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Does Spot Urinary Iodine Reflect Thyroid Dysfunction in Newborns? Single Center Experience

Author(s)

Hümeyra Acıkan[1], Nihal Hatipoğlu[2], Sabahattin Muhtaroğlu[3]

Affiliation(s)

[1]Kahramanmaraş Sütçü İmam University Faculty of Dentistry, Department of Basic Medical Sciences, Kahramanmaraş, Türkiye

[2]Erciyes University Faculty of Medicine, Department of Pediatric Endocrinology, Kayseri, Türkiye

[3]Erciyes University Faculty of Medicine, Department of Medical Biochemistry, Kayseri, Türkiye

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Abstract

Iodine is an essential trace element for all newborns. The aim of this study was to evaluate iodine levels during the neonatal period and conditions associated with iodine deficiency by examining thyroid function tests and anthropometric parameters. A retrospective analysis was performed on 169 screen-positive newborns who were referred to a tertiary pediatric endocrinology clinic. Newborns were classified according to iodine status and thyroid function. Evaluation was performed on 169 newborns, of whom 50.9% were female and 49.1% were male. The median spot urine iodine concentration (SUIC) of all the infants was 120 (70-195) µg/L. Iodine deficiency was the most common condition, occurring in 39.6%, and excessive iodine levels were present in 23.1%. Birth weight and body mass index were significantly lower in the iodine-deficient group, whereas thyroid stimulating hormone (TSH) levels were higher in the high-iodine group (all $p<0.05$). A weak positive correlation was observed between SUIC and TSH levels ($r=0.202$, $p=0.004$), whereas a weak negative correlation was observed between SUIC and free thyroxine levels ($r=-0.161$, $p=0.023$). In this referral-based cohort of screen-positive newborns, 28.4% were diagnosed with congenital hypothyroidism, 23.7% with subclinical hypothyroidism, and 47.9% were euthyroid. Iodine deficiency in newborns remains a relevant public health concern in our region. In addition, elevated iodine levels were detected in approximately one-fifth of the study population. Although iodine status was weakly correlated with thyroid function parameters, it did not influence the final thyroid diagnosis. These findings suggest that spot urinary iodine concentration is more appropriate for population-based assessment rather than individual diagnosis of thyroid dysfunction.

Keywords: Congenital hypothyroidism, iodine, newborn, thyroid dysfunctions

Introduction

Iodine is a vital trace element for the biosynthesis and structural integrity of thyroid hormones[1]. Both a deficiency and excess of iodine can affect thyroid hormone synthesis[2], and affects thyroid stimulating hormone (TSH) concentration through a negative feedback mechanism[3]. Thyroid hormones regulate growth, metabolism, and neurodevelopment and are essential for normal fetal brain and nervous system development. Adequate iodine intake is crucial for maintaining optimal thyroid hormone synthesis; therefore, alterations in maternal or neonatal iodine status may influence intrauterine growth and early

Correspondence: Nihal Hatipoğlu, Erciyes University Faculty of Medicine, Department of Pediatric Endocrinology, Kayseri, Türkiye
E-mail: nihalhatipoglu@yahoo.com **ORCID:** orcid.org/0000-0002-0991-6539

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anthropometric parameters such as birth weight and body proportionality. Both iodine deficiency and excess have been associated with variations in fetal growth patterns, further supporting a potential link between iodine status and neonatal anthropometric outcomes[4].

There is a high requirement for iodine during pregnancy due to the changing physiology and growing fetus[5].

Highlights

- Spot urine iodine concentration was evaluated in newborns with thyroid dysfunction.
- Iodine deficiency was common, while excess iodine was also frequently detected.
- Birth weight, body mass index, and thyroid stimulating hormone (TSH) differed according to iodine status.
- Spot urine iodine concentration showed a weak correlation with TSH and free thyroxine levels.
- Iodine status did not alter the final thyroid diagnosis in newborns.

Because iodine crosses the placenta directly, maternal and fetal iodine levels are significantly correlated. A pregnant woman with severe iodine deficiency is at risk of hypothyroidism for herself and the fetus.

Iodine deficiency during the intrauterine period causes irreversible neurodevelopmental damage to the fetus. Iodine deficiency is still a common cause of preventable intellectual disability[6]. In contrast, excess iodine causes hypothyroidism by inhibiting thyroid hormone synthesis via the Wolff-Chaikoff effect. Some iodine-containing supplements taken during pregnancy, topical antiseptics, and certain medications can cause excessive iodine intake and could indirectly affect the fetus and newborn[7]. A U-shaped relationship exists between iodine and thyroid hormone synthesis, with both insufficient and excessive iodine exposure increasing the risk of congenital hypothyroidism (CH) in newborns.

The International Council for the Control of Iodine Deficiency Disorders suggested that iodine status can be determined by urinary iodine levels[8]. Other biomarkers such as thyroid stimulating hormone, free triiodothyronine (fT3) and free thyroxine (fT4) are used to evaluate iodine status in pregnant women and newborn infants[9]. Compared to iodine-sufficient regions, individuals in iodine-deficient regions may have slightly higher TSH and fT3 concentrations, while fT4 may be slightly lower[10].

Another approach to estimating the iodine status of a region is neonatal TSH screening, which is commonly used to detect CH[11]. CH, a prevalent endocrine disorder in newborns with an incidence of 1 in 2,000-4,000, has been reported to be increasing[12]. In Türkiye, the birth prevalence of primary CH has been reported as 1:650[13].

To ensure normal cognitive and intellectual development, newborns should be routinely screened for CH, and if CH is detected, hormone replacement therapy should be initiated[14,15]. The definition of CH encompasses the causes of both permanent and transient hypothyroidism. Dysgenesis accounts for 85% of permanent CH cases, whereas iodine deficiency is the primary cause of temporary hypothyroidism[16]. Since iodine deficiency rates are high in Türkiye, the incidence of transient CH is also high (1/752-1/1236)[17].

This study aimed to assess iodine levels in newborns flagged during screening due to elevated TSH, to examine the correlation of spot urine iodine concentrations (SUIC) with anthropometric measurements and thyroid function tests, and to explore the association between thyroid dysfunction and iodine status.

Materials and Methods

The study included newborns referred to the Pediatric Endocrinology Clinic of Erciyes University during the past year due to abnormal newborn screening (heel prick test) results, particularly elevated TSH levels. This was a retrospective observational study. Urinary iodine levels were measured simultaneously with thyroid function tests at the time of referral. The necessary approvals were secured from the local ethics committee for the study This study was approved by the Ethics Committee of Clinical Research at the Faculty of Medicine, Erciyes University (approval no: 2021/567, date: 08.09.2021).

The demographic, anthropometric, and laboratory information of the newborns in the study was retrospectively retrieved from the Erciyes University Hospital Information Management System (HIMS). The study provides no definitive information on whether iodized or non-iodized salt was used during the gestational period, whether salt intake was restricted, whether the birth was by cesarean section or was normal, and whether antiseptics were applied after birth.

Cases were excluded if information could not be obtained from HIMS; if they had been treated in an external centre; if they had thyroid dysgenesis; if they had been born prematurely (<37 weeks); or if they exhibited SUIC values exceeding 500 µg/L, which may reflect acute iodine exposure, including possible contamination from iodine-containing antiseptics used in the peripartum period[18]. A total of 169 infants who had thyroid function tests and iodine levels measured on the same day and whose file information was available were included in the study.

The anthropometric measurements of all infants referred for outpatient heel blood screening during the first 2 weeks of life, including birthweight, length, and head circumference were determined by the same nurse using the same scales and recorded in their files. Body mass index (BMI) was determined by dividing the weight (in kg) by the square of the height (in meters). Specifically, BMI- standard deviation (SD) (z-scores) were calculated based on the World Health Organization (WHO) Child Growth Standards for infants and children, using the Lambda-Mu-Sigma method to ensure scientific validity and reproducibility[19].

The Sandell-Kolthoff reaction, using the WHO-recommended colorimetric ceric arsenic acid solution, with results reported in µg/L. TSH, fT4, fT3, and thyroglobulin (Tg) levels were analyzed using the electrochemiluminescence immunoassay, specifically the Roche Elecsys E170 from the United States of

America (USA). For newborns, the standard ranges were defined as 0.7-15.2 µIU/mL for TSH, 0.89-2.2 ng/dL for FT4, and 0.73-84 ng/mL for Tg. All laboratory analyses were performed in the accredited central laboratory of our institution following standardized internal quality control procedures.

According to the WHO, median spot urinary iodine concentration (SUIC) values are interpreted as follows: ≤99 µg/L indicate iodine deficiency, 100-199 µg/L indicate adequate iodine intake, 200-299 µg/L indicate more than adequate iodine intake, and ≥300 µg/L indicate excessive iodine intake, which may be associated with adverse health effects[9]. Based on this classification, newborns in the present study were categorized into three groups: iodine-deficient (SUIC ≤99 µg/L), normal iodine status (SUIC 100-199 µg/L), and high iodine status (SUIC ≥200 µg/L). This categorization uses inclusive boundaries to avoid ambiguity at the cut-off values. Primary CH was defined as serum fT4 <0.93 ng/dL (normal range: 0.93-1.71 ng/dL) and TSH >10 µIU/mL (normal range: 0.27-4.2 µIU/mL)[20]. Subclinical hypothyroidism was defined as TSH> 10 µIU/mL with fT4 within the normal range, and euthyroid status was defined as both values within the normal range. Within the Turkish national newborn screening program, a TSH level of 15 µIU/mL serves as the recall threshold. Newborns above this limit are reassessed approximately two weeks after birth with repeat thyroid function testing, and therapy is commenced if TSH persists above 10 µIU/mL[18].

Statistical Analysis

The study's data were statistically evaluated using SPSS version 23 (SPSS Inc., Chicago, IL, USA). The Shapiro-Wilk test, histogram, Q-Q graph, and skewness and kurtosis coefficients were used to assess whether the data followed a normal distribution. Variables that did not follow a normal distribution were presented as median (25^{th}-75^{th} percentile) values. For data with a normal distribution, descriptive statistics were given as mean ± SD, while categorical data were expressed as count (n) and percentage (%).

One-way analysis of variance was used to compare variables among three or more groups with normally distributed data, and Kruskal-Wallis analysis of variance was employed for variables that were not normally distributed. The Spearman correlation test (for non-normally distributed data) was used to assess correlations among infant TSH, fT4, Tg, and SUIC. Results were assessed using 95% confidence intervals, and a p-value less than 0.05 was considered to indicate statistical significance.

Results

An assessment was conducted of 169 newborns, comprising 50.9% females and 49.1% males with a mean age of 18.07±5.08 days, length of 51.96±2.56 cm, weight of 3850±570 g, and head circumference of 36.5 cm (35-37). The anthropometric and laboratory data of all the infants are presented in **Table 1**.

Retrospectively, SUIC results were obtained from newborns at a mean age of 3 weeks, and TSH values were examined. The median SUIC was 120 (70 -195) µg/L for both males and females, with no significant difference between the genders (p=0.367). The distribution of iodine status among newborns is presented in **Figure 1**. Iodine deficiency was identified in 39.6% of the infants, whereas excessive SUIC was observed in 23.1% of the infants. A comparative analysis across iodine status groups demonstrated statistically significant differences in birth weight (p=0.03), BMI (p=0.023), and TSH levels (p=0.031). No significant differences were detected in fT4 and Tg concentrations (p=0.281, p=0.291, respectively). According to the thyroid function test results (**Table 2**), 28.4% of the newborns were diagnosed with CH, 23.7% were diagnosed with subclinical hypothyroidism, and 47.9% were evaluated as euthyroid. The SUIC did not show a statistically significant difference across diagnoses (p=0.365).

When the relationship between SUIC and thyroid function tests was evaluated, a weak positive correlation with TSH levels (r=0.202, p=0.004) and a weak negative correlation with fT4 (r=-0.161, p=0.023) were observed. No relationship was found between SUIC and Tg (r=-0.045, p=0.291) (**Figure 2**).

Discussion

This study was conducted in a referral-based cohort of screen-positive newborns referred to a pediatric endocrinology clinic due to elevated TSH levels detected by the national newborn screening program. Accordingly, iodine levels and iodine-related factors were evaluated in this selected high-risk population at a single center. While iodine deficiency was detected in nearly 40% of newborns, excess iodine was detected

Table 1.
Anthropometric and laboratory data

N=169 (86 females, 83 males)	Values
Anthropometric data	
Age (day)	18.07±5.08
BW (g)	3245 (3040-3460)
Gestational age (day)	39.45 (38.37-40.00)
Weight (g)	3850±570
Weight (g)-SD	-0.04±1.09
Length (cm)	51.96±2.56
Length-SD	0.00 (-0.69-0.56)
Head circumference (cm)	36.50 (35.00-37.00)
Head circumference (cm)-SD	0.08 (-0.96-0.74)
BMI (kg/m^2)	14.16±1.47
BMI-SD	0.151±1.01
Laboratory data	
SUIC (µg/L)	120 (70-195)
TSH (µIU/mL)	10.17 (5.51-31.39)
fT4 (ng/dL)	1.31 (1.03-1.49)
Tg (ng/mL)	139.00 (66.40-300.00)

Values are presented as mean ± SD or median (25^{th}-75^{th} percentile), as appropriate according to data distribution
BMI: Body mass index, BW: Birth weight, fT4: Free thyroxine, SD: Standard deviation, SUIC: Spot urine iodine concentration, Tg: Thyroglobulin, TSH: Thyroid stimulating hormone

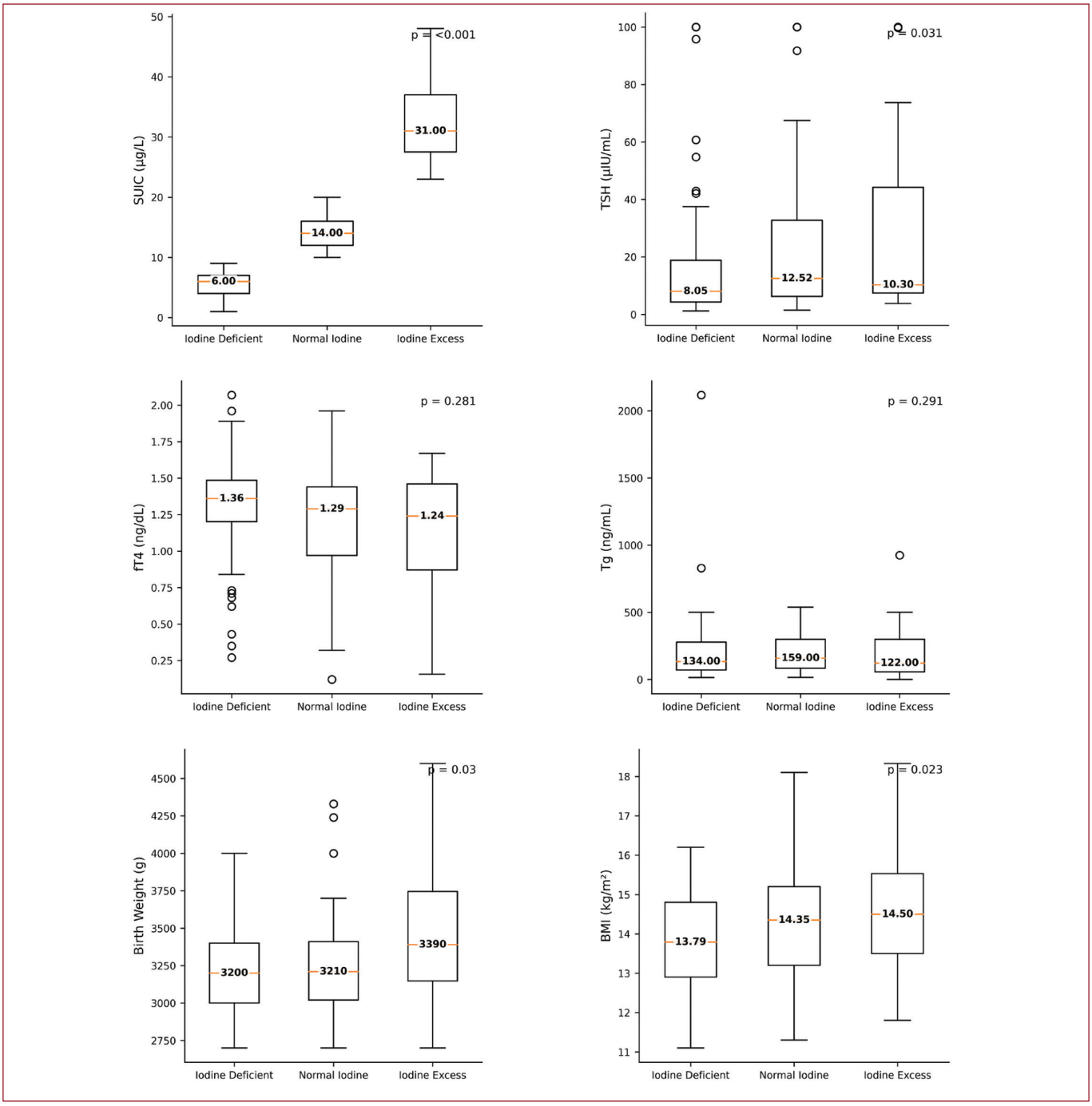


Figure 1. Distribution of laboratory and anthropometric parameters according to iodine status in newborns

BMI: Body mass index, fT4: Free thyroxine, SD: Standard deviation, SUIC: Spot urine iodine concentration, Tg: Thyroglobulin, TSH: Thyroid stimulating hormone

Table 2.
Statistical comparison of laboratory data according to thyroid dysfunctions

	Congenital hypothyroidism group (n=48)	Subclinical hypothyroidism group (n=40)	Euthyroidism group (n=81)	p-value
	Values	Values	Values	
Laboratory data				
SUIC (µg/L)*	170.60±110.90	142.00±90.40	144.50±110.40	0.365
TSH (µIU/mL)*	70.60 (36.22-100)[a]	14.1 (10.80-17.48)[b]	5.21 (4.07-7.46)[c]	**<0.001**
fT4 (ng/dL)**	0.61±0.21[a]	1.33±0.22[b]	1.43±0.19[b]	**<0.001**
Tg (ng/mL)*	300 (295-315)[a]	170.00 (92.20-300)[b]	85.50 (55.20-156.00)[c]	**<0.001**

Values are presented as mean ± SD or median (25^{th}-75^{th} percentile), as appropriate according to data distribution
*: Kruskal-Wallis test, the significance level is 0.05
**: One-way ANOVA test, the significance level is 0.05
Post-hoc test results are indicated by character ([a], [b], [c]). The same character indicate that there is no difference between them, and different character indicate that there is a significant difference between them
fT4: Free thyroxine, SD: Standard deviation, SUIC: Spot urine iodine concentration, Tg: Thyroglobulin, TSH: Thyroid stimulating hormone

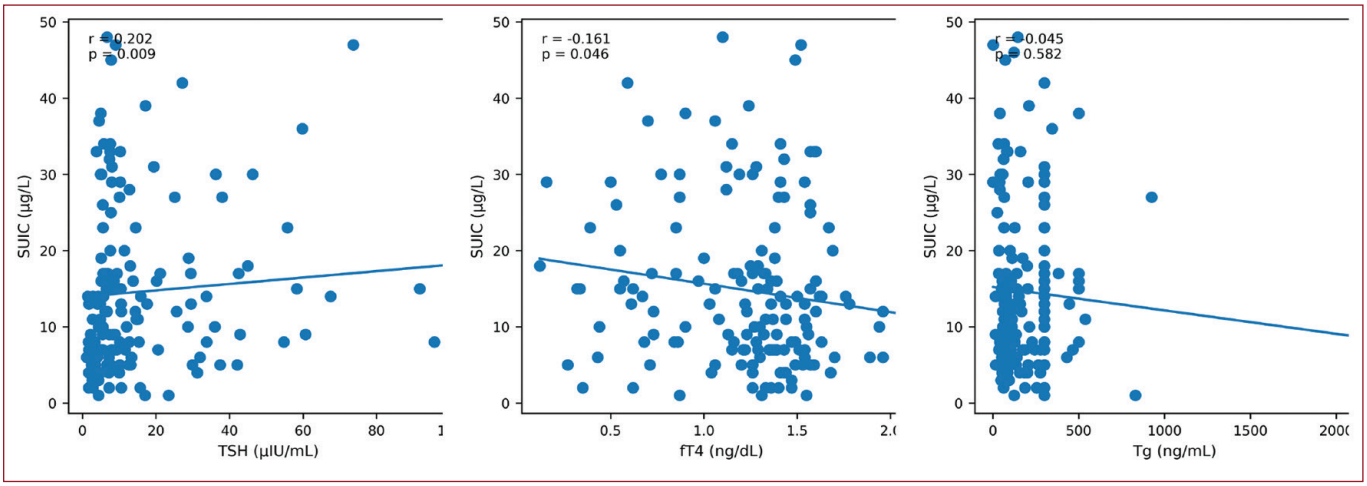


Figure 2. Correlation between urinary iodine concentration and thyroid function parameters in newborns

fT4: Free thyroxine, SD: Standard deviation, SUIC: Spot urine iodine concentration, Tg: Thyroglobulin, TSH: Thyroid stimulating hormone

in 23%. As expected, body weight was lower in those with iodine deficiency. Although iodine levels in patients with CH were similar to those in euthyroid infants and in infants with subclinical hypothyroidism, the findings of this study indicate that iodine deficiency and excess are still problems.

Iodine deficiency, which is common in all regions of the world, indirectly affects the population at all stages of economic development[21]. In a study conducted in 2020, insufficient iodine was found in the diets of 21 countries worldwide, with the lowest iodine intake observed in Madagascar and insufficient intake reported in European countries (Germany and Finland)[22]. Türkiye is considered to have mild-to-moderate iodine deficiency based on epidemiological data[23].

In a recent study evaluating iodine status in Türkiye, the overall median SUIC value in newborns was reported as 96 (41-191) µg/L overall and 97 (53-190) µg/L in the Central Anatolian region, where the present study center is located[24]. In our study, the median SUIC value was 120 (70-195) µg/L. However, the newborns included in our study represent a screen-positive, referral-based group rather than the general healthy newborn population. In our cohort, iodine deficiency was detected in 39.6% of the newborns, whereas 23.1% exhibited iodine excess. In contrast, another study, conducted within a neonatal screening and recall framework, reported a considerably higher median SUIC value of 279 µg/L and a high prevalence of iodine excess (61.2%) among newborns. These discrepancies likely reflect differences in study design, sample characteristics, and perinatal iodine exposure rather than true regional shifts in iodine status[18]. A study of 48 newborns in Tehran, Iran, reported an adequate median urinary iodine concentration (271 µg/L). However, CH was excluded from that study[25]. Unlike other studies conducted in this region, the current study included newborns with CH.

Iodine status groups differed significantly with respect to birthweight, BMI, and TSH levels. (p=0.03, p=0.023, p=0.031, respectively). The birth weight of infants with excess iodine was higher than that of infants in the other groups. Vural et al.[24], similarly reported that newborns with lower birthweight were at a higher risk of iodine deficiency. The observation indicated that the potential risk of iodine deficiency in newborns with a birthweight <3000 g was increased 1.47-fold (47%) compared to those with a birthweight >3600 g. In a study conducted in Spain, the highest median birthweight was observed in infants born to mothers with adequate SUIC values in the first or third trimester[26]. The TSH values differed significantly by iodine status. The median TSH level in the iodine-deficient group was 8.05 (3.85-13.17) µIU/mL; although this value was not low in absolute terms, it was relatively lower than in the adequate and iodine-excess groups. This observation may be attributed to the compensatory increase in T3 production, which maintains euthyroidism and suppresses TSH secretion even when T4 levels and iodine stores are low[27]. In contrast, the higher TSH levels observed in the iodine-excess group may reflect transient thyroid autoregulatory inhibition, known as the Wolff-Chaikoff effect, thereby increasing TSH concentrations. Furthermore, the neonatal thyroid gland exhibits unique regulatory characteristics, and the residual influence of maternal iodine status during the first month of life may modulate thyroid function test results. In another study examining the thyroid status of newborns with iodine deficiency in the same city as the present study, the TSH level was 5.4 (0.63-41.8) µIU/mL, which is similar to the TSH level in the iodine-deficiency group of the present study[28]. However, the previous study evaluated only infants with iodine deficiency, whereas the current study evaluated infants across all iodine statuses.

When SUIC was analyzed by thyroid dysfunction, no substantial differences were observed among the three groups in this study (CH, subclinical, and euthyroid); however, the highest numerical SUIC value was observed in newborns with CH. In a study conducted in the USA, blood iodine concentrations measured immediately after birth in infants with CH did not differ significantly from those of control-group infants. The lack of difference was attributed to the presence of newborns in the intensive care unit[29]. The same result was seen in the present study; however, there was no history of hospitalization, and iodine was measured in urine.

Study Limitations

This study has several limitations. First, it was conducted at a single endocrine center and included a limited number of newborns; therefore, the findings cannot be generalized to the entire country. Second, maternal iodine status and dietary intake were not evaluated. Additionally, BMI during the first month of life may be influenced by early postnatal fluid shifts and technical challenges in neonatal length measurement, potentially reducing its precision for neonatal assessment. To reduce potential bias, BMI was expressed as WHO-standardized SD scores rather than raw values, allowing comparability with internationally recognized growth references.

Despite these limitations, a major strength of the study is that detailed anthropometric measurements were obtained for all newborns that serum thyroid function tests were evaluated simultaneously with urinary iodine measurements. This comprehensive approach enabled us to assess the relationship between iodine status and CH, subclinical hypothyroidism, and euthyroidism.

Conclusion

Although the mean SUIC values in the newborns were normal, the number with iodine deficiency was higher. Although preventive measures have been taken against iodine deficiency, the results of this study demonstrate that there is still a high rate of iodine deficiency in newborn infants. This demonstrates the importance of the iodine supplementation program and the need to update it at regular intervals. Another important finding of this study was that approximately one-fifth of the cases had excessive iodine. This should be kept in mind as another possible cause of TSH elevation.

Ethics

Ethics Committee Approval: This study was approved by the Ethics Committee of Clinical Research at the Faculty of Medicine, Erciyes University (approval no: 2021/567, date: 08.09.2021).

Informed Consent: Because the study was designed retrospectively no written informed consent form was obtained from the patients.

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Footnotes

Author Contributions: Acıkan H: Concept, Design, Data Collection or Processing, Analysis or Interpretation, Literature Search, Writing; Hatipoğlu N: Surgical and Medical Practices, Analysis or Interpretation, Writing; Muhtaroğlu S: Concept, Design.

Conflict of Interest: The authors declare no conflicts of interest.

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