Sustained Elimination of iodine Deficiency in the Islamic Republic of Iran:

A SUCCESS STORY

Fereidoun Azizi, M.D

Professor of Internal Medicine & Endocrinology

Endocrine Research Center, Shaheed Beheshti University of Medical Sciences

Parvin Mirmiran, M.Sc

Instructor in Nutrition

Institute of Nutrition, Shaheed Beheshti University of Medical Sciences

Robabeh Sheikholesham, Ph.D.

Assistant Professor in Nutrition Epidemiology

Nutrition Department Ministry of health & Medical Education

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Iodine deficiency is recognized as the most common preventable cause of mental defects in the world today. It is estimated that 1.6 billion people in 130 countries are at risk of iodine deficiency disorders. Iodine deficiency causes abortions, stillbirths, motor skill disturbances, impaired growth, impaired cognitive developments, mental defects, deaf mutism, spastic weakness, paralysis and affects child learning capacity (lower IQ), women's health, the quality of life of communities and economic productivity. Yet IDD can be prevented by an inexpensive, cost effective method (salt iodisation) the most effective measure for the control and prevention of IDD.

Recognizing the importance of IDD prevention, the World Health Assembly, in 1991, adopted the goal of eliminating iodine deficiency as a public health problem by the year 2000. In 1990, world leaders endorsed this goal when they met at the World Summit For Children at the United Nations. It was reaffirmed by the International Conference on Nutrition in 1992. WHO and UNICEF therefore, recommended universal salt iodization (USI) as the main strategy to achieve elimination of IDD (1).

Since 1990, there has been tremendous progress in increasing the amount of adequately iodized salt. As a result, many countries are now on the threshold of achieving IDD elimination. In those countries, the emphasis will shift to ensuring that these achievements are sustained for all time.

Iodine deficiency disorders have been found to be endemic in many areas of Iran. For the first time epidemiological assessment of goiter as a major indicator of iodine deficiency was conducted in 1969 by the Institute of Nutrition. The results of this survey revealed that iodine deficiency is common in most cities and in the rural regions at the foot of the Alborz and Zagross mountains, the prevalence of goiter being between 10 to 60% in various provinces of Iran (2). No comprehensive studies had been carried out to examine the extent of iodine deficiency deficiency disorders (IDD), and no long-term preventive measure was taken. In 1983-84, after a gap of 15 years, reports by Azizi et al. pertaining to Shahriar (3), Tehran (4) and south-central province of Kohkyloyeh-BoyerAhmad (5) demonstrated low urinary iodine excretion and hyperendemic goiter in many regions. Subsequently they reported severe IDD in many villages located in the north of Tehran city (6, 7).

In 1995, thyroid status and neurologic, psychometric and auditory functions were reported by Azizi et al (6) in presumably normal schoolchildren, aged 6 to 16 years from three iodine deficient areas in Iran. The subjects from each area were placed into 3 groups A, B or C. Group A included individuals with retarded growth, high prevalence of visible goiter (83%), low T_4 (39%) and high TSH (70%). In group B 66% had a visible goiter and 7% had high serum TSH. In group C, visible goiter was present in 22% of the subjects but they had normal thyroid function. Urinary iodine excretion was low in all three groups. Head circumference was less in groups A and B, as compared to C. Pyramidal signs occurred in over half of the subjects in group A (hyperreflexia in 39% and crossed adductor reflex in 29%). The glabellar sign was present in 50% of group A and 20% of group B. Forty-four percent of the subjects in group A and 17% in group B had hearing deficits, as shown by audiometry. Psychomotor examination was performed using the Bender Gestalt test. A higher number of errors were evident in groups A and B, their psychomotor age being below their chronological age. The results of the Raven test showed mild impairment of IQ in group A, with 55% having IQs below 91 and 15% with IQs less than 70. The subjects in group B had IQs lower than group C, but higher than group A. There was a negative correlation betweens serum TSH and free thyroid indices and a positive correlation between TSH and the number of pyramidal signs. This study demonstrated that mild to moderate growth retardation and neurological, auditory and psychomotor impairments were present in apparently normal subjects residing in areas of iodine deficiency (6).

In another study, schoolchildren from three areas with different degrees of iodine deficiency were studied in Iran. In Randan, the prevalence of severe endemic goiter was accompanied by alteration in thyroid function, increased thyrotropin levels and retardation of both bone and psychomotor age and decreased intellectual quotient. In Tehran, where iodine deficiency is mild, visible goiter was present in 15% of schoolchildren but no alterations in thyroid function, serum thyrotropin, somatic or psychomotor development could be detected. In Zagoon, where the prevalence and severity of goiter were less than Randan but more than Tehran, thyroid function was normal but slightly decreased as compared to Tehran; somatic development was unaltered, but retardation in psychomotor development was evident and the mean intellectual quotient was less than that of Tehranian schoolchildren (Fig. 1).

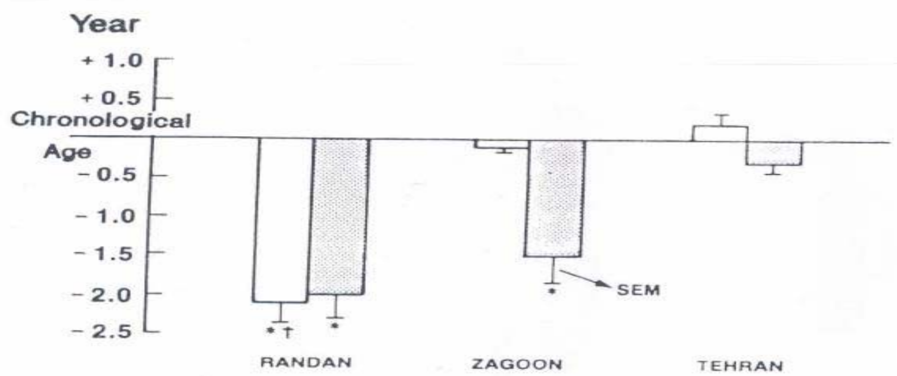

Fig 1. Difference between chronological age and psychomotor (□) and bone (□) ages in three groups of schoolchildren in Tehran and its suburbs. *p<0.001, as compared to values in Tehranian schoolchildren; † p<0.001, as compared to Zagoonian results. Note retarded psychomotor and bone ages in Randan and delay in only the psychomotor ages in Zagoon. From reference No. 7.

These findings indicate the occurrence of physical and psychomotor disturbances in apparently normal schoolchildren from areas of iodine deficiency. Alteration in psychomotor development may occur in children with moderate iodine deficiency despite normal physical growth (7).

Before iodide supplementation, median urinary iodine, in all locations surveyed, was below 100 µg/dl, being even ≤20 µg/dl in many regions (Table 1).

Table 1. Urinary iodine concentration in selected endemic and hyperendemic regions before iodized salt distribution. From references 8-15.

Location	Province	Urinary iodine (µg/L)
Kiga	Tehran (rural)	20±11
Randan	Tehran (rural)	12±5
Zagoon	Tehran (rural)	18±10
Keshar	Tehran (rural)	19±10
Tehran City	Tehran (urban)	39±19
Shahriar	Tehran (rural & urban)	71±39
Hanna	Esfahan (rural)	40±21
Yasuj	Boyer-Ahmand (rural)	34±39
Doruhan	Boyer-Ahmand (rural)	24±17

These findings prompted the Ministry of Health and Medical Education to form the Iranian National Committee for Control of IDD (INCCIDD) in 1988 (Fig 2).

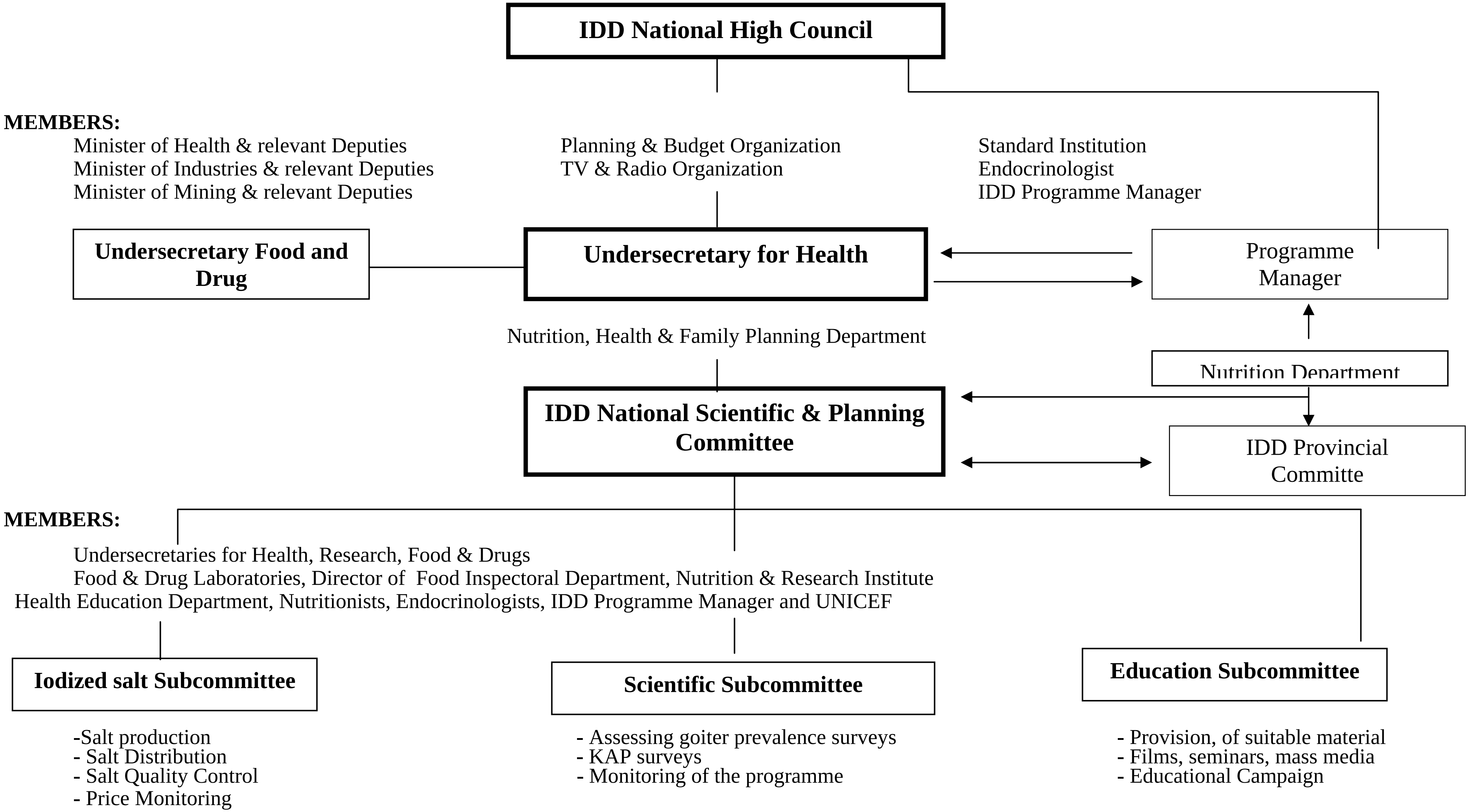

Fig 2. Organization of the Iranian National Committee for Control of IDD Translated. From reference No. 21.

Since 1989, IDD had been declared a health priority in the country. The INCCIDD prepared a national plan, which detailed objectives and strategies for IDD control. Salt iodization began in 1990. The production, distribution and consumption of iodized salt increased gradually, however a nation-wide survey in 1993 showed that less than 50% of the households were consuming iodized salt. INCCIDD announced universal salt iodization (USI) and all salt factories were obliged by the law to produce only idodized salt for household use, in 700 to 100 gram packages and an enhanced, more vigorous system of evaluation and monitoring was applied.

The IDD prevention program in Iran (8)

Under the National IDD Elimination Committee, a subcommittee for production and distributions related to USI activities:

- Identified related bodies and their functions;
- Defined guidelines and activities for each section and the tasks required at different levels;
- Developed training material and conducted the required training for salt producers, laboratory and health care workers.

Measures taken for USI monitoring include:

1. At production level:

1.1. Factories

- Daily sampling of continuous line of iodized salt from 8-10 lines, to assess the level of iodine with the titration method and registering in the logbook.

1.2. Food Safety Department:

- Inspection of iodized salt factories including:
    - Appropriate manufacturing;
    - Labeling;
    - Potassium iodate packages;

○ Storage of iodized salt;

○ Laboratory log books.

● Random sampling of iodized salt from factories and dispatch to the provincial food laboratory;

1.3. Food and Drug Laboratory

● Recording the results on special iodized salt assessment forms (ISAF) and sending these to national level officials through the provincial IDD committee;

● Assuring capability of the salt factory technician to perform titration method and their retraining if necessary.

2. At distribution level (urban areas)

By the environmental health specialists

● Sampling of existing salt in the market every three months by environmental health workers and analysis at the Food Laboratory;

● Recording the results of the testing on the ISAF (Iodized Salt Assessment Form) by the provincial food laboratories and its relaying to national level officials through the provincial IDD committee;

● Inspection of iodized salt at all sites where food is provided (restaurants, hospitals, day care centers, and canteens with rapid test kits);

● If tests show lack of iodine in the salt, importance of iodized salt is stressed and source of the defective salt is traced;

● Results of this testing is relayed to the national level officials the provinces.

3. Nutrition Department

● Computer data entry of all ISAFs from the provinces

- Half-yearly reports generated and feedback provided (IDD committees, labs, salt producers, Food Inspection Department, National Food Laboratory, Environmental Health Dept).
- Same procedures followed as with the market salt and feedback sent to related bodies

3.1 Integrated activities in rural areas

- Testing of salt with testing kits and education about importance of iodized salt provided by the Behvarz at the Health House:
- Local shops
- All households (once a year)
- Schools (every 6 months)
- Results of statistics of iodized salt utilization at the household registered on special stickers on the Vital Horoscope;
- Health technicians supervise Behvarz activities using a checklist

Rural checklists include:

- Is iodized salt available in the rural market?
- Has the Behvarz put the sticker of the iodized salt on the Vital Horoscope of the village?
- Have the schoolchildren been taught about the benefits of iodized salt?
- Are village shopkeepers aware of the reason why they should sell exclusively iodized salt?

3.2 National labs, quality assurance

- Bi-annually, National Food Laboratory sends blind samples of iodized salt to provincial food labs to ensure precision of their tests.
- Necessary training provided to laboratories with low performance ratings

● Surveys done to monitor USI

● Integration of questions on IDD into other public health surveys

● Surveys assess iodized salt utilization among households in rural and urban areas

● Each year, urinary iodine levels of 240 schoolchildren (8-10 yrs) in each province are also measured

National surveys in 1994, 1996, 1998, 2000 and 2004 have shown that more than 95% of the households were consuming iodized salt (9) (Fig 3). The results of survey done in the year 2000 showed that 94.5% in urban and 91.8% in rural areas were consuming iodized salt respectively.

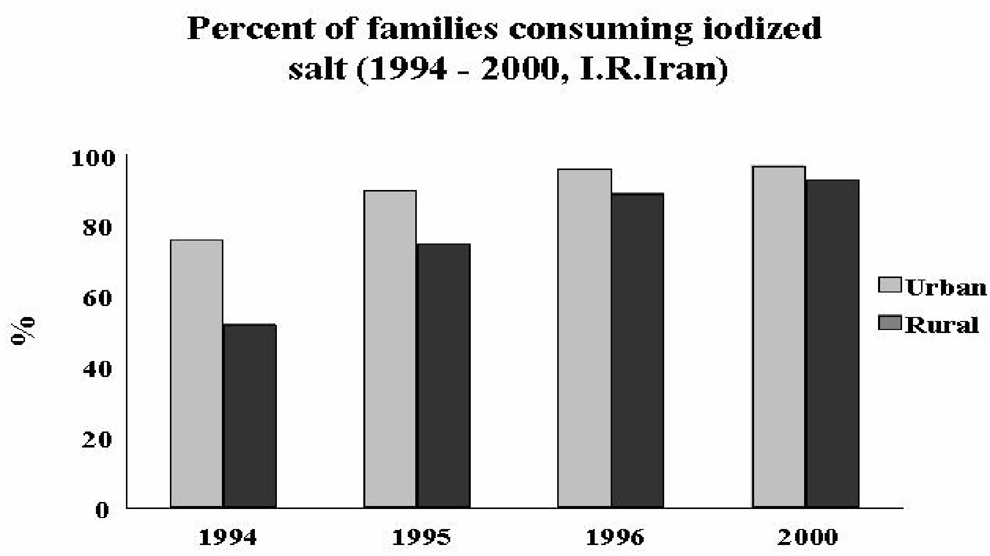

Fig 3. Survey on household salt utilization in 1994-97 in I.R. Iran Tehran. From reference No. 9.

In order to assure the quality of performance of provincial Food & Drug Control Labs and achieve uniformity, every year a salt sample with undisclosed iodine level is sent to each lab and the results and data are forwarded to Tehran. The results of monitoring from 1994 to 2000 are shown in Table 2.

Table 2. The quality of produced iodized salt based on iodine content Translated. From references 8 and 9.

Date	Total number	Good	Acceptable	Unacceptable
First half 1994	637	69	20	11
Second half 1994	476	67	19	14
First half 1995	423	73	21	6
Second half 1995	961	68	22	10
First half 1996	964	75	17	8
Second half 1996	791	68	26	6
First half 1997	879	73	20	7
Second half 1997	1154	74	20	6
First half 1998	1105	70	22	8
Second half 1998	1102	74	22	4
First half 1999	881	70	23	7
Second half 1999	1077	67	22	11
First half 2000	1202	67	24	9

* Iodide content of salt: Good: 40±10 ppm Acceptable: 51-55 or 15-29 ppm, non-acceptable: <15 or >55 ppm.

In 1996, the second national survey was conducted 7 years after the initiation of iodized salt production, 2 years after the implementation of the new law for mandatory consumption of iodized salt in households (10). The total number of pupils surveyed was 36178 of which 2917 had urinary iodine assessments. The percentage of girls surveyed in each province was between 49 to 51%, and the sex ratio was 1 in the country. 33%, 34% and 34% of all surveyed pupils were 8, 9 and 10 years of age, respectively. Approximately half of the schoolchildren in each province were from rural regions. In 16 of 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. There was no significant difference in goiter prevalence between boys and girls or schoolchildren of rural and urban regions.

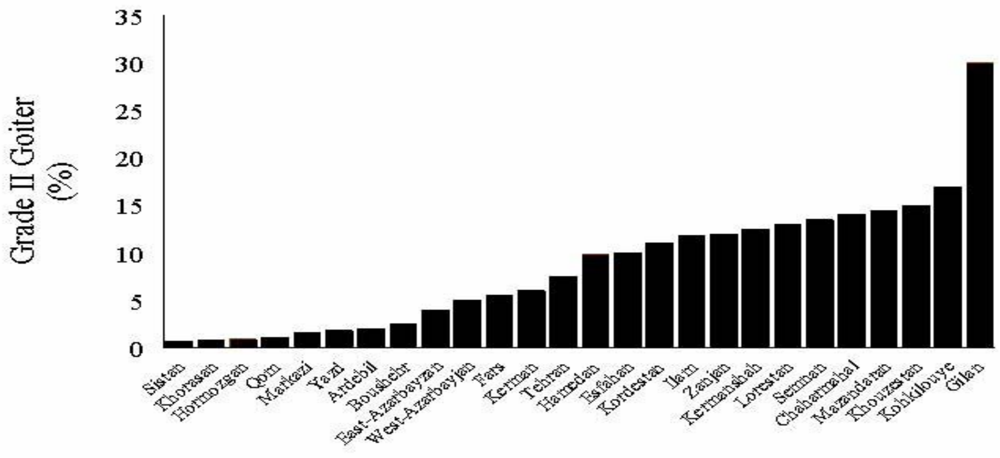

Fig 4. Percent schoolchildren with visible goiter in 26 provinces I.R.Iran, 1996. From reference No. 10.

In all 2917 schoolchildren, median urinary iodine excretion was 20.5 µg/dl. Two thirds of schoolchildren had urinary iodine between 10 to 30 µg/dl. 85.1% of children had urinary iodine equal to or in excess of 10 µg/dl. Mild, moderate and severe iodine deficiency was seen in 9, 2.3% and 3.6% had respectively. Fig 5 illustrates urinary iodine distribution in 8 to 10 year old schoolchildren of the country. There was no significant difference in urinary iodine excretion between boys girls and schoolchildren of rural and urban regions.

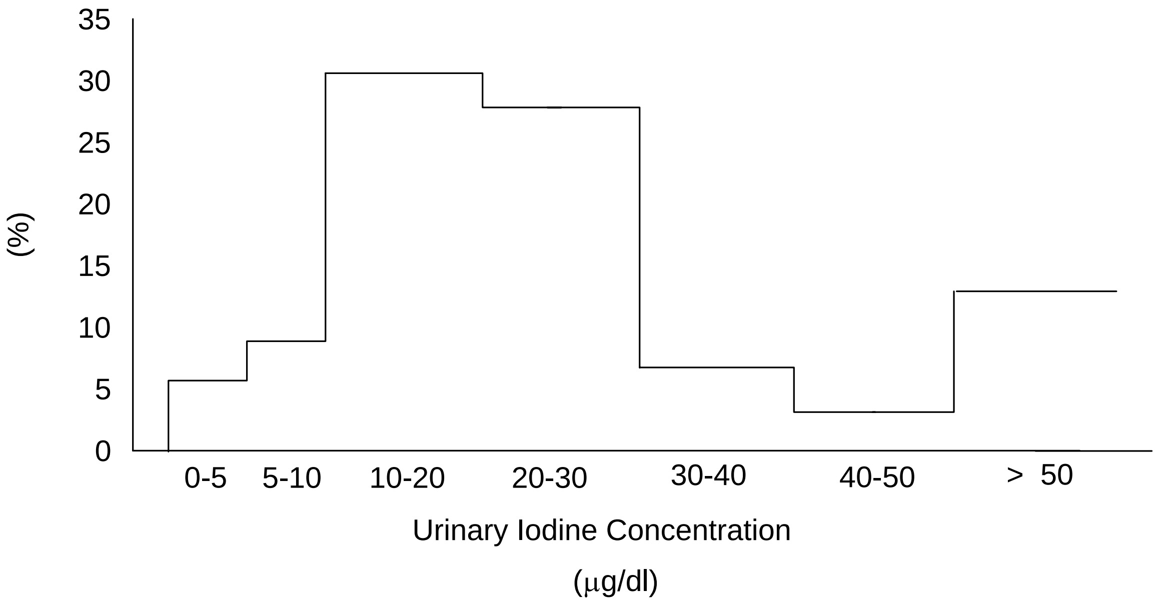

Fig 5. Distribution of urinary iodine concentration in 8 to 10 year old schoolchildren of 26 provinces, I.R. Iran, 1996. From reference No. 10.

Fig 6. Shows median urinary iodine excretion in schoolchildren of each of 26 provinces. The highest and lowest values belong to Guilan (North) and West-Azarbayjan (North-west) provinces, 65 and 13 µg/dl, respectively.

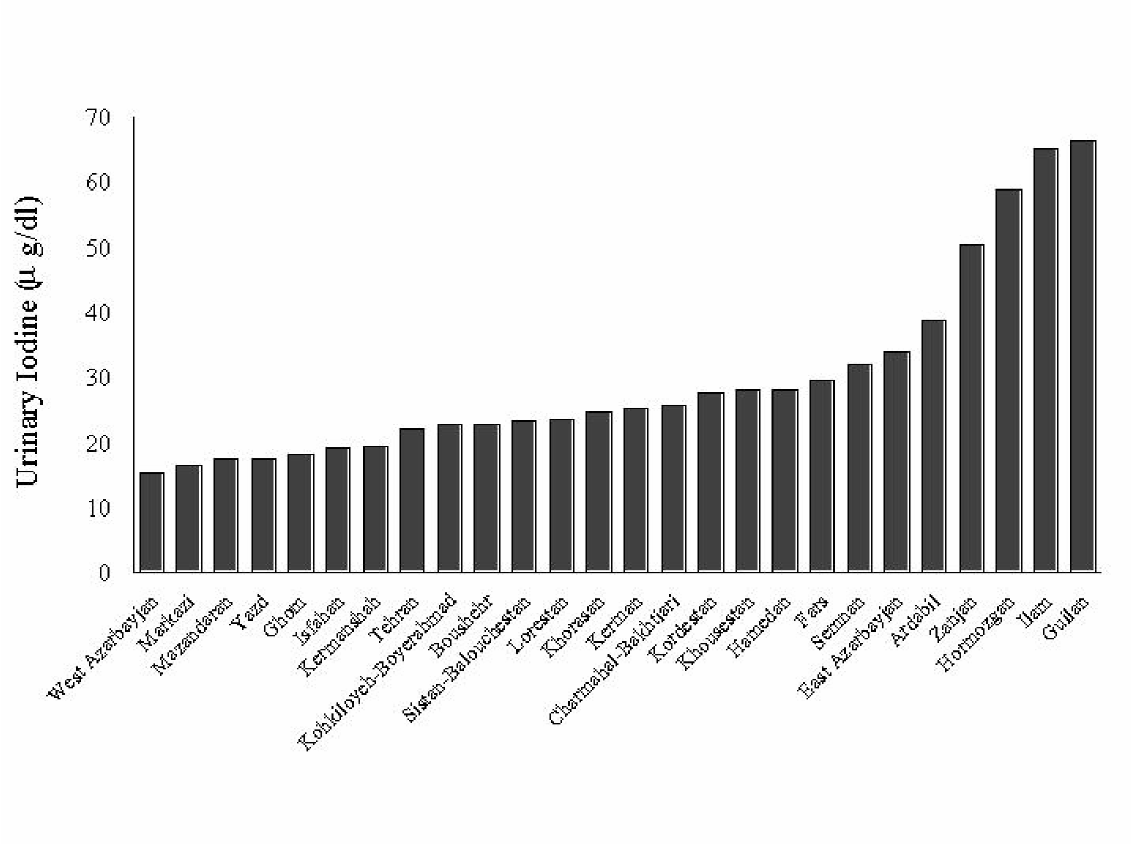

Fig 6. Median urinary iodine concentration in 8 to 10 year old schoolchildren of 26 provinces, I.R. Iran, 1996. From reference No. 10.

In Table 3, on the basis of urinary iodine excretion, all 26 provinces have been divided into 4 groups. In 9 provinces the median urinary iodine is between 13 and 19 µg/dl. In these provinces, 6.9% of schoolchildren have severe iodine deficiency. In 11 provinces the median urinary iodine is between 20 to 29 µg/dl and 2% of the children have severe iodinde deficiency. Median urinary iodine of 30-39 µg/dl and ≥50 µg/dl existed in 2 and 4 provinces with these schoolchildren having severe iodine deficiency of 0.4% and 1.7% respectively. In none of the 26 provinces, occurrence of urinary iodine of <50 µg/dl exceeded 70% of schoolchildren. There was no correlation between the prevalence or severity of goiter and urinary iodine excretion.

Table 3. Urinary iodine excretion in 26 provinces of I.R.IRAN, according to WHO/UNICEF/ICCIDD classification, 1996. From reference No. 10.

Median Urinary Iodine (μg/dl)	Provinces	Urinary iodine (μg/dl)			
		<2	**2-4.9**	**5-9.9**	**≥10**
13-19	W. Azarbayjan, Isfahan Ghom, Kerman, Kermanshah, Lorestan, Mazandaran, Yazd Markazi	6.9*	3.9	13.8	75.4
20-29	Boushehr, Tehran, Charmahal, Khorasan, Sistan-Balouchestan, Semnan, Fars, Kordestan, Kohkiloyeh, Hamedan, Khouzestan	2.0	1.7	7.0	89.4
30-39	E.Azarbaiejan, Ardabil	0.4	1.6	9.0	89.0
≥50	Ilam, Guilan, Hormozgan, Zanjan	1.7	0.9	3.2	94.2

* Numbers indicate percentage

In 1996 it was evident that the prevalence of goiter was still high in many provinces. Since the study was performed when the majority of people had used iodized salt only for 2 years, it was too early to expect that consumption of iodide result in reduction of goiter prevalence, because majority of 8 to 10 year old children had lived of their lives without adequate iodine supplementation.

It has been shown that thyroid size in children exposed to iodine deficiency in the first years of lives might fail to regress completely following consumption of iodized salt, and children born prior to iodine prophylaxis after 10 years after intervention, still had larger thyroid volume than children from iodine sufficient areas (11).

The most sensitive method for the monitoring and evaluation of an IDD control programme is the determination of urinary iodine excretion (12). Findings of the 1996 survey showed that the median of urinary iodine excretion in schoolchildren in Iran (20.5 µg/dl) was at the top of optimal range, i.e. 10 to 20 µg/dl, recommended by WHO/UNICEF/ICCIDD (17). In 20 of 26 provinces, the median urinary iodine was between 13 to 30 µg/dl and in 6 provinces, it was in a range that considered to be accompanied by an increased risk of iodine-induced hyperthyroidism (13). The reason for an increase in urinary iodine was then studied in Guilan province and it was attributed to increased consumption of salted food in the staple dietary habits of the population of this province (14). Guilan and other 5 provinces have been among hyperendemic regions, where in 1993 and 1994, iodine supplementation in the form of iodized oil injection had been made available. A repeat survey in one of these provinces, Ilam, has shown a decrease in mean urinary iodine to 20.5 µg/dl (15).

Another study was carried out to assess iodine status in Tehran in 1996 (16). 1146 families comprising 5140 subjects in the twenty districts of Tehran city, from all age groups, were randomly selected. Thyroid size was examined by palpation and graded according to the WHO classification. In 163 families selected randomly, thyroid size was determined by ultrasonography and urinary iodine was measured by the digestion method. Serum T_4, T_3 and TSH concentrations were also assayed by kits. Percentages of grades 1 & 2 goiter were 44 & 44% in females and 49 & 33% in males respectively. Median urinary iodine was 17.5 µg/dl. Mean serum T_4, T_3 and TSH were 8.41±1.4 µg/dl, 170±37 ng/dl and 1.4±0.8 µU/ml, respectively. In 118 children, aged 6-10 years, median urinary iodine was 17.5 µg/dl. Thyroid volume in children was 4.3±1.9 ml. No correlation was established between the thyroid volume and goiter grade. This study demonstrated the adequacy of iodine intake in the majority of families residing in Tehran.

In 1999, Azizi et al. attempted to measure thyroid volume by ultrasonography in Tehran in schoolchildren and compared them with WHO normative values. Cross-section studies were performed in 2016 schoolchildren, aged 6-15 years, in Tehran, 10 years after distribution of iodized salt. Data were collected on age, sex, weight, and height, thyroid size by palpation and ultrasonography, and urinary iodine. Age/sex and body surface area (BSA) upper limits (97^{th} percentile) of thyroid volume were derived. The goiter prevalence was 42% by palpation, 31% grade 1 and 11% grade 2. Median urinary iodine was 21.2 µg/dl. The 97^{th} percentiles were comparable in girls and boys of all ages. Applying the WHO thyroid volume references to the Tehranian children, showed no enlarged thyroid based on BSA and on age, even in 11% of children. In Tehranian children the best predictors of thyroid volume were BSA, height and weight. Using linear regression, the 97^{th} percentiles of thyroid volume from Tehranian children were lower than the corresponding references from the WHO normative values. The results indicated that a thyroid volume reference based on weight alone would perform as well as the one based on BSA. In addition, they concluded that until the adoption of a new applicable international reference for thyroid volume, the use of local reference in the screening of children for thyroid enlargement is recommended (17).

The third national survey and second national assessment on sustainability of control over iodine deficiency in Iran was conducted in 2001. More than 33000 schoolchildren were examined from all the 28 provinces of Iran by inspection and palpation methods for goiter grading and more than 3300 urine samples were collected from all provinces for the measurement of iodine concentration. Finally, the effects of a continuous and well-executed salt iodization program on the sonographically measured thyroid size of 7-10 yr Tehranian children during the iodine sufficiency era were assessed.

Goiter Rate and Urinary Iodine Excretion in Schoolchildren and Iodine Content of Salt

The study populations were schoolchildren aged 8-10 years with a mean age of 8.7±10.7 yr. Totally 33600 schoolchildren (168 clusters of 20 children), 16876 (50.2%) girls and 16718 (49.8%) boys were examined for goiter. In 10% of the study population urinary iodine was measured; in all, urinary iodine was measured in 33600 schoolchildren (168 clusters of 20 children each), 1200 schoolchildren being examined in each province. The sample size was 16575 (49.9%) in rural and 16837 (50.1%) in urban areas. In each province, 120 cases were evaluated for urinary iodine levels (60 cases in rural and 60 cases in urban areas). In each age group (8, 9 and 10 years old), 11200 schoolchildren were evaluated (400 cases in each province).

Total goiter rate was evaluated to be 9.8% after weighting the prevalence for the population size. Total goiter rates in Ilam, Chahar Mahal Bakhtiari, Hamadan, Khoozestan, Zanjan, Semnan, Sistan Baloochestan, Fars, Qom, Kordestan, Kerman, Kermanshah, Golestan and Gilan was over 10%. The prevalence of goiter grade 2 in 22 provinces was below 5% and in 6 other provinces (Boosheehr, Chahar Mahal Bakhriari, Sistan Baloochestan, Qom, Kordestan, Kermanshah) goiter rate did not exceed 10%.

Total, grade 1, and grade 2 goiters were present in 4670 (13.9%), 3686 (11%), and 984 (2.9%) children, statistics were significantly lower than the corresponding rates in the 1996 study (n=36178), i.e., 53.8%, 44.8%, and 9%, respectively ($p<0.0001$).

Goiter was present in 1970 (11.8%) urban and in 2700 (16.0%) rural children (odds ratio 1.4, 95% CI 1.35-1.53, $p <0.0001$). Of 16718 females 2160 (12.9%) and of 16876 males 2510 (14.9%) were goitrous (odds ratio 1.18, 95% CI 1.11-1.25, p<0.0001). Excluding grade 2 goiters, grade 1 goiter was present in 1704 (10.5%) of 16262 females and in 1982 (12.1%) of 16348 males (odds ratio 1.18, 95% CI 1.10-1.26, p<0.0001). Excluding grade 1 goiters, grade 2 goiter was present in 456 (3.0%) of 15014 females and in 528 (3.6%) of 14894 males (odds ratio 1.17, 95% CI 1.03-1.33, p=0.014).

Fig. 7 depicts the prevalence of goiter in different provinces in 1996 and 2001 and indicates significant reduction in total goiter rate in all provinces during a 5-year period; it is more significant in hyper endemic regions including Ilam, Hamedan, Kohkiloyeh Boyerahmed and Kermanshah. Sistan Baloochestan with higher goiter prevalence in 2001 is the only exception, which may due to interobserver variation caused by differences in evaluation of the two examiners between the years 1996 and 2001 and calls for further evaluation.

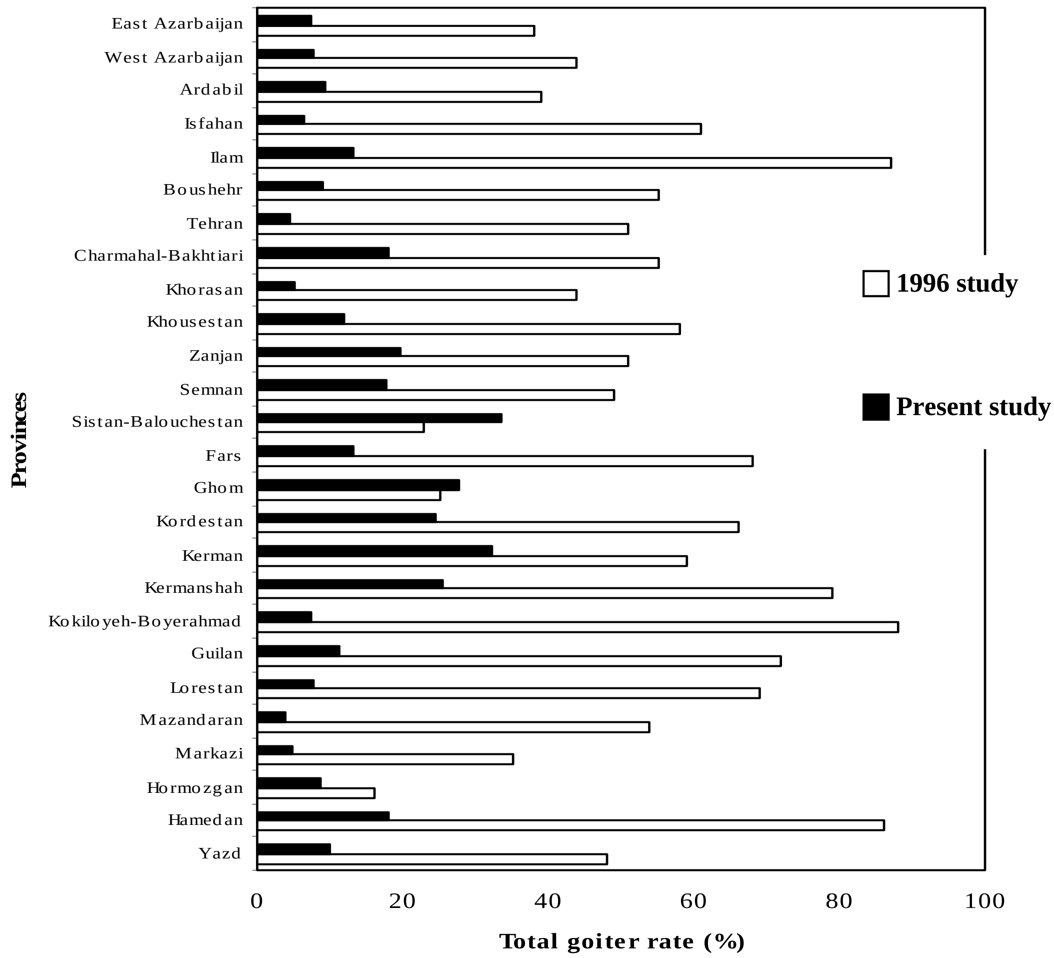

Fig. 7. Total goiter rates of twenty-four provinces in 2001 were significantly lower than those of the same provinces in 1996 (p<0.0001). Ghom showed no significant difference between two studies (p=0.10). Sistan-Balouchestan was the only province that showed higher goiter prevalence in 2001 as compared to 1996, i.e., 33.4% and 23.5%, respectively (p=0.002). No comparisons were made for total goiter rate in Ghazvin and Golestan because these provinces were governed by Zanjan and Mazandaran in 1996

UIC values

Totally 3329 urine samples were assayed in 2001. Median (range) and 95% CI of UIC values were 165 (18-410) and 183-190 μg/L, respectively. Frequency distribution of low (mild, moderate, and severe) and adequate iodine intakes in various provinces according to their median UIC levels are illustrated in Table 4.

Table 4. Classification of twenty-eight provinces of Iran according to median UIC values, Iran, 2001

Classification by Median UIC (µg/L)	Provinces (No. of urine samples)	UIC values (µg/L)*			
		<20	20-49	50-99	≥100
100-149	West Azarbaijan, Isfahan, Boushehr, Khorasan, Semnan, Golestan (n = 719)	0	9.6	19.5	70.9
150-199	East Azarbaijan, Ardebil, Ilam, Tehran, Charmahal, Khousestan, Zanjan, Sistan, Ghom, Kordestan, Kerman, Kermanshah, Kohkiloyeh, Guilan, Lorestan, Mazandaran, Markazi, Hormozgan, Hamedan, Yazd (n= 2370)	< 0.05	4.8	12.8	82.4
≥200	Fars, Ghazvin (n = 240)	0	3.8	7.9	88.3

* Numbers indicate percentage in each group of median UIC values.

UIC levels were not statistically different among 7 to 10 year old children (p=0.33). Median (range) UIC in urban areas (n=1667) was 160 (20-410) and in rural areas (n=1662) was 170 (18-400) µg/L (p=0.16). These values in males (n=1676) were 170 (20-410) and in females (n=1653) were 160 (18-400) µg/L (p=0.18).

UIC <100, between 100-199, and ≥200 µg/L were present in 655 (19.7%), 1520 (45.7%), and 1154 (34.7%) children, respectively. UIC was between 50-99 µg/L in 463 (13.9%) subjects, between 20-49 µg/L in 191 (5.7%) children, and less than 20 µg/L in only one (0.1%) subject. UIC≥300 µg/L was present in 631 (19%) schoolchildren. No association was seen between the presence of goiter and various UIC values, because goiter (grade 1 and 2) was present in 94 (14.4%) of 655 children with UIC <100 µg/L, in 217 (14.3%) of 1520 children with UIC of 100-199 µg/L, and in 172 (14.9%) of 1154 subjects with UIC ≥200 µg/L (p=0.89).

UIC values in 2001 vs. 1996

Median (range) and 95% CI values for UIC in 2001 were 165 (18-410) and 183-190 µg/L and in 1996 (n=2582) were 205 (10-5950) and 280-311 µg/L, respectively (p<0.0001). Central tendency measures of UIC values by provinces in the present and 1996 studies are shown in Figure 8.

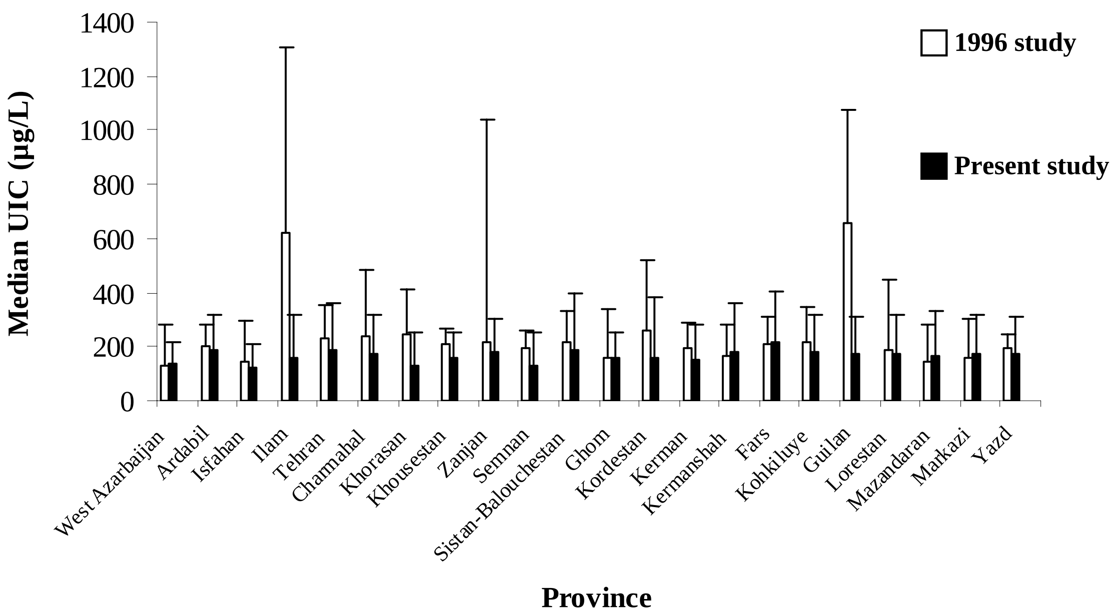

Fig. 8. Median (bars) and interquartile (whiskers) UIC values of twenty-two provinces in 1996 and 2001. Differences between UIC values in 2001 and 1996 were highly significant in Ilam, Khorasan, Khousestan, Semnan, Kordestan, and Guilan (p<0.0001), significant in Isfahan, Charmahal-Bakhtiari, Zanjan, Kerman, Kohkilouyeh-Boyerahmad, and Markazi (p values between 0.018-0.001), not quite significant in West Azarbaijan (p=0.046), and not significant in Ardabil, Tehran, Sistan-Balouchestan, Fars, Ghom, Kermanshah, Lorestan, Mazandaran, or Yazd (p>0.05)

Qualitative and quantitative measurement of iodine in salt

Qualitative assays performed by the health workers on site showed that 412 table salt samples were iodinated. No non-iodinated salts were found in our specimens.

Mean ± SD (95% CI) and median (range) iodine content of 410 household table salt samples determined by the titration method in 2001 were 32.7±10.1 (31.8-33.7) and 32.8 (2-75) ppm and of 395 samples in 1996 were 33.0±10.2 (32.0-34.0) and 32.8 (5-79) ppm, respectively ($p=0.79$). Frequency distributions of household table salts with iodine contents of <20, 20-40, and >40 ppm were 34 (8.3%), 294 (71.7%), and 82 (20.0%) in 2001 and 31 (7.8%), 284 (71.9%), and 80 (20.3%) in 1996, respectively ($p=0.97$).

Mean ± SD (95% CI) and median (range) iodine content of 297 factory salt samples in 2001 were 33.2±13.4 (31.7-34.7) and 32.8 (6-84) ppm and of 278 samples in 1996 were 33.8±13.2 (32.2-35.3) and 33.9 (8-91) ppm, respectively ($p=0.67$). Frequency distributions of factory salts with iodine contents of <20, 20-40, and >40 ppm were 51 (17.2%), 162 (54.5%), and 84 (28.3%) in 2001 and were 44 (15.8%), 152 (54.7%), and 82 (29.5%) in 1996, respectively ($p=0.89$). Median iodine contents of household table salts vs. factory salts were similar in 2001 ($p=0.57$) and in 1996 ($p=0.41$).

Thyroid volume by ultrasonography

Mean±SD and median (range) of height, weight, BSA, and BMI of children were 134±7.8 and 133 (116-159.5) cm, 28.5±6.9 and 27 (15-58) kg , 1.03±0.14 and 1.01 (0.72-1.53) m^2, 15.8 ± 2.6 and 15.1 (10.8-31.4) kg/m^2 respectively.

Data regarding thyroid volumes of 400 schoolchildren, aged 7-10 years were obtained in Tehran. There was a significant correlation between thyroid volume and values of height ($r=0.62$, $p<0.0001$), weight ($r=0.65$, $p<0.0001$), BSA ($r=0.68$, $p<0.0001$), and BMI ($r=0.41$, $p<0.0001$). Figure 9 illustrates thyroid volumes as a function of BSA in both sexes. Median (P50) and P97 of thyroid volumes of children by age and sex are shown in Table 5 and by BSA in Table 6.

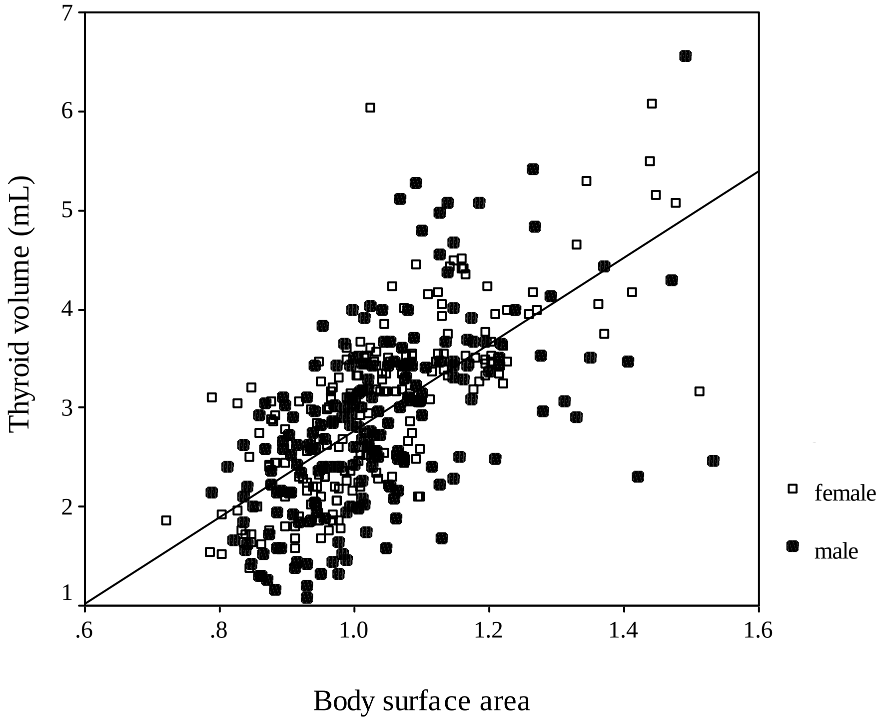

Fig. 9. Thyroid volume as a function of body surface area by sex

Table 5. Median (P50) and 97th percentile (P97) thyroid volumes by age and sex

Age (yr)	No. *	Total†			Male†			Female†		
		P50	**P97**	**Mean±SD‡**	**P50**	**P97**	**Mean±SD‡**	**P50**	**P97**	**Mean±SD‡**
7	100	2.29	3.47	2.34± 0.53	2.22	3.15	2.25±0.46**	2.34	3.51	2.44±0.58
8	100	2.45	3.60	2.42 ± 0.69	2.41	3.52	2.28 ± 0.72	2.45	3.68	2.55±0.64
9	100	3.34	5.29	3.46 ± 0.85	3.10§	5.34	3.41 ± 0.83	3.36§	5.39	3.50± 0.88
10	100	3.30	6.02	3.21 ± 0.94	3.42	5.77	3.40 ± 0.88	3.49	6.06	3.46±0.79

* There were 50 boys and girls in each age group (except for 46 eight-year old boys in 1999).
† Values of thyroid volume are presented in mL.
‡ Mean thyroid volumes were similar in females vs. males in 1999 and in 2001 using Student's t-test (P values => 0.053).
§ Because of non-Gaussian distribution of thyroid volumes, medians were compared using Mann-Whitney U test (P values => 0.405).
¶ Mean thyroid volume of 7-yr children was significantly lower in 2001 as compared to 1999 (P = 0.032).
** Mean thyroid volume of 7-yr males was significantly lower in 2001 as compared to 1999 (P = 0.027).

Table 6. Median (P50) and 97th percentile (P97) thyroid volumes by age and sex*

BSA (m^2)	No.	Mean ± SD †	P50	P97
0.9	79	2.2 ± 0.7	2.2	3.2
1.0	140	2.7 ± 0.7	2.7	4.0
1.1	88	3.3 ± 0.8	3.3	5.1
1.2	45	3.6 ± 0.6	3.5 ‡	4.9

* BSA values < 0.9 and > 1.2 had lower than 40 subjects in each group and were not compared.
† Mean thyroid volumes of all BSA groups were compared in 1999 vs. 2001 using Student's t-test (P values ≥0.08).
‡ Median thyroid volumes of those with BSA of 1.2 were compared in 1999 vs. 2001 using Mann-Whitney U test (P=0.21).

Impact of iodine supplementation in severely iodine deficient schoolchildren.

In villages Northwest Tehran, previous studies had shown ever iodine deficiency. Ten years after iodine suffementation, goiter rate decreased and urinary iodine increased significantly (Table 7).

Table 7. Total goiter rate and median urinary iodine in schoolchildren of villages before (1989) and 10 years after iodine supplementation (1999)

Village	Total goiter rate (%)				Median urinary iodine (μg/dl)	
	1989	1999*			1989	1999*
		All Schoolchildren	11-16 years old	6-10 years old		
Kiga	100	64	71	58	1.9	20.1
Keshar	99	52	53	51	1.8	20.1
Sangan	99	52	56	50	2.3	21.2
Randan	100	61	79	42	1.2	17.3
Zagoon	100	54	67	41	1.8	20.1
Total	99	57	72	41	1.8	19.4

* Present study

Significant decrease in grade 2 goiter was observed: Kiga: from 94 to 14%, Keshar: from 66 to 9.4 and Randan from 82 to 9.7%, P<0.001 (Fig. 10). 60% 0f the school children aged below 10 years and 30% of students above 10 years were not goitrous. Grade 2 goiter rates in the schoolchildren above and below 10 years of age were 3 and 19% respectively. The same figure for grade 1 was 37and 50%.

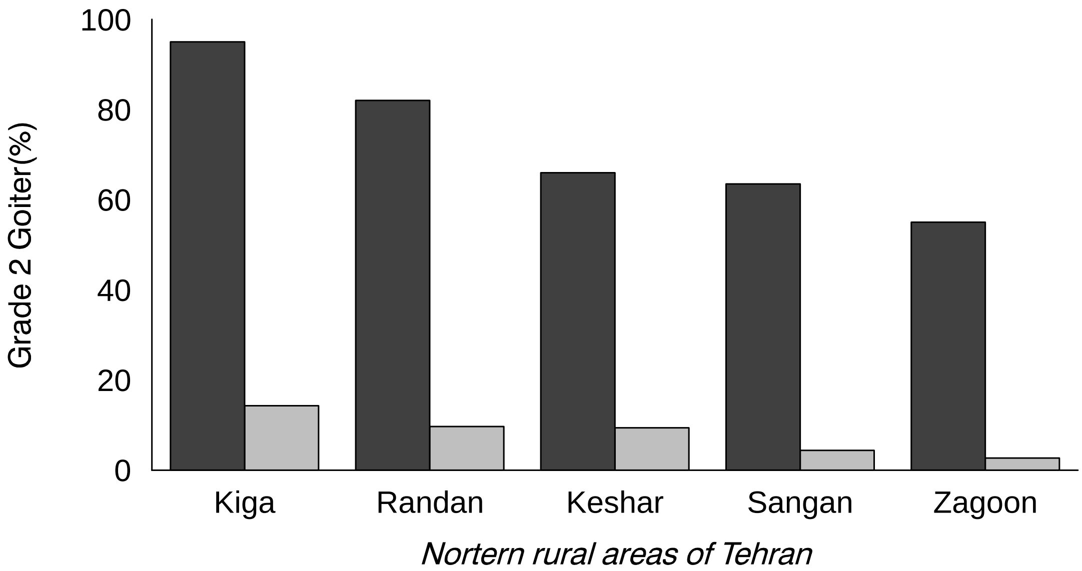

Fig. 10. Prevalence of grade 2 goiter in schoolchildren of five villages in 1989 and 1999 . The changes in goiter prevalence and severity were statistically significant in all villages at p<0.001

Urinary Iodine Concentration

In 1999 the median urinary iodine was above 17 µg/dl in all villages and 96% of the subjects had values above 10 µg/dl and no child had urinary iodine below 5 µg/dl. Median urinary iodine was 1.9 and 20.1 in Kiga, 1.8 and 20.1 in Keshar, 1.2 and 17.3 in Randan and 1.8 and 20.1 in Zagoon, in 1989 and 1999, respectively.

In 1989, many of schoolchildren were hypothyroid. Serum TSH levels between 5 and 10 µU/ml were 30% in Kiga and 22% in Randan and those of above 10 µU/ml were 40 and 24% in Kiga and Keshar, respectively. In 1999, no child had TSH ≥5.0 μU/ml or T_4<5.0 μg/dl.

Intelligence Quotient

In 1999, about 36 to 57% of schoolchildren had IQ above 100 and none had IQ below 70. In 1989, IQ above 100 was present in 20, 24, 17 and 45% of schoolchildren in Kiga, Keshar, Randan and Zagoon, respectively. Comparison of IQ in the two studies is shown in Table 8. Marked elevation of IQ in 3 of 4 villages is seen, the largest being 10 points in Randan.

Table 8. Comparison of mean and the frequency of IQ in schoolchildren of villages before (1989) and 10 years after iodine supplementation (1999)

Location	Year	Mean±SD	Intelligence Quotigent			
			≥100	90-100	70-90	>70
Kiga	1999	95 ± 11* (28)	35.7	28.6	35.7	0
	1989	89 ± 11 (95)	20	25	40	15
Keshar	1999	101 ± 12* (29)	37.9	34.5	27.6	0
	1989	96 ± 9 (39)	24	53	20	3
Randan	1999	99 ± 9.1* (14)	50	42.9	7.1	0
	1989	89 ± 15 (54)	17	36	38	9
Zagoon	1999	105 ± 11 (35)	57.1	43.3	8.6	0
	1989	102 ± 11 (20)	45	33	22	0

* P<0.02, as compared with 1989

There was significant decrease in the prevalence of goiter, marked reduction in serum concentrations of TSH and thyroglobulin and increase in serum T_4, 3 years following administration of iodized oil. These changes remained unaltered after 7 years of iodized salt consumption. In 1992 and 1999, all the pupils had normal serum T_4, T_3, TSH and thyroglobulin concentrations.

Hearing was abnormal in 44% of schoolchildren before intervention, and many showed mixed defects in audiometry, with high tone loss in 49%, conduction problems in 27% and sensoryneural deficit in 5% of subjects. Hearing threshold was 15.8±9.0 dB; it was between 10 and 15 in 57% and more than 15 dB in 46% of schoolchildren.

In 1992, three years after iodized oil injection, hearing threshold had significantly decreased from 15.6±5.9 to 10.2±4.6 dB (P<0.001) Hearing threshold was less than 10 in 42%, between 10-15 in 48% and above 15 dB in 10% of schoolchildren.

In 1999, following seven years of iodized salt consumption (10 years after the beginning of intervention) mean hearing threshold was 10.0±5.9, significantly lower than values before intervention (P<0.001). Hearing threshold was below 10 in 62%, between 10-15 in 28% and above 15 dB in 10% of subjects. The difference was statistically significant, as compared to hearing threshold distribution before intervention (Fig. 11). There was no difference in hearing threshold values between 1992 and 1999.

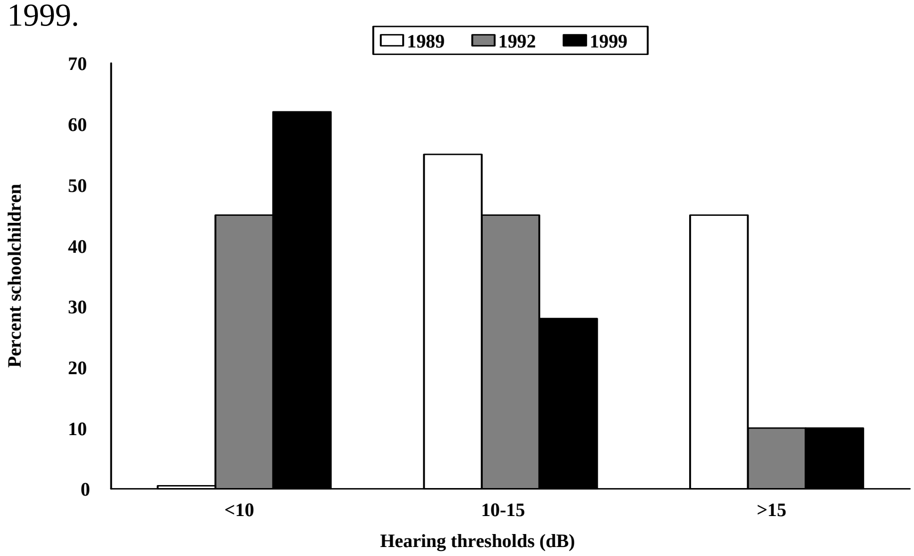

Fig. 11. Hearing thresholds in schoolchildren before intervention (1989), 3 years after iodized oil injection (1992) and 7 years following iodized salt consumption (1999)

Following national monitoring programs in 1996 and 2001, it was concluded that the I.R. Iran conducts an optimal sustainable programme for control of IDD. The I.R. Iran carries the following programmatic indicators:

a) An effective and functional national body (IDD Nation Committee), responsible to the government for the elimination of IDD, has been active since 1989. This multidisciplinary council relates to relevant fields of nutrition, medicine, industry and education etc. b) Political commitment to universal salt iodization and the elimination of IDD was made in 1989 and is sustainable. c) A responsible executive officer has been appointed for IDD control programme, since 1990. d) Universal salt iodization has been legalized since 1992. Ministry of Industry has announced that salt factories should produce only iodized salt for household use. e) I.R. Iran has been committed to assessment and reassessment of progress made in the elimination of IDD, with access to laboratories able to provide data on salt and urinary iodine. f) Public education Programmes and social mobilization on the importance of IDD and the consumption of iodized salt have been vigorously followed in the last 11 years. These programmes have been integrated into the health network, with full participation of Behvarz (rural health workers) in education and monitoring. g) Regular data on salt iodine at factory (daily), retail (monthly) and household levels (yearly) are collected in each province and analyzed by the National Committee. h) Regular laboratory data on urinary iodine in school-aged children with appropriate sampling for higher risk areas in each province on a yearly basis and nationally once every 5 years. i) Co-operation from the salt industry in maintenance of quality control is excellent, supervised by the IDD executive officer. j) Database with recording of results and regular monitoring procedures, particularly for salt iodine and urinary iodine is available in the Ministry of Health (MOH). Neonatal TSH has been measured in Tehran in 1989 and 1997-1999. This shows significant decrease in transient hyperthyrotropinemia and recall rate.

The I.R. IRAN therefore, fulfills all 10 programmatic indicators set by WHO/UNICEF/ICCIDD (1). According to these criteria, I.R. Iran appears to have achieved a sustainable IDD control programme since 1996. This has been recognized by WHO-EMRO in the year 2000 (18). Monitoring of IDD control programme is planned every 5 years to evaluate the sustainability of the programme.

In 2005, the world failed to meet the goal of elimination of iodine deficiency, presenting a dismal picture regarding the lack of success in many countries in development and sustainability of an efficient monitoring system; field evaluation of iodine levels in factories, retailers, sellers and households is not done regularly and when it is, it is mostly quantitative and lacks adequate program evaluation. In many countries the supporting laboratory network is not in place and urinary iodine measurement is available only in a few countries afflicted by IDD. Overall the national capacity for sustenance of IDD control is still fragile in such countries.

The afore-mentioned shortcomings do not diminish the unprecedented accomplishments in the control of IDD, as a non-communicable nutrition disease in the past 15 years. To quote Azizi (19), “they should remind us that USI, although achieved in the majority of countries where iodine deficiency is a major public health problem, is not sufficient by itself to eliminate IDD. The main objective should focus on suitable effective and sustainable iodine nutrition rather than on IDD control. Greater attention needs to be paid to the development of an efficient, sustainable and operating monitoring system in each country.”

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