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ORIGINAL ARTICLE

Iodine status of adults in Taiwan 2005–2008, 5 years after the cessation of mandatory salt iodization

Kam-Tsun Tang [a,*], Fan-Fen Wang [b], Wen-Harn Pan [c], Jiunn-Diann Lin [d], Ging-Shing Won [a], Wing-Keung Chau [e], Hong-Da Lin [a], Yao-Te Hsieh [c]

[a] *Division of Endocrinology and Metabolism, Taipei Veterans General Hospital, Taipei, Taiwan*
[b] *Department of Medicine, Yangming Branch, Taipei City Hospital, Taipei, Taiwan*
[c] *Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan*
[d] *Division of Endocrinology and Metabolism, Shuang Ho Hospital, Taipei, Taiwan*
[e] *Division of Hematology and Oncology, Taipei Medical University Hospital, Taipei, Taiwan*

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Background/Purpose: Iodine deficiency causes a broad spectrum of disorders across all ages. Mandatory salt iodization in Taiwan successfully reduced the goiter rate from 21.6% to 4.3% in schoolchildren surveyed in 1971. The program continued until 2003 when salt iodization was changed from mandatory to voluntary. The purpose of this study was to investigate the iodine status of Taiwanese individuals after the change in the iodine policy.

Methods: Urinary iodine (UI) was measured in samples from adults in the Nutrition and Health Survey in Taiwan 2005–2008.

Results: The median UI level was 100 μg/L, and the percentage of populations with UI levels below 100 μg/L and 50 μg/L was 50.1% and 15.1%, respectively, indicating that the iodine status was *borderline* adequate. Men had a higher UI level than women (102 μg/L vs. 98 μg/L, $p = 0.003$), and older individuals (age > 60 years) had a lower UI level than younger people, particularly in women. The iodine status of the population < 50 years was sufficient, but it was insufficient in older groups. Mild iodine insufficiency was noted in all areas of Taiwan except the Southern area and Penghu islands, with the lowest UI level of 79 μg/L in the Mountain area. Although the UI level of women of childbearing age (19–44 years) was 103 μg/L, there may be a risk of iodine deficiency during pregnancy.

Conflicts of interest: The authors have no conflicts of interest relevant to this article.

[*] Corresponding author. Division of Endocrinology and Metabolism, Department of Medicine, Taipei Veterans General Hospital, Taipei 112, Taiwan.

E-mail addresses: tang8228@gmail.com, kttang@vghtpe.gov.tw, tang.kt@msa.hinet.net (K.-T. Tang).

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Conclusion: The iodine nutrition of the Taiwanese population in 2005–2008 was borderline adequate, with insufficiency in some subgroups. Further monitoring of the iodine status is necessary.

Introduction

Iodine is a trace element required for hormone synthesis and essential in the development and the metabolic processes of vertebrate life. Iodine deficiency causes a broad spectrum of disorders (iodine deficiency disorders; IDD) including goiter, intellectual impairment, growth retardation, neonatal hypothyroidism, cretinism, and increased risk of fetal and infant mortality.[1] A meta-analysis showed that children and adults living in areas with severe iodine deficiency had a reduction in intelligence quotient of 12.45 and 13.5 points, respectively, compared with those living in areas without iodine deficiency.[2,3] In addition to cretinism, a rare extreme manifestation of iodine deficiency, subtle degrees of mental deficiency leading to impaired learning and intellectual capacity in children is a significant threat to the social and economic development of countries.[4] Eliminating iodine deficiency by the strategy of universal salt iodization has been recommended by World Health Organization (WHO) and United Nations Children's Fund (UNICEF) since the 1990s, and the number of countries with iodine deficiency has decreased from 126 in 1993 to 30 in 2013.[5] However, as a result of social and economic changes and a lack of awareness of iodine nutrition by the public and governments, the iodine status of the population in some countries deteriorated from sufficient to deficient.[6,7] The sustainability of the iodine program is an important issue that requires ongoing monitoring and adjustment by governments to protect their populations from IDD.

Taiwan was an iodine deficiency area and the iodine status has greatly improved after the implementation of national salt iodization program in 1967.[8] The median urinary iodine (UI) data of the Nutrition and Health Survey in Taiwan (NAHSIT) 2001–2002 indicated that the iodine status of Taiwanese people was adequate before the privatization of the former Bureau of Salt Administration (a government-run monopoly company) in 2003.[9] Thereafter, the salt iodization policy of Taiwan was changed from mandatory to voluntary. The flood of noniodized salt to the market, the increase in noniodized salt consumption by the food industries, and the promotion of a low-sodium diet to prevent cardiovascular disease in the population might influence the iodine status in the population.[10,11] To investigate the iodine status of Taiwanese people after the change in the salt iodization policy, we measured the iodine concentrations in urinary samples obtained from participants in the NAHSIT 2005–2008.[12]

Materials and methods

Study design

The NAHSIT was funded by the Food and Drug Administration, Department of Health, Taiwan, to investigate the dietary and nutritional status of the population, and to estimate the prevalence of nutritional deficiencies, over nutrition, and related health conditions, as well as determinants of poor nutritional and health status. The NAHSIT 2005–2008 surveyed Taiwanese citizens aged 0–6 years and $\geq$19 years. The survey adopted a multistaged, stratified, and clustered probability design, which has been described previously.[12] In brief, 358 districts and townships in Taiwan were designated into five sampling strata based on geographical location and population density (Northern 1, Northern 2, Central, Southern, and Eastern strata). National estimates of health and nutrition were based on the five strata. To enable analysis of particular lifestyle and dietary habits of ethnic minority groups in Taiwan, three additional strata, including Hakka areas, mountainous areas and Penghu Islands were created as specific population groups, which were independent of the national estimates of the five strata described above. The target population for UI measurement in this study included Taiwanese nationals aged 19 years and older. A total of 2823 urine samples were included in this study, which included 1652 samples from national estimates, 986 samples from specific population groups, and 185 quality control samples. Informed consent was signed by all participants and the study was approved by the Department of Health in Taiwan.

Urine sample preparation

Urine samples were collected after participants woke up in the morning and were taken to a mobile health examination center. Aliquots of urine were stored immediately into liquid nitrogen and shipped to Taipei within 2–3 days. The samples were then stored at −70°C in freezers located in the Academia Sinica until analysis.

Urinary iodine assay

The urinary iodine measurement was performed in the Laboratory of Thyroid Disorders, Taipei Veterans General Hospital, Taiwan in 2011. The urinary iodine was assayed by a modified microplate method based on the Sandell–Kolthoff reaction using ammonium persulfate as the oxidizing agent.[9,13–16] In brief, the digestion step was performed by pipetting 25 μL of standard iodine solutions and urine samples into a 96-well reaction plate (Applied Biosystems, Foster City, CA, USA), followed by addition of 50 μL/well of ammonium persulfate solution (freshly made, 1.35M; Sigma, St Louis, MO, USA). The microplate was covered with a 96-well full plate cover and digested in the GeneAmp PCR System 9700 Fast Thermal Cycler (Applied Biosystems) with a program of 95°C for 30 minutes and 4°C for 5 minutes. After digestion, the microplate was centrifuged at 1000 g for 3 minutes, and then proceeded to the Sandell–Kolthoff reaction step as previously described.[14] Aliquots (50 μL) of the resulting digestion were transferred to the corresponding wells of a 96-well reading plate (MicroWell; Nalge-Nunc International, Naperville, IL, USA), in which 100 μL of arsenious acid solution (0.05M; Sigma) was preloaded. After mixing the solution by shaking the plate in the microplate reader (Infinite F50; Tecan, Mannedorf, Switzerland), a 50 μL of ceric ammonium sulfate solution (0.019M; Wako Pure Chemical Industries, Osaka, Japan) was added into each well using a multichannel pipette as quickly as possible. The absorbance of the reaction mixture was read at 405 nm after sitting at room temperature (~25°C) for 30 minutes. The calibration curve was prepared for every plate by plotting the optical density values against the concentrations of standard solutions. The sample concentration was interpolated from the calibration curve. Pooled urines with low, medium, and high iodine concentrations, and potassium thiocyanate/L-ascorbic acid (final concentration 50mM) were included in each plate as internal quality controls to verify the accuracy of the assay and the success of digestion. External quality control samples were provided by the Ensuring the Quality of Urinary Iodine Procedures (EQUIP) program and were tested three times a year to ensure the quality of urinary iodine measurements. All samples were analyzed in duplicates in two separate assays. Samples with readings >400 μg/L were diluted with water to fit the calibration curve. Measurements were repeated for samples with discordant values exceeding 15%. The intra- and interassay coefficients of variation were <10% at iodine concentrations >20 μg/L.

Data analysis

The iodine status of a population was expressed as the median UI concentration of the sampled population. The criteria for classifying iodine nutrition of a population proposed by WHO/UNICEF/International Council for Control of Iodine Deficiency Disorder (ICCIDD) criteria are: <20 μg/L as severe iodine deficiency; 20–49 μg/L as moderate iodine deficiency; 50–99 μg/L as mild iodine deficiency; 100–199 μg/L as adequate iodine nutrition; 200–299 μg/L as above requirements; and ≥300 μg/L as excessive. In addition, not more than 20% of population should have a UI < 50 μg/L.[17]

Descriptive statistics and hypothesis testing were analyzed by SAS 9.2 (SAS Institute, Cary, NC, USA). Data are expressed as the median ± standard error or prevalence rates, and weighted for the unequal sampling probability to validate the results as representative of adults aged ≥ 19 years in the entire country. The significance of variation between sexes, ages, or areas of residence was evaluated by the Kruskal–Wallis test and multiple comparison (Dunn's test). The trend of changes in specific variables among age groups was analyzed using the Chi-square test for trend. Significance was taken as $p < 0.05$.

Results

Urinary iodine level

As shown in Table 1, the median UI level for the Taiwanese population aged ≥ 19 years was 100 μg/L [95% confidence interval (CI) 95–105]. When the data were analyzed in 10-year age groups, the median UI levels ranged from 87 μg/L to 103 μg/L, with the lowest level in those aged 60–69 years and the highest level in those aged 19–39 years. There was a tendency that the older the age group, the lower the median UI level. Seniors (age ≥ 70 years) had a significantly lower median UI level than people aged 19–29 years ($p = 0.026$). According to the criteria, adults younger than 50 years showed iodine sufficiency (median UI levels 101–102 μg/L), and those older than 60 years had mild iodine deficiency (median UI levels 87–88 μg/L), whereas those aged 50–60 years had borderline iodine deficiency (median UI level: 99 μg/L). The median UI level of all male adults was 102 μg/L (95% CI 96–109), with the lowest level (95 μg/L) at 60–69 years, and the highest level (107 μg/L) at 40–49 years. Overall, women had lower UI levels than men ($p = 0.003$). The median UI level of female adults was 98 μg/L (95% CI 90–106), and the lowest level was 77 μg/L in the 60–69 age group. Mild iodine deficiency was observed in men older than 60 years, whereas in women, mild iodine deficiency was found from the age of 50 years onwards.

As shown in Table 2, the percentages of the study population with UI levels <100 μg/L, <50 μg/L, and <20 μg/L were 50.1 ± 1.2%, 15.1 ± 0.9%, and 0.9 ± 0.2%, respectively. A slightly higher proportion of women than men had UI levels <100 μg/L (51.9 ± 1.7% vs. 48.4 ± 1.8%). The proportion of population with insufficient UI levels (<100 μg/L, <50 μg/L, and <20 μg/L) appeared to increase with age, reaching a peak at ≥70 years. Over 50% of women older than 50 years and 65.6% of women older than 65 years had UI levels <100 μg/L, whereas 25.8% of women aged ≥65 years had UI levels <50 μg/L.

The distribution of UI levels in adults is shown in Table 3. The percentage of adults with UI levels <100 μg/L, 100–199 μg/L, 200–299 μg/L, and ≥300 μg/L were 50.2%, 34.5%, 7.7%, and 7.6%, respectively. For the 50.2% of the population with UI levels <100 μg/L (iodine insufficient), the majority (35%) had mild deficiency; 14.3% had moderate deficiency; and 0.9% had severe deficiency. A higher percentage of men had adequate iodine nutrition than women in all age groups. The percentage of all adults, men, and women, with excessive iodine nutrition was 7.6%, 6.1%, and 9.2%, respectively.

As shown in Table 1, the median UI levels of the population in eight geographic areas ranged from 79 μg/L to 140 μg/L (men, 81–136 μg/L; women, 73–149 μg/L). The highest median UI level was found in Penghu Islands and the

Table 1 Urinary iodine levels by age, gender and strata of the Nutrition and Health Survey in Taiwan 2005–2008.

	Urinary iodine (μg/L)					
	Total		Male		Female	
	Median	95% CI	Median	95% CI	Median	95% CI
Age						
All (*n* = 1652)	100	95–105	102	96–109	98	90–106
19–29 y	102	87–118	103	86–120	103	78–128
30–39 y	103	91–116	103	88–118	103	82–124
40–49 y	101	89–114	107	89–125	101	83–119
50–59 y	99	86–111	101	84–118	89	69–109
60–69 y	87	75–98	95	77–113	77	61–93
≥70 y	88	78–99	98	82–114	79	64–95
Strata						
Northern area						
1st stratum	92	81–104	88	75–101	96	77–115
2nd stratum	95	84–106	97	85–109	93	74–112
Central area	95	86–105	99	86–112	94	79–109
Southern area	117	105–129	136	120–152	107	89–125
Eastern area	88	76–100	91	73–109	83	67–99
Hakka area[a]	95	86–103	95	85–105	88	73–103
Penghu Islands[a]	140	129–151	127	111–143	149	132–166
Mountain area[a]	79	68–90	81	63–99	73	58–88

[a] Hakka, Penghu Islands, and Mountain areas are ethnic minority groups with iodine nutrition parameters estimated independently (please see text for details).

Table 2 Distribution of urinary iodine levels < 100 μg/L, < 50 μg/L, and < 20 μg/L in samples from the Nutrition and Health Survey in Taiwan 2005–2008 by age and sex.

		Age (y)							*p*
		≥19	19–29	30–39	40–49	50–59	60–69	≥70	
Sample (*n*)		1652	194	173	292	307	317	369	
Population <20 μg/L									
Total	%	0.9	0.1	0.1	1.5	1.6	0.3	2.4	0.167
	SE	0.2	0.2	0.2	0.7	0.7	0.3	0.8	
Male	%	1.1	0.1	0.2	2.5	1.9	0.6	1.2	0.878
	SE	0.4	0.4	0.5	1.4	1.1	0.6	0.8	
Female	%	0.7	0	0	0.6	1.3	0	3.6	0.024*
	SE	0.3	0	0	0.6	0.9	0	1.4	
Population < 50 μg/L									
Total	%	15.1	10.0	15.0	17.4	14.4	18.2	20.8	0.014*
	SE	0.9	2.2	2.7	2.2	2.0	2.2	2.1	
Male	%	14.1	7.3	15.4	18.3	14.8	15.1	14.9	0.444
	SE	1.2	2.7	4.1	3.4	2.9	2.9	2.5	
Female	%	16.2	12.6	14.6	16.6	14.1	21.1	27.0	0.005*
	SE	1.3	3.3	3.7	3.0	2.8	3.3	3.4	
Population < 100 μg/L									
Total	%	50.1	45.9	48.2	48.6	51.2	57.5	59.2	0.010*
	SE	1.2	3.6	3.8	2.9	2.9	2.8	2.6	
Male	%	48.4	46.2	48.6	48.1	48.5	50.6	51.9	0.896
	SE	1.8	5.3	5.6	4.4	4.1	4.0	3.6	
Female	%	51.9	45.7	47.8	49.1	53.8	63.8	66.8	< 0.001*
	SE	1.7	4.9	5.2	4.0	4.0	3.8	3.6	

* Cochran–Armitage trend test, $p < 0.05$.
SE = standard error.

Table 3 Iodine status and urinary iodine distribution of the subjects in the Nutrition and Health Survey in Taiwan 2005–2008.

	Iodine status						
	Insufficient				Adequate	UI ≥200 μg/L	
	Severe	Moderate	Mild	Total		Above requirement	Excessive
Sex	<20 μg/L	20–49 μg/L	50–99 μg/L	≤99 μg/L	100–199 μg/L	200–299 μg/L	≥300 μg/L
(age ≥19 y)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
All	0.9	14.3	35.0	50.2	34.5	7.7	7.6
Male	1.1	13.0	34.4	48.4	37.2	8.3	6.1
Female	0.7	15.5	35.7	51.9	31.8	7.2	9.2

lowest was in the Mountain area. Men had a slightly higher median UI level in the Southern area (136 μg/L) than in Penghu Islands (127 μg/L), and both men and women had the lowest median UI level in the Mountain area. Other than the above-mentioned Southern area and Penghu Islands, the median UI levels in the other areas were 79–95 μg/L, suggesting mild iodine insufficiency.

To determine the status of iodine nutrition in women, including those of childbearing age, the data was also analyzed in three age groups: 19–44 years (young), 45–64 years (middle), and ≥ 65 years (old; Table 4). The median UI levels were 103 μg/L, 99 μg/L, and 88 μg/L, respectively. Men of all three age groups had median UI levels above 100 μg/L. The median UI level for women of childbearing age (19–44 years group) was 103 μg/L, and the prevalence of a UI concentration <100 μg/L and <50 μg/L were 46.5% and 13.8%, respectively. Apart from the young women, other age groups had median UI levels <100 μg/L. The older the age group, the lower the median UI level. The women in the ≥65 years group had the lowest median UI level of 78 μg/L. The percentage of the female population with UI levels <100 μg/L, 50 μg/L, and 20 μg/L also increased with age. Over 50% of the women in the middle and older age groups had UI levels <100 μg/L, and >20% of women in the old age group had UI levels <50 μg/L.

Discussion

Goiter was the fifth most common disease in Taiwan in the 1940s, and the implementation of mandatory salt iodization program in 1967 successfully reduced the prevalence of goiter in schoolchildren from 21.6% before the intervention to 4.3% in 1971.[8,18] NAHSIT 2001–2002 revealed that the median UI level of schoolchildren was 123 μg/L indicative of adequate iodine nutrition.[9] It inferred that the mandatory salt iodization had protected the population from iodine deficiency before the change of salt iodization policy in 2003. The present study measured the UI levels in samples from subjects in NAHSIT 2005–2008 to determine the iodine status under voluntary salt iodization, and to provide information for future reform of the national salt iodization program in Taiwan.

In the present study, the median UI level of adults is 100 μg/L, and the proportions of the adult population with UI level below 100 μg/L and 50 μg/L were 50.1% and 15.1%, respectively. Based on the WHO/ICCIDD criteria, the iodine status of the adult population in 2005–2008 was *borderline* iodine sufficiency.[17] It is reasonable to suggest that the reduction in median UI levels from 123 μg/L in 2001–2002 to 100 μg/L in 2005–2008 was related to the change of salt iodization policy. In a recent survey of 36 different salt brands in the market, only eight were iodized.[10] Although there were no available data of the percentage of households using iodized salt, the increasing noniodized salts emerging in the market is believed to affect the iodine intake in Taiwan. In 1940s, there was iodine deficiency in regions other than the Penghu Islands and the Southern area, and the Mountain area had the highest goiter rate.[18–20] After mandatory salt iodization, the population of all areas surveyed in 2001–2002 had become iodine sufficient, but there was a return to the previous iodine-deficient status in 2005–2008 that except Penghu Islands and Southern area, other areas were mildly iodine deficient with the lowest UI level in Mountain area. This observation probably reflects the reduction in the use of iodized salt in the population.

In 2002, Taiwan enrolled to be a member of World Trade Organization (WTO) and relaxed import prohibition. The Bureau of Salt Administration, a government-run monopoly

Table 4 Urinary iodine levels (μg/L) by sex, and young, middle, and old age of participants in the Nutrition and Health Survey in Taiwan 2005–2008.

Age (y)	Male					Female					Total				
	n	Median	Mean	Min.	Max.	*n*	Median	Mean	Min.	Max	*n*	Median	Mean	Min.	Max
19–44	233	103	121	16	812	249	103	154	21	3820	482	103	137	16	3820
45–64	274	105	169	12	4268	303	92	183	11	7004	577	99	176	11	7004
≥65	305	100	591	11	39846	288	78	141	13	4380	593	88	367	11	39846
≥19	812	103	199	11	39846	840	98	162	11	7004	1652	100	181	11	39846

company, was privatized in 2003, and the salt market of Taiwan was liberalized. In Europe, the European Union has been a WTO member since 1995. The European Salt Producers' Association declared in 2006 that they strongly advocate the implementation of the Universal Salt Iodization system in the European Union,[21] which ensures that there is adequate iodine intake for the entire population, and has no conflict of becoming a WTO member. IDD is an important public health issue, and salt iodization should be considered as a mandatory policy again in Taiwan.

Variations of iodine status among subgroups were observed in this survey. Women had a lower median UI level than males, and older people had a lower UI level than young adults, particularly in women. In surveys reported in the USA, lower UI levels existed in the elderly and in women.[5,22] There has been no national survey of UI levels of adults during the past 60 years in Taiwan. The largest survey of the goiter rate to assess iodine nutrition was in the 1940s.[18–20] At that time, a high goiter rate was observed in older people and women. The age of the peak goiter rates in the population (5.25%) and women (8.94%) was 50–54 years, and the female to male goiter ratio was 7.38:1.[18] Overall, it appears that elderly people, and particularly women, are at risk of iodine insufficiency. The reasons for this are unknown, but may be related to dietary variations, physiological requirements, and low-sodium diet to prevent cardiovascular diseases. The clinical consequences of IDD in adults are goiter, hypothyroidism, increased susceptibility to nuclear radiation, and iodine-induced hyperthyroidism (IIH) resulting from the body compensation for inadequate iodine intake.[4,17] People with underlying thyroid disorders, such as nodular goiter disease, are susceptible to IIH after iodine supplementation. It is noteworthy that elderly people often have subtle or undiagnosed cardiovascular disease and occult nodular goiter. IIH may aggravate underlying diseases and increase the risk of cardiac arrhythmia and osteoporosis. Unfortunately, there are no previous UI data in adults for comparison, so the actual change in iodine nutrition before and after the cessation of mandatory salt iodization is unclear. Further surveys of iodine status change are required to assess the impact of voluntary salt iodization.

Thyroid hormones are essential for normal neurodevelopment of the fetus and neonates.[1,2,23] Pregnant and lactating women and their offspring have long been considered to be the most vulnerable subgroups to iodine deficiency. Although pregnant women were not included in this study, women of childbearing age are particularly important and deserve special attention. The median UI concentration of women aged 19–44 years was 103 μg/L, and the prevalence of a UI concentration <100 μg/L and <50 μg/L were 46.5% and 13.8%, respectively. Women of childbearing age appeared to have sufficient iodine intake. However, pregnant women require greater iodine intake to compensate for the increased renal clearance of iodine and the transfer of iodine to the fetus.[23] The criteria of iodine sufficiency in pregnant women are much higher than in nonpregnant women (UI level 150–249 μg/L).[17] The fetus relies upon maternal iodine for thyroid hormone synthesis, particularly during the first trimester. Preliminary evidence showed that even mild iodine deficiency during pregnancy causes adverse effects on fetal cognitive function that are not corrected by iodine sufficiency during childhood.[23] Childbearing age women are often unaware of the pregnancy during the early weeks of gestation. Although women of childbearing age appeared to have a sufficient iodine intake in the present study, the median UI level suggests a risk of iodine deficiency during pregnancy. Iodine nutrition surveys should be carried out in pregnant and breastfeeding women in future NAHSIT surveys, and prenatal iodine supplementation, e.g., once-daily prenatal vitamins containing 150–200 μg iodine, may be helpful to prevent pregnant women from iodine deficiency.[24]

In conclusion, Taiwan achieved sufficient iodine status after introduction of the national salt iodization program in 1967. However, this good start was not supported by periodic monitoring of the iodine status in the population, or any adjustment of the program to adapt to the changing social context during these years. After the change in the salt iodization policy in 2003, the iodine nutrition of NAHSIT 2005–2008 is borderline adequate. The increase in non-iodized salt in the market, the increase consumption of processed food, and the global push towards a low-sodium diet to prevent cardiovascular diseases might negatively affect the iodine status in the population. Variations of iodine nutrition among subgroups were observed in this study, and the risks of vulnerable subgroups might be overlooked when relied on the UI level of schoolchildren to determine a country's iodine status.[25] Large sampling sizes covering different subgroups such as pregnant women, lactating women, and neonates should be included in the future surveys. Close monitoring of changes in iodine nutrition and the implementation of a new evidence-based iodization policy are required to avoid further deterioration of iodine nutrition in the Taiwanese population.

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