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Clinical And Laboratory Assessment of the Impact of Subclinical Hypothyroidism on the Severity of Hypertensive Disorders in Pregnant Women (Based on Data from Andijan Region)

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Abstract Subclinical hypothyroidism may represent a significant risk factor for hypertensive disorders during pregnancy. In the Andijan region, which is endemic for iodine deficiency, subclinical hypothyroidism is widespread; however, its association with hypertensive disorders remains insufficiently explored. This study aimed to evaluate the impact of subclinical hypothyroidism on the severity of hypertensive disorders in pregnant women. A total of 88 women with hypertensive disorders were examined and stratified by thyroid status: subclinical hypothyroidism (n = 46) and euthyroidism (n = 42). Anamnestic, clinical, laboratory, ultrasound data, and somatic symptoms were analyzed. Statistical processing was performed using the R program. Significant differences were identified between the groups in terms of age, frequency of severe preeclampsia, adverse obstetric outcomes, and levels of TSH, thyroglobulin, and anti-TPO antibodies. Women with subclinical hypothyroidism more frequently reported somatic symptoms, thyroid enlargement, and pronounced edema syndrome. The findings confirm the impact of subclinical hypothyroidism on the clinical course of hypertensive disorders and underscore the importance of thyroid screening in pregnant women living in iodine-deficient regions.

Keywords Pregnancy, Subclinical hypothyroidism, Hypertensive disorders, Thyroid hormones, Andijan region

1. Introduction

Hypertensive disorders (HD) during pregnancy remain one of the leading causes of maternal and perinatal morbidity. According to WHO, they occur in an average of 10% of pregnant women, and in low- and middle-income countries, this figure may exceed 17% [1,2,3]. During pregnancy, significant hormonal changes take place, including alterations in thyroid function. Even subclinical forms of thyroid dysfunction, such as subclinical hypothyroidism (SCH), can disrupt hormonal homeostasis and contribute to the development of complications, including preeclampsia [4,5]. SCH is characterized by elevated TSH levels with normal free T4 levels and is considered one of the factors in vascular dysfunction.

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In Uzbekistan, especially in iodine-deficient regions, the prevalence of SCH among pregnant women is estimated to be between 7–15%, and in the Andijan region around 12% [6,7]. Despite measures to prevent iodine deficiency, the coverage of iodine prophylaxis remains insufficient. Andijan region is an endemic area for iodine deficiency, which accounts for the high prevalence of SCH among women of reproductive age. However, the association between SCH and hypertensive complications of pregnancy in this region remains poorly studied.

Considering the multifactorial nature of HD risk including endocrine, genetic, environmental, and social aspects investigating the role of SCH in the development of hypertensive conditions becomes especially relevant. This is essential for improving diagnostics, prevention, and pregnancy management in the context of regional iodine deficiency.

The aim of the study was to assess the impact of SCH on the occurrence and course of hypertensive disorders in pregnant women in the Andijan region.

2. Materials and Methods

From November 2022 to April 2023, a case–control study was conducted at the Andijan branch of the Republican Specialized Scientific and Practical Center for Maternal and Child Health among pregnant women with hypertensive disorders (HD).

Inclusion and exclusion criteria: Included were women aged 18–40 years, with singleton pregnancies, in whom HD was diagnosed after the 20th week. Cases of chronic hypertension were excluded (N=88).

Data collection: Data were collected via an online questionnaire using the KoBoToolbox platform, which included sociodemographic, clinical, and laboratory parameters. As part of a comprehensive examination, patients underwent fetal and thyroid Doppler studies, clinical examination with assessment of somatic status, and laboratory investigations. On the second day of hospitalization, fasting venous blood samples were collected for the determination of TSH, triiodothyronine (T3), thyroxine (T4), thyroglobulin, anti-thyroid peroxidase antibodies (anti-TPO), and anti-thyroglobulin antibodies (anti-TG).

Diagnosis of SCH and HD was made according to the national guidelines of the Ministry of Health of Uzbekistan [7,8]. SCH was diagnosed with TSH > 4.2 μIU/mL and normal T4 (10.3–24.5 pmol/L) combined with elevated anti-TPO (>18 IU/mL). HD was defined as BP ≥140/90 mmHg without proteinuria; preeclampsia with proteinuria ≥0.3 g/L; severe preeclampsia with BP ≥160/110 mmHg and signs of organ dysfunction.

Ethical approval: The study was approved by the Ethics Committee of the Ministry of Health of the Republic of Uzbekistan (No. 1684/6-1 dated 27.09.2022).

Statistical analysis: Data were processed using R software (v.4.2.1) with tidyverse, rio, and here packages. Statistical differences were assessed using the Chi-squared test, Fisher's exact test, and Wilcoxon rank-sum test. The significance level was set at $p<0.05$.

3. Results

Based on thyroid profiles and endocrinologist consultations, participants with HD were divided into two groups: those with SCH (n = 46) and those with euthyroidism (n = 42). Comparative analysis revealed statistically significant differences in age and types of HD. Women with SCH were younger (27.0 [23.0–32.0] years) compared to euthyroid patients (31.0 [25.0–35.0] years; p = 0.048), which may indicate an earlier manifestation of thyroid dysfunction. The structure of hypertensive conditions also differed (p = 0.01): in the euthyroid group, HD and mild preeclampsia were more frequently diagnosed (28% and 49%, respectively), while in the SCH group, severe preeclampsia predominated (55% vs. 23%). This may indicate more pronounced vascular disturbances in the presence of thyroid dysfunction. Sociodemographic parameters (education, employment, place of residence) showed no significant differences (p > 0.05), indicating no apparent influence on the development of SCH in this sample (Table 1).

Women with SCH more frequently reported complicated outcomes of previous pregnancies (68% vs. 7.3% in the euthyroid group; p < 0.001), which may indicate a link between thyroid dysfunction and an increased risk of obstetric complications. The distribution of pregnancy-related nausea (toxicosis) across trimesters also differed (p = 0.035): in the SCH group, symptoms persisted more often into the second (34%) and third trimesters (3%), whereas in the euthyroid group, toxicosis was primarily confined to the first trimester (50%).

Table 1. Sociodemographic and clinical characteristics of patients with SCH and euthyroidism

Characteristics	Hypothyroidism N = 46[1]	Euthyroidism N = 42[1]	p-value[2]
Age	27.0 (23.0, 32.0)	31.0 (25.0, 35.0)	**0.048**
Diagnosis			**0.010**
GAH	8 (16%)	11 (28%)	
moderate preeclampsia	14 (29%)	19 (49%)	
severe preeclampsia	27 (55%)	9 (23%)	
Education			0.5
higher education	8 (17%)	5 (12%)	
secondary education	38 (83%)	37 (88%)	
Employment status			0.2
housewife	36 (78%)	30 (71%)	
employed	4 (8.7%)	9 (21%)	
student	6 (13%)	3 (7.1%)	
Place of residence			0.6
urban	5 (11%)	6 (14%)	
rural	41 (89%)	36 (86%)	

[1]n (%); Median (Q1, Q3)
[2]Wilcoxon rank sum test; Fisher's exact test; Pearson's Chi-squared test

Table 2. Obstetric history and pregnancy course in patients with subclinical hypothyroidism and euthyroidism

Characteristics	Hypothyroidism N = 46[1]	Euthyroidism N = 42[1]	p-value[2]
Adverse outcomes in previous pregnancy (AOPP)	28 (68%)	3 (7.3%)	**<0.001**
Toxicosis during pregnancy			**0.035**
In the 1st trimester	15 (52%)	13 (50%)	
In the 1st–2nd trimesters	10 (34%)	5 (19%)	
In the 2nd trimester	2 (7%)	0 (0%)	
In the 3rd trimester	1 (3%)	0 (0%)	
Surgical history	11 (24%)	22 (52%)	**0.006**

[1]n (%);
[2]Pearson's Chi-squared test

The frequency of prior surgical interventions was lower in the SCH group (24% vs. 52%; p = 0.006), which may reflect either characteristics of the sample or the potential influence of thyroid status on overall somatic burden and the need for surgical procedures.

Women with subclinical hypothyroidism (SCH) were significantly more likely to report symptoms such as nausea (67% vs. 40%; p = 0.014), fatigue (82% vs. 62%; p = 0.034), hair loss (67% vs. 45%; p = 0.044), bloating (58% vs. 33%; p = 0.022), dry skin (89% vs. 71%; p = 0.040), obesity (80% vs. 55%; p = 0.012), and brittle nails (53% vs. 9.5%; p < 0.001) compared to women with euthyroidism. These symptoms are likely associated with slowed metabolic processes, reduced mitochondrial activity, disrupted hair growth cycles, alterations in skin hydration, and slowed gastrointestinal motility features characteristic of hypothyroid states.

Table 3. Frequency of clinical symptoms in patients with SCH and euthyroidism

Characteristics	Hypothyroidism N = 46[1]	Euthyroidism N = 42[1]	p-value[2]
Nausea	30 (67%)	17 (40%)	**0.014**
Fatigue	37 (82%)	26 (62%)	**0.034**
Dizziness	25 (56%)	17 (40%)	0.2
Hair loss	30 (67%)	19 (45%)	**0.044**
Bloating	26 (58%)	14 (33%)	**0.022**
Aggressiveness	34 (76%)	33 (79%)	0.7
Dry skin	40 (89%)	30 (71%)	**0.040**
Obesity	36 (80%)	23 (55%)	**0.012**
Memory decline	38 (84%)	28 (67%)	0.053
Headache	27 (60%)	17 (40%)	0.069
Brittle nails	24 (53%)	4 (9.5%)	**<0.001**
Symptoms present before pregnancy	13 (28%)	10 (24%)	0.6

[1]n (%)
[2]Pearson's Chi-squared test

In contrast, no significant differences were found between the groups for complaints such as dizziness (41% vs. 36%), irritability (20% vs. 21%), memory decline (33% vs. 29%), headache (37% vs. 31%), or presence of symptoms before pregnancy (22% vs. 24%) (p > 0.05), indicating the nonspecific nature of these symptoms in relation to thyroid status.

Intergroup analysis revealed statistically significant differences in levels of thyroglobulin, TSH, anti-TPO, and anti-TG. At the same time, levels of free and total T3 and T4 remained stable, indicating a compensated state of thyroid dysfunction in SCH. Thyroglobulin levels were higher in patients with SCH (61 [38–87]) compared to those with euthyroidism (44 [17–67]; p = 0.050), possibly reflecting thyrocyte hyperplasia and compensatory tissue remodeling of the gland. Although the median value of anti-TPO was the same (3 IU/ml), the distribution range differed significantly (IQR: [3–5] in SCH vs. [2–6] in euthyroid; p = 0.042), suggesting increased autoimmune activity in the SCH group.

The most pronounced difference was observed in TSH levels: 4.42 [3.68–5.84] in the SCH group versus 1.60 [1.01–2.28] in the euthyroid group (p < 0.001), indicating compensatory pituitary stimulation in response to early thyroid hormone deficiency. Levels of free and total T3 and T4 showed no statistically significant differences (p > 0.1), confirming preserved hormonal output. The combination of elevated TSH, thyroglobulin, and changes in autoantibodies may serve as an early marker of initial restructuring of the hypothalamic–pituitary–thyroid axis.

Table 4. Thyroid hormone and autoantibody levels in patients with SCH and euthyroidism

Characteristics	Hypothyroidism N = 46[1]	Euthyroidism N = 42[1]	p-value[2]
Thyroglobulin	61 (38, 87)	44 (17, 67)	**0.050**
Anti-TPO	3 (3, 5)	3 (2, 6)	**0.042**
fT3	0.34 (0.18, 0.64)	0.31 (0.21, 0.51)	>0.9
fT4	7.92 (7.15, 9.00)	7.86 (6.95, 9.09)	>0.9
tT3	6.47 (4.85, 9.11)	6.50 (4.47, 8.39)	0.9
tT4	111 (97, 118)	110 (101, 123)	0.8
TSH	4.42 (3.68, 5.84)	1.60 (1.01, 2.28)	**<0.001**
Anti-TG	0 (0, 4)	2 (0, 8)	0.2

[1]Median (interquartile range)
[2]Kruskal–Wallis U-test

Table 5. Morphological characteristics of the thyroid gland and frequency of edema in patients with SCH and euthyroidism

Characteristics	**Hypothyroidism** N = 46[1]	**Euthyroidism** N = 42[1]	**p-value**[2]
Thyroid Ultrasound			**0.03**
No enlargement	10 (22%)	18 (43%)	
Enlarged	36 (78%)	24 (57%)	
Thyroid Gland Consistency			**0.047**
Soft	9 (16%)	2 (6.9%)	
Normal	36 (63%)	24 (83%)	
Firm	12 (21%)	3 (10%)	
Edema			**<0.001**
No edema	0 (0%)	13 (31%)	
In the upper limbs	0 (0%)	1 (2.4%)	
In the lower limbs	27 (59%)	12 (29%)	
In both upper and lower limbs	11 (24%)	10 (24%)	
In the lower limbs and facial area	1 (2.2%)	1 (2.4%)	
Facial area	1 (2.2%)	1 (2.4%)	
Generalized	6 (13%)	4 (9.5%)	

[1]n (%)
[2]Fisher's exact test; Pearson's Chi-squared test

Table 6. Laboratory parameters and blood group distribution in patients with subclinical hypothyroidism and euthyroidism

Characteristics	Hypothyroidism **N = 46[1]**	Euthyroidism **N = 42[1]**	p-value[2]
• **Proteinuria**	0.12 (0.05, 0.26)	0.03 (0.03, 0.10)	**0.003**
• **R-factor test**			0.3
Negative	6 (13%)	2 (4.8%)	
Positive	40 (87%)	40 (95%)	
• **Blood group**			**0.032**
I	6 (13%)	13 (31%)	
II	24 (52%)	19 (45%)	
III	13 (28%)	4 (9.5%)	
IV	3 (6.5%)	6 (14%)	
• **Urea**	8.26 (7.25, 9.10)	7.99 (7.27, 8.85)	0.3
• **Creatinine**	99 (86, 114)	95 (79, 106)	0.4
• **Total bilirubin**	18.6 (17.5, 19.8)	17.9 (15.5, 18.5)	0.14
• **Conjugated bilirubin**	7.1 (2.9, 16.3)	3.9 (0.0, 15.6)	0.5
• **Unconjugated bilirubin**	14.6 (3.1, 17.0)	11.0 (2.1, 16.8)	0.4
• **ALT**	0.57 (0.46, 0.67)	0.55 (0.48, 0.65)	0.8
• **AST**	0.48 (0.45, 0.55)	0.46 (0.43, 0.54)	0.2
• **Fibrinogen**	3.33 (3.10, 3.99)	3.55 (2.73, 4.33)	0.4
• **Mucus**	31 (67%)	37 (88%)	**0.021**

[1]n (%); Median (Q1, Q3)
[2]Wilcoxon rank sum test; Fisher's exact test; Pearson's Chi-squared test

Thyroid ultrasound findings more frequently revealed abnormalities in women with subclinical hypothyroidism (SCH): an increased thyroid volume was observed in 78% of SCH patients compared to 57% in the euthyroid group ($p = 0.03$). Normal thyroid size was more common in the euthyroid group (43% vs. 22%), suggesting possible compensatory hyperplasia in the context of SCH.

The consistency of the thyroid gland also differed between groups. A firm texture was detected in 21% of women with SCH versus 10% in those with euthyroidism. Conversely, normal consistency predominated in the euthyroid group (83% vs. 63%; $p = 0.047$), which may reflect fibrotic and inflammatory changes typical of autoimmune processes. Edema syndrome was more pronounced in the SCH group

($p < 0.001$). All patients with SCH exhibited some form of edema, whereas in the euthyroid group, 31% had no signs of swelling. Lower extremity edema was found in 59% of SCH cases versus 29% in the euthyroid group, while generalized edema occurred in 13% and 9.5% of cases, respectively. These manifestations may reflect fluid retention and impaired water–electrolyte balance, which are characteristic of hypothyroid conditions.

Statistically significant differences were found between patients with subclinical hypothyroidism (SCH) and those with euthyroidism across several laboratory parameters. The level of proteinuria was higher in the SCH group 0.12 [0.05–0.26] g/L compared to 0.03 [0.03–0.10] g/L in the euthyroid group ($p = 0.003$), potentially indicating impaired renal filtration due to endothelial dysfunction. Blood group distribution also differed significantly between groups ($p = 0.032$): blood group II (52%) and III (28%) were more frequent in the SCH group, whereas group I predominated among euthyroid women (31% vs. 13%). The potential relationship between blood type and thyroid status requires further investigation.

The presence of mucus in the urine was more frequently recorded in euthyroid patients 88% vs. 67% in the SCH group ($p = 0.021$), which may reflect differences in urinary tract function or metabolic processes. Other biochemical parameters (urea, creatinine, bilirubin, ALT, AST, fibrinogen) did not show significant intergroup differences ($p > 0.05$), supporting the notion of preserved systemic metabolic stability in the context of compensated SCH.

4. Discussion

This study revealed statistically significant differences between pregnant women with subclinical hypothyroidism (SCH) and those with euthyroidism in terms of age, severity of hypertensive disorders, frequency of clinical symptoms, and several laboratory and instrumental parameters. It was established that women with SCH were younger and significantly more likely to experience severe forms of preeclampsia. These findings are consistent with previous studies by Casey et al. (2005) and Wilson et al. (2012) [9,10], where SCH was considered an independent risk factor for complicated preeclampsia. Socio-demographic characteristics such as education, place of residence, and employment did not significantly influence the development of thyroid dysfunction, as also reflected in regional data from Central Asia [11].

Women with SCH were more likely to have had adverse outcomes in previous pregnancies, consistent with findings from Gietka-Czernel et al. (2021) [12]. Prolonged symptoms of toxicosis and a lower frequency of surgical interventions in anamnesis also require further investigation of underlying pathophysiological mechanisms. Somatic symptoms were significantly more common in the SCH group, including nausea, fatigue, hair loss, dry skin, obesity, and brittle nails all classical manifestations of hypothyroid states, as confirmed by clinical observations (Nazarpour et al., 2019) [13]. Meanwhile, nonspecific symptoms (dizziness, memory issues, emotional instability) did not differ between groups, indicating limited diagnostic value in assessing thyroid status.

The hormonal profile of SCH patients showed elevated levels of TSH, thyroglobulin, and thyroid autoantibodies, while free and total T3 and T4 levels remained stable suggesting a compensated phase of thyroid dysfunction [14]. Ultrasound findings more frequently showed enlarged thyroid volume and altered consistency in SCH patients, possibly indicating structural remodeling of autoimmune origin. Edema syndrome was significantly more prevalent in SCH patients, including both localized and generalized forms, reflecting fluid retention and impaired water-electrolyte balance typical of hypothyroidism, as described in the MSD Manual [15]. Laboratory analysis also revealed higher levels of proteinuria in SCH patients, suggesting endothelial dysfunction and impaired glomerular filtration, which has been described in cases of membranous nephropathy [16]. Differences in blood group distribution and mucus presence in urine also emerged, though they require further investigation and may reflect individual metabolic characteristics associated with SCH.

5. Conclusions

In conclusion, SCH in pregnant women is associated with more severe hypertensive complications, pronounced clinical manifestations, and notable laboratory deviations. These results support the inclusion of thyroid function screening and monitoring in standard pregnancy management protocols, especially in iodine-deficient regions.

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