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A Cluster of Thyrotoxicosis, Presenting with Muscle Weakness, at a Prison in Sakon Nakhon Province, Thailand, 2019

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Abstract

In April 2019, a cluster of prisoners with muscle weakness and palpitation was detected at Prison A in Sakon Nakhon Province, Thailand. An investigation was conducted to describe epidemiological characteristics, and to provide appropriate control measures. A descriptive cross-sectional study was done. Suspected cases were prisoners or prison officers who had at least one of the following manifestations: muscle weakness, palpitation, fatigue, increased perspiration, weight loss, or tachycardia during 1 Jan to 30 Sep 2019. Confirmed cases were suspected cases who had low thyroid-stimulating hormone (TSH) levels. We interviewed food suppliers and examined the food ingredients. Food samples were collected to test for thyroid hormone. Thirty confirmed cases and 61 suspected cases were found. The overall attack rate was 4.6%. Only male prisoners were affected. The majority of the cases had low TSH and low serum potassium levels. All cases had a history of eating pork offals. Pork offal was suspected as the cause of elevated tri-iodothyronine (T_3) and levothyroxine (T_4) levels. Establishing standard of food quality for food supplier and evaluation of food material could prevent future outbreaks.

Keywords: outbreak, thyrotoxicosis, thyroid hormone, pork offal, prison

Introduction

Thyrotoxicosis is a condition that occurs due to excessive thyroid hormone from any cause such as autoimmune disease, and excess iodine intake.[1] Specifically, thyrotoxicosis factitia refers to a condition of thyrotoxicosis caused by the ingestion of exogenous thyroid hormone.[2] It can be the result of excess drug, such as levothyroxine or as a thyroid tissue inadvertently removed from meat; which has resulted in two community outbreaks of thyrotoxicosis in the United States.[3,4] Moreover, there have been case reports that have described similar findings after consumption of beef sausage contaminated with thyroid tissue.[5,6] Classic symptoms of thyrotoxicosis include palpitations, muscle weakness, fatigue, weight loss, tachycardia and hand tremor. In relation to laboratory findings, patients with thyrotoxicosis factitia have low serum thyroid-stimulating hormone (TSH) levels. Serum tri-iodothyronine (T_3) and/or levothyroxine (T_4) may be elevated or normal, depending upon the degree of thyrotoxicosis while serum thyroglobulin (Tg) is suppressed.[7] Additionally, thyroid hormones also increase $3Na^+/2K^+$ ATPase activity leading to hypokalemia.[8] Discontinuation of thyroid hormone ingestion is usually the only treatment needed. When patients discontinue exposure to exogenous T_4, serum T_4 levels fall approximately 50 percent in seven days. T_3 is cleared more rapidly (serum half-life is approximately one day).[7]

In April 2019, the Department of Disease Control (DDC) in Thailand received a notification that there were 28 cases with muscle weakness, palpitation and fatigue at Prison A in Sakon Nakhon Province who received treatment at Hospital B. From all 8 specimens of blood collected from the cases, 7 specimens revealed hypokalemia and 1 out of 5 patients had low serum TSH levels. Then, after thyrotoxicosis had already

been diagnosed, the DDC, the Office of Disease Prevention and Control Region 8 Udon Thani, the Sakon Nakhon Provincial Health Office and Hospital B conducted an investigation beginning May 2019. The objectives were to confirm the diagnosis among those cases and outbreak, to describe epidemiological characteristics, and to provide recommendations and control measures.

Methods

We undertook a descriptive cross-sectional study of the thyrotoxicosis outbreak. The study population was both prisoners and prison officers in Prison A within the period 1 Jan to 30 Sep 2019. An active case finding was conducted using definition of patient under investigation (PUI). A PUI was defined as a prisoner or a prison officer at Prison A who had abnormal screening test: had a hand tremor or was unable to stand after squatting 3 times, or had muscle weakness during 1 Jan to 30 Sep 2019. A suspected case was defined as a prisoner or a prison officer at Prison A who had at least one of the following signs or symptoms during 1 Jan to 30 Sep 2019: muscle weakness, palpitation, fatigue, increased perspiration, weight loss, or resting pulse rate faster than 100 beats per minute (bpm). A confirmed case was defined as a suspected case who had low TSH levels (<0.3 µIU/mL).

All prisoners were screened by physicians using PUI definition. Then, prisoners and prison officers were interviewed and physically examined by physicians (Figure 1). Medical records of index cases were reviewed. A semi-structured questionnaire was used to collect information of demographic data, signs and symptoms, duration of imprisonment and history of food consumption.

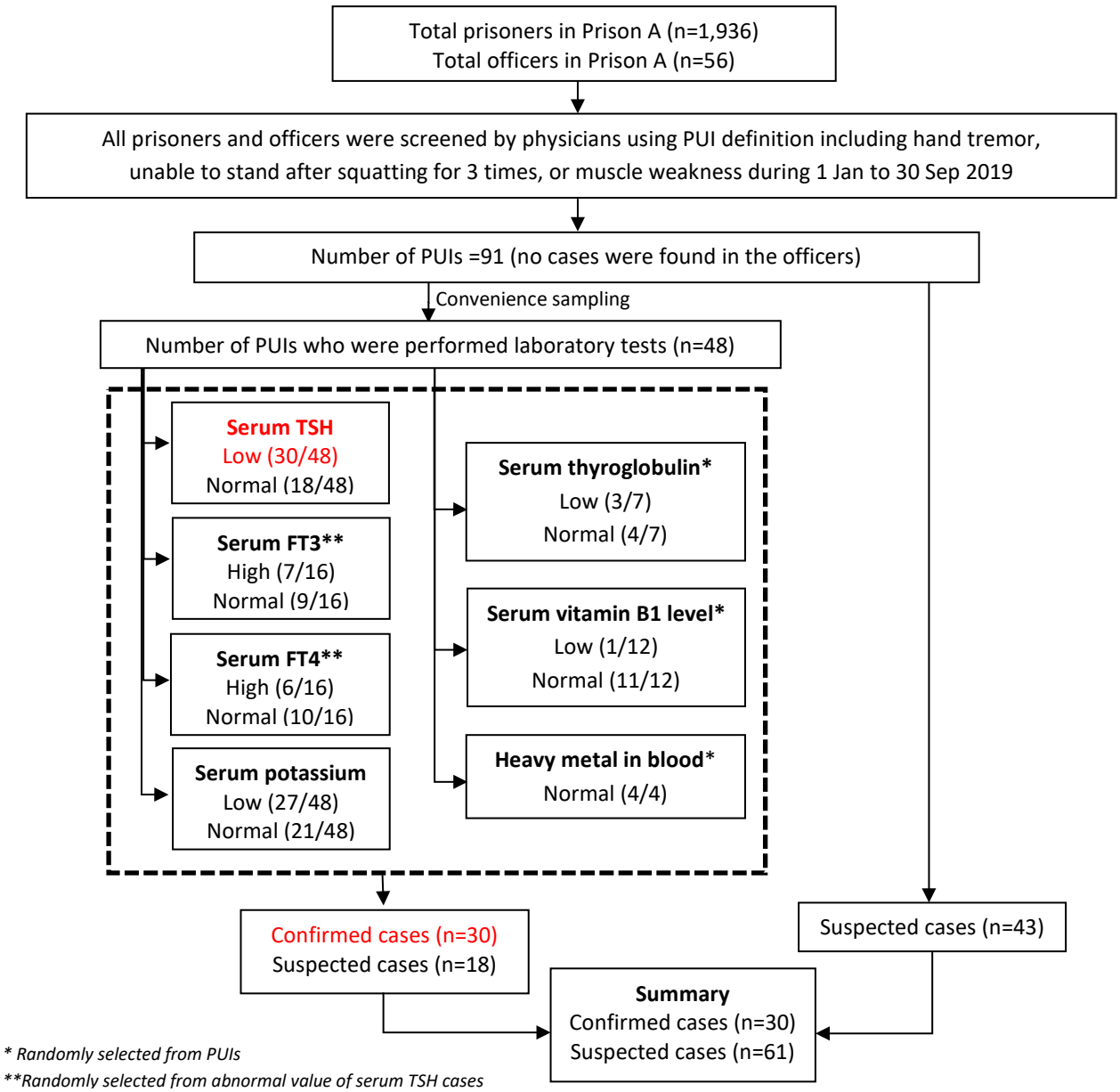

Figure 1. Diagram of active case finding in Prison A, Sakon Nakhon Province during 1 Jan–30 Sep 2019

Serum TSH and serum potassium were tested in suspected cases. Only cases who had abnormal TSH were tested for free T_3 and free T_4. Thyroid function test was performed at Hospital B. Suspected cases were randomly selected to test for serum vitamin B1, heavy metal in blood (Cadmium, Lead, Manganese), and serum thyroglobulin by convenience sampling. Vitamin B1, heavy metal in blood, and serum thyroglobulin were tested at the Center for Medical Diagnostic Laboratories, Faculty of Medicine, Chulalongkorn University, National Institute of Health (NIH) of Thailand, and BANGKOK R.I.A. LAB, respectively (Table 1).

Table 1. Normal values of laboratory testing

Test name	Specimen	Normal value	Unit
Thyroid-stimulating hormone (TSH)	Serum	0.3-3.6	µIU/mL
Free tri-iodothyronine (FT_3)	Serum	2.2-4.2	pg/mL
Free levothyroxine (FT_4)	Serum	0.8-1.7	ng/dL
Thyroglobulin (Tg)	Serum	3.5-77	ng/mL
Potassium	Serum	3.5-5.1	mmol/L
Vitamin B1	Serum	28-85	µg/L
Cadmium (Cd)	Blood	≤2	µg/L
Lead (Pb)	Blood	≤10	µg/dL
Manganese (Mn)	Blood	≤15	µg/L
Iodine level in table salt	Salt	2.0-3.0	mg/kg
Iodine level in fish sauce	Fish sauce	2.0-3.0	mg/kg
Iodine level in drinking water	Water	≤0.02	mg/L

For an environmental study, prisoners, prison officers, and food suppliers were interviewed. The suspected source of the outbreak was identified as follows: pork, pork offal and chickens supplied to Prison A during 2 Jul to 17 Sep 2019 which were randomly tested for T_3 and T_4 levels (measured as µg/g protein) by Division of Clinical Chemistry, Department of Medical Technology, Faculty of Associated Medical Sciences, Chiang Mai University. Because there was no standard laboratory values in food, food items including pork, pork offal and chickens from a registered market in Chiang Mai Province were collected by a veterinarian to be the best possible items for the control. Tissue lysates were prepared by extracting 20 mg of tissue samples with Radioimmunoprecipitation assay (RIPA) buffer. Protein concentration from the lysate supernatants were determined by Bicinchoninic acid (BCA) protein assay kit (Thermo Scientific). Total T_3 and T_4 in lysate supernatants were determined by Cobas e411 autoanalyzer (Roche) based on the principle of electrochemiluminescence immunoassay (ECLIA). Iodine levels of table salt, fish sauce and drinking water were measured at the Department of Medical Sciences.

Statistical Analysis

Continuous data were represented using median with inter-quartile range (IQR). Categorical data were presented using proportions and attack rate (AR). The data were analyzed using STATA® version 14.2 and Microsoft® Excel® 365. EpiData version 3.1 was used for data collection.

Ethics

Ethical clearance was omitted as this investigation was conducted as part of a response to a disease outbreak.

Results

Setting and General Description

Prison A located in Sakon Nakhon Province. There were 1,936 prisoners (1,769 males and 167 females) and 56 officers (54 prison officers and 2 nurses).

A Cluster of Thyrotoxicosis Description

There were 30 confirmed cases and 61 suspected cases; all were identified among prisoners. There was no case among prison officers. All cases were male. Overall attack rate was 4.6% (91/1,992) while specific attack rate among male prisoners was 5.1%. The median (IQR) age was 38 years (32-43 years). The epidemic curve indicated intermittent common source pattern. The indexes were reported in April, but retrospective investigation found that cases had begun in January. After cessation of pork offal purchasing, the number of cases declined (Figure 2). Median (IQR) duration of imprisonment of cases was 9 months (IQR: 6-22 months). In addition, suspected and confirmed cases had muscle weakness (93.8%). Fatigue and numbness were 70.8% and 64.6%, respectively. Other reported symptoms were increased perspiration (56.3%), weight

loss (45.8%) and palpitations (43.8%). From the physical examination, we found hand tremor (29.2%), thyroid enlargement (10.4%), thyroid tenderness (8.3%), pulse rate >100 bpm (8.3%) and exophthalmos (4.2%) (Figure 3). From prisoner interviews, all prisoners ate only the food provided by Prison A and had a history of consuming pork offal during 2018–2019. Additionally, in the monthly food menu, it was found that there was pork offal menu about 3 percent of food items per month (Figure 4).

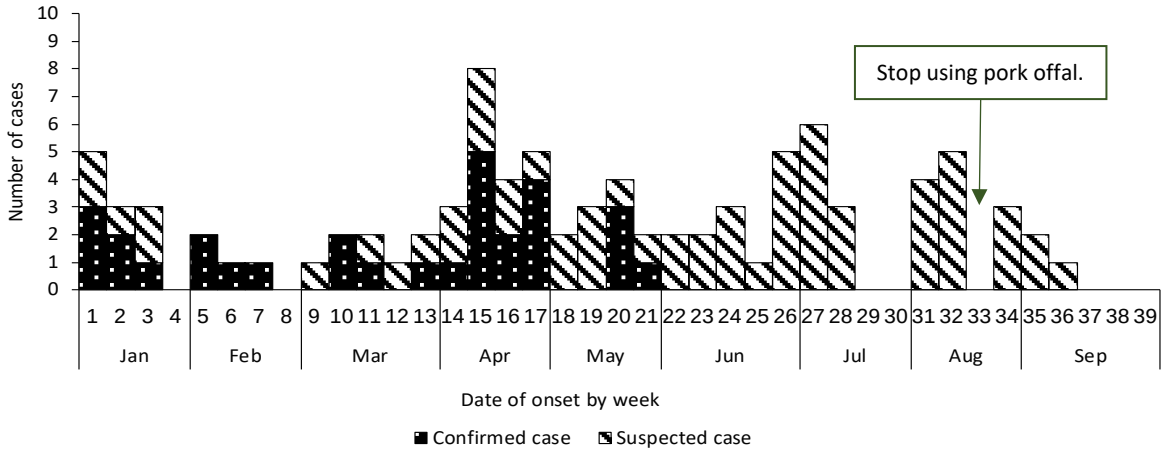

Figure 2. Number of thyrotoxicosis cases in Prison A, Sakon Nakhon Province during 1 Jan–30 Sep 2019 (n=91: confirmed=30, suspected=61)

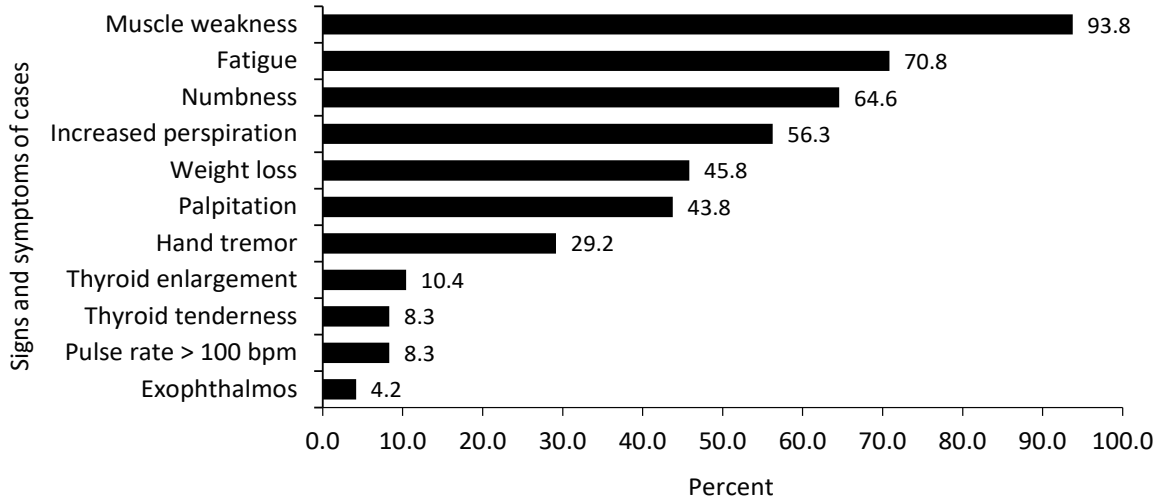

Figure 3. Signs and symptoms of thyrotoxicosis cases in Prison A, Sakon Nakhon Province during 1 Jan–30 Sep 2019 (n=48)

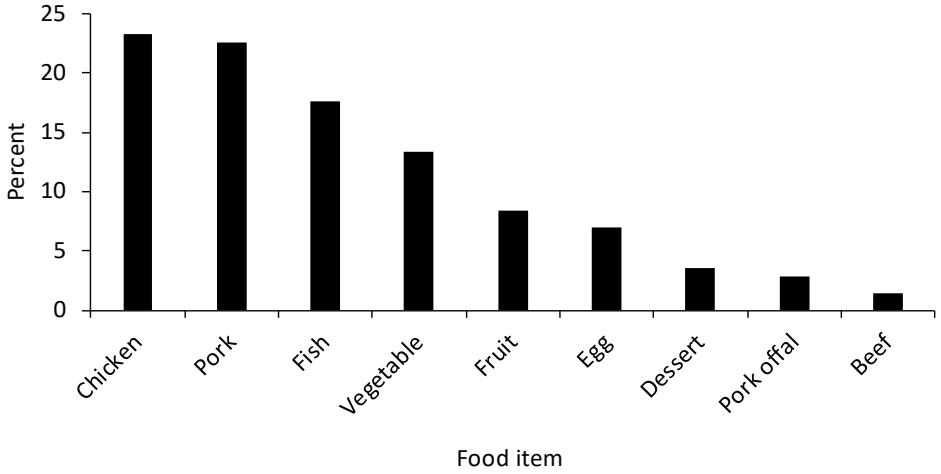

Figure 4. Percentage of food items consumed per month in Prison A, 2019 (n=142 food items)

Laboratory Study

We tested serum TSH levels by convenience sampling in 48 suspected cases showing 30 cases had low serum TSH (<0.3 µIU/mL). Free T_3 and free T_4 levels were elevated (>4.2 pg/mL and >1.7 ng/dL) in 7 of 16 cases (44%) and 6 of 16 cases (38%), respectively. Serum thyroglobulin levels were depressed (<3.5 ng/mL) in 3 of 7 cases (43%). Serum potassium levels were low (<3.5 mmol/L) in 27 of 48 cases (56%). Only 1 of 12 cases had low serum vitamin B1. Heavy metal in blood (Cadmium, Lead, Manganese) were normal in 4 cases measured.

Environmental Study

There were 9 zones in this prison; 8 male prisoner zones including kitchen, fieldwork, carpenters, cleaning, discipline training, education zone, outside working and nursing room and 1 female prisoner zone. Common food provided for the prisoners per month composed of chicken (23.2%), pork (22.5%), and fish (17.6%). Pork offal was 2.8% (Table 2). We sent the specimens by convenience sampling from Prison A including 8 pork samples, 7 chicken samples and 8 pork offal samples for T_3 and T_4 levels testing. In addition, pork (2 samples), chicken (1 sample) and pork offal (11 samples) from a registered market in Chiang Mai Province were tested as controls. We found that the median T_3 and T_4 levels in pork offal from Prison A including lung, bronchus, liver, spleen and intestine were 2 to 7 times higher than controls. In comparison, the median T_3 and T_4 levels in prison pork and chicken were nearly the same as controls (Table 2). Iodine levels in samples of table salt, fish sauce and drinking water from Prison A were within normal limit (Table 3).

Table 2. Laboratory of average T_3 and T_4 levels in pork, chicken, and pork offal

Specimen	Prison A			Control		
	Number of specimens	T_3 (µg/g protein)	T_4 (µg/g protein)	Number of specimens	T_3 (µg/g protein)	T_4 (µg/g protein)
Pork	8	1.92	4.34	2	1.32	3.08
Chicken	7	2.55	6.19	1	2.03	4.17
Pork offal	8			11		
• Lung	1	10.80	26.53	2	2.15	5.07
• Bronchus	1	10.70	24.84	2	2.14	5.36
• Liver	3	5.04	11.92	2	1.91	4.43
• Spleen	1	8.80	21.70	2	1.48	3.48
• Intestine	2	5.74	14.40	3	2.06	4.86

Table 3. Laboratory tests of iodine levels in table salt, fish sauce, and drinking water

Specimen	Iodine level	Expected level
Table salt	<3.0 mg/kg	2.0-3.0 mg/kg
Fish sauce	2.53 mg/kg	2.0-3.0 mg/kg
Drinking water	0.02 mg/L	≤0.02 mg/L

Discussion

Confirm Diagnosis

A cluster of thyrotoxicosis occurred in Prison A. Signs and symptoms among cases were compatible with thyrotoxicosis factitia that showed hyperthyroid manifestation. Decreased TSH, increased T_3 and T_4 with low serum thyroglobulin were also correlated with thyrotoxicosis factitia. Nonetheless, low vitamin B1 level was found in only one case. The magnitude of B1 deficiency was likely imprecise as symptoms were subjective and confirmatory physical examination had not been performed.

Characterize Outbreak

The number of cases had increased since January 2019. The overall attack rate in this outbreak was 4.6%. It was considered low extension when compared to previous outbreaks which occurred in Mae Hong Son and Sri Sa Ket Provinces during 2016 to 2017 in which the overall attack rate was 51.1% and 12.6%, respectively.[9] Furthermore, if laboratory had been tested for all prisoners, more cases might be found. The reason that the outbreak involved only male prisoners was the female prisoner's kitchen received food ingredients from a different source.

Identify Cause

We found high thyroid hormone levels in pork offal collected from the kitchen in Prison A that might be due to contamination which occurred during slaughtering process.[3] Consumption of food that is contaminated with thyroid hormone can cause thyrotoxicosis because the hormone is absorbed–similar

to the drug used in treatment of hypothyroidism. Thyroid hormone is heat stable, so it is not degraded by cooking.[3] Consumption of thyroid contaminated pork and chicken were the causes of the previous outbreaks.[10]

Action Taken and Follow Up

Active case finding, laboratory testing and environmental evaluation were done. We advised the officers for observing abnormal appearance of the meat as well as advised the officers to stop importing pork offal since 13 Aug 2019. Since then, there has been no further case after stopping purchase of pork offal for 2 weeks.

Limitations

Due to restrictions and authority in the prison setting, we could not implement the good sampling method for laboratory testing. Asymptomatic cases may be lost from this study. Besides, it was difficult to determine the amount eaten among cases. Thyroid contamination was not included in the food safety guideline in Thailand. We had no authority to obtain some important information such as pork offal source from the food suppliers. Due to limited resources, the preventive and control measures were not fully implemented. The supplier continued providing the pork offal leading to the prolonged outbreak.

Recommendations

The Department of Correction should set up the food quality standard for food suppliers and food ingredients inspection. Prisons should continue surveillance for thyrotoxicosis that was announced and performed simple case finding followed the PUI definition at least one month after the onset of the last case. Furthermore, thyroid hormone contamination as a food safety issue should be considered by Bureau of Food Safety Extension and Support, Ministry of Public Health. The Department of Livestock Development should also set up a slaughterhouse quality standard for thyroid contaminated prevention procedure. In addition, thyroid laboratory testing of food should be developed by the National Institute of Health of Thailand.

Conclusion

During January to September 2019, a thyrotoxicosis outbreak occurred in Prison A, Sakon Nakhon Province, Thailand. The outbreak affected only male prisoners with the overall attack rate of 4.6%. Pork offal was suspected because thyroid hormone levels in pork offal were higher than control. High thyroid hormone levels were found in pork offal which was collected from the kitchen in the prison. The contamination might occur during the slaughtering process. Establishing a standard of food quality for food suppliers and evaluation of food material could prevent future outbreaks.

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Suggested Citation

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