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IN THE NAME OF GOD

Subclinical hyperthyroidism and adverse pregnancy outcomes

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Introduction

- **Definition of subclinical hyperthyroidism (SH): A low (or undetectable) TSH level with a normal serum level of free T4 and normal serum total T3 level.**
- **SH is found in 0.4-1.7 % of all pregnancies.**
- **The prevalence of SH in iodine-insufficient areas is higher, which increases with aging and it is more common in parous pregnant women**

Introduction

- Previous studies have also revealed that overt hyperthyroidism is associated with some adverse pregnancy outcomes, such as placenta previa, intrauterine growth restriction (IUGR), preterm delivery, and neonatal thyrotoxicosis.
- The results of studies conducted on adverse consequences of subclinical hyperthyroidism on adverse pregnancy outcomes are still conflicting and inconclusive.

Objective:

We aimed to run a secondary analysis on data collected in the Tehran Thyroid and Pregnancy study (TTPs), to assess the adverse pregnancy outcomes of maternal SH by considering urinary iodine concentration.

Methods

Study design and participants

- This is a secondary analysis on data collected in TTPs.
- TTPs was a two-phase population-based study carried out among pregnant women receiving prenatal care.

Methods

Study design and participants

- These pregnant women were screened for thyroid dysfunction by collecting information on medical history, clinical examination, and thyroid laboratory tests, including TSH, T4 (TT4), T uptake, and TPOAb.
- Urinary iodine concentration (UIC) was measured in three urine samples.

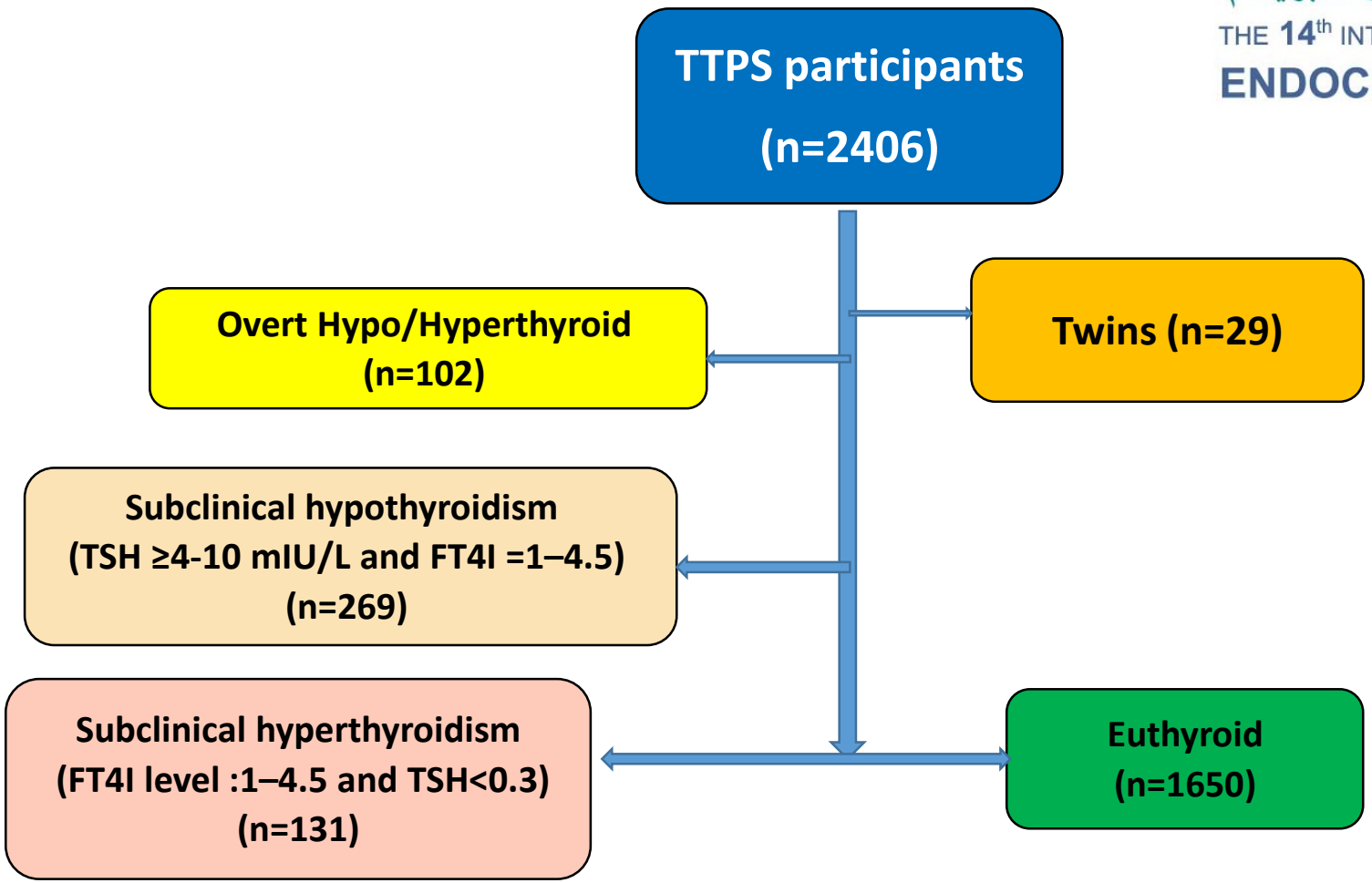
Methods

Exclusion criteria

- ❑ Twin pregnancies
- ❑ Overt thyroid dysfunction
- ❑ Subclinical hypothyroidism

SH is defined as normal FT4I level (1–4.5) and low TSH level (<5th percentile trimester-specific TSH value).

Flowchart of study:



Methods

Outcomes

Primary outcome:

- ❑ Preterm delivery

Secondary outcomes:

- ❑ Miscarriage,
- ❑ Placenta abruption,
- ❑ Stillbirth,
- ❑ Neonatal admission,
- ❑ The biometric neonatal parameters (BW, BH, BHC).

Results

Table. Adverse pregnancy outcomes in the study groups

* Characteristics	Subclinical Hyperthyroid (n=131)		Euthyroid (n=1650)	p-value[a]
Preterm delivery, n (%)	13 (12.3)		87 (6.7)	0.03
Miscarriage, n (%)	2 (1.9)		57 (4.3)	0.2
NICU admission, n (%)	12 (11.7)		111 (9.1)	0.3
Placental abruption , n (%)	1 (0.9)		7 (0.5)	0.5
Stillbirth, n (%)	0		6 (0.5)	1.0
Neonatal weight, mean (SD)	3279.5±501.0		3213.5±461.8	0.2
Neonatal height, mean (SD)	50.4±2.4		50.0±2.3	0.1
Neonatal head circumference, mean (SD)	35.0±1.4		34.7±1.7	0.07
Neonatal TSH (mIU/L), median (IQR)	1.1 (0.4- 1.9)	χ^2	1.0 (0.5- 1.9)	0.9

[a] P-value is calculated by t-test or Mann-Whitney U test or test for between-group comparisons, as appropriate. NICU, Neonatal Intensive Care Unit.

Results

Table 3. Generalized linear regression model analysis for pregnancy outcomes in study groups based on TSH cut-off values of 0.3 mIU/L and urinary iodine concentrations of 150 µg/l

Pregnancy outcomes*	Preterm Delivery		NICU admission		Head circumference (cm)		Neonatal height (cm)		Neonatal weight (g)	
Variable	OR (95% CI)	p-v	OR (95% CI)	p-v	Mean difference (95%CI)	p-v	Mean difference (95%CI)	p-v	Mean difference (95%CI)	p-v
TSH<0.3 mIU/L vs TSH≥0.3 mIU/L	2.27 (1.15,4.48)	0.02	1.59 (0.78,3.17)	0.2	0.28 (-0.10,0.66)	0.1	-0.02 (-0.54,0.51)	0.9	63.4 (-37.5,164.2)	
Urine iodine≥150 µg/l vs Urine iodine<150 µg/l	0.76 (0.46,1.28)	0.3	1.10 (0.68,1.75)	0.7	0.11 (-0.10,0.31)	0.3	0.02 (-0.27,0.32)	0.9	11.34 (-46.6,69.2)	
TSH× Urinary iodine	Adjusted OR (95% CI)	p-v	Adjusted OR (95% CI)	p-v	Mean difference (95%CI)	p-v	Mean difference (95%CI)	p-v	Mean difference (95%CI)	p-v
TSH≥0.3 mIU/L and Urine iodine≥150 µg/l	Reference Group		Reference Group		Reference Group		Reference Group		Reference Group	
TSH<0.3 mIU/L and Urine iodine<150 µg/l	2.06 (0.70 – 6.04)	0.2	1.10 (0.38-3.17)	0.8	0.30 (-0.18-0.78)	0.2	-0.03 (-0.72- 0.65)	0.9	36.6 (-96.1-169.3)	0.6
TSH<0.3 mIU/L and Urine iodine≥150 µg/l	4.61 (1.36 – 15.71)	0.01	1.37 (0.35-5.38)	0.6	0.09 (-0.61-0.79)	0.8	-0.84 (-1.83- 0.15)	0.09	-41.5 (-237.9-154.9)	0.7
TSH≥0.3 mIU/L and Urine iodine<150 µg/l	1.45 (0.84 – 2.52)	0.2	0.91 (0.56-1.49)	0.7	-0.14 (-0.35-0.07)	0.2	-0.08 (-0.39- 0.22)	0.6	-18.7 (-78.8-41.4)	0.5

*Adjusted for maternal age, parity, gestational age, BMI, and FTI.

BMI, body mass index; BP, blood pressure; TSH, thyroid-stimulating hormone; UIC, urinary iodine concentration; FTI, free thyroxine index.

Results

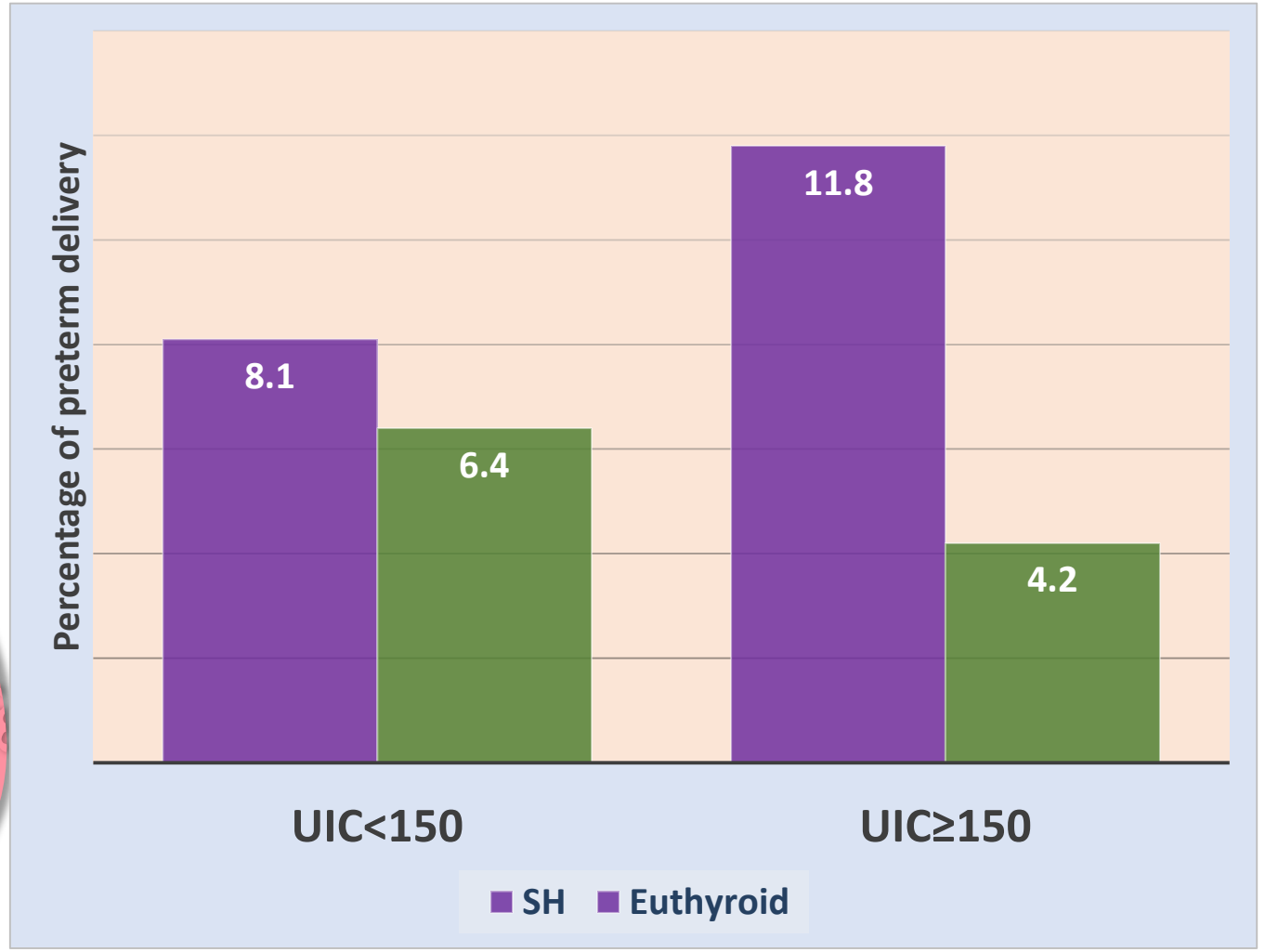


Figure . Percentage of preterm delivery based on the cutoff value of 150 for UIC level in women with SH and euthyroid women.

Discussion

- This study revealed that SH is associated with the increased odds ratio of preterm delivery, especially among mothers with UIC ≥ 150 µg/L, whereas there is no significant difference in neonatal admission and neonatal anthropometric parameters, including head circumference, weight, and height among SH and euthyroid groups in none of the subgroups of UIC (<150 or ≥150 µg/l).

Discussion

- This study showed that among those with UIC level ≥ 150 µg/L, the odds ratio (OR) of preterm delivery was **4.61 times higher** in the SH group, compared with those who were euthyroid

Discussion

- The association between thyroid dysfunction and preterm delivery can be due to the effect of thyroid hormones on the uterus.
- Thyroid hormone receptors, TSH, and thyrotropin-releasing hormone (TRH) receptors were observed in the myometrium of the primate uterus.

M. Hulchiy, H. Zhang, J. M. Cline, A. L. Hirschberg, L. Sahlin. Receptors for thyrotropin-releasing hormone, thyroid-stimulating hormone, and thyroid hormones in the macaque uterus: effects of long-term sex hormone treatment, Menopause 19(11) 2012 125

Discussion

- TSH can bind to human chorionic gonadotropin receptors, present in the human myometrium (R).
- However, the biological mechanism clearly explaining the effect of thyroid hormone disturbances on the induction of premature uterine contraction is still lacking and needs further studies.

C. Ticconi, A. Zicari, A. Belmonte, M. Realacci, C. V. Rao, E. Piccione. Pregnancy-promoting actions of HCG in human myometrium and fetal membranes, Placenta 28 2007 S137-S

Discussion

- Torlinska et al. (2018) in a prospective study on pregnant women reported **U-shaped relationships** between **urinary iodine concentrations and risks of preterm birth**.

B. Torlinska, et al. Iodine status during pregnancy in a region of mild-to-moderate iodine deficiency is not associated with adverse obstetric outcomes; results from the Avon Longitudinal Study of Parents and Children (ALSPAC), Nutrients 10(3) 2018 291.

Discussion

- The increased risk of preterm delivery associated with higher serum iodide levels and the possibility of a real U-shaped relationship based on the increased risk of preterm in both high and low iodine levels were also reported in Purdue-Smith's et al. (2019) study.

A. C. Purdue-Smithe, et al. The Joint Role of Thyroid Function and Iodine Status on Risk of Preterm Birth and Small for Gestational Age: A Population-Based Nested Case-Control Study of Finnish Women, Nutrients 11(11) 2019 2573.

Conclusion

- SH in women with higher iodine levels can lead to the increased preterm labor during their pregnancies.
- This result indicates the accelerating effect of SH on the existence of a possible U-shaped relationship between the increased premature risk and iodine levels.
- Iodine supplementation should be considered with caution in women with SH.
- Further studies on pregnancy outcomes of women with SH are highly recommended.


Thank you
for your attention