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Current iodine status In Turkey

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ABSTRACT. ***Objectives:*** **To evaluate the current nationwide iodine status in Turkey by determining urinary iodine concentrations (UIC) and household salt iodine content. A follow-up monitoring study was also conducted in 30 urban areas.** ***Methods:*** **A school-based survey was conducted in 2007 by using multistage 'proportionate to population size' (PPS) cluster sampling method. The study population was composed of 900 school-age children (SAC) from different urban, suburban, and rural areas. UIC and iodine content of the table salt used at home were analyzed.** ***Results:*** **Median UIC was 107 µg/l (147 in urban, 42 in suburban and rural areas, p<0.001). There were severe iodine deficiency (ID) in 7.2%, moderate and mild ID in 20.6% and 19.3%, of the SAC, respectively. UIC was sufficient (>100 µg/l) in 50% of the study population, whereas it was excessive (>300 µg/l) in 10.5% of them. Of the 900 salt samples, 662 (73.5%) were iodized and 508 samples (56.5%) contained adequately iodized salt (iodine content >15 ppm). UIC of the study population and salt iodine levels correlated well (r=0.42, p<0.001).** ***Conclusions:*** **Moderate to severe ID still exists in 27.8% of the Turkish population, which is much better compared to 1997 and 2002 surveys (i.e. 58%, 38.9%, respectively). The follow-up monitoring study (in 2007) demonstrated that ID has been eliminated in 20 of 30 cities surveyed, and median UIC was 130 µg/l. ID has been eliminated in most of the urban population, however, it is still an important problem in rural areas and in particular geographical regions, which should be the target of future programs.**
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INTRODUCTION

Elimination of iodine deficiency (ID) disorders (IDD) is an important health and social goal. ID at critical periods during early childhood results in impaired development of the brain and consequently in impaired mental function (1). Although global progress in controlling ID has been made in the recent years, this debilitating health issue continues to affect almost one in three individuals globally (2). In practice, the most commonly applied methods for correction of ID is universal salt iodization; i.e, the addition of a suitable amounts of potassium iodate to all salt for human and livestock consumption (3). Iodized salt is the best means for providing iodine to iodine-deficient populations. It is physiological, simple, practical, and effective (4, 5). The daily recommended nutrient intake for iodine proposed for pregnant, lactating women and children less than 2 yr old are 250, 250, and 90 µg/day, respectively (3, 6).
Until the 1990s total goiter prevalence (TGP) was the recommended indicator for assessing iodine status. However, TGP responds slowly to a change in iodine status and today urinary iodine is recommended as a more sensitive indicator of recent changes in iodine nutrition (7). While IDD affects the entire population, a school-based sampling method is recommended for urinary iodine concentrations (UIC) and TGP as the most efficient and practical approach to monitor IDD as this group is usually easily accessible and can be used as a proxy for the general population. The recommended strategy for IDD control is based on correcting the deficiency by increasing iodine intake through supplementation or food fortification. Four main components are required to implement the strategy: correction of ID, surveillance including monitoring and evaluation, inter-sectorial collaboration and advocacy and communication to mobilize public health authorities and educate the public (8).
The sustainable elimination of IDD requires that a) median urinary iodine levels in the target population are at least 100 µg/l and no more than 20% of values are below 50 µg/l; b) at least 90% of households are using salt with an iodine content of 15 parts per million (ppm) or more; and 3) there is evidence of sustainability, as judged by the attainment of at least 8 out of 10 specified programmatic indicators listed elsewhere (3). Monitoring and evaluating the impact of salt iodization on target communities are recommended to be performed every 5 yr (3).
As recommended by World Health Organization (WHO) and International Council for Control of Iodine Deficiency Disorders (ICCIDD), assessment and monitoring system, one major component of a sustainable programme to eliminate IDD, is being performed in Turkey since 1997. The first survey, carried out between 1997 and 1999, in Turkey showed that the country was severe to moderately iodine deficient [national median UIC 36 µg/l (range 14-78), goiter prevalence 31.8% (range 5-56%)]. In 14 of the 20 provinces surveyed, there was a severe to moderate ID. The other 6 provinces had mild ID. In that survey, none of the provinces had sufficient iodine status (9). Therefore, a national IDD control program had been implemented and mandatory salt iodization were

Key-words: Iodine content of table salt, iodine status, school-age children, urinary iodine concentration.

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applied by July 1998 with 50-70 mg/kg KI or 25-40 mg/kg KIO_3 added to the household salt.
The second survey was performed in 2002 in 30 cities. Over 7000 UIC of school-age children (SAC) were determined, and the result demonstrated an obvious improvement, yet it was not optimal for elimination of IDD (median UIC 53 μg/l) (10). These results representing nationwide iodine status of Turkey were consistent with regional surveys performed by different study groups (11-13).
In 2007, with the follow-up monitoring purposes, another survey was implemented in the same 30 areas, and the results demonstrated a gradual improvement in the country (median UIC 130 μg/l) (14). Nevertheless, all these nationwide surveys were performed in city centers, and they did not reflect the iodine status of suburban and rural areas. Besides, according to the last census (2007), in the last decade, there was a significant immigration (15). Therefore, we aimed to conduct another survey to evaluate the current iodine status that reflects the overall population including centrums, towns, and villages. Additionally, we studied iodine content of table salt. We, hereby, report both the results of this survey and results of the last follow-up monitoring study conducted in 2007.

STUDY POPULATION AND METHODS

Turkey is located in Anatolia and partly in South-eastern Europe. It is geographically divided into 7 regions: Marmara, Aegean, Mediterranean, Central Anatolia, Black Sea, Eastern Anatolia, and Southeastern Anatolia (16). It has 81 cities with overall 70,586,256 inhabitants according to 2007 census (15).
School-based survey was performed. Using multistage 'proportionate to population size' (PPS) cluster sampling method, 24 cities from all 7 geographical regions were determined: Balıkesir, Bursa, Istanbul, Kocaeli (Marmara Region), Afyonkarahisar, Izmir, Mugla (Aegean Region), Adana, Hatay, Kahramanmaraş, Osmaniye (Meditarrenean Region), Ankara, Konya, Nevşehir (Central Anatolia Region), Çorum, Ordu, Sinop (Black Sea Region), Elazığ, Erzurum, Tunceli (Eastern Anatolia Region), Batman, Diyarbakır, Gaziantep, and Şanlıurfa (Southeastern Anatolia Region). A list of the schools for each of these cities and enrollment informations were obtained. Again, the PPS method was used for selection of the school(s) and the pupils in that area.
With the permission of local scholastic and health authorities, the day before the survey, the children were announced to bring the salt that is used at home for cooking. On the day of the survey performed, salt samples and the morning urine samples of each pupil were collected. The urinary samples were sent to iodine laboratory of our department for determination of the UIC. Salt samples were sent to regional control laboratories of Ministry of Agriculture of Turkey.
External control of our iodine laboratory is periodically done by the EQUIP (Ensuring The Quality of Urinary Iodine Procedures) Program of CDC (The Centers for Disease Control and Prevention) (Atlanta, USA).
Urine samples were kept covered at 4 C, in deionized tubes and analyzed within 30 days from the collection. UIC were determined by using the method recommended by WHO-ICCIDD (Calorimetric ceric ion arsenous acid wet ash method based on Sandell-Kolthoff reaction), using Fisher® reagents and spectronic 20, Genesis autoanalyzer (3).
Salt iodine contents were measured using iodometric titration method.
These surveys were performed as a part of governmental duty, but also an informed consent was obtained from participants and their parents.

Statistical analysis

Since all continuous variables were non-normally distributed, they were expressed as median and interquartile ranges 25 and 75, and were compared with Mann-Whitney U test. Evaluation of normality was performed with the Kolmogorov Smirnov test. Categorical variables were compared with Pearson χ^2.
Pearson's correlation coefficients were computed to explore the relationship between UIC (μg/l) and salt iodine levels (ppm).
SPSS software v.13.0 (SPSS, Chicago, IL) was used for all statistical calculations.

RESULTS

Nine hundred SAC (6-14 yr old) were selected from 30 different schools located in 24 various cities (Table 1). Five hundred and ten of the pupils were living in urban areas, while the remaining 390 of them were living in suburban or rural areas. When they grouped according

Table 1 - *Overall population, sample size, urinary iodine concentrations (UIC) and salt iodine contents of the areas studied.*

Study area	Overall population	Sample size (no.)	Median UIC (μg/l)	Median salt iodine content (ppm)
1. DİYARBAKIR	1.460.714	30	21	0
2. TUNCELİ	84.022	30	103	20
3. ŞANLIURFA	1.523.099	30	105	0
4. ELAZIĞ	541.258	30	33	0
5. BATMAN	472.487	30	65	10
6. GAZİANTEP	1.560.023	30	130	37
7. İSTANBUL	12.573.836	150	154	32
8. BURSA	2.439.876	30	181	50
9. BALIKESİR	1.118.313	30	71	0
10. AFYONKARAHİSAR	701.572	30	185	38
11. KOCAELİ	1.437.926	30	167	40
12. ANKARA	4.466.756	60	142	39
13. NEVŞEHİR	280.058	30	87	0
14. KONYA	1.959.082	30	132	33
15. ADANA	2.006.650	30	40	0
16. OSMANİYE	452.880	30	27	33
17. HATAY	1.386.224	30	31	1
18. KAHRAMANMARAŞ	1.004.414	30	82	13
19. ERZURUM	784.941	30	32	2
20. SİNOP	198.412	30	338	35
21. ÇORUM	549.828	30	17	0
22. ORDU	715.409	30	203	43
23. İZMİR	3.739.353	60	170	31
24. MUĞLA	766.156	30	101	39
Total	42.223.289	900	107	29

to the geographical region they were living, 240 (26.7%) were from Marmara Region, 120 (13.3%) from Aegean Region, 120 (13.3%) from Mediterranean Region, 120 (13.3%) from Central Anatolia Region, 90 (10%) from Black Sea Region, 90 (10%) from Eastern Anatolia Region, and 120 (13.3%) were from Southeastern Anatolia Region.

UIC

Median UIC was 107 (46 to 180) µg/l. UIC of 65 SAC (7.2%) was <20 µg/l. One hundred and eighty-five (20.6%) were between 20 and 49 µg/l. One hundred and seventy-three (19.3%) of the pupils demonstrated mild ID (50-99 µg/l). Iodine status was optimal in 383 (42.4%) of the pupils examined (UIC was between 100 and 299 µg/l). The remaining 94 (10.5%) had excess iodine (>300 µg/l). The proportion of SCA with an UIC >500 µg/l was only 3%.

When the schools were analyzed with regard to their location, median UIC was 142 (90-205) in urban, whereas it was 52 (26-119) in rural and suburban areas ($p<0.001$). Frequencies of iodine deficiencies were also different in urban and rural areas (Table 2).

When the analysis was done for each geographical region separately, median UIC was 148 µg/l (98-216) in Marmara, 139 (80-234) in Aegean, 125.5 (82-170) in Central Anatolia, 172 (26-291) in Black Sea Regions, whereas it was 40 (27-82) in Mediterranean, 42 (26-105) in Eastern Anatolia, and 71 (29-134) µg/l in Southeastern Anatolia regions. The frequencies of ID were also varied in different geographical regions (Table 3).

Salt iodine levels

Two hundred and fifty-six (28%) of the salt samples were iodized with KI, and 406 (45.1%) with KIO_3.

One hundred and forty-one (55.1%) of the salt samples with KI, were appropriately (50-70 mg/kg) iodized, whereas 15 (5.9%) were excessively (>70 mg/kg), and the remaining 100 (39%) samples were insufficiently (<50 mg/kg) iodized. However, only 60 of these 100 insufficiently iodized salt samples contained >15 ppm iodine which is the lower limit recommended by WHO-ICCIDD (3).

Two hundred and forty-six (60.6%) of the salt samples with KIO_3 were appropriately (25-40 mg/kg) iodized, whereas 46 (11.3%) were excessively (>40 mg/kg), and the remaining 114 (28.1%) were insufficiently (<25 mg/kg) iodized or inappropriately preserved.

Overall, 662 (73.5%) of the salt samples were iodized. Overall, salt iodine content was 29.30 (0-41.6) ppm. However, 508 (56.5%) contained more than 15 ppm iodine. Besides, only 387 (43%) were appropriately iodized.

When the analysis performed for urban and rural areas separately, median salt iodine level was 33 (24-50) ppm in urban areas, whereas it was 2 (0-37) ppm in suburban and rural areas. When each geographical region separately analyzed, median salt iodine levels were 33 (26-51) ppm in Marmara, 35 (14-46) in Aegean, 6 (0-35) in Mediterranean, 34 (25-40) in Central Anatolia, 30 (0-49) in Black Sea, 2 (0-9) in Eastern Anatolia, and 0 (0-33) ppm in Southeastern Anatolia regions.

Median UIC of SAC using salt iodized with KI and KIO_3 was 150 (79 to 232) µg/l, and 130 (65 to 186), respec-

Table 2 - *Frequencies of median urinary iodine and comparison of both these frequencies and salt iodine levels of school-age children in urban and rural areas.*

Area	Median UIC (µg/l)					Median (IQR 25-75) salt iodine content
	0-19 (%)	20-49 (%)	50-99 (%)	100-299 (%)	≥300 (%)	
Urban (no.=510)	0.8	11.2	18.0	55.9	14.1 33	(24-50) ppm
Suburban and rural (no.=390)	16.2	32.8	20.8	24.6	5.6	2 (0-37) ppm
Overall (no.=900)	7.2	20.6	19.3	42.4	10.5	29 (0-42) ppm
p	<0.001	<0.001	0.30	<0.001	<0.001	<0.001

UIC: urinary iodine concentrations; IQR: interquartile range.

Table 3 - *Frequencies of median urinary iodine and comparison of both these frequencies and salt iodine levels of school-age children in each geographical region.*

Area	Median UIC (µg/l)					Median (IQR 25-75) salt iodine content
	0-19 (%)	20-49 (%)	50-99 (%)	100-299 (%)	≥300 (%)	
Marmara (no.=240)	0	9.2	16.3	61.5	13.0	33 (26-51)
Aegean (no.=120)	1.7	8.4	26.1	47.1	16.8	35 (14-46)
Mediterranean (no.=120)	10.0	53.3	17.5	14.1	5.0	6 (0-35)
Central Anatolia (no.=120)	0	6.7	30.0	57.5	5.8	34 (25-40)
Black Sea (no.=120)	20.0	12.2	10.0	33.3	24.4	30 (0-49)
Eastern Anatolia (no.=120)	15.6	40.0	16.7	24.4	3.3	2 (0-19)
Southeastern Anatolia (no.=120)	15.8	28.3	18.3	33.4	4.2	0 (0-33)
Overall (no.=900)	7.2	20.6	19.3	42.4	10.5	29 (0-42)
p	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01

UIC: urinary iodine concentrations; IQR: interquartile range.

tively (p=0.003). Salt iodine content was significantly correlated with UIC (r=0.42, p<0.001).
The follow-up monitoring study performed in 2007, examined 2280 SAC living in urban areas. The overall median UIC was 130 µg/l. It demonstrated that median UIC was sufficient (≥100 µg/l) in 20 of 30 cities surveyed (Fig. 1). In 8 city centers [Burdur, Hatay, Kahramanmaraş (Mediterranean Region), Kayseri (Central Anatolia Region), Bayburt, Çorum (Black Sea Region), Erzurum and Van (Eastern Anatolia Region)] median UIC was slightly (50-100 µg/l), and in 2 [Bitlis (Eastern Anatolia Region), and Diyarbakır (Southeastern Anatolia Region)] it was moderately (20-50 µg/l) low. Median UIC did not exceed the 300 µg/l value, in any of the areas studied (Fig. 1).

DISCUSSION

Reporting the results of UIC and salt iodine content in 2007, this report provides the current nationwide iodine nutrition status in Turkey. It represents a continuum of the previous reports on the estimated prevalence of IDD. There has been a gradual improvement in iodine status of the urban areas after 10 yr following the mandatory iodization of salt, yet the situation is serious in suburban and rural areas. In those areas a special attention is needed for the elimination of IDD. The iodine status correlates well with the salt iodine content. However, iodized salt consumption and thus iodine status differs significantly among the areas surveyed.
For programmes using iodized salt, monitoring of salt quality is important both for assessment of the iodine status of that population, and for identification and prevention of potential adverse effects of excessive iodization, such as iodine-induced hyperthyroidism (17). Our study demonstrated that median UIC of SAC using salt iodized with potassium iodide (KI) was higher compared to children using salt iodized with potassium iodate (KIO_3). KI in salt is not stable and can easily be lost by oxidation to iodine if the iodized salt is subjected appreciably to moisture in the salt, humid or excessively aerated environment; by exposure to sunlight or to heat; or by presence of impurities. It can also be lost if the iodized salt packages become damp, during the transfer of iodized salt. The industry tried to lessen this loss by the addition of stabilizers and/or drying agents such as magnesium carbonate or calcium carbonate. On the other hand, most people in iodine-deficient areas use unrefined salt that can be effectively supplemented with KIO_3 without adding carrier agents or stabilizers. Iodate is more stable under adverse climatic conditions than iodide and does not require stabilizers. It is also less soluble than iodide and less likely to migrate from the bag, but is only sparingly soluble in water at low temperatures. Potassium iodate breaks down rapidly in the human body and effectively delivers iodide to the thyroid gland for the synthesis of thyroid hormone (18). In recent years, most of the developed countries use potassium iodate (KIO_3) extensively for iodization of refined table salt. Salt industry is similarly changing and focusing on KIO_3 in Turkey.
The higher median UIC of SAC using potassium iodide compared to median UIC of SAC using potassium iodate seems to be in disagreement with the notion that iodate is more stable than iodide. This could be explained by the practice of salt iodization in Turkey. According to the codex for salt iodization in Turkey, salt iodized with potassium iodate should contain 25-40 mg/kg KIO_3 (14.8-23.7 mg/kg I^-), whereas salt iodized with potassium iodide should contain 50-70 mg/kg KI (38.2-53.5 mg/kg I^-). Twenty percent of the KIO_3 is lost before cooking, and another 20% during cooking, while 50% of KI is lost before cooking due to instability. Therefore, with the assumption of 6-10 g/day of salt *per capita* is consumed in Turkey, foods during consumption will contain 94-152 µg/day I^-, if the salt iodized with KIO_3; or 191-267 µg/day I^-, if with KI. We think that the higher median UIC of pupils using KI, compared to median UIC of pupils using KIO_3 is probably related to these factors.
Our survey demonstrated that in 11 of 24 areas studied were using salt with median iodine content <15 ppm, the minimum level recommended by WHO-ICCIDD. Furthermore, SAC living in 7 of these 11 areas

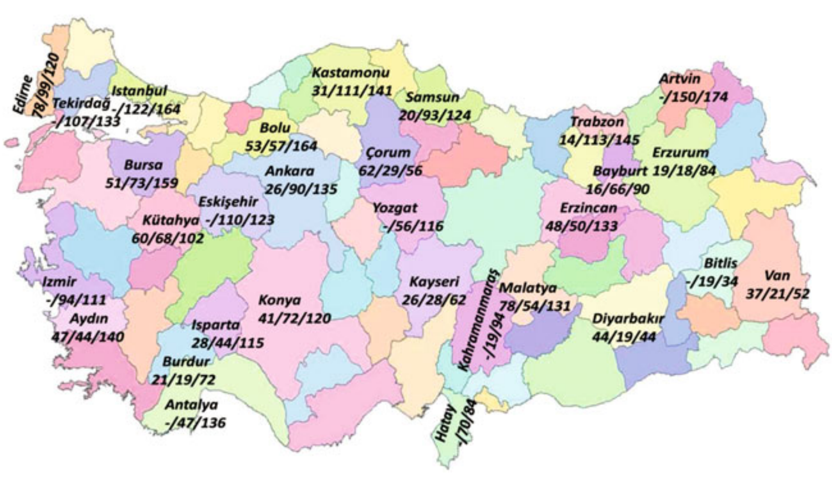

Fig. 1 - *Urinary iodine concentrations (µg/l) of school-age children of the 3 follow-up monitoring surveys (1997-1999/2002/2007) performed in city centers. Note that 20 city centers were studied in 1997-1999 survey. In the following 2 surveys 10 more city centers were included.*

were using salt with median iodine content of 0 ppm. Our survey reflects the salt used at home for cooking. Therefore, it is difficult to find in which process (production, marketing, packaging, handling, storage or consuming) the problem is and to what extent. Paying attention to the salt industry and to the aspects of production, transportation, iodization, packing, distribution, and marketing is of utmost importance. Non-compliance to laws of iodization should be controlled at the level of manufacturing and at the retail level if possible. Since an important difference exists between median levels of salt iodine content of urban and rural areas (33 and 2 ppm, respectively), and between particular geographical regions, erratic salt production and distribution patterns of iodized salt in rural areas where transportation is problematic should get more attention. Four of 5 large salt producers are well controlled and produces high-quality refined iodized salt in Turkey. However, there are more than 200 small producers which could explain the outstanding difference between urban and rural areas.

Excessive salt iodine was observed in 5.6% of salt iodized with KI, and in 11.3% of with KIO_3. Moreover, about 3% of the SAC was found to have excess UIC. The most probable causes of this iodine excess are excessive salt iodization, nutrient fortification, and use of multivitamin tablets. As one would expect, most of these children are living in more developed cities and metropolis. Unnecessary nutrient fortification, and use of multivitamin tablets should be avoided in metropolis.

Overall, iodine nutrition is much better, but still far to be optimal in Turkey. Important differences exist between urban and rural areas. These differences are possibly caused by different socioeconomical status and differentials in access to iodized salt. Climate differences may also play a minor role. More importantly, the lack of knowledge about the importance of the iodized salt in rural areas is possibly another factor. On the other hand, other than different consumption, conservation, and method of cooking of iodized salt also selenium deficiency, vitamin A deficiency and/or iron deficiency, diet habits, and environmental endocrine disrupters may explain the differences observed between urban and suburban/rural population (19). To the best of our knowledge, there is no study performed in Turkey to clearly answer these possibilities.

All agreed measures are available for both urban and rural areas. In the iodine-deficient areas, table salt iodization needs to be strengthened and fully implemented. Salt quality monitoring should be re-inforced to every salt producer ensuring that the level of salt fortification with iodine is adequate (20). The Ministry of Health of Turkey is working to strengthen monitoring and evaluation of national programs for the prevention and control of ID in suburban and rural areas. These programs include education the public on the need to prevent ID by consuming iodized salt, and thereby also increase consumer awareness and demand.

Noteworthy is the correlation between household coverage of iodized salt and prevalence of low iodine intake. Ten of the 11 cities where iodine content of the household-consumed salt was <15 ppm were iodine deficient. Some limitations of our study should be noted. First, our survey conducted with 900 SAC, and this may not be sufficient to extrapolate these data to nationwide. However, using multistage 'proportionate to population size' cluster sampling method in both this survey and the follow-up monitoring survey that was conducted with 2280 SAC, we think our results could be considered as reliable data for Turkey. Second, this survey does not give data for other vulnerable groups, such as pregnant or lactating women.

CONCLUSIONS

There has been substantial progress in the last 8-10 yr towards the elimination of ID in Turkey. However, the problem still continues mostly in rural areas, whereas excessive iodization does not seem to be a real problem at the moment. Improved iodine nutrition reflects the validity of the current mandatory iodine supplementation program of household salt. It also reflects the efforts made by the health authorities and the salt industry. However, the program should be fortified in rural areas, and additional effort is needed for ensuring the program continue and to cover all at-risk populations (i.e. pregnant and lactating women), in order to reach the goal of eliminating IDD.

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