The results of 16 years iodization: Assessment of iodine deficiency among school-age children in Antalya, Turkey

Gamze Celmeli1, Yusuf Curek1, Ikbal Ozen Kucukcetin2, Zumrut Arslan Gulten3, Sebahat Ozdem4, Sema Akcurin5, Iffet Bircan5
1University of Health Sciences, Antalya Training and Research Hospital, Clinic of Pediatric Endocrinology, Antalya, Turkey
2Akdeniz University, Health Science Faculty, Department of Nutrition and Dietetics, Antalya, Turkey
3 Akdeniz University, Department of Pediatrics, Antalya, Turkey
4Akdeniz University, Department of Biochemistry, Antalya, Turkey
5Akdeniz University, Department of Pediatric Endocrinology, Antalya, Turkey

What is already known on this topic?
Despite the highly effective salt iodization programs, ID continues to be a problem around the world.

What this study adds?
This study demonstrates the effect of the iodization program on the iodine status of the population in Antalya, 16 years after it was launched.

Abstract
Objective: Iodine deficiency (ID) continues to be a problem around the world. The present study investigates the prevalence of ID and goiter among school-age children (SAC) in the city center of Antalya, Turkey, aiming to show the effect of the iodization program on the nutritional iodine status, 16 years after it was launched.

Methods: A total of 1,594 school children aged 6–14 years were included in this cross-sectional study. The ID was evaluated based on median urine iodine/creatinine (UI/Cr) (μg/g) levels and median urinary iodine concentrations (UIC)(μg/l). UICs were measured using the Sandell-Kolthoff method, while goiter status was determined by palpation, and staged according to the WHO classification.

Results: The median UIC was found to be 174.69 μg/l (25th and 75th percentiles are 119.17–242.83 μg/l), and UIC was found to be lower than 50 μg/L in 6.5% of the population. The median UI/Cr increased from 62.3 μg/g to 163.3 and goiter rates decreased from 34% to 0.3% in the 16 years of the program. However, 19% of the population were classified as ID (mild, moderate or severe) and 11.5% as excessive iodine nutrition.

Conclusion: The comparison of two cross-sectional studies, carried out 16-years interval, shows that Antalya is no longer an iodine deficient region. That said, surveillance studies should be continued and the percentage of iodine deficient and iodine excess individuals in the population should be monitored to avoid emerging problems.

Keywords: iodine deficiency, prevalence, school-age children, Turkey

Introduction
Iodine is an essential trace mineral required for the synthesis of the thyroid hormones that play a critical role in normal growth and neurodevelopment in fetal life, infancy and childhood. Iodine deficiency (ID) causes wide spectrum damages in human development, from fetal life to adulthood. The clinical manifestations of iodine deficiency disorders (IDD) include miscarriage, stillbirth, neurologic and myxomatous cretinism, goiter, hypothyroidism, mental retardation, intellectual impairment and impaired physical development (1,2).

Despite the significant increase in the number of the iodine-sufficient countries as a result of the universal, highly effective salt iodization programs initiated by WHO and the International Council on Iodine Deficiency Disorders (ICCIDD) in 1990, there was still insufficient iodine intake in 29.8% (246 million) of the global school-age children (SAC) population in 2012 (3).

Knowledge of the prevalence and degree of ID is important, in that it provides information about the effectiveness of iodine prophylaxis in the population. The best indicators of iodine nutrition (IN) in a population are the percentage of households...
using adequately iodized salt and the prevalence of goiter and the median urinary iodine concentrations (UIC) among SAC or pregnant women (4).

The table salt iodization program was launched officially in Turkey in 1998. Erdogan et al. (5) reported a 31.8% goiter rate and a 58% moderate to severe ID in the Turkish population prior to mandatory iodization. Eight years after mandatory iodization, Erdogan et al. (6) reported that 27.8% of the population suffers from moderate to severe ID and ID remains as a serious public health problem in Turkey. Erdogan et al. (7) have emphasized that more than a decade of iodine prophylaxis is needed to eradicate goiter in a moderately iodine-deficient region.

To the best of our knowledge, the only study of community-based ID and the prevalence of goiter in Antalya, Turkey was conducted by Semiz et al. (8) in 1999, prior to the salt iodization program. Semiz et al. (8) reported mild-to-moderate ID in Antalya, Turkey with a 34% prevalence of goiter, and a 62.3 μg/g (10.7–136.9) median urinary iodine/creatinine (UI/Cr) ratio among SAC.

The aim of the present study is to evaluate ID according to urinary iodine levels and determine the prevalence of goiter through a physical examination of SAC in the city center of Antalya. The results will then be compared with those of the study conducted by Semiz et al. (8). In this wise, the status of IN in the population 16 years after the launch of mandatory salt iodization will be evaluated.

Method
The cross-sectional study was carried out between May and June 2015 and included 58 schools of the total 124 schools in the city center of Antalya, Turkey. For the study, 1,700 school children aged 6–14 years were selected from the total 61,092 students attending the schools using a probability proportional to population size cluster sampling method. After excluding 108 participants with chronic disease, regular medication uses or malnutrition, or those who could not provide urine samples under appropriate conditions, a total of 1,594 students were included in the study. None of the participants had been exposed to gadolinium, iodine or barium containing contrast material for the last 96 hours.

Written permission was taken from the Antalya Provincial Directorate of Health and the Antalya Province National Education Directorate. The study was approved by the Ethics Committee of Akdeniz University (Decision No. 269 of 27.05.2015) and was supported by the Akdeniz University Scientific Research Projects Coordination Unit (Project number: TSA-2016-962). Informed consent was obtained from the participants and their parents.

Early-morning spot urine samples were collected, ensuring no contamination, and goiter staging was assessed according to the WHO classification (grade 0: no goiter; grade 1: thyroid palpable but not visible; grade 2: thyroid visible with neck in normal position) by a pediatric endocrinologist. Urine samples were collected in iodized test tubes, and were transferred immediately to the laboratory where they were stored at -20°C.

The median UI/Cr (μg/g) and the median UIC (μg/l) were used in order to compare our results with the previous study conducted by Semiz et al. (8) in Antalya and with other studies in literature, respectively. Severe ID was defined as median UIC <20 μg/l, moderate ID as 20–49 μg/l and mild ID as 50–99 μg/l. Optimal IN was defined as median UIC 100–199 μg/l, more IN than required as 200–299 μg/l and excessive IN as >300 μg/l (4).

Urine levels in the urine were measured using the Sandell-Kolthoff method, as recommended by WHO and ICCIDD (4). Urine creatinine levels were measured spectrophotometrically using the Jaffe colorimetric method.

Statistical analysis
The data was analyzed using SPSS software (Statistical Package for Social Sciences, version 22). The values in the text are presented as median, 25th and 75th percentiles. The statistical analysis was performed using parametric (Student’s t-tests) or nonparametric (Mann-Whitney U-tests) tests, when appropriate. Values of P <0.05 were accepted as statistically significant.

Results
A total of 1,594 students, 839 male (52.6%) and 755 (47.4%) female, were included in the study. The mean age of the participants was 10.6±2.5 years.

The median UIC was found to be 174.69 μg/l (25th and 75th percentiles are 119.17–242.83 μg/l) among school children aged 6–14 years in the city center of Antalya, Turkey. The UI/Cr was lower than 50 μg/l in 6.5% of the sample. The percentages of participants with mild, moderate, severe ID and the IN status are shown in Table 1. Stage 1 goiter was detected in only five students (0.3%) upon physical examination.

When UI/Cr was evaluated for a comparison of the results with the 1999 study, the median was found to be 163.3 μg/l (25th and 75th percentiles are 108.3–254.8 μg/l) and the UI/Cr ratio was found to be lower than 50 μg/l in 4.4% of the population. The results were compared with those of the study conducted by Semiz et al. (8) in Antalya and with other studies in literature, respectively. Severe ID was defined as median UI/Cr <20 μg/l, moderate as 20–49 μg/l and mild as 50–99 μg/l. Optimal IN was defined as median UIC 100–199 μg/l, more IN than required as 200–299 μg/l and excessive IN as >300 μg/l (4).

In our study, although the median UIC was 174.69 μg/l, 19% of the population was classified as iodine deficient (mild, moderate or severe) (Table 1). Prevalence assessments from 2012 estimate that 75% of the children who are affected by low iodine intake live in iodine sufficient countries (3, 10). Gordon et al. (11) found that

Discussion
The cross-sectional study was carried out between May and June 2015 and included 58 schools of the total 124 schools in the city center of Antalya, Turkey with a 34% prevalence of goiter, and a 62.3 μg/g (10.7–136.9) median urine iodine/creatinine (UI/Cr) ratio among SAC. The UI/Cr ratio increased from 62.3 to 163.3 μg/g, the proportion of the population with below 50 μg/l UIC was found to 6.5% and the

The UI/Cr ratio increased from 62.3 to 163.3 μg/g, the proportion of the population with below 50 μg/l UIC was found to 6.5% and the

Discussion
The cross-sectional study was carried out between May and June 2015 and included 58 schools of the total 124 schools in the city center of Antalya, Turkey with a 34% prevalence of goiter, and a 62.3 μg/g (10.7–136.9) median urine iodine/creatinine (UI/Cr) ratio among SAC. The UI/Cr ratio increased from 62.3 to 163.3 μg/g, the proportion of the population with below 50 μg/l UIC was found to 6.5% and the
iodine supplementation improves cognitive function, even in mildly iodine-deficient children, and so the iodine sufficient countries should also monitor the percentage of affected individuals.

The second misleading problem is that the iodine status of SAC is generally representative of the adult population, but not of pregnant women and their newborns. In a recent study, Erdogan et al. (7) reported a median UIC of 117 μg/l and goiter prevalence of 1.3% among SAC in Ankara, Turkey's capital. In similar years, Oguz Kutlu et al. (12) reported a median UIC of 80.5 μg/l and goiter prevalence of 15.4% among pregnant women in Ankara, and indicated that UIC was below 150 μg/l in 72.8% of the pregnant women. In a recent large survey, the median UIC was found to be 73 μg/l among pregnant women in an iodine-sufficient metropolitan city. UIC was found below 50 μg/l in 36.6% of pregnant women and below 150 μg/l in 90.7% (13). There have been numerous studies to date highlighting the presence of ID in pregnant women and newborns in various countries where iodine appears to be adequate (14,15,16). These studies show that national iodization programs do not meet the increased iodine requirements of pregnant women. Accordingly, even iodine-sufficient countries should periodically screen these at-risk groups. And, there is a need for mandatory iodine supplementation programs for pregnant and lactating women.

Another population vulnerable to ID is those living in rural areas. In the 2009 survey, Erdogan et al. (6) found a significant difference among rural and urban areas in Turkey. There are many studies highlighting the difference in ID levels of rural areas (17,18). Therefore, this study does not reflect iodine levels in rural areas of Antalya. In societies where iodine intake is now sufficient, the fourth and a newly emerging problem is excessive iodine intake (median UIC greater than 300 μg/l). Recent national surveys found excessive iodine intake in 10 countries around the world (4). Nowadays, studies into excessive iodine intake have started to increase all around the world. Katagiri et al. (19) showed in a meta-analysis that chronic exposure to excess iodine is a risk factor for hypothyroidism. The mechanism behind hypothyroidism is thought involve an adaptation of the thyroid gland to excess iodine uptake (20,21). In China, the prevalence of subclinical hypothyroidism and thyroid nodules was found to be 20% and 15.5%, respectively, in the excess iodine areas, although the prevalence of subclinical and overt hyperthyroidism in the iodine deficient group was higher than in the excess iodine group (22). It has been shown that, after the start of mandatory salt iodization, the incidence of autoimmune thyroid disorder has increased in many countries (23,24). In the present study, UIC were 200–299 μg/l (more than required) in 28.1% of the population and were >300 μg/l (excessive iodine nutrition) in 11.5%. Accordingly, surveillance studies should be continued in iodine sufficient regions to prevent the growth of excess iodine as a problem. Measuring the ratio of urinary iodine to creatinine for population screening is expensive, and can be misleading in some cases, such as in the presence of malnutrition, and so is no longer recommended (4,25). In the present study, however, in order to be comparable with a previous study conducted in Antalya, we evaluated both UIC/Cr ratios as well as UICs.

Study Limitations and Strengths

In our study, we detected goiter in 0.3% of the population upon physical examination. Although palpation is the traditional diagnostic method, the sensitivity and specificity of palpation are poor in mild to moderate iodine deficient areas.

Percentages may be higher through measuring thyroid size by ultrasound. The strength of this study is its detailed demonstration of the outcome of 16 years of mandatory salt iodization in the same geographical region.

Conclusion

Our study shows that as a result of the application of an effective salt iodization program 16 years ago, Antalya is now an iodine sufficient region. Surveillance studies should be continued in SAC and in at-risk groups to ensure adequate iodine intake. The levels of ID and excess iodine intake in the population should be carefully monitored to avoid newly emerging problems.

Ethics

Ethics Committee Approval: The Ethics Committee of Akdeniz University (Decision No. 269 of 27.05.2015)

Informed Consent: Yes

Authorship Contributions

Surgical and Medical Practices: Gamze Celmeli, Yusuf Curek, Zumrut Arslan Gulten
Concept: Gamze Celmeli, Ikbbl Ozen Kucukcekin, Sema Akcurin
Design: Gamze Celmeli, Yusuf Curek, Sema Akcurin, Iflet Bircan
Data Collection or Processing: Gamze Celmeli, Yusuf Curek, Zumrut Arslan Gulten
Analysis or Interpretation: Gamze Celmeli, Ikbbl Ozen Kucukcekin, Sebahat Ozdem, Iflet Bircan
Literature Search: Gamze Celmeli, Ikbbl Ozen Kucukcekin, Zumrut Arslan Gulten, Sebahat Ozdem,
Writing: Gamze Celmeli, Sebahat Ozdem, Sema Akcurin, Iflet Bircan

Conflict of Interest: No conflict of interest

Financial Disclosure: No financial disclosure

References


Table 1. The distribution of iodine deficiency and iodine nutrition status in the city center of Antalya, Turkey

<table>
<thead>
<tr>
<th>Iodine Status</th>
<th>Median UIC (μg/l)</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe ID &lt; 20</td>
<td>38</td>
<td>2.4</td>
<td></td>
</tr>
<tr>
<td>Moderate ID 20-49</td>
<td>66</td>
<td>4.1</td>
<td></td>
</tr>
<tr>
<td>Mild ID 50-99</td>
<td>199</td>
<td>12.5</td>
<td></td>
</tr>
<tr>
<td>Optimal IN 100-199</td>
<td>654</td>
<td>40.5</td>
<td></td>
</tr>
<tr>
<td>More than required</td>
<td>454</td>
<td>28.1</td>
<td></td>
</tr>
<tr>
<td>Excessive IN &gt;300</td>
<td>183</td>
<td>11.5</td>
<td></td>
</tr>
</tbody>
</table>

ID: iodine deficiency, IN: iodine nutrition, UIC: urinary iodine concentration

Table 2. The comparison of two cross-sectional studies, carried out with a 16-years interval, in Antalya, Turkey

<table>
<thead>
<tr>
<th>Year</th>
<th>Median UI / Cr (μg / g)</th>
<th>The UI / Cr &lt; 50 μg / g</th>
<th>Goiter prevalence</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>1999*</td>
<td>62.3 (10.7-136.9)</td>
<td>20 % of population</td>
<td>34 %</td>
<td></td>
</tr>
<tr>
<td>2015</td>
<td>163.3 (105.3–254.8)</td>
<td>4.4 % of population</td>
<td>0.3 %</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

*reference 6.
UI / Cr: urine iodine / creatine