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Review Article

Iodine Deficiency Disorders in I.R. Iran: Past, Present and Future

Delshad H and Azizi F*
Endocrine Research Center, Shahid Beheshti University of Medical Sciences, Iran

***Corresponding author:** Fereidoun Azizi, Professor of Internal Medicine and Endocrinology, Endocrine Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences Tehran, P.O. Box: 19395-4763, I.R. Iran

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Abstract

Background: Although several years ago, iodine deficiency was prevalent in Iran, implementation of universal salt iodization programs targeting the eradication of Iodine Deficiency Disorders (IDD) was very effective and the I.R. Iran, since 1996 has met all criteria for the sustainable elimination of IDD.

Methods: This is a narrative literature review extracting relevant English and Persian language articles reporting the prevalence of iodine deficiency and iodine nutrition status of different target populations in Iran over 30 years. Published all internal (SID, Iran doc, Iran medex and, Magiran) and international (Web of knowledge, Pubmed, SCOPUS) literature between1988-2018, were searched, using the following medical subject heading terms: Iodine, IDD (iodine deficiency disorders), UIC (urinary iodine concentration), Goiter, IQ (intelligence quotient), thyroid hormone, Iodine and pregnancy, Iodine and breast feeding, as well as Iodized salt.

Results: The first report of iodine deficiency, as a nutritional problem in Iran, dates back to 1968; however, prevention of IDD has not been implemented then. After the Islamic Revolution in 1978, the first nation-wide survey in 1988 revealed that all provinces of the country were suffering from endemic goiter. It was then recognized as a major health problem by Ministry of Health in 1984. In 1990, salt factories began production iodized salt and in 1996, the second national survey indicated that about 50% of school-aged children had goiter, and their median urinary iodine excretion was 205μg/L. In the 3rd national survey conducted in 2001, total goiter rate and median UIC were 9.8% and 165μg/L, respectively, the 4th national survey conducted in 2007, seventeen years after iodized salt consumption by Iranian households, showed that the total goiter rate had decreased significantly to 5.7% and median urinary iodine was 145μg/L. In our last, the 5th national survey, conducted in 2013, all school-aged children showed adequate UIC, their median UIC being 161μg/L. The 1st national survey of iodine status and thyroid function of pregnant women in 2014, showed UIC of pregnant women to be 87μg/L, demonstrating that despite iodine sufficiency of school-aged children in Iran, iodine intake of pregnant women were inadequate. This was followed by implementation of the iodine supplementation program in pregnant women in 2017.

Conclusion: Since 1989, IDD has been accepted as a priority health problem in Iran. Production, distribution and consumption of iodized salt was begun in 1990. The first law requiring mandatory iodination of all salts for households use was passed in 1994, and in 2000 Iran was declared IDD free, confirming that well designed programmatic steps and mandatory iodized salt consumption are essential for achievement of a successful iodine deficiency control program.

Keywords: Iodine; UIC; Iodine deficiency disorders; Goiter; Iran

Introduction

As an essential micronutrient, iodine is necessary for human life. Iodine plays a major role in thyroid hormone synthesis, which is vital for body growth, neurologic development, and reproductive function during the different stages of life [1]. Iodine deficiency affects the physical and mental development of millions of people worldwide and is the main cause of preventable mental retardation [2]. The various disturbances resulting from inadequate iodine intake are collectively known as Iodine Deficiency Disorders (IDDs), a term introduced by Basil Hetzel in 1983 [3]. Salt iodination is a simple and feasible iodine supplementation [4,5] for control and elimination of IDD, and since 1960 remarkable progress has been documented in this field. Joint efforts by international agencies worldwide resulted in the achievement of iodine sufficiency by the year 2005; however many countries, even industrialized ones, are still iodine deficient. In 1990, just a handful of countries were considered to be iodine sufficient, whereas today, 70% of the world's population are consuming adequate iodized salt [6]. During the past decade the number of iodine deficient countries has decreased from 54 to 30, while the

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iodine sufficient ones have increased from 67 to 112; the number of those with excessive iodine intake has increased from 5 to 10. Although worldwide 90% of households consume adequately iodized salt, unfortunately consumption is still below 50% in 39 countries and 29.8% of school age children (246 million) worldwide are estimated to have insufficient iodine intake [7–9].

The normal content of body iodine is only 15-20mg and exogenous sources of iodine are needed to maintain normal levels of body iodine [10]. Iodine is efficiently absorbed from the intestine, while the thyroid gland takes up only 10% of the total iodine. In the chronic iodine deficiency state, the thyroid gland increases its uptake to 80% [11]. The primary source of iodine for the fetus is maternal iodine, which crosses the placenta and provides this essential nutrient to the fetus. In pregnant and lactating mothers iodine ingested is concentrated in their mammary glands, and approximately 40%-45% of the iodine ingested by mother appears in their breast milk [12,13]. Urinary iodine concentration (μg/L) is a useful indicator of recent iodine intake. According to WHO recommendations, urinary iodine excretions ranging between 100-199μg/L in school-aged children as well as adults, and levels between 150-249μg/L in pregnant women are considered adequate, based these recommendations, the prevalence of goiter should be less than 5% in iodine sufficient areas [14]. Since the body does not produce iodine, it has to rely on the diet for sufficient iodine intake, and the main cause of iodine deficiency worldwide is low iodine content in the diet. Universal salt iodization is a safe, cost-effective and sustainable strategy to provide adequate iodine for the body. It was recommended by the World Health Organization (WHO) and the United Nations Children's Fund (UNICEF) in 1994 to ensure sufficient intake of iodine by all individuals.

Three decades ago, moderate to severe iodine deficiency in the form of endemic goiter, retarded brain and mental development and cretinism were common in many parts of Iran [15,16]. The first report of IDD in Iran dates back to 1968 [17], although it was not recognized as a public health problem until 1980. The National Iranian Committee for Control of IDD was established in the Ministry of Health and Medical Education in 1989, this committee recommended universal salt iodination as the main sustainable program to be implemented for the prevention of iodine deficiency. This measure eventually led to the successful control and elimination of IDD in the country, based on which, the IR Iran declared to be an iodine-sufficient country by the WHO Eastern Mediterranean Regional Office in 2000 [18]. The aim of this narrative literature review is to review the data collection, policy making, programing, execution and monitoring of iodine nutrition in the I.R. Iran in the last 40 years after the Islamic Revolution and to gather and facilitate valuable background data in this field for future studies.

Methodology

This is a narrative literature review with an iterative approach in extracting relevant literature on the national control program for prevention and elimination of iodine deficiency disorders in the I.R. Iran. Search was restricted to literature sources in English and Persian published from 1988- 2018. Documented (SID, Iran doc, Iran medex and, Magiran) and international (Web of knowledge, Pubmed, SCOPUS) studies were searched to identify published and unpublished/in-progress studies, references, and citations of articles of interest using the following medical subject heading terms: Iodine, IDD (iodine deficiency disorders), UIC (urinary iodine concentration), Goiter, iodine deficiency among school children, national iodine deficiency disorders control program, IQ (intelligence quotient), thyroid hormone, Iodine and pregnancy, Iodine and breast feeding, as well as Iodized salt, reporting the prevalence of iodine deficiency and iodine nutrition status of different target populations in Iran over 30 years. A systematic search of pertinent journals was also undertaken. Articles related to the prevalence of IDD in different regions of Iran before and after mandatory salt iodization were included in this study.

Background of iodine nutrition in iran

The I.R. Iran was already considered to be among the countries most severely affected by iodine deficiency and endemic goiter was prevalent in most parts of the country. The first study of iodine nutrition in the country in 1968, reported prevalence of goiter ranging between 10 to 60% [17]; yet it was not 15 years later that this nutritional problem was recognized as a public health problem. Investigators of Endocrine Research Center and Food Technology and Nutrition Research Institute of Shahid Beheshti University of Medical Sciences and other investigators of the country conducted a few research projects in some provinces between 1983-84, these studies indicated that goiter was hyper-endemic and many subjects had low UIC. The first of these studies conducted in Shahryar, 35km south west of Tehran, reported presence of goiter in 54% of boys and 66% of girls, aged 6-18 years [19]; this group conducted another study in the East of Tehran in 1983, and showed that 68% of girls and 71% of boys were suffering from goiter [20]. The effects of iodine deficiency on various body systems were examined by a few studies between 1987-1989 in Tehran and some villages (Kiga, Keshar and Randan) located in the northwest of Tehran [21-25]. The apparently normal subjects residing in areas of iodine deficiency was found to have mild to moderate growth and physical retardation, neurological, intellectual, auditory and psychomotor disturbances. Physical growth retardation, prevalence of goiter and severity of hypothyroidism were higher in school children of Kiga than in Keshar, Randan and Tehran. School aged children in Kiga and Keshar had smaller head circumferences than Tehranian school children. Fifty percent of children in Kiga had pyramidal signs and lower IQ score which were more frequent than children of Keshar and Tehran. Psychomotor age was 1.7 years and 1.4 years lower than chronological age in Kiga and Keshar, respectively. The correlation between serum TSH and grades of pyramidal signs was positive ($r=0.331$, $P<0.025$). In a survey conducted in KohKilloyeh Boyerahmad, a province in the south west of the country, the prevalence of goiter was reported to be 95% and 87% in women and men, respectively [26]. Many surveys by Rajabian et al. from Khorasan [27], Hedayati et al. from Rasht [28] and unpublished studies by Omrani et al. from Fars, Zahedi Asl et al. in Khozestan, and Amini et al. from Isfahan showed that the goiter was endemic or hyperendemic in all of these provinces. Taking these findings into consideration, the Iranian National Committee for Control of IDD (INCCI) was established by the Ministry of Health and Medical Education in 1988.

Control of IDD in iran

The INCCI identified iodine deficiency as a major health problem of the community in 1989 and initiated production, distribution, and

consumption of iodized salt in 1990. Until 1993 only 70% of urban and 50% of rural households were consuming iodized salt, and 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 households were consuming iodized salt. Following organization of this committee, the first national survey showed that visible goiter (grade 2) was endemic in all provinces and hyper-endemic in the capital cities of five. All subjects in this study had UIC less than 100μg/L and in many localities it was below 20μg/L [29]. In 1995, a study was conducted in Shahriar by Azizi et al. following 5 years of salt iodization [30]. In 1984, before iodine supplementation, the prevalence of goiter in this region was 50% and 70% in men and women, respectively and the median UIC of subjects was 76μg/L (47.5% had UIC between 20 to 50μg/L) but after iodine supplementation, goiter rate was 40% and 51% in men and women, respectively and their median UIC was 185μg/L (65% had UIC between 100 to 250μg/L).

The second national survey (1996) indicated that 40% of boys and 50% of girls had only palpable goiter (grade 1) and all of them had adequate UIC (>100μg/L) [31]. This survey showed that the IDD elimination program and consumption of iodized salt by Iranian households had been very effective. One decade after universal salt iodization, studies were conducted in different provinces to determine the effects of iodized salt in preventing iodine deficiency, and a survey of schoolchildren from Gorgan province, indicated that 26.4% of subjects had goiter, but their UIC was 190μg/L [32]. In another study by Rajabian et al. in Tabas (south of Khorasan province), the prevalence of goiter after 10 years consumption of iodized salt had decreased from 34% to 25% [33]; two other studies also reported improved hearing thresholds and IQ scores of school children in the villages of Kiga and Randan [34,35]. In the year 2000, another study was conducted in Kiga, in which 212 school children from a severe iodine deficient area, before intervention (1989), 3 years after injection of 480 mg iodized oil (1992) and 7 years after consumption of iodized salt (1999), were selected. Compared to 1989, the goiter prevalence in 1992 and in 1999 was significantly lower and the increase in serum thyroxin was considerable. Of the school children, 44% had a mean hearing threshold of 15.8±5.9 Db, before iodine supplementation, whereas in 1989, 1992, and 1999, 46%, 11%, and 10% of school children had hearing thresholds > 15 Db, respectively [36]. The prevalence of goiter was studied 15 years after salt iodization in Isfahan province [37], and 19% of adults aged >20 years had goiter, of whom 18.6% had hypothyroidism and 33.5% had positive Thyroid Peroxidase Antibody (TPO Ab.) and median UIC of subjects was 180μg/L. The third national survey in 2001, indicated that only 9.8% of schoolchildren had grade 1 goiter and their median urinary iodine excretion was 165μg/L [38,39]. Seventeen years after universal salt iodization, the fourth national survey was conducted in 2007 [40,41]. The results of this survey showed that 98% of households in all provinces consume iodized salt and the prevalence of goiter was 5.7% in schoolchildren, all of whom had grade 1 goiter and their UIC was 145μg/L. The prevalence of goiter was significantly lower than previous studies and the UIC of schoolchildren was adequate (Figures 1 and 2). To prevent the recurrence of iodine deficiency in iodine-sufficient areas, every 5 years a surveillance program is mandatory [42], based on which the last national survey (the 5th) conducted in 2013, indicated that median UIC of school-aged children was

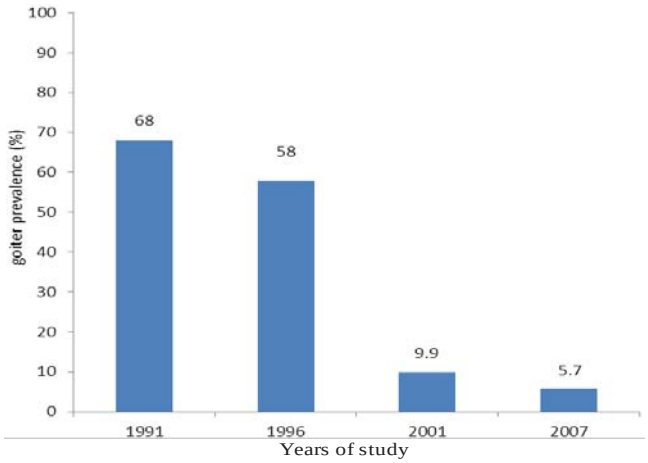

Figure 1: The trend of total goiter rate (%) before (1991) and after (1996, 2001, 2007) salt iodination in Iran.

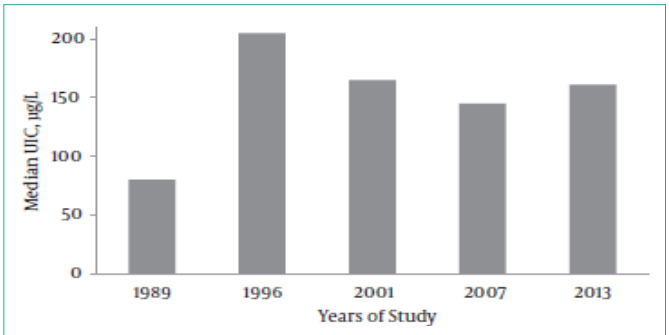

Figure 2: The median UIC of Iranian population before (1989) and after (1996 to 2013) IDD control program.

161μg/L. Household salt iodine content also was assayed for quality and quantity control. The coverage of iodized salt consumption among households was 98% in the country and mean±SD for salt iodine content was 38.6±10.1 ppm in households and 41.2±12.7ppm in factories [43].

In many studies, however adequate iodine intake of school-aged children and their median UIC do not accurately reflect the status of iodine nutrition in pregnant women. It has been suggested that even in an iodine-sufficient area, women during pregnancy and lactation may need iodine supplementation. Azizi et al. conducted a cross-sectional study between 1996 and 1998; this survey included 403 pregnant women from 4 cities, i.e Rasht, Ilam, Isfahan, and Tehran. Among 84% of pregnant women in Rasht, UIC was 200μg/L, although it ranged from 45 to 55μg/L in the other 3 cities. Altogether, in this study 51% of pregnant women had UIC below that recommended during pregnancy by scientific organizations [44]. Findings of other local studies have also demonstrated that more attention should be paid to iodine intake of pregnant women and lactating mothers in Iran. In a study of pregnant Tehranian women, Ainy et al. assessed inter-trimester and seasonal variations in Urinary Iodine Concentration (UIC) [45]; and found no seasonal fluctuations during pregnancy in median UIC, which was 193 (19-840), 159 (16-640), and 141 (16-400) μg/L in the 1st, 2nd, and 3rd trimesters, respectively ($P < 0.0001$) and more women had UIC < 150μg/L in the 2nd and 3rd *vs*. the

1st trimester of pregnancy.

Based on recent publications on iodine status of pregnant women over a few countries in the world which indicated mild to moderate iodine deficiency in this target group [46-53], in 2014 we organized the 1st national survey for assessing iodine intake and thyroid function of pregnant women in 10 provinces of the country [54], median UIC of subjects was 87.3μg/L, being 92.1, 86.0, and 76.8μg/L, in the 3 trimesters of pregnancy, respectively; 9% of these women had elevated serum TSH (6.6% subclinical, 2.4% overt hypothyroidism), 0.6% had low serum TSH, and positive TPO-Ab was found in 7.6 %. Results of this study, showed that despite iodine sufficiency of school children in Iran, pregnant women are suffering from moderate iodine deficiency. In 2017 this was followed by implementation of iodine supplement program in all pregnant women of the country and currently a national survey is examining the effects of this program on the UICs of this target group.

During pregnancy and lactation, thyroxin and iodine are transferred to the fetus and neonate, therefore pregnant women and lactating mothers need more iodine to compensate this requirement [55-57]. In iodine sufficient areas, pregnant women adjust their thyroidal iodine uptake to meet the increased iodine requirement for thyroid hormone production, whereas in iodine deficient regions, such adaptive mechanisms may fail to maintain adequate iodine stores [58,59]. Recently, it has been suggested that iodine intake during pregnancy is insufficient, even in the areas that had been iodine sufficient for several decades [60-63]. Accordingly, the American Thyroid Association (ATA) recommends that all women receive at least 150μg iodine daily as dietary supplements [64]. In keeping with recent guidelines of both the ATA [65] and the Endocrine Society [66], all pregnant and breastfeeding women need a daily intake of 250μg iodine, both in iodine-deficient and iodine-sufficient areas.

Conclusion

Three decades ago the I.R. Iran was included among the countries most severely affected by iodine deficiency. The first law requiring mandatory iodination of all salts for household use was passed in 1994. National surveys in the following years indicated that more than 95% of the households were consuming iodized salt. In 1996 in the second national survey conducted 7 years after the initiation of iodized salt production, 2-years following mandatory iodized salt consumption, the majority of schoolchildren had small goiters of grade 1 and median urinary iodine excretion was within adequate range in schoolchildren of all provinces. The third, fourth and fifth national survey were conducted every 5 years since year 2000 and the results indicated sustainable iodine sufficiency of Iranian schoolchildren. It is estimated that during first 20 years of proper iodine nutrition in the I.R. Iran, 20 million goiters have been prevented, 60 million points have been added to the IQ of children and adolescents and 16 billion Euro has been saved in health expenditure.

An excellent sustainable and well-monitored iodine deficiency control program has been implemented by the I.R. Iran. Determination of median UIC in school children and the monitoring of the quality of salt are vital for the continuing success of iodine sufficiency programs. However despite adequate iodine intakes of school children, Iranian pregnant women are suffering from moderate iodine deficiency for which iodine supplementation in this group has been initiated in 2017.

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