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Source / Izvornik: **Collegium Antropologicum, 2012, 36, 123 - 128**

Journal article, Published version

Rad u časopisu, Objavljena verzija rada (izdavačev PDF)

Permanent link / Trajna poveznica: <https://um.nsk.hr/um:nbn:hr:105:968485>

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Download date / Datum preuzimanja: **2024-08-17**



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# Current Status of Iodine Intake in Croatia – The Results of 2009 Survey

Zvonko Kusić<sup>1</sup>, Tomislav Jukić<sup>1</sup>, Sunčica Andreja Rogan<sup>1</sup>, Vesna Jureša<sup>2</sup>, Nina Dabelić<sup>1</sup>, Josip Staničić<sup>1</sup>, Marta Borić<sup>1</sup>, Ljerka Lukinac<sup>1</sup>, Ivan Mihaljević<sup>3</sup>, Ante Punda<sup>4</sup>, Aleksandar Smokvina<sup>5</sup>, Zlatko Topalović<sup>6</sup> and Marijan Katalenić<sup>7</sup>

<sup>1</sup> University of Zagreb, School of Medicine, »Sestre milosrdnice« University Hospital Center, Department of Nuclear Medicine and Oncology, Zagreb, Croatia

<sup>2</sup> »Andrija Štampar« School of Public Health, Zagreb, Croatia

<sup>3</sup> »J. J. Strossmayer« University, Osijek University Hospital Center, Department of Nuclear Medicine, Osijek, Croatia

<sup>4</sup> University of Split, Split University Hospital Center, Department of Nuclear Medicine, Split, Croatia

<sup>5</sup> University of Rijeka, Rijeka University Hospital Center, Department of Nuclear Medicine, Rijeka, Croatia

<sup>6</sup> »Centar« Primary Health Care Clinic, Zagreb, Croatia

<sup>7</sup> Institute of Public Health, Zagreb, Croatia

## ABSTRACT

*In 1996, due to persistence of mild to moderate iodine deficiency, new law on obligatory salt iodination with 25 mg of potassium iodide (KI) per kg of salt was implemented in Croatia. Along with a new law, a new program for monitoring of iodine prophylaxis was implemented. Investigations of goiter and iodine intake performed in 2002, demonstrated sufficient iodine intake in Croatia with overall median of urinary iodine concentration (UIC) for schoolchildren in Croatia of 140 µg/L. In 2002, thyroid volumes (TV) measured by ultrasound in schoolchildren from all four geographic regions of Croatia were for the first time within the normal range according to ICCIDD reference values. Nowadays, Croatia is internationally recognized as iodine sufficient country. The aim of the present study was to assess current status of iodine intake in Croatia. The investigation was carried out in 2009. A total of 386 schoolchildren aged 7–10 years from all four major geographic regions of Croatia, 103 euthyroid pregnant women and 36 women of child-bearing age from Zagreb, the capital, were included in the survey. Urinary iodine concentration (UIC) was measured in all participants. Thyroid volumes were measured by ultrasound in schoolchildren from the capital of Zagreb (N=101) and the village of Rude (N=56). In the time period 2002–2009, the content of KI was analyzed in 384 salt samples from Croatian salt plants and samples of imported salt. An overall median UIC for schoolchildren in Croatia was 248 µg/L. Median UIC in pregnant women was 159 µg/L, with 50% of samples below and under 150 µg/L. Median UIC in women of child-bearing age was 136 µg/L. Thyroid volumes in schoolchildren were within the normal range according to the new reference values. Mean value of KI/kg of salt in samples from Croatian salt plants was 25.5 mg/kg and 24.9 mg/kg in samples of imported salt. A total of 72/384 (18.8%) of salt samples didn't corresponded to the Croatian law on obligatory salt iodination. Presented data indicate sufficient iodine intake of the Croatian population. Current medians of UIC in schoolchildren in Croatia are significantly higher than medians measured in 2002. This indicates that other potential sources of iodine are present in Croatian diet that may contribute to overall iodine intake. Due to rising medians of UIC in schoolchildren in Croatia, it is important to conduct nutrition studies to identify potential sources of »silent prophylaxis« in order to avoid iodine excess.*

**Key words:** iodine sufficiency, Croatia, salt iodination, urinary iodine concentration (UIC), thyroid volume, schoolchildren, pregnancy, monitoring

## Introduction

Iodine deficiency has many adverse effects on growth and development<sup>1</sup>. These abnormalities are grouped under the term »Iodine Deficiency Disorders«<sup>1,2</sup>. Therefore,

the most vulnerable risk groups are fetuses, neonates and children. Despite the fact that iodine deficiency is the most common cause of preventable mental impair-

ment worldwide, it is still serious global public health problem. Based on current estimates, the iodine intake of 31.5% (266 million) school-age children worldwide is insufficient. The greatest proportion of children with inadequate iodine intake lives in the region of Europe (52.4%)<sup>3</sup>. In the general population, 2 billion people have insufficient iodine intake<sup>1,3</sup>. Assessment methods include urinary iodine measurement, goiter, newborn thyroid – stimulating hormone and blood thyroglobulin<sup>4</sup>. School-age children are the most efficient and practical target group for IDD surveillance because of high vulnerability, easy access, and applicability to a variety of surveillance activities. Urinary iodine is a more sensitive indicator of recent changes in iodine intake and is therefore the preferred indicator for assessing iodine nutrition in a population and monitoring progress of iodine interventions. Along with school-age children, assessing urinary iodine in women of childbearing age and pregnant women is also very important due to susceptibility of the developing fetus to iodine deficiency<sup>4</sup>.

Modern epidemiological investigations on goiter and ID in Croatia, as part of former Yugoslavia, began after the Second World War. At the time, endemic goiter was present in most parts of the country with a prevalence of 50–90% and presence of cretinism. It was estimated that over 2 million persons (about 11% of the population) had endemic goiter with 20,000 endemic cretins and 2000–4000 deaf-mute persons<sup>5,6</sup>. Resulting adverse effects on the general health and the mental and physical abilities of affected population were enormous. In the village of Rude near capital of Croatia, Zagreb, goiter was detected in 85% of schoolchildren with 2.3% of cretins in the village population<sup>6</sup>. In 1953 the first regulation on obligatory salt iodination for both human and animal consumption, requiring 10 mg of KI per kg of salt was established in former Yugoslavia. A three-fold reduction of goiter prevalence, together with disappearance of cretinism was recorded ten years later<sup>7</sup>. In 1992, the National Committee for Eradication of Goiter was founded. The Committee initiated new nationwide survey that was carried out at the beginning of 1990s. The survey demonstrated that mild to moderate ID still persisted in Croatia with the prevalence of goiter in schoolchildren 8–35% and UIC <100 µg/L in 66–83% of schoolchildren from continental parts of the country<sup>8,9</sup>. The new obligatory regulation, requiring 25 mg of KI/kg of salt was established in 1996. In 2002 Croatia has finally reached iodine sufficiency. Thyroid volumes measured by ultrasound and medians of UIC in schoolchildren from all four major geographic regions of Croatia were for the first time within the normal range according to the WHO/ICCIDD criteria. Overall median of UIC for schoolchildren in Croatia was 140 µg/L<sup>10,11</sup>. Both domestic and imported salt corresponded with the effective regulation on iodination. Nowadays, Croatia is internationally recognized as iodine sufficient country<sup>12</sup>. This study was performed 13 years after implementation of the new law on obligatory salt iodination with 25 mg of potassium iodide per kg of salt.

## Subjects and Methods

The study was performed in 2009.

### *Subjects – schoolchildren*

A total of 386 schoolchildren (215 boys and 171 girls) aged 6–10 years from all four major geographic regions of Croatia were included in the survey. In the North-western region the study group included 101 schoolchildren from the nation capital Zagreb and 56 schoolchildren from the nearby village of Rude. The village of Rude had the highest prevalence of goiter and cretinism before the introduction of iodine prophylaxis in Croatia<sup>13</sup>. In Slavonia, the eastern part of the country, the study included 71 of schoolchildren from Osijek. In Northern Adriatic region, the study included 98 schoolchildren from Rijeka and in the region of Dalmatia the study group included 60 schoolchildren from Split.

### *Subjects – pregnant women and women of child-bearing age*

A total of 103 healthy euthyroid pregnant women from the capital of Zagreb were included in the survey (30 in the first trimester, 58 in the second trimester and 15 in the third trimester of pregnancy). Median age of pregnant women was 31 (range 23–42 years). The study also included 36 women of child-bearing age from the capital of Zagreb. Median age of non-pregnant women was 31 (range 21–41 years). Pregnant and non-pregnant women taking medications for thyroid diseases and/or with previous history of thyroid disease were excluded from the investigation. Informed consent was performed from all participants. Iodine supplements in the form of KI (150–200 µg/day) were taken by 21 (20%) of pregnant women.

Ethical Committee of the »Sestre milosrdnice« University Hospital Center as well as Ethical Committee of the Ministry of Science, Education and Sport of the Republic of Croatia approved the study. Permission to examine the children was obtained from parents.

## Methods

### *Measurement of urinary iodine concentration*

The spot morning urine samples were taken from all participants (386 schoolchildren, 103 pregnant women and 36 women of child-bearing age). Urine samples were transported in refrigerator and frozen at –20°C before analysis. Urinary iodine was measured by modified colorimetric method based on Sandel-Kolthoff reaction<sup>14</sup>.

### *Measurement of thyroid gland volume by ultrasonography*

Thyroid volumes (TV) were measured by ultrasound in schoolchildren from the capital of Zagreb (N=101) and the village of Rude (N=56). Ultrasonography of the thyroid gland was performed with a real-time linear transducer (»Tosbee«, Toshiba, Japan) using 7.5–10 MHz.

Thyroid volume has been calculated with the following equation, according to Brunn and Block<sup>15</sup>:  $V=0.479 [(a1b1c1)+(a2b2c2)]$ , where: a represents length, b-width, c-breadth, 1-right lobe, 2-left lobe. Data were compared with the new international reference values for thyroid volume in iodine-sufficient schoolchildren<sup>16</sup>.

*Measurement of iodine salt content*

The content of potassium iodide in salt samples (150–200 mg) from Croatian salt plants as well as in imported salt was measured yearly from 2003 to 2009 as a part of the National Program for Monitoring of Iodine Prophylaxis. A total of 383 salt samples were analyzed. The content of potassium iodide in salt samples was measured by titration<sup>17</sup>. Measurements were performed in the Croatian Institute of Public Health.

**Results**

*Results of urinary iodine excretion in schoolchildren*

In 2009 medians of UIC in schoolchildren from Croatia were: 288 µg/L in Zagreb and 195 µg/L in the village of Rude, 281 µg/L in Osijek, 236 µg/L in Split and 205 µg/L in Rijeka (Table 1). An overall median of UIC for schoolchildren in Croatia was 248 µg/L. A total of 17.9% of samples had UIC<50 µg/L, 22.3% of samples UIC<100 µg/L,

while 77.7% of samples had UIC>100 µg/L. However, 36.7% of samples had UIC>300 µg/L (Figure 1).

*Results of thyroid volumes in schoolchildren from the capital of Zagreb and the village of Rude*

Thyroid volumes by ultrasound in schoolchildren from North-western region of Croatia (the capital of Zagreb

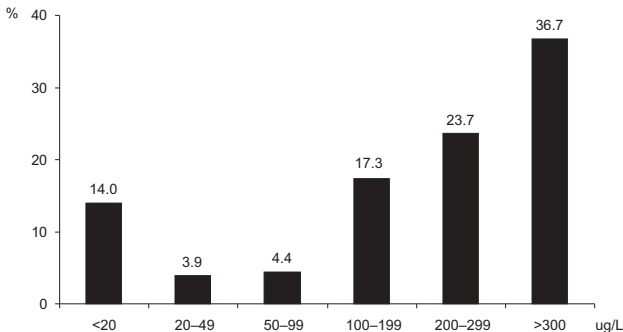


Fig. 1. The distribution of urinary iodine concentration in schoolchildren in Croatia (N=386), 2009.

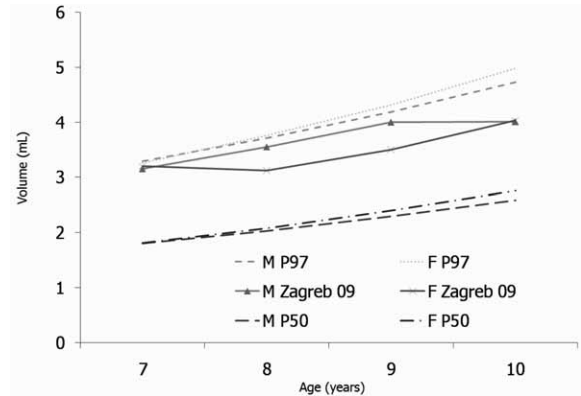


Fig. 2. Thyroid volumes in schoolchildren from Zagreb measured by ultrasound in 2009, M – Zagreb 09 (boys), F – Zagreb 09 (girls). Results are compared with reference values from Zimmermann et al.16.

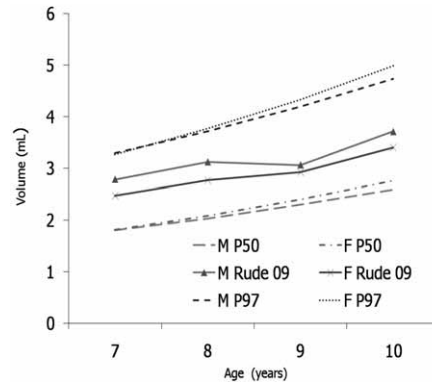


Fig. 3. Thyroid volumes in schoolchildren from the village of Rude in 2009; M – Rude 09 (boys), F – Rude 09 (girls). Results are compared with reference values from Zimmermann et al.16.

**TABLE 1**  
MEDIAN OF UIC IN SCHOOLCHILDREN FROM FOUR MAJOR GEOGRAPHIC REGIONS OF CROATIA IN 2009

Region of Croatia	No.	UIC (µg/L)		
		Median	<100 (%)	<50 (%)
North-western (Zagreb)	101	288	12.9	5.9
North-western (village of Rude)	56	195	35.7	30.4
Eastern (Osijek)	71	281	31.0	31.0
Northern Adriatic (Rijeka)	98	205	22.4	17.3
Dalmatia (Split)	60	236	11.7	15.0
Total	386	248	22.3	17.9

UIC – Urinary iodine concentration

**TABLE 2**  
URINARY IODINE CONCENTRATION IN PREGNANT WOMEN FROM ZAGREB IN 2009

Pregnancy (trimester)	No	UIC ( $\mu\text{g/L}$ )			
		Median	Range	<150 (%)	>150 (%)
1 <sup>st</sup>	30	107	1–557	53	47
2 <sup>nd</sup>	58	163	1–875	47	53
3 <sup>rd</sup>	15	145	1–796	53	47
Total	103	159	1–875	50	50

UIC – Urinary iodine concentration

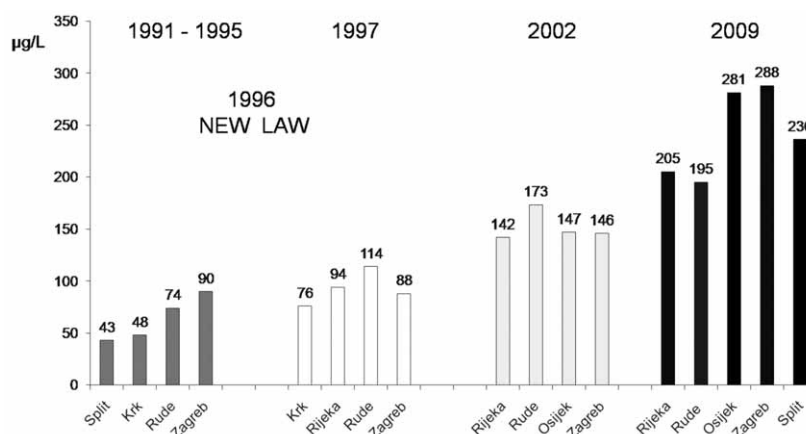


Fig. 4. Medians of urinary iodine concentration in schoolchildren in Croatia before and after the new law on obligatory salt iodination established in 1996.

and the village of Rude) were within the normal range according to the new international reference values for TV by ultrasound in iodine sufficient schoolchildren (Figures 2 and 3).

#### Results of urinary iodine concentration in pregnant women and women of child-bearing age

In 2009 Median UIC in 103 pregnant women from Zagreb was 159  $\mu\text{g/L}$ , with 50% of samples below and under 150  $\mu\text{g/L}$ . Median UIC in pregnant women in the 1<sup>st</sup> trimester of pregnancy was 107  $\mu\text{g/L}$ , in the 2<sup>nd</sup> trimester of pregnancy 163  $\mu\text{g/L}$ , while in pregnant women in the 3<sup>rd</sup> trimester of pregnancy median UIC was 145  $\mu\text{g/L}$  (Table 2). In 36 women of child-bearing age median UIC was 136  $\mu\text{g/L}$ .

#### Results of iodine content in salt samples

In a time period 2002–2009 a total of 384 salt samples were analyzed for iodine content. Mean value of KI/kg of salt in salt samples from Croatian salt plants was 25.5 mg/kg. Mean value of KI/kg of salt in salt samples of imported salt was 24.9 mg/kg. A total of 72/384 (18.8%) of salt samples didn't corresponded to the Croatian law on obligatory salt iodination.

## Discussion

Presented data indicate adequate iodine intake of the Croatian population. In 2009, medians of UIC in most of the schoolchildren from Croatia were in the range 200–300  $\mu\text{g/L}$  indicating more than adequate iodine intake. Thyroid volumes in schoolchildren from Zagreb and the village of Rude were within the normal range according to the new international reference values for TV by ultrasound in iodine sufficient schoolchildren. Median UIC in 103 pregnant women from Zagreb was 159  $\mu\text{g/L}$ . Current medians of UIC in Croatian schoolchildren are significantly higher than medians measured in 2002 (Figure 4). However, iodine content in salt revealed unchanged level of salt iodination corresponding to the new Croatian law established in 1996. This indicates that other potential sources of iodine are present in the Croatian diet that may contribute to overall iodine intake. Current medians of UIC in schoolchildren and pregnant women in Croatia are similar to United States National Health and Nutrition Examination Survey (NHANES) 2003–2004 iodine data with median UIC in schoolchildren aged 6–11-years of 229  $\mu\text{g/L}$  (246  $\mu\text{g/g}$  creatinine), median UIC of 181  $\mu\text{g/L}$  in pregnant women, and median UIC of 131  $\mu\text{g/L}$  in non-pregnant women<sup>18</sup>. Macedonia and neighbouring country Bosnia and Herzegovina have the same level of compulsory salt iodination.

ation as Croatia that ranges from 20 to 30 mg of iodine per kg of salt. Investigations of iodine intake from Macedonia conducted in 2007 revealed median UIC in schoolchildren of 241 µg/L<sup>19</sup>, and this result is in concordance with median UIC in schoolchildren in Croatia in 2009. However, median UIC in 228 pregnant women from Macedonia was slightly higher (199.7 µg/L in the first and second trimester of pregnancy and 174.9 µg/L in the third trimester of pregnancy)<sup>19,20</sup>. In Bosnia and Herzegovina (Tuzla), median UIC in 148 pregnant women without restriction of iodine intake was 156 µg/L while in 152 pregnant women with restriction of iodine intake median UIC was 133 µg/L<sup>21</sup>. These data indicate the importance of additional iodine intake in pregnant women with salt restriction. The American Thyroid Association has recommended that all women receive dietary supplements containing 150 µg of iodine daily during pregnancy and lactation and that all prenatal vitamins contain 150 µg of iodine<sup>22</sup>. However, these recommendations have not yet been adopted<sup>23</sup>. According to law, all salt in Croatia have to be iodized. There is a question whether

pregnant women in Croatia should take iodine supplements during pregnancy. It could be recommended in pregnant women with salt restriction. Croatia crossed a path from severe iodine deficiency detected in the 1950', to the period of mild to moderate iodine deficiency during the 1990', and finally, nowadays, iodine sufficiency has been achieved<sup>24</sup>. However, due to rising medians of UIC in schoolchildren it is important to conduct large nationwide survey in Croatia, continue to monitor the content of iodine in salt and conduct nutrition studies to identify potential sources of »silent prophylaxis« in order to avoid iodine excess.

### Acknowledgements

The research on goiter and iodine intake in Croatia was funded by the Ministry of Science, Education and Sport of the Republic of Croatia under grant 134-1342428-2430 for the project »Carcinogenesis in Thyroid and Goiter in Croatia«.

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Z. Kusić

University of Zagreb, »Sestre milosrdnice« University Hospital Center, Department of Nuclear Medicine and Oncology, Vinogradska 29, 10000 Zagreb, Croatia  
e-mail: zvonko.kusic@zgt.com.hr

### STANJE UNOSA JODA U HRVATSKOJ – REZULTATI ISTRAŽIVANJA PROVEDENOG 2009 GODINE

#### SAŽETAK

Zbog prisutnosti blagog do umjerenog nedostatka joda, u Hrvatskoj je 1996. godine uveden novi zakon o obveznom jodiranju soli s 25 mg kalij jodida (KI) po kilogramu soli. Uz novi zakon uveden je i novi program za kontrolu provođenja jodne profilakse. Istraživanja stanja gušavosti i unosa joda provedena 2002 godine, pokazala su dostatan unos joda u Hrvatskoj s ukupnim medijanom izlučivanja joda urinom u školske djece od 140 µg/L. Ultrazvučno izmjereni volumeni

štitnjače u školske djece iz sve četiri glavne regije Hrvatske bili su po prvi put u granicama normale prema referentnim vrijednostima ICCIDD (Međunarodnog vijeća za kontrolu poremećaja uzrokovanih nedostatkom joda). Hrvatska je danas međunarodno priznata kao zemlja s dostatnim unosom joda. Cilj ovog istraživanja bio je utvrditi sadašnje stanje unosa joda u Hrvatskoj. Istraživanje je provedeno 2009. godine. U istraživanje je uključeno 386 djece u dobi 7–10 godina iz sve četiri regije Hrvatske, 103 trudnice u eutireozi i 36 žena u generativnoj dobi iz Zagreba. Određivanje joda u urinu provedeno je u svih ispitanika. Volumeni štitnjače izmjereni su ultrazvukom u školske djece iz Zagreba (N=101) i sela Rude (N=56). U razdoblju od 2002. do 2009. godine, sadržaj joda u kuhinjskoj soli izmjereno je u ukupno 384 uzorka soli iz hrvatskih solana i uzoraka uvezene soli. Ukupni medijan izlučivanja joda urinom u školske djece u Hrvatskoj iznosio je 248  $\mu\text{g/L}$ . Medijan izlučivanja joda urinom u trudnica iznosio je 159  $\mu\text{g/L}$ , s 50% uzoraka s izlučivanjem joda urinom ispod 150  $\mu\text{g/L}$ , a 50% uzoraka iznad 150  $\mu\text{g/L}$ . Median izlučivanja joda urinom u žena u generativnoj dobi iznosio je 136  $\mu\text{g/L}$ . Volumeni štitnjače u školske djece bili su u granicama normale prema novim referentnim vrijednostima ICCIDD. Srednja vrijednost KI/kg soli u uzorcima soli iz Hrvatskih solana iznosila je 25,5 mg/kg, a u uzorcima uvezene soli 24,9 mg/kg. Ukupno 72/384 uzorka soli (18,8%) odstupala su od novog pravilnika o obveznom jodiranju soli. Prikazani podaci upućuju na dostatan unos joda u Hrvatskoj. Sadašnji medijani izlučivanja joda urinom su značajno viši u odnosu na medijane izmjerene 2002. godine. To upućuje da su drugi potencijalni izvori joda prisutni u Hrvatskim namirnicama koji mogu doprinijeti ukupnom unosu joda. Zbog rastućih medijana izlučivanja joda urinom u školske djece, neophodno je u Hrvatskoj provesti nutritivna istraživanja kako bi se utvrdili potencijalni izvori »tihe profilakse« s ciljem da se izbjegne prekomjeren unos joda.