



Epidemiology

Monitoring of salt iodisation programme in Iran; Health outcomes, shortages and perspective



Hamid Reza Shamsollahi^a, Maryam Nadarloo^a, Noushin Rastkari^b, Mika Sillanpää^{d,e},
Mahmood Yousefi^a, Hasan Pasalari^c, Ramin Nabizadeh^{a,b,f,*}

^a Department of Environmental Health Engineering, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran

^b Center for Air Pollution Research (CAPR), Institute for Environmental Research (IER), Tehran University of Medical Sciences, Tehran, Iran

^c Department of Environmental Health Engineering, School of Public Health, Iran University of Medical Sciences, Tehran, Iran

^d Laboratory of Green Chemistry, School of Engineering Science, Lappeenranta University of Technology, Sammonkatu 12, Mikkeli, Finland

^e Department of Civil and Environmental Engineering, Florida International University, 10555, West Flagler Street, Miami, FL, United States

^f Centre for Water Quality Research (CWQI), Institute for Environmental Research (IER), Tehran University of Medical Sciences, Tehran, Iran

ARTICLE INFO

Keywords:

IDD
Salt iodisation
Iran
Goiter
Congenital hypothyroidism

ABSTRACT

Iodine deficiency disorders include a wide range of metabolic and nonmetabolic disorders including goiter. To control IDD, the World Health Organization and responsible agencies in countries established daily iodine uptake. Almost all the countries in the world provide the required iodine through salt iodisation. IDDs are not completely eradicable, so monitoring the salt iodisation programme is necessary for control of IDDs. In Iran, a salt iodisation programme was started in 1996. In this study, we took salt samples from all legally produced salt brands in Iran in 30 provinces and measured iodine concentration. The results of the monitoring programme for iodine concentration in schoolchildren's urine was used to compare accessibility to iodized salts and health outcomes. The results show that more than 80% of available salts have a suitable or acceptable concentration of iodine. Despite large variance in iodine concentration in available salt in some provinces, the median of iodine concentration in salts is within an acceptable range. Also, the urinary concentration of iodine (national median = 161) confirms that shortage of iodine intake is very low in Iran. The high rate of salt consumption of the Iranian people also has a significant effect on iodine uptake, but can lead to hyperthyroidism and hypertension that must be controlled.

1. Introduction

Iodine deficiency disorders (IDDs) are a spectrum of disorders that can occur from the foetal stage to adulthood and is a widespread cause of diseases from goiter to neurological and metabolic disorders [1,2]. They have been common and of epidemic proportions around the world in recent decades. The World Health Organization (WHO) has therefore recommended a 150 µg/day guideline value for daily uptake of iodine in adults to control and restrict IDD incidence [3,4]. Besides WHO, countries around the world have established national standards for daily iodine uptake.

To achieve national standards of iodine uptake, many countries have planned and started a salt iodisation programme as a health intervention to control IDD prevalence. As WHO mentioned, IDDs are not eradicable, so the main purpose of a salt iodisation programme is

sustainable control of IDDs and they can come back if no control and monitoring programme is available [4,5].

In Iran, the first national standard for iodine content of salt was passed in 1996 at 40 ± 10 µg/gram for the supply of a sufficient daily iodine intake. To achieve this purpose, a salt iodisation programme was started after this legislation. Total goiter prevalence (TGP) in schoolchildren was about 40% in boys and 50% in girls when the programme was started [6]. Monitoring the programme has shown a decreasing trend in the goiter prevalence rate up to the present day [7].

In addition to consumption behaviours, the availability of sufficient iodine is an important factor influencing the success of salt iodisation programmes [8], so measurement and monitoring of commercially available salt for consumers is necessary for the evaluation of access to sufficient iodine and also for determination of areas with insufficient access to iodine at standard levels for corrective action.

* Corresponding author at: Centre for Water Quality Research (CWQI), Institute for Environmental Research (IER), Tehran University of Medical Sciences, Tehran, Iran. Email: rnabuzadeh@tums.ac.ir (R. Nabizadeh)

E-mail address: rnabizadeh@tums.ac.ir (R. Nabizadeh).

<https://doi.org/10.1016/j.jtemb.2018.11.004>

Received 22 September 2018; Received in revised form 30 October 2018; Accepted 6 November 2018

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Therefore, in this study we tried to evaluate iodine content of commercial salt in Iran, to determine the access rate to iodised salt and to investigate the relationship between iodine availability and urine iodine concentration (UIC) in schoolchildren as a predictor for incidence of growth disorders and goiter. We also measured UIC in pregnant women as an indicator of sufficient iodine uptake, and compared their UIC by congenital hypothyroidism (CH) incidence rate to determine iodine intake sufficiency in them.

2. Methods and materials

2.1. Salt sampling

Legally produced commercial salts with a production licence from the *Food and Drug Affairs Deputy of the Iranian Ministry of Health and Medical Education* numbered 70 commercial brands. All of them were sampled from all 30 provinces of Iran. The sample size was 1450. The iodine measurement of each sample was done by a measurement procedure repeated three times. Production date, claimed iodine content and time from production date were also documented for data processing. Most of the commercial brands had local distribution in some provinces and a few had national distribution. The samplers endeavoured to ensure that the sampling procedure covered all available brands in each province. The sampling was done during the spring and summer of 2016.

2.2. Calibration of measurement method

The iodine concentration of samples was measured by the standard titration method with sodium thiosulfate 0.005 N. In brief, to calibrate the titration method, analytical-grade NaCl (MERK-Germany) including 50-grammes of NaCl in each volumetric flask was studied by adding 10, 20, 40 and 80 µg of potassium iodate, raised to 250 ml by Milli Q water. The standard samples were titrated by sodium thiosulphate 0.005 N. The real (theoretical) concentration of iodine content in samples against measured I₂ concentration in standard samples by the regression model showed a linear and strong relationship between them ($R^2 = 0.9995$).

2.3. Measurement of iodine in salt samples

After calibration of the measurement method, the samples were prepared for measurement in the following order. First, 50 g of samples were dissolved in 250 ml of distilled water. Then, 1 ml H₂SO₄ (2 N) and 5 ml KI (10% w/v) were added to the samples. The samples were kept in a dark place for 10 min after a mellow yellow colour appeared in the samples. The samples were then titrated by 0.005 N Na₂S₂O₃ until a light-yellow colour appeared. Some drops of lugol's iodine indicator were added to the samples and titration was continued until the yellow colour disappeared. The volume of Na₂S₂O₃ consumed during titration was used to calculate the iodine concentration according to Eq. (1):

$$I = ((V \times F \times 0.1058) / W) \times 1000 \quad (1)$$

I = iodine concentration (µg/kg)

V = consumed volume of Na₂S₂O₃ (mL)

F = modifying coefficient for Na₂S₂O₃ solution

W = weight of dry salt sample (g)

2.4. Measurement of Urine iodine concentration in children

As WHO/UNICEF/ICCIDD indicated, UIC is associated with iodine intake. WHO/UNICEF/ICCIDD stated that UIC in the range 100 to 199 µg/l is an indicator of optimum iodine intake, so to determine sufficient consumption and intake rate in Iranian children, UIC in schoolchildren and adolescents from 5 to 14 years old in all provinces in

Iran was measured. The participants were of both sexes and chosen by random sampling. The number of participants in each province was according to its population proportion. The total number of participants was 2362 of both sexes (53% male, 47% female). The sampling method was Cluster sampling because this study was a survey study and every province assumed as a cluster. The number of samples in each province was fit to the population. The urine sampling was conducted morning and afternoon three days consecutively. Iodine measurement was repeated three times for each sample. The iodine measurement was done using the *Sandell-Kolthoff* reaction. Briefly, 1 mL zinc sulfate solution (0.35 mol/L), 2 mL sodium hydroxide solution (2 mol/L) and about 60 mg potassium chlorate were added to 1 mL of each urine sample. After mixing, the sample was dried in 115 C° and then was annealed in furnace with a temperature program. The final dried samples were dissolved in deionized water and the clear supernatant was collected after centrifugation. Some acidic solutions were added to the 2 mL supernatant and the final mixture was stirred and warmed in hot-air oven (20 min). After cooling, the absorbance of all the samples were measured in 430 nm by spectrophotometer [9]. For validation of measured UIC by *Sandell-Kolthoff* reaction, iodine concentration in the 20 of urine samples were measured by both ICP-OES (Spectro Arcos, Germany) as gold standard and *Sandell-Kolthoff* reaction. The measured values of two methods were compared by intraclass correlation (ICC) to determine *Sandell-Kolthoff* reaction accuracy [10].

2.5. Urine iodine concentration in pregnant women

One of the important IDD is congenital hypothyroidism (CH). CH has two types: permanent and transient. As WHO/UNICEF/ICCIDD indicated, UIC less than 150 µg/L is an indicator of insufficient iodine intake and may lead to some disorders such as CH in neonates [11], so UIC in the optimum range (150-249 µg/L) can be an indicator of low risk of CH incidence [12]. We therefore measured UIC in pregnant women. A total of 344 pregnant women in all Iranian provinces were chosen for this study by cluster sampling pattern. All of them were in the first trimester of pregnancy and had not yet started iodine supplement consumption. UIC was measured using the *Sandell-Kolthoff* reaction. Urine samples were taken morning and afternoon, three days consecutively.

2.6. Data collection and statistic analysis

The required national data including goiter prevalence, incidence rate and salt consumption rate were extracted from the final reports of a national survey of goiter in Iran and also from the *National STEPS Non-communicable Disease Risk Factor Survey Report in Iran (2016)*. All statistics analysis and graphs were prepared by Microsoft Excel and R software (3.4.4), and geographical distribution plots were prepared by ArcGIS version 10.6.

3. Results

The concentration of iodine in salt samples from each province is summarised in [Table 1](#). The WHO recommendation for adequate iodine concentration in salt is 15–55 ppm, 30 ppm as optimum and < 15 ppm as an inadequate value. According to this classification, 80% of our salt samples were of optimum value, 12% inadequate and 8% were adequate. Furthermore, according to the *Iran Ministry of Health and Medical Education* standard (40 ± 10 ppm: suitable, 20–29 ppm: acceptable, < 20 ppm: unacceptable), 49% of samples had a suitable content of iodine, 33% were acceptable and 18% had an unacceptable content on iodine. The distribution of salt samples in each province according to the Iranian standard and WHO guideline is shown in [Figs. 1 and 2](#).

A comparison of iodine concentration in salt in all provinces by ANOVA analysis showed significant differences between Lorestan, southern Razavi, northern Khorasan, Gilan and western Azerbaijan and

Table 1
Mean of iodine concentration in salt samples in the 30 provinces of Iran.

Province	Mean	Variance	Iran Health Ministry standard			WHO/UNICEF/ICCID guideline	
			Suitable %	Acceptable %	Unacceptable %	Sufficient	Insufficient
Western Azerbaijan	27.09	236.25	41	18	41	68	32
Eastern Azerbaijan	30.11	173.31	75	25	0	100	0
Esfahan	29.3	324.56	50	25	25	75	25
Ardebil	31.1	101.78	62	25	13	94	6
Alborz	32.14	100.06	67	25	8	96	4
Elam	29.53	168.82	75	25	0	100	0
Bushehr	32.66	74.8	43	57	0	100	0
Tehran	30.3	71.49	58	30	12	88	12
Chahar mahal	33.45	110.68	50	50	0	100	1
South Khorasan	27.3	76.39	37	26	37	79	21
Razavi Khorasan	23.86	109.03	37	26	37	79	21
Northern Khorasan	32.27	256.14	40	20	40	90	10
Sistan	25.18	71.49	67	16	17	83	17
Semnan	36.26	97.96	78	11	11	89	11
Zanjan	32.08	155.84	46	27	27	87	13
Khuzestan	31.03	339.35	67	25	8	78	22
Fars	30.45	145.44	56	22	22	100	0
Qazvin	32.93	33.1	64	36	0	100	0
Qom	26.58	39.88	40	40	20	100	0
Kordestan	34.73	299.58	67	13	20	80	20
Kermanshah	31.3	187.3	64	27	9	91	9
Kerman	30.6	167.23	69	12	19	81	19
Gilan	28.85	87.9	53	17	30	84	16
Mazandaran	39.53	56.53	100	0	0	100	0
Markazi	36.95	168.47	57	24	19	91	9
Lorestan	46.36	688.27	45	22	33	67	33
Hamedan	29.91	193.23	72	14	14	86	14
Hormozgan	33.42	28.65	48	27	25	84	16
Yazd	29.7	69.87	72	9	19	81	19
Golestan	37.45	61.33	63	18	19	90	10

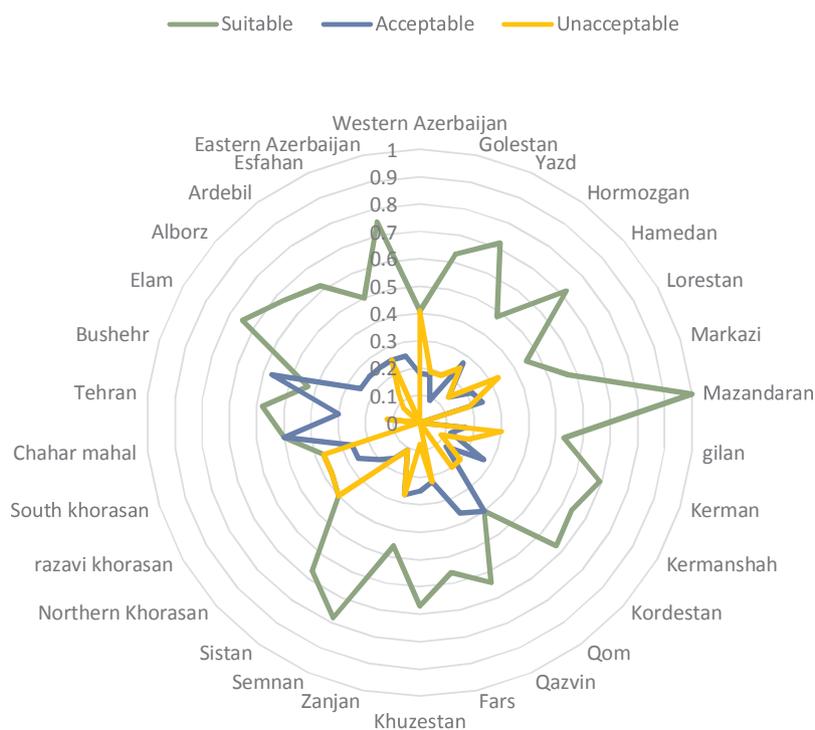


Fig. 1. Distribution of salt iodine content in salt samples in all provinces of Iran according to the Iranian standard.

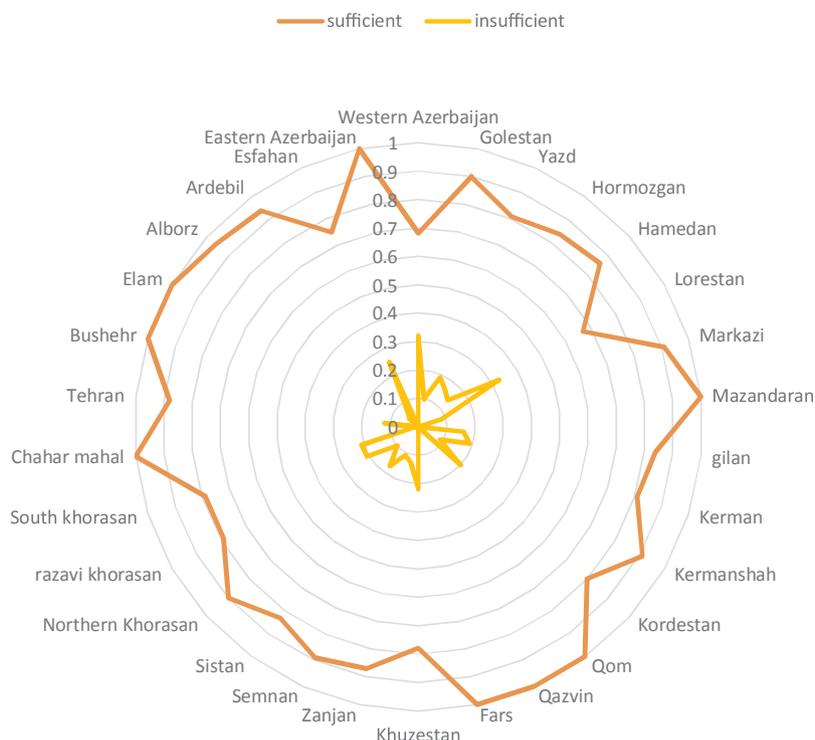


Fig. 2. Distribution of salt iodine content in salt samples in all provinces of Iran according to the WHO/UNICEF/ICCIDD guideline.

other provinces. (P value < 0.05). This indicates that the iodine concentration in these provinces is significantly lower than in the others.

The claimed iodine concentration on salt packages matched the value measured in the laboratory in 57% of the 1450 samples, in 9% it was more than was claimed and in 34% less. This could be because of fraud in production or other reasons, but regression analysis between time from the packaging date of the salt and differences between claimed and measured values showed a strong relationship ($R^2 = 0.98$).

Comparison of measured UIC by ICP-OES and Sandell-Kolthoff reaction was shown strong correlation between results of two methods ($ICC = 0.97$, $R^2 = 0.9973$). Thus, measured UIC in schoolchildren and pregnant women by Sandell-Kolthoff reaction was valid. The distribution of schoolchildren's UIC in three age groups is shown in Fig. 3. The distribution of pregnant women's UIC in all provinces is shown in Fig. 4.

4. Discussion

A comparison of mean salt iodine concentration in measured samples by Iranian standards shows that 20 provinces are in within a suitable range, 10 are in an acceptable range and none is in an unacceptable range. Distribution shows that, except for six provinces, all the others have commercial salt brands with insufficient iodine content. Figs. 1 and 2 show that distribution of salt with acceptable iodine content in all provinces is not the same. However, as shown in Table 1, in 24 provinces, more than 70% of available commercial salt has acceptable iodine concentration and, in the worst case in Iran, the accessibility is 60%. This rate, as stated by WHO/UNICEF/ICCIDD is about 70% globally [4].

Therefore, the access of the Iranian people to sufficient iodine is very good by global standards. The variation in salt iodine concentration in available commercial brands between different provinces is significant. The maximum value of variance was observed in Lorestan (Table 1). Despite a high value of variance there, about 70% of salt samples had acceptable iodine concentration.

Besides salt iodine content, another important factor in access sufficient iodine is iodine stability in salt. As several studies such as Diosady et al (1998) and Li et al (2010) have stated, there is strong

correlation between storage duration of salt in homes and the magnitude of differences between the claimed and measured values of salt iodine [13,14]. An initial solution for saving iodine content in salt could be packaging in smaller packages for faster consumption by families. As we found in this study, there is a direct relationship between the magnitude of difference between claimed and measured iodine concentration and time from production date. We were, however, unable to investigate this relationship in opened salt packages in homes. This suggests that future studies should involve storage duration.

Besides accessibility, an adequate consumption rate is an important factor in ensuring sufficient iodine intake. As shown in Fig. 3, UIC in children in all the provinces indicates sufficient iodine intake, although in some provinces there is surplus intake. ANOVA statistical analysis of UIC in children in each age group in various provinces shows significant differences between Hormozgan, Alborz, Hamedan, Zanjan, Qom, Kordestan and other provinces (P -Value > 0.05), but differences in UIC between three age groups in each province was not significant in any of the provinces (P -Value < 0.05). It shows that salt consumption behaviour changed not on account of age but of location and culture influence on salt consumption.

Iodine deficiency is one of the main risk factors in CH incidence, a major metabolic disorder in infancy. In the 1970s, CH screening programmes were begun around the world to determine CH incidence rate and define control programmes or monitoring of their efficiency. Several studies were done on CH incidence and prevalence rate around the world [15,16]. In 2003, the incidence rate in the United States was 1:1681, in Greek Cyprus it was 1:800 and in 2012 in France was 2.8:10,000 [17–19]. In Iran, in the latest published article about CH, Mehran et al reported the incidence rate as being 1:462 in live birth in 2011 [20]. Measurement of UIC in pregnant women is an essential for the control of the CH incidence rate and many countries try to measure this factor as an indicator for CH incidence. In this study, the median of UIC in pregnant women was $125 \mu\text{g.L}^{-1}$. Although, according to WHO/UNICEF/ICCIDD, this level of UIC is insufficient, it must be taken into account that this UIC values does not include iodine supplement usage, so the iodine uptake of pregnant women without iodine supplement is acceptable throughout Iran. In some provinces, UIC without

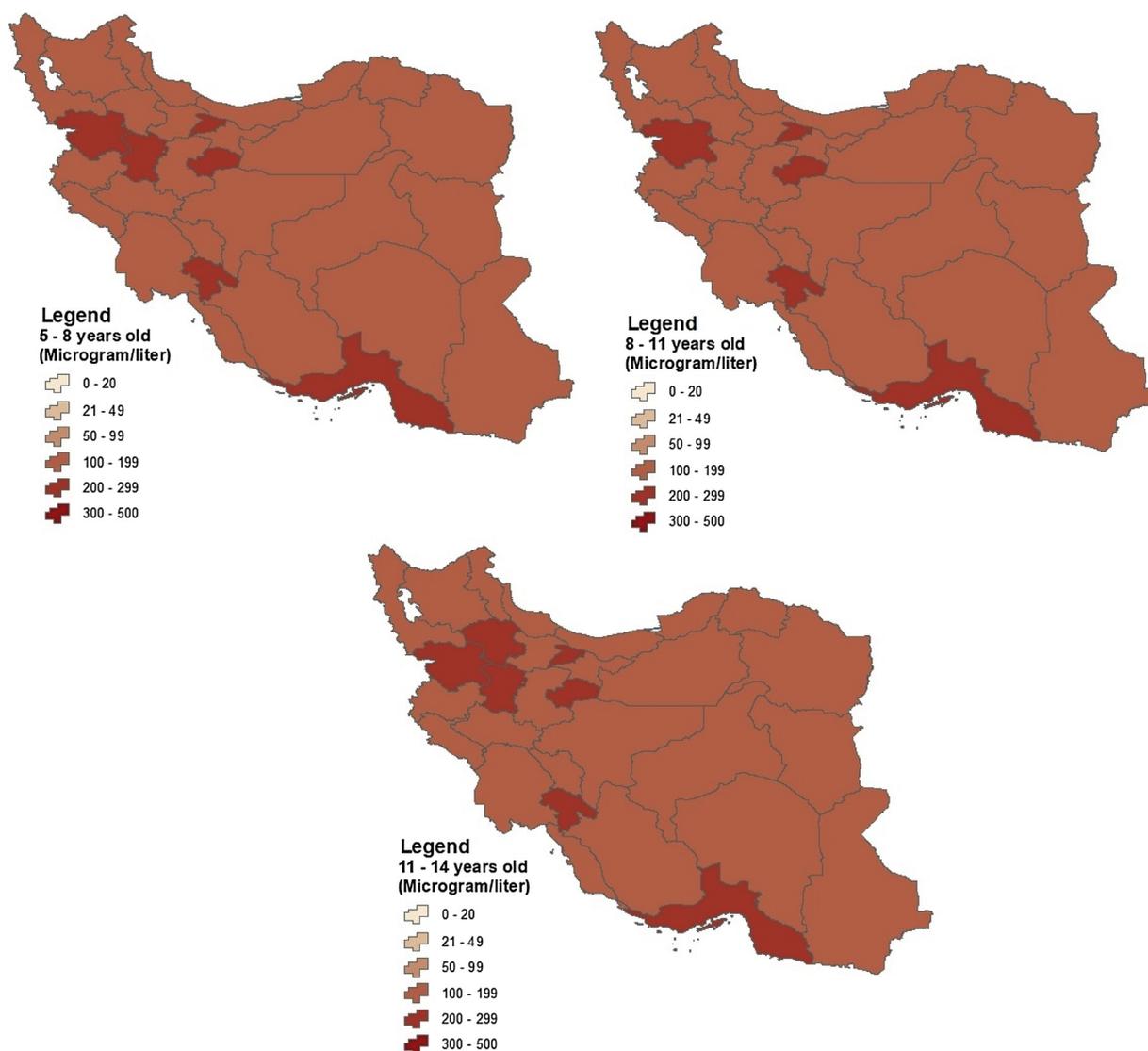


Fig. 3. Distribution of UIC in three age groups of children in Iran.

supplement usage is adequate. These provinces are exactly those where salt consumption is more than 8.9 g/day^{-1} according to the National STEPS Non-communicable Disease Risk Factor Survey Report in Iran (2016). This consumption rate can supply enough iodine, but increases the risk of hypertension in pregnant women, a disorder that must be controlled.

Besides of CH and failure to thrive, another indicator for the determination of sufficient iodine uptake is the goiter prevalence rate. As reported in the second report by the *Iranian Ministry of Health about Monitoring the Salt Iodisation Programme*, the prevalence of goiter in schoolchildren was 58% (1996). This rate was 9.8% and below 5% in monitoring reports in 2001 and 2007 and remained below 5% as mentioned in the monitoring report of 2014. Great success in this programme was a decrease of grade-2 goiter prevalence from 9% in 1996 to less than 0.5% in 2014. As WHO recommended, the urinary concentration of iodine should not be less than $100 \mu\text{g/l}$ [4]. In Iran in 2001, 5.7% of schoolchildren had a urinary concentration of iodine of less than $50 \mu\text{g/l}$, but in the monitoring programme report in 2014, the median of urinary concentration of iodine was $161 \mu\text{g/l}$, which is much higher than international guideline values and can assure health planners of the sufficient intake of iodine in society.

The Iranian salt consumption rate is a key factor in this study. As *Powles et al* (2013) mentioned, the salt consumption rate in Iran is twice

the recommended WHO limit [21]. The recommended value of salt consumption is about 5 g per day for prevention of hypertension. By this value, $30 \mu\text{g/gr}$ iodine in salt can provide daily uptake of $150 \mu\text{g}$ of iodine. According to the Iranian salt consumption rate, iodine uptake could be around $150\text{--}300 \mu\text{g/day}$. This is important for health planners because high salt uptake causes hypertension and extra iodine intake that can lead to hypothyroidism. An educational programme about both of these health outcomes could decrease their risk.

5. Conclusion

After about two decades from starting the salt iodisation programme in Iran, all the provinces in Iran have suitable access to iodised salt. More than 70% of commercial brands have sufficient iodine content according to national standards and WHO guidelines. Based on UIC, more than 70% of children aged 5–14 have sufficient iodine uptake although, in some provinces, the excess intake of iodine is worrying. Also, women's UIC shows a suitable intake of iodine without iodine supplement in pregnancy. Another sign of the success of salt iodisation programme in Iran is the decrease in goiter prevalence. Hence two major issues related to iodine and salt are education about suitable home storage and the worrying salt consumption rate of Iranian people that can lead to hypertension.

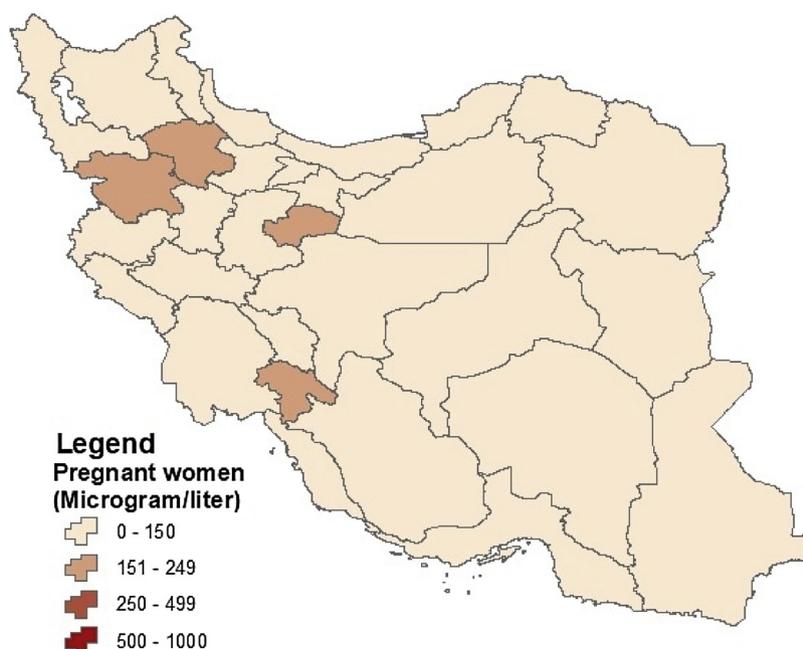


Fig. 4. Distribution of UIC in pregnant women in Iran.

Funding

This study was funded by the Institute for Environmental Health Research, Tehran University of Medical Sciences, Tehran, Iran (Grant number: 93-02-46-26044).

Conflict of interest

The authors of this article declare that they have no conflict of interests.

Acknowledgments

The authors are grateful to the Institute for Environmental Health Research, Tehran University of Medical Sciences, for financial support for this project. The authors are also grateful to Mr Yousef Chavepour for technical support in illustrations.

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