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Original Article

Normal values of thyroid gland in Isfahan, an iodine replete area

Atoosa Adibi, Mehri Sirous*, Ashraf Aminorroaya**,*
*Ehsan Roohi***, Mohsen Mostafavi***, Zahra Fallah****,*
*Azamossadat Tabatabaei****, Massoud Amini***

Abstract

BACKGROUND: Because of different values of thyroid volume in different populations, and the effects of different trace element and geographic substances on thyroid volume, we decided to evaluate thyroid volume and its determinants using ultrasound in healthy adults of Isfahan, a centrally located city in Iran, an iodine replete area.

METHODS: In a cross-sectional study, 1500 healthy adults were enrolled by cluster sampling. Serum TSH level and morning urine iodine level were measured. Thyroid exam was performed according to WHO criteria and history of previous or present thyroid disease was taken. If all the mentioned results were normal they were considered clinically normal. One third of these normal subjects referred for thyroid ultrasonography. If ultrasonography of thyroid parenchyma texture was normal, and there was no nodule by sonography (thyroid incidentaloma), thyroid volume was measured using ellipsoid formula ($X \times Y \times Z \times \pi/6$). Correlation between thyroid volume and age, sex, BMI, TSH level and urinary iodine concentration (UIC) was determined by Pearson correlation coefficient, t-Test and Kolmogorov-Smirnov. Thyroid volume more than 97% of this population was considered as goiter sonographically. Data expressed as mean ± SD, unless otherwise stated.

RESULTS: We finally studied 200 subjects (123 Males, 77 females, average age: 37.27 ± 11.80 Years). The overall thyroid volume was 9.53 ± 3.68 ml. Males thyroid volume (10.73 ± 3.44 ml) was significantly higher than the females one (7.71 ± 2.63 ml) ($P<0.001$). The thyroid volume ranges were 3-23.9 ml, 3.6-23.9 ml and 3-14.3 ml in all, males and females, respectively. Thyroid volume values more than 97 percentile of this reference range were 10.14 ml, 11.48 ml and 8.37 ml in all, males and females respectively, and were considered goiter sonographically. Thyroid volume had a positive correlation with age ($r = 0.163$, $P = 0.022$), but did not have correlation with serum TSH, UIC, and BMI, in both sexes. There was a strong correlation between thyroid volume, and height and body surface area ($r = 0.48$, $P<0.001$).

CONCLUSIONS: It was documented that thyroid volume is higher in male sex and increases with age, and have a positive correlation with body surface area and height.

KEY WORDS: Adult, thyroid, ultrasonography, volume.

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Ultrasound has become one of the primary imaging modalities for the assessment of the thyroid gland [1]. In areas without significant iodine deficiency disorders, where the prevalence of visible goiter is low, the sensitivity and specificity of palpation are poor and goiter prevalence can be estimated using thyroid ultrasound. [2,3] This is the most useful method for measurement of thyroid volume (TV) and can also be used to dis

*Assistant Professor, Department of Radiology, Medical School, Isfahan University of Medical Sciences, Isfahan, Iran.
**Professor of Endocrinology, Isfahan Endocrine & Metabolic Research center Isfahan University of Medical Sciences, Isfahan, Iran.
***Resident of Radiology, Department of Radiology, Isfahan University of Medical Sciences, Isfahan, Iran.
****General Practitioner, Isfahan Endocrine & Metabolic Research Center, Isfahan University of Medical Sciences, Isfahan, Iran.
Correspondence to: Dr Atoosa Adibi, Department of Radiology, Alzahra Hospital, Isfahan, Iran. e-mail: a_adibi@med.mui.ac.ir

criminate between cystic and solid lesions of gland synchronously [4-7]. Several factors are known to be involved in the regulations of TV and different reports of TV normal range are presented from different populations [8]. Mean TV was reported 8.55 cc (± 1.82) from Nigeria and they confirmed that their values are lower than other studies among Caucasians [1]. Another study from an iodine-replete individuals of Spain reported the median TV of 9.91 ml (CI: 9.09-10.05 ml) for males and 6.19 ml (CI: 6.02-6.92 ml) for females with significant difference between sexes [8]. A report from France while being a borderline iodine deficient area, calculated mean TV of 13.3 and 8.9 ml in males and females, respectively [8]. The median TV was reported lower significantly in a mild iodine deficiency area than in a moderate iodine deficiency area (11.9 ml vs. 13.6 ml, P<0.001) of Denmark [9]. It is suggested the need for population-specific references, for thyroid volumes and it's determinants in each area [7]. The aim of this study was to set normal values of TV in healthy adults of Isfahan and determine the criteria for goiter, sonographically.

Methods

We randomly selected 1500 adult people (age>20 years) in a cross-sectional study in Isfahan, a centrally located city in Iran, which is an iodine replete area, in 2006. [10] By a clustered random sampling method, 300 cases were selected from each of the five geographic areas of the city. Demographic data collection was performed and serum TSH level and urinary iodine concentration (UIC) were measured in each case. History of any present or previous thyroid disease was asked. Thyroid exam was performed by one expert examiner to rule out clinical goiter or thyroid nodule and considered normal clinically if the gland was neither palpable, nor visible [11]. If all the mentioned results were normal, they were considered clinically normal. One-third of these normal subjects referred for thyroid ultrasonography sequentially, which were totally 394 cases. 268 people accepted to be studied by sonography (68% acceptance). All ultrasounds were performed by one of the two radiologists using the same technical method. If ultrasonography of thyroid parenchymal texture was normal, and there was no nodule by sonography (thyroid incidentaloma), thyroid volume was measured using three dimensional ellipsoid formula ($X \times Y \times Z \times \pi/6$). TV values more than 97 percentile of this population was considered as goiter sonographically. Body mass index (BMI) (kg/m^2) was calculated for each subject, using Secca scale to measure height (HT) and weight (WT). Body surface area (BSA) was calculated from HT and WT according to the Du Bois formula [9].

Laboratory methods

Serum TSH was measured by IRMA method by Berthoud LB2111 unit Gamma counter equipment with its normal range of 0.3-4 mIu/L. Urinary iodine level was determined by the spectrophotometric method (405 wavelengths) from 5 ml fresh urine [12]. Values which were more than 10 µg/dl considered as sufficient iodine uptake.

Ultrasonography

Thyroid ultrasonography was performed with HS-2000 Honda ultrasound equipment with 7.5 MHZ linear probe. Cases were examined in a supine position with hyperextended neck by one of the two radiologists. Transverse (X), saggital (Y) and anteroposterior (Z) lengths of right and left lobes were measured and volumes calculated by three-dimensional ellipsoid formula ($V=\pi/6 \times X \times Y \times Z$) and expressed in ml [13]. The sum of both lobes volume was considered as TV. The isthmus was not taken into account in volume calculation.

Statistical Analysis

Data was entered to SPSS version 11. Student t-test was used for comparing means and ANOVA test was used to compare TV between age groups. The Kolmogorov- Smirnov test was applied to check normality of data. Correlation between thyroid volume and age, sex, BMI, BSA, TSH level and urinary iodine excretion was determined by Pearson correlation coefficient. Data expressed as mean ± SD, unless otherwise stated. All differences and

relationships were statistically significant at P<0.05. The study was approved by the ethics committee of Isfahan Endocrine and Metabolic Research Center and Isfahan University of Medical Sciences.

Results

Of 268 cases sequentially came for thyroid ultrasound, thyroid nodule and parenchymal heterogeneity were detected in 68 subjects. Sixty (23%) people had thyroid nodule and 8 (3%) cases had parenchymal abnormality in sonography and were excluded from the study. We finally studied 200 subjects representative of healthy population, according to history, palpation, ultrasonography and serum TSH level and UIC data (123 males, 77 females, average age: 37.27 ± 11.80 years). The overall TV was 9.53 ± 3.68 ml (range: 3-23.90 ml). Mean TV was 10.73 ± 3.44 ml (range: 3.60-23.90 ml) in males and 7.71 ± 2.63 ml (range: 3-14.30 ml) in females (P<0.001). There was statistically significant positive correlation between TV and age (r = 0.163, P = 0.022). Median UIC was 22 µg/dl (range: 10-42 µg/dl) and there was no correlation between TV and UIC (P = 0.352). The mean serum TSH level was 1.90 ± 0.30 mIU/L with no significant correlation between TV and TSH level (P = 0.367). In our cases, the average BMI was 25.16 ± 4.53 kg/m^2 and there was no significant correlation between TV and BMI (P = 0.112), but there was significant correlation between TV and subject's heights and BSA (r = 0.48, P<0.001 in both). There was neither significant correlation between age and serum TSH level nor between age and UIC (P = 0.929 and P = 0.078, respectively). Table 1 shows the participants demographic data, TSH level, UIC and TV in all cases, males and females. Figure 1, 2 and 3 show percentiles of TV in normal participants: all, males and females, separately. In this reference range, TV more than 97 percentiles were 10.14 ml, 11.48 ml and 8.37 ml in all, males and females, respectively, and were considered goiter sonographically.

Table 1. Demographic data, TV, TSH level and UIC in all normal participants, males and females.

	age# [years]	BMI# [kg/m2]	TV# [ml]	TSH# [mIU/L]	UIC* [µg/dl]
ALL	37.27 (11.80)	25.16 (4.53)	9.53 (3.68)	1.90 (0.30)	22.00
MALES	38.84 (11.47)	25.27 (4.48)	10.7 (3.44)	1.72 (0.78)	22.00
FEMALES	34.72 (12.21)	24.97 (4.65)	7.71 (2.63)	1.94 (0.80)	22.30

Data are presented as mean (SD). * Data are presented as median.

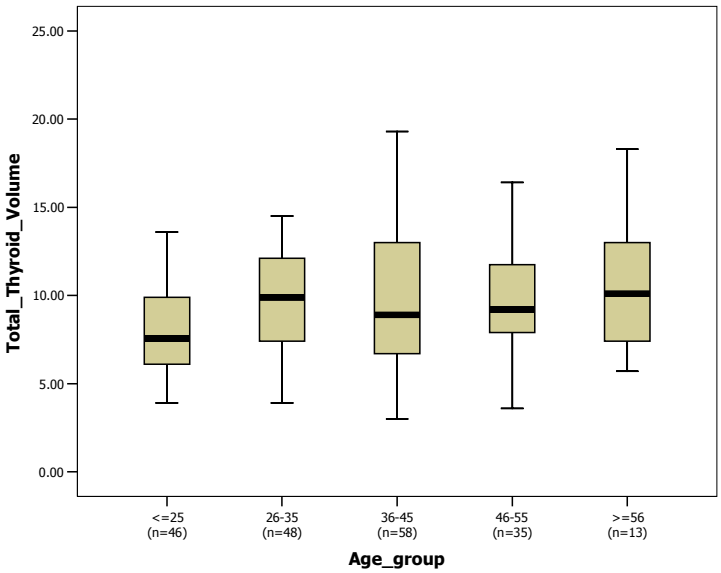

Figure 1. Thyroid volume in different decades in all normal participants.
*The mean TV differences were significant between the first and all other groups only (P<0.05).

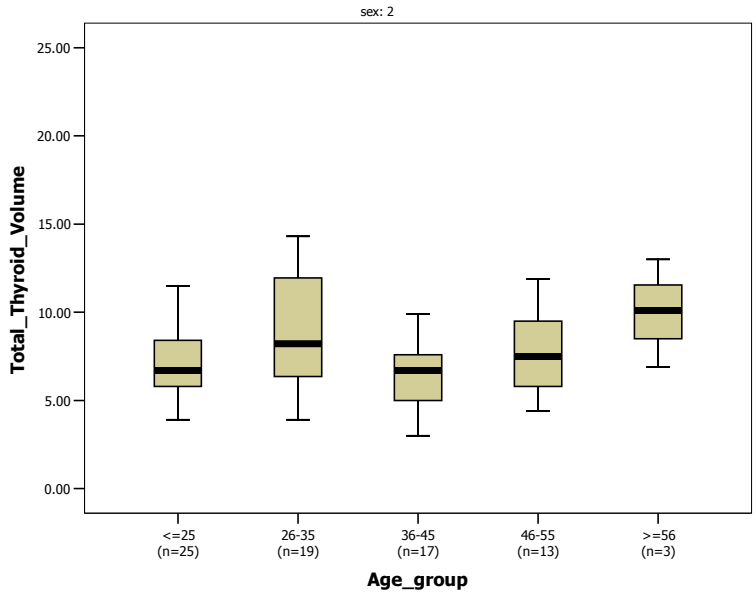

Figure 2. Thyroid volume in different decades in normal female participants.
*There was significant difference between mean TVs of the first (<25 years) and the second (26-35 years) groups (P = 0.03) and also between mean TVs of the second and the third (36-45 years) groups (P = 0.026).

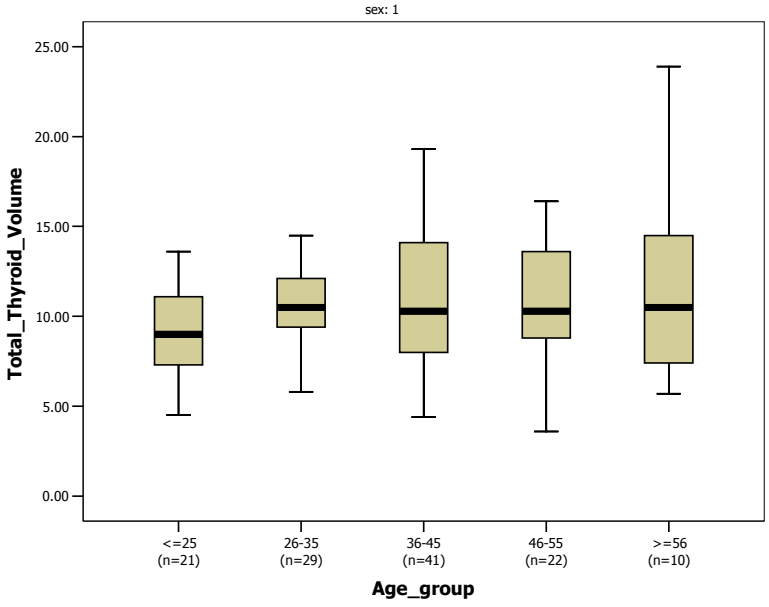

Figure 3. Thyroid volume in different decades in normal male participants.
*There was not any significant difference among mean TVs of different groups.

Discussion

This study presents the normal values of adult thyroid volumes in Isfahan region. Our measured mean TV was in agreement with reported values of Gomez et al [8], Tahir et al [14], and Berghout et al [15]. TV was correlated well with height in this study as was reported previously [8]. The Chinese TV studied by Hsiao and Chang was 7.7 ± 3.3 ml, which is slightly lower than ours and could be explained by the short

height of the Chinese population [16]. The total TV in our study was obviously less than that in Hegedus et al study [17], which was conducted in Copenhagen with reported volumes found 19.6 ml and 17.5 ml in males and females, respectively. It could be speculated that the Danish subjects were in fact iodine deficient to some degree [11]. Genetic background and environmental factors could contribute to the variations of the results in these different geographic areas [17]. We observed larger mean TV in males than in females, which is supported by other studies. Because structural anatomy is larger in male than that in female irrespective of BMI, this difference would be expectable [5,8,16,17]. Significant correlation was found between mean TV and age, which was reported by others too [15,17]. This was explained previously by a tendency towards higher serum TSH levels in advanced age or lower iodine intake in higher age groups [8,17]. But, we did not find any significant rise in TSH or drop in UIC with increasing age. Our selected group had normal TSH and UIC ranges, so this finding was expected because in previous reported studies all clinically normal subjects were enrolled irrespective of lab findings. Though some other data are against this finding [8,11,15]. This can be explained by decrease of lean body mass that is the active metabolic mass of body in elderly people [16]. We did not find any relationship between TV and UIC. Studies conducted in iodine sufficient countries do not support any association too [15]. But, those conducted in iodine deficient areas, differ significantly [11]. Because we selected subjects with adequate UIC, the results were expectable. The same is true for absence of relationship between TV and serum TSH level in this study. Previous controversies about this role are present suggesting that a wide variety of environmental agents may stimulate thyroid growth [15,17]. We observed absence of correlation between mean TV and BMI. In some studies TV had correlation with weight and height and also weakly with BMI or only with weight [11,15]. We suggest evaluating TV with lean body mass, which is the metabolic part of body to find any real relation. BSA showed the best correlation with TV previously, and we found a strong correlation too [17]. In conclusion, the clinical estimate of TV is prone to error. Therefore, it is necessary to know the regional reference values of thyroid volume in disease-free populations and its determinants. Mean TV of Isfahan was 9.53 ± 3.68 ml, which was significantly correlated with age and male sex. TV more than 97 percentiles were 10.14 ml, 11.48 ml and 8.37 ml in all, males and females, respectively, and were considered as goiter criteria, sonographically.

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