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ORIGINAL ARTICLE

Progress toward Eliminating Iodine Deficiency in the Republic of Georgia

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Iodine deficiency (ID) is the leading cause of preventable mental retardation worldwide. The most effective method of eliminating ID disorders (IDD) is promoting the widespread consumption of adequately iodized salt. To measure the impact of legislation banning the import and sale of noniodized salt, the Republic of Georgia government and UNICEF conducted a national survey of IDD prevalence in November 2005. <u>Materials and Methods</u>: A cross-sectional cluster survey of 970 school-aged children measured: 1) urinary iodine excretion (UIE), 2) prevalence of goiter by palpation, and 3) the iodine content of household salt. <u>Results</u>: The median UIE was 320.7 µg/L, and only 40 (4.4%) of 900 urinary samples were below 100 µg/L. Palpation of 4420 children revealed a total goiter rate of 32.4% (95% confidence interval [CI]=27.2-37.5). Of 957 salt samples analyzed with rapid salt testing kits, 867 (90.6%, 95% CI=86.9-94.3%) were adequately iodized (≥15 ppm), and only 39 (4.1%) had no iodine. Iodization of salt was validated in 136 random samples using iodometric titration; 94.1% (95% CI=89.1-97.2%) were adequately iodized. <u>Conclusions</u>: Due in part to effective legislation and implementation, Georgia now meets the primary World Health Organization criteria for IDD elimination (i.e., >90% of households using adequately iodized salt and <50% of population with UIE <100 µg/L). Findings of potential excessive iodine intake should be further examined. To maintain elimination of IDD, it is important to continue to enforce legislation and sustain Georgia's salt iodization program.

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Introduction

Iodine deficiency (ID) is a major public health problem worldwide. The consequences of ID, collectively referred to as ID disorders (IDD), include mental retardation, goiter, stillbirths and miscarriage, and impaired growth.[1] ID is the number one cause of preventable brain damage in childhood, and its devastating toll on intellectual capacity and work performance is the primary motivator behind efforts to eliminate IDD.[2-3] Promoting the consumption of adequately iodized salt through universal salt iodization is the most effective method for eliminating IDD.[4-5]

The Republic of Georgia, a country of 4 million inhabitants, is situated on the south Caucasus and borders Russia, Azerbaijan, Armenia, and Turkey. Because of low iodine concentrations in the water and soil, IDD are endemic in Georgia.[6] Since 1996, the government of Georgia and international partners, such as the United Nations International Children's Emergency Fund (UNICEF), have made efforts to implement universal salt iodization; these measures have included issuing a presidential decree in1996 requiring the iodization of salt,establishing the National IDD Council, formulating a tax exemption policy in 1997 for the import of iodized salt, and developing national standards for iodized salt in 1998.[7] In spite of these and other measures, IDD remained a public health problem. In 1996, 64% of school children were found to be affected by IDD, with a prevalence of goiter in mountainous regions of 54% to 78%.[6] A 1998 national survey showed that 80% of urinary iodine excretion (UIE) values were low (<100 µg/L) and that the prevalence of goiter by ultrasound was 36%.[8] Household consumption of adequately iodized salt (≥15 parts per million [ppm]) improved, however, from 8% in the 1999 Multiple Indicator Cluster Survey (MICS) to 67% in 2003.[9]

In February 2005, the government of Georgia enacted a law entitled "Prevention of Iodine and other Microelement and Vitamin Deficiencies," which banned the import and sale of noniodized salt. Currently all iodized salt in Georgia for both human and animal consumption is imported, and regulations mandate iodization at 40±15 ppm, in line with the World Health Organization (WHO) criteria of 20-40 ppm.[10] The aim of the present study was to measure the impact of the February 2005 salt iodization legislation on the prevalence of IDD and iodine concentrations of household salt. Information from the survey was also used to determine whether Georgia meets criteria for sustainable elimination of IDD recommended by the International Coordination Council for Control of Iodine Deficiency Disorders (ICCIDD), UNICEF, and WHO.[4] These criteria require that >90% of households use adequately iodized salt (≥15ppm), <50% of the surveyed population has UIE concentrations below 100 µg/L, and attainment of several programmatic indicators.

Materials and Methods

Study subjects and sampling: This cross-sectional school-based cluster survey of children aged 6-12 years measured 1) UIE, 2) the presence of goiter by palpation, and 3) the iodine content of household salt. The survey was designed in accordance with the methodology proposed by WHO, UNICEF, and the ICCIDD.[4]

Thirty secondary schools were selected with probability proportionate to size using national figures for school enrollment of schoolchildren in grades 1 to 7. In the second stage of sampling, 30 schoolchildren in grades 1-7 were randomly selected from each selected school for assessment of UIE and household salt. A total of 979 schoolchildren were selected(10% oversampling for potential nonresponse); 9 were excluded for not being in the intended age group (6-12 years).

For assessment of goiter, 200 schoolchildren were randomly selected from each of the 30 schools. For schools with total enrollment below 200, all schoolchildren were assessed (the size of clusters varied from 20 to 200). A support letter from the research team was sent to the family of each selected child with a short description of the project and a request to assist the research team for successful implementation of the survey. Written consent was obtained from the parents or guardian.

Laboratory and clinical assessment: During the school visits, the research team collected urine samples from pupils in sterile disposable cups. The urine was transferred into sealed 10-mL tubes and transported to the Central Laboratory of the National Centre for Nutrition in Tbilisi for storage at 4ºC. Iodine content was measured in the first 30 urine samples collected in each cluster (total of 900 samples) by serial dilutions at Centre Hospitalier Universitaire Saint-Pierre in

Brussels, Belgium. This laboratory is part of the International Resource Laboratories for Iodine (IRLI) Network.

For assessment of the iodization of household salt, 10-mL plastic tubes with screw tops were provided to the children who had been selected, who were asked to bring a sample of salt from their homes to school the following day. The children's parents were asked to complete a short questionnaire that requested them to note the manufacturer and expiration date of the household salt. The iodine content of household salt was measured in the schools by the field team using commercial rapid testing kits (MBI Kits International, India) in accordance with written instructions supplied with the kits.[11] The field team first used rapid testing kits for potassium iodate (KIO3) on each sample of salt. The estimated degree of iodization was assigned to one of three levels:

Adequately iodized (≥15 ppm): salt turned dark blue during the test.

Slightly iodized (<15 ppm): salt turned light blue during the test.

No iodine present (0 ppm): salt did not change colour.

All samples found to be negative (0 ppm) with the KIO3 kits were rechecked. If the salt sample still did not change color, the potassium iodide (KI) testing kit was used. Evaluation of iodization with KI discriminated only between ≥15 ppm (turned dark blue) and 0-15 ppm (did not turn dark blue).

To test for validity, approximately 20% of samples(5 samples per cluster) were randomly selected for testing with the WYD Iodine Checker (National Salt Research Center, Tianjin, China) in Tiblisi and testing for iodometric titration by the Institute of Endocriology and Metabolism, Academy of Medical Sciences of Ukraine. Due to laboratory limitations, only specimens positive for KIO3 with the rapid testing kit were subjected to further testing. Although iodometric titration is the reference standard for testing iodine in salt, it requires skilled laboratory personnel and is time-consuming.[10] The WYD Iodine Checker, which uses a single wavelength spectrophoto-mometer to measure the absorption of the iodine-starch blue compound, has been shown to be highly precise, accurate, and sensitive when compared to the titration method.[12] To compare the accuracy of the different testing methods, the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the rapid testing kit were calculated using the WYD Checker and titration as gold standards. Because only KIO3 samples were tested with the WYD Checker and titration, the performance of the rapid testing kits can be assessed only for potassium iodate.

The size of the thyroid gland was assessed by trained endocrinologists by visual inspection and palpation. Goiter was graded according to international classification.[4]

Statistical analysis: Statistical analyses were carried out using Epi Info (version 3.3.2;CDC, Atlanta, GA,USA), taking into account the cluster sampling. Sample weights were applied to account for unequal probabilities of selection due to variation in cluster size. Logistic regression was used for multivariate analyses, and chi-square tests wereusedto test for differences in proportions. Effect size was expressed as an odds ratio (OR) and 95% confidence interval (CI). Statistical significance was set at P<0.05.

Results

Of the 957 children who were ultimately included in the analysis (13 without a salt sample were dropped), 50.1% were male and the median age was 9 years.

A histogram of the UIE of the 900 urine samples collected is shown in Fig. 1. Only 4.4% had a UIE value below 100 µg/L, the WHO threshold for population-based ID.[4] The median UIE was 320.7 µg/L, and 19.3% had a UIE between 100-199 µg/L. Data on the presence of goiter (based on palpating the thyroid) among 4420 children are presented in Table 1. Using a logistic regression model, both female sex and age were associated with higher prevalence of goiter (odds ratio [OR] of 0.46, 95% confidence interval [CI]=0.21-0.98 and OR of 1.3, 95% CI=1.1-1.6, respectively). In contrast, there was no association between increasing concentrations of iodine in household salt or the urinary iodine concentration and prevalence of goiter (Table 1).

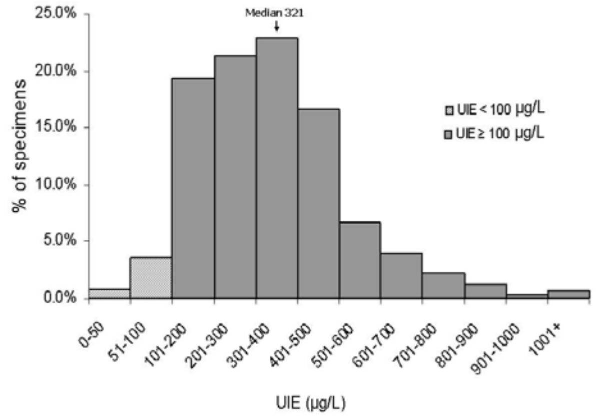

Figure 1. Distribution of urinary iodine excretion (UIE) in Georgia, 2005 (n=900).

Table 1. The prevalence of goiter in school-aged children in Georgia, 2005 (n=4420).

Grade of Goiter	Number	Percent (95% CI)	Median UIE (µg/L)
0	3092	67.6 (62.5-72.8)	316
1	1284	31.0 (26.3-35.6)	330
2	44	1.4 (0.5-2.3)	314
Total prevalence of goiter *	1328	32.4 (27.2-37.5)	321

Abbreviation: CI, confidence interval; UIE, urinary iodine excretion. *Total prevalence = prevalence of grades 1 and 2.

Field testing of 957 salt samples with rapid kits found that 867 (90.6%, 95% CI=86.9–94.3%) were adequately iodized (≥15 ppm), and 4.1% (95% CI=1.8–6.3%) had no iodine. Most salt was imported from Ukraine and Greece; small amounts of salt also came from neighboring countries, including Turkey, Armenia, and Russia. Salt from Ukraine or Greece was 6.0 times more likely to be adequately iodized than salt from other countries with known origin (P by chi-square <0.001). Furthermore, children from households consuming salt from Ukraine or Greece had significantly better iodine nutrition status than children consuming Turkish salt (median UIE by country of manufacture: 409 µg/L, Ukraine; 427 µg/L, Greece; and 119 µg/L, Turkey; P by Kruskal-Wallis test <0.01).

In the validation of salt testing with the rapid kits, a total of 122 samples were tested with the WYD Checker and 136 by titration. A total of 14 samples had insufficient quantity for analysis by both the WYD Checker and titration, and thus only titration was performed in these samples. Using the WYD Checker, the median iodine concentration was 29.2 ppm (range 2.2–51.9), and 82.0% of samples were adequately iodized (≥15 ppm). Using iodometric titration, the median iodine concentration was 40.2 ppm (range 9.5–74.1), and 94.1% of samples were adequately iodized (≥15 ppm). The rapid testing kit performed well in identifying adequately iodized salt as seen by its high sensitivity when either the WYD Checker or titration was used as the gold standard (Table 2). The proportion of positive rapid salt tests that truly were adequately iodized (as measured by the WYD checker or titration)was high (as seen by the high PPVs). On the other hand, the specificity, or percentage of samples that were not adequately iodized that the rapid kit correctly identified as such, was low. In 120 samples tested by both the WYD Checker and titration, the WYD Checker had high sensitivity, specificity, and PPV when titration was used as the standard (Table 2).

Table 2. Performance of the rapid test and WYD checker for detecting adequately iodized salt, Georgia, 2005

Assessment of Iodine Content	Reference	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Rapid Testing Kit	WYD Checker	96.0 (90.6-98.7)	18.2 (6.1-38.2)	84.2 (76.6-90.1)	50.0 (18.4-81.6)
Rapid Testing Kit	Titration	93.8 (88.5-97.1)	0.0 (0.0-31.2)	93.8 (88.5-97.1)	0.0 (0.0-31.2)
WYD Checker	Titration	86.7 (79.5-92.1)	85.7 (47.0-99.3)	99.0 (95.1-99.9)	71.4 (49.8-87.5)

Abbreviations: CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value.
Note: CI calculated using mid-p exact.

Discussion

In this national cross-sectional survey, we found that Georgia meets the primary criteria for sustainable elimination of IDD (i.e., more than 90% of households using adequately iodized salt and <50% of population with UIE<100 μg/L).[4] In less than 10 years, household consumption of adequately iodized salt has increased 10-fold, and the population with adequate iodine nutrition has increased 18-fold (Figure 2). Rates of goiter have also trended downward, as prevalence was 39% in 2003 and 32% in 2005 (based on palpation in the present survey).

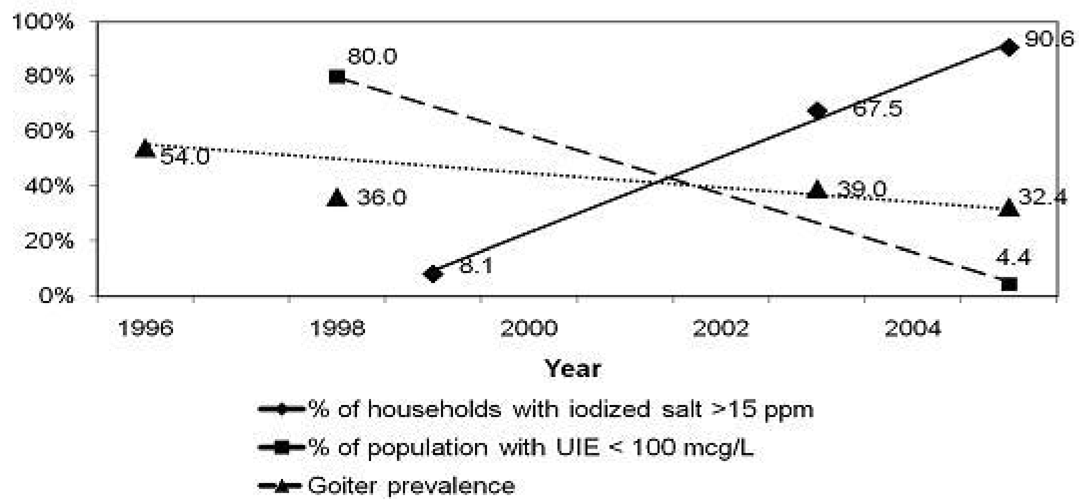

Figure 2. Results of efforts to eliminate iodine deficiency disorders in Georgia, 1998-2005.

Before the 2005 legislation on the iodization of salt, WHO targets were not reached in Georgia even with a strong IDD program and national standards for salt iodization. The remarkable and rapid achievement of eliminating ID in this country is likely due to legislation mandating the iodization of salt and effective implementation of such iodization. Fortification laws give the government authority to mandate compliance with food standards and become advocacy tools that demonstrate the government's commitment to combating micronutrient malnutrition.[13]

Important policy decisions were made in Georgia before the 2005 introduction of the law on iodizing salt that may help explain its rapid success in eliminating IDD. For instance, a strong regulatory structure was in place, and the government has been willing and able to enforce legislation on the iodization of salt. The chair of the Georgian National Fortification Alliance is also an influential member of parliament who regulates enforcement mechanisms. At the import level, all salt must pass through one of three major ports where the Customs Department provides a certificate of authenticity that the salt is iodized.[7] Legislation is also enforced at the wholesale and retail level by the Ministry of Agriculture, which monitors the distribution, storage, and labeling of salt for household consumption. The strong partnership between the government of Georgia, the salt industry, and UNICEF also makes accountability and enforcement of food fortification multisectoral.

Although legislation mandating the iodization of salt is an important early step, additional programmatic factors are important to sustain the elimination of IDD.[4] Some of these factors that are important for Georgia to endorse include ongoing political commitment to the elimination of IDD, having access to laboratories that provide accurate results on the concentration of iodine in salt and urine, a public education program, cooperation from the salt industry in maintaining quality control, and an ongoing monitoring and evaluation system.

The median UIE of greater than 300 ug/L that we found in school-aged children is likely explained by the fact that in Georgia the iodization of salt is truly universal. All salt, including salt for animal consumption, household salt, and salt used in the food industry, is iodized. Another factor to consider is that the patterns of food consumption among children (e.g., intake of bread) may differ from those of adults (children probably eat more bread), which may partly explain the more than adequate iodine nutrition status in our study group. Correspondingly, school-aged children may not be the best target group to assess the impact of continued efforts to ensure adequate iodine nutrition in Georgia, and other vulnerable groups, such as women of childbearing age, should be included in future surveys. Furthermore, a nationally representative cluster sample may not rule out pockets of iodine deficiency in certain regions of the country where consumption of iodized salt remains low. A valid assessment of iodine nutrition is important because excessive iodine intake (defined by WHO/UNICEF/ICCIDD as a median UIE > 300 ug/L) may lead to adverse effects, including subclinical hypothyroidism and autoimmune thyroiditis.[14] To prevent excess intake, the iodine content of salt can be adjusted, and the iodine levels in foods, such as dairy products and bread, may need to be regulated.

Because programs for iodizing salt do not always have an immediate impact on the prevalence of goiter, we were not surprised to find a goiter prevalence of 32% in the studied population in the presence of adequate iodine nutritional status. For example, in South Africa the prevalence of goiter in children did not decline after 12 months of mandatory salt iodization, even though their urinary iodine concentration improved.[15] The persistence of goiter in school-aged children in

Georgia likely reflects longstanding iodine deficiency, and it is known that enlarged thyroids in children who are iodine deficient at a young age may not regress completely after introduction of iodized salt.[16] During the early phase of a salt iodization program, goiter prevalence is a poor indicator because it reflects a population's history of iodine nutrition but not its present iodine status.[17] A limitation of the present study was that the prevalence of goiter was estimated by thyroid palpation. In areas with mild-to-moderate IDD, both the sensitivity and specificity of palpation are poor, and measurement of thyroid volume by ultrasound is preferable.[18] It is important to note that measurement of goiter may not be appropriate in short-term evaluations of the effectiveness of salt iodization programs.

In conclusion, our findings highlight that legislation mandating the iodization of salt and effective implementation can lead to increased consumption of iodized salt and elimination of IDD. Targeted evaluations of iodine status of high-risk groups, including women of childbearing age, pregnant and lactating women, and infants, need to be performed. In addition, potential excessive iodine intake in certain populations warrants further investigation and correction. Despite the apparent success of Georgia's salt iodization program, legislation needs to be enforced, and an effective monitoring and evaluation system needs to be introduced at all levels of the iodized salt supply to sustain the elimination of IDD.

Acknowledgments

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References

1. Hetzel BS. Iodine deficiency disorders (IDD) and their eradication. Lancet 1983; 2: 1126-9.
2. World Health Organization. Iodine and Health: A Statement by the World Health Organization. WHO/NUT/94.4. Geneva: World Health Organization; 1994.
3. Andersson M, Takkouche B, Egli I, Allen HE, de Benoist B. Current global iodine status and progress over the last decade towards the elimination of iodine deficiency. Bull World Health Organ 2005; 83:518-25.
4. World Health Organization, United Nations Children's Fund, International Council for Control of Iodine Deficiency Disorders. Assessment of the Iodine Deficiency Disorders and Monitoring their Elimination: a Guide for Programme Managers. WHO/NHD/01.1. Geneva: World Health Organization; 2001.
5. United Nations Children's Fund. The roadmap towards achievement of sustainable elimination of iodine deficiency: Operational guidance 2005 and beyond; 2005. New York: UNICEF. Available at: http://www.ceecis.org/iodine/01_global/00_mp/01_00_unicef_guidance_05.pdf. Accessed May 30, 2007.
6. United Nations Children's Fund. Achieving Universal Salt Iodization in Georgia: 2004-2005 Plan of Action. Unpublished conference report: "Strengthening Partnership for Elimination of Iodine Deficiency in Georgia," June 25-28 2004, Tbilisi, Georgia.
7. United Nations Children's Fund. Sustained Elimination of IDD through Universal Salt Iodization in Georgia 2001-2005. Annual progress report. Tbilisi, Georgia: Government of Georgia/UNICEF; 2004. Available at: http://www.ceecis.org/iodine/03_country/geo/03_08_geo.html. Accessed May 30, 2007.
8. Gerasimov G. IDD in Eastern Europe/Central Asia. IDD Newsletter 2002; 18: 33.
9. United Nations Children's Fund. Consumption of Iodized Salt in Georgia: Report on Households Sampling Survey. Tbilisi, Georgia: State Dept of Statistics/UNICEF; 2003. Available at: http://www.ceecis.org/iodine/03_country/geo/03_08_geo.html. Accessed May 30, 2007.

10. World Health Organization, United Nations Children's Fund, International Council for Control of Iodine Deficiency Disorders. Recommended Iodine Levels in Salt and Guidelines for Monitoring Adequacy and Effectiveness. WHO/NUT/96.13. Geneva: World Health Organization; 1996.
11. Sullivan KM, Houston R, Gorstein J, Cervinskas J. Monitoring universal salt iodization programmes. Atlanta: Program Against Micronutrient Malnutrition and Ottawa: Micronutrient Initiative; 2005. Available at: http://www.micronutrient.org/Salt_CD/4.0_useful/4.1_fulltext/pdfs/4.1.2.pdf. Accessed May 30, 2007.
12. Dearth-Wesley T, Makhmudov A, Pfeiffer CM, Caldwell K. Fast and reliable salt iodine measurement: evaluation of the WYD Iodine Checker in comparison with iodometric titration. Food Nutr Bull 2004; 25: 130-7.
13. Nathan R. Regulation of Fortified Foods to Address Micronutrient Malnutrition: Legislation, Regulations, and Enforcement. Ottawa, Canada: Micronutrient Initiative; 2000. Available at: http://www.micronutrient.org/salt-CD/4.0-useful/4.1-fulltext/pdfs/4.1.5.pdf. Accessed May 30, 2007.
14. Teng W, Shan Z, Teng X, Guan H, Li Y, Teng D, et al. Effect of iodine intake on thyroid diseases in China. N Engl J Med 2006; 354: 2783-93.
15. Jooste PL, Weight MJ, Lombard CJ. Short-term effectiveness of mandatory iodization of table salt, at an elevated iodine concentration, on the iodine and goiter status of schoolchildren with endemic goiter. Am J Clin Nutr 2000; 71: 75-80.
16. Aghini-Lombardi F, Antonangeli L, Pinchera A, Leoli F, Rago T, Bartomolei AM, et al. Effect of iodized salt on thyroid volume of children living in an area previously characterized by moderate iodine deficiency. J Clin Endocrinol Metab 1997; 82: 1136-9.
17. Zimmermann MB. Assessing iodine status and monitoring progress of iodized salt programs. J Nutr 2004; 134: 1673–7.
18. Zimmermann M, Saad A, Hess S, Torresani T, Chaouki N. Thyroid ultrasound compared with World Health Organization 1960 and 1994 palpation criteria for determination of goiter prevalence in regions of mild and severe iodine deficiency. Eur J Endocrinol 2000; 143: 727–31.