ULTRASONOGRAPHIC MEASUREMENT OF THYROID GLAND VOLUME IN TURKISH NEONATES AND ASSESSMENT OF REGIONAL DIFFERENCES

Original Article

TÜRK YENİDOĞANLARDA TİROİD GLAND VOLÜMLERİNİN ULTRASONOGRAFİK ÖLÇÜMÜ VE BÖLGESEL FARKLILIKLARININ DEĞERLENDİRİLMESİ

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ABSTRACT

Objectives: Our aim was to assess normative data regarding the thyroid gland volume of Turkish newborns with normal thyroid stimulating hormone levels and to detect whether regional differences existed.

Method: A total of 201 full-term newborns (term, 37–42 weeks; within 0–30 days of birth; 104 girls; 97 boys) from four different zones in Turkey (Marmara, Eastern Black Sea, Eastern Anatolian, and Aegean) were included in this study. Thyroid volumes were measured by ultrasonography by using a similar method, and the results were compared.

Results: In our study, the newborns' mean thyroid volume was 0.58 ± 0.19 mL. Thyroid volumes from the Marmara, Eastern Black Sea, Eastern Anatolian, and Aegean regions were 0.50 ± 0.12, 0.79 ± 0.23, 0.56 ± 0.16, and 0.43 ± 0.17 mL, respectively. The ultrasonographically assessed thyroid volume was significantly

greater for newborns from the Eastern Black Sea ($p < 0.001$), followed by the Eastern Anatolia, Marmara, and Aegean regions. No statistically significant difference existed among the latter three zones.

Conclusions: The neonates' normal thyroid volumes varied among the different regions. Newborns from the Eastern Black Sea region possibly have a greater thyroid volume because of a residual effect secondary to a history of iodine deficiency in that region, as well as a correlation between a mother and a neonate in terms of thyroid functions. Thus, in newborns from the East Black Sea region, additional screening tests may be added to routine screening in selected groups.

Key words: *ultrasonography; thyroid gland; Infant; newborn.*

ÖZET

Amaç: Bu çalışmada normal tiroid uyarıcı hormon düzeylerine sahip Türk yenidoğanlarının tiroid gland volümlerinin ultrasonografik ölçümü ve bölgesel farklılıklarının değerlendirimesi-amaçlanmıştır.

Metod: Türkiye'nin dört ayrı bölgesinden (Marmara, Karadeniz, Doğu Anadolu, Ege) toplam 201 yenidoğan (37–42 hafta; doğumun 0–30 günleri arası; 104 kız; 97 erkek) çalışmaya dahil edildi. Ultrasonografi ile tiroid volümleri ölçüldü ve sonuçlar karşılaştırıldı.

Results: Çalışmamızda yenidoğanların ortalama tiroid volümü 0.58 ± 0.19 mL bulundu. Marmara, Karadeniz, Doğu Anadolu, Ege Bölgelerindeki-yenidoğanlarda ultrasonografi ile ölçülen tiroid volümleri sırasıyla 0.50 ± 0.12, 0.79 ± 0.23, 0.56 ± 0.16, and 0.43 ± 0.17 mL idi. Karadeniz Bölgesinde ölçülen tiroid volümü diğer üç bölgedeki tiroid volümünden istatistiksel olarak anlamlı olacak şekilde büyüktü ($p < 0.001$). Marmara, Doğu Anadolu, Ege Bölgelerindeki yenidoğanlardaki tiroid volümleri arasında istatistiksel olarak anlamlı fark bulunmadı.

Sonuç: Yenidoğanların normal tiroid volümü bölgesel farklılıklara göre değişmektedir. Karadeniz Bölgesindeki yeni-doğanlarda tiroid volümü- muh-temelen bu bölgedeki iyot eksikliğine bağlı olarak daha fazladır. Bu nedenle, Karadeniz Bölgesindeki yenidoğanlarda rutin tarama testlerine ilave ek tarama testleri seçilmiş hastalarda düşünülebilir.

Anahtar Kelimeler: *ultrasonografi; tiroid gland; yenidoğan.*

INTRODUCTION

Ultrasonographic (USG) evaluation of the thyroid gland is a useful approach for the management of thyroid diseases. It can be used to determine the presence or absence of the gland, assess developmental abnormalities, and detect thyroid volume in neonates. It is also indicated for the evaluation of congenital hypothyroidism as determined on the basis of mass screening by using blood samples (1-5).

There have been many studies designed to ultrasonographically establish the size of the thyroid gland in school children, but few studies have been conducted in neonates (6-11). A few series has been reported in Turkish literature, from the Kayseri and Bursa regions, which have a history of moderate iodine deficiency (12,14). As regional factors may influence thyroid volume, determination of normative data in different regions is important to differentiate normal and abnormal values (9-11). Our aim was to evaluate thyroid volume in healthy neonates who had normal thyroid stimulating hormone (TSH) levels and who were from different zones in Turkey and to assess evidence of regional differences.

MATERIAL AND METHODS

A total of 201 full-term newborns (term, 37–42 weeks; within 0–30 days of birth) from four different zones in Turkey (Marmara, Eastern Black Sea, Eastern Anatolian, and Aegean) with a birth weight between the 10th and 90th percentiles of their mean gestational age were included in this study. Neonates with congenital malformations, mild to moderate jaundice, infections, and TSH level abnormalities upon routine neonatal screening were excluded. Neonates with a history of maternal thyroid disease or maternal smoking were also excluded. Volumetric measurements were performed by correcting for weight. The committees at each local institution involved in this study approved the study protocol, and informed written consent was obtained from the parents of the participating neonates.

The infants' height, weight, sex, gestational age, and current age were recorded before the USG examination. TSH values were measured in their venous blood on the fifth postpartum day by using a chemiluminometric technique. Infants with TSH levels of over 10 mU/L were excluded.

The ultrasonographic examinations were performed by four radiologists from four different centers in the Marmara, Eastern Black Sea, Eastern Anatolian, and Aegean regions that had at least 10 years of experience in USG examination. Thyroid gland volumes were measured by using the following: GE Medical Systems LOGIQ 9 (Milwaukee, WI, USA Systems), GE Medical Systems LOGIQ 500 (Milwaukee, WI, USA Systems), GE Medical Systems LOGIQ 7 (Milwaukee, WI, USA Systems), and GE Medical Systems VOLUSON 730 PRO V (Milwaukee, WI, USA Systems) that were calibrated by the manufacturer. All the scanners used in the four regions belonged to the same company. A 7.5-MHz linear transducer was used, and the transducer lengths were equal in all regions. The neonates were examined without sedation in a supine position and with their neck hyperextended. The width, length, and depth of both thyroid lobes were measured in the sagittal and axial planes, without compression. Duplicate measurements were performed by two examiners to assess interobserver variability for the first 20 neonates in each group. As high interobserver accuracy was determined and because of practical and ethical difficulties, one radiologist performed the examinations for the rest of participants. For each thyroid lobe, the maximum perpendicular anteroposterior and mediolateral dimensions were measured on a transverse plane at the largest diameter. The maximum craniocaudal diameter of each lobe was then measured on a longitudinal plane. The isthmus was not included. Thyroid volumes were calculated according to the following formula: (a × b × c) × 0.523 (**Figure 1**).

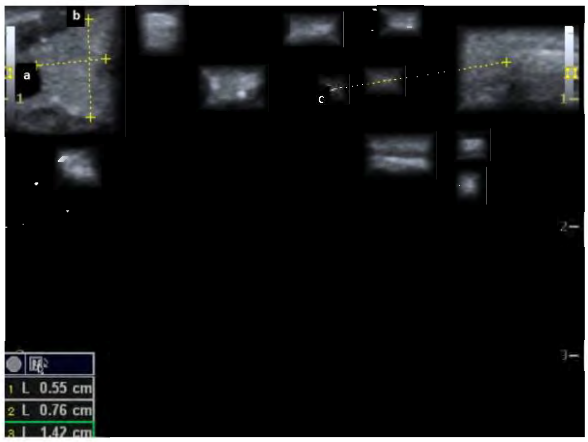

Figure 1. *Thyroid lobe measurements in the sagittal and axial planes.*

The right and left lobe volumes, as well as the total thyroid volumes, that obtained from the four regions were then compared.

Data analyses were performed using the Statistical Package for Social Sciences (SPSS for Windows, 10.0). All data were evaluated for a normal distribution with the Kolmogorov–Smirnov test. Because of differences in the participants' weight, the volumetric measurements were performed with and without a weight correction. A

covariance analysis program was used after a weight correction. Comparisons of the left and right lobe volumes without correction were made using the Student's *t* test. Comparisons among groups were made using the χ^2 test, according to sex distribution. Results were given by using a 95% confidence interval, and a p of <0.05 was considered significant.

RESULTS

The mean gestation was 39 weeks and 5 days (37–42 weeks) (Table 1). There was no statistically significant difference among the groups in terms of gestational age or sex (**Table 1**).

	Group I: Marmara Region	Group II: Eastern Black Sea Region	Group III: Eastern Anatolian Region	Group IV: Aegean Region	p
Gestational age (weeks)	39.60 ± 1.34	39.47 ± 1.04	39.52 ± 0.71	39.17 ± 0.99	0.34
Sex Female (n, %) Male (n, %)	27 (49.1) 28 (50.9)	25 (53.2) 22 (46.8)	25 (50) 25 (50)	22 (44.8) 27 (55.1)	0.91
Weight (g)	3478.91 ± 538.69	3285.11 ± 504.21	3620.92 ± 735.29	3249.00 ± 365.91	0.008*
Thyroid volume (mL)	0.50 ± 0.12	0.79 ± 0.23	0.56 ± 0.16	0.43 ± 0.17	<0.001**

Table 1. *The newborns' gestational age, sex distribution, weight, and thyroid volume in the four groups.*

**Differences existed among the weights of groups 1–3, groups 2–3, and groups 3–4 (p: 0.008).*

***Total volume measurements showed that neonates in the Eastern Black Sea region had significantly greater thyroid volumes than the other groups (groups 1–3, groups 2–3, and groups 3–4; p < 0.001).*

Thyroid lobe volumes (mL)	Right lobe		Left lobe		
	Mean	SD	Mean	SD	p
Group I: Marmara Region	0.26	0.14	0.25	0.09	NS
Group II: Eastern Black Sea Region	0.37	0.11	0.38	0.12	NS
Group III: Eastern Anatolian Region	0.31	0.14	0.31	0.14	NS
Group IV: Aegean Region	0.17	0.07	0.18	0.08	NS

SD, standard deviation; NS, not significant

Table 2. *Right and left thyroid lobe volumes in the four groups.*

The mean birth weight was 3429 ± 583 (2090–5100) g, with a statistically significant difference among the groups (p < 0.001) (**Table 1**).

The mean thyroid volume and weight were interrelated, which was consistent with literature, so a statistical analysis was performed after weight correction.

The newborns' mean thyroid volume was 0.58 ± 0.19 mL. The thyroid volumes from the Marmara, Eastern Black Sea, Eastern Anatolian, and Aegean regions were 0.50 ± 0.12, 0.79 ± 0.23, 0.56 ± 0.16, and 0.43 ± 0.17 mL, respectively. The newborns from the Eastern Black Sea region had significantly higher thyroid volumes (p < 0.001), followed by the Eastern Anatolian, Marmara, and Aegean regions, but no difference existed among the last three **(Table1).** There was no significant difference between right and left lobe volumes in the four regions **(Table2).** Regarding the ultrasonographic measurements of the thyroid volume, interobserver errors were 4.3%, 3.7%, 5.1%, and 4.7% for the Eastern Black Sea, Eastern Anatolian, Marmara, and Aegean regions, respectively.

DISCUSSION

Ultrasound is a promising, non-invasive method for neonatal thyroid imaging as well as for the assessment of thyroid size, in terms of volume. The assessment of normative data for each country or region is important to distinguish between normal and abnormal glands. Chanoine et al. (9) determined newborn thyroid volumes of 0.83 mL in Brussels, where there was a moderate iodine deficiency. Further, Ares et al. (10) reported a 0.92-mL thyroid volume in their series from Madrid. Then, in a study performed in Scotland, the mean volume was reported as 1.62 mL (11).

In Turkey, thyroid volumetric studies have been performed in school children and adults (8,15,16). To our knowledge, a few studies have been performed on newborns. In their Central Anatolian study, Kurtoglu et al. included newborns who had elevated TSH levels and reported thyroid volume as 1.21 mL (12). In another series in which newborns with normal thyroglobulin levels were recruited, the thyroid volumes were reported as 0.72 mL (13). Furthermore, Koksal et al. (14) determined neonatal thyroid volumes of 0.80 mL in a moderately iodine-deficient area. In our study, the newborns' mean thyroid volume was 0.58 ± 0.19 mL. Our findings are consistent with those of the latter two studies. The thyroid volumes from Marmara, Eastern Black Sea, Eastern Anatolian, and Aegean regions were 0.50 ± 0.12, 0.79 ± 0.23, 0.56 ± 0.16, and 0.43 ± 0.17 mL, respectively. Although the TSH levels in our series were within normal ranges, the total volume measurements showed that newborns from the Eastern Black Sea region had significantly greater thyroid volumes ($p < 0.001$).

Pregnancy is accompanied by changes in thyroid functions. In areas with sufficient iodine intake, the thyroid gland maintains stable free hormone levels, so changes in thyroid volume are minor. However, a mild iodine deficiency is associated with excessive thyroid stimulation in a healthy, pregnant woman (17, 18). With iodine deprivation, fetal thyroid stimulation occurs as soon as the thyroid gland begins to develop, leading to a relative compensatory increase in glandular size (19). Pregnancy constitutes a stimulus not only for a maternal thyroid, but also for a fetal thyroid gland. Glinoer et al. (18) treated one group of pregnant women who had minimal hypothyroidism by using a placebo, while the other group was administered exogenous iodine. The newborns from the mothers who were not given any iodine had significantly greater thyroid volumes than those in the other group (19). In another study performed on newborns of mothers who had minimal hypothyroidism that were treated with iodine tablets, decreased thyroid volumes were reported (20). In both studies (19,20), the newborns' TSH level was normal. It has not been entirely explained as to why the neonatal TSH levels were normal among the groups. However, similar findings have been reported in other studies on neonatal thyroid function in endemic goiter areas (17,18). One hypothesis is that the TSH level at birth does not reliably reflect fetal goitrogenesis, perhaps because this process occurs early during fetal development. Turkey is an area with a mild to moderate iodine deficiency, and the Black Sea region is the foregoing area in terms of endemic goiter, followed by the Eastern Anatolian, Marmara, and Aegean regions (21,22). We think the greater thyroid volumes in newborns from the Black Sea region may be because of a lower iodine level, as compared with the other regions, and it may also demonstrate a strong correlation between mother and baby in terms of thyroid functions.

Limitations in our study included the lack of detection of free serum T3, T4, or thyroglobulin, as well as urine iodine levels, in the newborns and mothers. As

our aim was to determine normative data, we recruited normal newborns with normal TSH values, which are considered to be the most sensitive indicator for monitoring iodine deficiency in several countries such as Japan, Australia, and most European countries (3,23,24). Since 2007, TSH screening has also been extensively used as a part of a neonatal thyroid function screening program in Turkey.

In conclusion, neonatal normal thyroid volumes vary among different regions. Local reference values should be used in thyroid volume assessment. Our results are in concordance with medical literature and can be used as reference values for these four regions. To our knowledge, this is the first multicentric study to assess the normative data of newborn thyroid volumes in Turkey. However, because of higher thyroid volumes in newborns from the East Black Sea region, additional screening tests may be added to routine screening in selected groups and this area should be investigated in terms of iodine status.

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