

Appropriate Iodine Nutrition in Iran: 20 Years of Success

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Abstract- Iodine is a trace element in the human body, its only known function is the synthesis of thyroid hormones. Effects of iodine deficiency, termed iodine deficiency disorders (IDD), include endemic goiter, hypothyroidism, cretinism, decreased fertility rate, increased infant mortality and mental retardation. 2.2 billion people worldwide are at risk for IDD. Of these, 30-70% have goiter and 1-10% have cretinism. Two decades ago the I.R. Iran was among the countries most severely affected by iodine deficiency, but during the last two decades has made much progress in the development of universal salt iodization strategies and IDD prevention, and since 1996 meets all WHO/UNICEF/ICCIDD criteria for the sustainable elimination of iodine deficiency.

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Introduction

Iodine is a trace element present in the human body in minute amounts. Its only confirmed role is the synthesis of thyroid hormones. Iodine is obtained primarily through the diet.

Dietary iodine is taken up readily from the gut in the form of iodide and then it is concentrated in the thyroid gland through blood circulation. In the follicle cells of the thyroid gland, 4 atoms of iodine are incorporated into each molecule of thyroxin (T_4) and 3 atoms into each molecule of triiodothyronine (T_3). These hormones are essential for neuronal and sexual development, growth and for regulating the metabolic rate, body heat, and energy (1). Consequently, severe iodine deficiency impairs thyroid hormonogenesis.

If the physiologic requirements of iodine are not met, a series of functional and developmental abnormalities occur, including thyroid function abnormalities, endemic goiter, cretinism, decreased fertility rate, increased perinatal death and infant mortality which are grouped under the general term of iodine deficiency disorders (IDD) (2-4).

Awareness regarding goiter and reports on cretinism go back to thousands and hundreds of years ago, respectively. The oldest report of goiter and iodine deficiency came from China (5). Five thousand years ago, the Chinese documented the occurrence of goiter and found seaweed to be effective in its treatment. In 1813, Courtois discovered iodine and the cause of goiter and cretinism were attributed to iodine deficiency (6). In

1846, Provost and Maffini proposed the theory of the role of iodine deficiency in the development of goiter. For the first time, Boussingault in Southern America suggested the usage of iodized salt in the treatment of goiter, but information on the extensive usage of preventive methods was not available until the 20th century. Marine and Kimball achieved the first successful experience in the campaign against iodine deficiency in Ohio through prescription of iodized salt (7).

Worldwide, iodine deficiency is the leading cause of preventable mental retardation (8,9). Twenty-nine percent of the world's population, living in approximately 130 countries, is estimated to live in areas of iodine deficiency. Of these persons, 30-70% have goiter and 1-10% have cretinism (10-15).

The recommended dietary allowance (RDA) is 150 $\mu\text{g/day}$ of iodine for adults and adolescents, 250 $\mu\text{g/day}$ for pregnant and lactating women and 90-120 $\mu\text{g/day}$ for children aged 1-11 years. The adequate intake for infants is 110-130 mcg/day (16-20). Replacement of iodine is most easily achieved by using iodized salt. Salt has been selected as the medium for iodine supplementation because intake is uniform across all socioeconomic strata and seasons of the year and the technology is simple and inexpensive (21-22). Since 1990, there has been tremendous progress in increasing the amount of salt, which is adequately iodized. As a result, many countries are now have achieved IDD elimination and some others are on the threshold of achieving this goal (23-25).

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History of IDD in Iran

Two decades ago the I.R. Iran was among the countries most severely affected by iodine deficiency and many parts of the country had been known as areas of endemic goiter. The first documented report of goiter in 1968 reported the prevalence of goiter to be between 10 to 60% (26). So this nutritional problem had been identified in Iran since 1968, but it was declared as a public health problem in early 1980. In 1983-84, after a gap of 15 years, various research projects conducted by the Endocrine Research Center and Food Technology and Nutrition Research Institute of Shahid Beheshti University of Medical Sciences and by other investigators in some provinces reported hyperendemia of goiter with low urinary iodine excretion in many subjects (27-37). The first of these studies conducted in Shahryar, 35 km south west of Tehran, reported the presence of goiter in 54% of boys and 66% of girls aged 6-18 years (27). Significant and reverse correlation was also found between the prevalence and severity of goiter and iodine content of drinking water and urinary iodine.

Another study by the same group in the East of Tehran in 1983, showed that 68% of girls and 71% of boys were goiterous with visible goiter found in 30% and 17.5% of girls and boys, respectively. In these studies, thyroid hormones measurements were at normal levels (28).

In the years 1987-1989 before the injection of iodized oil and salt iodization, a few surveys were conducted to find the effects of iodine deficiency on various body systems in Tehran and villages located in northwest of Tehran especially Kiga and Keshar (29,30). These studies demonstrated the occurrence of mild to moderate growth and physical retardation, neurological, intellectual, auditory and psychomotor disturbances in apparently normal subjects residing in areas of iodine deficiency.

Kimiagar et al. (31) reported more physical growth retardation and higher prevalence and severity of hypothyroidism and goiter in school children of Kiga than Keshar, Randan and Tehran. The mean height of 70% of girls and 54% of boys in Kiga fell below the third percentile of the height for age.

Neurological studies by Kalani et al. (32) in the same group revealed smaller head circumferences in schoolchildren of Kiga and Keshar than Tehran. Pyramidal signs were more frequent in the schoolchildren of Kiga (50%) than Keshar and Tehran. The most frequent finding was hyperreflexia, seen in 39% of subjects in Kiga. Among Primitive reflexes glabellar tap was present in approximately half of the

subjects in Kiga and 20% of subjects in Keshar and Tehran.

The survey by Sarshar et al. (33) reported lower IQ score for the students of Kiga than Keshar and Tehran. Psychomotor age was 1.7 years and 1.4 years lower than chronological age in Kiga and Keshar, respectively. There was a positive correlation between serum TSH and grades of pyramidal signs ($r=0.331$, $P<0.025$), and negative correlations between serum TSH and T4, T3, FT4I and FT3I. There was no correlation between serum TSH and age, height, weight, goiter grade, head circumferences, IQ, psychomotor and audiometric changes.

The survey in KohKilloveh Boyerahmad, a province reported the goiter prevalence of 95% and 87% in women and men, respectively (34). The visible goiter was more prevalent among women than men.

Many surveys in other provinces including the study in Khorasan, a province of Iran, by Rajabian et al. (35) and by Hedayati et al. (36) in Rasht and unpublished studies by Omrani et al. in Fars, Zahedi Asl et al. in Khozestan, a province of Iran, and Emami & Amini in Isfahan showed endemic or hyperendemic goiter. The survey in Neishabour reported goiter in 60% of school children of whom 2.5% had visible goiter (37).

These findings prompted the Ministry of Health and Medical Education to form Iranian National Committee for Control of IDD (INCCI) in 1988. After organization of this committee, a nation-wide survey was performed under the supervision of INCCI showed that goiter is endemic in all and hyperendemic in the capital cities of 5 provinces. Urinary iodine excretion were below 100 $\mu\text{g/L}$ in all and <20 $\mu\text{g/L}$ in many localities examined (38).

Control of IDD in Iran

Since 1989, IDD has been accepted as a priority health problem in Iran. The INCCI prepared a national plan for IDD control. Production, distribution and consumption of iodized salt was begun in 1990; however until 1993, only 70% of urban and 50% of rural households consumed iodized salt. The first law requiring mandatory iodination of all salts for households use was passed in 1994. National surveys in the following years indicated that more than 95% of the households were consuming iodized salt (39). In 1996 second national survey was conducted 7 years after the initiation of iodized salt production and 2-years following mandatory iodized salt consumption (40). In this survey which conducted in 26 provinces, total goiter rate was more than 40% in boys and over 50% in girls.

However, the majority of schoolchildren had small goiters of grade 1 and median urinary iodine excretion was within adequate range in schoolchildren of all provinces. In this study the median urinary iodine excretion was 200 µg/L, with 85% of subjects having urinary iodine of over 100 µg/L. Hence 2 years following mandatory iodized salt consumption, urinary iodine excretion indicated elimination of iodine deficiency (41), but the duration of iodine supplementation had not been enough adequate to reduce goiter prevalence significantly. The results of the 1996 survey revealed that overall median urinary iodine was above that recommended by WHO/UNICEF/ICCIDD (42). Therefore, the IDD elimination program using USI in Iran has proven to be very effective, 7 years after the initiation of salt iodization and Iran was recognized by WHO-EMRO as an iodine sufficient country by the year 2000 (43).

Monitoring of Iodine Nutrition in Iran

In 2001, the evaluation of the program was done as the third national survey (44). Goiter rate, UIC, and household salt iodine values were compared to those in 1996. Factory salt iodine was also compared in 2001 vs 1996. Weighted total goiter rate was 9.8% and median UIC was 165 µg/L. In 2001 vs 1996, mean ± SD for iodine salt content was 32.7 ± 10.1 vs 33.0 ± 10.2 ppm ($P=0.68$) in households and was 33.2 ± 13.4 and 33.8 ± 13.2 ppm ($P=0.57$) in factories, respectively. This study showed that after 7 years of optimized iodized salt supplementation in Iran, adequate UIC values and marked reduction in goiter rate have been achieved. Due to the continuous risk of recurrence of iodine deficiency in a previously iodine-deficient area (45), an every 5-yr surveillance program on sustainability of iodine sufficiency in Iran by the assessment of goiter prevalence and measurement of UIC has been conducted since 1996.

Therefore in 2007, the fourth national survey performed 17 years after the introduction of iodized salt to evaluate the current IDD status and monitoring the sustainability of the program in the country. The objectives of this survey were again to determine goiter prevalence, to assess urinary iodine excretion and to evaluate the iodine content of iodized salts in households, markets and factory levels. In this descriptive cross-sectional study, 36000 schoolchildren were evaluated for goiter by trained physicians. One-tenth of the subjects were randomly selected for urinary iodine determination. In this survey, samples of iodized salt for household use were collected for quality and

quantity control, and the content of household salt was measured in the field, using rapid testing kits; approximately 10% salt of samples were randomly selected for iodometric titration.

Results showed that households' consumption of iodized salt was 98% for all provinces. Total goiter rate was 5.7%, significantly reduced from previous surveys (Table 1). In 2007, the goiter rate was significantly lower than 1996 in all 30 provinces of Iran. The median urinary iodine of subjects was 145 µg/L. Today enhanced improvement in iodine nutritional status has been achieved as over 95% of Iranian households consumed adequate iodized salt. In 1989, the median urinary iodine concentration was less than 100 µg/L, but since 1996 it has consistently been over 100 µg/L. Similarly goiter rates decreased from 68%, in 1989, to 5.7%, in 2007.

After 10 years iodine supplementation two clinical trial conducted to evaluate the effect of iodine supplementation on making improvement in hearing threshold and IQ score of schoolchildren in Kiga (46, 47).

Table 1. Urinary iodine, serum T₄, T₃ and TSH concentration and intelligent quotients in schoolchildren before (1989) and 10 years after iodine supplementation (1999) in Kiga and Randan villages

| Variable | 1989 (n=246) | 1999 (n=40) |
|------------------------------|-----------------|----------------|
| Total goiter rate (%) | 100 | 63 |
| Median urinary iodine (µg/L) | 15.7 | 187 |
| Serum T ₄ (µg/dL) | 5.5(2.0) | 8.2(1.6) |
| Serum T ₃ (ng/dL) | 176 (38) | 141(23) |
| Serum TSH (mU/L) | 14.7(20.1) | 1.8(0.8) |
| TSH above 5 mU/L (%) | 40 | 0 |
| Intelligent quotient (IQ) | 89(13) | 97(10) |
| IQ below 70 (%) | 12 | 0 |

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

| Year | MUI (µg/L) | TGR (%) |
|------|------------|---------|
| 1989 | 12-82 | 68.0 |
| 1996 | 205 | 54.0 |
| 2001 | 165 | 9.8 |
| 2007 | 145 | 5.7 |

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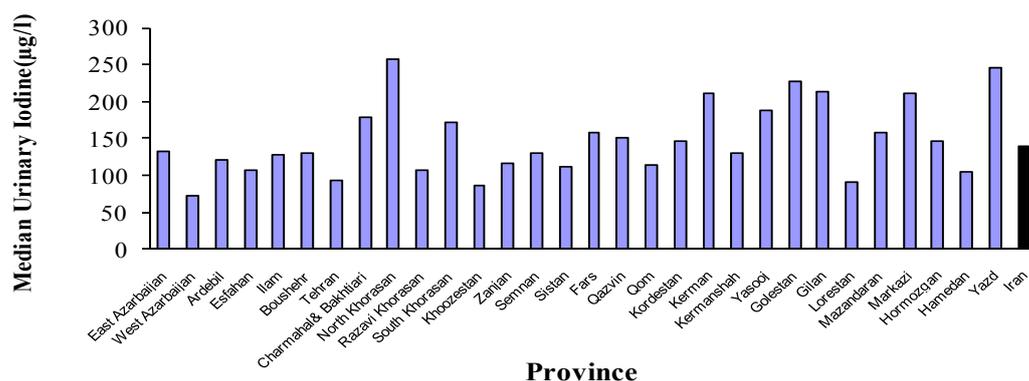


Figure 1. Median urinary iodine of various provinces of Iran in 2007

In year 2000, the study in Kiga and Randan villages reported restored normal thyroid function, a rise in urinary iodine and a fall in goiter rate irrespective of the time of iodine supplementation; whereas improvement in IQ score was reported in the group in which iodine supplementation in their mothers had been started 1 to 3 years before conception (46).

Another study in Kiga in the year 2000, on 212 schoolchildren of an area of severe iodine deficiency before intervention (1989), 3 yr after injection of 480 mg iodized oil (1992) and 7 yr after consumption of iodized salt (1999), showed significant decrease in the prevalence and severity of goiter and serum TSH and thyroglobulin concentration, and significant rise in serum T4 in 1992 and 1999, as compared to 1989. Hearing was abnormal in 44% of schoolchildren, before iodine supplementation with mean hearing threshold of 15.8 ± 5.9 and >10 dB in all children. Mean hearing threshold decreased to 10.2 ± 4.6 and 10.0 ± 5.9 , 3 and 10 yr after intervention ($P < 0.001$). Forty seven and 62% of children had thresholds <10 dB in 1992 and 1999,

respectively. Hearing thresholds >15 Db were detected in 46, 11 and 10% of schoolchildren in 1989, 1992 and 1999, respectively ($P < 0.001$). So this study demonstrated that hearing thresholds decreases following iodized oil administration and remains low via permanent consumption of iodized salt (47).

An excellent program for the control of IDD has been set up by the I.R. Iran; a sustainable and well-functioning iodization program is functioning with the following programmatic indicators: 1) From 1989, an effective and functional national office (IDD National Committee), responsible to the government for the elimination of IDD has been active; this council is multidisciplinary, involving the relevant fields of nutrition, medicine, industry, education etc; 2) Political commitment to universal salt iodization and the elimination of IDD, pledged in 1989, still continues until today; 3) A responsible executive officer had been appointed for the IDD elimination program, since 1990; 4) Legislation on universal salt iodization has been implemented since 1992. The Ministry of industries

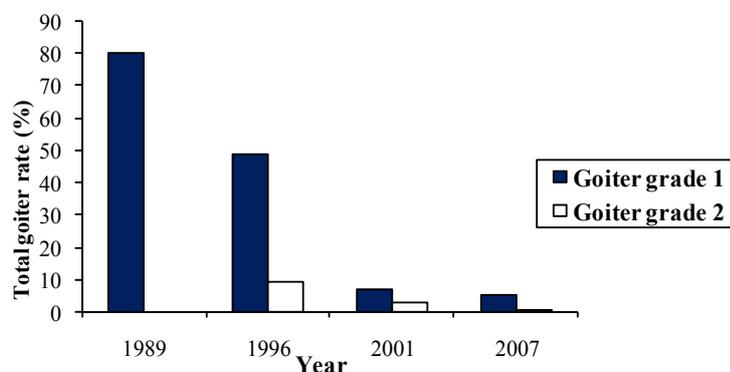


Figure 2. Total goiter rate in four national surveys (1989, 1996, 2001 and 2007)

made it mandatory for salt factories to produce only iodized salt for household use; 5) The country has performed an assessment and a re-assessment of progress in the elimination of IDD, with access to laboratories qualified to provide data on salt and urine iodine; 6) A program of public education and social mobilization on the importance of IDD and the consumption of iodized salt has been vigorously followed over the last 11 years. The program has been integrated into the health network, with full participation of the Behvarz (rural health worker) in education and monitoring; 7) Regular data on salt iodine at factory (daily), retail (monthly) and household levels (yearly) are collected in each province and analyzed by the IDD executive office; 8) Laboratory data on urine iodine in school aged children with appropriate sampling for higher risk areas is regularly being collected and processed in each province on a yearly basis and also at a national level every 5 yr; 9) Cooperation from the salt industry for the maintenance of quality control is excellent and it is supervised by the IDD executive officer; 10) A database with the records of results or regular monitoring procedures, particularly for salt iodine and urine iodine is available in the Ministry of Health and Medical Education. Neonatal TSH was measured in 1989 and 1999, and showed a significant decrease in transient hyperthyrotropinemia and recall rate.

The I.R. Iran therefore has fulfilled all 10 programmatic indicators set by WHO/ UNICEF /ICCIDD. According to these criteria, the IR of Iran has reached a sustainable IDD control program since 1996. The monitoring of the IDD control program, is scheduled for every 5-6 years, evaluates the sustainability of the program. We conclude that the implementation of a sustainable and well- monitored IDD control program needs many effective programmatic steps, in particular its integration into the health network; furthermore, it may require mandatory iodized salt consumption in certain situations.

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