IODINE STATUS AND THYROID FUNCTION IN LACTATING WOMEN AND INFANTS – A SURVEY IN THE ZAGREB AREA, CROATIA

Marina Prpić1, Maja Franceschi1,2,3, Valentina Vidranski1, Maria Andersson4,5, Michael B. Zimmermann5,6, Sandra Hunziker6, Milan Milošević7, Zvonko Kusić8 and Tomislav Jukić1,2,3

1Department of Oncology and Nuclear Medicine, Sestre milosrdnice University Hospital Centre, Zagreb, Croatia; 2School of Medicine, University of Zagreb, Zagreb, Croatia; 3Faculty of Medicine, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia; 4Division of Gastroenterology and Nutrition, Zurich University Children’s Hospital, Zurich, Switzerland; 5Iodine Global Network, Ottawa, Ontario, Canada; 6Human Nutrition Laboratory, Institute of Food, Nutrition and Health, Zurich ETH, Zurich, Switzerland; 7University of Zagreb, School of Medicine, Andrija Štampar School of Public Health, WHO Collaborative Centre for Occupational Health, Zagreb, Croatia; 8Croatian Academy of Sciences and Arts, Zagreb, Croatia

SUMMARY – Lactating women (LW) and infants have high dietary iodine requirements and are at risk of iodine deficiency. The aim of the study was to assess iodine status and thyroid function in LW and their breastfed infants in Zagreb, Croatia. The study included 133 LW and breastfed infant pairs. Urinary iodine concentration (UIC) and thyroid function parameters were measured in all subjects. In LW, breast milk iodine concentration (BMIC) was measured and iodine and salt rich food frequency questionnaire data were collected. Results of analysis indicated that 99.2% of the LW used iodized salt in household and 20.4% used iodine-containing vitamin and mineral supplements. Median (IQR) UIC was 75 μg/L (19.0-180.5 μg/L) in LW and 234 μg/L (151.0-367.5 μg/L) in infants, whereas BMIC was 121 μg/kg (87.8-170.8 μg/kg). Multivariate regression analysis revealed BMIC to be a significant predictor of infant UIC (p<0.001). Positive correlation was recorded between LW and infant thyroid function. This was the first study in Croatia demonstrating BMIC to be a reliable biomarker of iodine status during lactation and predicting iodine intake in breastfed infants. The study confirmed that mandatory salt iodization in Croatia ensured sufficient dietary iodine for LW and optimal iodine intake for breastfed infants via breast milk.

Key words: Breastfeeding; Infants; Iodine; Thyroglobulin; Thyroid hormones

Introduction

Iodine is an essential micronutrient and important component of thyroid hormones. Thyroid hormones are crucial for thermal and metabolic regulation, growth, development and function of many tissues, among which the most important are the brain and skeleton. Iodine is exclusively obtained through diet or iodine supplements1. Iodine requirements in infancy are high due to increased hormone synthesis. However, the infant thyroid has limited capacity for storing adequate amounts of iodine in response to high thyroid hormone requirements and intra-thyroidal meta-

Correspondence to: Assoc. Prof. Tomislav Jukić, MD, PhD, Department of Nuclear Medicine and Oncology, Sestre milosrdnice University Hospital Centre, Vinogradska c. 29, HR-10000 Zagreb, Croatia
E-mail: tomislav.jukic@kbcsm.hr
Received June 10, 2019, accepted September 24, 2019
bolic turnover\textsuperscript{2-4}. This period of infancy is a critical stage in the development of iodine deficiency\textsuperscript{5}. Severe iodine deficiency during infancy and early childhood results in increased mortality and morbidity, including goiter, delayed growth and development, as well as a broad spectrum of irreversible mental disorders, from cretinism to decreased intelligence and developmental testing scores\textsuperscript{6-8}. Breast milk is the only source of iodine for exclusively breastfed infants\textsuperscript{4}. The recommended daily iodine intake during lactation is 250 μg/day for women and 90 μg/day for children aged less than 2 years\textsuperscript{5,8}. Iodine is concentrated in human breast milk by the sodium iodide symporter in mammary glands and results in 20-25 times higher iodine concentration in breast milk than in plasma\textsuperscript{9,10}. Breast milk iodine concentration (BMIC) is associated with iodine intake of the mother and is a reliable biomarker of iodine status in lactating women (LW)\textsuperscript{11,12}. Studies suggest that the BMIC ≥100 μg/L indicates adequate iodine intake in lactating women\textsuperscript{9,13-15}, but data are equivocal\textsuperscript{16}.

Urinary iodine concentration (UIC) measurement is used to assess iodine status in the general population. Iodine status in infants is assessed by UIC\textsuperscript{6} and median UIC ≥100 μg/L indicates iodine sufficiency in infants\textsuperscript{6,10}, but the threshold is uncertain. Iodine status can also be assessed by thyroglobulin (Tg) concentration in serum samples\textsuperscript{17-21}. Thyroglobulin is a sensitive biomarker of iodine intake, as reported in schoolchildren\textsuperscript{18,21}, pregnant women\textsuperscript{19}, and 6- to 24-month-old infants\textsuperscript{20}, with the U-shaped curve. High Tg values are recorded in iodine deficiency but also in iodine excess. Thyroglobulin reference range in iodine-sufficient areas for adults and children is generally between 4 and 40 μg/L. Median Tg of <13 μg/L in schoolchildren\textsuperscript{18} and ≤10 μg/L\textsuperscript{19} in pregnant women indicates iodine sufficiency.

National programs of universal salt iodization have made remarkable progress in improving iodine status in general populations both in Croatia and worldwide. In 1996, Croatia introduced this preventive measure by legislation requiring 18-23 mg of potassium iodide (KI) \textit{per} kilogram of salt. This involved fortification of all salt for human and animal use\textsuperscript{21-24}. As a result, Croatia has reached iodine sufficiency, as demonstrated in national studies from 2002 and 2009, and in a regional study conducted in 2012, where median UIC in school-age children was 140 μg/L\textsuperscript{22,23}, 288 μg/L\textsuperscript{24}, and 205 μg/L\textsuperscript{21}, respectively. In the 2009 survey, median UIC for women of reproductive age was 136 μg/L and for pregnant women 159 μg/L\textsuperscript{24}. The mean KI content \textit{per} kg of salt measured in 2009, 2012 and 2015 demonstrated adequate iodine fortification of Croatian salt with values of 25.5, 24.9 and 23.8 (SD=3.1) mg/kg, respectively\textsuperscript{21,23,24}. A recently published international study presented data on iodine status in 73 LW/infant pairs in Croatia\textsuperscript{16}. However, detailed data on iodine status specific to LW and infants in Croatia are limited.

The aim of this study was to assess iodine status and thyroid function in LW/infant pairs in Zagreb, Croatia, and to evaluate UIC and BMIC for assessment of iodine intake in LW. Another aim was to assess interrelationship between lactating mothers’ and infants’ thyroid function parameters. We measured UIC, BMIC, thyrotropin (TSH), total thyroxine (tT4) and thyroglobulin (Tg) in all subjects.

### Subjects and Methods

We conducted a cross-sectional study in LW and their breastfed infants in Zagreb, Croatia between 2014 and 2016, as previously described by Dold \textit{et al.}\textsuperscript{16,25}. Approvals were obtained from the Ethics Committees of the Zurich ETH (EK 2013-N-82), Zurich, Switzerland, Sestre milosrdnice University Hospital Centre, Zagreb (EP-1356/14-9), and Zagreb West (109/15-2) and Zagreb Center (01-3751/1-2015) Primary Health Care Centers from Zagreb, Croatia.

Lactating women/infant pairs were recruited at pediatric clinics and through breastfeeding support groups at local Primary Health Care Centers in Zagreb. All LW were residents of the central, south and west parts of Zagreb, Croatia, for at least 12 months prior to recruitment to the study. Study inclusion criteria for LW were as follows: age 18-44, breastfeeding, no history of thyroid disease, no medication use for chronic disease, no exposure to iodine-containing contrast agents or drugs since childbirth.

Inclusion criteria for infants (infants aged 2-24 weeks and toddlers aged 6-24 months) were as follows: healthy and full-term (38-42 gestational weeks) singletons, normal birth weight (>2500 g), no history of thyroid disease, and not receiving any iodine-containing supplements. The term toddlers (age 6-24 months) referred to infants receiving both comple-
mentary foods and breast milk, similar to a recently published study.

All included infants together with their mothers constituted LW/infant pairs. During an interview, a trained physician explained the study to the mothers and their written informed consent was obtained. A questionnaire with questions addressed to both the LW and the infant was filled out during the interview. The questionnaire for LW collected information on the type of delivery, parity, total number of children, current cigarette smoking, education degree, use of iodine-containing supplements (currently and during pregnancy), frequency of iodine-containing food consumption (e.g., foods rich in salt and foods with natural high iodine content) and use of household iodized salt. LW were also asked about feeding practices for their infants, specifically consumption of breast milk, water, tea, juice and infant formula, canned, powdered or fresh milk, or complementary solid or semi-solid foods prepared at home, as well as salt intake.

Using the WHO/UNICEF criteria that define infant feeding practices, breastfeeding practices were divided into the following 3 groups: 1) exclusive (breast milk); 2) predominant (breast milk and liquids (water, water-based drinks, fruit juice)); and 3) partial (breast milk and solid or semi-solid foods, liquid, non-human milk and formula).

Breast milk was collected from LW to determine BMIC. Breast milk samples (10 mL) were obtained by manual expression into a plastic container, separated into aliquots and stored at -20 °C.

Spot urine samples and dried blood spot samples (DBS) were collected to determine UIC and thyroid function (Tg, TSH and tT4) in LW and infants.

Urine samples from LW were collected using sterile cups for urine collection and aliquoted into sterile Vacuette® tubes (yellow cap) (Greiner Bio-One, Kremsmünster, Austria). Infants’ spot urine samples were collected using a pad collection system (SteriSets Newcastle Urine Collection Pack Pediatric, Newcastle, UK). Urine samples were stored at -20 °C until analysis.

Dried blood spot samples were collected as five blood drops from a finger prick from LW and heel prick from infant and directly collected onto filter paper cards (Whatman 903 filter paper cards, GE Healthcare, USA). DBS cards were dried at room temperature for 24 hours, then placed into plastic bags and stored at -20 °C. DBS filter paper cards were sent at room temperature condition, while breast milk samples were sent stored on dried ice to Zurich ETH for analysis.

Breast milk iodine content was determined by multicollector-inductively coupled plasma mass spectrometry (MC-ICP-MS) with the use of isotope dilution analysis with iodine-129 and tellurium for mass bias correction. Pre-analytical procedure of breast milk samples involved the use of tetra-methyl-ammonium hydroxide for iodine extraction at 90 °C for 180 min.

Urinary iodine concentration in spot urine samples from LW and infants was determined at laboratory of the Sestre milosrdnice University Hospital Centre, Zagreb. We used a modification of the Sandell-Kolthoff reaction on AutoAnalyzer AA3 HR (Seal, Wisconsin, USA), with precision as a coefficient of variation below 10%.

DBS TSH and DBS tT4 were analyzed with Delfia NeoTSH and Neonatal T4 kits (Perkin Elmer, Waltham, Massachusetts, USA) using automated fluoroimmunoassay (GSP 2021-0010; Perkin Elmer, Waltham, Massachusetts, USA). DBS Tg analysis was done by a sandwich enzyme-linked immunosorbent assay (ELISA). All methods followed quality control rules with suitable QC materials. Normal reference ranges for TSH and tT4 as supplied by the manufacturer were as follows: TSH 0.1-4.5 mU/L and 0.1-3.7 mU/L for 60- to 155-day-old infants and for subjects aged 1-99 years, respectively; tT4 80-165 nmol/L and 65-165 nmol/L for 60- to 155-day-old infants and for subjects aged 1-99 years, respectively. Of note, DBS Tg reference ranges specific to LW and infants were not available.

Statistical analysis

Kolmogorov-Smirnov test was used to test for normal distribution of continuous variables. Normally distributed continuous data were reported as mean (± standard deviation) and evaluated with a 2-sided independent t-test for equal variances. Non-normally distributed interval data and ordinal data were reported as median (interquartile range, IQR) and evaluated using Mann-Whitney U test. Categorical variables were presented as counts (percentages) and evaluated using χ²-test. Pearson’s correlation coefficients were calculated between thyroid function markers, UIC and BMIC in LW and infants. All p values below 0.05 were considered significant. All statistical procedures
were performed using IBM SPSS Statistics version 25.0 (https://www.ibm.com/analytics/spss-statistics-software).

Results

A total of 133 LW/infant pairs fulfilled the inclusion criteria and were enrolled in the study (133 LW, 101 infants and 32 toddlers). Tables 1 and 2 summarize general characteristics of the LW and infants included in the study. All infants were breastfed; of them, 55% were exclusively breastfed, 20% predominantly breastfed additionally receiving plain water, flavored tea and juice, while 24% were partially breastfed. Infants partially breastfed received plain water (35%), infant formula (23%), and solid or semi-solid food (27%). None of the infants received iodine-containing supplements. Study results showed that 80.5% of LW had used iodine-containing supplements during pregnancy, 53.4% from birth, and 36.8% at the time of the study (Table 1).

Table 3 shows the frequency of iodine-containing food consumption during one month prior to the study. LW consumed bread, vegetables and fruits (60 meals per month), followed by cheese, meat, milk/yogurt (30-32 meals per month) and eggs (16 meals per month). Fish, salted meat and snack consumption was less than 10 meals per month. Meals were prepared

Table 1. Characteristics of lactating women

| Mothers: N=133 |          |
|---------------|----------|
| Age (yrs), mean ± SD | 31.5±4.7 |
| Number of children (total, including breastfed infants), median (IQR) | 1.0 (1.0-2.0) |
| Finished college/university as highest degree or level of completed education, n (%) | 100 (75.2) |
| Vaginal delivery, n (%) | 113 (85.0) |
| Number of breastfeeding sessions during 24 h, mean ± SD | 7.7±2.8 |

| Vitamin or mineral supplement use |          |
|----------------------------------|----------|
| During pregnancy, n (%) | 107 (80.5) |
| Containing iodine, n (%) | 21/107 (19.6) |
| Since birth, n (%) | 71 (53.4) |
| Containing iodine, n (%) | 11/71 (15.5) |
| Using supplement at the time of study, n (%) | 49 (36.8) |
| Containing iodine, n (%) | 11/49 (22.4) |

| Iodized salt use |          |
|------------------|----------|
| At home, n (%) | 132 (99.2) |
| Containing iodine, n (%) | 130/132 (98.5) |
| Used for cooking, n (%) | 130 (98.5) |
| At table, n (%) | 91 (68.9) |

Table 2. Characteristics of infants and breastfeeding practice

|                        | Infants (2-26 weeks) | Toddlers (27-96 weeks) | p   |
|------------------------|----------------------|------------------------|-----|
| Age (weeks), mean ± SD* | 12.6±7.1             | 40.0±11.0              | <0.001 |
| Gestational age (weeks), mean ± SD* | 39.5±1.7             | 39.5±1.2               | 0.956 |
| Birth weight (g), mean ± SD* | 3565.8±460.9          | 3413.4±392.5           | 0.072 |
| Number of breastfeeding sessions for 24 h, mean ± SD* | 8.2±2.5              | 6.2±3.2                | 0.002 |

Breastfeeding practice**

|                              | Infants | Toddlers | p   |
|------------------------------|---------|----------|-----|
| Exclusive breastfeeding, n (%) | 73 (72.3) | 1 (3.1) | <0.001 |
| Predominant breastfeeding, except for sweetened, flavored water, fruit juice, tea, n (%) | 24 (23.8) | 2 (6.3) | <0.001 |
| Partial breastfeeding, n (%) | 4 (3.9) | 29 (90.6) | <0.001 |
| Plain water use, n (%) | 16 (15.8) | 31 (96.9) | <0.001 |
| Infant formula use, n (%) | 18 (17.8) | 13 (40.6) | 0.008 |
| Solid or semisolid (mushy) food use, n (%) | 8 (8.9) | 28 (87.5) | <0.001 |

*independent t-test; **χ²-test
and eaten at home with the use of household iodized salt (98.5%), during cooking (98.5%) and additionally at the table (69.9%) (Table 3).

In LW, median (IQR) UIC was 75 μg/L (19.0-180.5 μg/L) and BMIC 121 mg/kg (87.8-170.8 mg/kg); in infants, median (IQR) UIC was 232 μg/L (130.5-383.0 μg/L). The BMIC positively correlated with infant UIC (r=0.415, p<0.001) (Fig. 1), but not with LW UIC (r=-0.165, p<0.085). Using multiple linear regression analysis, LW BMIC significantly predicted infant UIC (b=0.355; CI 0.51, 1.99, p<0.001).

Breast milk iodine concentration positively correlated with LW consumption of dairy products (milk and yoghurt) (r=0.262, p=0.006). However, BMIC did not correlate with any other iodine-containing food or with consumption of iodine-containing supplements. We observed no correlation between LW UIC and consumption of iodine-rich food, or with iodine-containing vitamin supplement use during pregnancy, from birth, or at the time of the study. LW consumption of fish (β=0.224, p=0.036, r²=23) was a positive predictor of infant UIC, while egg consumption addi-

---

**Table 3. Data on food consumption in lactating women during the last month reported in the food frequency questionnaire**

| Maternal intake of iodine rich foods (N=133), median (IQR) |
|----------------------------------------------------------|
| Number of meals consumed within the last 24 h before the study | 4.0 (3.0-5.0) |
| Prepared at home | 3.0 (3.0-4.5) |
| Prepared out of home | 0.0 (0.0-0.0) |
| Number of consumed meals during the last month, median (IQR) |
| Salted meat | 3.0 (3.0-4.5) |
| Bread | 60.0 (30.0-90.0) |
| Meat | 30.0 (16.0-32.0) |
| Cheese | 32.0 (16.0-60.0) |
| Salty snacks | 3.0 (1.0-8.0) |
| Milk/yoghurt (cup 0.25 L) | 30.0 (27.0-60.0) |
| Vegetables | 60.0 (32.0-90.0) |
| Fruit | 60.0 (30.0-77.0) |
| Fish | 8.0 (3.0-8.0) |
| Eggs | 16.0 (8.0-16.0) |

IQR = interquartile range

---

Fig. 1. Correlation of infant urinary iodine concentration (UIC) and lactating women breast milk iodine concentration (BMIC).

Fig. 2. Correlation of infant dried blood spot thyroglobulin (Tg) and lactating women total thyroxine (tT4).

Fig. 3. Correlation of infant and lactating women dried blood spot thyroglobulin (Tg).
tionally positively correlated with infant Tg (β=0.263, p=0.043, r²=54). Exclusive breastfeeding (r=-0.203, p=0.004) and number of breastfeeding sessions (r=-0.300, p<0.001) correlated negatively with LW UIC. Breast milk iodine content positively correlated with LW age (p=0.044) and negatively with infant age (r=-0.205, p=0.032). LW UIC positively correlated with infant age (r=0.322, p<0.001).

Thyroid function markers of LW/infant pairs are presented in Table 4. Median (IQR) TSH, tT4 and Tg values of LW were 0.3 (0.3-0.6) mU/L, 65.5 (49.8-85.3) mmol/L and 5.3 (2.8-10.6) μg/L, respectively. In infants, median (IQR) TSH, tT4 and Tg were 0.6 (0.4-1.0) mU/L, 95.0 (67.5-117.0) mmol/L and 13.8 (7.4-32.6) μg/L, respectively. In both LW and infants, TSH levels were within the normal range. No significant correlations were found between infant UIC, LW UIC or BMIC and LW/infant TSH, tT4 and Tg. LW TSH, tT4 and Tg positively correlated with infant TSH, tT4 and Tg (p<0.001), respectively (Figs. 2 and 3).

Discussion

This was the first study to report on the iodine status, BMIC and thyroid function in LW and infants in Croatia. According to the last population study, Croatia is an iodine sufficient country, based on median UIC measurement in school-age children. The results of this study suggest that LW UIC alone is a less reliable indicator for assessment and monitoring of iodine status in LW and their infants. Median BMIC in our study population was >100 μg/kg (121 μg/kg), indicating adequate iodine status in LW. Median UIC of 75 μg/L in the mothers was below the WHO threshold, but recent data suggest that UIC is not a reliable biomarker of iodine status during lactation. We observed negative correlation between UIC and BMIC of the LW.

Our results suggest that iodine is preferentially excreted in breast milk, likely as a physiologic compensatory mechanism to ensure adequate iodine intake to weaning infants in order to preserve enough iodine for thyroid hormone synthesis, as recently observed by Dold et al. They suggest the use of a wide BMIC reference range of 60-465 mg/kg for assessment of iodine status in exclusively breastfeeding women residing in iodine sufficient regions. Nazeri et al. report similar results of adequate BMIC and low UIC in LW.

We observed a significant correlation between BMIC and infant UIC, suggesting that BMIC may be used as a predictor for infant iodine status in exclusively breastfed infants. Median UIC in infants was 232 μg/L. However, infant daily urinary volume is around 0.5 L, much lower than in adults (1.5 L). Accordingly, estimated daily iodine excretion in infants can be calculated as UICx0.5 L. Most of the infants were exclusively breastfed, while the remaining infants received infant formula or semi-solid and solid foods. Exclusive breastfeeding and number of breastfeeding sessions were in negative correlation with LW UIC, which could be explained physiologically as more iodine being shifted by mammary gland natrium iodide symporter to breastmilk with each breastfeeding session. Infant age was negatively correlated with BMIC, but positively correlated with LW UIC. This reflects a decline of BMIC over time as the needs of older infants for consumption of breast milk decrease with the introduction of semi-solid and solid foods. There was

| Table 4. UIC, BMIC, and thyroid function markers in lactating women, infants and toddlers |
|----------------------------------------|----------------|----------------|------|
|                                       | Lactating women | Infants (2-26 weeks) | Toddlers (27-96 weeks) |
|                                       | N=133 | N=101 | N=32 |
| UIC (μg/L)*                           | 75.0 (19.0-180.5) | 234.0 (151.0-367.5) | 208.5 (102.0-375.3) |
| TSH (mU/L)*                           | 0.3 (0.3-0.6) | 0.6 (0.4-1.05) | 0.6 (0.4-0.8) |
| tT4 (mmol/L)*                         | 65.5 (49.8-85.3) | 95.0 (67.5-117.0) | 79.0 (64.3-99.0) |
| Tg (μg/L)*                            | 5.3 (2.8-10.6) | 13.8 (7.4-32.6) | 19.6 (15.1-40.7) |
| BMIC (μg/kg)*                         | 121.0 (87.8-170.8) | - | - |

*Mann-Whitney U test: difference between infants and toddlers; values are median (IQR); UIC = urinary iodine concentration; BMIC = breast milk iodine concentration; TSH = thyrotropin; tT4 = total thyroxine; Tg = thyroglobulin
no statistically significant difference between infant and toddler UIC (p=0.502). The main source of dietary iodine in LW in Croatia is iodized salt; 99.2% of LM reported use of salt (Table 1). Dairy products are another important dietary iodine source and we observed positive correlation between BMIC and consumption of cows’ milk and yoghurt. Median (IQR) iodine concentration in cows’ milk in Croatia is reported to be 279 μg/L (242–322 μg/L), a rather high value compared to other European countries.

According to data from food frequency questionnaire, the mean daily milk consumption of LW was 0.25 L (Table 3). This provided a rough estimate of 70 μg of LW median daily iodine intake from cows’ milk.

Study results revealed euthyroid hormonal status in both LW and their infants. No significant correlation between BMIC and infant TSH, tT4, Tg, or between infant UIC and infant TSH, tT4 or Tg was demonstrated. No specific reference ranges for thyroid function tests are available for LW. Lower mean tT4 concentrations have been reported in LW compared with non-pregnant, non-lactating women. The thyroid hormone profile in LW resembles hypothyroid or iodine deficiency state with low T4 and low reverse T3.

However, LW in the present study had low TSH but still within the normal range. Obviously, with iodine metabolism shifting from thyroid to mammary gland, thyroidal iodine metabolic turnover in LW may be decreased compared to non-lactating state to preserve enough iodine for infants. Low Tg level in LW with median value of 5.3 μg/L may reflect hypo-stimulation of the thyroid gland, a physiologic adaptation during the breastfeeding period (Table 4).

Thyroglobulin in infants was higher, with median value of 13.8 μg/L in infants and 19.6 μg/L in toddlers, reflecting increased iodine metabolic turnover in comparison to older children, as iodine intake in infants/toddlers from Zagreb was in the sufficient range. Serum Tg levels are normally higher in infancy than in older children or adults.

However, no specific reference range in infants/toddlers is available for the DBS Tg assay used in our study. Maternal TSH, tT4 and Tg concentrations were positively correlated with infant tT4, TSH and Tg, respectively. Pal et al. have recently reported a similar positive correlation between LW and infant thyroid hormones and TSH profiles, but only in the iodine deficient group defined with UIC <100 μg/L. Most of the Croatian LW had UIC less than 100 μg/L.

Conclusion

This study confirms that mandatory salt iodization in Croatia ensures sufficient dietary iodine for LW and optimal iodine nutrition for breastfed infants via breast milk. We observed a positive correlation between LW and infant thyroid function parameters. BMIC is a reliable biomarker of iodine status during lactation in LW and predicts iodine intake in breastfed infants.

Acknowledgment

Funding for this study was provided by the Global Alliance for Improved Nutrition, Geneva, Switzerland, UNICEF, Zurich ETH and with support of the Croatian Science Foundation (IP-2014-09-6499).

References

1. Velasco I, Bath SC, Rayman MP. Iodine as essential nutrient during the first 1000 days of life. Nutrients. 2018;10(3). doi: 10.3390/nu10030290
2. Zimmermann MB. The importance of adequate iodine during pregnancy and infancy. World Rev Nutr Diet. 2016;115: 118-24. doi: 10.1159/000442078
3. Delange F. Screening for congenital hypothyroidism used as an indicator of the degree of iodine deficiency and of its control. Thyroid. 1998;8(12):1185-92. doi: 10.1089/thy.1998.8.1185
4. Stinca S, Andersson M, Herter-Aaeberli I, Chabab L, Cherkawi M, El Ansari N, et al. Moderate-to-severe iodine deficiency in the “first 1000 days” causes more thyroid hypofunction in infants than in pregnant or lactating women. J Nutr. 2017; 147(4):589-95. doi: 10.3945/jn.116.244665
5. World Health Organization/International Council for the Control of the Iodine Deficiency Disorders/United Nations Childrens Fund (WHO/ICCIDD/UNICEF). Assessment of the iodine deficiency disorders and monitoring their elimination. Geneva: World Health Organization, 2007.
6. de Escobar GM, Obregón MJ, del Rey FE. Iodine deficiency and brain development in the first half of pregnancy. Public Health Nutr. 2007;10(12A):1554-70. doi: 10.1017/S136898007360928
7. Zimmermann MB. The role of iodine in human growth and development. Semin Cell Dev Biol. 2011;22(6):645-52. doi: 10.1016/j.semcdb.2011.07.009
8. Andersson M, de Benoist B, Delange F, Zupan J, Secretariat W. Prevention and control of iodine deficiency in pregnant and lactating women and in children less than 2-years-old: conclusions and recommendations of the Technical Consultation. Public Health Nutr. 2007;10(12A):1606-11. doi: 10.1017/S136898007361004
Iodine status and thyroid function in lactating women and infants

9. Semba RD, Delange F. Iodine in human milk: perspectives for infant health. Nutr Rev. 2001;59 (8):269–78. doi:10.1111/j.1753-4887.2001.tb05512.x

10. Andersen SL, Moller M, Laurberg P. Iodine concentrations in milk and in urine during breastfeeding are differently affected by maternal fluid intake. Thyroid. 2014;24(4):764–72. doi: 10.1089/thy.2013.0541

11. Azizi F, Smyth P. Breastfeeding and maternal and infant iodine nutrition. Clin Endocrinol (Oxf). 2009;70(5):803–9. doi: 10.1111/j.1365-2265.2008.03442.x

12. Ordookhani A, Pearce EN, Hedayati M, Mirmiran P, Salimi S, Azizi F, et al. Assessment of thyroid function and urinary and breast milk iodine concentrations in healthy newborns and their mothers in Tehran. Clin Endocrinol (Oxf). 2007;67(2):175–9. doi: 10.1111/j.1365-2265.2007.02857.x

13. Pal N, Samanta SK, Chakraborty A, Chandra NK, Chandra R, Gowachirapant S, et al. Thyroglobulin is a sensitive measure of both deficient and excess iodine intakes in children and indicates no adverse effects on thyroid function in the UIIC range of 100-299 μg/L: a UNICEF/ICCIDD study group report. J Clin Endocrinol Metab. 2013;98(3):1271–80. doi: 10.1210/jc.2012-3952

14. Nazeri P, Kabir A, Dalili H, Mirmiran P, Azizi F. Breast milk iodine concentrations and iodine levels of infants according to the iodine status of the country of residence: a systematic review and meta-analysis. Thyroid. 2018;28(1):124–38. doi: 10.1089/thy.2017.0403

15. Dror DK, Allen LH. Iodine in human milk: a systematic review. Adv Nutr. 2018;9(Suppl 1):347S–57S. doi: 10.1093/advances/nmy020

16. Dold S, Zimmermann MB, Aboussad A, Cherkaoui M, Jia Q, Jukić T, et al. Breast milk iodine concentration is a more accurate biomarker of iodine status than urinary iodine concentration in exclusively breastfeeding women. J Nutr. 2017;147(4):528–37. doi: 10.3945/jn.116.242560

17. Pearce EN, Caldwell KL. Urinary iodine, thyroid function, and thyroglobulin as biomarkers of iodine status. Am J Clin Nutr. 2016;104Suppl 3:898S–901S. doi: 10.3945/ajcn.115.110395

18. Zimmermann MB, Aeberli I, Andersson M, Assey V, Yorg JA, Jooste P, et al. Thyroglobulin is a sensitive measure of both deficient and excess iodine intakes in children and indicates no adverse effects on thyroid function in the UIIC range of 100-299 μg/L: a UNICEF/ICCIDD study group report. J Clin Endocrinol Metab. 2013;98(3):1271–80. doi: 10.1210/jc.2012-3952

19. Stincu S, Andersson M, Weibel S, Herter-Aeberli I, Fingerhut R, Gawarchirapant S, et al. Dried blood spot thyroglobulin as a biomarker of iodine status in pregnant women. J Clin Endocrinol Metab. 2017;102(1):23–32. doi: 10.1210/jc.2016-2829

20. Farebrother J, Zimmermann MB, Assey V, Castro MC, Cherkaoui M, Fingerhut R, et al. Thyroglobulin is markedly elevated in 6- to 24-month-old infants at both low and high iodine intakes and suggests a narrow optimal iodine intake range. Thyroid. 2019;29(2):268-77. doi: 10.1089/thy.2018.0321

21. Jukić T, Zimmermann MB, Granić R, Prpić M, Krilić D, Juresa V, et al. Sufficient iodine intake in schoolchildren from the Zagreb area: assessment with dried blood spot thyroglobulin as a new functional biomarker for iodine deficiency. Acta Clin Croat. 2015;54(4):424–31.

22. Kuscić Z, Jukić T. History of endemic goiter in Croatia: from severe iodine deficiency to iodine sufficiency. Coll Antropol. 2005;29(1):9–16.

23. Kuscić Z, Novosel SA, Dabelić N, Punda M, Rončević S, Labar Z, et al. Croatia has reached iodine sufficiency. J Endocrinol Invest. 2003;26(8):738–42.

24. Kuscić Z, Jukić T, Rogan SA, Jureša V, Dabelić N, Staničić J, et al. Current status of iodine intake in Croatia – the results of 2009 survey. Coll Antropol. 2012;36(1):123–8.

25. Dold S, Zimmermann MB, Jukić T, Kuscić Z, Jia Q, Sang Z, et al. Universal salt iodization provides sufficient dietary iodine to achieve adequate iodine nutrition during the first 1000 days: a cross-sectional multicenter study. J Nutr. 2018;148(4):587–98. doi: 10.1093/jn/nxy015

26. Wawchinek O, Eber O, Petek W, Wakonig P, Güarakar A. Bestimmung der Harnjod- ausscheidung mittels einer modifizierten Cer-Arsenit-Methode. Berichte ÖGKC. 1985;8:13–5.

27. Stincu S, Andersson M, Erhardt J, Zimmermann MB. Development and validation of a new low-cost enzyme-linked immunosorbent assay for serum and dried blood spot thyroglobulin. Thyroid. 2015;25(12):1297–305. doi: 10.1089/thy.2015.0428

28. Dold S, Baumgartner J, Zeder C, Krzystek A, Osei J, Haldimann Z, et al. Optimization of a new mass spectrometry method for measurement of breast milk iodine concentrations and an assessment of the effect of analytic method and timing of within-feed sample collection on breast milk iodine concentrations. Thyroid. 2016;26(2):287–95. doi: 10.1089/thy.2015.0317

29. Iwatani Y, Amino N, Tanizawa O, Mori H, Kawashima M, Yabu Y, et al. Decrease of free thyroxin in serum of lactating women. Clin Chem. 1987;33(7):1217-9.

30. Stuebe AM, Meltzer-Body S, Pearson B, Pedersen C, Greven K. Maternal neuroendocrine serum levels in exclusively breastfeeding mothers. Breastfeed Med. 2015;10(4):197–202. doi: 10.1089/bfm.2014.0164
Sažetak

UNOS JODA I FUNKCIJA ŠTITNJAČE U DOJILJA I DOJENČADI
– ISTRAŽIVANJE NA PODRUČJU GRADA ZAGREBA

M. Prpić, M. Franceschi, V. Vidranski, M. Andersson, M. B. Zimmermann, S. Hunziker, M. Milošević, Z. Kusić, T. Jukić

Dojilje i dojenčad imaju povećane zahtjeve za unos joda pa su pod rizikom nedostatnog unosa joda. Cilj istraživanja bio je ispitati unos joda i funkciju štitnjače u dojilja i njihove dojenčadi. U istraživanje je uključeno 133 para dojilja i dojenčadi s područja grada Zagreba. U svih ispitanika određena je koncentracija joda u mokraći i funkcija štitnjače, dok je dodatno u dojilja određena koncentracija joda u majčinu mlijeku i prikupljeni su podaci o unosu hrane koja sadrži jod i sol. Prema rezultatima istraživanja 99,2% dojilja koristilo je jodiranu kuhinjsku sol, a 20,4% vitamine i minerale s jodom. Medijan (interkvartilni raspon) izlučivanja joda mokraćom iznosio je 75 μg/L (19,0-180,5 μg/L) u dojilja i 234 μg/L (151,0-367,5 μg/L) u dojenčadi. Medijan (interkvartilni raspon) izlučivanja joda u majčinu mlijeku iznosio je 121 μg/kg (87,8-170,8 μg/kg). Multivarijatna regresijska analiza pokazala je statističku povezanost, odnosno da koncentracija joda u majčinu mlijeku predviđa koncentraciju joda u mokraći njihove dojenčadi (p<0,001). Takoder je utvrđena pozitivna povezanost parametara funkcije štitnjače u dojilja i dojenčadi. Ovo je prvo istraživanje u Hrvatskoj koje pokazuje da je mjerenje koncentracija joda u majčinu mlijeku pouzdan pokazatelj unosa joda u dojilja i predvija unos joda u dojenčadi. Istraživanje potvrđuje da program univerzalnog jodiranja soli u Hrvatskoj osigurava dostatan unos joda u dojilja i dojenčadi.

Ključne riječi: Dojenje; Dojenčad; Jod; Tireoglobulin; Hormoni štitnjače