

Eighteen Years of Continuously Sustained Elimination of Iodine Deficiency in the Islamic  
Republic of Iran: The Vitality of Periodic Monitoring

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**Running title:** Sustained elimination of iodine deficiency in Islamic Republic of Iran (I.R. Iran)

**Key words:** Goiter, Iodine, Iodized salt, Urinary iodine

## ABSTRACT

**Background:** Two decades ago the Islamic Republic of Iran (IR Iran) was among countries most severely affected by iodine deficiency. The IR Iran has since achieved great success in the control and elimination of iodine deficiency disorders (IDD) following the national salt iodization program, initiated in 1989. The aim of the study was to evaluate the effectiveness of sustained consumption of iodized salt by Iranian households and the current status of iodine nutrition in all 30 provinces of Iran.

**Methods:** Goiters, measured by palpation, and urinary iodine concentration of children were assessed. In this descriptive cross-sectional study, 36000 schoolchildren (18000 girls and 18000 boys), aged 8 to 10 year-old, were randomly selected, from October 2007 to February 2008, from 30 provinces of the country. Goiter prevalence and urinary iodine excretion in schoolchildren and the iodine content of salt at household, factory and distribution levels were measured.

**Results:** The goiter rate in the country was 6.5 % (6 % grade 1 and 0.5 % grade 2), and the weighted goiter rate was 5.7 %. The total goiter rate in Hamedan, Zanjan, Kermanshah, Mazandaran and Gilan provinces was over 10 %. The median urinary iodine was 140  $\mu\text{g/l}$ . Urinary iodine levels of 20-50, 50-99 and  $\geq 100$   $\mu\text{g/l}$  were noted in 15.3%, 19.8% and 64.9% of the samples, respectively. In four provinces, the median urinary iodine was lower than 100  $\mu\text{g/l}$ . The mean ( $\pm\text{SD}$ ) and median salt iodine values were 23.2 ( $\pm 13.8$ ) and 34.7 ppm respectively at the production level, and 32.4 ( $\pm 14.7$ ) and 32.3 ppm respectively at the distribution level. Ninety-eight percent of households consumed iodized salt, 58% of households had appropriate salt storage, and 27% of the household salts contained less than 20 ppm.

**Conclusions:** The I.R. Iran has achieved much in the development of universal salt iodization strategy and elimination of IDD and currently meets all criteria for sustainable elimination of

iodine deficiency. However, the lack of adequate iodine nutrition in some provinces necessitates special attention and proper monitoring.

Thyroid  
Eighteen years of continuously sustained elimination of iodine deficiency in the Islamic Republic of Iran: The vitality of periodic monitoring (doi: 10.1089/thy.2011-0156)  
This article has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

## INTRODUCTION

Iodine is an essential nutrient for humans (1). Although the importance of adequate iodine intake is obvious and outstanding efforts by international agencies have resulted in a worldwide pledge of achieving iodine sufficiency by the year 2005 (2-5), there are still many regions, even in most industrialized countries of the world, that are suffering from iodine deficiency (6-10). Despite remarkable progress in the control of the iodine deficiency disorders (IDD), these global areas still have a significant public health problem in sustaining the control of IDD.

Two decades ago the I.R. Iran was among the countries most severely affected by iodine deficiency (11,12). This nutritional problem had been identified in Iran in 1968 (13), but had not declared a public health problem until early 1980. Since then, an effective national program of dietary iodine supplement via universal salt iodization has resulted in sustainable preventive programs for IDD, and the country has achieved great success in IDD control and elimination leading to its recognition in 2000 by WHO-EMRO (Eastern Mediterranean Regional Office) as an iodine sufficient country (14). Once the criteria of iodine repletion have been achieved (15), the sustainability of iodine sufficiency then becomes the major concern. One of the major causes of failure in IDD elimination programs is the sense of complacency toward maintenance of adequate iodine intake in a population (16). Since the establishment of the Iranian National Committee for Control of IDD (INCCIDD) in 1989, monitoring of IDD control programs are scheduled every 5 years to evaluate the sustainability of the program. A nationwide survey in 1989 of goiter by palpation showed that goiter existed in schoolchildren in most provinces at rates of between 30-80% (17) and the median urinary iodine was 12-82  $\mu\text{g/l}$  in various parts of the country. Production, distribution and consumption of iodized salt was begun in 1990 and the

second national survey, 6-years following the start of iodized salt consumption, was conducted in 1996. This indicated that total goiter rate was still above 40%, however the median urinary iodine excretion was 200  $\mu\text{g/l}$ , with 85% of subjects having urinary iodine of over 100  $\mu\text{g/l}$  (18). In 2001, an evaluation of the program was conducted as the third national survey (19), indicating that the median urinary iodine was 165  $\mu\text{g/l}$ , and the total goiter rate was 9.8%. The present study is the fourth national survey as a part of the 5 yearly surveillance programs on sustainability of iodine sufficiency in the I.R. Iran.

## **MATERIAL AND METHODS**

In this cross-sectional study, performed between October 2007 and February 2008, goiter rate and urinary iodine levels in schoolchildren and the amount of iodine content of salt at factory and distribution sites and households were measured.

### **Goiter rate and urinary iodine concentration**

To estimate goiter prevalence, 30 clusters of 40 schoolchildren, aged 8-10 years (1200 subjects, equal number of girls and boys), were selected in each province. Overall 36000 schoolchildren were selected for goiter assessment by seven trained physicians. Thyroid size was assessed using the palpation method and classified into grades 0-2 according to the classification of WHO/UNFCEF/ICCIDD (15). To reduce inter observer differences in goiter assessment by the palpation method (20), seven general physicians were trained under supervision of an experienced endocrinologist of the study, prior to initiation of the survey. Each physician had to grade goiter status in 60 children. Kappa co-efficient of agreement was calculated for validation. All examiners had the highest Kappa for detection of goiter. One-tenth of the subjects were randomly selected for urinary iodine determination and 120 (equal numbers of rural and urban) urine samples were obtained from each province. Spot urine samples (10 ml) were collected

between 08.00 and 11.00 a.m. while children attended school. Urine samples were transferred in screw-top plastic bottles on ice to the laboratory of the Research Institute for Endocrine Sciences and kept frozen at  $-20^{\circ}\text{C}$  until the time of iodine measurement at the end of the study.

### **Iodine content of salts**

*a) At factory and distribution levels:* Five samples from different parts of the factory site, from each of the 56 iodized salt producing factories that were active at the time of the study, and 100 samples from distribution sites in each province, were collected and sent to the food and drug control laboratory of the health center for in each province. There quantitative iodine measurement was performed.

*b) At households:* Samples of iodized salt for household use (400 samples from each province) were collected for quality and quantity control, and the content of household salt was measured in the field, using rapid testing kits. Approximately 10 % of salt samples were randomly selected and transferred to the laboratory for food and drug control of the health center in each province for iodometric titration.

### **Laboratory measurement**

All urine samples were assayed for iodine concentration by three trained technicians at the Research Institute for Endocrine Sciences laboratory, using the acid digestion method (21,22). The laboratory is reference laboratory of the region and regular quality control is done. A median urinary iodine concentration (UIC)  $< 100\mu\text{g/l}$  was considered representative of iodine deficiency. Mild, moderate, and severe iodine deficiency were considered if the median UIC was 50-99, 20-49, and  $<20\mu\text{g/l}$ , respectively. Median UICs of 100-199, 200-299, and  $>300\mu\text{g/l}$  were considered adequate, more than adequate, and excessive, respectively (15). The intra-assay coefficient of variation (CV) of UIC measurement method for concentrations of 3.5, 15, and 38

$\mu\text{g/l}$  were 11.2%, 8.2%, and 9.4% respectively, and the inter-assay CV values for these concentrations were 12.5%, 8.9%, and 10.3%, respectively.

For qualitative salt iodine measurement, rapid test kits were used (23). Quantitative salt iodine measurements were performed by the iodometric titration assay (24) and values were shown in parts per million (ppm). The titration method has been standardized by the Research Institute for Endocrine Sciences and approved by the Ministry of Health and Medical Education (MHME) for uniform measurement of salt iodine in the laboratories for food and drug control of the health center of each province. Inter-examiner differences in various provinces have been shown to be negligible for the titrimetric method of determining salt iodine content.

### **Statistical analyses**

Chi-squared test was used for comparison of categorical variables. For continuous variables, Student's t, analysis of variance (ANOVA), Mann-Whitney and Kruskal-Wallis ANOVA tests were used according to normality of their distribution. Correlations between continuous numerical variables were assessed by Spearman's Rank and Pearson coefficients. SPSS 9.05 software package (SPSS, Inc. Chicago, IL) was used for the statistical analysis and  $P < 0.05$  was considered as significant.

## **RESULTS**

### **Goiter rate:**

Totally 36000 schoolchildren, aged 8-10 years, in 30 clusters of 40 children from each of 30 provinces of the country, participated in this study. The prevalence of total goiter rate (TGR) was 6.5% (6% grade 1 and 0.5% grade 2). After weighting goiter prevalence for the size of the population in each province, TGR was calculated to be 5.7%. The TGRs in Hamedan, Zanjan,

Kermanshah, Mazandaran and Gilan provinces was over 10 %. Apart from these 5 provinces, the TGR in 25 provinces was 4.5 % (4.4 % grade 1 and 0.1 % grade 2).

#### **Urinary iodine concentration:**

The median UIC in 36000 schoolchildren was 140.5  $\mu\text{g/l}$ . Figure1 depicts median UICs of all provinces in bar graphs. UICs of 20-50, 50-99 and  $\geq 100$   $\mu\text{g/l}$  were found in 15.3%, 19.8% and 64.9% of the population, respectively. There was no significant difference in UIC between boys and girls or between rural and urban areas. None of the provinces had median UIC less than 20 or above 300  $\mu\text{g/L}$ . In Khoozestan, Tehran, Lorestan and Western Azarbaijan, median UIC was between 50 to100  $\mu\text{g/l}$ . In 8 provinces (Western Azarbaijan, Tehran, Khoozestan, Zanjan, Sistan-baluchestan, Ghom, Lorestan, Hamedan) over 20 % of schoolchildren had UIC less than 50  $\mu\text{g/l}$ .

#### **Salt iodine at production level:**

Mean ( $\pm\text{SD}$ ) and median (range) of iodine concentrations in salt at the production level were 23.2 ( $\pm 13.8$ ) and 34.7 (26.5- 40.2) ppm, respectively. Iodine levels of less than 20, of 20-40 and of  $\geq 40$  ppm were observed in 12, 70 and 18% of samples, respectively.

#### **Salt iodine at distribution level:**

Mean ( $\pm\text{SD}$ ) and median (range) of iodine level concentrations were 32.5 ( $\pm 14.8$ ) and 32.3 (26.4-43.0) ppm, respectively. Iodine levels of  $< 20$ , of 20-40 and of  $\geq 40$  ppm were observed in 17, 52 and 31 % of samples, respectively.

#### **Salt iodine at household level:**

Ninety-eight percentage of households consumed iodinated salt and 82 % used crystallized iodized salt. Salt storage was appropriate in 58 % of households. Quantitative assays

of household salt samples showed that median iodine content was 30 ppm. Iodine level < 20, 20-40 and  $\geq$  40 ppm were observed in 27, 53 and 20% of household salts, respectively.

Figure 2 shows the distribution of salt iodine content at different levels in this study.

## DISCUSSION

The results of this national survey, conducted in 2007-2008, indicated sustainable elimination of iodine deficiency disorders and favorable urinary iodine values in school-aged children of 30 provinces of Islamic Republic of Iran (Table 1). In fact, this survey was a part of the IDD elimination program, which monitors the stages of the program every 5 years in Iran. Although goiter prevalence has decreased to a favorable rate, and median urinary iodine indicates overall adequate iodine nutrition, findings in some provinces and the presence of up to 20% salt samples with less than 20 ppm iodine at household level may imply the risk of iodine deficiency in some areas. This situation is of particular importance during for pregnant and lactating women and their infants. It may impair growth and neurodevelopment of the offspring and increase infant mortality.

Compared to 1996 and 2001, the TGR was significantly decreased in the majority of provinces, with no alteration in the salt iodine content. In this survey the TGR was 6.5 % (6 % grade 1 and 0.5% grade 2) with weighted TGR of 5.7 %, significantly lower than the corresponding rates of 53.8 % ( 44.8 % grade 1 and 9 % grade 2) among 36178 schoolchildren in 1996 and 13.9 % ( 11% grade 1 and 2.9 % grade 2) among 36000 schoolchildren in 2001 ( $P<0.001$ ). Figure 3 shows the prevalence of TGR in the year 1989 and decrease of the TGR in monitoring surveys in 1996, 2001 and 2007.

The median UIC of schoolchildren in this study was 140.5  $\mu\text{g/l}$ . This value was 205  $\mu\text{g/l}$  in 1996 and 165  $\mu\text{g/l}$  in 2001(Table 2), when the median UIC in urban areas was 160  $\mu\text{g/l}$  and in

rural areas was 170  $\mu\text{g/l}$  ( $P=0.16$ ). But this was 230  $\mu\text{g/l}$  in urban vs 205  $\mu\text{g/l}$  in rural areas in 1996 ( $P=0.04$ ). Values of UIC of  $<100$  and  $>100$   $\mu\text{g/l}$  were present in 19.7 and 80.3 % of children in 2001 and in 14.2 % and 85.8 % children in 1996, respectively ( $P<0.0001$ ). The median UIC values, however, were higher than the WHO/UNICEF/ICCIDD optimal levels in many provinces two years after the 1996 enactment of the law on mandatory salt iodization in Iran. But after 7 years of national salt iodization, an optimal median UIC level was obtained among schoolchildren without any change in salt iodine content. It is unclear whether the reduction in median UIC values from 1996 to 2007 in our study is due to a dietary change in schoolchildren or some other environmental factors. A similar downward trend was primarily observed between National Health and Nutrition Examination Surveys (NHANES) 1 and 3 in the USA; however, median iodine finally stabilized at adequate UIC levels on further follow ups (25). This condition is particularly important in pregnant and lactating women, whose low iodine intakes could be accompanied by detrimental outcomes in vulnerable populations such as neonates, infants, and young children (1). In this study the median urinary iodine of schoolchildren in Khoozestan, Tehran, Lorestan and Western Azarbaijan, was between 50 and 100  $\mu\text{g/l}$ . In 8 provinces (Western Azarbaijan, Tehran, Khoozestan, Zanjan, Sistan-baluchestan, Ghom, Lorestan, Hamedan) over 20 % of schoolchildren had a UIC less than 50  $\mu\text{g/l}$ . The persistence of a proportion of subjects with low urinary iodine or indeed a fall in median urinary iodine in these areas, despite unchanged method for urinary iodine measurement over the period 1996 to 2007, could be due to iodized oil injection during earlier years of salt iodization program, improper iodine content of salts or changes of dietary habits, particularly in young people.

Since 1996, the mean ( $\pm\text{SD}$ ) and median (range) salt iodine at the production level have not changed significantly, as current values are 23.2 ( $\pm 13.8$ ) and 34.7 (26.5- 40.2) ppm

respectively while corresponding values in 1996 for 278 factory salt samples were 33.8 ( $\pm 13.2$ ) and 33.9 (8-91) ppm and for 297 samples in 2001 were 33.2 ( $\pm 13.4$ ) and 32.8 (6-84) ppm, respectively ( $P=0.57$ ). Frequency distributions of factory salts with iodine contents of <20, 20-40, and >40 ppm were 12%, 70% and 18% in 2007, 17.2%, 54.5%, and 28.3% in 2001 and 15.8%, 54.7%, and 29.5% in 1996, respectively ( $P=0.89$ ). Neither did median iodine contents of household salt samples show significant differences during last three periods, being 30 ppm in 2007 and 32.8 ppm in both 2001 and 1996 ( $P=0.68$ ). The frequency distributions of household table salts with iodine content of <20, 20-40, and >40 ppm were 27%, 53%, and 20% in 2007, 8.3%, 71.7%, and 20.0% in 2001, and 7.8%, 71.9%, and 20.3% in 1996, respectively ( $P=0.97$ ). Figure 4 compares the median UIC and salt iodine content in three national surveys after IDD control program.

The results of the 2007 national survey were indicative of favorable urinary iodine values in school-aged children of 30 provinces. The TGR declined in comparison to the last survey. This result, occurring 17 years after the beginning of salt iodization and 12 years after more than 50 % of households have been consuming iodized salt, was foreseen (Table 2). The prevalence of goiter in 12 provinces was less than 5 %, in 13 provinces it was 5 to 10 %. Only 5 provinces have a goiter prevalence of more than 10 %. The noticeable decrease in the prevalence of grade 2 goiter (from 9 % in 1996 to 2.9 % and 0.5 % in 2001 and 2007, respectively) is of high importance. Of the 5 provinces, (Hamedan, Gilan, Mazandaran, Kermanshah and Zanjan), with goiter prevalence over 10 %, the prevalence of goiter showed no change in Zanjan and Hamedan, in comparison with 2001; in Kermanshah, the TGR decreased from 23.9 % in 2001 to 10.8 % in 2007, but in Gilan and Mazandaran there was a significant increase from 11.3 % and 4 % in 2001, to 18.5 % and 14.9 % in 2007, respectively. Since clinical assessment of low grade goiter has

less validity due to high inter-observer variation, and because the examiners in the two surveys were not the same, these two factors may be responsible for this discrepancy rather than a true change in TGR. The median UIC of over 100  $\mu\text{g/l}$  in the provinces with TGR>10 %, indicates that the grading of goiter might have been inaccurate and further assessment is needed. On the other hand, the median salt iodine content within the optimal range of 20-40 ppm, from 1996 to 2007, suggests that deficiency of available salt iodine content does not seem to explain the persistence of elevated goiter rate in some of the provinces. Assessment of other goitrogens, e.g., nutritional habits, deficiencies of selenium (26,27), iron (28,29), vitamin A (30), and endocrine disruptions (31,32) might be useful in detecting the underlying causes of goiter rate in rural/urban areas of the country, where goiter rate is still high despite adequate iodine intake. However, since low iodine content of soil is the main factor responsible for iodine deficiency, IDD's return whenever there are inadequate iodine supplies to the population at risk or sustainability of the monitoring program is interrupted.

For many countries with IDD control programs, sustainability has become a major focus (33). There is much evidence of IDD relapse in some countries that had previously been successful in controlling IDD. In several countries in which IDD had been eliminated by universal salt iodization (USI), control programs faltered, and IDD recurred (34-39). In Guatemala, their previously effective iodized salt program deteriorated, and currently the median urinary iodine concentration is less than 100  $\mu\text{g /l}$ , and new cases of cretinism have appeared (34). In regions of the former USSR, successful, long-term iodized salt programs have lapsed, and IDD has returned. In Azerbaijan, the current GR is 86 % and the median UI is 54  $\mu\text{g /l}$ , indicating moderate to-severe IDD (35). Similar patterns of IDD recurrence were also demonstrated in Kazakhstan, Kyrgyzstan, and other neighboring countries (34). The

reemergence of IDD also has reported from industrialized countries previously thought to be iodine sufficient, such as Australia and New Zealand (36,37). A recent cohort study in school-aged children by Zimmermann and et al., in an area of endemic goiter in Morocco, described changes in thyroid function after sudden interruption of USI (38). Moroccan children (6–16 y old), with severe IDD, received iodized salt for one year, normalizing their median urinary iodine and decreasing thyroid volume by 34%, but because of practical and financial constraints, salt iodization was discontinued and the improvements in IDD control parameters reversed rapidly following cessation of salt iodization. New research by Vanderpump suggests that the U.K. population is iodine deficient. A systematic assessment of UIC from 810 U.K. girls aged 14 to 15 years revealed that 69 percent were lower than 100  $\mu\text{g}/\text{l}$ ; this is consistent with iodine deficiency according to WHO standards. In addition, 18 percent had UIC levels lower than 50  $\mu\text{g}/\text{l}$  (39). Overall, these data suggest that IDD control programs are fragile, and depend on a strong, long-term commitment from governments, donors, consumers, and the salt industry (40).

To ensure the achievement of goals in any public health interventional program, monitoring of the indicators is a vital element of an effective and sustained program for the control and elimination of iodine deficiency. Since most countries, including the I.R. Iran, have now started to implement IDD control programs, urinary iodine rather than thyroid size is emphasized as the principal indicator of impact. In areas free of iodine deficiency, where most individuals have low grade goiter, thyroid ultrasonography is necessary for the assessment of thyroid volumes. It would therefore be worthwhile to design the next national program of monitoring of iodine deficiency control with a view to determining goiter rates by thyroid ultrasonography for more precise assessment of goiter prevalence in different provinces of the country.

In conclusion, the well-monitored salt iodization program in Iran has ultimately resulted in optimization of UIC, and drastically decreased the goiter rate 18 years after universal salt iodization, although the later effect appeared some years after normalization of UIC. The median urinary iodine of schoolchildren was as adequate as those reported in 1996 and 2001, indicating a well established sustainable IDD program in the I.R. Iran. However, lack of adequate nutrition in a few provinces of Iran is a major cause of concern, necessitating prompt attention of the authorities of the Ministry of Health, salt producers and other officials responsible for promotion, implementation and monitoring of the Iranian Program for Elimination of Iodine Deficiency Disorders and, last but not least, the need for periodical monitoring of any IDD control program following elimination of IDD.

## ACKNOWLEDGMENT

This project was supported, in part, by grants from the Budget and Programming Organization, Ministry of Health and Medical Education. We would like to express our appreciation and acknowledgement to the officials and colleagues at the Ministry of Health and Medical Education and the branches in all provinces, our colleagues at the Research Institute for Endocrine Sciences of Shahid Beheshti University of Medical Sciences, UNICEF and related officials and personnel all over the country for their cooperation and assistance throughout this project conducted for monitoring and evaluation of IDD. Their invaluable efforts and contributions played a major role in the results documented in this final report. We would like to thank Ms. N. Shiva for the English editing of the manuscript.

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Table 1- Sustainable elimination of iodine deficiency disorders in the Islamic Republic of Iran;  
data from the 2007 national survey

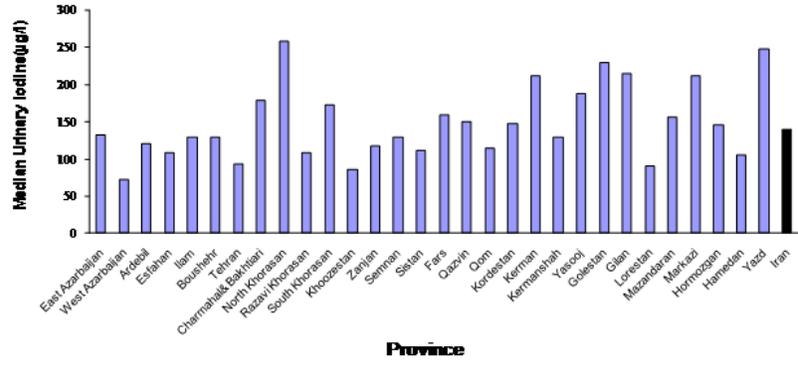
<b>Indicator</b>	<b>Results</b>
1. Salt iodization	
Proportion of households consuming effectively iodized salt	>98%
2. Goiter rate	5.7 %
3. Urinary iodine	
Median (n=3600)	140 µg/L
Proportion below 100 µg/L	19.8%
Proportion below 50 µg/dl	15.3%
4. Programmatic Indications	
Attainment of the indicators listed <sup>(9)</sup>	All 10

Table 2- Changes in median urinary iodine (MUI) and total goiter rate (TGR) in school-age children between **1989** and **2007**

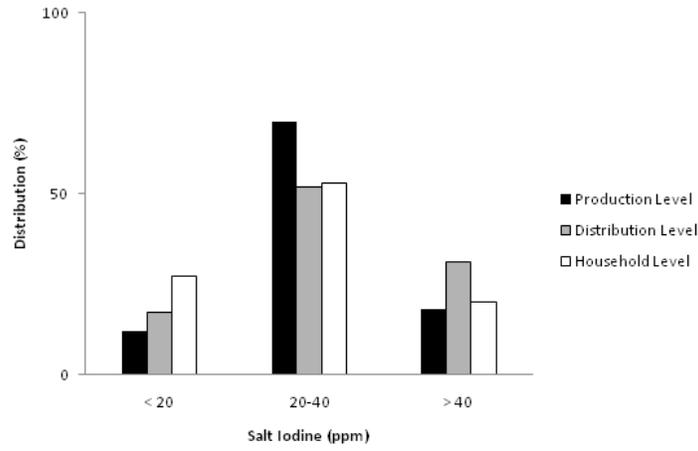
<b>Year</b>	<b>MUI</b> <b>(<math>\mu\text{g/L}</math>)</b>	<b>TGR</b> <b>(%)</b>
1989	12-82	68.0
1996	205	54.0
2001	165	9.8
2007	145	5.7

## Legend to Figures

- Fig.1. Median urinary iodine of various provinces of I.R.Iran in 2007.  
From each province between 80-120 samples of urine were collected.  
All urinary iodine concentrations are presented in  $\mu\text{g/l}$ . In Khoozestan, Tehran, Lorestan and Western Azarbaijan, median urinary iodine is lower than  $100\mu\text{g/l}$ .
- Fig.2. Distribution (%) of salt iodine content (ppm) at production, distribution and household levels
- Fig.3. Total goiter rate in different provinces of I.R. Iran in 1996 and 2007.  
Total goiter rate (TGR) was significantly decreased in the majority of provinces compared to 1996, with no alteration in the salt iodine contents. In this survey TGR of the country was 5.7% which was significantly lower than the corresponding rate of 53.8% in 1996( $P<0.001$ ).
- Fig.4.Total goiter rate (%) in four national surveys; 1989(before) and 1996, 2001 and 2007 (after IDD control program).
- Fig.5. The median urinary iodine concentration ( $\mu\text{g/l}$ ) and salt iodine content (ppm) in three national surveys over the period 1996-2007 (after IDD control program).

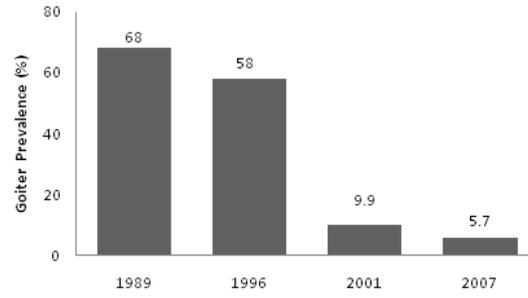


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