

The Story of The Croatian Village of Rude after Fifty Years of Compulsory Salt Iodination in Croatia

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ABSTRACT

The village of Rude is situated near Zagreb, the capital of Croatia in the last Alpine valley on Balkan. In the past, the village was well-known area of severe iodine deficiency disorders (IDD). In 1952', distinguished Croatian endocrinologist Professor Josip Matovinović carried out detailed village survey. Goiter prevalence in school-age children was 85.0% (with 2.3% of cretins in the village). In 1953, the first regulation on compulsory salt iodination with 10 mg of KI/kg of salt was established in former Yugoslavia. Ten years later a dramatic decrease in goiter prevalence was recorded in all endangered areas of the country and no new cretins appeared. However, at the beginning of 1990' mild to moderate iodine deficiency still persisted in Croatia. In 1991, the village of Rude survey demonstrated goiter prevalence in school-age children of 35.0% and median of urinary iodine excretion (UIE) of 7.4 µg/dL. In 1996, the new obligatory regulation with 25 mg of KI/kg of salt was established in Croatia. The study aim was to monitor IDD status in the village after the new law on compulsory salt iodination. Measurements of UIE and thyroid volumes (Tvol) by ultrasound were performed in 7–11-y-old schoolchildren living in the village of Rude. Medians of UIE and body surface area (BSA)-adjusted Tvol in boys and girls were calculated. The study included 84 children in 1997, 132 in 2000, 72 in 2002, 85 in 2003 and 46 in 2004 for UIE measurement. Thyroid volumes were measured in 1999 (43 boys and 26 girls) and in 2005 (22 boys and 26 girls). Data were compared with the new WHO/ICCIDD reference values. Medians of UIE in schoolchildren from the village of Rude demonstrated rising values in µg/dL: 11.4 in 1997, 14.3 in 2000, 17.3 in 2002, 15.4 in 2003 and 19.0 in 2004. Significant decrease in BSA-adjusted Tvol was recorded from 1999–2005 in boys and girls from the village of Rude and in 2005 Tvol were within the normal range according to the new international reference values for Tvol in iodine-sufficient schoolchildren. As a result of increased iodine prophylaxis, IDD no longer exist in Croatia. Monitoring of IDD status in the village of Rude after new law on compulsory salt iodination in Croatia demonstrated rising medians of UIE together with significant reduction of Tvol. In 2005, Tvol in schoolchildren from the village of Rude were within the normal range according to the new international reference values for Tvol in iodine-sufficient schoolchildren.

Key words: iodine deficiency, goiter, salt iodination, urinary iodine excretion, thyroid volume, schoolchildren, the village of Rude

Introduction

The village of Rude is situated about 25 km southwest of Zagreb, the capital of Croatia (Figure 1), in the valley of the river Rudarska Gradna, the last Alpine valley on Balkan, bordered with mountains Plešivica, Črnc and Oštrc. The village of Rude probably dates back from early middle-ages, but some data indicate that copper mines had already existed in this area since antic ages. The village was named after the mines that were exploited in

this area; »Rude« in Croatian language means ores in English. The valley was settled with German miners from Saksonia in XVI century by Croatian noble family Zrinski¹ and foreign owners of the mines. German miners remained in this area, marrying with Croatian girls. The community kept some old habits but their native German language was forgotten. Besides the mining, the agriculture was the main activity of the inhabitants.



Fig. 1. Geographic location of the village of Rude.

In the past, the village was well-known area of severe iodine deficiency, and therefore the object of many epidemiological investigations. Endemic goiter was the most common disease of the village population. In 1952, distinguished Croatian endocrinologist Professor Josip Matovinović carried out detailed village survey². The goiter was detected in 83% of 865 individuals with increasing prevalence with age. Goiter prevalence in schoolchildren and adolescents was 85.0%. It was the place with the highest prevalence of goiter in Croatia before the introduction of compulsory salt iodination in former Yugoslavia in 1953. Professor Matovinović³ gave detailed description of the life in the village at the beginning of the 1950's: »The houses were small and over-crowded, with an average of five family members per household. The essential dietary products were corn bred, potatoes and beans, with little meat or milk. Wine was an important source of calories – 7.4% drank more than one liter per day, and 83% of children consumed alcohol«. A young girl

»without a neck« wasn't considered beautiful and even angels in the local church were also represented with goiter (Figure 2). Drinking water from wells and small brooks contained an average of 1.3 and 0.43 µg iodine per liter respectively. The most tragic complication of iodine deficiency in the village was endemic cretinism. There were 20 cretins in the village (2.3% of the village population). The majority was severely mentally retarded. Professor Matovinović described cretins as good, poor fellows who depended inseparably to the life of his mother. After her death they were condemned to isolation and death, as it was described in the sentence: »Her care for her unfortunate child reflected boundless love, terror of his disease, the height of ignorance and superstition, torment of guilt, and desolation of hopelessness. She was aware that after her death her beloved cretin would most likely suffer from neglect, malnutrition, or die in confinement«³.

Salt Iodination in Former Yugoslavia

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.

Ten years later a dramatic decrease in goiter prevalence was recorded in all endangered areas of the country and no new cretins appeared⁴. In endemic areas the structure of growth normalized and there was an increase of intellectual abilities and success in school among children. However, the goiter was still found in 20–30% of children.

The Village of Rude Survey in 1991–1993

At the beginning of the 1990's The National Committee for Eradication of Goiter and Control of Iodine Prophylaxis was founded. The Committee initiated a comprehensive epidemiological research with the aim of determining the state of iodine intake in different parts of Croatia^{5,6}. A part of the nationwide survey was carried out in the village of Rude⁶. A total of 200 schoolchildren were included in the village survey (110 boys and 90 girls). The prevalence of goiter among schoolchildren was determined by palpation of the neck according to the PAHO/WHO classification⁷. Urinary iodine excretion was measured by the instructions of ICCIDD/WHO and modified colometric method based on the Sandell-Kalthoff reaction⁸. The results of the investigation demonstrated that iodine deficiency in the village still persisted. Goiter was detected in 26% of schoolchildren aged 7–11 years (n=88) and in 43% of schoolchildren aged 12–15 years (n=112). The urinary iodine excretion in those children (n=118) varied between 0.5–19 µg/dL with a median of 7.4 µg/dL. Only few were distinctly low and 30% were below 5 µg/dL, while 80% were below 10 µg/dL. The overall prevalence of goiter in the village was 35%⁶.



Fig. 2. Angel with goiter in the local church near the village of Rude, where 85% of the children had goiter in 1950'.

The New Regulation and Successful Elimination of Iodine Deficiency Disorders in Croatia

In 1996, the new obligatory regulation requiring 25 mg of KI/kg of salt was established in Croatia^{9,10}. In 2002, thyroid volumes and medians of urinary iodine excretion from all four major Croatian regions were for the first time within the normal range according to the WHO/ICCIDD reference values. An overall median of urinary iodine excretion for all four major geographic regions of Croatia was 14.0 µg/dL^{11–14}. Both domestic and imported salt corresponded with the effective regulation on iodination.

The Village of Rude Surveys after the New Obligatory Regulation

The study aim was to monitor IDD status in the village after the implementation of the new law on compulsory salt iodination in Croatia.

Measurement of UIE and thyroid volume by ultrasound was performed in 7–11-y-old schoolchildren living in the village of Rude. The prevalence of goiter in schoolchildren was assessed by neck ultrasound using 7,5 MHz linear transducer (Tosbee, Toshiba, Japan). Urinary iodine excretion was measured by the instructions of ICCIDD/WHO and modified colometric method⁸. Medians of UIE and body surface area – adjusted thyroid volumes in boys and girls were calculated. The study included 84 children in 1997, 132 in 2000, 72 in 2002, 85 in 2003 and 46 in 2004 for UIE measurement. Thyroid volumes were measured by ultrasound in 1999 (43 boys and 26 girls) and in 2005 (22 boys and 26 girls). Data were compared with the new international reference values for thyroid volume in iodine-sufficient schoolchildren¹⁵.

Medians of urinary iodine excretion in schoolchildren from the village of Rude demonstrated rising values: from 7.4 µg/dL in 1991, and after the new regulation 11.4 µg/dL in 1997, 14.3 µg/dL in 2000, 17.3 µg/dL in 2002, 15.4 µg/dL in 2003, and 19.0 µg/dL in 2004 (Table 1). Significant decrease in BSA-adjusted thyroid volumes was recorded from 1999 to 2005 in boys (Figure 3) and girls (Figure 4) from the village of Rude. In 2005, Tvol in schoolchildren from the village of Rude were within the

TABLE 1
URINARY IODINE EXCRETION IN SCHOOLCHILDREN FROM THE VILLAGE OF RUDE

Year of survey	Number of children	Median (µg/dL)	< 5 µg/dL (in %)	< 10 µg/dL (in %)
1997	84	11.4	10.7	41.7
2000	132	14.3	5.6	26.4
2002	72	17.3	8.3	26.4
2003	85	15.4	14.1	25.9
2004	46	19.0	6.5	23.9

normal range according to the new international reference values for Tvol in iodine-sufficient schoolchildren.

Discussion

As a result of increased iodine prophylaxis, IDD no longer exist in Croatia. Nowadays, Croatia is internationally recognized as iodine sufficient country¹⁶. Monitoring of the IDD status in the village of Rude after new law on compulsory salt iodination in Croatia demonstrated rising medians of urinary iodine excretion in schoolchildren together with significant reduction of thy-

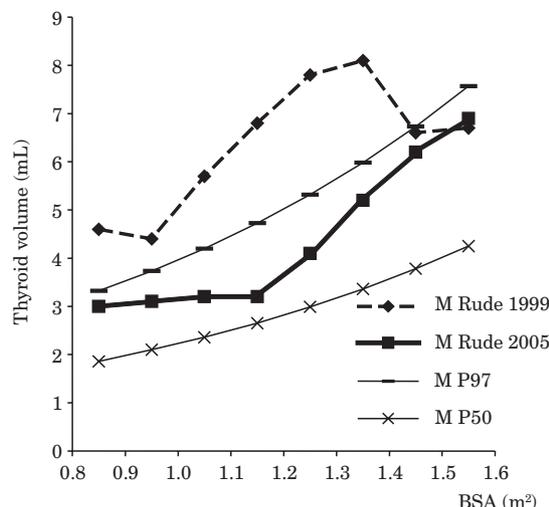


Fig. 3. Thyroid volumes in boys from the village of Rude in 1999 (M Rude 1999) and 2005 (M Rude 2005) adjusted for body surface area (BSA) together with 50th percentile (M P50) and 97th percentile (M P97) of new international reference values.

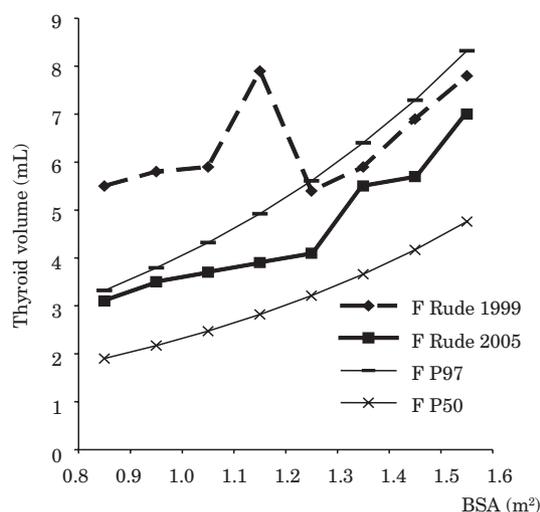


Fig. 4. Thyroid volumes in girls from the village of Rude in 1999 (F Rude 1999) and 2005 (F Rude 2005) adjusted for body surface area (BSA) together with 50th percentile (F P50) and 97th percentile (F P97) of new international reference values.

roid volume in both boys and girls. Thyroid volumes in schoolchildren from the village of Rude adjusted for BSA were in 2005 within the normal range according to the new international reference values for thyroid volume in iodine-sufficient schoolchildren. The struggle against iodine deficiency disorders in Croatia will contribute to the benefit of future generations

REFERENCES

1. GUŠIĆ B, Do Anthropogeographic factors take a strumigenic effect. In: FERBER, M, KOVAČEVIĆ M. (Eds) Drugi Jugoslavenski Simpozij o Endemskoj Gušavosti (KOMNIS, Zagreb, 1961). — 2. FERBER E, MATOVINOVIĆ J, KOVAČIĆ N, R. BUZINA R, Higijena, 7 (1956) 295. — 3. MATOVINOVIĆ J, Ann Rev Nutr, 3 (1983) 341. — 4. BUZINA R, Am J Clin Nutr, 23 (1970) 1085. — 5. KUSIĆ Z, ĐAKOVIĆ N, KAIĆ-RAK A, KARNER I, LECHPAMMER S, MESAROŠ-ŠIMUNČIĆ E, PETROVIĆ I, RONČEVIĆ S, SMOJE J, STANIČIĆ A, VALENT I, DELANGE F, J Endocrinol Invest, 19 (1996) 210. — 6. KUSIĆ Z, LECHPAMMER S, Coll Antropol, 21 (1997) 499. — 7. DELANGE F, BASTANI S, BENMILLOUD M, Definitions of endemic goiter and cretinism, classification of goiter size and severity of endemias, and survey techniques. In: DUNN JT, PRETELL E, DAZA CH, VITERI FE (Eds) Towards the eradication of endemic goiter, cretinism and iodine deficiency (Pan American Health Organization, PAHO/WHO Scientific Publication No. 502., Washington, 1986). — 8. WAWSCHINEK O, EBER O, PETEK W, WAKONIG P, GURAKAR A,

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ÖGKC, 8 (1985) 13. — 9. KUSIĆ Z, Lijec Vjesn, 118 (1996) 306. — 10. KUSIĆ Z, LECHPAMMER S, DELANGE F, J Endocrinol Invest, 20 (1997) 346. — 11. KUSIĆ Z, NOVOSEL SA, DABELIĆ N, PUNDA M, RONČEVIĆ S, LABAR Ž, LUKINAC LJ, NOTHIG-HUS D, LECHPAMMER S, STANIČIĆ A, KAIĆ-RAK A, MESAROŠ-KANJSKI E, KARNER I, SMOJE J, MILANOVIĆ N, KATALENIĆ M, JUREŠA V, SARNAVKA V, J Endocrinol Invest, 26 (2003) 738. — 12. KUSIĆ Z, IDD Newsletter, 5 (2003) 27. — 13. KUSIĆ Z, JUKIĆ T, Coll Antropol, 29 (2005) 9. — 14. KUSIĆ Z, JUKIĆ T, DABELIĆ N, ROGAN SA, RONČEVIĆ S, LUKINAC LJ, NOTHIG-HUS D, KARNER I, STANIČIĆ A, PUNDA M, SMOJE J, Thyroid, 15 (Suppl 1) (2005) 174. — 15. ZIMMERMAN MB, HESS SY, MOLINARI L, DE BENOIST B, DELANGE F, BRAVERMANN LE, FUJIEDA K, YOSHIYA I, JOOSTE PL, MOOSA K, PEARCE EN, PRETELL EA, SHISHIBA Y, Am J Clin Nutr, 79 (2004) 231. — 16. VITTI P, DELANGE F, PINCHERA A, ZIMMERMANN M, DUNN JT, Lancet, 361 (2003) 1226.

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PRIČA O SELU RUDE PEDESET GODINA NAKON UVOĐENJA OBVEZNE JODNE PROFILAKSE U HRVATSKOJ

SAŽETAK

Selo Rude smješteno je nadomak Zagreba u posljednjoj Alpskoj dolini na Balkanu. To je područje u prošlosti bilo poznato po teškom nedostatku joda. Eminentni hrvatski endokrinolog svjetskog ugleda, profesor Josip Matovinović proveo je 1952 u Rudama opsežno epidemiološko istraživanje i utvrdio prevalencija gušavosti u školske djece od 85,0% (uz 2,3% kretena u seoskoj populaciji). Godine 1953 prvi zakon o obveznoj jodiranju soli sa 10 mg KI/kg soli uveden je u bivšoj Jugoslaviji. Deset godina kasnije zabilježeno je dramatično smanjenje prevalencije gušavosti u svim zahvaćenim područjima Hrvatske uz nestanak kretinizma. Međutim, početkom 1990-tih blagi do umjereni nedostatak joda još uvijek je postojao u Hrvatskoj. Godine 1991, epidemiološko istraživanje stanja gušavosti u selu Rude pokazalo je prevalenciju gušavosti u školske djece 35,0% uz medijan izlučivanja joda urinom 7,4 µg/dL. Godine 1996 uveden je u Hrvatskoj novi zakon o obveznom jodiranju soli s 25 mg KI/kg soli. Cilj ovoga istraživanja je praćenje stanja gušavosti i unosa joda u selu Rude nakon uvođenja novog zakona o obveznom jodiranju soli. Provedeno je višestruko mjerenje izlučivanja joda urinom i ultrazvučno mjerenje volumena štitnjače u školske djece u dobi od 7 do 11 godina. Dobivene podaci su prikazani kao medijani izlučivanja joda urinom te volumeni štitnjače u dječaka i djevojčica usklađeni prema površini tijela. U istraživanje izlučivanja joda urinom uključeno je 84 školske djece u 1997 godini, 132 u 2000, 72 u 2002, 85 u 2003 i 46 školske djece u 2004 godini. Ultrazvučno mjerenje volumena štitnjače provedeno je 1999 godine (43 dječaka i 26 djevojčica) i 2005 godine (22 dječaka i 26 djevojčica). Podaci su uspoređeni s novim referentnim vrijednostima WHO/ICCIDD. Medijani izlučivanja joda urinom u školske djece u selu Rude porasli su nakon novog zakona (µg/dL): 11,4 u 1997, 14,3 u 2000, 17,3 u 2002, 15,4 u 2003 i 19,0 u 2004 godini. Značajno smanjenje volumena štitnjače usklađenih prema površini tijela utvrđeno je u dječaka i djevojčica iz sela Rude, a u 2005 godini te vrijednosti bile su granicama normale u odnosu na nove referentne vrijednosti WHO/ICCIDD. Kao rezultat uvođenja novog zakona o obveznom jodiranju soli 1996 godine danas je iskorijenjena gušavost u školske djece u Hrvatskoj i općenito svi poremećaji uzrokovani nedostatkom joda.