A Sentinel Survey in Remote Western Thailand Indicates that School-Aged Children and Reproductive-Aged Women of the Indigenous Pwo Karen Community are Iodine Sufficient

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Short title: Sentinel Survey Indicates the Indigenous Pwo Karen are Iodine Sufficient

Abbreviations: BMI, Body Mass Index; IDD, Iodine Deficiency Disorders; INMU, Institute of Nutrition Mahidol University; IQR, Interquartile Range; OR, Odds Ratio; RDA, Recommended Dietary Allowance; SAC, School-Aged Children; UIC, Urinary Iodine Concentration; USI, Universal Salt Iodization; WHO, World Health Organization; WRA, Women of Reproductive Age



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Abstract

Indigenous peoples are often not routinely included in iodine programs because of language barriers and remote access, and may thus be at higher risk of iodine deficiency disorders, which could adversely impact their quality of life. We conducted this cross-sectional study in the remote Pwo Karen community of Thailand to determine the urinary iodine concentration (UIC) of school-aged children (SAC) and women of reproductive age (WRA) and investigate the iodine content in household salt. We measured UIC in spot urine samples from healthy SAC and WRA, administered a questionnaire, estimated daily iodine intake and collected household salt samples to determine salt iodine concentration. The median UIC (range) of SAC (n=170) was 192 (136 - 263) µg/L, which was significantly higher than WRA (n=306) [147 (89 – 233) μ g/L] (P < 0.001). The estimated daily iodine intake in the SAC and WRA were 135 and 195 µg/day, respectively. The median (range) iodine concentration in rock and granulated salts consumed in the households were 2.32 (0.52 – 3.19) and 26.64 (20.86 – 31.01) ppm, respectively. Surprisingly, use of iodized salt and frequency of seafood consumption were not significant predictors of UIC in these two groups. Our data suggest that school children and women of the Pwo Karen community have sufficient iodine intake, indicating the Thai salt iodization program is effectively reaching even this isolated indigenous community. Sentinel surveys of remote vulnerable populations can be a useful tool in national iodine programs to ensure that program coverage is truly universal.

Keywords: iodine status; sentinel survey; indigenous people; urinary iodine concentration; iodine content in salt; school-aged children; reproductive-aged women

Introduction

Iodine is an essential micronutrient involved in metabolism, growth, and brain development in animals and humans ⁽¹⁾. Iodine deficiency causes a broad spectrum of adverse effects, including goiter, infertility, and increased risk of cretinism or thyroid cancer. Inadequate iodine, which is required for thyroid hormone production, affects thyroid hormone production, termed iodine deficiency disorders (IDD) ^(1; 2; 3). Iodine deficiency is a global public health problem affecting all groups of people, especially women more than men. Although severe endemic iodine deficiency has largely disappeared in most parts of the world, mild-to-moderate iodine deficiency is still widespread globally, especially in Asia ⁽⁴⁾. To combat iodine deficiency, salt iodization is recommended as the most cost-effective way of delivering iodine to the target population ⁽⁵⁾. The World Health Organization (WHO) recommends iodized salt consumed in the household should contain 15 – 40 ppm of iodine ⁽²⁾.

In Thailand, the iodine surveillance prevention and control program has been operated continuously since 1989. Part of the strategy to drive this matter is to develop data management and research. Accordingly, salt iodization and iodine supplementation in vulnerable groups such as pregnant women and children living in remote areas are the most common strategies (6). The iodine status and effects of iodine supplementation in these populations are therefore continuously monitored (7; 8; 9; 10). From the surveillance data (2015-2016) of iodine status collected by the Bureau of Nutrition, Department of Health, Thailand, the median urinary iodine concentration (UIC) among children aged between 3-5 years and the elderly groups indicated an adequate iodine intake. In addition, the urinary iodine status among Thai pregnant women during 2015-2020 indicates an optimal iodine status (11). However, the iodine status among school-aged children (6-12 years) and women of reproductive age (15-49 years) has not been elucidated. In recent years, the quality of iodized edible salt in Thai households was estimated by a random inspection. The result showed that more than four-fifths of Thai households consumed adequate iodine content in salt, 20-40 ppm $^{(11)}$. Although surveillance of Thai people's iodine status indicated appropriate daily intake of iodine in children 3-5 years old, elderly, and pregnant women, the iodine status of indigenous people living in Thailand has not been specifically revealed. Indigenous people are one of the most marginalized people in many societies in terms of being excluded from access to socioeconomic rights, and this is especially the case with healthcare (11). Most countries have inaccurate or no published statistical

data for these people. Hence, systematic information on health, morbidity, and mortality is rare and fragmented ⁽¹²⁾.

To reach the IDD surveillance programs in indigenous people, this study thus aims to determine the iodine status of indigenous communities of two priority population subgroups, including schoolaged children and women of reproductive age, and to investigate the iodine content in household salt. In addition, The results can also be considered and strengthened for the Universal Salt Iodization (USI) program in the country, which can be described as covering indigenous peoples.

Methods

Study design and study site

The cross-sectional study was conducted in Laiwo Subdistrict, Sangkhlaburi District, Kanchanaburi Province, Thailand. This subdistrict is located in Thungyai Naresuan National Wildlife Sanctuary adjacent to the Myanmar border. Access to this community is only by four-wheel drive vehicle or motorcycle. There are six villages with 1,352 households in Laiwo Subdistrict. The population is 6,183 inhabitants—3,283 males and 2,900 females ⁽¹³⁾. Due to a limitation in transportation and accessibility, only three villages were purposively collected for data collection, including Sanephong, Kongmongta, and Koh Sadueng.

Participants

The participants were divided into two groups- school-aged children (SAC) and women of reproductive age (WRA). We aimed to recruit a sample of 300 SAC and 300 WRA. This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects were approved by the Center of Ethical Reinforcement for Research, Mahidol University (MUCIRB 2022/178.3006). Written informed consent was obtained from all The study protocol was registered on the ClinicalTrials.gov subjects. platform at https://clinicaltrials.gov/ (identifier: NCT05920603). After receiving the name list of villagers in each village, the sample quota in each selected village was estimated using a proportional selection technique. The inclusion and exclusion criteria were considered to recruit eligible participants in each village for the study. Inclusion criteria were 1) healthy SAC (6-12 years old) or healthy WRA (15-49 years old) who was not diagnosed by a doctor having serious medical conditions; 2) living in the study area; and 3) willing and able to give informed consent for participation in the trial. Exclusion criteria were 1) pregnant women, 2) breastfeeding women, and 3) people who have moved out from the village. A simple random sampling using a lottery method was used for

participant selection. For the SAC, it was found that the actual total of eligible children (n = 219) was less than the required number, so all of them were invited.

Study procedure

The sample collection period was from April to July 2023. The core research team presented the project at the monthly village meetings of all three villages and at Ban Kongmongta Subdistrict Health Promotion Hospital to invite interested local people to join the research team in each village. The local people who were fluent in reading and writing Thai and could translate between Karen and Thai were selected to be local researchers. After selection, 3 males and 23 females were selected to participate as local researchers and were given a clear explanation of the project details. Most of the local researchers had experience in data collection in their villages. Then, all local researchersattended training from the core research team on 1) how to complete the general information questionnaire, 2) how to collect urine samples, and 3) how to collect salt samples.

Data collection and analysis

Questionnaire. The WRA and guardians of SAC completed the questionnaire that included: 1) age of participants; 2) weight and height of participants; 3) perception about iodized salt; 4) Intent to purchase iodized salt for household consumption; 5) whether salt was used more as a seasoning or a condiment in the household; 6) whether more salt or more fish sauce was used in the household (these two condiments are widely used in Thailand); and 7) frequency of household seafood consumption per week; never, 1–2 times, 3–4 times, or over 4 times.

Urinary iodine concentration. Spot urine samples were collected from eligible participants (SAC and WRA) at home in the morning using a small plastic bottle and zip-lock plastic bag. The urine samples were transported on ice to the Institute of Nutrition, Mahidol University (INMU), aliquoted into microcentrifuge tubes, and stored at -20°C until analysis. At INMU, the iodine concentration in urine was measured in duplicate using the Pino modification of the Sandell-Kolthoff reaction (14).

Iodine content in salt. Participants were asked for two tablespoons of salt commonly used in their households. The salt samples were transported to INMU, and stored under dry and shielded from light conditions until analysis. The iodine content in salt was measured using the iodometric titration technique ⁽¹⁵⁾.

Daily iodine intake. Urinary iodine concentration and body weight were used to estimate iodine intake through the formula of the U.S. Institute of Medicine ⁽¹⁶⁾:

UI (μ g/L) x 0.0235 x body weight (kg) = daily iodine intake (μ g)

Data and statistical analysis

Data analysis was performed using the SPSS version 21 statistical package (SPSS Corp., USA). The Kolmogorov-Smirnov test was used to assess normal data distribution. It was reported as the mean \pm SD, while nonparametric values were reported as the median with interquartile range (IQR). The Mann–Whitney U-test was used to test the UIC difference between SAC and WRA. To determine the association between the selected sociodemographic predictors and UIC, a binary logistic regression was conducted. Statistical significance was considered for P < 0.05.

Results

Characteristics of participants

A total of 170 school-aged children (SAC) and 306 women of reproductive age (WRA) were recruited from the three villages. The SAC comprised a similar proportion of gender (84 males and 86 females), with a mean age of 9.3 ± 2.0 years, while the WRA had a mean age of 32.5 ± 10.7 years. The mean weights of SAC and WRA were 30.2 ± 12.2 kg and 56.4 ± 12.0 kg, respectively. The mean heights of SAC and WRA were 128.1 ± 18.3 cm and 153.9 ± 6.2 cm, respectively. The body mass index (BMI) of WRA was 23.85 ± 5.1 kg/m². Regarding perception about iodized salt, most of SAC (62.9%) and WRA (74.8%) were aware of iodized salt. Regarding the households information collected from WRA and guardians of SAC, there was little difference in intention to buy or not to buy iodized salt for household consumption in both groups. The majority of households of both participant groups used salts as a seasoning (SAC, 99.4%; WRA, 99.3%), and consumed salt more than fish sauce (SAC, 98.2%; WRA, 96.7%). About two-thirds of both participant groups consumed seafood 1 - 2 times per week (SAC, 57.1%; WRA 63.1%) (Table 1).

Iodine content of salt consumed by the participating household

A total of 370 salt samples (162 rock salt and 208 granulated salt) were obtained from 280 households (91.0%). Among 280 households, households that consumed two types of salts, only rock salt, and only granulated salt were 90 (32.1%), 72 (25.7%), and 118 (42.1%), respectively. The median iodine content with interquartile range (IQR) in rock and granulated salts was 2.32 (0.52 – 3.19) ppm and 26.64 (20.86 – 31.01) ppm, respectively. Most rock salt (99.4%) had an iodine content of less than 15 ppm, while most granulated salt (75.0%) had adequate iodine content of 15 – 40 ppm. In other words, rock salt is a non-iodized salt, whereas granulated salt is an iodized salt. (Table 2).

Urinary iodine concentration (UIC)

The median UIC with IQR of SAC [192 (136 – 263) μ g/L] was significantly higher than WRA [147 (89 – 233) μ g/L] (P < 0.001) (Figure 1). According to WHO criteria ⁽²⁾, 40.0% of SAC and 37.6% WRA had a UIC that fell between 100 – 199 μ g/L, 1.8% of SAC and 8.5% of WRA had a UIC < 50 μ g/L, while 20.0% of SAC and 14.1% of WRA had a UIC \geq 300 μ g/L (Table 3). The median UIC of 192 μ g/L in SAC with a mean age of 9.3 years and a mean body weight of 30.2 kg was related to a median iodine intake of approximately 135 μ g/day. While among WRA with a mean age of 32.5 years and a mean body weight of 56.4 kg, their median UIC of 147 μ g/L corresponded to a median iodine intake of approximately 195 μ g/day.

Association of sociodemographic variables and UIC

The odds ratio (OR) for having UIC < 100 μ g/L, according to household use of granulated salt, which is an iodized salt, and frequency of seafood consumption per week, were determined. Accordingly, SAC whose households did not use iodized salt (OR 1.175, 95% CI 0.358 - 3.854, P = 0.791) and did not consume seafood in the past week (OR 1.024, 95% CI 0.407-2.578, P = 0.960) were not associated with having UIC < 100 μ g/L. In the same way, households of WRA that did not use iodized salt (OR 1.200, 95% CI 0.688 – 2.095, P = 0.521) and the individuals who did not consume seafood in the past week (OR 1.346, 95% CI 0.772 – 2.348, P = 0.295) were not associated with having UIC < 100 μ g/L (Table 4).

Discussion

According to WHO guideline for fortification of food-grade salt with iodine, salt iodization is the desired strategy to prevent and control IDD at the population level. At least 90% of households, a representative population, should access an iodized salt with iodine content between 15 – 40 ppm ⁽¹⁷⁾. In the present study, the majority (74.3%) of the Karen households consumed granulated salt with a median iodine content of 26.64 (20.86 – 31.01) ppm, while 35.7% of them consumed rock salt with a median iodine content of only 2.32 (0.52 – 3.19) ppm. Nevertheless, participants who used both rock and granulated salt in their households were not asked which type of salt they used more often. The current finding was consistent with the previous study in remote Australian Indigenous communities that iodized table salt was most commonly consumed (71.7%) among all salt purchased ⁽¹⁸⁾. More than 95% of the Karen people regularly used salt in cooking rather than as a condiment and consume more than fish sauce, which is a rare iodine-fortified condiment that is popular with Thais of all ages, as shown in the 2017 Food Consumption Behavior Survey in Thailand ⁽¹⁹⁾.

To determine iodine sufficiency, the median UIC of SAC (192 µg/L) and WRA (147 µg/L) in the Karen community indicated adequate iodine nutrition (2). In addition, no more than 20% of SAC and WRA population should have a median UIC < 50 µg/L (2); only 2% of SAC and 9% of WRA had values less than this cut-off. Our finding is consistent with the Iodine Global Network (IGN) Global Scorecard 2021, which showed adequate iodine intake of Thai SAC (4). Interestingly, approximately one-fifth of SAC (20%) and more than one-seventh of WRA (14%) had excessive levels of median UIC (≥ 300 µg/L) (2). Based on the IGN Global Scorecard 2021, 11 out of 194 countries have shown excessive iodine intake in the SAC population (4). However, UIC assessment in spot urine samples in this study should be considered because it may be affected by several factors, such as hydration status and daily variation in iodine intake (20; 21). The study from Barloggio et al. stated that assessing thyroglobulin complementary with adjusting the UIC using urinary creatinine could strengthen the validity of the result rather than relying on UIC alone (22). To estimate the daily iodine intakes in the population, the formula of the U.S. Institute of Medicine has widely been used ^(7; 16; 23). This study revealed that the daily iodine intakes of SAC (135 µg/day) and WRA (195 µg/day) were higher than the recommended dietary allowance (RDA) for iodine (2). Although the daily iodine intake of the participant group did not reach the international reference values for upper intakes of iodine (24), the high level of iodine status in this Karen community is still a concern.

To determine the possible causes affecting the iodine status of the Karen people, the findings showed that the use of iodized salt and frequency of seafood consumption per week was not associated with having UIC < 100 μg/L in both SAC and WRA. It indicates that the type of salt and seafood consumption are not good predictors of inadequate iodine intake in this Karen community. The other predictors of insufficient iodine status may be considered, such as salt storage, industrialized seasoning consumption, and processed food consumption (25; 26). Besides considering insufficient iodine levels, excessive iodine intake should also be followed up. As findings, almost half of the SAC (47.7%) and one-third of WRA (34.0%) had UIC above the requirement. Adverse consequences of excessive iodine intake may activate hyperthyroidism, hypothyroidism, goiter, and/or thyroid autoimmunity (24; 27). Accumulating iodine intake reaching excess levels may be caused by various sources, including iodized salt, drinking water, milk, certain seaweeds, dietary supplements containing iodine, and processed foods and condiments composed of iodized salt (28; 29). All-source intake should be carefully considered (24). Nevertheless, most people generally well-

tolerate to excess iodine exposure or ingestion, except in some susceptible individuals $^{(30)}$. Discretionary choice consumption among SAC in Tanzania can cause one-third of the children to have UIC > 500 µg/L. Most frequently consuming potato chips and fried cassava with discretionary salt added was likely caused by the excessive iodine intake in SAC $^{(31)}$. Thus, a more elaborate and quantitative food frequency questionnaire or a 24-hour dietary recall should be additionally applied to determine additional foods that are possible sources of excessive iodine consumption in further study. Although several limitations are discussed, the strengths of this study are also described. This is the first study that evaluates iodine sufficiency in the Pwo Karen communities in Thailand. Since most people in the communities speak and understand the Karen language more than the official Thai language, training local people, mostly village health volunteers, to be data collectors are advantageous because they comprehend their community context and understand the context of health surveillance and prevention. Moreover, they may play a key role in assisting the Primary Health Care Unit in monitoring the health of people in their communities in the future.

The findings affirm that the universal salt iodization program in Thailand is steady, as indicated by the majority consumption of iodized salt among the indigenous population in remote areas. The strengths of the majority of iodized salt intake in this population should continue to be assured. However, iodine intake above the requirement of the Pwo Karen people should be closely monitored to determine the cause of this problem. These data should be confirmed in a larger population with an additional dietary assessment to ensure these marginalized people are receiving appropriate iodine intake, reducing the risk of many adverse health and nutrition consequences. In addition, the IDD surveillance program should continue to be actively extensive for all groups of people in the country.

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Table 1. Characteristics of school-aged children (SAC) and women of reproductive age (WRA)

Vesiables	SAC	WRA	
Variables	n = 170	n = 306	
Age, y	9.3 ± 2.0	32.5 ± 10.7	
Child's gender			
Male:female, n:n	84 : 86		
Weight, kg	30.2 ± 12.2	56.4 ± 12.0	
Height, cm	128.1 ± 18.3	153.9 ± 6.2	
BMI, kg/m ²	-	23.85 ± 5.1	
Perception about iodized salt, %			
Yes	62.9	74.8	
No	37.1	25.2	
Intent to purchase iodized salt, %			
Yes	44.1	43.1	
No	40.0	42.8	
Do not know	15.9	14.1	
Greater salt consumption for, %			
Cooking	99.4	99.3	
Condiment	0.6	0.7	
Greater consumption of, %			
Salt	98.2	96.7	
Fish sauce	1.8	3.3	
Seafood consumption per week, %			
Never	42.4	29.1	
1-2 times	57.1	63.1	
3-4 times	0.6	5.9	
Over 4 times	0	2.0	

 $^{^{-1}}$ Values are mean \pm SD

kg, kilogram; cm, centimeter; m, meter; BMI, body mass index

Table 2. Iodine content in household salt (n = 370)

Type of solt	Iodine content*			n	
Type of salt	< 15 ppm	15 – 40 ppm	> 40 ppm	. n	
Rock	(99.4) [84.3]	(0.6)[0.6]	0	162	
Granule	(14.4) [15.7]	(75.0) [99.7]	(10.6) [100.0]	208	
n	191	157	22	370	

^{*}number of salt sample (Row %), [Column %]

Table 3. Median (IQR) urinary iodine concentration in school-aged children (SAC) and women of reproductive age (WRA)

Median urinary iodine concentration (μg/L) ¹	Frequer	Frequency (%)		
	SAC	WRA		
	(n = 170)	(n = 306)		
< 20	1 (0.6)	3 (1.0)		
20 - 49	2 (1.2)	23 (7.5)		
50 – 99	18 (11.0)	61 (19.9)		
100 - 199	68 (40.0)	115 (37.6)		
200 - 299	47 (27.7)	61 (19.9)		
≥ 300	34 (20.0)	43 (14.1)		

⁻¹ WHO (2007) criteria for iodine sufficiency in school-aged children and women with reproductive age ⁽²⁾.

 $\textbf{Table 4.} \ \ \text{Odds ratio (OR) of iodine deficiency ($<$100 $\mu g/L$) in school-aged children (SAC) and women of reproductive age (WRA).}$

	SAC		WRA		
n (%)	OR (95% CI)	Р	n (%)	OR (95% CI)	Р
31 (19.9)	1.175 (0.358-	0.791	83 (29.2)	1.346 (0.772-	0.295
	3.854)			2.348)	
125 (80.1)	1 [Ref]		201 (70.8)	1 [Ref]	
72 (42.4)	1.024 (0.407-	0.960	89 (29.1)	1.200 (0.688-	0.521
	2.578)			2.095)	
98 (57.6)	1 [Ref]		217 (70.9)	1 [Ref]	
	31 (19.9) 125 (80.1) 72 (42.4)	31 (19.9) 1.175 (0.358- 3.854) 125 (80.1) 1 [Ref] 72 (42.4) 1.024 (0.407- 2.578)	31 (19.9) 1.175 (0.358- 0.791 3.854) 125 (80.1) 1 [Ref] 72 (42.4) 1.024 (0.407- 0.960 2.578)	31 (19.9) 1.175 (0.358- 0.791 83 (29.2) 3.854) 125 (80.1) 1 [Ref] 201 (70.8) 72 (42.4) 1.024 (0.407- 0.960 89 (29.1) 2.578)	31 (19.9) 1.175 (0.358- 0.791 83 (29.2) 1.346 (0.772-3.854) 2.348) 125 (80.1) 1 [Ref] 201 (70.8) 1 [Ref] 72 (42.4) 1.024 (0.407- 0.960 89 (29.1) 1.200 (0.688-2.578) 2.095)

¹Twenty-eight households (SAC, missing 18 data; WRA, missing 22 data) did not provide salt samples.

All P values are given with logistic regression; 95% CI 95% is a confidence interval.

Ref, reference value

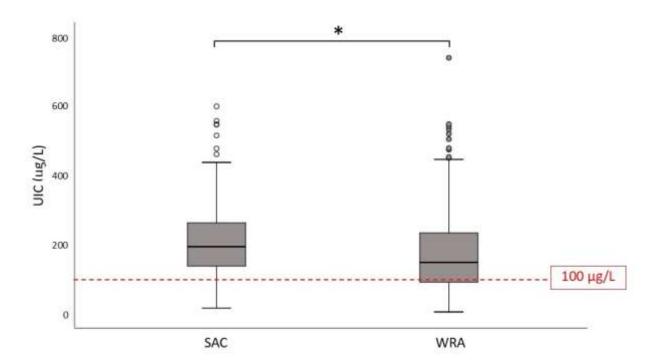


Figure 1. Urinary iodine concentration (UIC) of school-aged children (SAC) and women of reproductive age (WRA). Horizontal lines and boxes represent the median and the interquartile range, respectively. Whiskers indicate SD. The stippled horizontal line represents the epidemiological criteria for assessing adequate iodine intake based on the median UIC (2). * (P < 0.001) indicates a significant difference in UIC (Mann–Whitney U-test).