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ORIGINAL ARTICLE

Normative Values for Thyroid Volume and Tracheal Index in Healthy Turkish Newborns in an Iodine Sufficient Region

TUZCU G et al. Normative Values of Thyroid Gland Dimensions in Newborns

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What is already known on this topic?
- Each community must determine its own normative values for accurate assessment of neonatal thyroid dimensions.
- In previous studies, local neonatal thyroid volume normative values for various regions of our country were given, but there is no data on tracheal index.

What this study adds?
- Normative thyroid volume and tracheal index data of healthy newborns of our city, where an iodine-sufficient society lives, are presented.
- A handheld US device can be used to calculate the neonatal tracheal index.

Abstract
Objective: The study aims to determine the normal values of thyroid volume and tracheal index in healthy term newborns born in an iodine-sufficient population. Additionally, we investigated the usability of a handheld device for assessing the tracheal index.
Methods: Thyroid imaging was performed at 0-2 days and 15-30 days using handheld and portable ultrasound devices. Thyroid volume and tracheal index were calculated using standard formulas.
Results: A total of 144 healthy term newborns with a mean birth weight 3230 g were enrolled. The normal thyroid volume for the entire population was 0.66 ± 0.25 ml at 0-2 days, which significantly increased to 1.12 ± 0.33 ml at 15-30 days ($p<0.01$). There were no significant differences in thyroid volume between genders in either age group ($p=0.246$ and $p=0.879$). Thyroid volume correlated with birth weight, length, and head circumference, with the strongest correlation being with birth weight ($r=0.404$, $p<0.001$; $r=0.252$, $p=0.002$; $r=0.223$, $p=0.007$, respectively). The tracheal index at 0-2 days was 1.84±0.30 in girls, 1.82±0.27 in boys, and 1.83±0.29 overall. At 15-30 days, it was 1.99±0.23 in girls, 2.00±0.28 in boys, and 1.99±0.25 overall. Similar to thyroid volume, the tracheal index increased with age ($p<0.01$), with no significant gender differences in either age group ($p=0.593$ and $p=0.886$). Thyroid volume and tracheal index were moderately correlated in both measurements ($rho=0.538$, $p<0.01$). Measurements of the trachea, and thyroid lobe widths using portable and handheld ultrasound devices were correlated ($r=0.449$, $p<0.01$; $r=0.638$, $p<0.01$; $r=0.497$, $p<0.01$). There was also a correlation between tracheal index measurements using both devices in both the first and second measurements.
Conclusion: This study provides normative data on thyroid volumes and tracheal index in newborns from an iodine-sufficient population. The tracheal index can estimate thyroid size when volume calculation is not feasible and handheld ultrasound devices are effective for this assessment.
Keywords: Newborn thyroid volume, tracheal index, handheld ultrasonography

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Introduction

Congenital hypothyroidism (CH) is the most common endocrine disorder in the neonatal period, occurring in approximately 1:2000 - 1:3000 live births. The majority (85%) of cases are due to thyroid dysgenesis (aplasia, hypoplasia or ectopy) (1). The gold standard method for evaluating the thyroid gland is ultrasonography (US), which provides critical information on the structure, anatomical location, and size of the thyroid gland, thereby aiding in the etiological assessment of CH (2).

US evaluation of the thyroid gland, when conducted by a trained sonographer, offers detailed information rapidly without the risks associated with radiation or contrast agents. Moreover, its widespread use and easy accessibility present additional advantages(3).

The size of the thyroid gland in the neonatal period is influenced by factors such as gestational age, ethnic background, and iodine status. Consequently, it is recommended that each community establish its own normative values for accurate evaluation (4).

During thyroid US imaging, the US probe should be placed in the transverse plane, and the entire embryological path of the thyroid should be scanned from the base of the tongue to the mediastinum (5). The conventional method for assessing thyroid size involves calculating thyroid volume by measuring the width, length, and height of the gland (3, 6). However, in newborns with short necks and increased adiposity, accurately assessing the anatomical features and measurements of the thyroid gland can be challenging (7). Furthermore, in the absence of a dedicated probe for measuring the thyroid's longitudinal axis, a three-dimensional evaluation of the gland becomes impractical. In such cases, a simpler method known as the tracheal index can be used. The tracheal index is calculated by the ratio of the sum of the widths of both thyroid lobes to the width of the trachea (8).

This study aimed to determine the normal values of thyroid volumes and tracheal index in healthy newborns born in Aydın, a region with sufficient iodine levels (9). Additionally, the study evaluated the feasibility of using a handheld ultrasound device to assess thyroid size in newborns, a method has gained significant interest in recent years and has been found effective in assessing thyroid tissue in older children (10).

Materials and Methods

This prospective cohort study included healthy term newborns aged 0-2 days, born between January 1, 2023, and December 31, 2023, at Aydın Adnan Menderes University and Aydın Maternity and Children's Hospital, Türkiye. Exclusion criteria included congenital anomalies, low birth weight (<2500 grams), prematurity (<37 weeks), multiple pregnancies, refugees, and newborns of mothers with thyroid disease or other chronic conditions (such as diabetes mellitus, and hypertension). Thyroid imaging was performed on newborns aged 0-2 days, with follow-up assessments conducted when they were 15-30 days old.

Thyroid US imaging was conducted using a portable US device (Samsung HM70 EVO - POCUS) by an experienced radiologist, and a handheld US device (Sonostar C5PL) by a pediatric endocrinologist. The endocrinologist performing measurements with the handheld ultrasound device had previously received training in device usage and thyroid ultrasound imaging, with three years of experience, and was conducting these procedures as part of clinical practice (10). Two researchers, using both the handheld and portable ultrasound devices, performed independent, blinded measurements. Necessary adjustments were made in each case to ensure optimal image clarity during the measurements with the handheld ultrasound device.

Subjects were positioned in supine with their necks extended. Measurements of each thyroid lobe, including the longitudinal length, were obtained in three planes using a portable US device. Thyroid volume for each lobe was calculated using the following formula: [anterior-posterior (AP) x medio-lateral (ML) x longitudinal] x $\pi/6$ (5), and expressed in milliliters.

The tracheal index is calculated as the ratio of the sum of the maximum widths of the right and left lobes in the mediolateral line on a transverse section of the thyroid gland to the tracheal width at the level of the thyroid.

Tracheal Index = (Right Lobe Width + Left Lobe Width) / Tracheal Width

Since the measurement method in trachea index is mediolateral line, the difference in measurement during inspiration and expiration is not significant. (Figure 1) (8).

The longitudinal measurements required to calculate thyroid volume could not be performed using the handheld ultrasound device, due to the probe length being unsuitable for the anatomy of the newborn's neck. Therefore, measurements from the handheld ultrasound device were used only for calculating the tracheal index, as volume data could not be provided. To assess the reliability of the handheld ultrasound device, the tracheal index data were compared between the results obtained from the two devices.

Statement of Ethics: All procedures involving human participants in this study were conducted in accordance with the ethical standards of the institutional and/or national research committee, as well as the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the non-interventional ethics committee of Aydın Adnan Menderes University (Ethics no: 2022/213). Informed consent was obtained from all participants.

Statistical Analysis

Statistical analysis was performed using the Statistical Package for Social Science (SPSS) version 21 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.). Descriptive statistics were presented as mean and standard deviation for normally distributed data, and as median, minimum, and maximum values for non-normally distributed data. The normality of continuous variables was assessed using descriptive statistics, skewness and kurtosis coefficients, histogram, and the Shapiro-Wilk test. The chi-square test was used for categorical data. For comparing two independent groups, the t-test was used for normally distributed data, and the Mann-Whitney U test for non-normally distributed data. For variance analysis, ANOVA was used for normally distributed data (with Tukey post hoc test if variances were homogeneous and Tamhane's T2 test if variances were not homogeneous); otherwise, the Kruskal-Wallis H test was used (with Dunn's test for post hoc analysis). Bland-Altman analysis was used to assess the consistency of measurement data. Pearson's correlation was used for normally distributed data, and Spearman's correlation was used for non-normally distributed data. The Type I error level was set at 0.05.

Results

The study included 144 healthy term newborns, of whom 49.3% were female. The gestational age of the subjects were 38.8 ± 1.30 weeks, birth weight was 3230 ± 426 grams, and the birth length was 48.5 ± 2.13 cm. All subjects had capillary TSH levels within the normal range (< 5.5 mU/L).

On days 0-2, the thyroid volume was 0.64 ± 0.26 ml in girls and 0.68 ± 0.23 ml in boys (p>0.05). The mean thyroid volume for the entire population was 0.66 ± 0.25 ml. Between days 15-30, the thyroid volume was 1.12 ± 0.33 ml in girls, 1.13 ± 0.33 ml in boys, and 1.12 ± 0.33 ml for the entire population. Thyroid volume significantly increased in the second measurement as the infants grew (p<0.01) (Table 1). No significant differences in thyroid volume were found between genders in both age groups (p=0.246 and p=0.879, respectively).

There was a correlation between thyroid volume and birth weight, length, and head circumference, with the strongest correlation being with birth weight (r=0.404, p<0.001; r=0.252, p=0.002; r=0.223, p=0.007, respectively) (Figure 2). Thyroid volumes according to birth weight standard deviation (SD) are presented in Table 2.

On days 0-2, the tracheal index was 1.84±0.30 (1.85) in girls, 1.82±0.27 (1.82) in boys, and 1.83±0.29 (1.82) in the entire population. Between days 15-30, it was 1.99±0.23 (1.99) in girls, 2.00±0.28 (1.90) in boys, and 1.99±0.25 (1.94) in the entire population. Similar to thyroid volume measurements, the tracheal index increased with age (p<0.01), but no significant differences were found between genders in either age group (p=0.593 and p=0.886, respectively) (Table 3).

Thyroid volume and tracheal index were moderately correlated in both the first and second measurements (rho=0.538, p<0.01) (Figure 3). Measurements of the trachea and the right and left thyroid lobe widths using both portable and handheld ultrasound devices were correlated (r=0.449, p<0.01; r=0.638, p<0.01; r=0.497, p<0.01, respectively). In both the first and second measurements, there was a correlation between tracheal index measurements using both portable and handheld ultrasound devices (Table 4).

Discussion

This study, which aimed to determine the normal thyroid volume values and tracheal index in healthy term newborns in an iodine-sufficient region (9), as well as to evaluate the feasibility of handheld ultrasound devices for these measurements. It provides essential normative data for thyroid volume and tracheal index, stratified by gender and by early and late neonatal periods.

Thyroid volume

Numerous studies from various regions of Turkiye and around the world have investigated thyroid volume. These studies have demonstrated that thyroid size varies based on ethnic background, geographical features, dietary habits, and particularly iodine status. Consequently, it is recommended to use community-specific normative data when assessing thyroid size (4).

In Turkiye, studies conducted in Bursa and Kayseri in 2008, and in Trabzon in 2012, reported larger thyroid sizes in newborns compared to our findings (11-13). This discrepancy may be attributed to the long-standing iodine sufficiency in our region, supported by the national iodized salt program initiated in 1998.

When compared with data from regions with mild to moderate iodine deficiency around the world, the thyroid volumes in our study were found to be lower (5, 14, 15). While we attribute this to residing in an iodine-sufficient community, we also recognize the potential influence of other confounding factors. In our study, thyroid volumes were observed to increase over time, from the initial measurements to those taken on days 15-30. This increase in thyroid volume aligns with the expected growth patterns in newborns. Additionally, no significant differences were observed between genders in either age group, which is consistent with existing literature (5, 14, 16).

When examining the relationship between thyroid volume and birth weight, length, and head circumference, the strongest correlation was with birth weight, although thyroid volume was correlated with all parameters. When assessing thyroid volume according to birth weight, it was observed that thyroid volume increased with each increase in weight SD in both genders. The only exception was seen in boys between +1 and +2 SD; however, the small sample size of this group precludes a definitive assessment. While the correlation between thyroid volume and auxological parameters is well-documented (16), larger-scale studies with a homogenous weight distribution are needed to recommend assessing thyroid size based on birth weight.

Tracheal index

Measuring the long axis of the thyroid gland in neonates is technically challenging, which has led to the idea of evaluating thyroid size based solely on transverse plane imaging, a concept that has been considered for several years. While various techniques have been attempted, the calculation of the tracheal index, first introduced by Yasumoto et al., has gained wider acceptance (8). However, it is ideal to have normative data for tracheal index, similar to thyroid volume, that is specific to each population. In this study, we aimed to determine the tracheal index norms for newborns in Aydın, an iodine-sufficient region.

The study found that the tracheal index increased with age, similar to thyroid volume, and did not differ between genders. Additionally, both thyroid volume and tracheal index showed a moderate correlation in both the first and second measurements (rho = 0.538, $p < 0.01$). A study conducted in an iodine-sufficient population in Brazil, found a weak correlation between thyroid volume and tracheal index (14). We believe that our study supports this relationship and demonstrates the applicability of the tracheal index in neonates, where three-dimensional measurements are challenging.

In the literature, cases with a tracheal index below 1.7 and low uptake in scintigraphy have been considered as thyroid hypoplasia (17). In this study, we propose that in our region, newborns with a tracheal index below 1.49 could be evaluated as having thyroid hypoplasia. However, larger series of studies are required to establish definitive thresholds.

Additionally, measurements made using portable and hand-held ultrasound devices demonstrated a correlation between the tracheal index and the widths of both the right and left thyroid lobes. The bedside handheld US device can be utilized in routine evaluations by trained clinicians due to its easy accessibility and practicality in assessing thyroid size.

Study Limitations

In our study, we were unable to perform longitudinal measurements with the handheld ultrasound device due to the incompatibility of the device's long axis with the anatomy of the newborn's neck. Instead, we were able to measure the widths of both lobes and the trachea in the transverse section and only compared these data. Including a comparison of thyroid volume would have increased the robustness of our study.

Although previous studies have demonstrated that Aydın is an iodine-sufficient region, the urinary iodine levels of the mothers and newborns were not measured in this study, which is one of its limitations.

Conclusion

This study provides valuable normative data on thyroid volume and tracheal index for newborns in an iodine-sufficient region. The findings emphasize the importance of region-specific references for thyroid measurements and support the use of portable ultrasound devices as reliable tools for assessing tracheal index in newborns. Further research in diverse geographical and iodine status contexts will help to expand the understanding of normal thyroid size in newborns.

Ethics

Study approval statement: The study was approved by the non-interventional ethics committee of Aydın Adnan Menderes University (Ethics no: 2022/213).

Consent to participate statement: Informed consent in this study was taken from all participants.

Conflict of Interest Statement

The authors declare that they have no conflict of interest.

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Author Contributions

Concept: Ahmet Anık Design: Ahmet Anık Data Collection or Processing: Ahmet Anık, Göksel Tuzcu, Reyhan Deveci Sevim, Ayşe Anık, Mustafa Gök Analysis or Interpretation: Reyhan Deveci Sevim, Ahmet Anık Literature Search: Reyhan Deveci Sevim, Göksel Tuzcu Writing: Reyhan Deveci Sevim, Göksel Tuzcu, Ahmet Anık.

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Data Availability Statement: All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

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Table 1. Normal thyroid volume by age and gender

	n	**Thyroid volume (ml) 0-2. day**	**Thyroid volume (ml) 15-30. day**	**p**
Girls	71	0.64± 0.26	1.12 ± 0.33	**<0.01**
Boys	73	0.68 ± 0.23	1.13± 0.33	**<0.01**
Total	144	0.66 ± 0.25	1.12 ± 0.33	**<0.01**

ml: millilitres

Table 2. Thyroid volume normal values according to birth weight

	Boys Thyroid volume (ml)			**Girls Thyroid volume (ml)**		
Weight (SD)	**Mean±SD (median)**	**-2 SD**	**+2 SD**	**Mean±SD (median)**	**-2 SD**	**+2 SD**
-2 - -1 (n=13)	0.50±0.16 (0.43)	0.18	0.82	0.45□0.17 (0.46)	0.11	0.78
-1 - 0 (n=32)	0.71±0.23 (0.68)	0.25	1.17	0.62□0.18 (0.62)	0.26	0.98
0 - 1 (n=23)	0.75±0.23 (0.76)	0.29	1.21	0.72□0.25 (0.73)	0.22	1.22
1 - 2 (n=5)	0.71±0.19 (0.78)	0.33	1.09	1.19□0.48 (1.31)	0.23	2.15

SD: standard deviation, ml: millilitres

Table 3. Tracheal index by age and gender

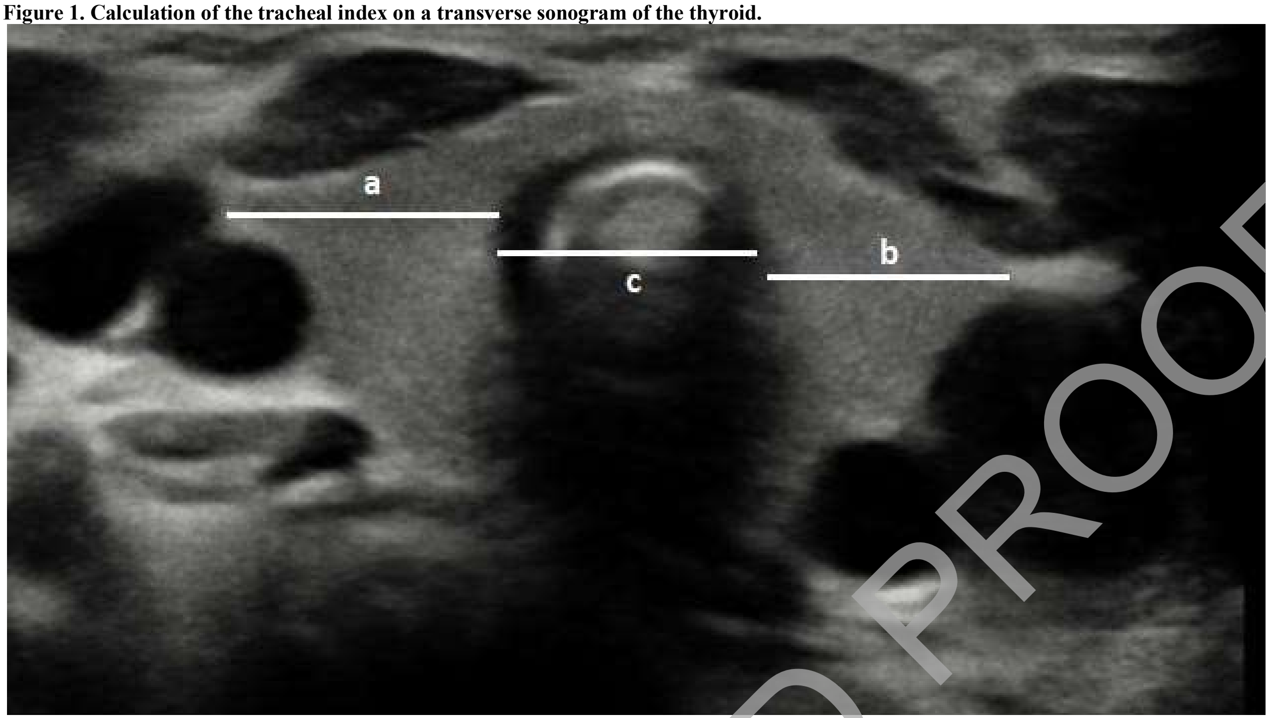
	n	**Tracheal index Mean±SD (median) 0-2. day**	**Tracheal index Mean±SD (median) 15-30. day**	**p**
Girls	71	1.84±0.30 (1.85)	1.99±0.23 (1.99)	**<0.01**
Boys	73	1.82±0.27 (1.82)	2.00±0.28 (1.90)	**<0.01**
Total	144	1.83±0.29 (1.82)	1.99±0.25 (1,94)	**<0.01**

SD: standard deviation
The tracheal index is calculated as the ratio of the sum of the maximum widths of the right and left thyroid lobes in the transverse section to the width of the trachea at the thyroid level.

Table 4. Correlation of tracheal index measure with handheld and portable ultrasound devices

		Portable device (First measurement)	**Portable device (Second measurement)**
Handheld device (First measurement)	r	0.520	
	p	**<0.001**	
Handheld device (Second measurement)	r		0.421
	p		**0.001**

Figure 1. Calculation of the tracheal index on a transverse sonogram of the thyroid.



(The sum of the maximum width of each thyroid lobe (a+b) divided by the width of the trachea at the level of the thyroid (c) gives the transverse sonogram tracheal index)

Figure 2. Correlation of thyroid volume with birth weight

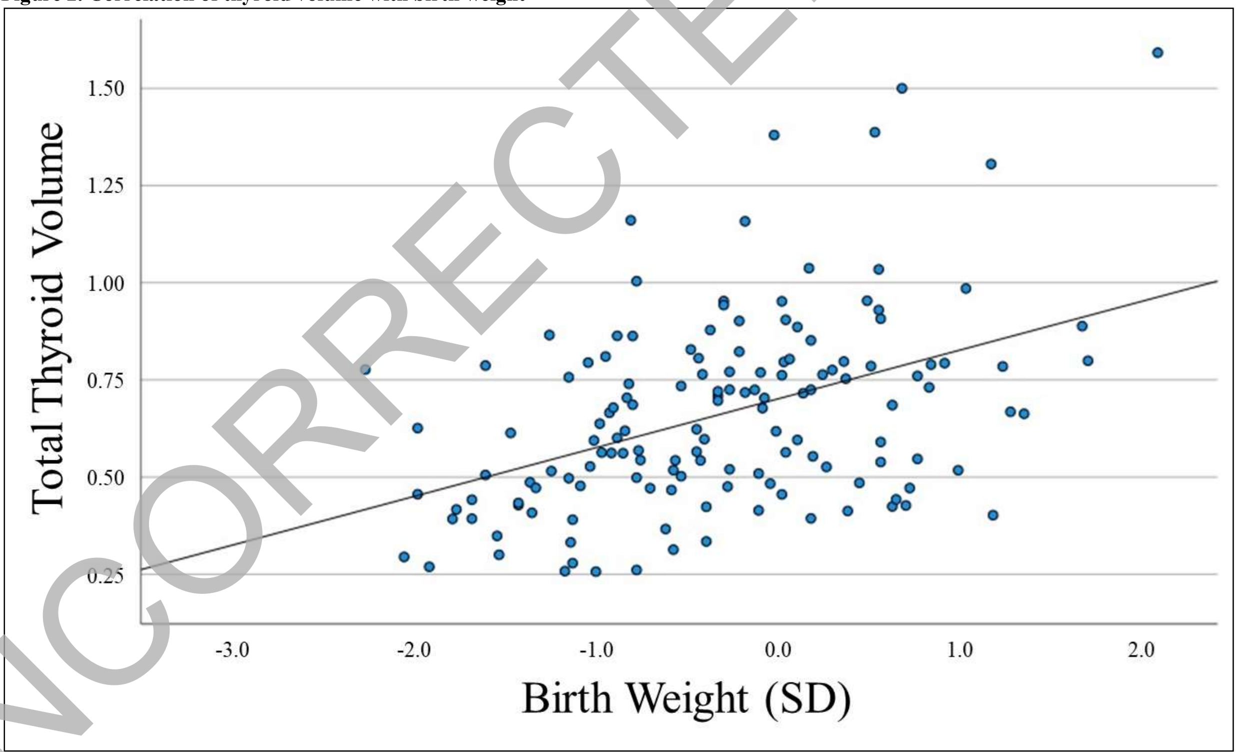


Figure 3. Correlation of tracheal index and thyroid volume