THYROID VOLUME, URINARY AND MILK IODINE IN MOTHERS AFTER DELIVERY AND THEIR NEWBORNS IN IODINE-REPLETE COUNTRY

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Objective. To estimate thyroid volume (ThV) in primiparous (PP) and multiparous (MP) mothers (MO) and their newborns (NB) as related to their urinary iodine and thus contribute to the question on the interrelation between iodine intake during the pregnancy and thyroid function in pregnant women.

Methods. The ThV by ultrasound was estimated in a total of 258 MO (108 PP and 150 MP)) and their newborns on the 4th-7th day after delivery. There were 227 in term and 31 preterm (before 37th week) deliveries. In addition, ThV was estimated in double amount of controls (216 vs. PP and 300 vs. MP) in the same age range and nearly age matched which were either nulliparous or did not have delivery within last 12 months.

Urinary iodine concentration was estimated in spot urine samples obtained from 75 MO and their NB and milk iodine in 44 milk samples obtained between the 4th and 7th day after delivery.

Results. On the first week after delivery, the ThV in all 258 MO was significantly higher than that in 516 of nearly age matched females (mean±S.D.: 14.87±4.93 ml vs. 10.61±4.02 ml, resp., P<0.01). Although the ThV was lower in 108 PP than in 150 MP women (mean±S.D.: 13.85±4.51 ml vs. 15.59±5.11 ml, resp., P<0.01), it was still significantly higher (P<0.01) than that in a double amount of nearly age matched controls for PP (9.96±3.15 ml) and MP (11.07±4.48 ml).

Mean ThV found in all 258 NB was 0.60±0.21 ml (median 0.5 ml, range 0.2-1.6 ml), the values in those born in term being higher than in preterms (mean±S.D. 0.62±0.20 ml vs. 0.45±0.12 ml; P<0.01). No correlation was found between the ThV and body weight in NB. However, significant correlation was found between the ThV in all 257 NO and their NB (r=0.292, P<0.05).

The mean value of urinary iodine in mothers on the first week after delivery was 9.0±7.2 μg/dl (median 6.1, range 3.0-47.2). The average urinary iodine in primiparous was slightly higher than that in multiparous mothers (10.3 vs. 8.4 μg/dl; not significant). In newborns, the mean urinary iodine in the first week after birth was 11.6±7.6 μg/dl (median 6.5, range 0.7-45.0).

Conclusions. The finding of about 30 % higher ThV in 258 mothers after delivery than that in double amount of nearly age matched women (P<0.01) who were either nulliparous or did not have delivery at least within last 12 months shows that, in spite of general satisfactory iodine intake in Slovak population, the iodine intake during pregnancy was not satisfactory. This is supported by the data on urinary iodine which was higher in primiparous than in multiparous women.

Key words: Thyroid volume – Ultrasound – Mothers – Newborns –Urinary iodine – Human milk iodine

Pregnancy with several hormonal changes and increased demand for iodine may result, especially in iodine deficient countries, in the increase of thyroid volume (Rasmussen et al. 1989; Romano et al. 1991; Glinoer et al. 1992 a,b; Filteau et al. 1994). Among the hormonal changes a major role is played by in-

crease of chorionic gonadotropin and estrogens, but also by the production of thyroid hormones which depends on the intake of iodine the need for which is increasing (Glinoer et al. 1990, 1992 a,b, 1993, 1996, 1997).

The synthesis of thyroid hormones in fetal thyroid starts from about 20th week of gestation. These hormones together with the transplacental transfer of maternal thyroxine play decisive role in the fetal growth and differentiation. The fetal thyroid needs about 25 μg iodine per day (Glinoer et al. 1992; Boehles et al. 1993) which comes from the maternal blood via the placenta. Such loss of iodide plus the increased renal iodide clearance result at least in a relative iodine deficiency in the mother. In the second and third trimester the level of TSH in the mother is increasing and even the relative iodine deficiency results in increasing sensitivity of her thyroid to the TSH, the growth effect of which may appear even at the high normal blood level (Glinoer et al. 1994; Glinoer 1997).

The function of fetal thyroid is entirely dependent on the iodide supply from the mother and on the functional status of her thyroid. The development of neonatal goiter from intrauterine iodine deficiency is prevented by sufficient prenatal iodine intake which should result in neonatal ioduria higher than 5 μg/dl (Delange and Buergi 1989), while more severe deficiency results in the impaired maturation of central nervous system.

Iodine intake in Slovakia during the last about 45 years may be considered satisfactory as supported namely by the recent European Thyromobil Study (Delange et al. 1997). From this appears that any serious disorders of central nervous system cannot be expected. However, even under the satisfactory iodine intake some relative iodine deficiency during the pregnancy may appear which may result in the increase of thyroid volume in both the mother and newborn. The aim of this study was to contribute to this question.

Subjects and Methods

Subjects. A total of 258 mothers and their newborns were examined on the 4th-7th day after delivery. Among the mothers 108 were primiparous (mean age 22.5 years, range 17-34) and 150 multiparous (mean age 28.2 years, range 17-44). There were 227 in term and 31 preterm (before 37th week) deliveries. In addition, thyroid volume was estimated in double amount of controls (216 vs. primiparous and 300 vs. multiparous women) in the same age range and nearly age matched which were either nulliparous or did not have delivery within last 12 months.

Thyroid volume. Thyroid examination was performed by a real-time instrument (ALOCA SSD 630, Japan) using a 7.5 mHz linear transducer. ThV for each lobe (ml) was calculated according to the ellipsoid formula: width cm x length cm x thickness cm x correction factor of 0.479 (Brunn et al. 1981). In newborns, the thyroid volume was measured according to Simpson, the apparatus used being equiped with the appropriate softweare (Fig. 1).

Urinary iodine. The estimation of urinary iodine concentration was performed in spot urine samples obtained from 75 mothers and their newborns. The aliquots of 250 μl urine were digested in thermoblock at 110-115 °C with 750 μl perchloric acid for 60 min. For final evaluation, Sandell-Kolthoff reaction under temperature and time control was used followed by spectrophotometry at 410 nm. The results were expressed in terms of μg/dl.

Iodine in human milk. In 44 mothers the concentration of iodine in milk samples obtained between the 4th and 7th day after delivery was estimated using dry-ash alkaline digestion in muffle oven at 420 °C followed by Sandell-Kolthoff reaction as described above. The results were expressed in terms of μg/dl.

Statistical evaluation. Student's t-test for unpaired values, regression analysis and one way ANOVA were used.

Results

Thyroid volume in mothers. On the first week after delivery, the thyroid volume in all mothers (N=258) was significantly higher than that in 516 of nearly age matched females of the same age range who either were not yet pregnant at all or did not have delivery within the last 12 months (mean±S.D.: 14.87±4.93 ml vs. 10.61±4.02 ml, resp., $P<0.01$). Although the thyroid volume was lower in primiparous (N=108) than in multiparous (N=150) women (mean±S.D.: 13.85±4.51 ml vs. 15.59±5.11 ml, resp., $P<0.01$), it was still significantly higher ($P<0.01$) than

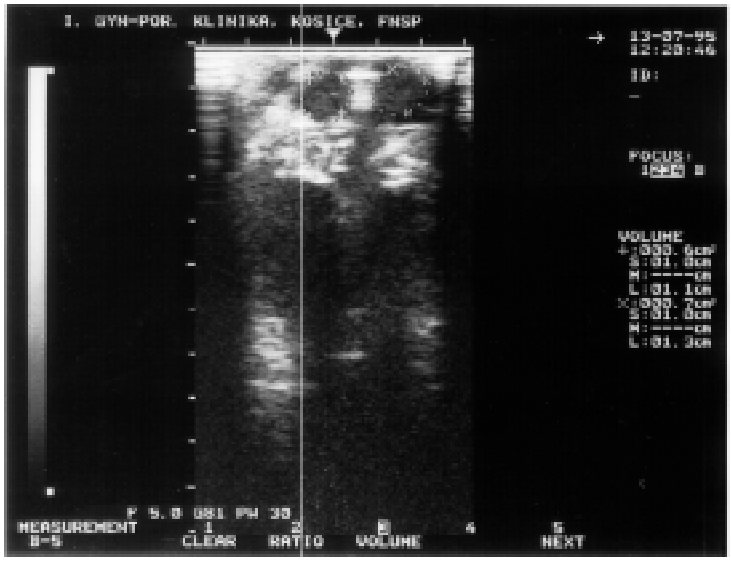

Fig. 1
Method of thyroid volume estimation in newborns according to Simpson. The circles show individual lobes of the thyroid as located on both sides of the larynx.

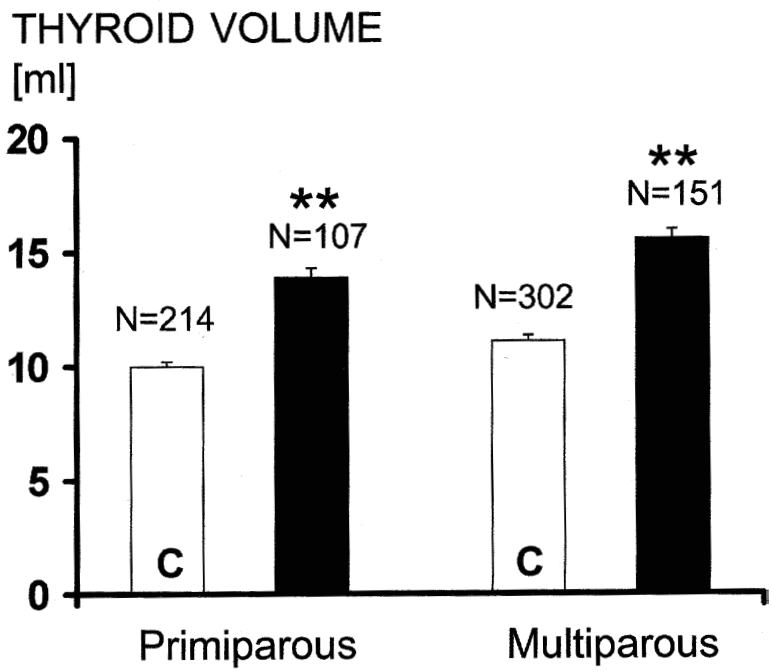

Fig. 2
Thyroid volume in primiparous (N= 107) and multiparous (N=151) mothers (black columns) and the double number of nearly age matched control women (C - white columns) who were either nulliparous or did not have delivery within last 12 months. Means and S.E. ** = P<0.01 vs. appropriate control.

that in a double amount of nearly age matched controls for primiparous (9.96±3.15 ml) and for multiparous (11.07±4.48 ml) women (Fig. 2).

In a total of 26/258 (10.1 %) mothers the thyroid volume was >22.0 ml which, in pregnant women, is considered as goiter (Glinoer et al. 1996). Such in-

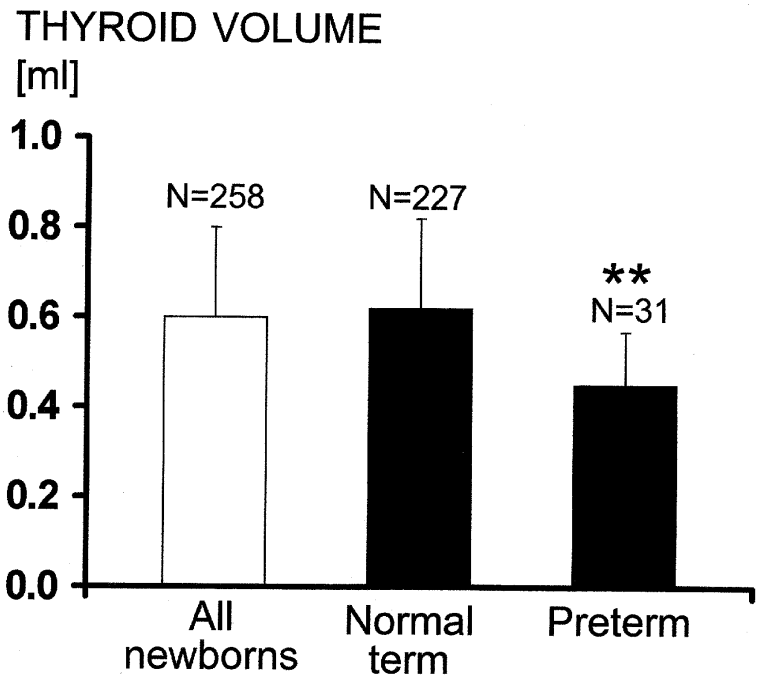

Fig. 3
Thyroid volume in all newborns (N= 258) white column) and in these born in normal term (N= 227) and preterm (N= 31) as shown in black columns. Mean and S.E. ** = P<0.01 vs. all newborns and these born in normal term.

crease was more frequent (P<0.05) in multiparous (20/150, 13.6 %) than in primiparous women (6/108, 5.6 %). In contrast, significantly higher frequency of smaller thyroids (<18.0 ml) was found in primiparous (93/108; 86,1 %) than in multiparous women (101/150; 67.3 %; P<0.001).

Thyroid volume in newborns. Mean thyroid volume found in all 258 newborns was 0.60±0.21 ml (median 0.5 ml, range 0.2-1.6 ml), the values in those born in term being higher than in preterms (mean±S.D. 0.62±0.20 ml vs. 0.45±0.12 ml; P<0.01; Fig. 3). The volume >1.0 ml was found in 16 newborns (6.2 %) and that >1.3 ml in 4 of them.

The thyroid volume <1.0 ml was found in 242 (93.8 %) and that in the range of 0.2-0.5 ml was found in 120 newborns. The frequency of small thyroid volumes (e.g. between 0.2 and 0.5 ml) was about the same in primiparous (51/108; 47.2 %) and multiparous women (69/150, 46.0 %), while the frequency of very small volumes (e.g. 0.2 to 0.3 ml) was higher in primiparous (24/108, 22.2 % vs. 20/150, 13.3 %, P<0.05, resp.). The frequency of the volumes >1.0 ml in multiparous women (11/150; 7.3 %) was about the same as in primiparous (5/108, 4.6 %).

No correlation was found between the thyroid volume and body weight in newborns. However, significant correlation was found between the thyroid volume in the mothers and their newborns (r=0.292, P<0.01).

Urinary iodine in mothers. The mean value of urinary iodine in mothers on the first week after delivery was 9.0±7.2 μg/dl (median 6.1, range 3.0-47.2). There was no difference between primiparous and multiparous mothers, although the excretion in primiparous ones was slightly higher (the mean of 10.3 vs. 8.4 μg/dl). In addition, there was no difference in urinary iodine between the mothers who had delivery in term and these who had it preterm (median 6.3 vs. 5.9 μg/dl). There was no correlation between urinary iodine in mothers and their thyroid volume.

Urinary iodine in newborns. In newborns, the mean urinary iodine in the first week after birth was 11.6±7.6 μg/dl (median 6.5, range 0.7-45.0). The median in these born in term was 6.6 μg/dl and that in preterms was 5.5 mg/dl. Significant correlation (r= 0.372, P<0.01) was found between urinary iodine in mothers and their newborns. Similarly as in

Table 1
Thyroid volume and urinary iodine in mothers after delivery

Authors	Country	N	Thyroid volume (ml) Mean ± S.D.	>22.0	Urinary iodine
Rasmussen et al. (1989)	Denmark	20	24.1 ± 2.2	30 %	not indicated
Brander et al. (1989)	Finland	21	13.7 ± 2.3	????	not estimated
Romano et al. (1991)	Italy	18	11.8 ± 1.3 (untreated)	????	mean 37.0 μg/24h
		17	10.1 ± 1.1 (treated)	????	mean 30.5 μg/24h
Glinoer et al. (1990)	Belgium	179	15.0 ± 6.8	????	median 45 μg/l
Boehles et al (1993)	Germany	61	14.4 (range 4.5-66.8)	????	58 μg/g Cr
Pedersen et al. (1993)	Denmark	56	about 12.4	????	53 μg/l
Berghout et al. (1994)	Netherlands	10	9.4 ± 3.0	????	not shown
Liesenkoetter et al. (1996)	Germany	38	20.1 ± 9.0 (treated)	????	104.5 μg/g Cr
		70	20.0 ± 11.0 (untretaed)	????	54.9 μg/g Cr
Hnikova et al (1996)	Czech Rep.	50	mean 12.0 (treated)	????	62 μg/l
		50	mean 14.3 (untreated)	????	43 μg/l
Smyth et al. (1997)	Ireland	115	16.0 ± 0.7	????	76 ± 5.7 μg/l
Tajtakova et al. (this study)	Slovakia	258	14.9 ± 4.9	10 %	mean 83 μg/l

mothers, the mean values of urinary iodine in newborns of primiparous were higher (not significantly) than these in newborns of multiparous mothers (13.1 vs. 10.3 μg/dl). There was no correlation found between thyroid volume and urinary iodine in newborns.

Iodine in mother milk. The mean level of iodine in mother milk was 8.9±14.1 μg/dl (media 5.5, range 4.3-75.1). It was observed that these afte Caesarean section had higher values. The average value in primiparous was unsignificantly higher than that in multiparous (10.5 vs. 8.1 μg/dl), while median was the same (5.5 μg/dl).

Discussion

In this cross-sectional study the thyroid volume found in 258 mothers 3-5 days after delivery was about 30 % higher than that in double amount of nearly age matched women who were either nulliparous or did not have delivery at least within last 12 months. In this respect the findings are comparable with longitudinal ultrasound studies in Denmark (Rasmussen et al. 1989; Pedersen et al. 1993), Belgium (Glinoer et al. 1990, 1995), Ireland (Smyth et al. 1991) and Italy (Romano et al. 1991), while in Netherlands Berghout et al. (1994) did not find any increased volume in ten longitudinaly followed pregnant women (Tab. 1). Among these countries, the iodine intake in Netherlands is considered sufficient, while that in the other countries (Belgium, Denmark, Italy and Ireland) is considered moderate or low. Thus, the difference between no increase in thyroid volume in Netherlands vs. increase in other countries is explained by the different iodine intake, e.g. sufficient in Netherlands and unsufficient in the other countries. This explanation may be challenged by the findings in Germany by Liesenkoetter et al. (1996) who were not able to prevent an increase of maternal thyroid gland volumes during pregnancy even by the daily administration of 300 μg potassium iodide.

Since the recent study of thyroid volume and urinary iodine in adolescents from 12 European countries showed the lowest thyroid volume and highest

Table 2
Thyroid volume and urinary iodine in newborns

Authors	Country	Thyroid volume (ml)	Urinary iodine
Chanoine et al. (1991)	Belgium	median 0.76 (N=85)	not estimated
Boehles et al. (1993)	Germany	median 0.61, range 0.28-1.50 (N=65)	median 30 µg/l
Glinoer et al. (1994)	Belgium	0.76±0.23 (0.2-1.4) treated (N= 46) 1.05±0.34 (0.2-2.5) (N= 48)	not shown
Liesenkoetter et al. (1995)	Germany	0.7 (0.5-1.6) supplemented (N= 38) 1.50 (0.4-2.6) (N= 70)	106 µg/g Cr 56 µg/g Cr
Hnikova et al. (1996)	Czech Rep.	mean 0.60 (treated, N=50) mean 0.60 (untreated, N=50)	60 µg/l 45 µg/l
Tajtakova et al. (this study)	Slovakia	0.6 ± 0.2 (N=258)	mean 113 µg/l

Cr = creatinine

urinary iodine in Netherlands and Slovakia (Delange et al. 1997), it may be suggested that Slovakia belongs to iodine-replete countries. This apparently results from well organized and monitored mandatory supply of iodized salt since early fifties and may be supported even by several other field studies showing low thyroid volume in large numbers of adolescents and adults (Langer et al. 1994; Tajtakova et al. 1998; Langer et al. 1998). However, when taking the iodine-replete status of both the Slovak and Dutch general population into account, the difference between no increase of thyroid volume in pregnant women in Netherlands and increase of that in Slovakia should be considered. One possible explanation may be that, although in Slovakia the iodine intake is considered satisfactory, it might be still slightly deficient for pregnant women. Such view may be supported by our findings of urinary iodine showing the median values between 5 and 10 µg/dl.

The thyroid volume in newborns found in this study was similar to that reported by several authors (Tab. 2). This is true namely for the lower limit of the range (e.g. 0.2-0.3 ml), while the mean values and upper limits appear to differ according to iodine intake and urinary iodine. Thus, in newborns of iodine supplemented mothers the upper limit was 1.4 ml (Glinoer et al. 1994) and 1.6 ml (Liesenkoetter et al. 1995) compared to 1.6 ml in this study, while the respective means were 0.7, 0.7 and 0.6 ml. However, in the newborns of unsupplemented mothers the upper limit was 2.5 ml (Glinoer et al. 1994) and 2.6 ml (Liesenkoetter et al 1995) and respective means were 1.05 and 1.5 ml which was definitely higher than the values found in this study.

Thyroid volume higher than 1.3 ml was found in 16 newborns. However, the frequency of such thyroid volume in newborns of multiparous mothers was higher (11/16) than that in primiparous ones (5/16) and, similarly, the thyroid volume higher than 22.0 ml was more frequent in multiparous (20/26) than in primiparous ones (6/26). This finding might result from repeated pregancies in multiparous women who were thus even repeatedly exposed to relative iodine deficiency. If so, it may be suggested that namely such women should be supplemented by small doses of iodide.

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Accepted: January 15, 1999