

Sustained Elimination of Iodine Deficiency within the third decade after Compulsory Iodine Supplementation Policy in South of IRAN

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Abstract

Background: Recently, some studies in Iran have shown mild to moderate iodine levels in the adults and pregnant population despite iodine sufficiency in children. We designed this study to evaluate the urine iodine status and salt intake of adult household of the city of Sadra, Fars province in southern Iran and to assess its possible influencing factors.

Method: Participant households for this cross-sectional study were chosen based on randomized cluster sampling. Two subjects over 18 years of age from each household were invited. 92 subjects (24 men, 68 women) were enrolled. Subjects were asked for 24-hour urine collection, examined for thyroid disorders and sent for thyroid ultrasonography and thyroid function tests. Urine samples were tested for iodine, sodium and creatinine levels. Household salt intakes were estimated.

Results: Median urine iodine content (UIC) in the population was 175 (IQR: 117 – 250) $\mu\text{g/L}$ and the median salt consumption per person per day was 9.59 (IQR: 7.34 – 14.55) gr. Gender, methods of salt storage, goiter or thyroid nodules, salt added by cooking stage or subclinical hypothyroidism had no effect on UIC while individuals with hypertension and lower education levels had significantly lower iodine levels. UIC had a significant positive correlation with urine sodium and TSH levels and a negative correlation with thyroid volume and T4.

Conclusion: Iodine status in the adult population of city of Sadra is categorized as sufficient despite inadequate iodine levels in Tehran. Contributing factor can be the higher use of salt or possible high environmental iodine concentrations in Sadra.

Introduction

Iodine deficiency is the most prevalent preventable cause of mental disability. [1] It has long been recognized as a micronutrient essential for neural development and growth. [2] Iodine deficiency disorders (IDD) can include symptoms including hypothyroidism, goiter, spontaneous abortion and cretinism. Chronic iodine deficiency has also been linked to follicular thyroid carcinoma. [3] Sufficient iodine levels in adults is crucial based on its links to possible follicular carcinoma and its role in pregnant women for development of fetus. [1]

Based on the World Health Organization (WHO) guidelines, urine iodine levels of a representative group can demonstrate the iodine sufficiency status of a population. [4] Approximately 80% of consumed iodine from the last 24–48 hours is excreted in urine. [5]

Despite global efforts to curb iodine deficiency by measures such as salt iodine fortification, some previously, iodine sufficient countries have experienced a resurgence of iodine deficiency. Based on the Iodine Global Network report, Norway, Finland and Germany have experienced iodine insufficiency in 2019 despite being classified as iodine sufficient previously. [6] The United States has also seen dramatic decrease in urine iodine levels from 1974 to 2010. [1]

Recently, some studies in Iran have shown mild to moderate iodine levels in the adults and pregnant population [7, 8] despite iodine sufficiency in children. [9] Nazeri et al believe that the reduction of daily salt intake can contribute to the reduction of urine iodine levels as demonstrated in their study. [8] Based on this, we designed this study to evaluate the urine iodine status and salt intake of adult household of the city of Sadra, Fars province in southern Iran and to assess its possible influencing factors in comparison to results from the study by Nazeri et al in Tehran.

Method

This cross-sectional study was performed in the city of Sadra, located in Fars province, southern Iran. Samples were chosen based on cluster sampling. The city was divided into four districts, of which 25 households were randomly selected in each district. Twenty-four hour urine samples were taken from two residents of each household. Additionally, a pre-weighted container of iodized salt was given to each household to exclusively use for 14 days, including during food preparation and in table salt shakers; after which the amount of salt used was measured and divided by the number of people in each household. A questioner was also given and participants were asked for gender, age, education level, thyroid disorder and related drug use history, blood pressure and related drug use history, salt container storage (in sunlight vs. dark and out of sunlight) and the cooking stage in which the salt is usually added (before cooking, during cooking, after cooking). Participants were also examined and underwent ultrasonography for goiter or thyroid nodules, thyroid volume was calculated based on length, width, and depth of thyroid gland using this formula: $\text{width} \times \text{length} \times \text{depth} \times \pi / 6$. Subjects were also invited for blood sampling and measurement of thyroid function tests including thyroid stimulating hormones (TSH), thyroxine (T4) and triiodothyronine (T3). Urine containers were sent to Valfajr health center in Shiraz stored at -20°C until analysis. Signed informed consent was taken from all participants and the study was approved by the Shiraz University of Medical Sciences ethics committee (Code:IR.SUMS.MED.REC.1398.568). Inclusion criteria were age of above 18 years old and residence in urban Sadra city. Exclusion criteria included thyroid disorders or use of thyroid related drugs, diuretic medications, pregnancy or lactation.

Urine iodine content (UIC) were measured based on Sandell-Kolthoff method as recommended by the WHO and reported as $\mu\text{g/L}$. [4, 10] Inter and intra-assay coefficient of variation were 9.6% and 10.4% respectively. Urine sodium levels were measured as mEq/L with coefficient of variation of 2%. WHO guidelines only define $> 100 \mu\text{g/L}$ median UIC in adults as sufficient. As a result, UIC cut-offs intended for school children and extended to the general population by the WHO are used as proxy. Medians of $< 20 \mu\text{g/L}$, $20-49 \mu\text{g/L}$, $50-99 \mu\text{g/L}$, $100-199 \mu\text{g/L}$ UIC are labeled as severe deficiency, moderate deficiency, mild deficiency, and adequate respectively.[7] Completion of 24 hour urine collection was assessed using urine creatinine levels. Urine creatinine levels under 500 mg per day were considered incomplete and thus excluded.

Median and interquartile range (IQR) of UIC levels are reported as recommended by the WHO. Significant differences between quantitative variables are compared using Mann-Whitney U and Kruskal-Wallis

tests. Correlation between variables are assessed using two-sided Spearman's Rho. Statistical analyses were performed using SPSS software version 25.0 (SPSS, Chicago, IL, USA). Statistical significance is determined with a P value of < 0.05 with a confidence interval of 95%.

Results

Median UIC in the population was $175 \mu\text{g/L}$ (IQR: $117\text{--}250 \mu\text{g/L}$) and the median salt consumption per person per day was 9.59 gr (IQR: $7.34\text{--}14.55 \text{ gr}$). Median thyroid volume was 8.9 ml (IQR: $6.6\text{--}12.4 \text{ ml}$). Median urine sodium content was 138 mEq/L (IQR: $99\text{--}186 \text{ mEq/L}$). Mean TSH, T4 and T3 were $3.72 \pm 9.55 \text{ mIU/L}$, $8.99 \pm 1.92 \mu\text{g/dL}$ and $138.2 \pm 20.12 \text{ ng/dL}$ respectively.

Table 1 demonstrates the median UIC and the statistical difference between each characteristic.

Table 1
Urine iodine levels in the study's participants based on characteristics

	n	UIC		P
		Median (µg/L)	IQR (µg/L)	
Gender				
Male	24	188	150–268.8	0.405
Female	68	175	108–247	
Hypertension				
No	72	188	133–258.8	0.016*
Yes	20	133	71–184.8	
Salt Storage				
Out of Sunlight	45	175	102.5–244	0.845
In Sunlight	12	166.5	83–250	
Thyroid nodule or goiter				
No	57	188	102.5–257.5	0.286
Yes	24	175	133–208.3	
Education Level				
Below High School	46	150	79–225	0.009*
High School graduate	39	213	150–275	
College graduate or higher	7	184	150–275	
Salt added at cooking stage				
Before food preparation	56	186	119–262.5	0.286
During food preparation	20	150	83–225	
After food preparation	16	179	133–231	
Subclinical Hypothyroidism				
No	81	175	111–250	0.909
Yes	11	183	117–213	

	n	UIC	P
Thyroid Volume			
< 7 ml	24	225	150–271
7–10 ml	24	175	104–253
> 10 ml	32	162.5	83–213

No statistical difference in UIC was found regarding factors including gender, method of storage, presence of goiter or thyroid nodules, salt added by cooking stage or subclinical hypothyroidism. Subjects with hypertension or lower education levels had significantly lower iodine levels.

Table 2 shows Spearman's correlation between UIC and quantitative values.

Table 2
Spearman's Rho correlation between urine iodine content ($\mu\text{g/L}$) and quantitative factors.

Factor	n	Correlation Coefficient	P
Urine Sodium level (meq/L)	48	0.599	< 0.001
TSH (mIU/L)	92	0.208	0.046
T4 ($\mu\text{g/dL}$)	92	-0.245	0.018
T3 (ng/dL)	92	-0.043	0.686
Salt used per day (gr)	84	0.184	0.095
Thyroid volume (ml)	80	-0.244	0.029

UIC had a statistically significant positive correlation with urine sodium and TSH levels and a significant negative correlation with T4 and thyroid volume. There was no significant correlation between UIC and salt consumed per day. Figures 1a to 1d illustrate the scatter dot graphs between UIC and urine sodium, thyroid volume, TSH and T4 levels.

Discussion

Median UIC of the adult population in the city of Sadra was $175 \mu\text{g/L}$, which categorizes the iodine status of the population as adequate based on WHO guidelines. The results found in our study is significantly higher than $70 \mu\text{g/L}$ found in adults (72.9 and $68.9 \mu\text{g/L}$ in men and women respectively) and the $87.3 \mu\text{g/L}$ in the pregnant population of Tehran. [7, 8] Median UIC in this study is similar to median UIC of $200 \mu\text{g/L}$ and $186.1 \mu\text{g/L}$ in 8–10 year old school-children of Shiraz (capital of Fars province) and Iran respectively. [9] Median UIC in adults worldwide includes $144 \mu\text{g/L}$ in China [11], $110 \mu\text{g/L}$ in US [12], 46

µg/L in Italy [13] and 124.66 µg/L in Spain [14]. Results from our study indicated that national efforts to curb iodine deficiency is still successful 28 years after the introduction of 1994 Salt Iodization Act.

Despite worldwide efforts to combat iodine deficiency, many countries have experienced decreased median UIC levels while some have experienced iodine insufficiency resurgence. Median UIC has decreased from 133 µg/L in 2010 to 110 µg/L in US women of reproductive age and from 320 µg/L in US general population in 1974 to 133 µg/L in the same population in 2013. [12] Previously iodine sufficient countries such as Norway, Finland and Germany have been categorized as iodine insufficient based on the latest IGN report. [6] Iodine insufficiency has also reoccurred in the past in countries such as France, Australia and UK due to dietary changes. [1, 15, 16] In some countries such as Columbia and Argentina decrease in UIC levels has been attributed to lack of proper iodine status monitoring and public health strategies. [8, 17–20]

In Iran, studies have also shown reduction in UIC levels. Median UIC in adults of Tehran has dropped from 232 µg/L (1996) to 100 µg/L (2010). [8] Similar results have also been found in Tehranian pregnant women (186 µg/L in 1998 to 87.3 µg/L in 2014) and in Iranian school children (205 µg/L in 1996 to 161 µg/L in 2013). [7, 21–22] Nazeri et al believe that the reduction in salt consumption in Iran can be an attributable factor. [8] Indeed, salt intake per person in Tehran has dropped from 10 gr per day (2000) to 8.4 gr per day (2009) with similar results seen in Yazd and Isfahan. [8, 23] In Shiraz, Babaali et al found that daily consumption of salt in Shiraz was 7.1 gr. [24] In our study, we found a much higher median of 9.59 gr salt consumed per day in Sadra adults. This number is much closer to the results found in 2000 Tehran adults. The higher use of Salt in Sadra can be a contributing factor to its higher UIC levels.

In our study, we found no significant difference in iodine levels between genders. Similar results were found by Nazeri et al. [8] However, in studies by Iacone et al and Tayie et al, men had higher UIC levels. [25, 26] We found a significant negative correlation between hypertension and UIC levels. Similar results were found by Usha Menon et al. [27] Meanwhile, Tayie et al found no correlation between those factors, while Liu J et al found a positive correlation between UIC levels and high blood pressures. [28] Also, we found that better education levels were associated with significantly higher UIC levels. Similar results were found in Tehran by Nazeri et al when using univariate logistic regression. However, this statistical significance was diminished when adjusting for household salt iodine content and daily salt intake, suggesting that these factors were interconnected when leading to lower UIC levels. [8] Based on these results, we hypothesize that subjects with higher education levels are more likely to use iodized salt.

In our study, we found a positive correlation between TSH and UIC levels and a negative correlation between T4 and UIC levels, which is in contrast to the negative correlation seen between these two factors especially in iodine deficient areas. [29] Some previous studies showed no direct association between UIC and serum TSH or T4. [30] Some the other such as NHANES III found that higher urinary iodine excretion was significantly related to higher TSH concentration. [31] Although in our study, individuals with higher level of urinary iodine excretion had higher TSH and lower T4 levels, these concentrations were within the

physiologic range. It seems that distribution of TSH shifted toward the right in iodine sufficient area could be affected by the hereditary and genetic influences on the set-point of thyroid hormone. [32]

During food preparation, some methods such as heating and washing can decrease the amount of salt iodine content. Microwaving, boiling, rice washing and poor salt preservation conditions including storage in sunlight can decrease the effective iodine content. [33] The WHO expects approximately 20% salt iodine loss from retail until food served at table. [4] Despite this, in our study we found no significant difference in UIC between subjects storing salt in the dark and those storing in direct sunlight. In addition, there was also no difference in UIC between those that add salt before food preparation, those that add salt during food preparation and those that add salt after the food is fully prepared.

We found no significant correlation between daily salt intake per person and UIC levels. However, we found a significant positive correlation between UIC and urine sodium content, which is more accurate method of measuring salt consumption. [34, 35] Similar results were found by Nazeri et al. These results along with results from other studies [8, 36–37] and the WHO declaration illustrate the link between salt consumption and iodine status. This can also further link the higher UIC levels found in Sadra city and the city's higher use of salt consumption in comparison to the results from Tehran.

In this study, we found a negative correlation between thyroid volume and UIC. Iodine deficiency has goitrogenic effect and this negative correlation is anticipated. Some previous studies explained that association between iodine status and thyroid volume is inconsistent; and have reported that there is no correlation between thyroid volume and UIC in iodine sufficient areas. [38, 39] It seems that volume of thyroid gland is population-specific and some genetic and environmental factors contribute to thyroid volume variation especially in iodine sufficient areas. [40]

Conclusion

Iodine status in the adult population of city of Sadra is categorized as sufficient despite inadequate urine iodine levels in adult and pregnant population of Tehran, capital city of Iran. A considerable contributing factor can be the higher use of salt in Sadra in comparison to that of Tehran. High environmental iodine concentrations such as high water iodine content can also be hypothetical factors. Studies with larger sample sizes and in other parts of the country are warranted.

Statements And Declarations

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Data Availability: The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval: This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Shiraz University of Medical Sciences (Code:IR.SUMS.MED.REC.1398.568)

Consent to participate: Informed consent was obtained from all individual participants included in the study.

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Figures

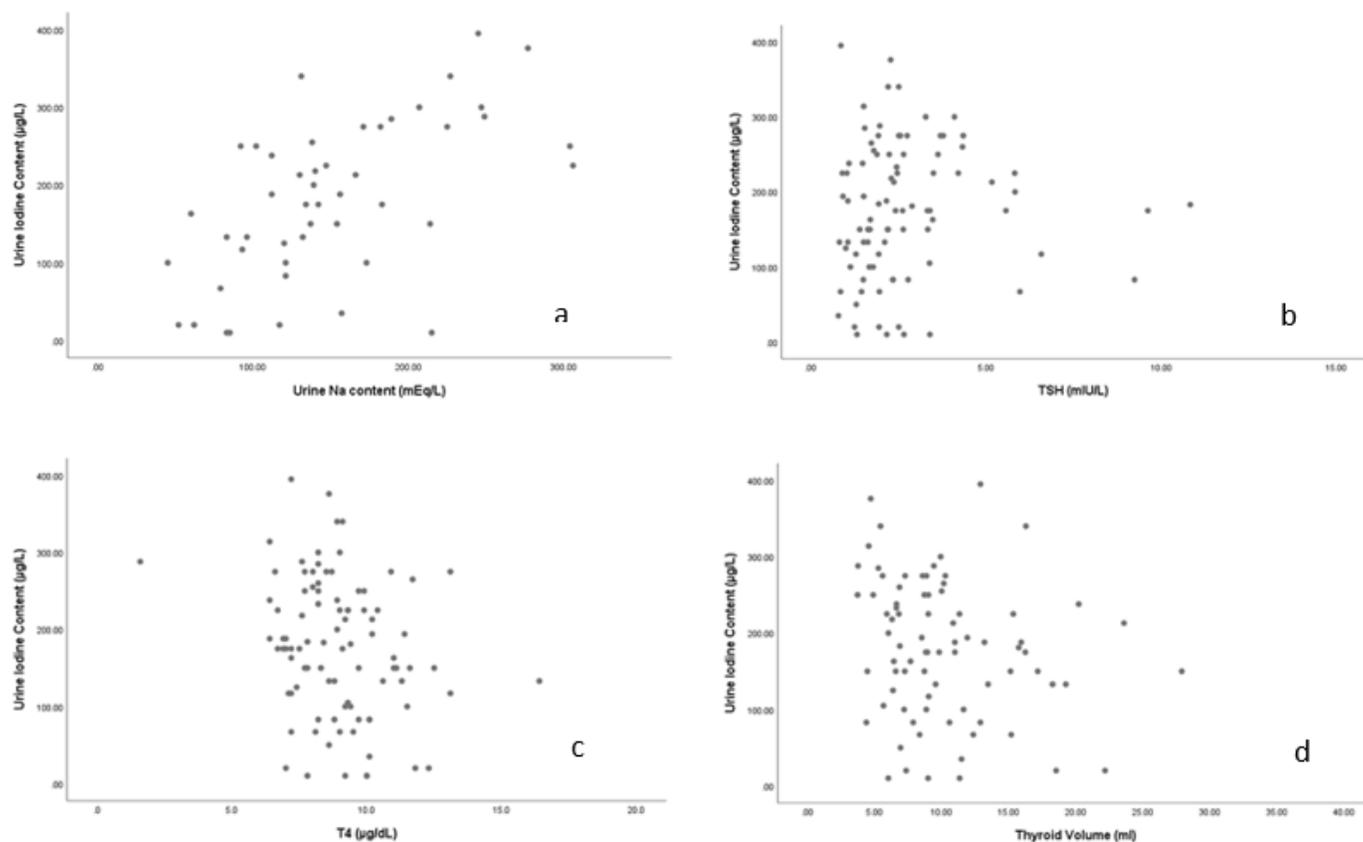


Figure 1

Scatter plot of urine iodine content with urine sodium content (a), TSH (b), T4 (c), and thyroid volume (d) in subjects.