ORIGINAL ARTICLE

Iodine Deficiency Disorders in the South of Iran during 1989-2012: A Surveillance System Report

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Abstract

Background: Iodine deficiency disorders (IDD) have been recognized as a major public health problem worldwide. Consequences of IDD include goiter, hypothyroidism, and intellectual disability followed by retarded growth and development of the brain. This report aimed to determine the state of IDD in Fars province, south of Iran.

Methods: In this study, we gathered data from all scientific papers, published and unpublished reports of IDD surveillance system, results of IDD-related surveys and all data from the center for disease control (CDC) at provincial and national levels during 1989-2012. Five main IDD indices are summarized, interpreted, and then organized in graphs and tables.

Resuits: After formation of national committee of IDD followed by launching of extensive iodine delivery, most of IDD indices have improved. The percentage of iodized salt intake has increased from 0 to near 100%, and that of salt with adequate amount of iodine has increased to 94.5%. Median of urinary iodine concentration (UIC) has always been higher than the acceptable value (≥100 µg/L) and 68% of people had a mean of UIC ≥100 µg/L. The percentage of TSH (Thyroid-Stimulating Hormone) >5 mU/L in the screened newborns has persistently been less than 1% during 2005-11. Prevalence of goiter has declined from 68% in 1989 to 1.3% in 2007.

Conclusion: Present findings address those efforts to combat iodine deficiency which were effective. According to the small sample size and also the fact that some data have been derived at the national level, we recommend that a comprehensive population-based survey should be carried out with sufficient sample size to achieve information with high accuracy and precision.

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Introduction

Iodine is an essential element for human survival since it is essential for making thyroid hormones. Iodine is also required for growth and development of the brain, even before birth. Iodine deficiency, through disrupting the brain development, builds iodine deficiency disorders. Iodine deficiency reduces the average IQ of people as much as 13.5, and increase the prevalence of goiter and other thyroid disorders in the population. Iodine deficiency during pregnancy can cause severe cretinism, abortion and stillbirth.[1] Brain damage due to iodine deficiency is easily preventable.[2] More than 2 billion people worldwide in 1990 were at risk of IDD. According to the reports of World Health Organization (WHO) and United Nations Children's Fund (UNICEF), more than 30% of school-aged children (260 million) suffer from insufficient iodine intake.[1]

For the first time in the world, iodized salt has been used to prevent goiter in 1924 by Kimball, Michigan in America, where the prevalence of goiter was estimated 38.6%. After distribution and consumption of iodized salt in that state, the prevalence of goiter dropped to about 9% in 1929.[3] This program continued, so the iodized salt was used in many parts of the world in 2008 and according to UNICEF's report, the percentage of iodized salt consumption in developing countries has raised to nearly 70% of the countries, Figure 1.[1]

In spite of over 30 years of legislation of iodized salt production, however, 38 million infants are at risk of IDD worldwide. Most of them are living in South Asia and Africa, Figure 2.[1,4]

In 1960s, Iran was known as one of the iodine deficiency areas. Emami et al study conducted in 1969 showed that goiter, as a manifestation of iodine deficiency, was endemic with a range of 10 to 60% in many provinces in Iran.[5] This means that a population of over 20 million people were at risk of IDD.[6] Goiter was so prevalent that a study conducted in Kohgilooye and Boyrahmad province in 1985 showed that the prevalence of goiter in some areas of the province has reached 100%.[7] However, until 1983 no any decision was taken to identify the magnitude of IDD for its prevention and control issues.[8] In 1990, by formation of national committee of IDD in Iran, universal Iodized supplementation, especially iodized salt, was prioritized. With continuation of this policy in later years, the prevention of IDD in the country was realized. After this, Iran has obtained the highest percentage of households consuming iodized salt, Figure 3.[1] Only after two decades of hard work in this way, Iran satisfied the WHO criteria against IDD in the late 2000s and reported that Iran belonged to areas with no iodine deficiency in the Middle East.[9] After extensive preparation and distribution of iodized salt in the country, the WHO declared that the IDD parameters have reached an acceptable value.[10]

Since inadequate iodine in the soil and water is the main cause of iodine deficiency, the IDD can occur whenever iodine supply policy is stopped. The available evidence indicates that in countries where iodine delivery was disrupted, IDD can return with lag.[11,12] Loss of a clear, organized and constant evaluation and monitoring of receipt and consumption of dietary iodine intake could make us unable to combat IDD.[13,14] Thus, periodic and regular monitoring of the median of UIC should be done to ensure iodine delivery sufficiency among population.[15]

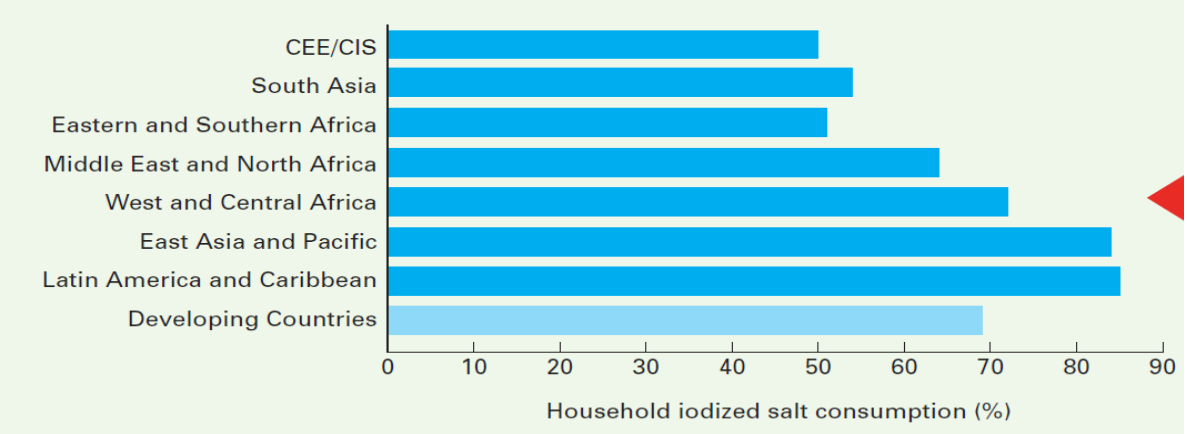

Figure 1: Consumption of iodized salt by households in different regions of the world, 2001-2006.

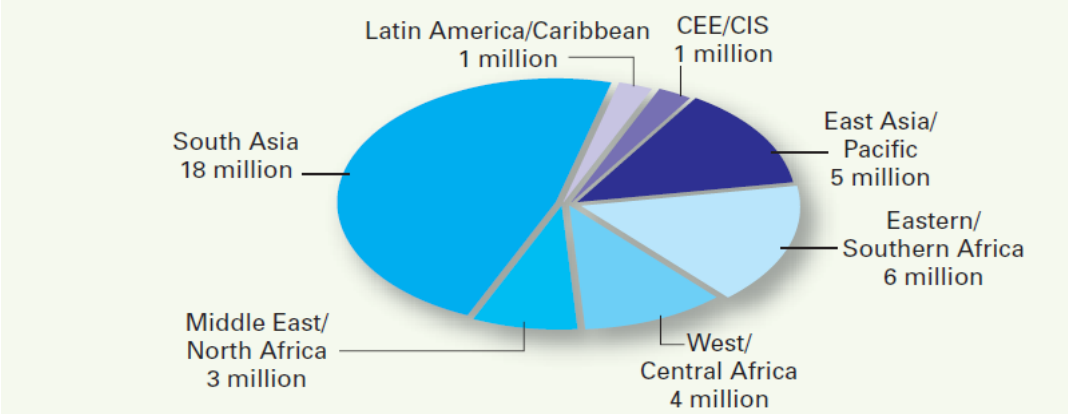

Figure 2: Distribution of infants at risk of IDD in different regions of the world, 2001-06.

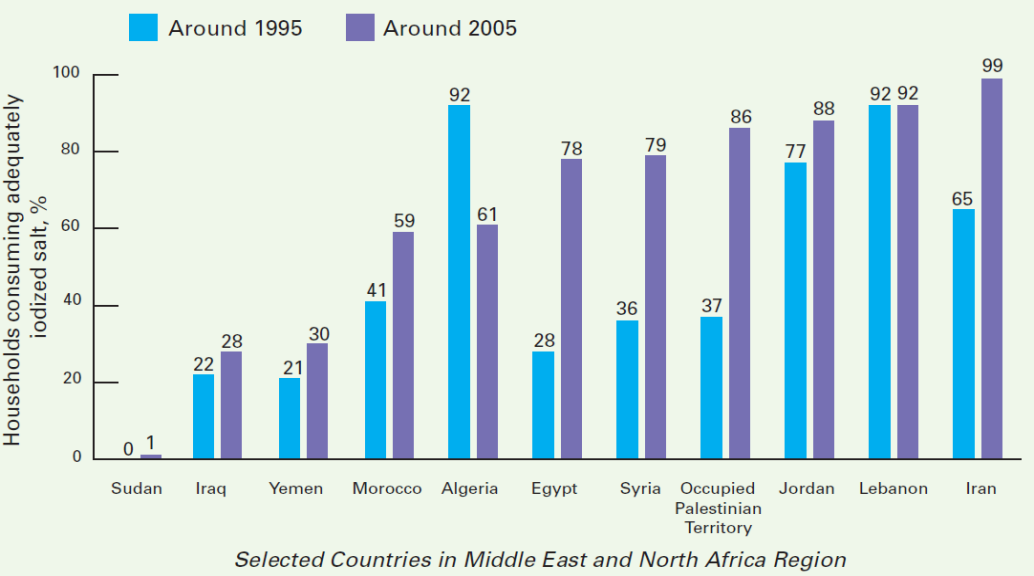

Figure 3: Percentage of households consuming iodized salt in the Middle East and North Africa countries, in 1995 and 2005.

To investigate and monitor any program in health care system, the most important step is preparation and presentation of the report of monitoring and evaluation of surveillance system.

Periodic reports are an integral component of any surveillance system that should be prepared, printed and distributed by authorities periodically.[16,17] National IDD control surveillance system guarantees the implementation of IDD and measures compliance with the standards of instruction.[18]

Therefore, this report aimed to reveal surveillance effectiveness of prevention and control of iodine deficiency disorders in Fars province, south of Iran, with a population of more than 4.5 million people and an area of over 122,000 square kilometers, during 1989-2011.

Methods

To prepare this report, we included all IDD information in 2 parts: first, secondary data including scientific papers in Medline, Iran Medex and periodic reports published by the Ministry of Health and second, CDC reports that were annually distributed by health vice-chancellors of Shiraz University of Medical Sciences (SUMS). Indices of evaluation of IDD prevention and control program include the following:[1,18,19]

- **Prevalence of Goiter:** The term goiter refers to the abnormal enlargement of the thyroid gland. Goiter prevalence is measured in two ways: physical examination and ultrasound. Ultrasound method is feasible and accurate, but because it is costly, it is not used in many countries. However, clinical examination due to the high accuracy, low cost and availability is used as a first step to investigate the prevalence of goiter in most countries. In this report, to estimate goiter prevalence, clinical examination was used. To determine the prevalence of goiter, the age group of 8-10 year old students was selected because they are more accessible, belong to the higher risk group and also are representative of the entire population.[18,19] All students were examined by skilled and trained physicians. Clinical examination was done at a room with enough light. The subject to be examined stood in front of the examiner, who looked carefully at the neck for any sign of visible thyroid enlargement. The subject was then asked to look up and fully extend the neck. This pushed the thyroid forward and made any enlargement more obvious. Finally, the examiners palpated the thyroid by gently sliding their own thumb along the side of the trachea (wind-pipe) between the cricoid cartilage and the top of the sternum. Both sides of the trachea were checked. The size and consistency of the thyroid gland were carefully noted. To check and reduce variation between examiners, 5% of the subjects were re-examined by another examiner under supervision of a skillful physician.[20] Goiters are classified into 3 grades by WHO as shown in Table 1:[21]

Table 1: Simplified classification of goiter by palpation

Grade	Finding in clinical examination
0	This is when the goiter is not palpable or visible even when the neck is extended.
1	When the goiter is palpable
1A	Goiter detected on palpation
1B	Goiter palpable and visible when neck extended
2	Goiter visible when neck is in the normal position
3	Large goiter visible from distance

To estimate the prevalence of goiter, the total samples were 1200 students (600 samples in urban and 600 samples in rural areas) and selected from male and female school children in grade two to four elementary schools by cluster random sampling.

- **Median of urinary iodine concentration:** Some of the absorbed iodine is excreted in the urine. Thus,

an important index for measuring iodine delivery and iodine sufficiency as well as a simple method for monitoring the iodine status among the population is the median of UIC.[22] There are various methods for measuring iodine in the urine, but the validity and reliability, speed, and technical requirements, cost and safety are characteristics that help us to choose the method. According to the mentioned properties, the selected method for estimation of iodine in the urine is *ammonium persulfate*. IDD classification based on urinary iodine is shown in Table 2:[18]

To estimate the median of UIC, 240 school children aged 8 to 10 years old studying in 48 schools were randomly selected from each cluster. Biochemical test was taken with acid digestion method at 10 ml urine sample.[23]

- **The amount of iodine in salt:** Adding iodine to salt is safe, cost-effective and tolerable. The cost of adding iodine to salt is so low and negligible. Adding iodine to salt has 3 phases of decision phase, implementation phase and phase of continuity in salt iodinization. In phase 3, to monitor sufficient iodine in salt, we must periodically assess the amount of iodine in salt. The ideal goal is that about 90 to 100% of household salt should have iodine.[18,19] According to literature recommendations, for most of countries iodine ≥20 ppm[18] and for Iran iodine ≥ 15 ppm[19] have been considered. To determine the amount of iodine in salt, it was assessed annually with iodometry kit.[1]

- **Percentage of households that consume iodized salt:** The purpose is that more than 90% of households should consume iodized salt.[18,19]

- **TSH and T4:** Ordinarily, due to its high cost, hormonal assay is not used for epidemiological studies and population surveys. In areas with moderate to severe iodine deficiency, TSH and T4 measurements identify hypothyroidism. Nevertheless, measuring the hormone is used to show long term effect of iodine delivery.[18] In countries that implement screening program in infants for congenital hypothyroidism, if the percentage of TSH>5 mU/L is more than 5%, it indicates iodine deficiency in that region.[19] However, some of the researchers indicate if the percentage of TSH>5 mU/L in infants is less than 3%, it indicates the adequacy of iodine intake.[24]

Results

Median of UIC in children aged 8 to 10 in 2001 to 2011 was measured; all values were greater than 100 micrograms per liter (acceptable and standard value), Figure 4.

Table 2: Epidemiological criteria for assessing iodine nutrition based on median of UIC of school-age children (≥6 years)

Median of urinary iodine (mU/L)	Iodine intake	Iodine status
<20	Insufficient	Severe iodine deficiency
20-49	Insufficient	Moderate iodine deficiency
50-99	Insufficient	Mild iodine deficiency
100-199	Adequate	Adequate iodine nutrition
200-299	Above requirements	Likely to provide adequate intake for pregnant/lactating women, but may pose a slight risk of more than adequate intake in the overall population
≥300	Excessive	Risk of adverse health consequences (iodine-induced hyperthyroidism, autoimmune thyroid diseases)

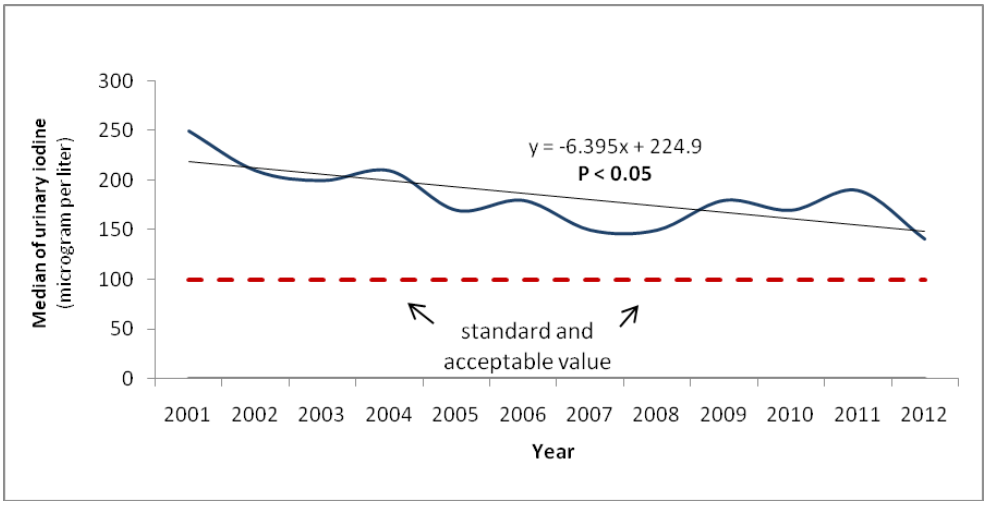

Figure 4: Median of UIC in schoolchildren aged 8 to 10 from 2001 to 2012.

The results of three national surveys in 1996, 2001 and 2007 showed that the median of UIC in 8 to 10 year old students in the province was higher than the national levels (Table 3).

Monitoring results in 2007 showed that the median of UIC for boys was higher than girls in Fars province.[25] (Table 4)

Likewise, that report also showed that 67.8% of pupils aged 8 to 10 had median UIC >100 µg/L, (Table 5).[25]

In other studies conducted in 1994 and 2004 among schoolchildren, it was shown that 64.3% in Shiraz and 40% in Marvdasht were goitrous. (Tables 6 and 7).[26,27]

However, a national study[1] showed that the prevalence of goiter by physical examination in children aged 8 to 10 has significantly declined to an acceptable level of 1.3% in 2007 (1% and 1.5% in urban and rural regions, respectively), Figure 5.[25,27,28]

Prevalence of goiter reached its lowest value (1.3%) in 2007; however, goiter prevalence was higher in girls than boys, Table 8.[25]

This study[1] also showed that 94.5% of household salt in Fars province was iodized, Table 9.

Table 3: Comparison of median of UIC (µg/L) at national and provincial levels

Year	1996	2001	2007	2012
Country	205	165	140	-
Fars Province	280	220	156	141

Table 4: Median of UIC (µg/L) in Fars province by sex and location, 2007.

Sex	Male	Female	Total
Location			
Urban	128.3	180.2	150
Rural	121.1	169.8	161.5
Total	124.7	174.5	159.4

Table 5: Distribution (%) of median of UIC (µg/L) among pupils 8-10 years old in Fars province, 2007.

Median of UIC	<50	50-100	>100
Location			
Urban	13.3	18.3	68.3
Rural	16.4	16.4	67.3
Total	14.8	17.4	67.8

Table 6: Prevalence (%) of goiter by clinical examination among pupils 6-10 years old in Shiraz, 1994.

Age	Number	Grade				Total prevalence
(Year)		0	1a	1b	2	
6	420	32.1	18.6	36.7	12.6	67.9
7	364	31.3	16.8	37.9	14	68.7
8	376	47.1	14.9	31.4	6.6	52.9
9	421	31.1	14	42.3	12.6	68.9
10	394	37.8	14.5	35.8	11.9	62.2
Total	1975	35.7	15.7	36.9	11.6	64.3

Table 7: Prevalence (%) of goiter by clinical examination among pupils 8-13 years old in Marvdasht, 2004.

Age	Number	Grade			Total prevalence
(Year)		0	1	2	
8	200	65	32.5	2.5	35
9	199	61.8	34.7	3.5	38.2
10	200	54.5	42	3.5	45.5
11	199	57.3	40.2	2.5	42.7
12	193	61.1	36.3	2.6	38.9
13	197	62.9	36	1.1	37.1
Total	1188	60.4	37	2.6	39.6

1 Data derived from national monitoring of IDD published by Iran's ministry of health, 2007.

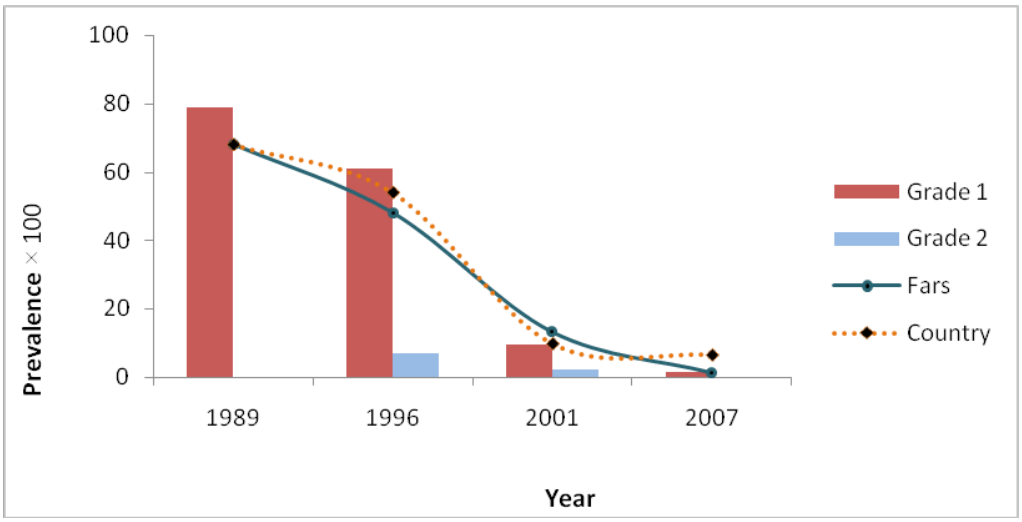

Figure 5: Prevalence of goiter in national and proventioal levels in selected years

Table 8: Prevalence (%) of goiter (both grades 1 and 2) among *pupils* 8-10 years old in Fars province, 2007.

Age	8	9	10	Total
Sex				
Girl	1.3	0.6	3.1	1.7
Boy	0.4	1.3	1.3	1
Total	0.8	1	2	1.3

Table 9: Indices of iodized salt intake in Fars province households, 2007

Index	Refined salt	Color changing by Kit	Amount of iodine in salt (ppm)				Quality of salt storage in house	
			<15	15-29	30-50	>50	Suitable	Unsuitable
Percentage (95% of CI)	98.3 (97–99.5)	94.5 (92.3–96.7)	0	71.4 (38–100)	94.5 (0–62)	0	94.5 (65.5–74.7)	94.5 (25.3–34.5)

Since 1989, after public education and iodizing salt intake, the percentage of iodized salt (≥15 ppm) in rural households has considerably increased in Fars province[2], Figure 6.

ANIS[3] survey conducted in urban and rural areas of Fars province in 2008 revealed that 98% of households were using iodized salt.

Congenial hypothyroidism screening program was launched in 2005 and has continued to now; in this period, 457,289 newborns were screened and 961 congenital hypothyroidism cases were diagnosed[4]. Percentage of TSH>5 mU/L in all these years was less than 5% according to national goal and even less than 3% according to WHO goal,[24] Figure 7. It should be noted that in all these years, median UIC was more than 100 micrograms per liter and nearly 100% of the households were using iodized salt.

Discussion

International Classification of Diseases introduces the IDD as one of the four main causes of developmental disorders in children in the world.[29] Until the decade of 1960, no scientific study has been conducted on iodine deficiency in Iran. Epidemiology of goiter, as one of the major indices of iodine deficiency, has been conducted for the first time by the National Institute of Nutrition in Iran in 1969.[5] In 1989, the national committee was formed to combat iodine deficiency disorders. The priority of the committee was iodine delivery to all households via iodine enrichment of salt intake.[1] Now this question arises that "what is the effect of implementation of these educational, nutritional, and cultural interventions?" To answer it, we collected all IDD-related scientific papers, published and unpublished reports in national or provincial level, and also from CDC and vital horoscope in the past 25 years. After extraction of their finding, we have depicted IDD status according to its indices in this report.

The results showed that after performing educational and interventional programs in 1989 and mandatory law of production of iodized salt for edible use in 1994,[19] production of iodized salt increased gradually and then more households were using iodized salt (≥15 ppm). Therefore, since 2001 onwards,

2 Date derived from rural vital horoscope in Fars province
3 Anthropometric and Nutrition Indicators Survey
4 Data were derived from a report of non-communicable department of health deputy of SUMS

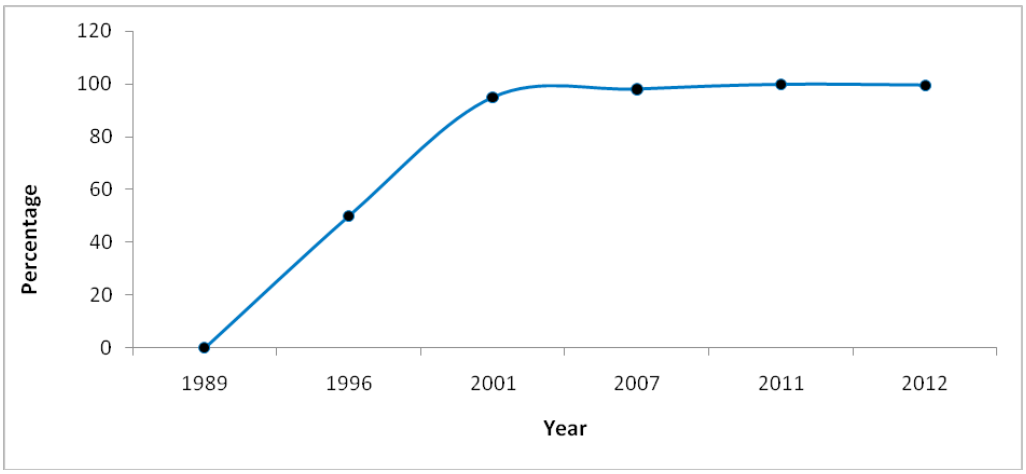

Figure 6: Percentage of households that have cosumed iodized salt in rural areas in Fars province, 1989-2012.

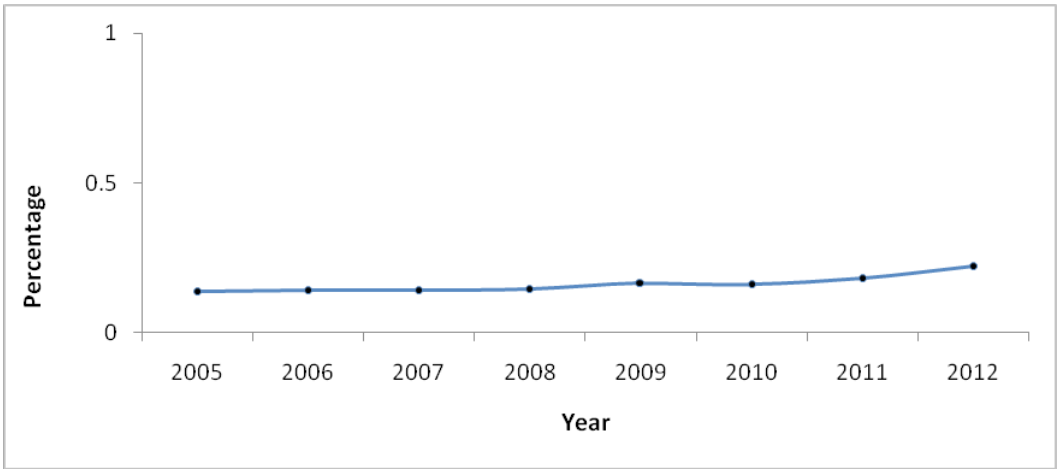

Figure 7: Percentage of TSH>5 mU/L in screened newborn in Fars province, 2005-12.

most households (over 95%) have used iodized salt, Figure 3. Iodized salt program has been considered as an important way to combat IDD.[1] Iodine enrichment of salt is considered as the lowest cost, easiest way and most effective method to fight against IDD.[1,18] National goal is that 90% of households use iodized salt.[19] This goal cannot be achieved except by good coordination and cooperation of industry sector and policy makers of public health. Availability and accessibility to iodized salt by households has increased in the last two decades in many countries and regions of the world.[1,2,30] Iran is one of the most successful countries in the region which has achieved the highest rank of the areas without iodine deficiency in the Middle East, Figure 3.[1,9] although many areas of the world are still at risk of iodine deficiency, Figure 8.[22]

Report of UNICEF in 2007 indicated that overall progress in iodized salt production has been declining during the past decades in the world. Now, global prevalence of goiter compared to 1993 has increased as much as 23%.[31] According to the latest report by the WHO in 2007, 31.5% of the students (286 million) and 2 billion people in the world (31%) had inadequate intake of iodine. 52.4% of the students in Europe, 48.8% in the Eastern Mediterranean, 22.7% in the West Pacific and 10.6% in America have not enough iodine intake.[32,33]

Measuring UIC, particularly in school-age children as representative of the general population, is considered as appropriate and acceptable outcome indices of iodine delivery. In fact, UIC indicates the desirability of iodine sufficiency in all stages of production, distribution and consumption of iodized salt in a community.[1,2] Figure 1 and Tables 3 and 4 show that the median of UIC in a last decade was more than the standard value (≥100 µg/L). National goal of IDD is that the percentage of people with UIC of more than 100 micrograms per liter reaches over 50%.[19] Table 5 shows that the UIC of more than 100 micrograms per liter was 65%.[25] New research shows that during 2003 to 2011 the number of countries with sufficient UIC has reduced from 54 to 32. In contrast, the number of countries that have had insufficient UIC has increased from 67 to 105. Nevertheless, some countries such as Malaysia and even New Zealand are suffering from inadequate iodine intake so the mean of UIC was 79 and 68, respectively.[34,35] With all the success in application of iodine delivery, still

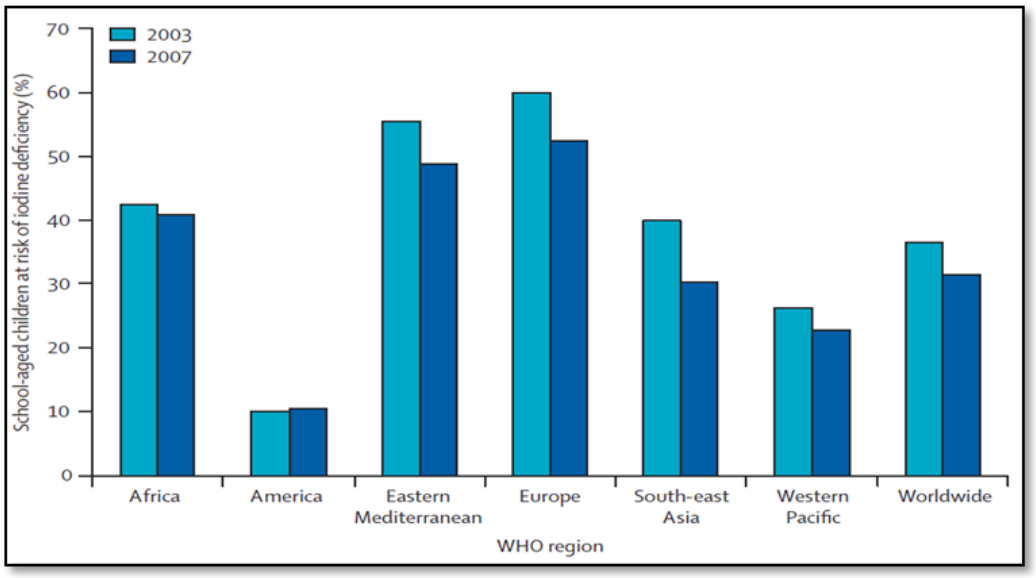

Figure 8: Prevalence (%) of iodine deficiency based on urinary iodine (<100 mU/L) among school-aged children in different WHO regions in 2003 and 2007.

nearly 260 million students worldwide, most of whom belong to the Southeast Asia and Africa, are suffering from insufficient iodine intake. However, global trend of goiter prevalence shows an improved trend.[1,36]

The prevalence of goiter is taken as an important method to assess the long-term iodine intake. The results of various studies indicate that since the past two decades the prevalence of goiter, based on clinical examination, among 8 to 10 year old students has decreased from 70% to 1.3% (1% in urban and 1.5% in rural areas).[25,26,28] Figure 5 shows the dramatic decrease in goiter prevalence; this means the success in national program on production and consumption of iodized salt has started in 1989 and continued till present. There is a close relationship between UIC and goiter so that an increase in UIC is accompanied by a decrease in prevalence of goiter.[19,37]

In countries where screening for congenital hypothyroidism in neonates has been done, percentage of TSH>5 mU/L is recognized as a key index of iodine deficiency. One of the objectives of iodine sufficiency is that the percentage of TSH>5 mU/L should be less than 5%.[1,19] Hypothyroidism screening has been launched in Fars province since 2005 and continued to now. In this period, the percentage of TSH>5 mU/L in infants was less than 5%, Figure 7. These values indicate success in iodine delivery.

Articles and data used in this report had some limitations. For example, some results of a national survey can just be assigned at the provincial level and cannot be generalized to each city or rural and urban communities singly. Data of consumption of iodized salt are obtained from vital horoscope in rural areas. Lack of data in the urban areas provided little information on IDD situation there. Another limitation of IDD surveillance system was lack of complete list of educational, cultural and nutritional interventions. It was better to record all interventions with all their details in a notebook or a file. Lack of systematic and periodic monitoring and evaluation of IDD surveillance system was another limitation. Failure to submit periodic reports, can not only confine the policy makers to have enough information about the status of IDD, but also make them unaware about the effects of all interventions.

In spite of neglecting some steps of surveillance system of IDD, however, all IDD control indices were improved in the last two decades. Success in national IDD control depends on continuation of iodine delivery sufficiency. Disregarding any component of the IDD program could result in failure to combat IDD. So, it has been seen in some countries with good iodine delivery that IDD has returned to their communities by negligence in a part of surveillance system.[11-14] Nowadays, in addition to iodizing salt, other methods such as fortification of bread with iodized salt and even enrichment of eggs with iodine could improve the median of UIC.[38,39] Therefore, exact implementation of all phases of surveillance system including data collection, analysis, interpretation, and preparation and publication of systematic reports should be considered as the cornerstone of our tasks. Finally, we recommend that a comprehensive survey should be done to achieve precise and accurate information.

Recommendation

- Many of the data are related to 2007 and new information is not available. So, it is recommended that a comprehensive survey with a sufficient sample size should be conducted in all cities of Fars province

in 2013. It is necessary to measure all IDD-related indices in that survey. The answer to the question of whether or not we are in the process of eliminating IDD depends on the availability of the mentioned indicators plus assurance of national multi-sector coalition, political commitment, legislation and supportive regulations on universal salt iodization, reporting of national program progress every three years, laboratories' ability to provide accurate data, public education and social mobilization, routine availability of data on salt iodine content at factory and home levels, and availability of population-based routine data.[19] If the result of that survey shows us that we are fully successful in achieving the surveillance system objectives, it is better to conduct such study every 3 years to monitor the IDD surveillance with the following objectives:

-Estimating goiter prevalence by both clinical examination and ultrasound (to assess the validity and reliability of clinical methods),

-Checking the amount of iodine in salt intake from factory to houses,

-Measuring UIC in schoolchildren aged 8 to 10 years, male and female, urban and rural areas,

-Assaying UIC in pregnant mothers as a vital index of IDD surveillance evaluation and iodine sufficiency,

-Adding congenital hypothyroidism screening data, such as thyroid TSH, as an important index in evaluating IDD surveillance system, and

-Evaluating the percentage of households in which iodized salt is consumed.

● Setting up a system for collecting data at various centers such as clinics, hospitals, laboratories, pharmacies and factories,

● Revising of surveillance data forms to be corrected for potential problems,Preparing and distributing surveillance system reports periodically, and

● Setting up a register center to record and maintain all the documents, including the details of executive tasks, raw data files, educational media, and articles in the same geographic area. In this center, systematic reports including the results of all monitoring and evaluation efforts (with strengths and weaknesses of interventions) should be available at all times.

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Conflict of Interest: None declared

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