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# ULTRASONOGRAPHIC ANALYSIS OF THE THYROID GLAND DURING PREGNANCY

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SUMMARY - The aim of the study was to determine whether pregnancy induced ultrasonographically detectable changes of the thyroid gland. It is a very interesting clinical feature, because some parts of inland Croatia were an endemic goiter area before the implementation of the 1996 act on salt iodination. Sixty-six pregnant women with no history of thyroid disease were repeatedly examined by ultrasound during the course of pregnancy. The size and echostructure of the thyroid were estimated. The thyroid volume increased slightly during pregnancy, but mostly remained within the normal range for particular age. A significant thyroid volume enlargement was observed in third trimester as compared with either first trimester (p=0.02) or control group (p=0.01). Mild goiter of 16% was found in pregnant women in comparison to control group. Morning urine sample, thyroid hormone, TSH and thyroid antibodies were also analyzed in 89 women. Median urine iodine was 8.8 μg/dL. Sixty percent of pregnant women had an iodine concentration below 10 μg/dL. In four out of nine subjects with goiter, urinary iodine excretion was below 5 μg/dL. Elevated serum TSH concentration was recorded in three (3%) women, however, they were euthyroid at the time of the study. Results of the study supported the hypothesis that thyroid volume and thyroid function adapt to the physiologically increased iodine and energy demands. The possible goitrogenic effect of pregnancy could be prevented by an increased iodine intake by diet rich in iodine.

Key words: *Thyroid gland - ultrasonography; Pregnancy complications; Thyroid gland - anatomy and histology*

## Introduction

The state of mild to moderate iodine deficiency persisting in many European countries has important consequences on the target groups of population such as lactating women, neonates, and young infants. During pregnancy, complex changes occur in the function of maternal endocrine glands, along with cardiovascular and hemodynamic changes[1].

Thyroid function in pregnant women undergoes stimulatory events: 1) high human chorionic gonadotropin (hCG) levels, associated with functional and anatomical thyroid stimulation; 2) increase in serum thyroid binding globulin (TBG) and lowering of free hormone concentration; and 3) increased renal clearance of iodide[2]. The alterations in maternal thyroid function during gestation are intrincate and as yet incompletely understood.

In the state of mild or marginally low iodine intake, gestation is in a significant number of women associated with relative hypothyroxinemia, increased thyroglobulin, and enlarged thyroid. The main consequence of maternal iodine deficiency is fetal and neonatal hypothyroidism[3].

In the early '80s and '90s, investigations of goiter incidence in north Croatia (Zagreb area)[4] showed the incidence of goiter to be between 19% and 35% in normal population. At the end of 1996, a new regulation of salt iodination was introduced as part of the nationwide program of

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iodine deficiency disorders control[4]. Therefore, pregnant women from the Zagreb area could be expected to have developed goiter and thyroid function disturbances. The aim of the study was to determine the incidence of goiter among pregnant women.

## Subjects and Methods

*Subjects*

Eighty-nine pregnant women, mean age 26.7 years, were included in the study. Ultrasonographic analysis during the course of pregnancy was performed in 66 of 89 women, i.e. in the first (T1), second (T2) and third (T3) trimester of gestation in 29, 38 and 38 women, respectively. Six women underwent ultrasonographic examination in each of the three trimesters; 26 women were examined on two occasions, and others had one ultrasonographic examination during the course of gestation.

There were 18 multiparae (10 with two, and eight with three previous deliveries). The women with high levels of thyroid autoantibodies were excluded from ultrasonographic analysis.

A control group consisted of 31 age-matched non-pregnant healthy volunteers, none of whom had previously been pregnant.

Morning urine samples were collected once, twice or three times per week during pregnancy (n=138). Only 11 women gave their urine samples in each trimester. None of the study group subjects received iodine-containing supplements during gestation.

Fasting blood samples were obtained from all women for determination of triiodothyronine (T3), tetraiodothyroinine (T4), thyroid stimulating hormone (TSH), and thyroid autoantibodies.

*Methods*

The procedure of ultrasonographic scanning was performed using an 8 MHz linear transducer (Toshiba, Japan). Two specialists generally obtained transverse and longitudinal scans of the thyroid with the subjects in the position of neck hyperextension (a pad placed under the shoulders), at the same time of the day, i.e. early in the morning. The size of the thyroid and its echostructure were estimated. Total thyroid volume was calculated using the following equation:

V=0.475 ((a1b1c1)+(a2b2c2)), where a=length, b=width, c=breadth, 1=right lobe, and 2=left lobe[5]. Volume determinations were performed without knowledge of previous results. Thyroid volumes greater than 18 mL were considered to be enlarged.

Wilcoxon test for unpaired data was used in statistical analysis of thyroid volume differences between gestation trimesters.

TSH concentration was determined in serum samples by use of immunoradiometric (IRMA) kits (TSH-IRMA, DPC, USA; normal range 0.23-4.5 mU/L). Urine iodine concentration was measured by our own modification of Wawschinek's colorimetric method based on Sandell-Kolthoff reaction (control group median, 10 μg/dL)[6].

*Results*

Initial ultrasonography (menstrual week 14) revealed no detectable goiter. Median thyroid volume was 12 mL, an mean value was the same (range 7-15 mL). The slight increase in thyroid size recorded in T2 (median 13, mean 12.6 mL) was not statistically significant in comparison with T1 and control group (Table 1).

*Table 1. Thyroid volume (mean and median) according to pregnancy trimesters*

| Trimester | n | Thyroid volume (mL) | |
|---|---|---|---|
| | | mean | median |
| I | 29 | 11.8 | 12 |
| II | 38 | 12.6 | 13 |
| III | 38 | 14.1 | 15 |
| Control group | 31 | 11.3 | 12 |

A tendency toward thyroid enlargement was observed in T3, however, neither median nor mean thyroid volume exceeded 18 mL (range 7-28 mL). In T3, goiter was found in nine (16%) women, one of them showing enlarged goiter already in T2; it should be noted that in this woman thyroid volume was not measured in T1. The women with a history of several deliveries had no larger thyroids than primiparae, with the exception of one woman with euthyroid goiter in T2 and T3.

Figure 1 shows thyroid enlargement in T3 versus T1 and control group. Comparison of thyroid volume measurements in T3 with those in T1 and control group yielded a statistically significant difference.

Median thyroid volume in non-pregnant women was 12 (range 7-14) mL, without any echographic changes of the parenchyma. Most pregnant women had a uniformly homogeneous ultrasonographic appearance; three women

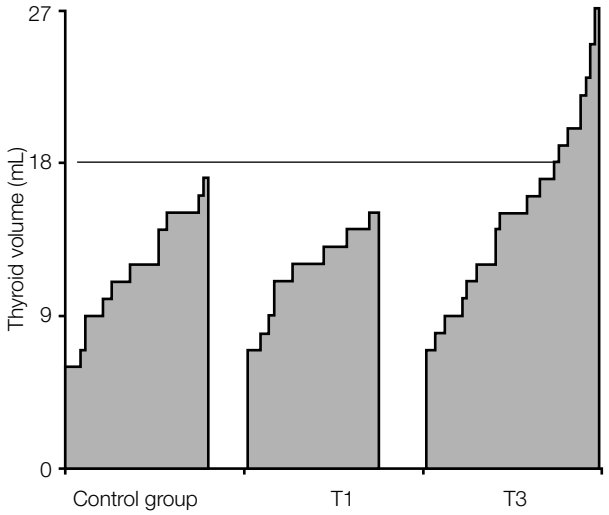


*Fig. 1. Comparison of thyroid volume between T1, T3 and control group; p (T1:T3)=0.02; p (T3:control group)=0.01; thyroid volume >18 mL=enlarged thyroid.*

had slightly diffuse parenchymal changes. Only two of them showed nodular changes (nodes of less than 1 cm), both of them on the first examination.

*Urine iodine excretion*

The distribution (% prevalence) of urine iodine excretion is shown in Fig. 2. Median urine iodine excretion was slightly lower in pregnant study women than in non-pregnant controls (study group median, 8.8 μg/dL; control group median, 10.0 μg/dL). Forty per cent of pregnant women had urine iodine excretion of more than 10 (μg/dL, and 16% lower than 5 μg/dL).

Nine women with verified goiter had median urine iodine excretion of 5.6 μg/dL, four (45%) of them <5 μg/dL. None of them had any impairment of thyroid function. The correlation between the level of urine iodine excretion and thyroid volume (r=-0.485) in these subjects is illustrated in Fig. 3. There was no statistically significant difference (p>0.05).

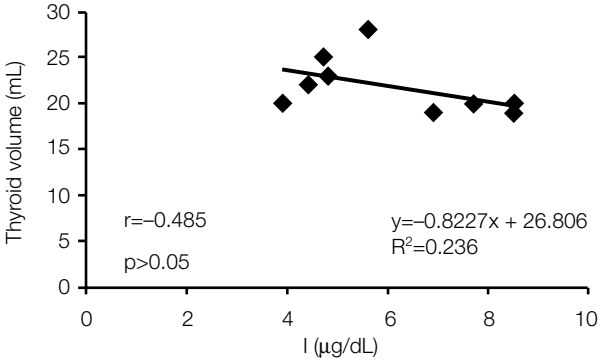


*Fig. 3. Correlation between the level of urine iodine excretion and thyroid volume.*

*Maternal TSH concentration*

A histogram of TSH concentration in maternal serum, presented in Fig. 4, shows that only three (3%) women had elevated TSH values (>4.5 mU/L), with no increase in the

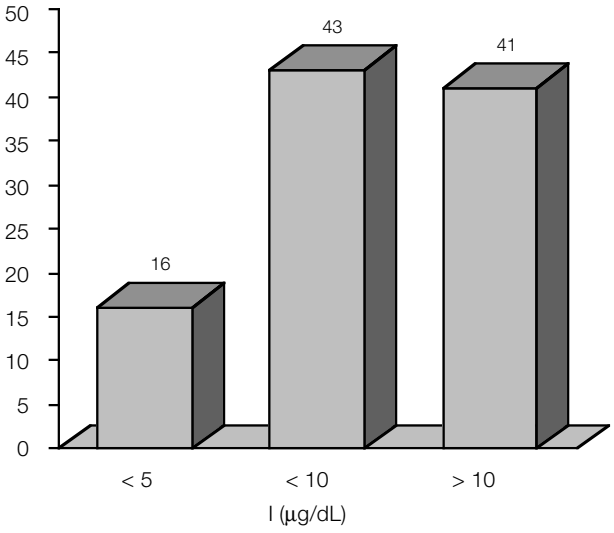


*Fig. 2. Histogram of urinary iodine concentration during pregnancy (n=138); median concentration=8.8 μg/dL).*

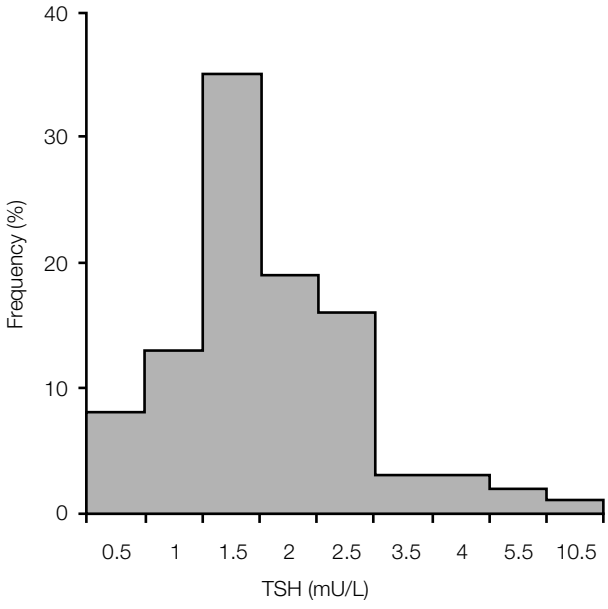


*Fig. 4. TSH concentration in serum of pregnant women (n=89).*

level of autoantibodies and no thyroid hormone impairments. Other study group women were euthyroid.

*Discussion*

Before the era of ultrasonic, high-resolution thyroid volume determination, reports were based on thyroid palpation, which is now considered inaccurate. In many European countries, palpation or ultrasound examination were used in numerous studies to assess thyroid volume during pregnancy.

In areas with an adequate iodine intake, thyroid volume neither increases during pregnancy nor it differs from a control group[7]. Cross-sectional studies in which the size of the thyroid was assessed by inspection and palpation were performed before the '80s in areas with sufficient iodine intake. These authors failed to find any difference between pregnant and control women[8-10]. In 1994, a longitudinal and prospective ultrasonography study performed in the Netherlands showed no difference in thyroid size during pregnancy[11].

On the other hand, many authors observed thyroid size changes in iodine deficient countries. In Denmark, Rasmussen et al.[12] and Pedersen et al.[13] found thyroid enlargement by 20% and 31%, respectively. In Belgium characterized by moderate iodine deficiency, Glinoer et al.[14] recorded a thyroid volume increase by 18% in 1990 and by 30% in 1995.

Therefore, we initiated this preliminary prospective study in 89 subjects, which revealed 16% of the pregnant women in Croatia to develop goiter during gestation. In almost 60% of study subjects, the urine iodine excretion was below 10 μg/dL. It was even more pronounced in goitrous pregnant women: 45% of these women showed a urine iodine excretion of less than 5 μg/dL. The non-significance of the relatively high coefficient of correlation was probably due to the small number of study subjects.

The question arises whether the observed increase in thyroid volume during pregnancy reflected the goitrogenic effect of pregnancy, or should be regarded as a pathologic condition indicating relative iodine deficiency. In 1999, in a randomized sample of the Zagreb population, a urine iodine concentration of <5 μg/dL was found in 8.9%, and of <10 μg/dL in 44.6% of subjects[15]. These data are not comparable, but strongly point to great differences.

Rasmussen et al.[12] indicated in the early '90s that body weight, presence of thyroid autoantibodies, smoking habits, and increased vascularity of the region could aggravate thyroid enlargement.

Serum TSH increase was found in only 3% of study subjects, calling for appropriate treatment. Thus, it is not very likely that the size of thyroid increases during pregnancy only as the result of stimulation by TSH. Anyway, this gives rise to the question of routine screening for hypothyroidism in pregnancy (as proposed by the American Association of Clinical Endocrinologists), however, the cost/benefit ratio is an unsurmountable problem for our community. Unfortunately, the present study did not include the levels of TSH in newborns, which is obviously an issue to be tackled in future investigations.

In conclusion, a 16% thyroid volume increase was demonstrated in a small number of pregnant women. A urine iodine excretion of less than 5 μg/dL was found in 16% of all study women, and in four of the nine women with goiter. The fact that nearly 60% of study subjects had iodine concentration in the urine below 10 μg/dL appears to be quite disturbing. It could be explained by the state of mild iodine deficiency in this part of Croatia. This study will therefore be continued in parallel with the national program of the struggle against iodine deficiency disorders. The results of the present study strongly call for serious consideration of an additional iodine supply.

*Acknowledgment*

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Sažetak

## ULTRAZVUČNA ANALIZA ŠTITNJAČE U TRUDNOĆI

*S. A. Novosel, S. Rončević, Lj. Lukinac, D. Nöthig-Hus, R. Herman i Z. Kusić*

U kontinentalnim dijelovima Hrvatske prije uvođenja novoga pravilnika o jodiranju soli 1996. godine zabilježena je endemska gušavost. Stoga je svrha ovoga istraživanja bila utvrditi postoji li i u kojoj mjeri gušavost, odnosno povećanje volumena štitnjače u trudnica sa zagrebačkog područja. Šezdeset šest zdravih trudnica u kojih prethodno nije postojala bolest štitnjače u više je navrata pregledano ultrazvukom, pričem je određen volumen i ehostruktura štitnjače. Utvrđen je porast volumena štitnjače u sva tri trimestra trudnoće koji je, međutim, prelazio gornju granicu normalne veličine štitnjače (18 mL) i to uglavnom u trećem trimestru. Značajan porast veličine štitnjače ustanovljen je u trećem trimestru u odnosu na prvi trimestar (p=0,02) te na kontrolnu skupinu (p=0,01). Umjerena guša nađena je u 16% trudnica u odnosu na kontrolnu skupinu. U skupini od 89 trudnica određena je koncentracija joda u mokraći, koncentracija hormona štitnjače, TSH te tiroidna protutijela. Utvrđen je medijan koncentracije joda u mokraći od 8,8 μg/dL, a 60% trudnica imalo je koncentraciju nižu od 10 μg/dL. U četiri od devet trudnica s ustanovljenom gušom razina joda bila je ispod 5 μg/dL. Povišena razina TSH u serumu nađena je u 3% trudnica, ali uz normalne razine hormona štitnjače. Ovim smo ispitivanjem potvrdili očekivani porast volumena štitnjače u trudnoći kao posljedicu povećane potrebe za energijom i jodom. Stoga zaključujemo da se očekivani goitrogeni učinak trudnoće može spriječiti prehranom obogaćenom jodom.

Ključne riječi: *Štitna žlijezda - ultrazvuk; Komplikacije trudnoće; Štitna žlijezda - anatomija i histologija*