Trends in Clinical and Medical Sciences

PSR Press

Article

Thyroid volume and its correlation with thyroid function in central India

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Academic Editor: Dr. Augustine Ibegbu
Received: 10 January 2023; Accepted: 7 May 2023; Published: 25 May 2023.

Abstract: Introduction: Thyroid gland volume is highly variable as it is greatly influenced by age, gender, anthropometric measurements, and geographical location. It has become essential for every population to determine the reference range of their normal thyroid gland volume in healthy individuals. This, in turn, will help the population in grading goitre and guide large-scale iodine monitoring programs. Ultrasound, being more precise than clinical examination in identifying enlarged thyroid glands, overcomes the problems of overestimation of goitre prevalence and marked interobserver variability associated with palpation estimates. A nomogram of thyroid volume in our environment is important to serve as a reference point in managing patients with thyroid pathologies, especially goitre. The purpose of this study was to establish reference ranges of total thyroid volume among the normal adult population in central India using ultrasonography and correlate it with thyroid function tests.
Methods and Material: A prospective cross-sectional study was conducted in a tertiary care hospital. A total of 410 healthy subjects were included. B-mode Ultrasonography was used to measure the total thyroid volume by combining the volume of both lobes obtained using the ellipsoid formula. Blood samples were taken for thyroid function tests. Age-specific reference values for thyroid volume were obtained.
Statistical analysis used: IBM Statistical Package for the Social Sciences (SPSS) software for Windows, Version 26.0. Armonk, NY: IBM Corp was used for analysis.
Results: The mean total thyroid gland volume of all study subjects was 6.90 ± 1.74 ml. Males had a significantly higher gland volume (7.30 ± 1.86 ml) compared to females (6.63 ± 1.61 ml) ($P < 0.001$). The volume of the right lobe was significantly greater than that of the left lobe in both genders (3.76 ± 0.96 ml vs 3.14 ± 0.89 ml, $P < 0.001$). No significant correlation was found between gland volume and thyroid function tests.
Conclusions: We attempted to contribute to establishing the reference values for our local population, and further large studies are required to establish nationwide reference values of thyroid gland volume.

Keywords: Thyroid volume; Ultrasonography; Thyroid function; Adult.

1. Introduction

Thyroid is a vital endocrine gland of our body, which is located superficially within the infrahyoid compartment of the neck. It lies against the C5 to T1 vertebral level in a space outlined by muscles, trachea, esophagus, carotid arteries, and jugular veins. The thyroid gland is involved in the production, storage, and release of thyroid hormones, namely thyroxine (T4) and triiodothyronine (T3). These hormones are essential for various physiological actions within the body, including the regulation of body metabolism and the growth and development of individuals.

The size and shape of the thyroid gland vary widely in normal individuals. Typically, in tall individuals, the lobes have an elongated shape, whereas in shorter individuals, they are more oval [1]. Numerous physiological and pathological factors can affect thyroid volume. Anthropological factors such as aging, gender, weight, height, body mass index (BMI), waist-to-hip ratio (WHR), lean body mass (LBM), blood

group, body surface area (BSA), reproductive state, and hormonal changes all influence thyroid volume in normal individuals. Additionally, certain socioeconomic factors such as dietary iodine intake, consumption of excess goitrogens, smoking, alcohol consumption, and geographical locations can also impact thyroid volume in normal individuals.

Thyroid volume estimation is particularly important in various pathological situations, including iodine deficiency goiter, thyroiditis, and others. Several methods can be used to estimate thyroid size and volume, such as palpation, ultrasonography, radionuclide study, computed tomography (CT), MRI, etc. As the gland is located superficially, it can be easily palpated. However, there is a lack of consensus regarding which palpation system best describes the size of the thyroid gland: one based on estimated weight or one based on other variables, such as the presence of a visible prominence. The scarcity of data comparing different methods of thyroid examination or size determination makes it challenging to recommend the use of one method over another.

Goitre is a common clinical condition characterized by an enlarged thyroid with increased thyroid volume (TV). It serves as a functional biomarker for assessing iodine status in individuals and populations. The diagnosis of goitre is typically made through inspection and palpation. However, these methods have poor sensitivity and specificity due to their subjective nature, which can be influenced by examination circumstances, the experience of the examiner, and the anatomical variations in the neck of the individual being examined [2]. Estimating thyroid volume using ultrasound (US) scans is more precise than clinical examination in identifying enlarged thyroid glands. Ultrasonographic estimation of thyroid volume overcomes the problems associated with overestimation of goitre prevalence and the marked interobserver variability associated with palpation estimates.

Goitre, as determined by ultrasound, is defined as glands with a volume exceeding the 97th percentile of the normal population. As a result, most epidemiological studies utilize ultrasound for the assessment of goitre prevalence and iodine status. Sonography has improved with the development of high-frequency transducers, enabling a more detailed study of the thyroid gland. Consequently, the World Health Organization (WHO) and the International Council for the Control of Iodine Deficiency Disorders (ICCIDD) now consider sonography as the diagnostic method for assessing goitre [3]. Ultrasound is a non-invasive, rapid, inexpensive, easily available, safe, and comfortable technique. In addition to measuring thyroid size, ultrasound can also detect non-palpable nodules, estimate the size of nodules, and characterize their properties.

Several countries, including Western countries and neighboring regions, have conducted sonographic studies to assess thyroid volume in both children and adults. Various researchers have measured thyroid volume and obtained different values for normal euthyroid patients. However, data on thyroid volume among adults are limited in India, as most field studies have focused on school children. To the best of our knowledge, there is currently limited data on the normal volume of the thyroid gland among the adult population in India. In the central Indian population, the normal volume of the gland has not been established to date, and there is a lack of reference values for thyroid volume in this population.

This study aimed to establish a local reference for thyroid volume in the central Indian population using ultrasound and to correlate it with thyroid function tests.

2. Material and Methods

2.1. Study Population and Design

This study was a time-bound, hospital-based cross-sectional study conducted in a tertiary healthcare institution located in the central part of India. Approval was obtained from the Institutional Scientific and Ethics Committee. The study was conducted from February 2021 to July 2022. A total of 410 patients who were referred to the Department of Radiodiagnosis for an ultrasound examination indicated for any non-thyroid pathology were included in the study.

2.2. Inclusion Criteria

- Patients aged 18 to 60 years.
- Patients referred to the Department of Radiodiagnosis for an ultrasound examination indicated for any non-thyroid pathology.

- Patients willing to take part in the study.

2.3. Exclusion Criteria

- Females during menstruation, pregnancy, or those who have delivered within the last 12 months.
- Subjects with clinical evidence of thyroid/endocrine disorder.
- Subjects with a known history of thyroid disease or with a positive family history of thyroid disease.
- Subjects taking anti-thyroid drugs or any drugs that alter thyroid hormone metabolism.
- Subjects showing any abnormality in the gland during thyroid ultrasound scan.
- Subjects who did not consent to participate in the study.

2.4. Sample Size Determination

The sample size was determined using Fisher's statistical formula:

$$n = \frac{z^2 pq}{d^2}$$

for populations greater than 10,000. It was calculated to be 384 as shown below:

Where:

$n =$ Desired sample size

$z =$ Standard deviation, set at 1.96 for a 95% confidence level

$p =$ Proportion in the target population estimated to have a particular characteristic

$q = 1.0 - p$

$d =$ Degree of accuracy desired, usually set at 0.05

Therefore,

$$n = \frac{1.96^2 \cdot 0.5 \cdot 0.5}{0.05^2} = 384.$$

However, a sample size of 410 was used.

2.5. Technique

The procedure was explained to all participants, and informed consent was obtained. The participants were asked questions about their history of previous thyroid disease or surgery as stated in the questionnaire. Questions on any anti-thyroid medication, pregnancy, and last childbirth were also asked. Patients were examined in a supine position with a pillow placed under the shoulders to aid in the extension of the head. All examinations were performed using a real-time ultrasound machine fitted with a high-resolution linear transducer (7-12 MHz). Ultrasound gel was applied over the anterior neck (thyroid area), and the transducer was placed directly on the skin over the thyroid area. Images of each lobe and the isthmus were obtained in longitudinal (see Figure 1) and transverse planes (see Figure 2). Longitudinal (length), transverse (width), and depth (AP) measurements were taken in centimeters (cm). The right and left thyroid volume data were obtained and analyzed separately. The isthmus was not included in the sum.

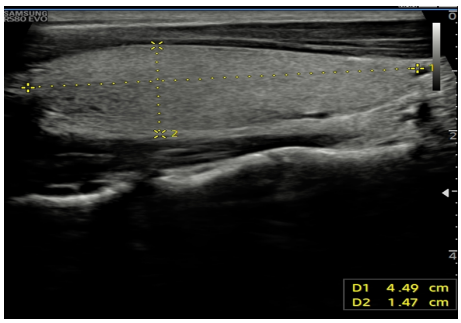

Figure 1. Longitudinal ultrasound scan of the thyroid, showing measurement of the longitudinal (Ls) and antero-posterior diameters of the thyroid lobe

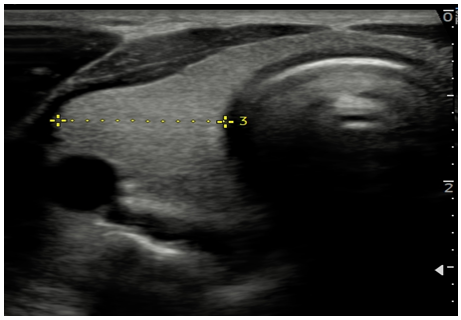

Figure 2. Transverse ultrasound scan of the thyroid

Due to its cone-shaped structure, its lobe is supposed to mimic an ellipsoid and its volume is calculated from the equation of Brunn et al. [4] using the ellipsoid model formula by multiplying the length (L) by width (W) by depth (d) in cm by a correction factor 0.479 for each lobe.

Thyroid volume was calculated using the Brunn expression:

$$V_{US} = 0.479 \cdot L \cdot W \cdot T\,.$$

The total thyroid volume was the sum of volumes of both lobes. Isthmus volume was not taken into account.

$$V_{\text{Thyroid}} = V_{\text{RL}} + V_{\text{LL}}\,.$$

The participants were then asked to get their thyroid profile (T3, T4, TSH) done, and subsequently their results were obtained and recorded.

2.6. Data analysis

The data obtained from the structured questionnaire was entered into a computer to generate a computerized database for subsequent analysis and processing using SPSS version 26.0. Statistical parameters such as student's t-test were used for association between different variables. A p-value of 0.05 or less was considered statistically significant. The results were presented in the form of tables, charts, and graphs.

3. Results

A total of 410 adults were recruited, comprising 172 (41.9%) males and 238 (58.1%) females. The number of females was more than the males. The total mean age for the subjects was 35.22 $\pm$ 11.76 years, with the majority (42.4%) lying in the age group of 18-30 years. The mean age for males was 35.59 $\pm$ 12.17 years (range 18-60), and for females, it was 34.96 $\pm$ 11.46 years (range of 18-60). The lowest number of individuals (12.4%) were in the age group of 51-60 years. The distribution of patients according to age is given in Figure 3.

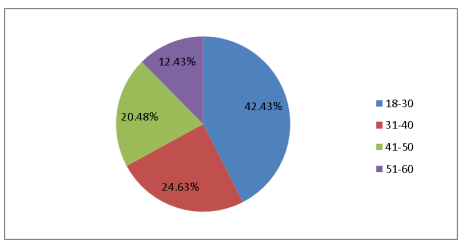

Figure 3. Distribution of patients according to age

Table 1. Mean total volume, right and left lobe volumes in our population

		Mean volume(in ml)	Median	Std. deviation	Variance	Minimum volume(in ml)	Maximum volume(in ml)
Mean statistics	Right lobe	3.7623	3.7600	0.96999	0.941	1.31	
	Left lobe	3.1475	3.2050	0.89570	0.802	1.13	7.42
	Total volume	6.9098	6.8900	1.74998	3.062	2.44	15.66

Table 1 shows the mean total volume, right and left lobe volumes in our population. The total mean thyroid volume in our study was 6.90 ± 1.74 ml. The maximum thyroid volume was found to be 15.66 ml, while the minimum volume was 2.44 ml. The majority of patients (81.95%) had their thyroid volume between 5 to 10 ml, while only 4.14% of the patients had their volume above 10 ml. The highest mean total thyroid volume of 7.45 ± 1.84 ml was seen in the 31-40 age group, while the lowest of 6.58 ± 1.74 ml was seen in the 18-30 age group. The mean total gland volume in the 18-30, 31-40, 41-50, and 51-60 age groups were 6.58 ml, 7.45 ml, 7.03 ml, and 6.71 ml respectively (Table 2). The total thyroid volume gradually increased till the 31-40 age group and then it decreased. However, the difference in TGV among the age groups was not statistically significant (P > 0.05). Figure 4 shows the variation of thyroid volume in different age groups.

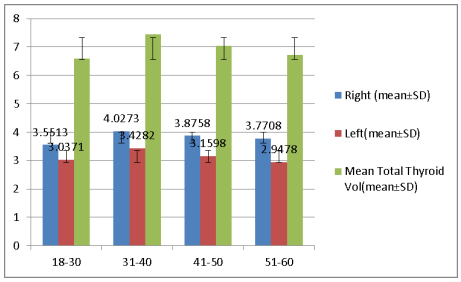

Figure 4. Variation of thyroid volume in different age groups

Table 2. Variation of total thyroid volume in different age groups

Age group	Right lobe vol (Mean±SD)	Left lobe vol(Mean±SD)	Total vol(Mean±SD)
18-30	3.5513±.95055	3.0371±.87908	6.5884±1.74789
31-40	4.0273±1.03557	3.4282±.92279	7.4555±1.84448
41-50	3.8758±.91312	3.1598±.89703	7.0356±1.66566
51-60	3.7708±.85007	2.9478±.77942	6.7186±1.43008

The mean right lobe volume was 3.76 ± 0.96 ml, while that for the left lobe was 3.14 ± 0.89 ml. The right lobe had a significantly higher volume than the left (p < 0.001). Furthermore, the mean right lobe volume in males and females was also found to be greater than their corresponding left lobe volumes.

The total mean thyroid volume for males was 7.30 ± 1.86 ml (range 2.87-15.66 ml). Among male patients, the highest mean total volume of 7.98 ± 2.22 ml was seen in the 31-40 age group, while the lowest mean volume of 6.73 ± 1.55 ml was seen in the 51-60 age group. The mean total gland volume in the 18-30, 31-40, 41-50, and 51-60 age groups of the male population were 7.33 ml, 7.98 ml, 6.86 ml, and 6.73 ml respectively. The total thyroid volume in the male population first increased until the 31-40 age group, then decreased as the age advanced further. However, this association was not statistically significant (p > 0.05). The variation of thyroid volume in male population is given in Figure 5 and Table 3.

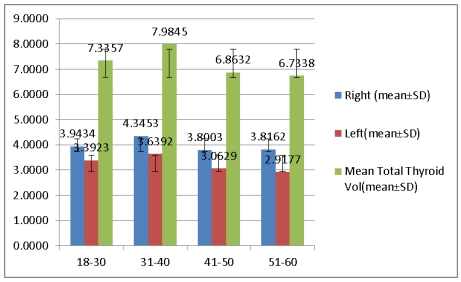

Figure 5. Variation of thyroid volume in male population

Table 3. Variation of thyroid volume in male population

Age Group	Right lobe vol(mean±SD)	Left lobe vol(Mean±SD)	Total thyroid Vol(Mean±SD)
18-30	3.9434±.94197	3.3923±.91566	7.3357±1.75844
31-40	4.3453±1.18676	3.6392±1.14775	7.9845±2.22149
41-50	3.8003±.86852	3.0629±.93591	6.8632±1.66125
51-60	3.8162±.86413	2.9177±.77332	6.7338±1.55885
Overall	3.98±.99	3.32±.98	7.30±1.86

The total mean thyroid volume for females was 6.63 ± 1.61 ml (range 2.44-13.76 ml). Among female patients, the highest mean total volume of 7.15 ± 1.67 ml was seen in the 41-50 age group, while the lowest mean volume of 6.03 ± 1.52 ml was seen in the 18-30 age group. The mean total gland volume in the 18-30, 31-40, 41-50, and 51-60 age groups of the female population were 6.03 ml, 7.13 ml, 7.15 ml, and 6.70 ml respectively (Table 4). The total volume showed an increasing trend until the 41-50 age group, and after that, it decreased. However, this increase in volume with age was not statistically significant ($p > 0.05$). The variation of thyroid volume in female population is presented in Figure 6 and Table 4.

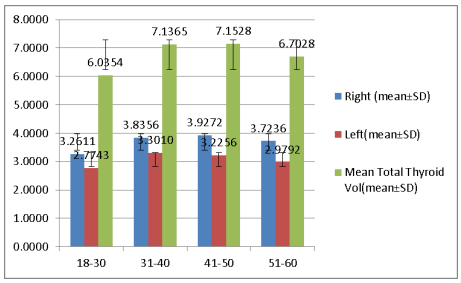

Figure 6. Variation of thyroid volume in female population

Table 4. Variation of thyroid volume in female population

Age group	Right (Mean±SD)	Left(Mean±SD)	Mean total thyroid vol (Mean±SD)
18-30	3.2611± .85128	2.7743±.75373	6.0354±1.52722
31-40	3.8356±.88874	3.3010±.73726	7.1365±1.50575
41-50	3.9272±.94745	3.2256±.87302	7.1528±1.67520
51-60	3.7236±.85033	2.9792±.80041	6.7028±1.31489
overall	3.60±.92	3.03±..81	6.63±.1.61

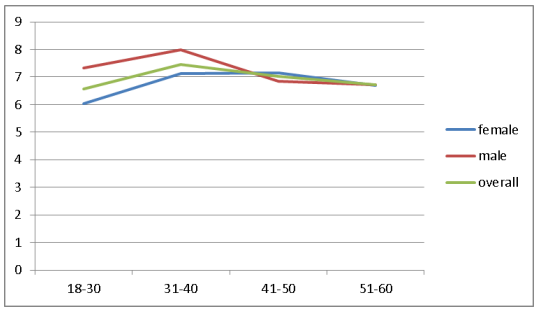

Figure 7. Variation of total volume in overall, male and female populations

The mean T3 level, T4 level, and TSH level in our study came out to be 1.09 ng/ml, 8.25 mcg/dl, and 2.63 uIU/ml respectively. No significant variation of hormone levels with age was noted. Variation of total volume in overall, male and female populations is shown in Figure 7 and mean thyroid hormone levels in male and female populations is given in Table 5. The comparison of thyroid volume studies in different countries is given in Table 6.

Table 5. Mean thyroid hormone levels in male and female populations

	Mean T3 level(in ng/ml)	**Mean T4 level(in mcg/dl)**	**Mean TSH level(in uIU/ml)**
Males	1.07 ±0.21	7.95 ±1.52	2.60 ±0.77
Females	1.11 ±0.23	8.47 ±1.63	2.66 ±0.84
Overall	1.09 ±0.22	8.25 ±1.57	2.63 ±0.76

Table 6. Comparison of thyroid volume studies in different countries

Author	**Number of subjects**	**Age range(in years)**	**Mean thyroid vol in ml ± SD**	**Country**
Current Study	410	18-60	6.90 ± 1.74	Central India
Guo et al. [5]	1991	29-52	9.0	China
Salaam et al. [6]	400	>18	6.03±2.49	Nigeria
Morna et al. [7]	320	18-95	6.8±2.5	Ghana
Sahin et al. [8]	461	18-61	12.98±2.53	Turkey
Turcios et al. [9]	100	17-60	6.6±0.3	Cuba
Kamran et al. [10]	421	21-82	6.26±2.89	Pakistan
Kayastha et al. [11]	485	1-83	6.62±2.50	Nepal
Gomez et al. [12]	268	15-70	8.22±3.92	Spain

4. Discussion

The total mean thyroid volume in our study was 6.90 $\pm$ 1.74 ml. The mean thyroid volume in our study was comparable to the studies done in other Southeast Asian and African countries. It came out to be less compared to the European, Mediterranean, and Chinese population. It is proposed that thyroid volume differs with geographical locations due to differences in iodine availability, smoking habits, alcohol consumption, and the presence of goitrogens in the diet [13].

The study has also reported that the mean total gland volume (TGV) was significantly greater in males (7.30 $\pm$ 1.86 ml) when compared to females (6.63 $\pm$ 1.61 ml) ($p < 0.001$). This was in concordance with the studies conducted by Guo et al. [5], Memon et al. [14], Alazigha et al. [15], Sahin et al. [8], Nafisi et al. [16], Seker et al. [17], Adibi et al. [18], and Gomez et al. [12].

Many explanations have been given for the difference in TGV between the two genders. Nafisi et al. [16] and Hegedus et al. [19] suggested that the difference in body weight between males and females was the reason for this difference in TGV. Abidi et al. [18] and Berghout et al. [20] proposed that the difference in lean body mass between the two genders could be an answer for the increased TGV in males. Salaam et al. [6] proposed that this may be due to the fact that males have an increased body mass index compared to females of the same age. Some researchers also suggested that the larger size of anatomical structures in males can also be an answer for the increased TGV in males. However, these results were contrary to the studies done by Morna et al. [7] in Ghana, Turcios et al. [9] in Cuba, and Kayastha et al. [11] in Nepal, who all reported that the difference in mean TGV between males and females was insignificant ($p > 0.05$).

The mean right lobe volume (3.76 $\pm$ 0.96 ml) of the thyroid was significantly greater than that of the left lobe volume (3.14 $\pm$ 0.89 ml) ($p < 0.001$). Furthermore, the mean right lobe volume in males and females was also found to be greater than their corresponding left lobe volumes. This was in accordance with the studies conducted by Salaam et al. [6], Memon et al. [14], Alazigha et al. [15], Sahin et al. [8], Kamran et al. [10], and Seker et al. [17]. The asymmetry between the two lobes of the thyroid gland is probably due to the presence of adjacent structures. The esophagus is normally deviated towards the left side of the midline. It is suggested that the deviation of the esophagus gives more space to the right lobe of the thyroid to grow, resulting in a larger volume of the right lobe.

The total gland volume first increased and then decreased with age. The mean total gland volume in the 18-30, 31-40, 41-50, and 51-60 age groups is 6.58 ml, 7.45 ml, 7.03 ml, and 6.71 ml respectively. However, the difference in total gland volume among the age groups was not significant ($p > 0.05$). Hence, in our study, no statistically significant association was observed between thyroid volume and age. This was in accordance with the studies conducted by Nafisi et al. [16], Salaam et al. [6], Morna et al. [7], and Turcios et al. [9], who also reported no significant association between thyroid volume and age ($p > 0.05$). This was contradictory

to the studies of Kamran et al. [10], Seker et al. [17], and Kayastha et al. [11], who all stated a significant association between thyroid volume and age.

The total thyroid volume in the male population first increased until the 31-40 age group and then decreased as the age advanced further. Similarly, the total gland volume in the female population increases until the 41-50 age group and then decreases in the 51-60 decade. However, the difference in total gland volume among both male and female age groups was not statistically significant ($p > 0.05$). Similar findings were also reported in the studies of Lamichhane et al. [21] in Nepal and Guo et al. [5] in China. Guo et al. stated that the trend of thyroid volume increasing with age was observed in men under 40 years and women under the age of 52 years.

The mean T3 level, T4 level, and TSH level in our study came out to be 1.09 ng/ml, 8.25 mcg/dl, and 2.63 uIU/ml, respectively. No significant variation of hormone levels with age was noted. The mean T3 level was almost the same in both genders (1.07 ng/ml in males vs. 1.11 ng/ml in females). The mean T4 level was slightly higher in females (8.47 mcg/dl) than males (7.95 mcg/dl), while the mean TSH level was almost the same in both genders.

Spearman's rank correlation coefficient and Pearson's R coefficient were applied to look for any association between thyroid volume and thyroid hormone levels in the body, and no significant correlation was found between the two variables. This was in concordance with Adibi et al. [18], who also did not find any correlation between thyroid volume and serum TSH levels in their study.

The thyroid volume ranges were 2.44-15.66 ml, 2.87-15.66 ml, and 2.44-13.76 ml in all, males, and females, respectively. Goiter by ultrasound is defined as glands with a volume more than the 97th percentile of the normal population. The 97th percentile volume is calculated by applying the formula Mean + 2.17 SD. The 97th percentile of thyroid volume in our study came out to be 10.67 ml. Hence, any person having a total thyroid volume above 10.67 ml can be sonographically diagnosed with goiter in our population. Similarly, the volume cut-off to consider goiter in males and females was 11.33 ml and 10.12 ml, respectively. These cut-off values are somewhat similar to the values provided by Adibi et al. [18] in Iran. They conducted a study on 200 adults with a mean age of 37.27 years in Isfahan, Iran and concluded that volumes more than 10.14 ml, 11.48 ml, and 8.37 ml in all, males, and females, respectively, should be considered goiter sonographically.

5. Conclusion

A normogram of thyroid volume in our environment is important to serve as a reference point in managing patients with thyroid pathologies, especially goiter. To our knowledge, this is the first reference of thyroid volume measured by ultrasonography in the central parts of India. These values are recommended as reference values for use in our region. According to this data, we tried to contribute to the establishment of the reference values in our country. As the thyroid volume is associated with anthropometric measurements, genetic and environmental factors, we recommend further studies on a national scale to establish standard national reference values of normal thyroid volume in India.

Author Contributions: All authors contributed equally to the writing of this paper. All authors read and approved the final manuscript.

Conflicts of Interest: The authors declare that they do not have any conflict of interests.

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