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Assessment of Iodine Status in a Referral-Based Euthyroid Adult Population in Aydın Province: Spot Urinary Iodine Concentration, Iodine/Creatinine Ratio, and Serum Thyroglobulin Levels

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ABSTRACT

Objective: To assess iodine status in adults with euthyroid in Aydın province using spot urinary iodine concentration (UIC) and the urinary iodine-to-creatinine (I/Cr) ratio and to evaluate the relationship between serum thyroglobulin (Tg) and iodine status.

Methods: This retrospective study included 162 euthyroid and anti-Tg-antibody-negative adults evaluated between 2023 and 2025, with simultaneous spot UIC, urinary creatinine, and serum Tg measurements. Participants were classified per World Health Organization (WHO) criteria as iodine-deficient (UIC <100 µg/L) or iodine-sufficient (UIC ≥100 µg/L). Serum Tg was compared between groups using the Mann–Whitney U-test, and its relationship with UIC and the I/Cr ratio was assessed by Spearman correlation.

Results: Of the 162 participants, 123 (75.9%) were iodine-deficient and 39 (24.1%) were iodine-sufficient; median UIC and serum Tg for the whole group were 63.0 µg/L and 13.27 ng/mL, respectively. Median serum Tg was significantly higher in the iodine-deficient group than in the iodine-sufficient group (15.11 vs 9.49 ng/mL; U = 1807.5, *P* = .021). Serum Tg showed weak but significant negative correlations with both spot UIC (rho = –0.184, *P* = .019) and the I/Cr ratio (rho = –0.205, *P* = .009).

Conclusion: Despite weak individual-level correlations with urinary iodine measures, serum Tg was significantly elevated in iodine-deficient participants, supporting its potential role as a population-level biomarker of iodine status rather than an individual diagnostic tool. Given the lack of validated Tg reference values for adults, these findings underscore the need for locally derived thresholds and further validation in larger, prospective cohorts.

Keywords: Biomarker, creatinine ratio, iodine deficiency, iodine, spot urinary iodine concentration, thyroglobulin

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INTRODUCTION

Iodine is an essential trace element for the synthesis of thyroid hormones (triiodothyronine and thyroxine) and plays a critical role in normal growth and neurodevelopment. Both iodine deficiency and iodine excess can lead to thyroid dysfunction and disease.[1] Globally, iodine deficiency remains one of the most prevalent micronutrient deficiencies, affecting approximately one-third of the world's population. Even in countries where iodized salt policies are in place, regular monitoring of local populations is necessary due to variability in individual iodine intake.[2]

At the population level, the most widely used indicator for assessing iodine status is the measurement of spot urinary iodine concentration (UIC). Because approximately 90% of ingested iodine is excreted in the urine, UIC is a practical and readily applicable indicator reflecting recent iodine intake.[3] However, the use of UIC at the individual level has important limitations; due to intra- and inter-day variability in hydration status and iodine intake, a single spot measurement reflects only the preceding 24-48 hours

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of intake.[4] It has been reported that more than 10 repeated measurements are required to determine individual iodine status with 20% precision, which restricts feasibility in both clinical practice and large-scale studies.[5] The iodine-to-creatinine (I/Cr) ratio, corrected for urinary creatinine levels, aims to partially compensate for dilution effects arising from hydration; however, this approach carries its own limitations, as creatinine excretion is influenced by age, sex, muscle mass, and diet.[4,6]

Serum thyroglobulin (Tg) is a complementary functional biomarker recognized by the World Health Organization (WHO) for assessing iodine status at the population level.[2] Unlike spot UIC, Tg reflects nutritional iodine history extending weeks to months into the past and is less susceptible to day-to-day biological variability.[7] Importantly, the relationship between Tg and iodine intake is not linear but U-shaped, with elevated Tg observed at both low and high iodine intakes; therefore, a single Tg value should always be interpreted alongside urinary iodine measurements.[8]

A widely adopted Tg cutoff of approximately 13 ng/mL, indicating adequate iodine intake, was derived from a multinational study of school-age children and has since been used as a reference for population-based screening.[9] However, this pediatric-derived threshold has not been validated in adults, and whether it retains diagnostic relevance in this population remains unclear. Studies using repeated urine sampling have shown that Tg performs close to chance level as an individual-level predictor of iodine status,[10] suggesting its main utility lies at the population rather than the individual level.[11] Despite this recognized potential, adult-specific data validating Tg as a population biomarker particularly alongside direct urinary iodine indices remain scarce.

To the authors' knowledge, no locally derived data on iodine status in Aydın province are currently available in the literature. Although Aydın, situated on the Aegean coast, is a region where seafood consumption may be relatively high, the iodine status of the local population should be determined through direct measurement rather than assumption, given its urban–rural distribution, dietary diversity, and uncertain adherence to salt iodization. To the authors' knowledge, this study is the first to jointly evaluate spot UIC, the I/Cr ratio, and serum Tg in a euthyroid adult population, with the aim of defining the prevalence of iodine deficiency in Aydın province and assessing the relationship between serum Tg and iodine status at both the individual and group levels.

METHODS

Study Design and Participant Selection

This study is a single-center, observational, analytical, and cross-sectional study based on the retrospective review of records from the Biochemistry Laboratory of Aydin Adnan Menderes University Training and Research Hospital. Records of individuals who presented to the laboratory between 2023 and 2025 and for whom UIC, urinary creatinine, and serum Tg measurements were simultaneously available on a single request were reviewed.

Inclusion criteria were as follows: Thyroid-stimulating hormone (TSH) value within the normal reference range (0.27-4.2 mIU/L; euthyroid), negative anti-Tg antibody status (<115 IU/mL; Abbott Alinity i reference range), and age 18 years or older. Individuals with a known diagnosis of thyroid disease, those using medications affecting thyroid function (levothyroxine, antithyroid drugs, etc.), anti-Tg antibody-positive individuals, pregnant individuals, and records with missing data for any of the relevant laboratory parameters were excluded. A total of 162 individuals meeting these criteria were included in the study.

The study was approved by the Non-Interventional Clinical Research Ethics Committee of Aydin Adnan Menderes University (Approval No: 2026/245; Date: 22.06.2026).

Grouping was based solely on spot UIC. According to WHO criteria, individuals with a UIC <100 µg/L were classified as iodine-deficient, and those with UIC ≥100 µg/L as iodine-sufficient. The I/Cr ratio was not used for grouping purposes and was evaluated only as a secondary iodine indicator in the correlation analysis with Tg, as the WHO defines population-level iodine status classification exclusively on the basis of spot UIC, and no internationally accepted threshold value exists for the I/Cr ratio.

Laboratory Measurements and Analytical Methods

Serum Tg and anti-Tg levels were measured by chemiluminescent microparticle immunoassay (CMIA) using the Abbott Alinity i automated analyzer (Abbott Laboratories, Abbott Park, IL, USA). The lower limit of detection (LoD) and limit of quantification (LoQ) for the serum Tg assay were 0.09 ng/mL and 0.14 ng/mL, respectively. Spot urinary iodine concentrations were measured by an external laboratory using inductively coupled plasma mass spectrometry (ICP-MS). Urine samples were stored at 2-8°C for 2-3 days prior to being transported to the external laboratory under a cold chain. The intra-assay and inter-assay coefficients of variation (CV%) for the ICP-MS method were 1.43% and 5.46%, respectively. Urinary creatinine concentrations were measured using the Creatinine2 assay on an Alinity c automated clinical chemistry analyzer (Abbott Laboratories, Abbott Park, IL, USA), part of the Alinity ci-series platform. The assay employs a kinetic alkaline picrate method (modified Jaffé method), in which creatinine reacts with picric acid under alkaline conditions and the rate of formation of the creatinine–picrate complex is measured photometrically at 500 nm.

For each individual, spot UIC (µg/L), urinary creatinine level (g/L), I/Cr ratio (µg/g), and serum Tg level (ng/mL) were recorded. The urinary I/Cr ratio was calculated by dividing spot UIC by urinary creatinine.

Statistical Analysis

The conformity of data to a normal distribution was assessed using the Shapiro–Wilk test. Categorical variables were presented as frequency and percentage (%), and between-group comparisons were performed using the chi-square test with Yates' continuity correction for 2×2 tables. Continuous variables not conforming to a normal distribution were expressed as median and interquartile range [Q1-Q3]. Median serum Tg levels between the iodine-sufficient and

Main Points

- *In a cohort of 162 euthyroid adults in Aydın province, 75.9% were iodine-deficient (UIC < 100 µg/L) based on spot urinary iodine concentration.*
- *Serum thyroglobulin (Tg) was significantly higher in iodine-deficient participants than in iodine-sufficient ones (median 15.11 vs. 9.49 ng/mL; p = 0.021), despite only weak correlations with individual UIC and I/Cr ratio (rho = −0.184 and −0.205, respectively).*
- *These findings suggest serum Tg reflects iodine status at the population/group level rather than the individual level, supporting its use as a complementary biomarker alongside UIC.*

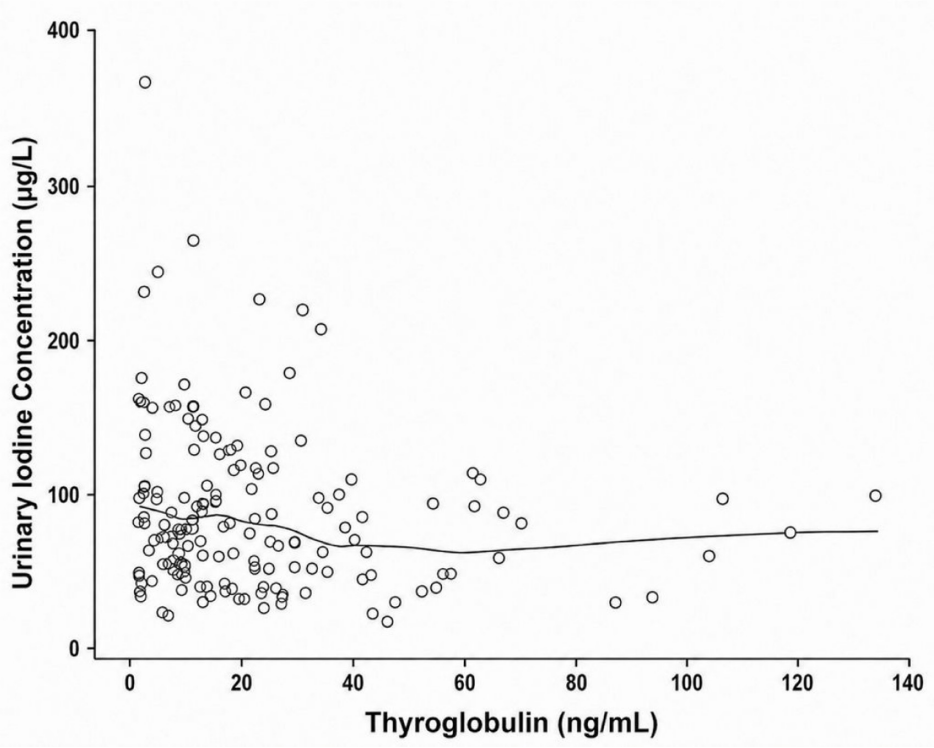

Figure 1. Scatter plot illustrating the relationship between Tg level and urinary iodine concentration. Each dot represents 1 individual. The curve was obtained using the LOESS (locally weighted scatterplot smoothing) method with 50% of the observations included in each local fit (span = 0.50) and the Epanechnikov kernel to visualize the potential non-linear trend in the data.

iodine-deficient groups were compared using the Mann–Whitney *U*-test. The relationship between serum Tg level and both spot UIC and I/Cr ratio was evaluated by Spearman rank correlation analysis. The locally weighted scatterplot smoothing (LOESS) curve presented in Figure 1 was generated using 50% of the observations in each local fit (span = 0.50) and the Epanechnikov kernel. Polynomial degree was not a user-selectable parameter in the SPSS Chart Editor and was therefore not independently specified. The curve was used only for descriptive visualization. The threshold for statistical significance was set at $P < .05$. All analyses were performed using SPSS 22.0 statistical software (IBM Corp., Armonk, NY, USA).

RESULTS

A total of 162 individuals meeting the inclusion criteria were analyzed. The median spot UIC of the study group was 63.0 µg/L and the median serum Tg level was 13.27 ng/mL. The demographic and clinical characteristics of the study group are presented in Table 1.

Table 1. Demographic and Clinical Characteristics of the Study Group

Variable	All Participants (N = 162)	Iodine Deficient (n = 123)	Iodine Sufficient (n = 39)	*P*
Sex, Female, n (%)	130 (80.2%)	99 (80.5%)	31 (79.5%)	1.000
Age (years), median [Q1-Q3]	46 [38-54]	46 [39-54]	45 [34-52]	.329

Chi-square test with Yates' continuity correction was used for the sex comparison; Mann–Whitney *U*-test was used for the age comparison.

Of the participants, 123 (75.9%) were classified as iodine-deficient (UIC <100 µg/L) and 39 (24.1%) as iodine-sufficient (UIC ≥100 µg/L). Because Tg levels did not conform to normal distribution, non-parametric methods were used for between-group comparisons. Median Tg levels were 15.11 [6.80-33.25] ng/mL in the iodine-deficient group and 9.49 [2.71-18.84] ng/mL in the iodine-sufficient group; the difference between the 2 groups was statistically significant ($P = .021$) (Table 2).

A weak but statistically significant negative correlation was found between serum Tg and spot UIC. Similarly, a weak but significant negative correlation was observed between serum Tg and the I/Cr ratio, with a coefficient similar in magnitude to that obtained with spot UIC (Table 3).

The relationship between serum Tg and spot UIC is illustrated in Figure 1. The LOESS curve in the scatter plot, generated using a span of 0.50 and the Epanechnikov kernel, displays a slight trend suggesting that the relationship may not be linear (Figure 1).

DISCUSSION

In this study, the relationship between iodine status and serum Tg was evaluated in a euthyroid adult population. It was found that the

Table 2. Comparison of Serum Thyroglobulin Levels According to Iodine Status

Urinary Iodine Level	n	Tg, median [Q1-Q3]	*P*
<100 µg/L (iodine-deficient)	123	15.11 [6.80-33.25]	.021
≥100 µg/L (iodine-sufficient)	39	9.49 [2.71-18.84]	

Mann-Whitney $U = 1807,5$; $Z = -2,315$.

Table 3. Correlation Between Serum Thyroglobulin Level and Urinary Iodine Indicators

Variable	n	Spearman rho	*P*
Tg – spot UIC	162	−0.184	.019
Tg – I/Cr ratio	162	−0.205	.009

Spearman rank correlation test was used in the correlation analysis.

majority of the study group (75.9%) fell within the iodine-deficient category, that median Tg levels in iodine-deficient individuals were significantly higher compared to iodine-sufficient individuals (15.11 ng/mL vs 9.49 ng/mL), and that serum Tg showed a weak but significant negative correlation with spot UIC and the I/Cr ratio at the individual level.

The median UIC of the study group (63.0 µg/L) indicates that iodine deficiency is prevalent among the euthyroid adults included in the study. Although iodine status has generally improved following the mandatory salt iodization program initiated in Türkiye in 1998, marked regional and demographic disparities and mild-to-moderate deficiencies persist.[12,13] Ozpinar et al[14] reported median urinary iodine levels of 77.5 µg/L in Istanbul, 58.8 µg/L in Isparta, and 69.8 µg/L in Kayseri in a study conducted among non-pregnant adult women in 3 different cities, identifying mild iodine deficiency in all 3 settings. These findings demonstrate that regional iodine deficiency persists in adult populations in Türkiye despite the mandatory iodization policy. In contrast, Karpuzoğlu et al[15] reported a median UIC of 122 µg/L in the Turkish adult population and concluded that the community was iodine-sufficient, and a recent cross-sectional study by Memiç-İnan et al[13] conducted in Amasya likewise found adequate iodine levels in the majority of adult participants. The median UIC of 63.0 µg/L in the study group, with 75.9% of individuals falling within the iodine-deficient category, indicates a markedly lower iodine status than the values reported in these studies. This discrepancy most likely stems from the fact that this study encompasses a laboratory-referral-based sample rather than a community-based one; individuals presenting with simultaneous requests for UIC, creatinine, and Tg may represent a group in whom there is clinical suspicion regarding thyroid function or nutritional status, and therefore a selection bias toward iodine deficiency cannot be excluded. Taken together, these data suggest that while iodine sufficiency has been largely achieved in school-age children at the national level, deficiency persists in adults, particularly in certain regions. Indeed, the Europe-wide mapping study conducted within the framework of the EUthyroid project highlighted that iodine deficiency is more prevalent in adult populations than in school-age children across many countries, including Türkiye, and that this group should be addressed as a priority in surveillance programs.[16]

The significant difference in Tg observed between the iodine-deficient and iodine-sufficient groups supports the capacity of Tg to discriminate iodine status at the group level, consistent with numerous studies in the literature.[6,9,17] However, the weak correlation coefficients at the individual level (rho = −0.184 for Tg–UIC; rho = −0.205 for Tg–I/Cr) demonstrate that the use of Tg for individual diagnostic purposes is limited, in agreement with the review by Ma and Skeaff[17] encompassing 12 observational adult studies, and consistent with the confounding factors identified by Krejbjerg et al[3] in the large-scale DanThyr cohort study—age, sex, smoking status, thyroid nodularity, and anti-Tg positivity. Notably, the median Tg value of the study group (13.27 ng/mL) nearly coincides with the 13 ng/mL threshold derived from school-age children by Zimmermann et al[9], which has not been validated in adult populations. While this coincidence may suggest that the population sits at the borderline between deficiency and sufficiency, whether it is biologically meaningful or incidental cannot be determined with the available data, underscoring the need for adult-specific, age- and sex-standardized Tg reference ranges.

The correlation coefficient between the I/Cr ratio and Tg (rho = −0.205) was numerically similar to that obtained with spot UIC (rho = −0.184). Given the small magnitude of this difference, and in the absence of a formal statistical comparison of dependent correlation coefficients, it cannot be concluded that creatinine correction meaningfully reduces hydration-related variability in the dataset; this difference should be regarded as exploratory rather than confirmatory. This interpretation is further constrained by the fact that the WHO defines population-level iodine deficiency exclusively on the basis of spot UIC, with no internationally accepted threshold for the I/Cr ratio[2]; the I/Cr threshold used in the study is therefore an adaptation from the literature with limited direct comparability to the WHO criterion, and creatinine correction of spot urine samples is not consistently superior to UIC alone.[16,18] Krejbjerg et al[3] reported that estimated 24-hour urinary iodine excretion was a stronger predictor of Tg than spot UIC in adult cohorts, underscoring the inadequacy of single spot measurements in fully capturing individual iodine status and its relationship with Tg.

The relationship between Tg and iodine is known to be U-shaped; however, only 1 individual in the study group had a UIC ≥300 µg/L, making it impossible to evaluate the right arm of this relationship (i.e., the rise in Tg with excessive iodine intake).[19] The LOESS curve in the scatter plot displayed a slight non-linear trend, but the very small number of individuals with high iodine levels precluded a clear demonstration of the U-shaped pattern described in the literature. Therefore, the negative correlation observed in the population largely reflects the deficiency-to-sufficiency range, and larger, more balanced samples including individuals with excessive iodine intake will be needed to confirm the U-shaped relationship.

This study has several limitations. First, as the study is retrospective and cross-sectional in design, causal relationships cannot be established. Second, as noted above, the laboratory-referral-based nature of the sample may have introduced a selection bias toward iodine deficiency, limiting generalizability to the general adult population of Aydın province. Third, the single-time collection of spot urine samples means that individual iodine status may have been influenced by day-to-day variability, a limitation frequently emphasized in the literature. Fourth, the sample size (N = 162) remained limited, particularly in the iodine-sufficient subgroup (n = 39), which may have restricted statistical power and complicated the interpretation of subgroup analyses. Finally, although age and sex were available and did not differ significantly between groups (Table 1), the absence of detailed data on other variables that may influence Tg levels such as smoking status, thyroid nodularity, and dietary habits precluded multivariable analysis.

CONCLUSION

In conclusion, the findings indicate that serum Tg may serve as a useful complementary biomarker for monitoring iodine status at the population level, particularly in settings where iodine deficiency remains prevalent among euthyroid adults. Given the absence of validated, adult-specific Tg reference ranges, prospective, community-based

studies accounting for relevant confounders are needed to confirm its clinical utility.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: Ethical committee approval was received from the Non-Interventional Clinical Research Ethics Committee of Aydin Adnan Menderes University (Approval No: 2026/245; Date: 22.06.2026).

Informed Consent: Patient consent was waived due to the retrospective design of the study.

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