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การระบาดของโรคพิษเมทานอลจากยาดองเถื่อนใน 3 ชุมชน จังหวัดชลบุรี ประเทศไทย

A study of methanol poisoning outbreak from infused liquor in three communities, Chonburi, Thailand

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บทคัดย่อ

วัตถุประสงค์ : วันที่ 20 ตุลาคม 2562 กองระบาดวิทยา กรมควบคุมโรค ได้รับรายงานว่าพบผู้ป่วยด้วยอาการแน่นหน้าอก อาเจียนเป็นเลือดหลังดื่มยาดอง มาโรงพยาบาลชลบุรี จำนวน 14 ราย เสียชีวิต 1 ราย ทีมสอบสวนโรคได้ดำเนินการสอบสวนในวันที่ 21-22 ตุลาคม 2562 เพื่อยืนยันการวินิจฉัยและการระบาดของโรค ศึกษาระบาดวิทยาของการเกิดโรค ค้นหาปัจจัยเสี่ยงของการเกิดความรุนแรงของโรค และให้คำแนะนำมาตรการในการควบคุมป้องกันโรค

รูปแบบและวิธีวิจัย : ศึกษาเชิงพรรณนาโดยทบทวนเวชระเบียน ตรวจหาสารพิษในยาดองที่เกี่ยวข้อง ศึกษาเชิงวิเคราะห์เพื่อระบุปัจจัยที่เกี่ยวข้องกับความรุนแรงของผู้ป่วย ตรวจสอบแหล่งผลิตยาดอง และกระบวนการผลิต

ผลการศึกษา : จากผู้ดื่มยาดอง 25 ราย ใน 3 ชุมชน พบผู้ที่มีอาการ 22 ราย (ร้อยละ 88.0) เสียชีวิต 5 ราย ผู้ป่วยร้อยละ 50.0 เข้ารับการรักษาในโรงพยาบาล จำเป็นต้องฟอกเลือด ร้อยละ 31.8 มัธยฐานอายุเท่ากับ 42 ปี (IQR=16.3) มัธยฐานระยะเวลาแฝง (latent period) เท่ากับ 17 ชั่วโมง อาการที่พบมากที่สุด คือ สับสน (ร้อยละ 40.9) รองลงมา คือ คลื่นไส้/อาเจียน (ร้อยละ 36.4) และการมองเห็นผิดปกติ (ร้อยละ 18.2) ผู้ป่วยส่วนใหญ่ตรวจเลือดพบ High anion gap ระดับเมทานอลในตัวอย่างยาดองมีค่าสูงเกินมาตรฐาน (36.2 g/dl) การดื่มสุราในปริมาณสูงมีความสัมพันธ์อย่างมีนัยสำคัญกับความรุนแรงของผู้ป่วย (Coefficient 833.4,

95%CI 207.9-1459.0) ในด้านกระบวนการผลิตผู้ขายผสมยาดองขึ้นเองแล้วเดินหาบเร่ขายตามแต่ละบ้าน อย่างไรก็ตามทีมสอบสวนโรคไม่สามารถระบุส่วนประกอบของยาดองโดยละเอียดได้เนื่องจากผู้ผลิตหลบหนี
สรุปผลการศึกษา : พบผู้ป่วยจากการดื่มยาดองปนเปื้อนเมทานอล โดยอัตราการตายของผู้ป่วยอยู่ในเกณฑ์เฉลี่ยใกล้เคียงกับเหตุการณ์อื่น ๆ และยังพบความบกพร่องทางสายตาถาวร ปริมาณการดื่มยาดองส่งผลต่อความรุนแรงของอาการอย่างมีนัยสำคัญทางสถิติ มาตรการที่ดำเนินการในพื้นที่ ได้แก่ แนะนำให้ให้ความรู้ด้านสุขภาพเกี่ยวกับพิษของเมทานอลและเสริมสร้างการบังคับใช้กฎหมายเกี่ยวกับการขายสุราเถื่อน
คำสำคัญ : การระบาด, เมทานอล, ชลบุรี, ยาดอง

ABSTRACT

Objective : On October 20, 2019, the Department of Disease Control was notified that 14 patients had experienced chest tightness, nausea, and hematemesis after ingesting a new formula-infused liquor believed to be mixed with a toad and had gone to Chonburi Hospital. One of them died. Subsequently, the Joint Investigation Team conducted an investigation on October 21–22, 2019, to verify the diagnosis, perform active case finding, identify severity factors, and provide recommendations.

Methods : We reviewed medical records and conducted a descriptive study. The implicated liquor was sent for the determination of toxic substance levels. An analytic study was performed to identify factors associated with the severity among the patients. The distribution point and the production process of the liquor were also investigated.

Results : Of 25 liquor drinkers living in 3 communities in Chonburi, 22 cases (88.0%) were identified; 5 of them died. Fifty percent of them were hospitalized; 31.8% required hemodialysis. The median age was 42 years old (IQR=16.3). The median latent period was 17 hours. The most common symptom was confusion (40.9%), followed by nausea/vomiting (36.4%) and abnormal vision (18.2%). Most of the cases exhibited a high anion gap. Methanol levels in two liquor samples were extremely high (36.2 g/dl). A high amount of liquor drinking was significantly associated with the severity of cases (Coefficient 833.4, 95%CI 207.9-1459.0). The maker illegally mixed the infused liquor and distributed the liquor door-by-door. The components of the infused liquor cannot be identified.

Conclusion : A confirmed cluster of methanol poisoning was caused by the ingestion of methanol-contaminated infused liquor. No toad was involved. The case fatality rate was within the average range of previous outbreaks. Permanent visual impairments were detected. The amount of infused liquor consumed was statistically significant among severe and non-severe cases. Health education on methanol poisoning and strengthened enforcement on selling illegal liquor are recommended.

Keywords : Outbreak, Methanol, Chonburi, Infused liquor

Background

Infused liquor can be made in various ways, often by mixing rice whiskey with various herbs. Sometimes, a combination of poisonous animals is believed to enhance sexual performance and treat certain diseases.[1] Despite being an ancient local tradition, infused liquor is illegal under the Alcohol Beverage Control Act, B.E. 2551.[2]

The toxic substances found in the liquor are generally divided into two types: those naturally occurring in the production process and those intentionally mixed by the manufacturer for some perceived benefit.[3] Methanol is one of the toxic substances that can contaminate illegal liquor.[3] People can be exposed to methanol through vapors, ingestion, and dermal or eye contact.[4] The suspected toxic substances in illegal liquor, besides methanol, include cyanide, bufotoxin, organophosphate, carbamate, detergent, and heavy metals such as cadmium, mercury, and arsenic.

Methanol can be metabolized to formaldehyde and formic acid, which are toxic to the central nervous system. This can lead to delirium, seizures, coma, respiratory depression, complete blindness, and death.[5] The lowest amount of methanol that can cause blindness is 3.2 grams per person, and the lethal dose is 15.8 grams per person.[6] The effects of methanol contamination have resulted in high morbidity and mortality worldwide. In Thailand, according to the National Health Database, the incidence was 1.8 per million population in 2017, decreasing to 1.2 and 0.7 per million in 2018 and 2019, respectively. Despite this decreasing trend, the number of methanol poisoning cases continues, predominantly in the northern part of the country.

On October 20, 2019, the Department of Disease Control was notified that 14 patients had experienced chest tightness, nausea, and hematemesis after ingesting a new formula-infused liquor believed to be mixed with a toad and had gone to Chonburi Hospital. One of them died. Subsequently, the Joint Investigation Team investigated on October 21–22, 2019, to verify the diagnosis, perform active case finding, identify severity factors, and provide recommendations.

Methods

Operational definition

- New formula-infused liquor is illicit alcohol suspected of causing current health threats in the community. It is allegedly made by a suspected individual, who reportedly mixed the liquor with a toad and distributed it during the study period.

Descriptive study

A descriptive study included interviewing the involved people, active case finding, and reviewing medical records. Our target population was the people that exposed to the new formula-infused liquor living in three communities: Samed Subdistrict, Muang District, Chonburi Province, from October 13 to November 13, 2019, who were exposed to infused liquor. We

reviewed the methanol poisoning situation in Chonburi Province from Chonburi Hospital. We reviewed medical records from Chonburi Hospital and a private hospital that the patients visited. Moreover, we interviewed cases, their relatives, and villagers through door-to-door screening and broadcasting using a car announcement with semi-structured questionnaires. Furthermore, we conducted interviews with doctors using unstructured questionnaires the purpose of obtaining differential diagnoses. Variables included in the review were sex, age, underlying disease, address, signs and symptoms, onset date and time, treatment, duration from onset to death, complications, drinking frequency, reasons to drink alcohol, type of beverages, reasons for choosing beverages, and places to buy alcohol. Furthermore, we examined the methanol poisoning situation in Chonburi Province from medical records at Chonburi Hospital from January 1, 2014, to November 13, 2019. For the environmental study, we explored the locations of group drinking in the communities to identify the infused liquor distribution point by interviewing villagers and observing their activities. We used Epi Info™ version 7.2 to calculate the percentage, ratio, median with Q1 and Q3.

Case definition

Suspected case: Any person who lived in the three communities in Chonburi Province, had a history of ingesting new formula-infused liquor during October 13 to November 13, 2019, and met one of the following criteria:

- Died or exhibited at least two of the following symptoms: coma, restlessness, seizure, confusion, dizziness, headache, abnormal vision, palpitation, nausea/vomiting, or abdominal pain.

- Laboratory criteria: High anion gap metabolic acidosis (Na^+- Cl^-- $HCO3^-$ ≥ 12 mmol/L)[7]

Confirmed case: A suspected case who had a blood methanol level > 20 mg/dL or a blood formic acid level > 9 mg/L.[8]

Laboratory study

We collected samples from the cases and the environment, including the new formula-infused liquor from the suspected cases' houses. For the cases, we sent blood samples from the intensive care unit (ICU) hospitalized suspected cases to Ramathibodi Hospital, which included six blood samples for methanol, four blood samples for formic acid, and four blood samples for cyanide. Additionally, we sent two blood samples to the Division of Environmental and Occupational Diseases to test for ethanol, methanol, formic acid, mercury, cadmium, and arsenic. We reviewed laboratory results from the medical records at Chonburi Hospital to evaluate severity, which included blood sodium, potassium, bicarbonate, chloride, and anion gap for all cases.

For the environment, two samples of the new formula-infused liquor from suspected cases' houses were sent to Ramathibodi Poison Center to test for organophosphate and

carbamate. Moreover, we sent them to the Division of Environmental and Occupational Health to test for ethanol, methanol, formic acid, mercury, cadmium, and arsenic.

Analytic study

We conducted a retrospective cohort study to identify prognostic factors for severity. The study population comprised all suspected and confirmed cases from the descriptive study. We classified the target population into two groups: severe cases, which included any patient who died or was admitted to the ICU, and non-severe cases, which included any patient treated as an inpatient in a general ward, outpatient, or through self-treatment. The study variables included sex, age, the amount of infused liquor ingestion, and the duration from onset to treatment. Analytical statistics were determined using linear regression with Epi Info™ version 7.2.

Results

Descriptive study

This methanol outbreak occurred in Chonburi Province, located in the eastern part of Thailand. The most common occupation among the people who were exposed to the infused liquor in these three communities was labor (86.4%). The houses were predominantly rental row houses, and the villagers live in close proximity to each other.

According to the review of methanol poisoning cases at Chonburi Hospital, there were no reports in the last five years. However, some cases were diagnosed as methanol poisoning in October 2019, which marks the starting point of this outbreak.

A total of 25 people who consumed the new formula-infused liquor were identified. Twenty-two cases met the case definition, divided into seven confirmed cases and 15 suspected cases in three communities. The overall attack rate within the group with a history of consuming the infused liquor was 88.0% (22/25). The attack rates for communities A, B, and C were 87.5%, 100.0%, and 75.0%, respectively. There were five deaths, resulting in a case fatality rate (CFR) of 22.7%. Among the survived cases, eight (47.1%) were treated as inpatients, and four cases (36.4%) had permanent visual problems. Regarding the characteristics of the cases, the median age was 42 years old (Q1-Q3 = 37.0-53.3). The male-to-female ratio was 1.4:1. The median latent period was 17 hours (Q1-Q3 = 13.5-24.5). Most of the cases (94.4%) had a high anion gap. Seven cases (31.8%) required hemodialysis. Most of the cases were laborers (86.4%), followed by the unemployed (9.1%) and merchants (4.6%). The five most common symptoms were confusion (40.9%), followed by nausea or vomiting (36.4%), fatigue (31.8%), chest discomfort (27.3%), and unconsciousness (27.3%) (Figure 1).

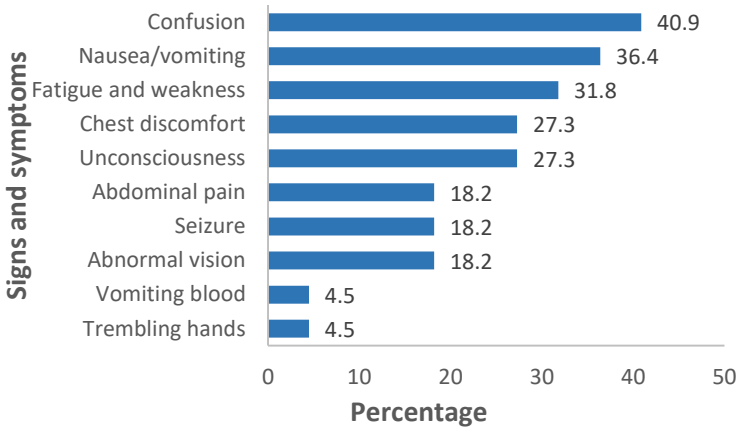


Figure 1. The signs and symptoms of methanol poisoning cases, October 21–November 13, 2019 (n=22)

The epidemic curve (Figure 2) shows that the onset of the cases began on the morning of October 19. The curve resembles a point common source. The suspected exposure time for the first case was from October 17-18. As observed from the decreasing number of cases and the absence of new cases after October 22, it suggests that the source may have been stopped.

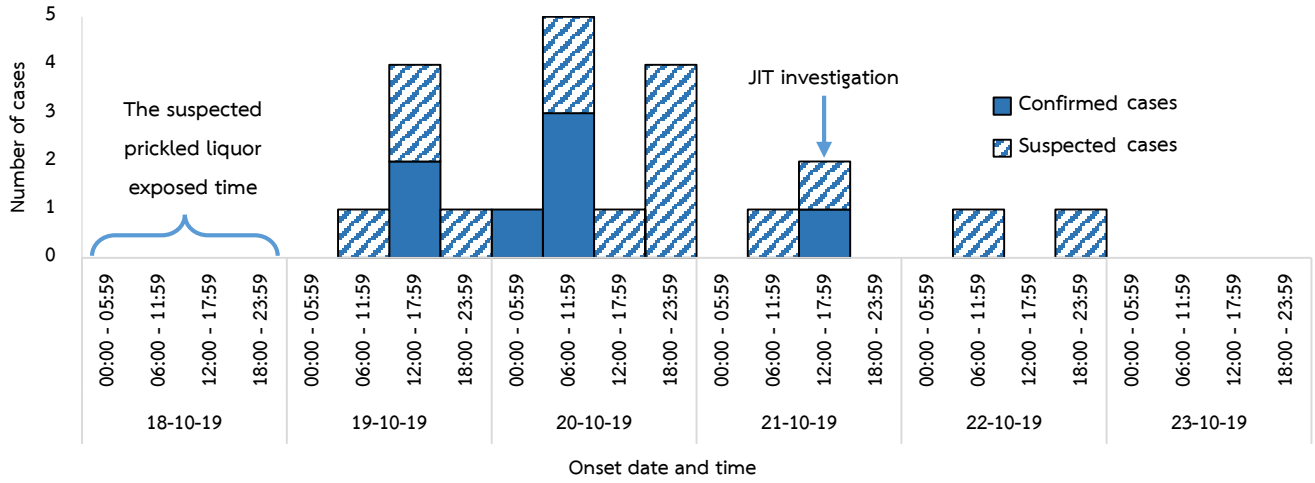


Figure 2. The number of methanol poisoning cases by date and time of onset, from October 13 to November 13, 2019 (n=22)

The treatment included ethanol via nasogastric feeding as an antidote. Supportive treatment comprised proton pump inhibitors (PPIs), supplemented vitamins such as thiamine, folic acid, and vitamin B6, as well as supportive intravenous fluids and electrolyte-adjusting agents. For patients with severe electrolyte imbalances, acute hemodialysis was administered. Endotracheal intubation was performed in patients with acute respiratory failure (seven cases). All inpatients were monitored for signs, symptoms, and blood electrolytes.

One-third of the cases drank alcohol daily, followed by only special events at 20.7%. The major reason for cases to consume alcohol was being persuaded by friends (73.3%), followed by socializing (53.3%), having a lot of free time (33.3%), and stress relief (20.0%). The primary factor influencing beverage selection was the cheap price and containing special properties, accounting for 40.0% of the cases. The most common place to buy alcohol was the community grocery store (73.3%), followed by delivery (26.7%), convenience stores (13.3%), and the flea market (6.7%).

The environmental study revealed the distribution of cases in Community A, including the liquor maker's house and the location of group drinking. The new formula-infused liquor maker had moved to live in Community A for about two months. Initially, he sold Thai cotton candy but switched to selling the new formula-infused liquor for approximately 15 days. In the beginning, he bought infused liquor from other stores to sell in Community A. Afterward, he started making his new formula of infused liquor for about a week and distributed it to nearby villagers without explicitly informing them of the liquor components. The maker walked around the community, distributing the liquor door-to-door. Not only in Community A, but the maker also distributed his product to other sellers in Communities B and C. According to the interviews, no one knew the components of the infused liquor. The patients stated that the liquor maker provided them with no information, only mentioning that it was a new product and encouraging them to try it. Furthermore, when investigating the rumor about liquor being infused with a toad, we identified its cause. The rumors that this new liquor was mixed with a toad originated from a journalist who took a picture of a toad jumping in the maker's house and spread it out. Consequently, the villagers believed that the liquor is a mixture involving a toad.

Laboratory study

Laboratory results of the cases showed that 5 out of 6 blood specimens had blood methanol levels higher than the toxic level. The median blood methanol level was 22.3 mg/dL (Q1-Q3=20.1-134.6). The median formic acid level was 958.5 mg/L (Q1-Q3=205.9-1712.8). The results of blood sample from cases (n=4) for formic acid, mercury, cadmium, and arsenic are presented in Table 1.

Table 1. Laboratory results of methanol poisoning biomarkers from cases

Laboratory testing of human biomarkers (unit)	Number of specimens over toxic level	Substance level
Methanol (mg/dL)	5/6	Median 22.3 (Q1, Q3=20.1, 134.6)
Formic acid (mg/L)	4/4	Median 958.5 (Q1, Q3=205.9, 1,712.8)

Laboratory testing of human biomarkers (unit)	Number of specimens over toxic level	Substance level
Ethanol (mg/L)	0/2	4.7 and 356.4
Cyanide (mg/L)	0/4	Median 0.1 (Q1, Q3=0.0, 0.1)
Digoxin (ng/mL)	0/1	<0.9
Mercury (μg/L)	2/2	2.4 and 3.4
Cadmium (μg/L)	2/2	0.2 and 1.9

The laboratory testing of the infused liquor showed methanol levels higher than the toxic level in 2 out of 2 specimens, with concentrations of 48.3 and 63.7 %weight/volume. Additionally, it tested positive for ethanol, with a median concentration of 56.0 %weight/volume. The results of infused liquor samples (n=2) for formic acid, organophosphate, carbamate, mercury, cadmium, and arsenic are illustrated in Table 2.

Table 2. Laboratory results of the new formula-infused liquor collected from the cases' houses

Laboratory testing of infused liquor (unit)	Number of specimens over toxic level	Substance level	
		Specimen from community A	Specimen from community B
Methanol (%w/v)	2/2	48.3	63.7
Ethanol (%w/v)	0/2	61.6	36.2
Formic acid (mg/L)	0/2	9.0	8.4
Mercury (μg/L)	0/2	$4.5x10^{-2}$	$4.0x10^{-2}$
			0.1
Cadmium (μg/L)	0/2	0.1	
Arsenic (μg/L)	0/2	1.3	0.7

Analytic study

In the analytic study to evaluate prognostic factors associated with severe symptoms among cases, in addition to the four variables we assessed, the amount of infused liquor ingestion emerged as a significant prognostic factor with an adjusted coefficient of 4.5x10-4 and a 95% confidence interval of $2.7x10^{-5}$-$8.8x10^{-4}$. (Table 3)

Table 3. The prognostic factors of severe symptoms compared between severe cases and non-severe cases

Variables	Severe (n=9)	Non-severe (n=13)	Coefficient	95%CI	P-value
Sex; No. of males (%)	6 (46.2)	7 (53.8)	-0.12	-0.6-0.3	0.67
Age (years); Median (Q1, Q3)	46 (37, 61)	42 (37, 47)	5.8	-5.3-16.9	0.50
Amount of infused liquor ingestion before symptom (ml.); Median (Q1, Q3)	700 (250, 1300)	100 (63, 212.5)	833.4	207.9-1459.0	0.04
Duration onset to treatment (Median, hours)	14.2 (4.2, 25.0)	19.3 (0.5, 35.8)	-3.4	-20.4-13.7	0.92

Control measures

We provided health education to villagers about the dangers of illegal liquor through leaflets and car announcements. We communicated risks and aimed to prevent panic within the community. Additionally, Chonburi Hospital strengthened methanol poisoning surveillance by using the ICD-10 code.

Discussion

This study confirms a methanol poisoning outbreak in three communities in Chonburi Province. There are four pieces of evidence supporting the causation of methanol poisoning. First, blood methanol levels were found to be higher than the lethal level, which is more than 90 mg/dl. Second, high anion gap metabolic acidosis was observed in 94.4% of the cases, and methanol is one of its causes. Third, visual disturbance is one of the toxic effects of methanol. Four cases (36.4%) experienced eye complications. Previous studies on methanol poisoning have shown that the most common complications occur in the eyes (16.2%-55.0%).[11-12] Our study reported a lower percentage, which could be attributed to appropriate treatment. Fourth, the blood levels of other potentially toxic substances were below toxic levels. This could be explained by these substances not being included in the purification process, as believed by the liquor maker. These pieces of evidence strongly support the methanol

outbreak. Moreover, monitoring blood levels of methanol, electrolytes, and following up on eye complications were deemed necessary.

In terms of severity, the Case Fatality Rate (CFR) was similar to that observed in previous outbreaks, with serious health consequences identified. The CFR was 22.73%, and the rate of eye complications was 36.4%. Previous studies have reported CFRs ranging from 18% to 50%, and eye complications ranging from 16.2% to 55%.[13-14] The CFR in our study is lower than in others, likely due to the dilution of mixed ethanol with infused liquor before consumption or the intake of ethanol after consuming infused liquor, which serves as an antidote for methanol.

Regarding the prognostic factors for severe symptoms, the amount of infused liquor ingestion significantly differed between the severe and non-severe groups. According to a previous study, the concentration of biological exposure indices and clinical symptoms of methanol exposure might have a dose-response relationship. (5) Since the median amount of infused liquor ingestion among non-severe cases was higher than the lethal dose (90 mg/dL), this could be attributed to early and proper treatment, leading to a higher survival rate. Therefore, early and proper management might contribute to a decrease in mortality.

Infused liquor legalization is controversial. On one hand, many formulas of infused liquor were historically used as medication, representing valuable local wisdom. On the other hand, infused liquor has been associated with fatalities and permanent disabilities. (1) There is a concern that contaminated substances can be produced in substandard production processes. Nevertheless, if infused liquor legalization is considered, adherence to standard production must be a priority.

Limitation

We could not directly inquire about the process of methanol contamination from the liquor maker as he has been evading police arrest. Moreover, this study is subject to some information bias stemming from the level of consciousness of the cases. Additionally, there is some missing data (16.0%), including onset date, consumption date and time, and the amount of infused liquor ingestion due to the mentioned altered level of consciousness, which may introduce some inaccuracy into the data. We attempted to mitigate this by aggregating information from various sources other than the patients, such as patients' relatives, neighbors, and medical records, to obtain the most accurate data.

Recommendations

Office of Disease Prevention and Control, Region 6 (ODPC6), Chonburi Provincial Health Office, administrative officers, local police, and the Excise Department conducted a joint inspection of the sales of alcoholic beverages in Chonburi Province. The Office of the Consumer Protection Board should strengthen control measures and monitor liquor production in Thailand. Additionally, the Office of the Alcohol Control Committee and the

Bureau of Risk Communication and Health Behavior Development at the Department of Disease Control (DDC) should publicize the risks associated with methanol consumption.

Conclusion

A confirmed cluster of methanol poisoning occurred due to methanol-contaminated pickled liquor ingestion in three communities on September 21–22, 2019. No toad was involved. The case fatality rate was within the average range of other previous outbreaks. Permanent visual impairments were detected. The amount of infused liquor drinking was statistically significant among severe and non-severe cases. Health education on methanol poisoning and strengthened enforcement on selling illegal liquor are recommended.

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