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Correlation of thyroid hormones with levels of iron and selenium in women with hypothyroidism in Basrah, Iraq

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ABSTRACT

Introduction and aim. Trace elements play a critical role in thyroid hormone synthesis and metabolism; however, data on their combined alterations in hypothyroid women from the Middle East remain limited. This study aimed to evaluate the relationship between serum selenium (Se) and iron (Fe) levels and thyroid function in women with overt and subclinical hypothyroidism compared with euthyroid controls.

Material and methods. In this case-control study, 312 women were enrolled, including 194 patients with hypothyroidism and 118 age- and body mass index-matched euthyroid controls recruited in Basra, Iraq. Serum thyroid-stimulating hormone (TSH), free thyroxine (FT4), iron (Fe), and Se were measured using standardized automated assays.

Results. Hypothyroid women had significantly higher median thyroid-stimulating hormone levels than controls (4.51 [1.9–7.5] vs. 1.45 [0.98–2.1] mU/L; $p<0.0001$) and lower median free thyroxine concentrations (12.48 [9.0–16.47] vs. 16.73 [14.16–20.59] pmol/L; $p<0.0001$). Serum iron levels were significantly reduced in hypothyroid patients (11.52 [7.79–15.83] vs. 15.90 [10.47–19.42] $\mu\text{mol/L}$; $p<0.0001$), as were selenium levels (0.81 [0.55–1.12] vs. 1.45 [1.18–1.92] $\mu\text{mol/L}$; $p<0.0001$). Age correlated positively with thyroid-stimulating hormone (Spearman's $\rho=0.449$, $p<0.001$) and negatively with free thyroxine ($\rho=-0.301$, $p=0.007$), while no significant correlations were observed for iron or selenium.

Conclusion. Women with hypothyroidism exhibited combined selenium and iron deficiencies alongside marked hormonal disturbances. To our knowledge, this is one of the first large case-control studies in women from southern Iraq to simultaneously assess selenium and iron status in relation to thyroid function.

These findings support the potential clinical relevance of routine micronutrient assessment in hypothyroid patients, particularly in regions with known dietary deficiencies.

Keywords. hypothyroidism, iron, selenium, trace elements, women

Introduction

Hypothyroidism is an endocrine disorder characterized by a severe reduction in circulating thyroid hormones. Common etiologic factors include autoimmune thyroid disease, thyroidectomy, or therapeutic iodine radiotherapy. Even in iodine-replete regions, prevalence may reach 11.7%.^{1,2} Epidemiological data on thyroid disorders in the Middle East are limited and largely anecdotal; however, Basra is considered a highly endemic area, with local findings indicating a particularly high prevalence of hypothyroidism among women.³ Thyroid hormones are essential for numerous physiological processes, including thermoregulation, carbohydrate, protein and lipid metabolism, electrolyte balance, and mineral homeostasis.⁴ Among the micronutrients implicated in thyroid function, selenium (Se) and iron (Fe) are indispensable for thyroid hormone synthesis and metabolism.⁵

Although the total selenium content of the human body is relatively small (10–20 mg), the thyroid gland contains one of the highest concentrations per gram of tissue, reflecting its strong dependence on selenoproteins (SePs) for normal function.^{6,7} During thyroid hormone synthesis, hydrogen peroxide (H_2O_2) is required as an oxidizing agent for iodination. However, excessive H_2O_2 – particularly in the context of iodine deficiency and elevated TSH – can lead to oxidative injury of thyrocytes. Selenium-dependent enzymes, including glutathione peroxidases (GPxs) and thioredoxin reductases (TRs), function as key thiol-redox systems that neutralize H_2O_2 and lipid hydroperoxides, thereby maintaining cellular membrane integrity and limiting oxidative damage.⁸

The GPx family consists of several isoenzymes (GPx1–GPx6). GPx1 is abundant in the cytosol and reduces H_2O_2 and free hydroperoxides, while GPx3 and GPx4 are particularly relevant within the thyroid gland. GPx3 acts extracellularly, whereas GPx4 (phospholipid hydroperoxidase) regulates phospholipid and cholesterol hydroperoxide reduction, contributing to membrane stability and apoptotic control.⁹ Through these mechanisms, selenium plays a central role in antioxidative and inflammation-protective defense. Insufficient selenium intake decreases GPx activity, weakens antioxidative capacity, and increases the risk of thyrocyte injury and apoptosis. Additionally, selenium is required as a cofactor for iodothyronine deiodinases, which convert thyroxine (T_4) to the biologically active triiodothyronine (T_3), supporting normal thyroid hormone metabolism and protecting the gland from oxidative stress.^{10,11} According to the World Health Organization, the recommended daily selenium intake for adults is 55 μg .¹²

Selenium availability varies considerably worldwide. Selenium-rich soils are found in regions such as Australia, Ireland, and North America, whereas large areas of Europe, New Zealand, and China are selenium-poor. Importantly, several Middle Eastern countries, including Iraq, have been reported to exhibit

low-to-moderate selenium intake due to poor soil selenium content, potentially predisposing their populations to marginal selenium deficiency and altered thyroid hormone metabolism.¹³

Iron is also essential for normal thyroid function. It acts as a cofactor for thyroid peroxidase (TPO), the heme-containing enzyme that catalyzes iodination and coupling reactions during thyroid hormone synthesis. Iron deficiency reduces TPO activity, thereby impairing the production of thyroid hormones. Furthermore, as a key component of hemoglobin, iron supports oxygen delivery to tissues and participates in multiple enzymatic pathways essential for cellular metabolism. Iron deficiency may also diminish erythropoiesis and decrease erythropoietin secretion, further contributing to impaired thyroid hormone synthesis.¹⁴ Despite the established role of selenium and iron in thyroid hormone metabolism, data on their simultaneous alterations in women with hypothyroidism from the Middle East remain scarce. To our knowledge, this is one of the first studies in southern Iraq to jointly evaluate selenium and iron status in relation to thyroid function in a large female case–control cohort.

Aim

The aim of this study was to assess the relationship between serum selenium and iron levels and thyroid function in women with overt and subclinical hypothyroidism compared with euthyroid controls, addressing the lack of data from the Middle Eastern population.

Material and methods

Study design and subjects

The present retrospective case-control study was organized at the Faiha Specialized Diabetes, Endocrine, and Metabolism Center (FDEMC) laboratories in Basra, Southern Iraq, from November 2024 to May 2025.

Ethical approval

The study was approved by the Institutional Review Board of the College of Pharmacy, University of Basrah (Approval No. EC 81, dated 10/11/2024). Written informed consent was obtained from all participants prior to study enrollment.

Participants and eligibility criteria

Enrollment included women clinically diagnosed with primary and subclinical hypothyroidism, as established through clinical evaluation and laboratory tests for thyroid function, particularly serum FT4 levels and TSH concentrations. A control group of euthyroid women has been established to enable comparative analyses. The participants were selected based on predefined eligibility criteria as follows:

Inclusion criteria

- Women aged 18–78 years, covering both the reproductive period and the menopausal transition, which may influence thyroid function and mineral metabolism.
- Clinically diagnosed primary (overt) hypothyroidism, defined as:
 - TSH > 4.2 mU/L
 - FT4 < 12 pmol/L
- Clinically diagnosed subclinical hypothyroidism, defined as:
 - TSH > 4.2 mU/L
 - FT4 within the normal reference range (12.0–21.9 pmol/L)
- Reference ranges (manufacturer instructions):
 - TSH: 0.27–4.2 mU/L
 - FT4: 12.0–21.9 pmol/L

Exclusion criteria

Participants were excluded if they had any of the following:

- other thyroid diseases (e.g., autoimmune thyroid disorders such as Hashimoto's thyroiditis), excluded based on review of available medical records
- major systemic conditions (e.g., diabetes mellitus, chronic kidney disease),
- use of hormonal contraceptives or any nutritional supplements (e.g., selenium, iron, multivitamins),
- smoking,
- malabsorption syndromes,
- pregnancy,
- other endocrine disorders,
- lack of consent to participate.

Levothyroxine treatment status was recorded descriptively and was not used as an exclusion criterion.

A summary of the selection process is presented in Figure 1.

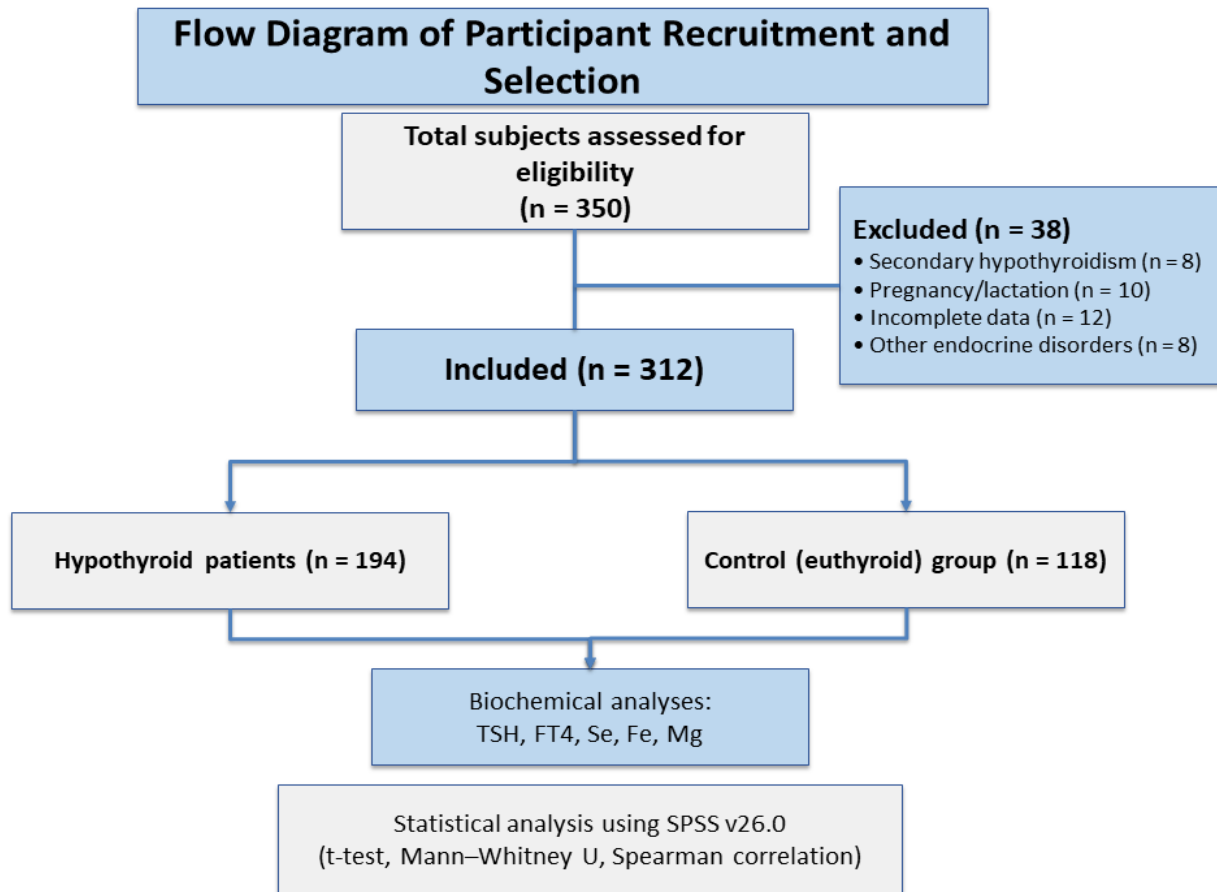


Fig. 1. Flow diagram of participant recruitment and selection process

Dietary and lifestyle considerations

To minimize dietary and lifestyle confounding, women taking any nutritional supplements (selenium, iron, or multivitamins) were excluded, and all participants were recruited from the same geographical and socioeconomic background. Dietary intake and lifestyle behaviors were not quantitatively assessed and are acknowledged as a methodological limitation; however, the shared environmental and cultural dietary patterns of the study population help reduce major variability in selenium and iron intake.

Sample size calculation

Sample size was calculated based on expected differences in serum selenium and iron levels between hypothyroid and euthyroid women, assuming an effect size of $d=0.35$ – 0.40 , $\alpha=0.05$, and power= 0.90 .¹⁵ A structured questionnaire was administered to collect demographic information, including questions on nutritional habits, socioeconomic status, medication use, and family history.

Blood collection and biochemical measurements

Following a 12-hour period of overnight fasting, a venous blood sample of approximately 5 mL was taken from all patients and controls under strict aseptic conditions and transferred to a sterile yellow top gel tube. Blood samples were allowed to clot and centrifuged at 5000 rpm for 5 minutes to obtain serum. Serum was isolated and preserved at -20°C till examination.

Thyroid hormone measurements

Serum thyroid hormones (FT4 and TSH) were computed via electrochemiluminescence immunoassay using a cobas e411 analyzer (Roche Diagnostics, Germany).¹⁶

Trace-element measurements

Serum iron was quantified in vitro on the Roche/Hitachi Cobas C311 system (Roche Diagnostics, Germany) through a Ferrozine colorimetric endpoint by using IronGen.2 reagents, where the absorbance at 570 nm is directly related to iron concentration.^{17,18}

Serum selenium was determined using a colorimetric assay (Elabscience®, Cat. No. E-BC-K776-M, China) according to the manufacturer's protocol. Selenium Assay Validation and Performance – The assay was performed on a microplate reader at 420 nm (range 415–425 nm). Intra- and inter-assay precision coefficients of variation (CV) were 0.3–0.4% and 0.5–0.7%, respectively, and mean recovery was 103.7%. A colorimetric method was selected due to its validated analytical performance—adequate sensitivity for physiological selenium levels, excellent precision (CV <1%), and high recovery—while being fully compatible with our laboratory workflow and high-throughput processing. Selenium concentrations were reported in SI units (μmol/L) and were consistent with the Results section.

Statistical analysis

Data were processed with SPSS, version 26.0 (IBM, Armonk, NY, USA). Normality was tested by Kolmogorov-Smirnov test. Quantitative variables were presented as mean±SD for normally distributed ones or median (Q1–Q3) for those not following a normal distribution. Baseline differences of means were examined using an independent-samples t-test or Mann-Whitney U test as appropriate, and for categorical variables, the Chi-square (χ^2) test was used. Associations were tested using Spearman's rank-correlation coefficient (ρ). Statistical significance was set at a two-tailed $p < 0.05$. Graphs were made on GraphPad Prism, version 8 (USA).

Results

Demographic, reproductive, and anthropometric characteristics of the study population

A total of 312 women, including 118 controls and 194 hypothyroid patients, were included in a retrospective analysis. Baseline characteristics are shown in Table 1.

The two populations did not differ for a common age; the median ages were 41 and 43.5 years respectively ($p=0.446$), confirming that the groups were age-matched. With respect to residence distribution, for hypothyroid women, more lived in city areas (71.6%) than controls (61.8%); however, the difference was not significant ($p=0.08$).

Income status differed markedly between groups ($p<0.0001$): low-income individuals were more frequent among hypothyroid cases (42.2%) than among controls (16.9%), while high-income participants were fewer (7.2% vs. 18.6%, respectively).

Marital status did not vary significantly ($p=0.614$); most participants in both groups were married, and the proportions of single, divorced, and widowed women were comparable. Irregular and menopausal cycles were markedly more frequent in the hypothyroid group, and amenorrhea occurred exclusively among hypothyroid patients (11.9%). Childbearing history also differed significantly ($p=0.0004$), as nearly all controls had given birth (97.5%) compared with 85% of hypothyroid women.

Anthropometric data were largely comparable between groups. Median height was 1.59 m in both ($p=0.489$). The mean body weight tended to be higher in hypothyroid patients (79.5 ± 18.4 kg) than controls (75.3 ± 18.1 kg), though the difference narrowly missed statistical significance ($p=0.051$). Similarly, BMI values were slightly higher among hypothyroid women (31.5 ± 6.7 kg/m²) than controls (29.8 ± 5.3 kg/m², $p=0.117$).

Among hypothyroid patients, the median disease duration was 5 years (range: 2–8 years). Approximately half (49.5%) reported a family history of thyroid disease, a rate significantly higher than in controls (0%; $p<0.0001$), suggesting a potential familial or genetic predisposition. Regarding levothyroxine therapy, most patients (61.3%) were receiving 50 µg daily, 32.5% were on 100 µg daily, 4.1% were taking 50 µg twice daily, and 2.1% had discontinued treatment.

Table 1. Demographic and clinical characteristics of the study participants*

Variable	Control (n=118)	Hypothyroid (n=194)	p
Sociodemographic data			
Age (years), median (range)	41 (26–55)	43.5 (30–58)	0.446
Residence, n (%)	Urban 73 (61.86 %)	Urban 139 (71.6 %)	0.08
	Rural 45 (38.14 %)	Rural 55 (28.3 %)	

Income status, n (%)	Low 20 (16.94 %)	Low 82 (42.2 %)	<0.0001
	Medium 76 (64.4 %)	Medium 98 (50.5 %)	
	High 22 (18.64 %)	High 14 (7.2 %)	
Marital status, n (%)	Single 12 (10.16%)	Single 31 (15.9%)	0.614
	Married 96 (81.35%)	Married 133 (68.5%)	
	Divorced 0 (0%)	Divorced 4 (2%)	
	Widow 10 (8.47%)	Widow 26 (13.4%)	
Reproductive characteristics			
Cycle status, n (%)	Regular 59 (50 %)	Regular 18 (9.3 %)	<0.0001
	Irregular 21 (17.79 %)	Irregular 75 (38.6 %)	
	Menopause 38 (32.2 %)	Menopause 78 (40.2 %)	
	Amenorrhea 0 (0 %)	Amenorrhea 23 (11.8 %)	
Childbearing, n (%)	Yes 115 (97.46 %)	Yes 165 (85 %)	0.0004
	No 3 (2.54 %)	No 29 (14.9 %)	
Anthropometric data			
Height (m), median (range)	159 (1.54–1.64)	1.59 (1.55–1.63)	0.489
Weight (kg), mean±SD	75.3±18.1	79.5±18.4	0.051
BMI (kg/m ²), mean±SD	29.75 ± 5.3	31.54 ± 6.7	0.117
Disease-related data			
Duration of disease (years), median (range)	–	5.0 (2.0–8.0)	–
Family history of disease, n (%)	No 118 (100 %)	Yes 96 (49.4 %) No 98 (50.5 %)	<0.0001
Levothyroxine therapy, n (%)			
50 µg 1×1	–	119 (61.3 %)	–
50 µg 1×2	–	8 (4.1 %)	–
100 µg 1×1	–	63 (32.4 %)	–
Discontinued	–	4 (2.0 %)	–

* Data were tested for normality using the Kolmogorov–Smirnov test; normally distributed data are presented as mean±SD and non-normal data as median [interquartile range, IQR], comparisons were performed using the t-test, Mann–Whitney U, Chi-square, or Fisher’s exact test, as appropriate

Comparison of biochemical and clinical parameters between control and patient groups

Descriptive and comparative analyses were conducted for serum TSH, FT4, Fe, and Se across the control and hypothyroid groups. As the data were not normally distributed, intergroup comparisons were performed using the Mann-Whitney U test, and differences were considered statistically significant at $p < 0.05$.

Hypothyroid patients showed a significant increase in TSH levels compared to the control group ($p < 0.0001$), which was associated with a large effect size ($r = 0.50$, CI: 2.1–3.4). In contrast, the concentration of FT4 was significantly lower in the hypothyroid group ($p < 0.0001$), with a large effect ($r = -0.7$, 95% CI: -7 to -2.8). In addition, serum levels of iron and selenium were significantly decreased in hypothyroid patients compared with controls ($p < 0.0001$). Reduction in Fe showed a moderate effect size ($r = 0.36$, 95% CI: -4.8 to -1.8), while that of Se was high ($r = 0.64$, 95% CI: -0.78 to -0.56).

A comprehensive summary of these findings is presented in Table 2.

Table 2. Comparison of TSH, FT4, iron, and selenium levels between control and patient groups*

Parameter	Control (Median [IQR])	Patient (Median [IQR])	p	Effect size (r)	95% CI of difference
TSH (mU/L)	1.45 (0.98–2.1)	4.51 (1.9–7.5)	<0.0001	0.5	2.10 to 3.40
FT4 (pmol/L)	16.73 (14.16–20.59)	12.48 (9.0–16.47)	<0.0001	0.7	-7.00 to -2.80
Fe ($\mu\text{mol/L}$)	15.90 (10.47–19.42)	11.52 (7.79–15.83)	<0.0001	0.36	-4.80 to -1.80
Se ($\mu\text{mol/L}$)	1.45 (1.18–1.92)	0.81 (0.55–1.12)	<0.0001	0.64	-0.78 to -0.56

* Values are expressed as median [interquartile range, IQR], statistical significance between groups was assessed using the Mann–Whitney U test, effect sizes (r) were interpreted as small (0.10–0.29), moderate (0.30–0.49), or large (≥ 0.50)

The pattern of the results is also represented by comparison in Figure 2, showing trends toward hormonal and biochemical changes between study groups. The graph presents an evident negative relationship between thyroid function and trace-element status. Error bars represent the interquartile range, reflecting variability within each group, particularly the wider dispersion of TSH levels among hypothyroid patients, consistent with differences in disease severity and treatment status.

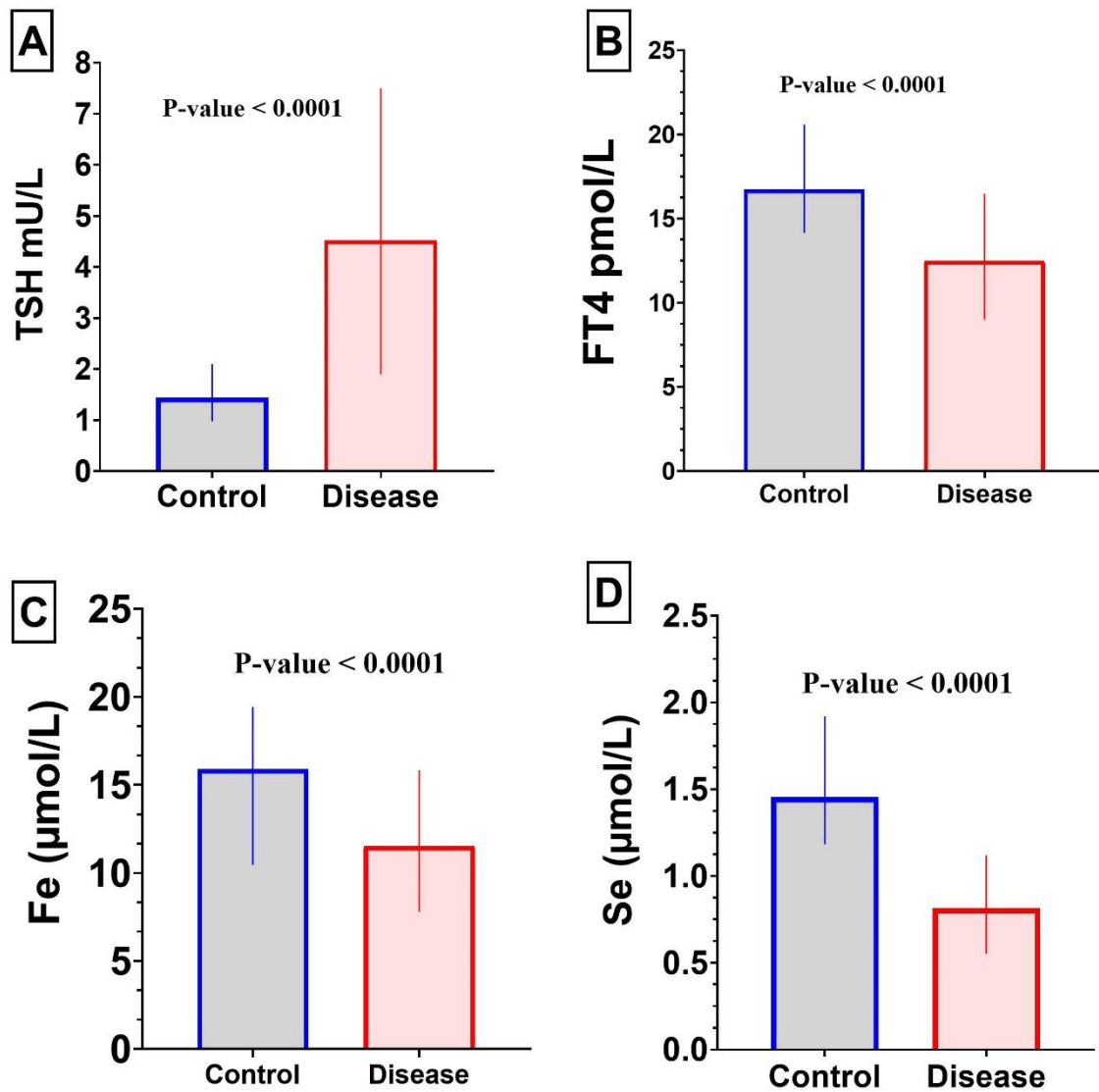


Fig. 2. Comparative visualization of (A) TSH, (B) FT4, (C) iron, and (D) selenium levels in hypothyroid patients and control subjects, values are expressed as median (interquartile range, IQR), and group comparisons were analyzed using the Mann-Whitney U test

Statistical correlation results between age and each biochemical parameter in the hypothyroid group

The correlation between age and various categories of biochemical parameters in hypothyroid patients was calculated by Spearman's rank correlation coefficient (ρ). As reported in Table 3, there was a statistically significant moderate positive correlation between age and serum TSH ($\rho=+0.449$, $p<0.001$), showing that also TSH increases with aging. This indicates that the severity of thyroid failure or the extent of pituitary input becomes more severe with increasing age.

Inversely, serum FT4 negatively correlated with age ($\rho=-0.301$, $p=0.007$), showing the decrease of T4 concentration in the bloodstream with aging.

Age was not associated with serum iron ($p=-0.068$, $p=0.559$) or selenium ($p=-0.152$, $p=0.187$). These results show that the trace-element status of hypothyroid patients is age-independent. The lack of correlation between serum levels of Fe and Se could indicate that changes are less influenced by age than by nutritional or pathological causes.

Table 3. Spearman's correlation between age and biochemical parameters in patients with hypothyroidism

Parameter	Spearman's ρ (Correlation coefficient)	p	Interpretation
TSH (mU/L)	+0.45 \uparrow	<0.0001	significant moderate positive correlation – TSH levels tend to increase with age
FT4 (pmol/L)	-0.30 \downarrow	0.007	significant negative correlation – FT4 levels decrease slightly as age increases
Fe ($\mu\text{mol/L}$)	-0.06 \downarrow	0.559	no significant correlation – serum iron is independent of age
Se ($\mu\text{mol/L}$)	-0.15 \downarrow	0.187	weak and non-significant negative trend – selenium levels slightly decrease with age, but not significantly

Discussion

The present study investigated the relationship between thyroid hormones and two essential trace elements – selenium and iron – in women diagnosed with hypothyroidism in Basra, Iraq. Although the hypothyroid and euthyroid groups were comparable in age and BMI, they differed significantly in income, menstrual regularity, parity, and family history – factors frequently associated with thyroid dysfunction and hormonal imbalance. The clear elevation in TSH and reduction in FT4, selenium, and iron among hypothyroid participants support the hypothesis that altered trace-element status may contribute to impaired thyroid hormone production, disturbed metabolism, and diminished antioxidative defense within the thyroid gland.¹⁹

Hypothyroid women exhibited a markedly lower median serum selenium concentration (0.81 $\mu\text{mol/L}$) compared with the control group (1.45 $\mu\text{mol/L}$), consistent with findings reported from Iran and other selenium-deficient regions.²⁰ Reduced selenium status – together with elevated TSH and lower T3/T4 ratios – may reflect impaired deiodination and weakening of the thyroid's antioxidative capacity, thereby reducing its functional reserve. DIO1 and DIO2, the key enzymes responsible for converting T4 into biologically active T3, are selenoproteins containing selenocysteine at their catalytic centers; their activity depends directly on adequate selenium availability. Experimental studies show that selenium-deficient

animals exhibit significantly reduced DIO1 and DIO2 activity across tissues including liver, kidney, and brain.²¹

A recent review by Köhrle emphasized that the thyroid gland retains high selenium levels and expresses multiple selenoproteins, including deiodinases, and that selenium deficiency impairs both thyroid hormone production and metabolism through decreased selenoprotein expression.²² In women with primary or subclinical hypothyroidism, low selenium may therefore reduce peripheral T4-to-T3 conversion, potentially causing relative T3 deficiency or increased rT3 formation, thereby diminishing thyroid hormone action in peripheral tissues. This provides a physiological rationale for the associations observed in the present cohort.

The absence of a strong association between selenium and FT4 in our results may reflect the multifactorial nature of thyroid regulation, where oxidative stress, genetic variation, and other micronutrient deficiencies influence hormone kinetics. In some individuals, normal T4-to-T3 conversion may be maintained despite low selenium through compensatory mechanisms such as hierarchical selenium distribution to essential selenoproteins and adaptive upregulation of DIO2 activity in peripheral tissues.

Nonetheless, the inverse relationship between selenium and TSH suggests that reduced selenium status may compromise negative-feedback regulation along the hypothalamic-pituitary-thyroid (HPT) axis. Given that the thyroid is one of the organs richest in selenium, adequate selenium intake is critical for maintaining redox homeostasis and protecting thyrocytes from H₂O₂-induced oxidative injury during hormone biosynthesis.^{23,24} Epidemiological evidence supports these findings: Wu et al. reported a 3.6-fold higher prevalence of hypothyroidism among individuals with low selenium status, and serum selenium showed an inverse association with autoimmune thyroiditis, subclinical hypothyroidism, and goiter (odds ratio: 0.47–0.75). Experimental studies likewise demonstrate that selenium deficiency negatively affects T3 production and degradation, consistent with reduced DIO1 activity.²⁵

In addition to selenium deficiency, hypothyroid women in this study had significantly lower serum iron concentrations. This aligns with previous research showing that iron deficiency impairs thyroid function.^{26,27} Iron is indispensable for thyroid hormone synthesis because TPO – the enzyme responsible for iodide oxidation and coupling – is heme-dependent. Iron deficiency reduces TPO activity, thereby impeding thyroid hormone biosynthesis. Beyond TPO, iron deficiency may also disrupt peripheral thyroid hormone activation. A 2023 review by Garofalo et al. reported that iron deficiency interferes with thyroxine deiodinase activity and reduces T4-to-T3 conversion.¹⁴

Although the exact molecular pathways remain incompletely defined, experimental and clinical evidence strongly supports an effect of iron status on thyroid hormone metabolism. Beard et al. demonstrated that iron-deficient anemic rats have markedly reduced hepatic 5'-deiodinase activity and lower plasma T3 turnover, indicating impaired peripheral conversion of T4 to T3.²⁸ More recent data by Monko et al. showed that cellular iron deficiency disrupts thyroid-hormone-regulated gene expression in developing

hippocampal neurons, underscoring the importance of iron for downstream T3-dependent transcription.²⁹ In Chinese women during early pregnancy, Li et al. reported that low iron status was associated with alterations in thyroid hormone markers, including lower FT4.³⁰ A 2021 systematic review and meta-analysis by Luo et al. further concluded that iron deficiency is a significant risk factor for thyroid dysfunction, partly through impaired deiodinase activity and reduced T4-to-T3 conversion.³¹

In the present cohort, low serum iron may therefore impair peripheral deiodination and exacerbate hormonal imbalance, compounding the deficit associated with primary thyroid failure. It is also possible that low selenium and iron reflect consequences of hypothyroidism rather than primary causes, as thyroid hormone deficiency is known to reduce gastric absorption, impair intestinal motility, and alter iron mobilization.³² Additionally, iron deficiency reduces TPO activity, further impairing thyroid hormone synthesis.³³ This bidirectional interaction underscores the importance of screening for micronutrient deficiencies in hypothyroid patients, particularly in regions where dietary deficits are common. Improving selenium and iron intake may offer meaningful benefits for thyroid function and clinical outcomes.^{34,35} Previous studies investigating trace and toxic metals in hypothyroid and goitrous populations also support the concept that disturbances in essential elements such as selenium and iron occur alongside alterations in other biologically relevant metals, reinforcing the importance of comprehensive micronutrient assessment in thyroid disorders.^{36–39}

Correlation analysis showed a moderate positive relationship between TSH and age, and a weak negative relationship between FT4 and age, suggesting that older hypothyroid patients tend to exhibit higher TSH and lower FT4 levels.⁴⁰ In contrast, age showed no significant association with selenium or iron, indicating that their levels may be shaped more by nutritional, metabolic, or disease-related factors than by chronological aging.⁴¹ These findings are consistent with evidence that aging alters the HPT axis through impaired TSH metabolism, altered pituitary sensitivity, and diminished negative feedback.

The inverse association between age and FT4 observed in this study suggests that aging may exacerbate declining thyroid hormone production or reduce peripheral T4-to-T3 conversion. Although healthy older adults often maintain normal FT4 through compensatory TSH increases, such compensatory mechanisms may be insufficient in individuals with hypothyroidism. The lack of age-related variation in selenium or iron supports the notion that trace-element status reflects external nutritional and physiological determinants rather than aging alone.^{40,42}

Clinical implications

These findings underscore the potential clinical value of assessing selenium and iron status in women with hypothyroidism, particularly in regions with known micronutrient deficiencies such as Basra. Optimizing dietary intake or considering targeted supplementation may support thyroid hormone metabolism and

improve clinical outcomes; however, therapeutic recommendations should await confirmation from controlled interventional studies.

Study limitations

This study has several limitations. Dietary intake of selenium and iron was not evaluated, and other relevant factors – including vitamin D status, inflammatory markers, and autoimmune thyroid antibodies – were not assessed, all of which may influence thyroid function or trace-element metabolism. The cross-sectional design limits causal inference, and unmeasured confounders may persist despite group matching.

Future directions

Future research should incorporate longitudinal and interventional study designs to clarify the directionality of the observed associations and to determine whether correcting selenium and iron deficiencies can improve thyroid hormone profiles, deiodinase activity, or patient-reported outcomes. Randomized controlled trials are particularly needed to establish causality and to identify subgroups of hypothyroid women who may benefit most from micronutrient optimization.

Conclusion

In conclusion, women with hypothyroidism exhibited significantly lower selenium and iron levels together with marked disturbances in thyroid hormone parameters. These findings support a close association between trace-element status and thyroid dysfunction. The observed age-related changes in thyroid-stimulating hormone and free thyroxine further emphasize the complexity of thyroid regulation in hypothyroid women. Future interventional studies are needed to determine whether correcting selenium and iron deficiencies may improve thyroid function and clinical outcomes.

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Declarations

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Author contributions

Conceptualization, R.S. and F.H.; Methodology, M.H.; Software, R.S.; Validation, R.S. and F.H.; Formal Analysis, M.H.; Investigation, M.H.; Resources, R.S.; Data Curation, F.H.; Writing – Original Draft Preparation, M.H.; Writing – Review & Editing, R.S.; Visualization, F.H.; Supervision, R.S. and F.H.; Project Administration, M.H.

Conflicts of interest

The authors declare no competing interests.

Data availability

The corresponding author can be contacted to request access to the data, which will be made available upon reasonable request.

Ethics approval

The study was approved by the Research Ethics Committee of the University of Basrah, College of Pharmacy (Approval No. EC 81, dated 10/11/2024), and conducted in accordance with CIOMS/WHO ethical guidelines and the Belmont Report.

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