package for social science (SPSS) version 23 software for analysis. Results were presented as frequencies and proportions for categorical data and mean \pm SD for continuous variables. Correlations were used to test the relationship between one variable and another, p=0.05 was considered significant for the study population.

RESULTS

Five hundred randomly selected healthy adults with no apparent clinical, or pathologic evidence of thyroid disease were recruited for the study, comprising 260 males, representing more than half of the respondents (52.0 %) while 240 (48.0%) were females (Figure 3).

The ages of the patients ranged from 18 to 80 years. The mean age for the study population, males and females were 40.7 ± 15.80 years; 40.0 ± 16.20 years and 38.7 ± 14.90 years respectively. A significant proportion 117 (19.9%) of the population was of the age range 21-30 years, followed by the age range of 31-40 years with 113

(22.6%), while the least population 2 (0.40%) was of the age category 71-80 years as shown in (Figure 4).

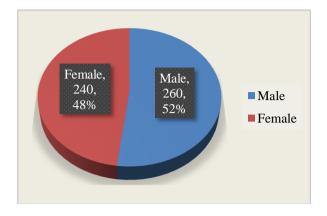


Figure 3: Gender distribution of respondents.

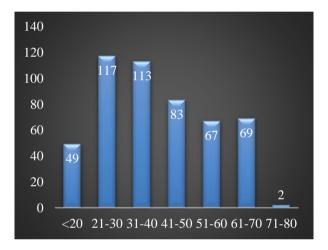


Figure 4: Age distribution of respondents.

Patients with tertiary education were in the majority 269 (53.8%) while 131 (26.2%) had secondary education. Eighty-eight (17.6%) and 12 (2.4%) patients had primary and no formal education respectively as depicted in (Figure 5).

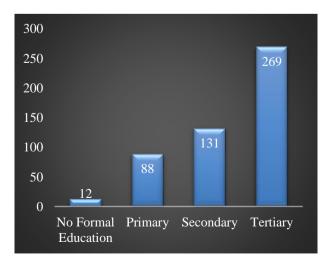


Figure 5: Educational attainment of respondents.

The mean total thyroid gland volume for both lobes in the entire population of the study was 6.91 ± 2.41 cm³, with a range of 2.56-13.82 cm³ as seen in (Table 1). The mean total thyroid gland volume increases with increasing age till the sixth decade, with the highest recorded value of 7.22±2.88 cm³ at the 51-60 age group, while the least recorded value was 6.60 ± 2.48 cm³ at the 21-30 years age group. There was a statistically significant increase in thyroid gland volume with increase in age (p=0.009).

Table 1: Thyroid gland volume for the study
population.

Thyroid volume (n=500)	Min.	Max.	Mean	SD	P value
Right lobe (RL)	1.31	7.12	3.56	1.14	
Left lobe (LL)	1.25	6.70	3.35	1.10	0.000
Total (TTV)	2.56	13.82	6.91	2.41	

The mean thyroid volume for both lobes in males was 7.09 ± 2.60 cm³. There is a steady increase in male thyroid gland volume with age up to the fifth decade. The highest and least recorded values of 7.53±2.95 cm³, and 6.88 ± 3.09 cm³ were observed at the 41-50 and 21-30 years age category respectively (Table 2). There was a statistically significant volume increase with increasing age (p=0.044). The mean thyroid volume for both lobes in females was 6.73±2.38 cm³. The female thyroid gland volume has its highest recorded value of 7.54 ± 2.64 cm³ at the sixth decade and its lowest value of 6.15 ± 2.70 cm³ at the second decade as seen in (Table 3). There was no statistically significant volume increase with increasing age (p=0.055). There was a consistent steady increase in thyroid gland volume with age for the general, male and female population until at least the fifth or sixth decade.

Table 2: Distribution of age with the male thyroidgland volume.

Age (years)	%	Mean RL±SD	Mean LL±SD	Mean TTV±SD
<20	28	3.36 ± 1.00	3.37±1.16	6.73 ± 2.60
21-30	43	$3.64{\pm}1.45$	3.24±1.16	6.88±3.09
31-40	62	4.01 ± 1.54	3.46 ± 1.21	7.47 ± 3.08
41-50	46	4.06±1.39	3.47±1.19	7.53±2.95
51-60	38	3.72 ± 1.24	3.25 ± 1.16	6.97 ± 3.08
61-70	41	3.55 ± 1.22	3.42 ± 1.22	6.97±2.72
71-80	2	3.50±0.10	3.58 ± 0.10	7.08 ± 0.68
P value		0.013	0.012	0.044
$\sum \mathbf{X}$	260	3.69±1.13	$3.40{\pm}1.03$	7.09 ± 2.60

The mean right lobe volume (RLV) was 3.56 ± 1.14 cm³ and that of males and females were 3.69 ± 1.13 cm³ and 3.43 ± 0.98 cm³ respectively. The mean left lobe volume (LLV) was 3.35 ± 1.10 cm³ and that of males and females

were 3.40 ± 1.03 cm³ and 3.30 ± 1.01 cm³ respectively. The right lobe volume was significantly greater than the left lobe (p=0.000).

The total thyroid gland volume significantly correlated with the individual's height, body surface area (BSA), weight, age and body mass index (BMI) as seen in (Table 4). The highest correlation was found with height (r=0.256, p<0.05)), followed by BSA (r=0.178, p<0.05). The total thyroid gland volume increases with increasing body height (Figure 6) and body surface area respectively, the body parameters that best correlated with thyroid gland volume in our study. In addition, the male subjects were taller than their female counterparts with a male to female heights of 1.68 ± 0.09 m and 1.63 ± 0.09 m respectively.

Table 3: Distribution of age with the female thyroidgland volume.

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Age	%	Mean	Mean	Mean	
(years)	/0	RL±SD	LL±SD	TTV±SD	
<20	28	3.08 ± 0.91	3.07 ± 0.91	6.15 ± 2.70	
21-30	43	3.34±1.0	3.24 ± 0.96	6.58 ± 2.07	
31-40	62	3.57±1.01	3.56 ± 1.01	7.13±2.29	
41-50	46	3.31±0.79	3.31±1.15	6.62±1.65	
51-60	38	3.85 ± 1.07	3.69±1.11	7.54±2.64	
61-70	41	$3.40{\pm}1.10$	2.92 ± 0.93	6.32 ± 2.92	
71-80	0	0	0	0	
P value		0.099	0.032	0.055	
$\sum \mathbf{X}$	240	3.43±0.98	$3.30{\pm}1.01$	6.73±2.38	

Table 4: Correlation between thyroid gland volume and the anthropometric parameters (n=500).

Anthropometric indices	Pearson's correlation (r)	P value
Height	0.256	0.000
BSA	0.178	0.000
Weight	0.149	0.001
Age	0.090	0.000
BMI	0.009	0.004

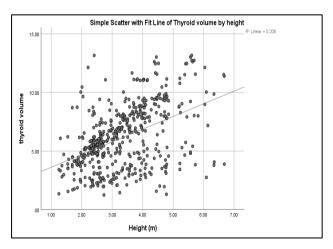


Figure 6: Correlation between total thyroid volume and body height.

DISCUSSION

A normogram of the thyroid volume of 500 subjects in our environment was estimated based on cross-sectional ultrasonographic measurements of the thyroid gland. We also studied the relation of the thyroid volume with age, sex, height, weight, body mass index (BMI), and body surface area (BSA).

The mean total thyroid gland volume for both lobes in the entire population of our study was $6.91 \text{ cm}^3 + 2.41$ (range 2.56-13.82 cm³). This value was much lower than those previously recorded by Servet et al, Ahidjo et al, Ertan et al, and Ivanac et al, who separately reported total thyroid gland volumes of 13.0cm³±6.27 in Turkey, 8.55 cm³±1.82 in Maiduguri, Nigeria, 12.98 cm³±2.53 in Turkey and 10.68 $cm^{3}\pm 2.82$ in Croatia respectively.^{14,17,23,24} Our value was, however slightly higher than that recorded by Mahrukh et al and Salaam et al, which was 6.26cm³±2.89 in Karachi and 6.03 cm³±2.49 in Jos Nigeria respectively.^{4,21} However, comparable to our study were the values obtained by Silvia et al, Kayastha et al and Mohamed Y et al which were 6.60 cm³ \pm 0.26 in Cuba, 6.629 cm³ \pm 2.5025 in Nepal and 6.44 cm³ \pm 2.44 in Sudan respectively.^{5,12,19} The reason for the variations in thyroid gland volume was attributable to determinant factors that interact in a complex way. They include age, gender, dietary iodine intake. consumption of goitrogenic vegetables(cruciferous), ethnicity, massive iodization programs by governments and according to our findings, anthropometric parameters, like weight, height, BMI and BSA.^{3,5,12,21} It is to be noted that the mean thyroid gland volume in the studied population of Karachi, Pakistani and Jos, Nigeria by Mahrukh et al and Salaam et al respectively, was much lower than that of the rest of the other countries.^{4,21} This is in agreement with the known severe and prolonged iodine deficiency status of Pakistan till the recent past, which is believed to be the answer for the small thyroid gland in the studied population.⁴ For the Jos. Nigerian study, increasing use of iodine supplementation in the recent years could be one of the factors reducing the iodine deficiency, previously prevalent in the country, thus reducing the total thyroid gland volume.21

Our study also reported that the mean thyroid volume was significantly greater in males when compared to the females (M:F=7.09cm³ \pm 2.60:6.73 cm³ \pm 2.38). Mahrukh et al from Karachi in 2014, Ahidjo et al from Maiduguri Nigeria in 2005, Mohamed et al from Sudan in 2011, Salaam et al from Jos Nigeria in 2011 and Ertan et al from Turkey in 2010 had also reported significantly greater thyroid gland volume in males than females.^{4,17,19,21,23} Many explanations have been given for the difference in thyroid gland volume between the two genders. Laszlo et al suggested the difference in body weight between male and female as the reason for this difference in thyroid gland volume.^{25,26} Reza et al and Adidi et al proposed that the difference in lean body mass between the two genders

could be the reason for an increased thyroid gland volume in males.^{25,27} However, these findings were contrary to the study done in other countries. Kayastha et al from Nepal in 2010 and Xu et al from Atlanta in 1999 reported no significant difference in the mean TGV in males and females.^{12,28} However, the Kayastha et al study did prove significant correlation between TGV and anthropometric measurements, namely body surface area (r=0.444, p<0.0001), weight (r=0.443, p<0.0001), body mass index (r=0.371, p<0.0001), and height (r=0.320, p<0.0001). Our study showed that the right lobe volume of the thyroid gland was significantly greater than that of the left lobe in both genders (p < 0.05). This was collaborated by parallel reports from Asia. Africa and Europe. The Asian reports included that by Makrukh et al in 2014, Servet et al in 2010, and Ertan et al in 2015.^{4,14,23} The African reports mainly from Nigeria by Tahir et al in 2002, Ahidjo et al in 2005, Salaam et al in 2020, and Mohamed et al in 2011 from Sudan as well as a European report by Gordana et al in 2004.^{16,17,19,21,24} The reports were all in agreement with the fact that the mean volume of the right lobe of the thyroid gland was significantly greater than that of the left lobe in both genders.^{4,14,16,17,19,21,23,24} The asymmetry between the two lobes of the thyroid gland is probably simply due to increased vascularization of the right lobe compared to the left.^{21,30} Other investigators are, however of the view that the asymmetry may be due to the presence of adjacent structures, like the oesophagus, which is normally deviated towards the left side of the midline, thus giving more space to the right lobe of thyroid to grow resulting in the larger volume of the right lobe.^{4,29} Another, though yet to be fully understood theory suggests that thyroid asymmetry is associated with handedness of an individual.²⁹ Thyroid lobal asymmetry is also believed to be regulated by the central nervous system (CNS) through the unilateral differentiation of the hypothalamus on the thyroid gland.^{21,29} In all these permutations, our study did not find sufficient evidence to support the association of handedness or esophageal position with thyroid lobe asymmetry. This was most probably due to the very small sample size of left-sided handers and subjects who had centrally located esophagus. Also, no subject was recruited with the esophagus deviated to the right! A previous report by Yildirim M et al³¹ did not find any association between handedness and total thyroid volume or the volume of the right lobe. This therefore calls for further investigation with a larger sample size of left-sided handers and subjects with different esophageal positions. Our index study showed a consistent and steady increase in thyroid gland volume with increasing age for the total, male and female populations until at least the 5^{th} or 6^{th} decade. For the total and male populations, there was a statistically significant increase in thyroid gland volume with increasing age (p<05). For the female population there was no statistically significant volume increases with increasing age (p=0.055). The highest mean thyroid gland volume in our study was 7.22cm³±2.88 at the 51-60 years age category. No obvious explanation could be given for these findings, thus necessitating further research. However, these accounts are, in partial agreement with a previous study by Servet et al who reported thyroid gland volume increase with increasing age till the age of 65 years.¹⁴ In a similar study on the South-Asian population of Nepal in 2010 by Kayastha et al the largest thyroid gland volume was found at the age range 70-79 years.¹²

The total thyroid gland volume in our study significantly correlated with the individual's height, body surface area (BSA), weight, age and body mass index (BMI). Highest correlation was found with height (r=0.256, p<0.05), while the least was with body mass index (r=0.009, p<0.05). This was in agreement with earlier reports by Kayastha et al in 2010 and Gordana et al in 2004, who also reported that thyroid volume correlated well with body parameters especially body surface area (r=0.444, p<0.0001) and body height (r=0.37, p=0.001) respectively.^{12,24} Similarly mean heights of male was more than that of the females in our study (M:F=1.68:1.63 m). This finding corroborated well with earlier investigators.^{3,12,14,17,21,24}

Limitations

Limitation of current investigations were; apart from the that thyroid gland volume measured fact bv ultrasonography is a highly operator-dependent procedure, the sizes and contour irregularities of the neck presented difficulties in ultrasound examination of these patients There was also sample size limitation, necessitating a call for larger samples in future research to increase the statistical power of the study. Again, for lack of resources, this study was done using a 2dimensional ultrasound machine, instead of a 3dimentional ultrasound scanner which would have given a more accurate estimate of the thyroid gland volume.

CONCLUSION

Age specific normative thyroid volume was estimated in our environment which will be useful in the clinical diagnosis, grading and management of goiter. Our estimated mean thyroid volume is significantly lower when compared to previous studies among Caucasians and some Asian communities. Thyroid volume, in our study, best correlated with height, then BSA and weight. As such height-specific reference values should be the best local reference values to be used in the clinical evaluation of thyroid volume. The mean thyroid volume in the males is higher than in the females. The volume of the right lobe of the gland was significantly greater than the left in both genders.

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