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1 **RESULTS FROM THE NATIONAL STRATEGY FOR IMPROVEMENT OF**
2 **IODINE NUTRITION IN BULGARIA. STUDY ON CHILDREN AND**
3 **PREGNANT WOMEN LIVING IN IODINE DEFICIENT AREA**

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18 **ABSTRACT**

19 *Background:* A significant part of Bulgaria is considered as iodine-deficient
20 area. The National strategy for prevention and control of iodine deficiency disorders
21 (IDD) was developed in 1994 and regular surveys undertaken during 2000-2003
22 indicated a normalization of iodine supply in Bulgarian population, including some risk
23 population groups (children, schoolchildren, pregnant women). Despite the results
24 achieved, mandating periodic cohort surveys for tracking the disappearance of iodine

deficiency are necessary. *Objective:* The aim of this study was to evaluate the results from the National strategy for improvement of iodine nutrition in children and pregnant women, living in iodine deficiency area in Bulgaria 15 years after its update. *Subjects and methods:* Subjects of study were 73 children aged 9.21 ± 2.07 years (29 boys and 44 girls) and 16 pregnant women living in the town of Asenovgrad. Urinary iodine concentration was measured and used as an index of iodine intake. *Results:* The median urinary iodine of the inspected children was between 100-199 $\mu\text{g/L}$, which is an indicator of optimal iodine nutrition. Almost 1/3 of the children (31.5%) were with iodine deficiency. The median urinary iodine concentration of the inspected 16 pregnant women was 127.0 $\mu\text{g/L}$, which is an indicator of insufficient iodine intake. *Conclusion:* Despite the normalization of iodine supply during the last years in the risk population groups of children and pregnant women, a considerable part of them are with iodine deficiency. Recommendations about improvement of health education and iodine nutrition of risk population groups were made.

Key words: Urinary iodine; Children; Pregnant women; Iodine nutrition

INTRODUCTION

The iodine deficiency regions in Bulgaria comprise 1/3 of the country territory and subsequently, a frequent occurrence of goiter was reported in mid 50's. The first national program for control of iodine deficiency disorders (IDD) was introduced in Bulgaria in 1958 with the major measure salt fortification with KI. As a result of this strategy, goiter frequency decreased from 56 % in 1956 to 12.1% in 1974 (Gatseva and Argirova 2009).

The iodine prophylaxis was neglected during the period of transition from regulated to market-oriented economy taking place in the country in 90's. The strategy for prevention and control of IDD in Bulgaria was updated in 1994. Iodine supply in Bulgaria was improved during the following 10 years due to several efforts to increase iodine intake by using iodized salt in bakeries and food processing industries. National surveys undertaken during 2000-2003 confirmed the successful putting into practice of the National strategy for prevention and control of IDD in Bulgaria and indicated a normalization of iodine supply in Bulgarian population, including risk population groups. Despite the results achieved, the level of information of population concerning the health consequences of iodine deficiency and correct prophylaxis was found as insufficient. Therefore, in the National action plan "Food and Nutrition 2005-2010" was included an instruction on the iodine deficiency problems for general practitioners, an introduction of health education lessons in schools and a large scale general public information by using appropriate flyers (Gatseva and Argirova 2009).

The aim of this study undertaken in May 2009 was to evaluate the results from the National strategy for improvement of iodine nutrition in children and pregnant women, living in iodine deficient area of Bulgaria 15 years after its update.

MATERIALS AND METHODS

Subjects of study were 73 children aged 9.21 ± 2.07 years (29 boys and 44 girls) and 16 pregnant women aged between 20 and 33 years living in the town of Asenovgrad. It is situated in South Bulgaria, at the foot of the Rodopi Mountain, which is known for its low iodine in the environment. Mean age of the studied boys was $9.31 \pm$

2.30 years and that of the girls 9.22 ± 2.05 years without significant difference between the both groups ($P = 0.8725$, $t = 0.1611$). The study practically covers all of the patients of the general practitioner aged between 7 and 11 years. Only two of the pregnant women that were patients of the same GP did not agree to participate in the survey. There were no other criteria for inclusion/exclusion in the study. Informed consent for participation in the survey was obtained from the children and their parents and from the pregnant women. Ethical Committee of Medical University in Plovdiv, Bulgaria approved the research. The participants completed a short questionnaire by using “yes” or “no” answers concerning the iodine intake from table salt and other sources (e.g. supplementary tablets), familial thyroid disorders and underlying or chronic diseases.

Urine samples were collected during prophylactic examinations. Iodine concentration was measured by the Sandell-Kolthoff reaction (Dunn et al.1993), which comprised the reduction of ceric ammonium sulfate (yellow) to cerous form (colorless) by arsenious acid. The process was catalyzed by iodine in a concentration-dependent manner. Working protocol was based on the recommendations of the International Council for the Control of Iodine Deficiency Disorders (ICCIDD) (Dunn et al 1993; Ohashi et al.2000; Gnat et al.2003). Urine samples (0.25 ml) were pipetted into 13 x 100 mm glass tubes and mixed with 1 ml of ammonium persulfate (1 M in distilled water, freshly prepared). After heating for 60 minutes at 100°C and then cooling to room temperature, the digested samples were mixed with 2.5 ml arsenious acid (0.5 M in 2 M H_2SO_4) and let stand for at least 15 minutes. Thereafter, 0.3 ml ceric ammonium sulfate (0.02 M in 1.75 M H_2SO_4) was added at 30-second intervals between successive tubes. The absorbance at 420 nm of each sample was read exactly 20 minutes after the addition of ceric ammonium sulfate. A set of KIO_3 calibrators within the range 50 –

300 µg/l iodine was ran at the beginning and end of each series of urine samples. Distilled water was used as a zero calibrator. The concentration of each standard was plotted against optical density at 420 nm and regression analysis was applied for calculation of the iodine concentration in urine samples. Each urine sample was analyzed in duplicate.

Median values for urinary iodine were used to evaluate the iodine status of studied groups according to the recommendations of WHO, UNICEF and ICCIDD (ICCIDD, WHO and UNICEF 2001). Data were statistically analyzed by using SPSS for Windows computing program (SPSS Inc, Chicago, IL). Comparisons between groups were conducted using dependent t-tests for matched samples and the level of significance was set at $P<0.05$.

RESULTS

The median urinary iodine of the inspected boys and girls was between 100-199 µg/L, which is an indicator of optimal iodine nutrition. There was no difference ($P>0.05$) between the median urinary iodine concentrations found for the boys and girls groups (Table 1).

Table 1 here

Figure 1 presents the relative parts (%) of the studied boys and girls with iodine deficiency (UI <100 µg/L); with optimal iodine nutrition (UI 100-199 µg/L) and more than adequate iodine intake (200-299µg/L) (Fig.1).

Figure 1 here

Almost 1/3 (31.5%) of the children (12.3% of the boys and 19.2% of the girls) had iodine deficiency. Most of the children having iodine deficiency were between 7 and 8 years. With optimal iodine nutrition were 56.2% of the children (24.7 % of the boys and 31.5% of the girls). With more than adequate iodine intake were 12.3% of the inspected children (2.7% of the boys and 9.6% of the girls). The relative parts of boys and girls with adequate and more than adequate iodine intake differ significantly ($P<0.05$).

Data from the filled questionnaires showed that iodized salt had been used in all children's families (100%) over the last 15 years. None of the children reported for additional iodine supplementation with iodine-containing tablets. For familiar thyroid disorders and chronic diseases reported 9 children (12.3%).

The median urinary iodine concentration of the inspected pregnant women was 127.0 $\mu\text{g/L}$ (95% confidence interval 97.07-175.55 $\mu\text{g/L}$), which is indicator for insufficient iodine intake in pregnancy (WHO 2005).

Figure 2 shows the relative parts of the studied pregnant women with different iodine status, assessed on the basis of the new WHO recommendations. (Fig. 2).

Figure 2 here

Data from the filled questionnaires showed that 100% of the inspected women have used iodized salt over the last years. All of the pregnant women reported about intake of tablets, containing minerals (Mg and Fe) and vitamins (folic acid); iodine supplementation was not prescribed by their general practitioner. For familiar thyroid disorders and chronic diseases reported 12.5% of the pregnant women.

DISCUSSION

Iodine is an essential micronutrient required for the production of the thyroid hormones that regulate growth, development, metabolism, and reproductive function in all age groups. Fetal and child development suffers the greatest impact from low levels of thyroid hormone and the greatest risk of iodine deficiency disorders. Urinary iodine (UI) is the most reliable indicator to assess, monitor and evaluate the iodine nutrition of the population (ICCIDD, WHO and UNICEF 2001). The median urinary iodine of the studied children is comparable to those found in previous Bulgarian studies (Gatseva et al. 2006; Ivanova 2004; Lozanov et al. 2004). These data show a steady positive effect of the strategies for elimination of IDD in this region in Bulgaria.

However, unfavorable result of the study was that 31.5% of the children were with iodine deficiency (mild, moderate and severe) despite the introduced and successfully realized strategy for elimination of iodine deficiency during the last 15 years in Bulgaria.

During pregnancy, thyroid hormone production increases by 50 percent; this requires a greater intake of iodine to maintain thyroid function and thyroid hormone production. Thus, pregnant women represent a highly risk group, as even mild iodine deficiency during pregnancy could induce transitory hypothyroidism (Moleti M et al. 2008). The most significant consequences of iodine deficiency during pregnancy are the adverse effects on the reproductive and thyroid function of maternal and newborn organism, as well as on the mental development of offspring (Pearce 2008; Zimmermann and Delange 2004).

Assuming a mean iodine bioavailability of 92% and a modest increase in renal iodine clearance during pregnancy, recommended daily iodine intake of 200-250 µg/L

during pregnancy corresponds to a median UI of $\geq 150 \mu\text{g/L}$ in adult pregnant women (Zimmermann 2007). New recommendations from WHO consider as an adequate iodine intake in pregnancy that corresponding to a median UI $150\text{-}250 \mu\text{g/L}$ (WHO 2005). Thus, a median UI $50\text{-}150 \mu\text{g/L}$ found in the present study for pregnant women's group can be defined as mild-to-moderate deficiency.

With insufficient iodine intake were 10 (62.5%) of the studied pregnant women having urinary iodine excretion below $150 \mu\text{g/L}$. Their relative part is higher compared to the part of pregnant women having adequate and more than adequate iodine intake. Recent studies reported about inadequate iodine intake in many pregnant women in Western Europe (Antonangeli et al. 2002; Liesenkötter et al. 1996; Delange 2007; Zimmermann and Delange 2004). These results suggest that monitoring of iodine status during pregnancy is a must because of increased iodine requirement. The conclusion of experts is that more surveys of pregnant women are required because they are the group most susceptible to the effects of iodine deficiency (de Benoist et al. 2008; WHO 2007).

There is no special Bulgarian legislation regarding iodine supplementation in pregnancy and breastfeeding. The practice is that medical care providers such as GPs and obstetricians/gynecologists decide whether pregnant women in their practice should have iodine supplements prescribed. It has been suspected (but no evidence is available to support this), that women in Bulgaria when pregnant may reduce their intake of salt added at the table and during cooking. The influence that health care providers and health education may have on habitual dietary practices during pregnancy is therefore growing. Recommendation for detailed information about risks of iodine deficiency during the first weeks of pregnancy was made in the National action plan "Foods and Nutrition 2005-2010".

1 There are two limitations that need to be acknowledged and addressed regarding
2 the present study. The first limitation concerns the fact that ioduria is a “moment
3 picture” of the iodine status and may vary during the day and/or day-to-day. The
4 second limitation has to do with the extent to which the findings can be generalized
5 beyond the groups studied. The number of patients is too limited for broad
6 generalizations. However, numerous studies from our group have led to similar
7 conclusions – despite the normalization of iodine supply in the last years in the risk
8 population groups of children and pregnant women, a considerable part of them are with
9 iodine deficiency, assessed on the basis of urinary iodine excretion.

10 This study brought up some questions as well. Is it necessary to undertake a re-
11 esteem of the strategies for control of iodine deficiency, especially in pregnant women,
12 living in endemic area? Can we suppose a presence of multiple deficiencies such as
13 selenium deficiency in this area in Bulgaria provided that selenium is an essential trace
14 element, which takes part in iodine and thyroid metabolism? These questions can be
15 answered after purposeful epidemiological investigations in risk population groups.

17 **Conflict of interest**

18 The authors declare that they have no conflict of interest.

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FIGURE LEGENDS

Fig. 1 Status of iodine nutrition of the studied children according to the criteria of WHO, UNICEF, and ICCIDD (2001). The status was assessed on the basis of urinary iodine (UI) excretion and classified as: iodine deficiency – $UI < 100 \mu\text{g/L}$; adequate iodine intake – $UI 100\text{--}200 \mu\text{g/L}$; more than adequate iodine intake – $UI > 200 \mu\text{g/L}$

Fig. 2 Status of iodine nutrition in pregnant women after the new WHO recommendations (2005). The status was assessed on the basis of urinary iodine (UI) excretion and classified as: insufficient iodine intake – $UI < 150 \mu\text{g/L}$; adequate iodine intake – $UI 150\text{--}250 \mu\text{g/L}$; more than adequate iodine intake – $UI > 250 \mu\text{g/L}$

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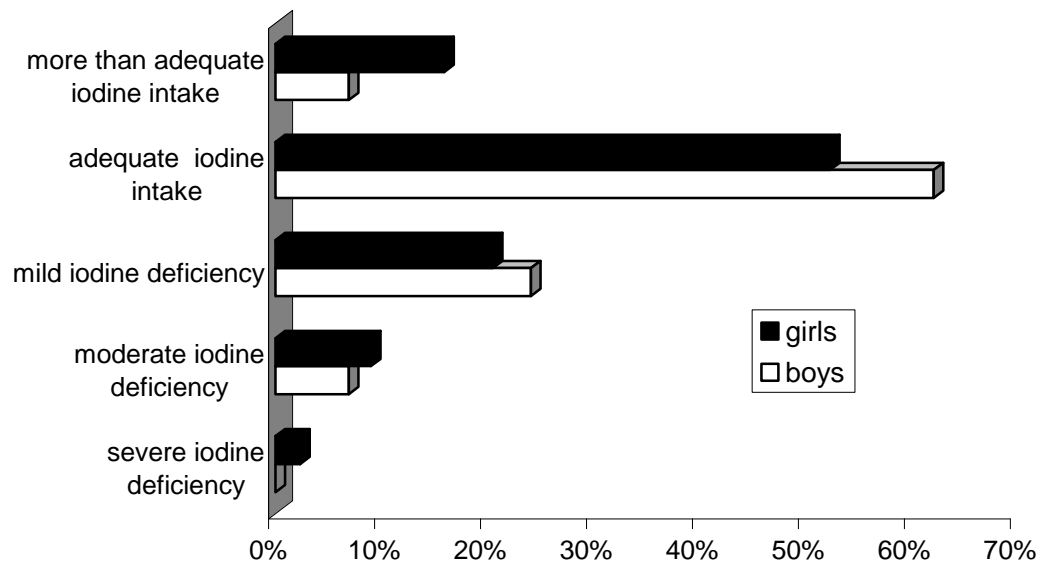


Figure 1.

The figure is Microsoft Office Excel Chart

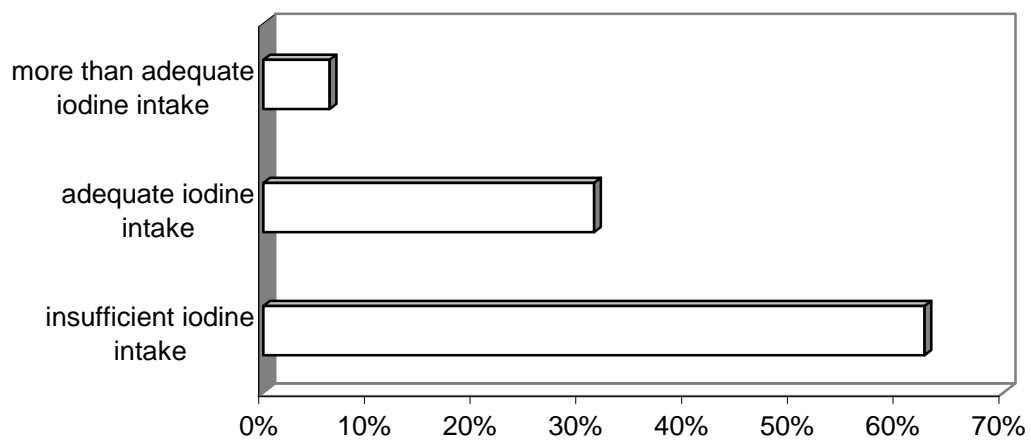


Figure 2.

The figure is Microsoft Office Excel Chart

1 **Table 1.** Urinary iodine concentrations (µg/L) in the studied children

Indices	Boys	Girls
Number of children	29	44
Mean ± SEM	127.48 ± 9.96	134.11 ± 9.76
Median (50 th percentile)	123.0	125.0
95% confidence interval	107.07 – 147.90	114.40 – 153.83
min	24.0	9.0
max	241.0	276.0
Statistical indices	t = 0.4570; P = 0.6491	

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