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Stable Iodine Intake During Pregnancy and Children's Thyroid Screening Outcomes After the 2011 Fukushima Nuclear Disaster in Japan: A Municipality-based Descriptive Study

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Abstract

Objectives: Stable iodine intake is an essential preventive strategy against thyroid cancer following a nuclear disaster. However, the rate of stable iodine intake during pregnancy and thyroid outcomes among their children have remaifned unclear.
Methods: This observational study used data from a thyroid screening program at Research Institute of Radiation Safety for Disaster Recovery Support in Fukushima, Japan. The participants were children from Miharu Town, which implemented stable iodine intake during the Fukushima Nuclear Disaster, born between March 15, 2011 and March 31, 2012. Thyroid ultrasound results were stratified according to stable iodine intake.
Results: This study included 86 children born after the disaster. A total of 34.9% (30 of 86) of their mothers reported taking stable iodine during pregnancy. As for thyroid screening outcomes, none of the children required detailed thyroid examination.
Conclusions: The intake rate of stable iodine during pregnancy was about 1/3 within the traceable municipality after the Fukushima Nuclear Disaster, which was lower than the previously reported number of 63.5% among children. Awareness-raising and effective communication toward pregnant women would be important for nuclear disaster preparedness. There were no participants who required further thyroid examination in this study.

Stable iodine intake is an important preventive strategy for thyroid cancer after nuclear emergencies along with evacuation, sheltering, and restricting the consumption of contaminated materials.[1,2] The administration of stable iodine saturates the thyroid gland, thereby blocking the internal radiation exposure of the thyroid by blocking the uptake of radioactive iodine.[1] Iodine thyroid blocking is recommended for children, adolescents, and pregnant women by the World Health Organization and national regulatory authorities, including the Food and Drug Administration in the US.[1,3] It has been reported that iodine blocking was performed from neonates to adults in Poland after the Chernobyl accident.[4,5] However, information on stable iodine intake and thyroid screening results in actual nuclear disaster cases is limited.

On March 11, 2011, the Great East Japan Earthquake and tsunami occurred, followed by the Fukushima Daiichi Nuclear Power Plant (FDNPP) accident. After the release of radioactive substances, nearby residents were unintentionally exposed to them.[6,7] In the absence of established nuclear disaster response plan, there was a lack of consistent national-level instructions on intake of stable iodine tablets.[8] However, as a subnational-level decision to protect local residents, 7 local municipalities distributed stable iodine to residents and 4 instructed on the intake of stable iodine.[9] This was implemented in collaboration with pharmacists and public health nurses when physicians were absent in some situations. Earlier than the official initiation of the Fukushima Health Management Survey,[10] Research Institute of Radiation Safety for Disaster Recovery Support (RSDRS) has been conducting voluntary thyroid screening since 2012 in cooperation with municipalities, including Miharu Town.[11] This screening program has been collecting screening data and questionnaire-based information including the use of stable iodine. Among children after the FDNPP accident, the intake rate was 63.5% among children in Miharu Town.[12]

Pregnant women are another recommended group for stable iodine due to concerns about the transfer of radioactive iodine to the fetus, as the fetal thyroid becomes functional by the end of the first trimester.[1,13] Despite the recommendation, the actual situation regarding the intake of stable iodine among pregnant women after the Fukushima Nuclear Disaster remains unknown. This study aimed to examine the intake rate of stable iodine during pregnancy at the disaster, as well as the relationship between children's thyroid screening outcomes and the use of stable iodine during pregnancy. This information could be beneficial for nuclear disaster preparedness.

Materials and Methods

Study Design, Setting, and Participants

This observational study obtained data from a thyroid screening program conducted at RSDRS in Fukushima Prefecture, Japan. Geographical locations of RSDRS, FDNPP, and Miharu Town were shown in Figure 1. RSDRS is a public interest incorporated foundation established in response to the FDNPP accident by the founder of health care corporation Seireikai group, which holds Hirata Central Hospital, a privately run and sole hospital with 143 beds. The participants in this study were children in Miharu Town, which implemented stable iodine intake during the Fukushima Nuclear Disaster, born between April 1998 and March 2012. They underwent thyroid screening at the RSDRS from March 15, 2011, which was the day of the nuclear accident, and March 2012 (Japanese fiscal year 2011). Miharu Town provided and instructed stable iodine intake at the time of the Fukushima Nuclear Disaster.[9] Participants who did not respond to the questionnaire regarding stable iodine intake were excluded. To explore the potential impact of non-response bias on stable iodine intake, we conducted a sensitivity analysis as below. Participants born 293 days or more after the accident were considered to have been not yet conceived at the time of the disaster and excluded.

Thyroid screening at RSDRS

RSDRS has been conducting voluntary thyroid screenings since 2012. This program had operated independently of the Fukushima Health Management Survey (FHMS), which had monitored the general population in Fukushima Prefecture.[14] Notable differences were observed between these 2 screening programs, particularly regarding the timing and the participants involved. RSDRS initiated thyroid screening earlier than FHMS at a municipality level.

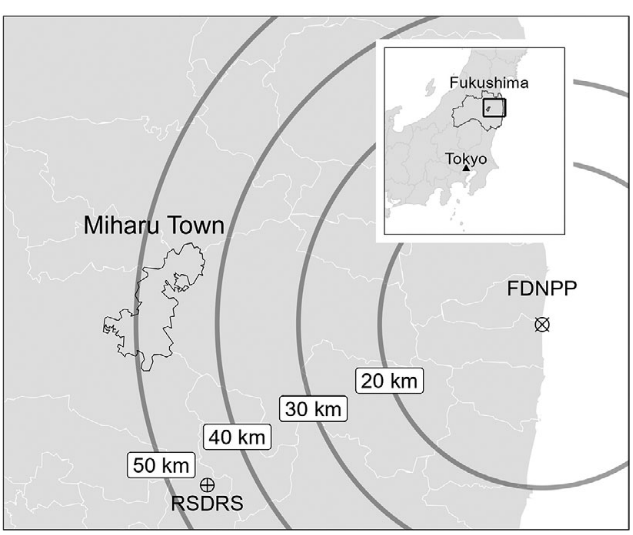

Figure 1. Geographical locations of Miharu Town, Fukushima Daiichi Nuclear Power Plant (FDNPP), and Research Institute of Radiation Safety for Disaster Recovery Support (RSDRS).

Self-administered questionnaire

Before thyroid cancer screening at RSDRS, all guardians of the participating children were asked to complete a self-administered questionnaire that included information on the participants' and their guardians' intake of stable iodine after the disaster. While the term "guardians" was used, responses were assumed to be primarily from mothers, although the possibility of fathers or other guardians cannot be excluded. All the questionnaires were collected at RSDRS.

Thyroid ultrasound screening outcomes

Thyroid ultrasound results were evaluated by a Board Certified Otorhinolaryngologist by Japanese Society of Otorhinolaryngology-Head and Neck Surgery (CS). The screening results were classified into the following 4 categories:

A1: No nodules or cysts are found in the thyroid gland. The thyroid gland was considered normal.
A2: Although nodules or cysts are found, they are benign or of low concern. Specifically, cysts are 20.0 mm or less in diameter and nodules are 5.0 mm or less in diameter. This is also considered to be a normal state of the thyroid.
B: Nodules are greater than 5.1 mm in diameter and/or cysts >20.1 mm. Alternatively, any nodules or cysts found to possess suspicious characteristics regardless of size are also classified as B. These cases are recommended for a more detailed examination known as a "confirmatory examination."
C: Cases requiring immediate detailed investigation due to the possibility of malignancy, regardless of nodule or cyst size.

Data and variables

The data extracted from the thyroid screening database included the ages of participants at the time of the screening and at the time of the disaster, sex, whether the participant took stable iodine orally after the disaster, and their mothers' intake of stable iodine, increased iodine-rich seaweed intake after the disaster, and presence or absence of voluntary evacuation. Because pregnancy-related information was lacking, the duration of pregnancy was assumed to be the longest full-term period in the main analysis. Participants born 293 days or more after the accident were considered to have been not yet conceived at the time of the disaster. Additionally, 3 sensitivity analyses were conducted as described in the Analytical Methods section. Children born between the accident of the FDNPP (March 15, 2011) and 292 days thereafter were categorized according to their pregnancy trimester at the time of the disaster: the first trimester (up to 12 weeks), the second trimester (13–28 weeks), and the third trimester (29–40 weeks).[15] The trimester of pregnancy was estimated from the difference in the number of days between the birthdate and the date of the FDNPP accident. Thyroid screening outcomes, including thyroid volume (mm^3), parenchymal heterogeneity (or homogeneity), and thyroid screening results, were retrieved.

Analytical methods

Continuous variables were presented as means and standard deviations. The participants' characteristics were classified into 2 groups: the intake group and no intake group. For categorical variables, associations were evaluated using Fisher's exact test, while continuous variables were assessed using t-tests to compare the means between different groups. *P* values less than 0.05 were considered indicative of statistical significance.

As for non-responses on stable iodine intake, the following sensitivity analysis for nonresponse were performed. For each scenario, the

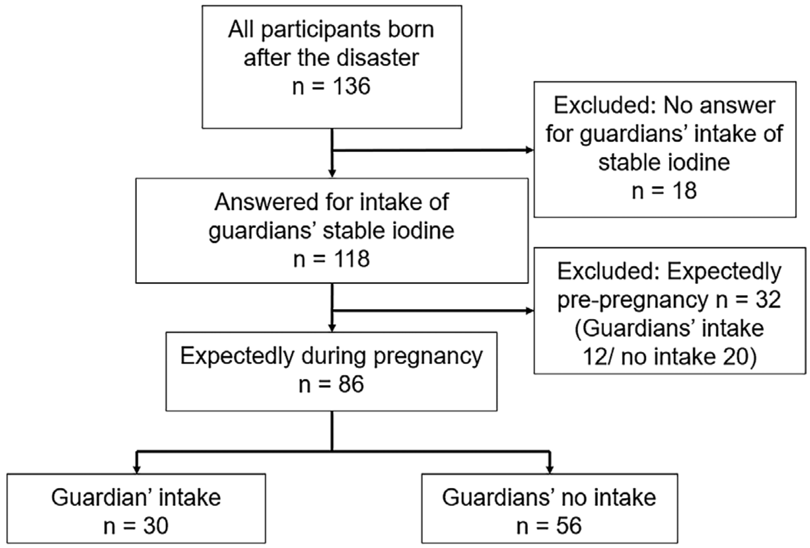

Figure 2. Participants flow chart.

rate of stable iodine intake and thyroid screening outcomes were examined.

Sensitivity analysis 1. All non-respondents took stable iodine. All participants without response were assumed to take stable iodine. This assumption aims to evaluate the maximum possible uptake rate of stable iodine among the study population.

Sensitivity analysis 2. No non-respondents took stable iodine. Conversely, none of the non-respondents were assumed to take stable iodine. This scenario aims to assess the minimum possible uptake rate.

As for the assumption of pregnancy period, the following sensitivity analyses were performed.

Sensitivity analysis 3. Two hundred and seventy-three days or 39 weeks, which was most frequent week from Japanese data.[16]

Sensitivity analysis 4. Two hundred and eighty days or 40 weeks.

Sensitivity analysis 5. Three hundred days or 42 weeks 6 days, which was the longest assumption including post-term delivery.

All analyses were performed using R version 4.4.1 (http://www.r-project.org).

Ethical considerations

This study was approved by the ethics board of Hirata Central Hospital (2017-0321-2), Kyoto University (R1459) and Fukushima Medical University (30180). Written informed consent was obtained from the guardians of all the participants.

Results

In this study, there were 136 participants who were born after the disaster. 18 participants were excluded from this specific analysis due to the absence of data on the mothers' iodine intake. The mothers' stable iodine intake information was available for a total of 118 participants. Among these, 32 were assumed pregnant post disaster and excluded. For this post-disaster pregnancy group, stable iodine intake was reported for 12 mothers, whereas 20 did not take stable iodine. The remaining 86 participants were assumed pregnant at the time of the disaster (Figure 2).

Table 1 showed 30 mothers (34.9%) took stable iodine, while 56 (65.1%) did not. From a sensitivity analysis including non-respondents (10 out of 18 were assumed pregnant at the time of the disaster), it was found that the proportion ranged from a maximum of 43.8% to a minimum of 30.2%. Of all children, 45.3% were female, and the mean age at the time of testing was 10.22 years (standard deviation SD 1.27), with no difference between the 2 groups.

Table 1. Participants expectedly during pregnancy at the time of the disaster, stratified with mothers' stable iodine intake

	Overall (*n* = 86)	Yes (*n* = 30)	No (*n* = 56)	*P* value
Sex (Female/Male, %)	39/47 (45.3/54.7)	16/14 (53.3/46.7)	23/33 (41.1/58.9)	0.364
Age at test (mean, SD)	10.22 (1.27)	10.17 (1.34)	10.25 (1.24)	0.773
Expected trimester (%)				0.656
- First trimester	22 (25.6)	9 (30.0)	13 (23.2)	
- Second trimester	30 (34.9)	11 (36.7)	19 (33.9)	
- Third trimester	34 (39.5)	10 (33.3)	24 (42.9)	
Evacuation status (%)	64/22 (74.4/25.6)	24/6 (80.0/20.0)	40/16 (71.4/28.6)	0.446
Seaweed intake (%)	81/5 (94.2/5.8)	27/3 (90.0/10.0)	54/2 (96.4/3.6)	0.337
Final result (A1/A2, %)	28/58 (32.6/67.4)	9/21 (30.0/70.0)	19/37 (33.9/66.1)	0.811
Volume (mm^3) (mean, SD)	6613.57 (2196.60)	6472.61 (2573.35)	6689.09 (1987.11)	0.666
Heterogeneity (%)	85/1 (98.8/1.2)	30/0 (100.0/0.0)	55/1 (98.2/1.8)	1

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As for the trimester, 22 (25.6%) mothers were in the first (intake 9 vs no intake 13), 30 (34.9%) in the second (intake 11 vs no intake 19), and 34 (39.5%) in the third trimester (intake 10 vs no intake 24); it did not differ between the groups ($p = 0.656$). The proportion of evacuation history was 20.0% among mothers taking stable iodine and 28.6% for those who did not ($P = 0.446$). Among those whose mothers took stable iodine, 10.0% increased iodine-rich seaweed intake after the disaster, compared to 3.6% in the group without iodine intake ($P = 0.337$).

Regarding thyroid ultrasound results, most participants were classified as A2 (67.4%), A1 (32.6%), and no B or C. There was no difference between the iodine intake and non-intake groups ($P = 0.811$). The mean thyroid volume and the parenchymal structure showed similar proportions of homogeneity across both groups.

Discussion

The present study examined the intake rate of iodine intake among pregnant women, their characteristics, and thyroid outcomes. An important finding from our study is the lower intake rate of stable iodine among pregnant women (34.9%), compared to that among children in a previous report (63.5%).[12] While stable iodine intake did not appear to influence the need for detailed thyroid examinations in this study, it would play an important role in protecting the thyroid from radioactive iodine, as recommended.[1]

No difference was found with trimester, child's sex, voluntary evacuation, or post-disaster dietary habits classified with stable iodine intake during pregnancy. In the previous study involving children aged 0-9 years at the time of the FDNPP accident, lower children's age and parents' intake of stable iodine were associated with children's intake.[12] However, in this study, which examined stable iodine use during pregnancy, no factors associated with mothers' intake were found.

Informing pregnant women about stable iodine is crucial due to its potential effect on the fetal thyroid gland. However, generally, they may face challenges in accessing the medication, such as nausea, vomiting, and concerns about teratogenic effects.[17–19] It should be noted that long-term adverse effects from a single dose of stable iodine have not been observed.[20] Additionally, obtaining stable iodine can become more difficult later in pregnancy due to factors like impending delivery or hospitalization. From the perspective of nuclear disaster preparedness, pregnant women, including those who wish to have children, should also be prioritized and communicated to appropriately implement stable iodine prophylaxis. Barriers and facilitators of stable iodine implementation at the municipal and prefecture levels, as well as the intake of distributed tablets at the individual level, need to be further investigated and discussed in future research.

There were no participants who required a detailed thyroid gland examination, regardless of whether their mothers took stable iodine. Thyroid screening results were consistent with the findings from the FHMS, which found similar thyroid screening results among those exposed as children to the nuclear disaster in Fukushima, Japan.[21,22] This result may be attributed to the relatively low radiation doses following the Fukushima nuclear disaster, which may have limited the impact of radioactive exposure on the thyroid.[23] In addition, a previous study showed that the usual iodine intake was sufficient in those areas.[24] The number of participants requiring detailed thyroid examinations was thus not high in this study.

This study had some limitations. First, while all responses were collected from guardians, the analysis assumed that the majority were from mothers. The possibility of responses from fathers or other guardians cannot be excluded, yet this remains valuable information on radiation protection during pregnancy. Second, the timing of pregnancy was an estimate based on the assumption of full-term pregnancies to the maximum extent. However, the results from 3 sensitivity analyses consistently showed lower intake rates. Third, as the number of participants was not large, it might be difficult to examine the possible associations, being unable to perform additional inferential statistics. However, this study collected data from as many participants as possible, corresponding to the number of births in the same town for the fiscal year 2011.[25] Importantly, in terms of thyroid ultrasound outcomes, no participants required a detailed thyroid examination. Participants who did not respond regarding their guardians' stable iodine intake were excluded from the study. This exclusion may introduce a participation bias. However, sensitivity analyses of the cases of 18 individuals who did not respond regarding stable iodine were conducted. Whether all the 18 mothers took stable iodine or not, the numbers in both cases would be lower than the previously reported 63.5% among children. Notably, data from Chernobyl showed a thyroid cancer incidence of 66 per 100 000 person-years for individuals under 18 years old with stable iodine intake, versus 96 per 100 000 without.[1,26] Fourth, due to periodic revisions of the questionnaire used for this screening practice, we were unable to ask participants why they did not take stable iodine. However, based on discussions with staff of RSDRS, the assumed reasons for no intake would include impending delivery or hospitalization, as previously mentioned. Lastly, the findings from this study pertain to 1 municipality and may not be generalizable to all 4 municipalities where stable iodine intake was instructed. Yet, conducting surveys in the other municipalities was difficult due to mandatory evacuations, making this study unique in its scope.

In conclusion, as an immediate response after the Fukushima nuclear disaster, pregnant women had lower iodine intake rates than children. To ensure better nuclear disaster preparedness in the future, it is essential to focus on awareness-raising and effective communication among pregnant women. Regarding thyroid screening results, there were no participants who required further thyroid examination in this study.

Supplementary material. The supplementary material for this article can be found at http://doi.org/10.1017/dmp.2025.10048.

Data availability statement. The datasets generated for this study were not publicly available; however, they are available upon reasonable request from the authors, subject to approval from Hirata Central Hospital.

Author contribution. Conception and design (all authors); data collection (YN, CS, MT); data analysis (YN, MT); interpretation of the results (all authors); drafting of the article (YN, AG); critical revision of the article for important intellectual content (all authors); final approval of the article (all the authors).

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Competing interests. FO is currently employed by SUSMED Inc. However, SUSMED Inc had no role in any aspect of the study. The findings and conclusions presented in this study are solely of the authors alone. Outside the submitted work, YN received personnel fees from Japan Association for Clinical Engineers, Japan Society for the Promotion of Science, and EUCALIA Inc., a grant from Japan Medical Association, and a donation from Datack Inc.

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