

## Iodine deficiency in pregnant women and in their neonates in the central Anatolian region (Kayseri) of Turkey

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Severe iodine deficiency disorders may have been eradicated in many parts of the world, but milder forms still exist and may escape detection. The aim of this study was to assess the iodine nutritional status of pregnant women and their newborns, and the prevalence rates and severity of iodine deficiency in the Kayseri region, which has appeared to be iodine deficient in previous studies. A cross-sectional voluntary screening study was performed in the Maternity Unit of the University Hospital. Seventy pregnant women and their babies participated in this study. Iodine deficiency with high prevalence of goiter, low urinary iodine excretion and high serum thyroglobulin concentrations were recognized among pregnant women and their babies in Kayseri. Regular administration of iodine, starting at preconception or in early pregnancy and continuing during the period of nursing, is recommended in these regions.

**Key words:** thyroid function, thyroglobulin, thyroid volume, urinary iodine, pregnant women, newborn.

Iodine deficiency remains an important public health problem for almost all countries worldwide. An estimated one-third of the world's population is currently exposed to the risk of iodine deficiency disorders (IDD). These disorders are caused by insufficient iodine intake and, in some areas, goitrogenic factors in the diet. Their negative impact on the health of individuals and societies, and thus on national economic development as well, is tremendous<sup>1-6</sup>.

The spectrum of health problems caused by iodine deficiency includes goiter stillbirth and hypothyroidism. However, its most severe consequence is mental retardation due to brain damage occurring during fetal development as a result of maternal hypothyroidism. Indeed, iodine deficiency is the world's greatest single cause of preventable brain damage in childhood. While cretinism is the most extreme outcome, of much greater significance are the subtler degrees of mental impairment that lead to poor school performance, reduced intellectual ability and impaired work capacity. Iodine-deficient communities have been found to score 10-15

points lower on IQ tests than iodine-replete ones. These disorders can be prevented by ensuring adequate iodine intake, which is the primary objective of the current worldwide drive to eliminate IDD<sup>7-13</sup>. According to the dietary allowances of iodine, as endorsed by the International Council for Control of Iodine Deficiency Disorders (ICCIDD) and the World Health Organization (WHO), the ideal iodine intake should be 150 mg/d for normal adults and 200 mg/d for pregnant (and lactating) women<sup>14,15</sup>.

Turkey has long been known as a mild to moderate iodine deficient area according to the figures obtained from previous epidemiological studies<sup>16-21</sup>. It is believed that total goiter prevalence in Turkey is as high as 30.5%, and that of visible goiter 6.7%<sup>20</sup>. It was also shown that goiter prevalence did not fall below 2% in any region, and may increase up to 50% in some<sup>20</sup>. Turkey is geographically a mountainous region with volcanic properties, so lack of iodine in the soil is an expected finding underlying endemic goiter. Parameters of iodine status in Central

Anatolia (Kayseri province and mountainous region) have shown severe iodine deficiency in previous cross-sectional studies<sup>17-21</sup>.

In this study we analyzed the iodine nutritional status of pregnant women and their babies, and the prevalence rates and severity of iodine deficiency in an area of suspected moderate to severe iodine deficiency (region of Kayseri).

### Material and Methods

We enrolled 70 pregnant women and their newborns into a cross-sectional voluntary screening study. The use of iodized salt was elicited by detailed history. All the subjects were apparently healthy women and none of them gave any history of thyroid disease, nor were they taking any thyroid modifying medication. The women were admitted for delivery at Erciyes University Maternity Unit. They gave birth to apparently healthy full-term babies. The Ethical Committee of the Faculty of Medicine approved the protocol.

Thyroid volume (TV) measurements were performed by ultrasound (Toshiba, 7.5 MHz linear transducer). Each lobe of the thyroid gland was assessed separately by measuring the three main diameters, and the total volume of the thyroid was calculated by the algorithm  $\pi/6$  height x width x depth<sup>22</sup>. In pregnant women, TV greater than 18.0 ml was considered as thyroid stimulation or hypertrophy and greater than 22.0 ml was considered as goiter<sup>23</sup>.

The upper limit of TV in newborns is 1.5 ml<sup>24</sup>.

The estimation of urinary iodine (UI) concentration was performed in spot urine samples obtained from all mothers and their newborns on the 5<sup>th</sup> day after delivery. Urine specimens were stored at  $-70^{\circ}\text{C}$  until required for analysis. Final evaluation was done with reversed-phase high-performance liquid chromatography (HPLC)<sup>25</sup>. The results were expressed in terms of  $\mu\text{g/L}$ . Classification of the severity of IDD in mothers was according to the cut-off points of UI excretion values; thus, UI values ( $\mu\text{g/L}$ ) less than 20 were considered severe, between 20 and 49 as moderate, between 50 and 99 as mild and greater than 100 as adequate<sup>4</sup>. The iodine deficiency in neonates was regarded to be mild with UI concentration between 31-50  $\mu\text{g/L}$ , moderate in the range 30-15  $\mu\text{g/L}$  and severe when values were less than 15  $\mu\text{g/L}$ .

The women provided approximately 10 ml venous blood just before delivery. A doctor or a trained midwife obtained cord blood samples (10 ml) during delivery. The blood samples were allowed to coagulate at room temperature before separation of the serum by centrifugation. The serum samples were frozen within 1 h of sampling and then kept frozen at  $-70^{\circ}\text{C}$  pending analysis.

Free triiodothyronine (FT3) and Free thyroxine (FT4) were measured by radioimmunoassay (Amersham UK). TSH (Amersham UK) thyroglobulin (Tg) (CIS Bio International, France) were determined using a sensitive immunoradiometric assay.

In mothers, biochemical criterion of excessive thyroid stimulation was defined as serum Tg greater than 30 ng/ml<sup>23,26</sup>. Cord blood normal Tg level is 2-54 ng/ml<sup>27</sup>.

In the absence of iodine deficiency, the frequency of neonatal TSH above 5 mU/L whole blood (or 10 mU/L serum) is less than 3%. A frequency of 3%-19.9% indicates mild IDD. Frequencies of 20%-39.9% and above 40% indicate moderate and severe IDD, respectively<sup>4,28,29</sup>.

### Statistical Analysis

All data processing was done with the Statistical Package for Social Sciences SPSS 10.0 software for Windows. Commonly used statistical methods (median, proportions) were applied to analyze the data. The data were found to be not normally distributed. The level of significance in all statistical tests was set at  $p \leq 0.05$ . The Mann-Whitney U test and Pearson's correlation were used for independent variables.

### Results

Only 23% of the mothers had access to iodized salt.

### Serum Studies

The median concentrations (and ranges) of neonatal TSH, Tg, FT3 and FT4 were 7.4 (1.06-30.54) mU/L, 71.6 (7.07-598.12)  $\mu\text{g/L}$ , 1.3 (0.64-4.29) pg/ml, and 1.3 (0.65-2.52) ng/dl, respectively. The corresponding levels for the mothers during labor were 2.2 (0.82-4.85) mU/L, 25.7 (0.38-185.18)  $\mu\text{g/L}$ , 1.3 (0.72-2.74) pg/ml, and 1.2 (0.78-2.07) ng/dl, respectively (Table I).

The median neonatal serum concentrations of TSH and Tg were significantly higher than the corresponding maternal levels ( $P < 0.0001$ ,

$P < 0.0001$ , respectively). There were no significant differences between the median neonatal concentrations and corresponding maternal levels of FT3 and FT4. There was a significant correlation between the newborn and maternal levels of FT3 ( $r: 0.32$ ,  $p < 0.05$ ) (Fig. 1).

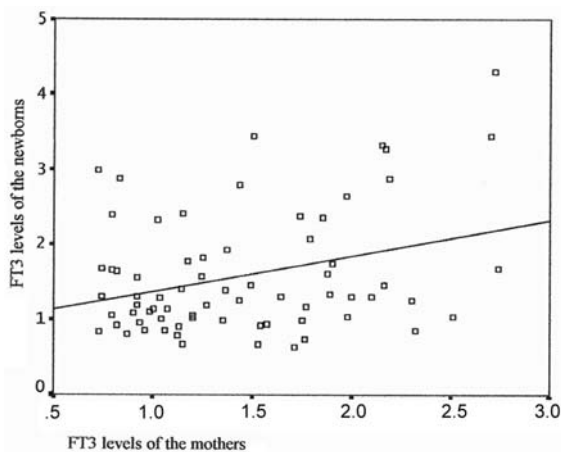
#### Urinary Iodine in Mothers

The median value of UI in mothers in the first week after delivery was  $30.2 \mu\text{g}/\text{dl}$  (range 3.20-171.50). There was no correlation between UI TV. Severe iodine deficiency ( $\text{UI} < 20 \mu\text{g}/\text{L}$ ) was detected in 33%, moderate deficiency (20-

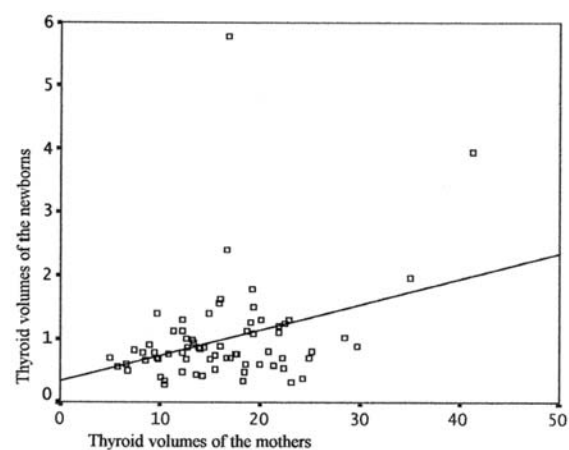
**Table I.** Median Serum Concentrations (and Ranges) of Tg, TSH, FT3, FT4, TV and UI in Pregnant Women During Labor and in Their Neonates

Parameter	Pregnant women during labor	Neonates
Tg (ng/ml)	25.7 (0.38-185.18)	71.6 (7.07-598.12)
TSH (mU/L)	2.2 (0.82-4.85)	7.4 (1.06-30.54)
FT3 (pg/ml)	1.3 (0.72-2.74)	1.3 (0.64-4.29)
FT4 (ng/dl)	1.2 (0.78-2.07)	1.3 (0.65-2.52)
TV (ml)	15.7 (4.90-41.19)	0.8 (0.28-5.78)
UI ( $\mu\text{g}/\text{L}$ )	30.2 (3.20-171.50)	23.8 (3.20-95.30)

Tg: Thyroglobulin, FT3: Free triiodothyronine, FT4: Free thyroxine, TV: Thyroid volume, UI: Urinary iodine.



**Fig. 1.** Correlation between free triiodothyronine (FT3) (pg/ml) levels of the mothers and their newborns ( $r: 0.32$ ,  $p < 0.05$ ).



**Fig. 2.** Correlation between thyroid volumes (ml) of the mothers and their newborns ( $r: 0.34$ ,  $p < 0.05$ ).

#### Thyroid Volumes in Mothers

In the first week after delivery, median TV found in all 70 women was 15.7 ml (range 4.90-41.19). Thyroid gland volume was in excess of the normal value of 18 ml in 37% of the women. Goiter was diagnosed in 17%.

#### Thyroid Volumes in Newborns

Median TV found in all 70 newborns was 0.8 ml (range 0.28-5.78). Volume  $> 1.5$  ml was found in eight newborns (11.4%). There was a significant correlation between the newborn and maternal thyroid volumes ( $r: 0.34$ ,  $P < 0.05$ ) (Fig. 2).

49  $\mu\text{g}/\text{L}$ ) in 33% and mild deficiency (50-99  $\mu\text{g}/\text{L}$ ) in 24% of the mothers. The UI excretion was normal ( $> 100 \mu\text{g}/\text{L}$ ) in 10% of these women.

#### Urinary Iodine in Newborns

In newborns, the median UI in the first week after birth was  $23.8 \mu\text{g}/\text{dl}$  (range 3.20-95.30). Severe iodine deficiency ( $\text{UI} < 15 \mu\text{g}/\text{L}$ ) was detected in 27%, moderate iodine deficiency (15-30  $\mu\text{g}/\text{L}$ ) in 33% and mild deficiency (31-50  $\mu\text{g}/\text{L}$ ) in 23% of the babies. The UI excretion was normal ( $> 50 \mu\text{g}/\text{L}$ ) in 17% of these newborns.

There was a significant correlation between the newborn and maternal UI levels ( $r: 0.24$ ,  $p < 0.05$ ) (Fig. 3).

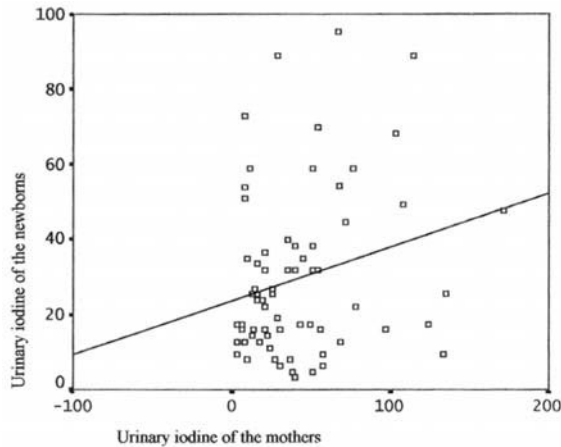


Fig. 3. Correlation between urinary iodine levels of the mothers and their newborns ( $0.24$ ,  $p < 0.05$ ).

## Discussion

Iodine deficiency causes developmental abnormalities in all age groups. These include not only goiter with impaired thyroid function but also decreased fertility, increased perinatal mortality, retarded growth, and impairment of mental development, including its extreme form, endemic cretinism<sup>6</sup>. The most detrimental effects of inadequate iodine intake appear in pregnant women and in children<sup>7-9</sup>. In 2001 alone, some 50 million children were born without any preventive measures having been taken against IDD during pregnancy<sup>3</sup>.

Urinary iodine is an indicator to assess present iodine intake<sup>6</sup>. There is an agreement that spot urine samples from a representative fraction of the population provide accurate information on the status of iodine nutrition. In our study, the UI excretion was adequate ( $>100 \mu\text{g/L}$ ) in only 10% of these mothers and in only 17% of their newborns ( $>50 \mu\text{g/L}$ ). The median values of UI in mothers and their babies on the 5<sup>th</sup> day after delivery were 30.2 (range 3.20-171.50) and 23.8 (3.20-95.30)  $\mu\text{g/L}$ , respectively, supporting that Kayseri is an area of moderate iodine deficiency<sup>4</sup>.

In this study, the median TVs of women and their babies were 15.7 ml (4.90-41.19) and 0.8 ml (0.28-5.78), respectively. In the same region, Kurtoğlu et al.<sup>21</sup> found a higher median TV of the newborn (1.26 ml) in 1994. The

volume of the thyroid gland was in excess of the normal value of 18 ml in 37.1% and goiter was diagnosed in 17.2% of the women ( $\text{TV} > 22 \text{ ml}$ ). Goiter ( $\text{TV} > 1.5 \text{ ml}$ ) was diagnosed in 11.4% of the newborns. In these findings, TV of the women and their babies in the Kayseri region pointed to mild iodine deficiency.

In population studies, Tg is a sensitive marker of iodine deficiency<sup>30,31</sup>. Median Tg levels of the mothers and their babies were 25.7 ng/ml (range 0.38-185.18) and 71.6 ng/ml (range 7.07-598.12), respectively. In 30 newborns (42.9%), cord Tg levels were above 54 ng/dl. In 29 mothers (41.4%), serum Tg levels were above 30 ng/dl. High serum levels of Tg in both mothers and newborns reflect that Kayseri is an iodine deficiency endemic area in Turkey<sup>17,21</sup>. In 27.1% of newborns, cord blood TSH level was above 10 mU/L; none of the mothers had serum TSH levels above 5 mU/L. Neonatal thyroid screening appears to be a particularly sensitive index in the monitoring of iodine supply at a population level<sup>28,29</sup>. In our study, the frequency of cord serum TSH above 10 mU/L (5 mU/L blood) was 27.1%, indicating moderate iodine deficiency.

Salt iodization is arguably the most effective way to correct iodine deficiency in the long run<sup>32</sup> and is currently the preferred method for iodine repletion in Turkey. However, the circumstances leading to severe iodine deficiency in remote areas may in turn govern the success of the efforts toward correction. In Turkey, iodization of table salt was initiated in 1968 on a voluntary basis, when the use of potassium iodide was approved by the revised food codex. According to recent numbers from the Ministry of Health, iodized salt production of the major salt companies increased to 57% of their entire production in 1999. Now, whole table salt has to be iodized; however, iodization of industrial salt is not enforced. Although iodization of table salt is now legally enforced, this is in fact impossible to establish countrywide. There are more than 400 salt manufacturers in Turkey, most of which are small local producers. These local manufacturers use traditional, old-fashioned methods in salt production, and they do not have the substructure appropriate for salt iodization. In many small places like these villages, the population rely on these local manufacturers using primitive technology<sup>16,19</sup>. Recently, the Health Ministry started to work on a national salt iodization program to improve

iodine intake nationwide, but the level of utilization of iodized salt is far from sufficient to improve iodine status. In our study, only 23% of the mothers had access to iodized salt.

Regular administration of iodine, starting at preconception or in early pregnancy and continuing during the period of nursing, is recommended in these regions.

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