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Editorial

Control Arbovirus Infections through Control of Mosquito Population

Angela Song-En Huang, Senior Editor

In the World Health Organization's Dengue Global situation update published in December 2023, it was reported that worldwide, the number of dengue cases, outbreaks, and occurrence in previously unaffected areas had all increased substantially during the year.[1] Even though dengue outbreaks may occur in cycles of every 3 to 4 years, the situation reported in 2023 was unprecedented.

With climate change, the warmer temperatures have expanded the geographic distribution of *Aedes aegypti* and *Aedes albopictus* mosquitos, the main vectors that transmit dengue virus. Notably, Europe, not usually a region considered to have dengue fever, had continued to report locally-acquired cases in several countries; and in South America, 2023 marked a year with expansion of dengue geographically and rapid increase in cases. The number of cases had continued to rise in 2024, especially in Brazil, where cases are at a 10-year high.[2,3]

Even though dengue fever is endemic in much of the Asia Pacific region, the region saw a rise in the number of cases 2023. Of note, Thailand and Bangladesh had seen cases in 2023 increase 3 and 5 times, respectively, over 2022 levels. In Taiwan, dengue outbreaks expanded into geographic areas previously unaffected by the disease.

Vector control strategies, mainly breeding site reduction, had been the mainstay of disease control strategy. Removing bottles, tires, buckets, and pots which lead to stagnant water reduces the chance for mosquitos to lay their eggs. While this approach successfully reduces populations of the *Aedes* mosquitoes, it is labor-intensive and requires sustained community engagement. These efforts frequently lose effectiveness as communities become desensitized to repeated messaging and fail to internalize these practices to consistently eliminate mosquito breeding sites.

With nearly 2 million cases reported in Brazil during the first 10 weeks of 2024, Brazil is implementing a mass dengue vaccination program targeting children, who are more likely to be hospitalized because of dengue fever. This program, however, will not cover the elderly, another high-risk group for hospitalization, as the vaccine is not approved to be used among the elderly.[4]

The global health community will be eagerly awaiting the results of Brazil's vaccination campaign. If successful, it could pave the way for dengue vaccines to become an added tool, complementing vector control efforts, in the overall strategy in managing dengue outbreaks.

With Timor-Leste currently experiencing concurrent arboviral outbreaks of dengue, Zika, and chikungunya[5], it is a stark reminder that even if mass dengue vaccination is effective in reducing dengue associated morbidity and mortality, because the *Aedes* mosquitoes that transmit dengue fever may also spread zika and chikungunya viruses, vector control may remain an important part of disease control strategies.

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Factors Associated with Influenza-like Illness among Inmates in an All-male Prison, Songkhla Province, Thailand, 2023

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Abstract

On 9 Feb 2023, the Office of Disease Prevention and Control Region 12 Songkhla was informed of an influenza-like illness (ILI) cluster in an all-male prison in Songkhla Province. We investigated to identify the causative agent, possible sources and risk factors, and provide control measures. We conducted an active case finding by interviewing inmates and officers. Prison facilities and hygiene behaviors of inmates and officers were inspected. A retrospective cohort study was performed. Basic and effective reproductive numbers were estimated. The overall attack rate was 12.6% (474/3,648). Most cases were inmates from Wing C (80.4%). There were no severe cases or deaths. Of ten specimens tested, all were positive for influenza B/Victoria lineage, V1a.3a.2. Fifty-four percent of inmates had received influenza vaccine within the last 12 months. A mismatch between the viral strain in the vaccine and the one causing this outbreak likely contributed to the outbreak as the vaccine provided to the inmates was manufactured during the previous year's influenza season. Vaccine effectiveness was 36.2% against ILI. Having high-risk conditions (adjusted odds ratios (AOR) 2.83, 95% confidence interval (CI) 1.27–6.32) and sharing drinking glasses (AOR 2.02, 95% CI 1.21–3.36) were significant risk factors. The basic reproductive number for ILI in this outbreak was 1.36. The effective reproductive number ranged from 0.18–3.69. For effective management of ILI outbreaks in prisons, a continuous program of influenza vaccination following updated World Health Organization recommendations and a comprehensive surveillance system with rigorous respiratory illness management practices are suggested.

Keywords: influenza, prisons, viral strain, vaccine effectiveness, reproductive numbers

Introduction

Seasonal influenza is a leading cause of morbidity and mortality. The World Health Organization (WHO) estimates an annual average of 3 to 5 million severe illnesses and 290,000 to 650,000 deaths due to influenza worldwide.[1] The highest burden of influenza is in Sub-Saharan Africa and Southeast Asia.[2] In Thailand, the incidence of influenza lower respiratory tract infections was 1231.1 and the mortality rate 3.0 per 100,000 population in 2017.[3] The Department of Disease Control reported that around 80,000 influenza cases and 41 clusters of influenza-like illness (ILI) occurred in 2022. Of these clusters, 19 (47%) occurred in correctional facilities.[4]

Annual influenza vaccination is recommended for all individuals aged six months or older, prioritizing those facing high risk of severe illness, including the elderly (age over 65 years), pregnant women, immunocompromised individuals, and individuals with obesity or chronic medical condition.[5,6] A national influenza vaccination policy has been in effect in Thailand since 2004; seasonal influenza vaccines being provided to healthcare personnel, individuals under the age of two years or over the age of 65 years, and other vulnerable populations.[7] In addition, these vaccines are offered to inmates belonging to high-risk groups as part of a prison wellness initiative.[8]

On 9 Feb 2023, the Office of Disease Prevention and Control Region 12 Songkhla (ODPC-12) was alerted of an outbreak of ILI affecting approximately 100 inmates in an all-male prison in Songkhla Province, Thailand. An investigation was conducted by healthcare staff from ODPC-12, Songkhla Provincial Public Health Office, and Songkhla Hospital on 10 Feb 2023. The objectives of the investigation were to verify the outbreak, describe its epidemiological characteristics, identify associated factors, and provide recommendations.

Methods

Epidemiological Investigation and Descriptive Study

We interviewed prison staff and inmates and reviewed the infirmary records. Suspected ILI cases were inmates or prison officers who, during 18 Jan to 9 Mar 2023, developed at least one of the following symptoms: fever (either body temperature ≥38 °C or self-reported), rhinorrhea, cough, sore throat, and dyspnea. Confirmed cases were suspected cases whose nasopharyngeal swabs were positive for influenza or SARS-CoV-2 viruses. A semi-structured questionnaire was used for data collection. Information on demographic characteristics, clinical history, and associated factors such as smoking status, influenza vaccination status, hygiene behaviors, and infection control measures were obtained.

Prison staff and inmates who met the criteria for a suspected case were classified according to their risk of developing severe ILI. The following conditions were considered to be high-risk: age ≥65 years, chronic lung, heart, liver, and/or kidney diseases, diabetes mellitus, hypertension, body mass index over 30 kg/m^2, and immunocompromised status. Prison staff and inmates who did not meet these criteria were classified as low risk. We also screened for cases with severe symptoms (dyspnea, stupor, dehydration, respiratory rate more than 24 times per minute, or oxygen saturation equal to or less than 94%) and prolonged illness (having body temperature over 38 °C for more than 48 hours).

Laboratory Study

We collected ten nasopharyngeal swabs from suspected cases who were symptomatic on the day of investigation.[9] All specimens were tested for respiratory pathogens using real-time polymerase chain reaction (RT-PCR) for influenza and antigen test kit for SARS-CoV-2 at the Regional Medical Sciences Center Region 12 Songkhla.[10,11] Positive specimens were sent for pathogen identification by whole genome sequencing.

Environmental Study

For the environmental characteristics, we inspected the physical structures of prison facilities, including dormitories, dining areas, workshops, handwashing areas, and visiting rooms. The living conditions, routine activities, and sanitation behaviors of inmates in the prison were directly observed during a walk-through survey. Prison staff, including wardens and nurses, were interviewed about the prison entry procedures, respiratory illness screening protocol and management algorithm.

Analytic Study

We conducted a retrospective cohort study among all inmates in Wing C where the outbreak initially occurred. Inmates who were not available for the interview on the investigation day were excluded. Sample size was calculated using parameters from a previous study of an ILI outbreak in a prison.[12–14] The minimum sample size required to achieve 80% power with 95% confidence interval was 55 participants each in the exposed and unexposed cohorts. The key exposure factor of interest was sleeping near cases. The primary outcome was the incidence of ILI symptoms among inmates from 18 Jan to 9 Mar 2023. ILI symptoms comprised having a body temperature over 38 °C and either cough or sore throat. The dependent variables were age, risk category, smoking status, influenza vaccination status, and hygiene practices. Participants were considered to be vaccinated if they had received the latest dose of influenza vaccine at least 14 days but no more than 12 months prior to the onset of symptoms, or before the date of investigation for asymptomatic cases.[5]

Statistical Analysis

We used R version 4.2.1 for the statistical analysis.[15] For the descriptive study, categorical data were presented as frequencies and percentages while continuous data were presented as median and percentile. The basic reproductive number (R_0) was estimated using the attack rate of ILI among inmates from Wing C prior to interventions using R_0 package.[16] The effective reproductive number (R_t) was estimated using the Walling and Teunis method with a lognormal serial interval distribution and a mean of

3.7 days and standard deviation of 2.0 days.[17,18] For the analytic study, we employed univariable analysis by calculating crude relative risks (RR) using a two-by-two table and multivariable logistic regression for multivariable analysis to determine factors associated with ILI. Known variables from a literature review and variables with p-values less than 0.05 from the univariable analysis were included into the multivariable analysis. Adjusted odds ratios (AOR) with corresponding 95% confidence interval (CI) were presented. Vaccine effectiveness (VE) against ILI was estimated as 100% × (1 – AOR).

Ethics

This study was part of the routine outbreak surveillance and response activities of the Thai Department of Disease Control, Ministry of Public Health. Verbal informed consent was acquired before the interview and specimen collection.

Results

Clinical Setting

The outbreak occurred in a male-only prison facility in Songkhla Province, Thailand. It is a central prison which exclusively receives inmates transferred from other correctional facilities. The Department of Corrections, Ministry of Justice set the prison capacity at 2,755 inmates; however, the population at the time of the investigation was 3,648. Additionally, there were 108 correctional and nine healthcare officers present.

In 2022, the prison received a total of 3,556 doses of influenza vaccines. Of these, 1,443 doses were trivalent vaccines for the 2021–2022 northern hemisphere influenza season, and 537 doses were quadrivalent vaccines for the 2022 southern hemisphere influenza season. The trivalent vaccines provided did not contain the strains of influenza virus (influenza B/Victoria, V1A.3a.2) later identified in this outbreak.

Outbreak Description

We identified 471 inmates and three nurses that met our case definitions of suspected (464) and confirmed (10) cases for an overall attack rate of 12.59% (474/3,765). The median (interquartile range) age of the cases was 36 years (30–42 years). As shown in Table 1, the wing-specific attack rate was highest in Wing C. A total of 68 inmates with prolonged illness were treated with oseltamivir. There were 44 cases with high-risk conditions. No hospitalized cases or deaths were reported. Of ten nasopharyngeal swab specimens tested, all were positive for influenza B/Victoria lineage, V1a.3a.2.

Table 1. Attack rates of an influenza B outbreak in a prison among inmates and staff during 18 Jan–10 Mar 2023, Songkhla Province, Thailand (n=3,765)

	Onset date of the first case	Cases/total	Attack rate (%)
Inmates			
Wing A	-	0/257	0.00
Wing B	6 Feb 2023	44/788	5.58
Wing C	25 Jan 2023	381/795	47.92
Wing D	8 Feb 2023	25/780	3.21
Wing E	11 Feb 2023	20/801	2.50
Wing F	16 Feb 2023	1/227	0.36
Prison officers	**31 Jan 2023**	**3/117**	**2.56**
Total		**474/3,765**	**12.59**

The epidemic curve of the ILI outbreak is shown in Figure 1. On 25 Jan 2023, a 35-year-old hypertensive man from Wing C developed fever, cough, sore throat, and rhinorrhea. He visited the prison infirmary on the same day and was sent back to his living quarters after receiving supportive care. He had been in prison for one year and had never left the facility. He had been participating in workshops at the educational center every day since 1 Feb 2023, and had received the seasonal influenza vaccine provided by the prison during the past year. A number of inmates from Wing C reported having respiratory symptoms on the following days. On 6 Feb 2023, a prison nurse noticed that over 40 inmates visited the infirmary due to respiratory symptoms, exceeding the median number of 15 per day. On 9 Feb 2023, the hospital and ODPC-12 were notified. The outbreak subsequently spread to Wings B, D and E. The onset of the last known case was on 5 Mar 2023 and no further case was identified after 10 Mar 2023. Based on the epidemic curve and the high attack rate, we found that the R_0 for this event was 1.36 (95% CI 1.32–1.40) and as shown in Figure 2, the R_t on the investigation day was 1.71 (ranging from 0.18–3.69 throughout the course of the outbreak).

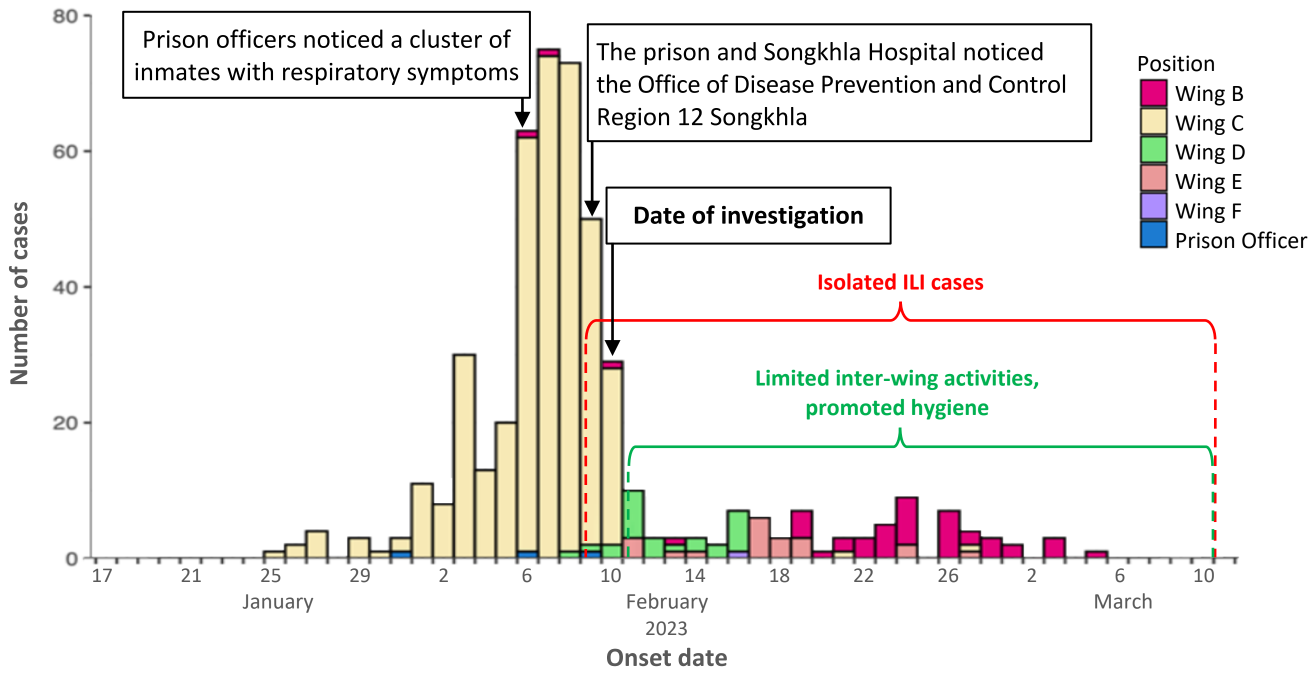

Figure 1. Number of influenza B cases in a prison by date of onset during 18 Jan–10 Mar 2023, Songkhla Province, Thailand

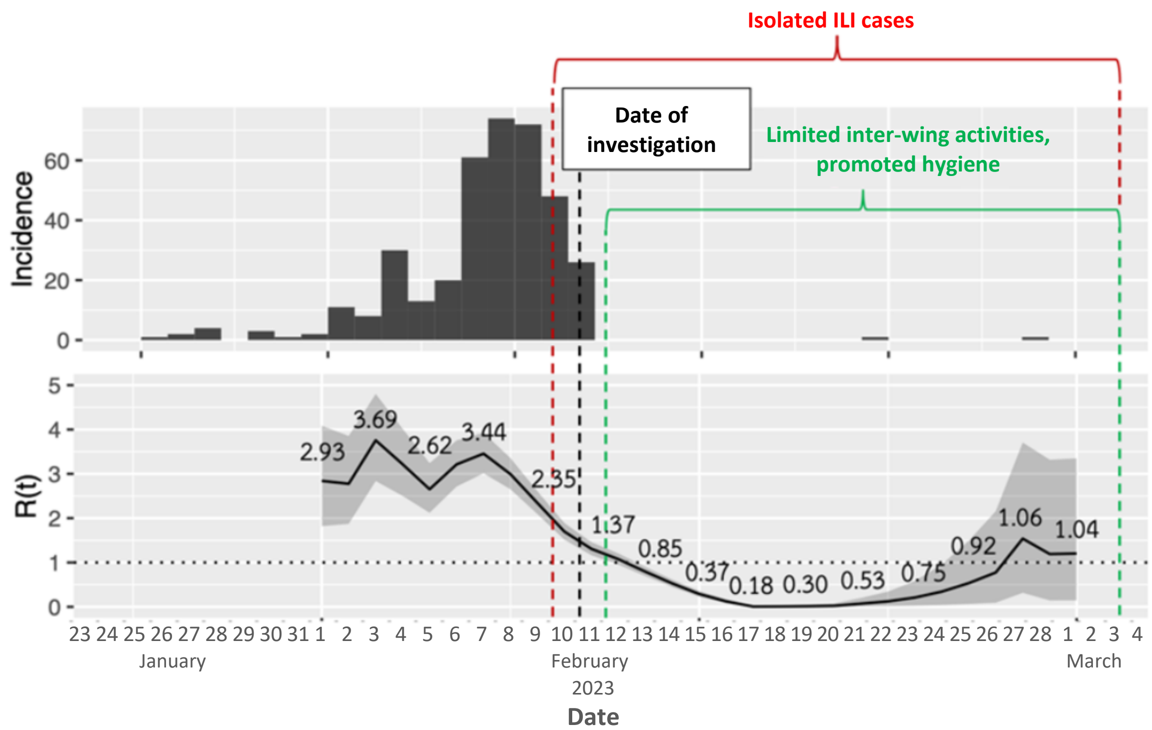

Figure 2. Effective reproductive numbers of an influenza B outbreak in a prison during 18 Jan–10 Mar 2023, Songkhla Province, Thailand

Environmental Study

The prison facility has six zones: a kitchen zone (Wing A), a high-security zone (Wing B), an education zone (Wing C), a zone for new inmates (Wing D), a zone for vulnerable inmates (Wing E), and an infirmary zone (Wing F). Each zone has one to two dormitories with eight to nine cells per dormitory. Each cell houses approximately 10 to 120 inmates who sleep on the floor with a personal pillow and blanket. The sleeping space per person ranges from 1.16 to 1.60 m^2. There are isolation rooms for inmates with respiratory symptoms in all dormitories. All inmates stayed in their wings and followed a fixed routine. The only exception was during daily workshops in an educational center in Wing C, where selected inmates from all wings participated in the activities with external instructors. These instructors received body temperature screening prior to entering the prison.

It was found that approximately 20% of inmates washed their hands after doing activities and using toilets; soap was frequently unavailable. Food was often shared directly, without the use of a serving spoon. Drinking fountains with shared cups were available, but some inmates used them without washing the cups first.

Since the beginning of the COVID-19 pandemic, the prison adopted a respiratory screening protocol. Upon admission, new inmates underwent a five-day solitary confinement period in Wing F followed by an additional five days in quarantine rooms in Wing B with other new inmates. If an inmate exhibited respiratory symptoms during quarantine, they were immediately isolated, and the remaining inmates' quarantine period was extended by an additional five days. Inmates who left and re-entered the prison were isolated for five days in Wing F and another five days in their assigned wing. Inmates requiring frequent visits to the hospital or court hearings were permanently relocated to an isolation zone in Wing F. Due to space constraints, inmates with mild respiratory symptoms that did not meet the criteria for ILI were not isolated.

Other preventive measures included restrictions on direct contact between visitors and inmates, requiring telephone conversations through a glass wall. Inmates were also mandated to wear face masks at all times and promptly report any respiratory symptoms to prison officers. Prison nurses were responsible for monitoring the number of inmates with respiratory illnesses and notifying local health officers if the number of inmates with ILI exceeded 20–30 per day. Notably, all records were maintained in paper format and were not summarized daily, resulting in a delayed outbreak notification. Furthermore, these preventive measures were not consistently enforced, and with varying degrees of compliance.

Analytic Study

Of 795 inmates in Wing C, 792 were available to be interviewed and were recruited into the analytic study. Having high-risk conditions and sharing drinking cups with other inmates were significant risk factors for ILI with AOR of 2.83 (95% CI 1.27–6.32) and 2.02 (95% CI 1.21–3.36), respectively (Table 2). At the time of the outbreak, 54.28% (1,980/3,648) of inmates were vaccinated. From the multivariable analysis, the VE of the influenza vaccine was 36.19% (AOR 0.64, 95% CI 0.33–1.22) against ILI.

Table 2. Univariable and multivariable analyses of factors associated with ILI among inmates of Wing C during 18 Jan–10 Mar 2023, Songkhla Province, Thailand

Variable	Case no./total no. among exposed individuals	Case no./total no. among unexposed individuals	Univariable analysis (n=792) RR (95% CI)	Multivariable analysis (n=402) AOR (95% CI)
Age	-	-	-	0.99 (0.96–1.02)
High risk (vs. low risk)	20/82	119/710	1.46 (0.96–2.20)	2.83 (1.27–6.32)
Current or former smoker (vs. never)	119/686	15/92	1.06 (0.65–1.74)	1.36 (0.61–3.01)
Vaccinated (vs. unvaccinated)	114/660	25/132	0.91 (0.62–1.35)	0.64 (0.33–1.22)
Sharing drinking cups	74/324	65/468	1.64 (1.22–2.22)	2.02 (1.21–3.36)
Being coughed or sneezed on	33/103	65/461	2.27 (1.58–3.26)	1.38 (0.74–2.59)
Sleeping near cases	62/234	40/266	1.76 (1.23–2.52)	2.00 (0.77–5.16)
Eating near cases	61/244	47/345	1.84 (1.30–2.59)	2.25 (0.74–6.85)
Working near cases	52/210	49/287	1.45 (1.02–2.05)	0.42 (0.14–1.25)

RR: relative risk. AOR: adjusted odds ratio. CI: confidence interval. vs: versus

Public Health Response

On 9 Feb 2023, a daily screening program for respiratory symptoms was initiated for all inmates by prison officers. Inmates with ILI were isolated and monitored for signs of severe symptoms for five days after symptoms onset. Activities involving inmates from more than one wing and activities with external instructors were postponed until eight days after the onset of the last known case. Correctional facilities to which inmates were transferred during the time of the outbreak were informed of the outbreak situation.

Discussion

Outbreak management in correctional facilities is challenging due to multiple factors. Insufficient health data management and lack of awareness of respiratory illnesses among inmates contributed to the delay in outbreak detection and control. The R_t was observed to be declining at the time of the investigation, suggesting that the outbreak had already entered the receding stage. Additionally, overcrowding at the prison meant there was limited space for inmate isolation. This led to the rapid spread of ILI among inmates. Similar issues have been reported in previous outbreaks.[19–21]

The most likely source of the ILI outbreak was the entrance of visiting instructors. The outbreak began in Wing C, where educational sessions were held. Although there is a screening guideline for visitors, it was not effective in detecting asymptomatic carriers which account for up to 36% of ILI cases.[22] Another possible source of the outbreak was inmates and prison staff who exited and re-entered the prison prior to the beginning of the outbreak. However, the only cases among these groups were prison nurses who cared for inmates with ILI.

Hygiene behaviors played an important role in the transmission of ILI among inmates. The environmental survey revealed the sharing of drinking cups, working, eating, and sleeping near cases, and being coughed or sneezed on; this was also confirmed by the univariable analysis. These findings are consistent with previous studies which found that poor hygiene behaviors, such as sharing drinking cups and inadequate handwashing, are linked to ILI in prisons.[12,23,24] In this event, upon adjusting for covariates, only sharing drinking cups remained significant.

The R_0 of ILI in this outbreak was 1.36 (95% CI 1.32–1.40), which is higher than the median R_0 of seasonal influenza (1.28) reported by Biggerstaff et al.[25] On the other hand, a study of an influenza outbreak in a Thai prison by Karnjanapiboonwong et al. estimated an R_0 of 4.50.[19] The R_0 of outbreaks in confined settings tend to be larger than those in the general population due to the increased contact rates.[26] Prison overcrowding can accelerate the spread of infection by increasing the number of opportunities for transmission between individuals.

The outbreak of ILI in an all-male prison in Songkhla Province, Thailand was caused by the influenza B/Victoria, V1A.3a.2 virus. This virus is antigenically similar to the influenza B/Austria/1359417/2021-like virus, which is recommended to be included in the 2023 influenza vaccine composition for both northern and southern hemispheres.[27] As of 2023, circulating influenza B/Victoria has not shown resistance to antiviral medications.[28] The percentage of influenza incidence caused by Influenza B virus in Thailand has increased from 15% in 2022 to 30% in 2023. However, influenza A/H3 virus remained the predominant circulating strain in Thailand.[29] We found that influenza vaccination was not effective in reducing the likelihood of ILI. These findings could be explained by the following reasons. Firstly, the effectiveness of influenza vaccines is reduced when the strains of influenza in the vaccine do not match the circulation strain. A meta-analysis by Tricco et al. found a VE of 77% (95% CI 18–94%) for matched influenza B strains and 52% (95% CI 19–72%) for mismatched influenza B strains.[30] Secondly, the outcome of interest in this study was ILI, which is non-specific to any respiratory pathogens. The VE against ILI identified by a syndromic definition will always be lower than that against laboratory-confirmed influenza.[31]

This study has some limitations. First, the retrospective design could have introduced recall bias, as the cases may have been more likely to remember details of past exposure to symptomatic inmates than the non-cases, leading to an overestimation of the measure of association. Second, the prison did not keep well-organized records of vaccination status and medical conditions of inmates. This resulted in incompleteness of the data provided. Third, the source of the outbreak could not be confirmed due to the unverified illness status of external instructors. Finally, the VE in the study was estimated using a non-laboratory-based case definition. This could have led to an overestimated VE against influenza infection.

We recommend improving the sensitivity of the respiratory illness surveillance system in the prison by incorporating a daily summary of infirmary data and establishing a lower threshold for timely notification. Also, the respiratory illness screening and management algorithm should be strictly followed. This includes examining visitors and external instructors for respiratory tract symptoms before entering the prison and isolating all inmates with respiratory symptoms once detected. Personal drinking cups should be provided to inmates in dormitory rooms and dining areas, and handwashing facilities should include soap and alcohol gel. Routine health education sessions on general and respiratory hygiene should be conducted for inmates and prison officers. Seasonal influenza vaccines with updated viral strains based on WHO recommendations should be prioritized for distribution, particularly in high-risk settings such as correctional facilities.

Conclusion

This study confirms an outbreak of ILI caused by influenza B/Victoria, V1A.3a.2 among prison inmates. Overcrowded conditions in the prison facilitated transmission of the virus. Although more than half of the inmates were vaccinated, the vaccine strains did not match the circulating strain, resulting in lower vaccine effectiveness. From the analytic study, sharing drinking cups was a significant risk factor for ILI. Control measures such as isolating symptomatic inmates and limiting inter-wing activities were implemented. To mitigate future ILI outbreaks, recommendations include enhanced surveillance systems, stricter respiratory illness management algorithms, lower notification thresholds, and prioritized routine vaccination with WHO-recommended and updated viral strains.

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Association between Air Pollution Relating to Agricultural Residue Burning and Morbidity of Acute Cardiopulmonary Diseases in Upper Northern Thailand

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Abstract

In Northern Thailand, increasing seasonal agricultural residue burning has led to public concern about health risks. This study aimed to examine the associations between air pollutants related to agricultural residue burning and morbidity from acute cardiopulmonary diseases in upper Northern Thailand in 2018. An ecological study was conducted. Emergency room visits and hospitalizations for chronic obstructive pulmonary disease (COPD), stroke, myocardial infarction (MI), and asthma were extracted from the National Electronic Health Record database. We interpolated air pollution data to estimate weekly pollutant concentrations, including PM_{10}, $PM_{2.5}$, carbon monoxide, nitrogen dioxide, sulfur dioxide and ozone from 1 Jan to 31 Dec 2018. Associations between air pollution and health outcomes were analyzed using a mixed effect model incorporating different lag structures. Overall pollutant concentrations exceeded WHO air quality standard levels throughout March and April, which is the end of forest burning prohibition campaign. Morbidity from COPD, stroke, MI and asthma slightly increased over March–April. For every increase in $PM_{2.5}$ level of 10 µg/m^3, the relative risk of COPD, stroke, MI and asthma 1 week later was 1.10 (95% CI 1.09–1.12), 1.06 (1.05–1.08), 1.06 (1.04–1.08) and 1.06 (1.01–1.12), respectively. The effects of agricultural residue burning should be highlighted and policies should be developed to deter this practice.

Keywords: air pollution, acute cardiopulmonary diseases, agricultural residue burning, burning prohibition campaign

Introduction

Air pollution is one of the leading contributors to the global burden of diseases. Approximately 98% of Southeast Asia's population live in places where air quality does not meet WHO air quality standard levels.[1,2] Exposure to ambient particulate matter is the fifth leading risk factor for deaths worldwide.[3] Air pollution in both urban and rural areas was estimated to cause more than four million premature deaths worldwide in 2016.[1,3] Approximately 90% of premature deaths from air pollution are from people living in low and middle income countries, including Thailand.[1] Exposure to air pollution has been known to increase morbidity and mortality of cardiopulmonary diseases.[4,5] Specifically, an increase in fine particulate matter ($PM_{2.5}$) of 10 µg/m^3 was associated with a 6% increased risk of cardiopulmonary death.[5]

Major sources of air pollution include industry, road traffic, households, and agricultural residue burning. However, satellite remote sensing of active fire data suggests that air pollution in Southeast Asia, particularly Myanmar, Lao PDR, Cambodia and upper Northern Thailand, is unique; and occurs principally from wildfires.[6–8] Wildfires can emit multiple air pollutants including particulate matter, carbon monoxide (CO), nitrogen dioxide (NO_2), sulfur dioxide (SO_2) and ozone-forming chemicals (O_3).[9–11] In upper Northern Thailand, wildfires occur almost every year and affect people's health, property, the regional economy, society and the environment.[6–8] Each year, the wildfire season, which causes air pollutant emissions during January to May, has a negative impact on respiratory health and vision.[8] Gathering of forest products, such as fuel wood, mushrooms and bamboo, and agricultural residue burning for land clearing are the major contributing factors.[7] Concern is growing as air pollution levels in upper Northern Thailand poses a threat to the population's health.

Although several studies reporting the association between air pollution and cardiopulmonary diseases have been conducted, only a few studies have investigated the health effects caused by agricultural residue burning. This information could help policymakers prepare medical resources for patients with acute cardiopulmonary disease, especially within the week after air pollution levels rise. This study aimed to describe the levels and dynamics of air pollutants, morbidity of acute cardiopulmonary diseases, and examine associations between air pollutants and morbidity for acute cardiopulmonary diseases in the upper northern area of Thailand.

Methods

Overview of Study

This was an ecological study using secondary time series data and including two datasets; air pollution data and health outcome data. The study population were people visiting an emergency room (ER) or admitted to hospital and diagnosed with acute cardiopulmonary diseases in eight provinces (Chiang Mai, Chiang Rai, Nan, Phrae, Lampang, Lamphun, Phayao and Mae Hong Son) in the upper northern region of Thailand from 1 Jan to 31 Dec 2018. Health outcomes were defined based on the international classification of diseases-10th revision (ICD-10). We identified cardiopulmonary diseases including chronic obstructive pulmonary disease (COPD) (J44), cerebrovascular diseases (stroke) (I60–I69), myocardial infarction (MI) (I20–I24) and asthma (J45–J46). Regarding air pollution data, six pollutants, including coarse particulate matter (PM_{10}), fine particulate matter ($PM_{2.5}$), CO, NO_2, SO_2, and O_3, were collected and integrated into spatial interpolation models to estimate weekly air pollutant concentrations. Associations between the air pollutants and health outcomes were analyzed using district-week as the unit of analysis.

Estimation and Pattern of Air Pollution

In order to estimate the spatiotemporal distribution of air pollution, national air pollution records provided by the Pollution Control Department, Ministry of Natural Resources and Environment were extracted. Date were recorded hourly from all air quality monitoring stations in Thailand and gathered at the Data Center in the Bureau of Air Quality and Noise Management, Pollution Control Department, Ministry of Natural Resources and Environment.

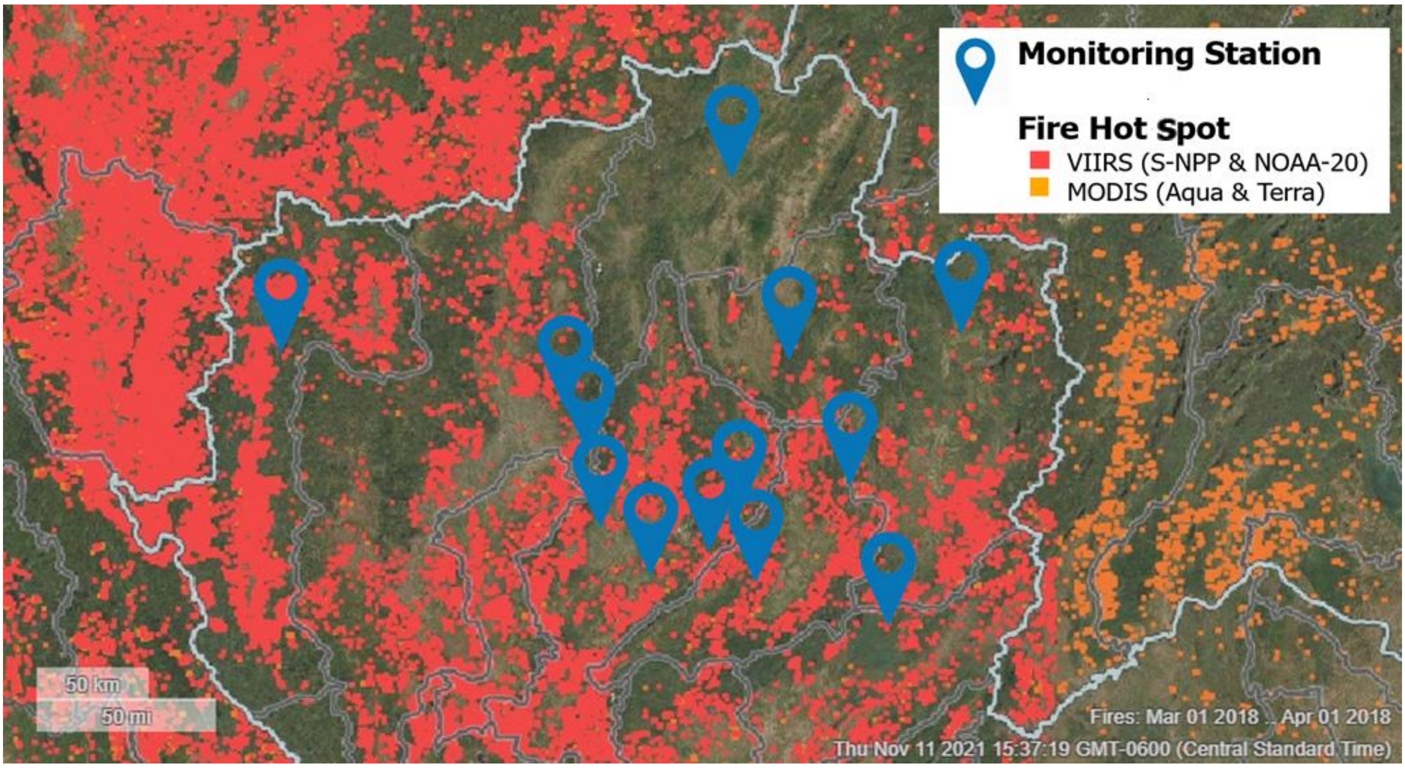


Figure 1. Distribution of air pollution monitoring stations and fire hot spots in the upper Northern Thailand, March–April 2018[12]

We obtained hourly air pollutant data from 13 monitoring stations in upper Northern Thailand to describe the seasonal pattern of air pollution between 2013–2018 to observe seasonality (Figure 1).[12] For each monitoring station, the pollutant level within each station on an hourly basis each day was aggregated. If the hourly pollutant level was not recorded, a 3-hour moving average was used to impute the missing data before calculating a daily average pollution level. Spearman's correlation was used to assess the correlation among each pollutant. We used a Simple Kriging interpolation model[13] in order to estimate the spatial distribution of air pollution concentration in 10,000 grids (100×100). Air pollution concentrations were then aggregated into districts using zonal statistics and averaged from daily to weekly time units. We used the R language and environment (packages: gstat, raster, maptools, sp, field) to analyze the data.[13-14]

To better understand patterns of wildfire in the study area, we obtained fire hot spots during exceeding pollution period in 2018 from Fire Information for Resource Management System which is provided by National Aeronautics and Space Administration (NASA) (https://firms.modaps.eosdis.nasa.gov).

Spatiotemporal Distribution of Health Outcomes in 2018

Morbidity from acute cardiopulmonary diseases was calculated by extracting the secondary health data from the National Electronic Health Record (NEHR) database. NEHR was provided by the Health Data Center, Ministry of Public Health. All medical institutions of the Ministry of Public Health in Thailand have the authority to report individual health records into the which were coded by diagnosis according to the ICD-10. We obtained daily counts of acute cardiopulmonary diseases in each district. Aggregation of healthcare facility address and week of onset by district-week was performed to estimate the spatiotemporal distribution of diseases in each district-week unit.

Association between Air Pollution and Health Outcomes

As this time series data of health outcomes had repeated measurements in the same district in different weeks, mixed effects models, which contain both fixed and random effects, were selected for analysis in this setting where repeated measurements were made on the same statistical units.[15,16] Districts were treated as a random effect.

Various lag structures between air pollution and health outcomes have been identified in previous studies, therefore, we initially examined separate models with different lag structures, including single-week lag from lag-0 to lag-2 (lag-0 refers to the air pollution in the current week and lag-1 and lag-2 refer to 1 and 2 weeks prior to the current week, respectively).[17,18] Furthermore, models assessing the associations between health outcomes and both single- and multiple-pollutants were fit. PM_{10}, $PM_{2.5}$, CO, NO_2, SO_2 and O_3, were included in the single-pollutant models while $PM_{2.5}$, adjusted for the other pollutants, was included in the multiple-pollutants models. A variance inflation factor (VIF) was estimated to identify the severity of multicollinearity. All pollutants with a VIF greater than 10 were excluded from the multiple-pollutant models. All of these models were fit using different lag structures.

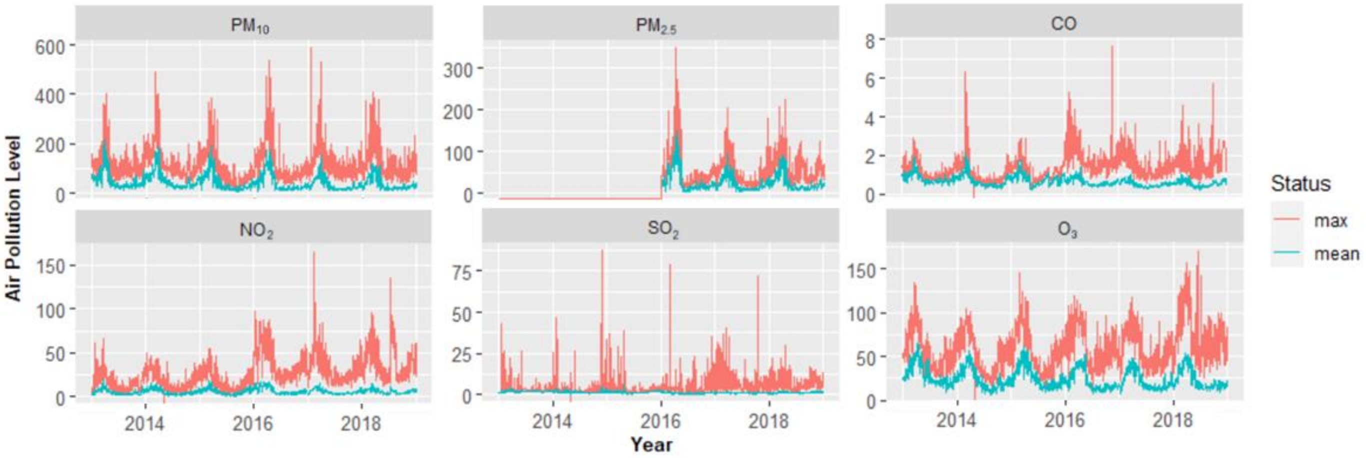
After establishing various models, concentration response (CR) relationships were developed to estimate the relative risk (RR) which was calculated based on the relationship between RR, CR-coefficients and a 20% change in air pollution concentrations.[18] A CR-coefficient was assigned as the slope of the log-linear relationship between ambient air pollution concentrations and morbidity, while a 20% change in air pollution concentrations was defined as a 20% difference in maximum concentration and mean concentration of each pollutant in that year.[18] The CR at each change in air pollution concentration was visualized with curves of the central estimation of RR and their 95% uncertainty intervals.

Results

Estimation and Pattern of Air Pollution

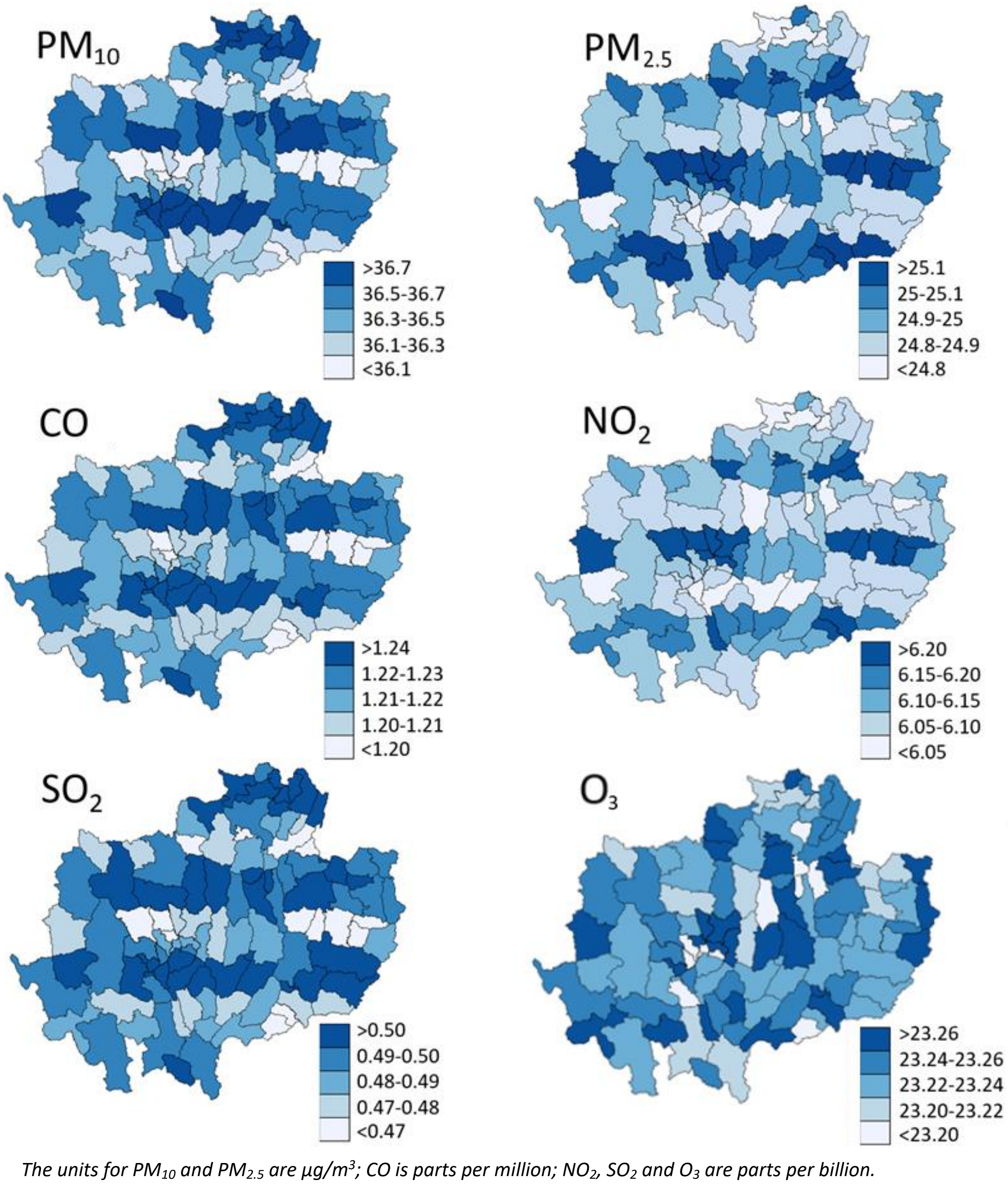
Air pollution data were obtained from 12 of the 13 monitoring stations; the station in Mae Hong Son Province (located in the farthest northwest) was not functioning on the required days. Most pollutant concentrations were monitored by at least 10 stations.

As shown in Figure 1, the fire hot spots distributed throughout the northern parts of Thailand and the neighboring countries exceeded WHO pollution levels in March and April 2018. All air pollutants, especially PM_{10} and $PM_{2.5}$, exceeded WHO standards from the middle of February to the end of April from 2013–2018 (Figure 2). The annual average air pollution concentration in 2018 from 97 districts in the eight provinces is illustrated in Figure 3. There were strong to very strong correlations among most pollutants with correlation coefficients ranging from 0.68–0.99 (all *p*-values <0.01), while CO exhibited correlations ranging from 0.25–0.40 (all *p*-values <0.01).



The units for PM_{10} and $PM_{2.5}$ are µg/m^3; CO is parts per million; NO_2, SO_2 and O_3 are parts per billion.

Figure 2. Time series of air pollution concentrations of PM_{10}, $PM_{2.5}$, CO, NO_2, SO_2 and O_3 in upper Northern Thailand, 2013–2018



The units for PM_{10} and $PM_{2.5}$ are µg/m^3; CO is parts per million; NO_2, SO_2 and O_3 are parts per billion.

Figure 3. Annual average air pollution concentrations in 97 districts in upper Northern Thailand, 2018

Spatiotemporal Distribution of Health Outcomes

Air pollution related morbidities from 97 districts in the eight provinces were extracted and then each district data were aggregated into 5,044 (97×52) district-week units. However, the number of ER visits and hospitalizations dropped to nearly zero during August and September 2018 (Figure 4).

The number of ER visits and hospitalizations for patients with acute cardiopulmonary diseases in this region was 53,668, including 31,706 for COPD (537 per 100,000 populations), 12,190 for stroke (206 per 100,000 populations), 6,164 for MI (104 per 100,000 populations) and 3,416 for asthma (22.8 per 100,000 populations). Each disease showed a minimal fluctuation in the number of ER visits month by month with a slightly higher number of visits early in the year for COPD, stroke and MI. The annual incidence of these four diseases in the 97 districts is illustrated in Figure 5.

Figure 4. Incidence of chronic obstructive pulmonary disease (COPD), stroke, myocardial infarction (MI) and asthma admissions or emergency room visits by month of onset, upper Northern Thailand, 2018

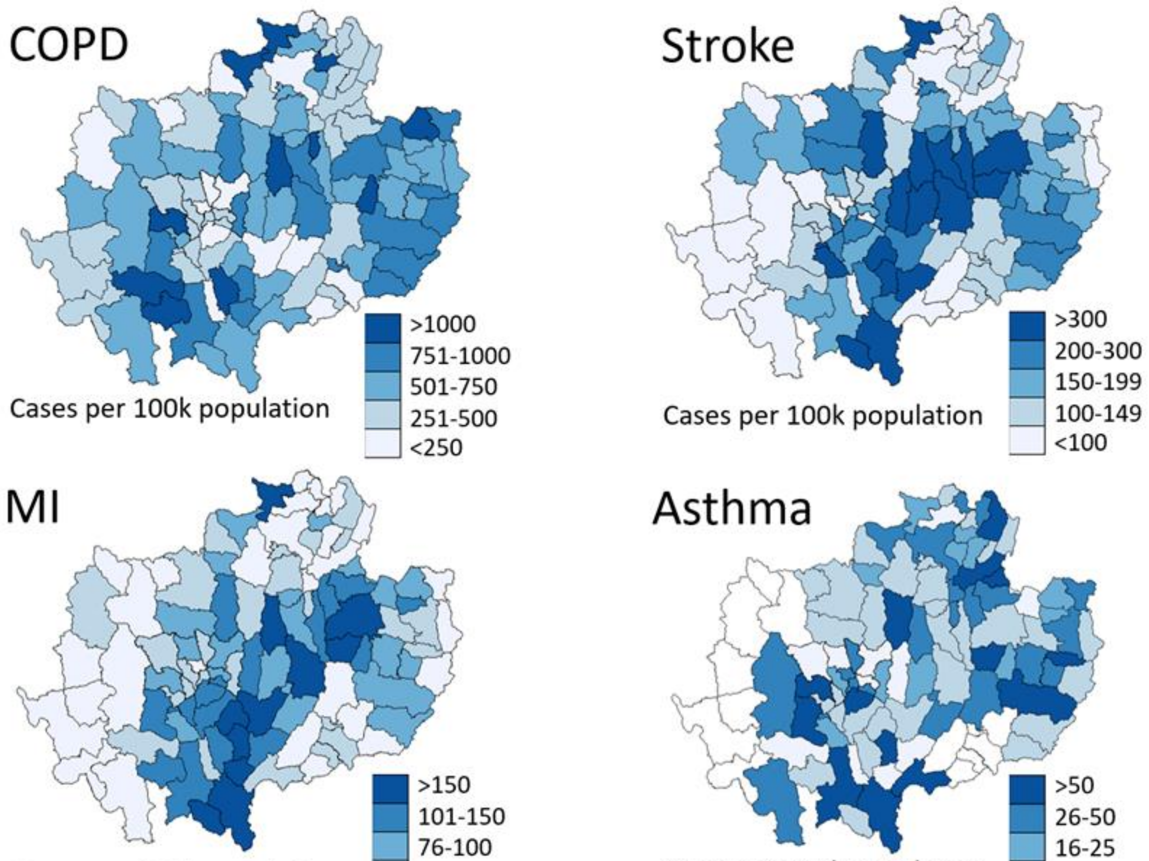


Figure 5. Incidence of chronic obstructive pulmonary disease (COPD), stroke, myocardial infarction (MI) and asthma admissions or emergency room visits in 97 districts of upper Northern Thailand, 2018

Associations between Air Pollution and Health Outcomes

Morbidity data in August and September were excluded due to an unexplainable decline during those two months. Therefore, the other 4,074 district-week units were included in the analysis. In order to estimate relative risks, a 20% difference between the maximum pollutant levels and mean pollutant levels were determined, which were 11 μg/m^3, 10 μg/m^3, 0.12 ppm, 0.86 ppb, 0.06 ppb and 5.08 ppb for PM_{10}, $PM_{2.5}$, CO, NO_2, SO_2, and O_3, respectively.

For the single-pollutant model, all pollutants were identified as significant risk factors to develop all cardiopulmonary diseases in all selected lag structures, except for asthma at lag-0. For pollutants, the 20% difference between maximum pollutant and mean pollutant change of PM_{10} and $PM_{2.5}$ had the highest impact on all cardiopulmonary diseases (relative risks 1.02–1.18), whereas CO had the lowest impact on cardiopulmonary diseases (relative risks 1.01–1.05). In addition, CO was not statistically associated with MI and asthma at lag-0 and the moving average lag (Table 1).

Analysis of the different lag structures revealed that lag-1 had the highest association between all cardiopulmonary diseases and PM_{10} and $PM_{2.5}$, while lag-2 had the highest corresponding associations for CO, NO_2, SO_2, and O_3, compared to lag 0 and the moving average lag (Table 1).

Table 1. Summary of relative risks for chronic obstructive pulmonary disease (COPD), stroke, myocardial infarction (MI) and asthma for a 20% change in mean ambient air pollution concentration, upper Northern Thailand, 2018

Pollutant	Lag structure	COPD			Stroke			MI			Asthma		
		RR	LCI	UCI	RR	LCI	UCI	RR	LCI	UCI	RR	LCI	UCI
PM_{10}	L0	1.06	1.05	1.07	1.02	1.01	1.04	1.02	1.00	1.04	1.02	0.97	1.08
	L1	1.10	1.09	1.11	1.06	1.05	1.08	1.06	1.04	1.08	1.06	1.01	1.12
	L2	1.10	1.09	1.11	1.06	1.04	1.07	1.07	1.05	1.08	1.07	1.02	1.12
$PM_{2.5}$	L0	1.06	1.05	1.07	1.02	1.01	1.04	1.02	1.00	1.03	1.02	0.96	1.08
	L1	1.10	1.09	1.12	1.06	1.05	1.08	1.06	1.04	1.08	1.06	1.01	1.12
	L2	1.10	1.09	1.11	1.06	1.04	1.07	1.06	1.05	1.08	1.07	1.02	1.12
CO	L0	1.01	1.00	1.02	1.01	1.00	1.03	1.01	0.99	1.03	1.01	0.97	1.06
	L1	1.05	1.05	1.06	1.05	1.04	1.06	1.04	1.03	1.06	1.05	1.01	1.10
	L2	1.04	1.03	1.04	1.03	1.01	1.04	1.02	1.01	1.04	1.04	0.99	1.09
NO_2	L0	1.05	1.04	1.05	1.02	1.01	1.03	1.02	1.01	1.04	1.03	0.99	1.08
	L1	1.10	1.09	1.11	1.07	1.06	1.09	1.08	1.07	1.10	1.10	1.05	1.15
	L2	1.09	1.08	1.10	1.07	1.06	1.08	1.08	1.06	1.09	1.12	1.07	1.17
SO_2	L0	1.05	1.05	1.06	1.03	1.01	1.04	1.03	1.01	1.04	1.05	1.00	1.09
	L1	1.07	1.06	1.08	1.04	1.03	1.06	1.04	1.03	1.06	1.07	1.02	1.11
	L2	1.05	1.04	1.06	1.02	1.01	1.04	1.03	1.02	1.05	1.06	1.00	1.00
O_3	L0	1.06	1.05	1.07	1.03	1.01	1.04	1.02	1.00	1.04	1.01	0.96	1.05
	L1	1.09	1.08	1.10	1.06	1.04	1.07	1.05	1.04	1.07	1.05	1.00	1.10
	L2	1.09	1.08	1.10	1.06	1.04	1.07	1.05	1.04	1.07	1.06	1.01	1.10

20% change in mean ambient air pollution level for PM_{10}: 11 μg/m^3, $PM_{2.5}$: 10 μg/m^3, CO: 0.12 PPM, NO_2: 0.86 parts per billion (PPB), SO_2: 0.06 PPB, and O_3: 5.08 PPB. COPD: chronic obstructive pulmonary disease. MI: myocardial infarction. RR: relative risk. LCI: lower confidence interval. UCI: upper confidence interval.

For multiple-pollutants models, PM_{10} and O_3 were excluded due to VIF exceeding 10. After adjusting for CO, NO_2, and SO_2, $PM_{2.5}$ was significantly associated with COPD. However, there were no associations between $PM_{2.5}$ and stroke or MI after adjusting for SO_2 or SO_2 combined with other pollutants (Table 2). We illustrated the association between cardiopulmonary diseases and $PM_{2.5}$ adjusting for CO at lag-0 using CR-curves and found a slight exponential relationship (Figure 6).

Table 2. Summary of relative risks of chronic obstructive pulmonary disease (COPD), stroke, myocardial infarction (MI) and asthma for a 20% change in mean $PM_{2.5}$ adjusting for CO (lag-0), NO_2 and SO_2, upper Northern Thailand, 2018

Main Pollutant	Adjusted Pollutant	COPD			Stroke			MI			Asthma		
		RR	LCI	UCI	RR	LCI	UCI	RR	LCI	UCI	RR	LCI	UCI
$PM_{2.5}$	CO	1.13	1.11	1.16	1.03	1.01	1.05	1.02	1.00	1.04	1.02	1.00	1.03
	SO_2	1.06	1.02	1.10	0.97	0.95	1.00	0.96	0.92	1.00	1.01	0.98	1.03
	NO_2	1.13	1.09	1.16	1.02	0.99	1.04	1.00	0.97	1.03	0.97	0.95	1.00
	CO+SO_2	1.06	1.02	1.10	0.97	0.95	1.00	0.95	0.92	0.99	1.01	0.98	1.04
	CO+NO_2	1.12	1.07	1.16	1.01	0.99	1.04	1.00	0.97	1.03	0.97	0.94	1.00
	NO_2 + SO_2	1.06	1.02	1.11	0.97	0.94	1.00	0.94	0.91	0.98	0.96	0.94	1.00
	NO_2 + SO_2 + CO	1.06	1.02	1.11	0.97	0.94	1.00	0.94	0.91	0.98	0.97	0.94	1.00

We excluded PM_{10} and O_3 due to a variance inflation factor (VIF) >10. COPD: chronic obstructive pulmonary disease. MI: myocardial infarction. RR: relative risk. LCI: lower confidence interval. UCI: upper confidence interval.

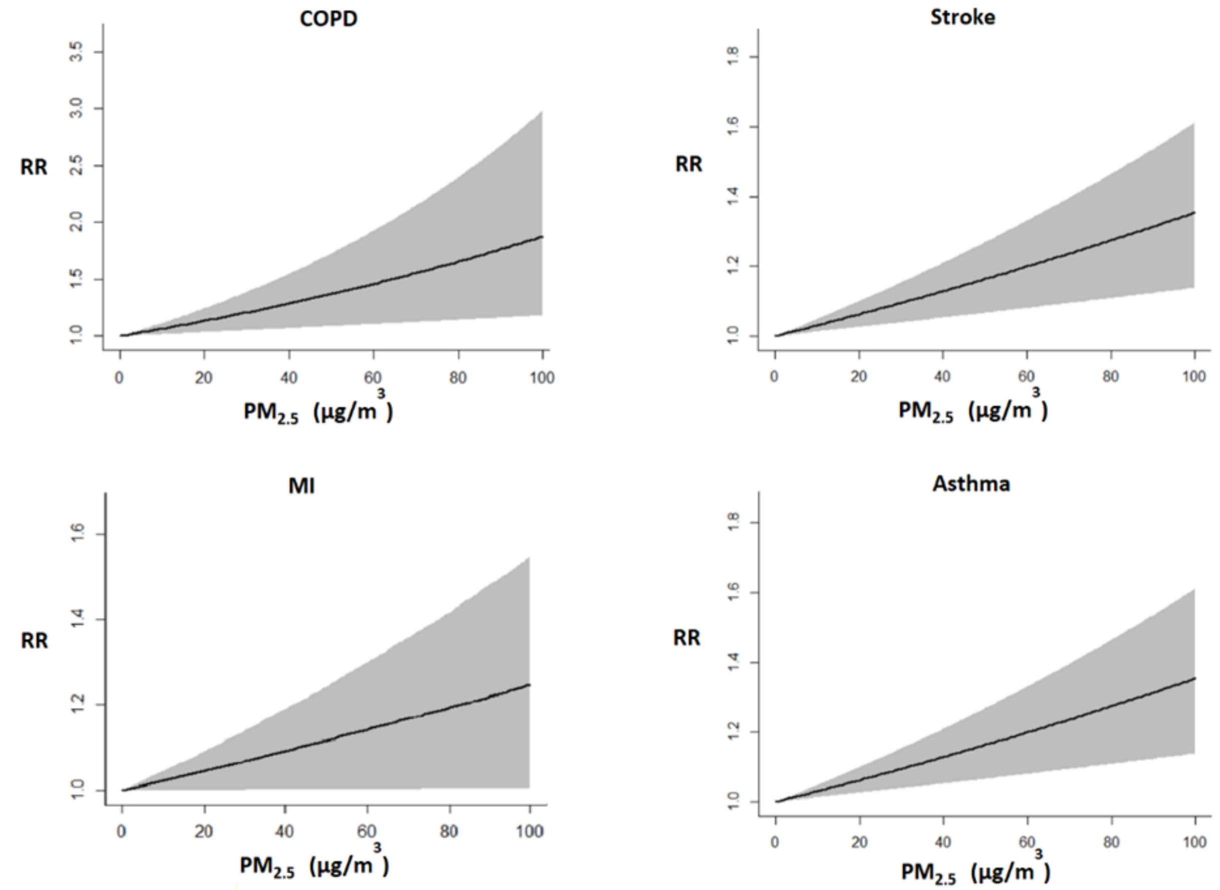


Figure 6. Concentration response relationship curves showing the adjusted relative risk of $PM_{2.5}$ adjusting for CO and cardiopulmonary diseases in upper Northern Thailand, 2018. Shaded areas represent 95% confidence intervals

Discussion

This is one of the few studies on the acute and sub-acute effects from agricultural residue burning related to air pollution associated with cardiopulmonary diseases using data from a large disease registry. We illustrated the association of air pollution related to agricultural residue burning with other air pollutants.

The excessive pollutant levels are likely due to wildfires and is supported by other researchers.[7–9] All pollutants had strong to very strong correlations with each other, especially PM_{10}, $PM_{2.5}$, and O_3, which might originate from the same source of pollutants (wildfires), thus the analytic study was mindful of perfect collinearity among those pollutants. For all pollutants, the mean daily pollutant levels were higher than standard concentrations issued by the World Health Organization's Air Quality Guideline, especially after the end of forest burning prohibition campaign.[18] This finding provides evidence that the campaign could be promoted to control air quality and should be expanded in both time and scope to include agricultural residue burning.

Corresponding with the excessive air pollution, the morbidity associated with acute cardiopulmonary diseases in upper Northern Thailand was high compared with previous annual reports of average morbidity in other regions of Thailand, based on the 2017 Thai Annual Epidemiological Surveillance Report (AESR) and the United States National Hospital Ambulatory Medical Care Survey (NHAMCS).[20,21] On the other hand, morbidity from asthma was slightly lower than that reported by the AESR and much lower than the NHAMCS.[20,21] Asthma morbidity from the National Electronic Health Record was likely to be underestimated, probably due to the strict diagnostic criteria in Thailand for patients that need pre–post bronchodilator for diagnosis.[22] However, only a few community hospitals in Thailand have spirometers.[23] Moreover, we found an unexplained and abnormally large decline in the number of ER visits and hospitalizations from all diseases of interest during August and September, which might be due to errors of reporting during the beginning of the fiscal year.

We found that all pollutants had statistically significant associations with stroke, MI and COPD. For stroke, our findings were consistent with previous studies for PM_{10} and $PM_{2.5}$.[4,5,24] Comparing with different sources of air pollution, our strength of association for $PM_{2.5}$ and stroke at lag-0 is similar to previous studies. The previous study in Ireland identified the pollutant source from domestic solid fuel burning during winter.[23] While, the previous study in China identified the pollutant source from industrial production and traffic congetion.[24] This finding may suggest that air pollution from wildfire contributes a similar impact on stroke compared to other sources of pollution. For MI, our findings are consistent with previous studies from around the world.[4,5,26,27] We found that the strength of association between PM_{10} and MI at lag-0 was slightly lower than reported in a previous study from Poland where pollution was identified from residential areas and small-industry, and in Beijing, China where pollution was identified from traffic and industry.[26,27] This finding suggests that air pollution from wildfire has a slightly lower impact on MI compared to other sources, which could be explained from other hazardous chemical pollutants from traffic and industry-related pollutants such as benzene, perchloroethylene, and methylchloride.[28–30]

Concerning COPD, our findings are consistent with previous studies assessing its associations with PM_{10}, $PM_{2.5}$ and NO_2 concentrations.[4,5,16,31,32] Compared with different sources of air pollution, the strength of association between $PM_{2.5}$ and COPD at lag-0 was slightly lower compared to a previous study in Beijing, China which was associated from traffic and industry.[31] It was also higher than in Taiwan where pollutant sources were identified from sea-land breezes and desert dust storms.[32] For three of these diseases, with the same level of $PM_{2.5}$, air pollution due to agricultural residue burning had a similar, or perhaps higher, impact compared to other sources of air pollution. This could be explained by other confounders, for instance, chemical related pollutants, weather, or physical activities. Asthma, however, was not significantly associated with most of the other air pollutants, except SO_2, which could be due to a lack of consistency and accuracy of NEHR for reporting asthma.

According to our models which analyzed different lag structures, lag-1 had the highest relative risk on health outcomes for almost all pollutants, followed by lag-2 and lag-0. Therefore, the effect of air pollution on cardiopulmonary diseases does not peak during the initial period of air pollution, but was stronger during the week after the event. This finding is compatible with previous studies in the US, China, Brazil, and Thailand.[16,33,34] This could be because of the natural history of diseases and delays in emergency room visits.

This study has several limitations which should be acknowledged. First, there were a limited number of air monitoring stations and some of them were clustered in particular areas. Interpolation methods were used to solve this limitation; however, accuracy may have been compromised. Secondly, the associations of health outcomes were estimated from modeled air pollutants, not from direct pollutant measures. Thirdly, ecological fallacy could potentially occur by inferring that associations at the aggregate level rather than the individual level: if we infer into aggregate level, ecological fallacy would not be the issue. Fourthly, confounding bias may have occurred if unmeasured potential confounders such as temperature, humidity, chemical related pollution, or physical activities in each area, are correlated with pollutants and the illnesses reported in this study.

Conclusion

In Northern Thailand, the morbidity from COPD, stroke, MI and asthma slightly increased since the middle of March, 2018, which is consistent with pollutant concentrations exceeding standard levels after March. This period marks the end of the agricultural residue burning season and the increasing air pollution levels were significantly associated with COPD, stroke and MI. Air pollution from agricultural residue burning had almost similar or even higher health impacts compared to other sources of air pollution. Therefore, we suggest using air pollutant data to estimate and monitor the trend of air pollution-related diseases and increase the number of air pollution monitoring stations in Northern Thailand. Specifically, disease prevention and control authorities should use the air pollutant data in available areas to estimate and monitor the trend of air pollution-related diseases. The magnitude of air pollution-related diseases should be reported to authorities to monitor trends as part of disease surveillance systems. For healthcare facilities in the affected areas, after an increase in pollutants is detected, the number of air pollution-related diseases should be estimated using CR-curves. Adequate preparation for essential resources in hospitals is recommended. For national health data organization, consistency and accuracy of NEHR should be studied and closely monitored and forecasted. For the Pollution Control Department, due to the limited number of air pollution monitoring stations in the affected area, we recommend increasing the number of stations, especially in areas affected by wildfires. Forest burning prohibition campaign should be promoted, expanded its period, and should include neighboring countries.

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Conflicts of Interest

The authors declare no conflict of interest.

Author Contributions

Conceptualization, S.W., H.P. and P.T.; methodology, S.W., H.P. and P.T.; software, S.W. and C.J.; validation, S.W., P.T. and C.J.; formal analysis, S.W., C.J. and P.T.; resources, S.W. and P.T.; data curation, S.W. and C.J.; writing—original draft preparation, S.W. and C.J.; writing—review and editing, H.P. and P.T.; visualization, S.W. and C.J.; supervision, H.P. and P.T.; project administration, S.W.; All authors have read and agreed to the published version of the manuscript.

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Acute Gastroenteritis Outbreak in a Rural Area in Perak, Malaysia, 2022

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Abstract

An outbreak of acute gastroenteritis was identified in a rural village in Perak, Malaysia, on 22 Jun 2022, following the detection of 20 cases. The Larut, Matang, and Selama District Health Office implemented public health measures to control the outbreak. We detected 25 cases during 22–24 Jun 2022, among private boarding school students and residents. Half (52%) of the cases were aged between 11 and 15 years, 68% were male, and 44% were students. Common symptoms included vomiting (88%), abdominal pain (76%), and diarrhoea (72%). No food was suspected based on food diaries, as there was no common food eaten by all cases. The epidemic curve showed a point-source pattern. Mapping of cases demonstrated that all cases used water for drinking, cooking, and other domestic usages that were supplied by the same gravity feed system. Several empty containers of carbofuran-containing insecticide and nematicide, used for agriculture, were found near the gravity feed system route at an altitude higher than its inlet. No known pathogen was isolated from the rectal swabs of cases. This acute gastroenteritis outbreak was suspected to have occurred from drinking water contaminated with chemicals such as carbofuran. After excluding other possible causes, health education to the villagers, particularly on the appropriate use of insecticides nearby the source of water supply with good cooperation from the local communities had helped successfully controlling the outbreak.

Keywords: acute gastroenteritis, insecticide, chemical, gravity feed system

Introduction

Acute gastroenteritis is a condition wherein inflammation occurs in the stomach as well as the small or large intestine. Presenting symptoms include abdominal pain, nausea, vomiting, and diarrhoea, which normally resolve within 14 days.[1] The main causes are infectious agents such as viruses, bacteria, and parasites. Larut, Matang, and Selama (LMS) is a district in Perak State, Malaysia. The LMS District Health Office monitors acute gastroenteritis cases in the district through a surveillance system whereby notifications are received from all public healthcare facilities in the district. On 22 Jun 2022, the LMS District Health Office received a notification of 11 acute gastroenteritis cases seeking treatment at a nearby health clinic on 21 Jun 2022. They were all male students aged between 11 and 15 years old who were staying in a private boarding school in a rural area within the LMS District. Further nine cases were detected on 22 Jun 2022. These involved people in the same locality where the school is located. Therefore, an outbreak of acute gastroenteritis was declared on 22 Jun 2022, and the district rapid response team was activated to investigate the event. The objectives of the investigation were to present descriptive epidemiological characteristics, identify possible sources for the outbreak, and implement public health measures to control the outbreak.

Material and Methods

The operation room of the LMS District Health Office was activated during the outbreak to synchronize all actions and commands.

Operational Case Definition

Anyone who lived in a rural village within LMS District and experienced at least one of the following symptoms including nausea, vomiting, abdominal pain or diarrhoea, between 19 and 24 Jun 2022, was defined as a case.

Active Case Detection

The detection of cases was conducted on 24 Jun 2022, based on the operational case definition. Due to limited resources, we visited 39 premises and met 189 (21.6%) of the 876 residents. We conducted face-to-face interviews using a standard investigation form [FWBD/KRM/ BG/001 (Pindaan 2006)] and a food diary form.

Epidemiological Analysis

We conducted a descriptive epidemiological analysis of all identified cases, including their close contacts. The variables included socio-demographic characteristics such as age, gender, and occupation, as well as date of onset of symptoms, clinical manifestation, food intake, and significant movement history. Data were coded, manually checked for any inconsistencies, duplication, and missing values, and analyzed using the Statistical Package for the Social Science (SPSS), version 21.0. Descriptive results were presented as follows: quantitative data were presented using the mean and standard deviation, whereas qualitative data were presented using frequency and percentage. An epidemic curve was constructed based on symptom onset dates. A map of cases in this outbreak was done to identify the possible source.

Environmental Assessment and Laboratory Study

The area around and above the gravity feed system (GFS) catchment, which was surrounded by a durian orchard at the peak of the hill, was inspected to detect any illegal activity at the river that supplied the GFS. This GFS is a system that was built to supply untreated water to a community from a river through a structure that water will directly flow using force of gravity to the consumers. Water samples were taken from the GFS at various points as listed below and sent to Malaysia Chemistry Department (Perak Branch) for chemical pesticides (Alpha-BHC, Beta-BHC, Lindane, Delta-BHC, Heptachlor, Heptachlor exo epoxide, Alpha Endosulfan, Beta Endosulfan, Endosulfan sulphate, 4,4-DDE, 4,4-DDD, 4,4-DDT, Aldrin, Dieldrin, Endrin, Methoxychlor, Endrin Aldehyde, Alpha Chlordane and Gamma Chlordane), light metal [NH_3-N, (NO_3+NO)N, Fluoride, Chloride, Ferum, Manganese and Aluminium), heavy metal (Arsenic, Mercury, Cadmium, Plumbum, Chromium, Argentum, Cuprum, Zinc, Magnesium, Natrium, Selenium, Sulphate, Chloroform, $CHCl_2Br$, $CHBr_2Cl$, $CHBr_3$) and bacteriological (total coliform and *Escherichia coli*) using Membrane Filtration Method analysis: a) two water samples from the river at the altitude above the water catchment area; b) one water sample from the GFS catchment area; c) two water samples from the GFS outlet in the private boarding school; and d) one water sample from the GFS outlet in a randomly selected case's house.

We randomly took eight rectal swab samples from eight cases and sent them to a public health laboratory in Ipoh, Perak, Malaysia, for culture and drug sensitivity tests for pathogenic enteric bacteria. Two water-selling dispenser machines in these villages were also identified and inspected for cleanliness, and the source of the water supply was determined. Water from the outlets of these machines was tested for pH, turbidity, and the presence of residual chlorine, coliform, *Bacillus cereus, Coagulase-positive Staphylococci, Escherichia coli, Salmonella spp.,* and total plate count.

Ethics

An ethical approval for this study was obtained from the Medical Research and Ethics Committee of the Ministry of Health, Malaysia on 26 Jan 2023 [Reference number: NMRR ID-22-02381-CBQ (IIR)].

Results

Descriptive Epidemiology

Socio-demographic characteristics

There were 25 cases detected in this outbreak through both passive and active case detection activities, with an attack rate of 2.85%. Most of them were male (68%), aged between 11 and 20 years (60%). Almost half of them were students who stayed in a private boarding school (44%), followed by housewives (20%), durian orchard farmers (16%), other students (8%), and the remaining three cases were a businessman, a private sector worker, and a government officer. Most of the students from the private boarding school consumed water that was supplied by the GFS only and underwent the same daily activity in the school. Meanwhile, 72% of cases consumed water from a low-cost water-selling dispenser machine for drinking and cooking in addition to GFS water (Table 1).

Table 1. Socio-demographic characteristics of cases linked to an acute gastroenteritis outbreak in a rural village in Perak, Malaysia, from 22 to 24 Jun 2022 (n=25)

Characteristics	Frequency	Percentage
Age group (years)		
0–10	0	0.0
11–20	15	60.0
21–30	4	16.0
31–40	3	12.0
41–50	2	8.0
51–60	0	0.0
More than 60	1	4.0
Age (years)		
Mean (SD)	23.0 (14.86)	
Minimum	11	
Maximum	73	
Gender		
Male	17	68.0
Female	8	32.0
Occupation		
Student (private boarding school)	11	44.0
Housewife	5	20.0
Durian orchard farmer	4	16.0
Other students	2	8.0
Businessperson	1	4.0
Private sector worker	1	4.0
Government officer	1	4.0
Water source		
GFS only	7	28.0
GFS and water-selling dispenser machines	18	72.0

GFS: gravity feed system. SD: standard deviation

Clinical manifestation

Most cases presented with vomiting (88%), abdominal pain (76%), and diarrhoea (72%). Other symptoms included nausea (24%), dizziness (8%), and myalgia (4%). None of the cases developed a fever (Table 2).

There were 18 cases (72%) who had received out-patient treatment, while seven did not seek treatment at any healthcare facility as they claimed to have very mild symptoms.

Epidemic curve

The first and last onset were on 21 Jun 2022, at 3:30 AM and 22 Jun 2022, at 2:50 AM, respectively. Most cases developed symptoms on 21 Jun 2022, between 4:00 PM and 8:00 PM. The outbreak was declared on 22 Jun 2022, and ended on 24 Jul 2022. The epidemic curve suggested a point-source outbreak with a single exposure (Figure 1).

Table 2. Clinical manifestation of cases linked to an acute gastroenteritis outbreak in a rural village in Perak, Malaysia, from 22 to 24 Jun 2022 (n=25)

Clinical Manifestation	Frequency	Percentage
Vomiting	22	88.0
Abdominal pain	19	76.0
Diarrhoea	18	72.0
Nausea	6	24.0
Dizziness	2	8.0
Myalgia	1	4.0

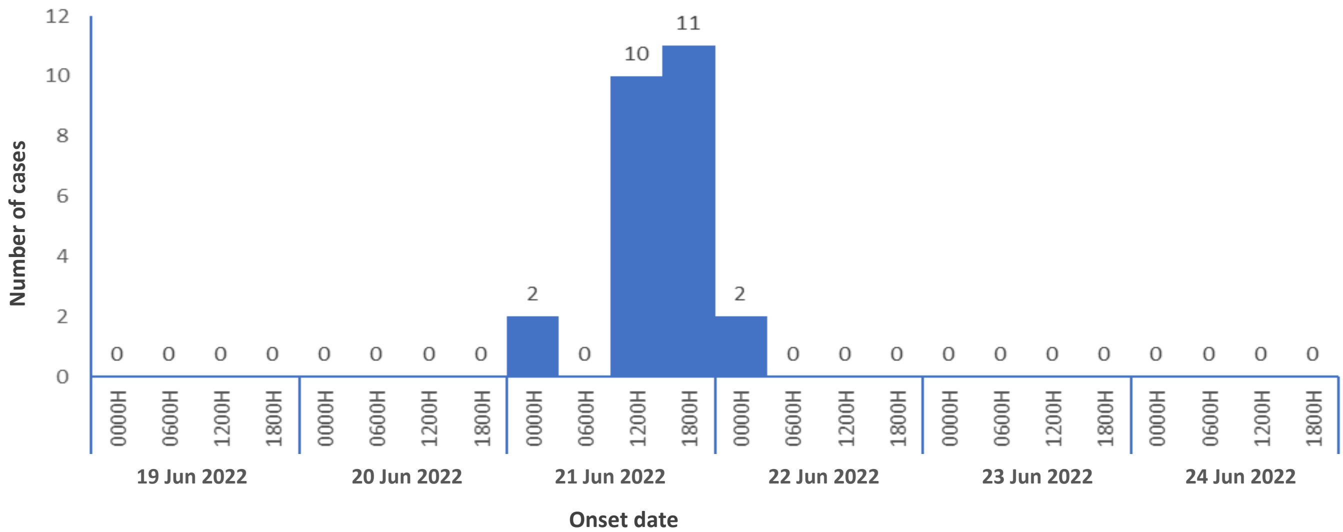

Figure 1. Epidemic curve of an acute gastroenteritis outbreak in a rural village in Larut, Matang, and Selama District, Perak, Malaysia, from 22 to 24 Jun 2022

Mapping of cases

The same GFS outlet supplied untreated water directly to all cases and other residents. Figure 2 shows the location of the cases' houses with respect to the water supply from the GFS outlet.

Food diary

There was no common food eaten by all cases, and none of them had any history of eating or drinking from the same restaurant or food stall except for students from the private boarding school who ate the same food provided by the school. Most residents of the villages also ate foods they cooked at home. In fact, none of the cases reported any abnormal appearance, taste, or smell of the food they consumed prior to the onset of symptoms. Thus, no specific food was identified as the possible cause of this outbreak.

Environmental Assessment and Laboratory Study

Gravity feed system

The GFS water catchment from the river as well as higher-altitude areas up to the peak of the hill were surrounded by a durian orchard. Chemical smells were detected nearby the GFS inlet, and several empty containers of insecticide and nematicide that contain carbofuran 3% w/w (anticholinesterase carbamate) as their active ingredient were also found near the inlet.

Analysis of all water samples taken from the GFS found that all chemical pesticides, namely Alpha-BHC, Beta-BHC, Lindane, Delta-BHC, Heptachlor, Heptachlor exo epoxide, Alpha Endosulfan, Beta Endosulfan, Endosulfan sulphate, 4,4-DDE, 4,4-DDD, 4,4-DDT, Aldrin, Dieldrin, Endrin, Methoxychlor, Endrin Aldehyde, Alpha Chlordane, and Gamma Chlordane, were found to be lower than the mandatory standard value. Furthermore, none of the light metal, namely NH_3-N, $(NO_3+NO)N$, Fluoride, Chloride, Ferum, Manganese, and Aluminium, as well as the heavy metal, namely Arsenic, Mercury, Cadmium, Plumbum, Chromium, Argentum, Cuprum, Zinc, Magnesium, Natrium, Selenium, Sulphate, $CHCl_2Br$, $CHBr_2Cl$, and $CHBr_3$, in the water samples exceeded the Malaysia Drinking Water Quality Standard. However, the level of chloroform ($CHCl_3$), a type of heavy metal, in a water sample was 0.204 mg/L, which exceeded the maximum acceptable value of 0.2 mg/L. Nevertheless, no test was done to identify the presence of carbofuran.

Bacteriological analysis of all water samples showed that the total coliform level at the GFS water catchment area and one of the houses with water supplied by the GFS exceeded 16,000/100 mL, based on the most probable number technique.

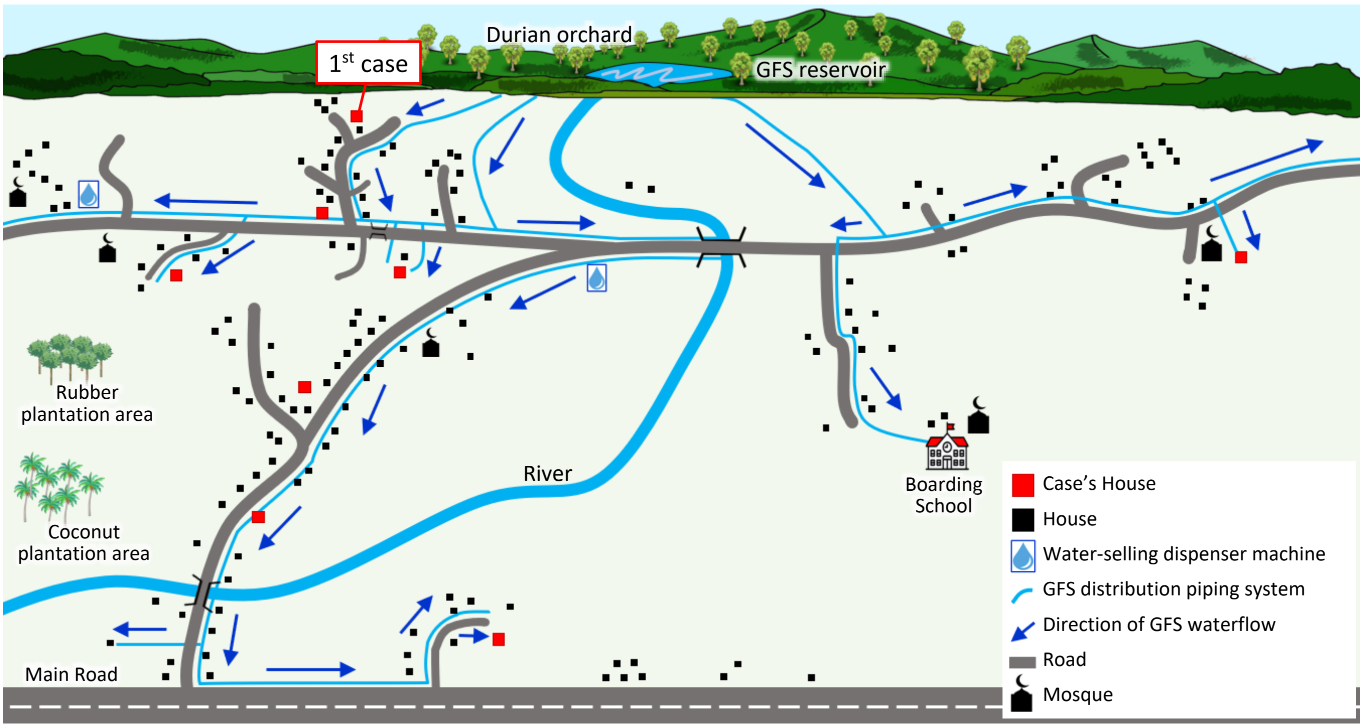

Figure 2. Mapping of cases of acute gastroenteritis outbreak in a rural village in Larut, Matang, and Selama District, Perak, Malaysia, from 22 to 24 Jun 2022

Inspection of water-selling dispenser machines

Two suspected dispensing machines received treated water supplies from the Perak Water Authority, and their outer surfaces were clean and well maintained. An analysis of the water from these machines showed low free residual chlorine (0.07 mg/L and 0.02 mg/L, respectively). Both the pH and turbidity levels of the water from these machines did not exceed the maximum acceptable value. Analysis to detect the presence of coliform, *Bacillus cereus, Coagulase-positive Staphylococci, Escherichia coli, and Salmonella spp.* was found to be negative except for the total plate count (7.5×10^1 CFU/mL and 1.1×10^2 CFU/mL, respectively).

Clinical Sample Analysis

Analysis of all rectal swab samples taken randomly from eight cases did not isolate any pathogenic enteric bacteria.

Health Education

Health education about the importance of consuming treated water for drinking and cooking was given to all cases and their household family members, other residents who were met during the active case detection activity, and teachers at the private boarding school. They were also advised to avoid consuming water from the GFS water supply for any activity if the water was turbid or had an abnormal smell. Pamphlets on food poisoning prevention were also distributed to all villagers, as was the proper usage of insecticides, especially near rivers that supplied water to the villagers.

Discussion

This acute gastrointestinal outbreak involved a group of community members in a rural area with an attack rate of 2.85%. A higher attack rate was previously reported in closed institutions, such as 55% among residents and 25% among employees at a geriatric convalescent facility in Los Angeles County in 1988 and 40% in a secondary school in Pathum Thani Province, Thailand, in 2022.[2,3]

The symptoms experienced by all cases were generally mild and did not require hospitalization. Most cases presented with vomiting, abdominal pain, and diarrhoea. However, none of them presented with fever, which is one of the main symptoms normally experienced by most food- and water-borne bacterial infectious disease cases.[4] Furthermore, no known pathogenic enteric bacteria were isolated from all rectal swab samples.

All cases consumed water from the same GFS. The presence of coliform in the GFS water that exceeded its maximum acceptable value may indicate the presence of pathogenic microorganisms such as viruses, bacteria, or protozoa.[5] They are commonly found in the environment, such as soil or vegetation, and inside mammals' intestines, including humans, particularly *Escherichia coli.*[6]

However, a systematic review and meta-analysis study by Gruber et al. found that fecal coliform had no significant association with diarrhoea.[7] Although those infected by *Escherichia coli* may present with abdominal cramps, fever, vomit, and diarrhoea, bacteriological analysis of all GFS water samples in this outbreak only found a high total coliform, and none of them isolated *Escherichia coli.*[8] Thus, the presence of total coliform in the water samples could not be significantly linked with this outbreak occurrence. Nevertheless, the source of infection from viruses and other microorganisms cannot be excluded because no test was conducted for virus analysis on both clinical and water samples in this outbreak, as water can be contaminated by bacteria, viruses, protozoa, and helminths, as well.[9]

Analysis of water samples from both water-selling dispenser machines discovered low free residual chlorine, which indicates the chlorine level for disinfecting waterborne microorganisms was low.[10] Moreover, the high total plate count in both water samples indicates a high level of microorganisms (mold, yeast, and bacteria) in the water samples.[11] However, clinical sample analysis did not support the epidemiological link between the water consumed by these machines and this outbreak.

Next, the analysis of water from the GFS at various points showed that none of the specific chemical pesticides nor light metal exceeded the mandatory standard value and Malaysia Drinking Water Quality Standard. The test for specific heavy metal also produced similar findings, except for chloroform in one sample. The presence of chloroform in raw water can be a result of contamination by pesticides. This is because chloroform has been used as an ingredient in pesticide production.[12] Although chloroform can also be produced naturally in the water by the chlorination process (mainly water and wastewater), there is no history of this river having been chlorinated previously.[13,14]

In fact, chloroform ingestion may adversely affect a human's health in ways that include central nervous system depression, respiratory depression, delayed hepatotoxicity, severe gastrointestinal injury, and dermatitis.[15] However, all cases in this current outbreak merely presented with mild symptoms and signs and mostly involved the gastrointestinal tract.

Further investigation had discovered that the same source of GFS water is continuously consumed by villagers for domestic use, but the epidemic curve shows a point source with single exposure. Thus, it is more likely to have recent environmental contamination. In fact, carbofuran-containing insecticides and nematicides are normally used seasonally, especially near the durian season, to eliminate unwanted pests on the fruit.

Therefore, a chemical, namely carbofuran, is highly suspected as the source of this outbreak in comparison with an infectious cause. This is based on the symptoms presented by all the cases and is further supported by the fact that none of the rectal swab samples that were taken from more than 30% of the cases had isolated any known pathogenic enteric bacteria. According to the Centers for Disease Control and Prevention, those who consume carbofuran tend to present with vomiting, abdominal cramps, diarrhoea, nausea, headache, miosis, blurred vision, sweating, salivation, lassitude, muscle twitching, incoordination, and convulsions as a result of the inhibition of blood cholinesterase, which later affects the function of both the central nervous system and peripheral nervous system.[16,17] An exposure to chemical such as carbofuran is commonly immediate or shortly after exposure and the cases in this outbreak may had consumed the flowing contaminated water that resulted in different time of exposure with different time of onset.

Moreover, several empty containers of insecticides and nematicides containing carbofuran were found at higher altitudes in the GFS water catchment area, suggesting their use may possibly contaminate the water that is consumed by the villagers. Carbofuran is an anticholinesterase carbamate that is frequently used in agriculture.[18] It can contaminate food, water, and air, adversely affecting human health. Thus, all cases may have consumed river water through GFS that was contaminated by carbofuran, as it supplies water to all the affected premises, even though there was no supportive laboratory evidence due to no water analysis for carbofuran was conducted.

The exposure at every premises is transient as the water flows continuously through the GFS, where possibly carbofuran-contaminated water becomes diluted, resulting in the dose of exposure becoming lower as the distance from the GFS inlet increases. The high number of cases from the private boarding school can be explained by the similar time of exposure to the water from the GFS among them. Nevertheless, some residents who were not working in the villages may not have been exposed to the water at the time it flowed into their house.

During the outbreak, health education for the villagers was intensified, particularly on the proper usage of insecticides near the river that supplies water to the GFS. This was successfully conducted through strong efforts to build trust, respect, and a good relationship with the local communities. Subsequently, there were no additional cases reported with an epidemiological link to this outbreak.

Limitations

This outbreak involved a rural area with a large number of residents. Therefore, we were unable to visit all premises or interview all residents in this area due to limited resources. Furthermore, the results of the analysis should be interpreted with caution, as there was a possibility of non-response bias given that some residents who may have been affected by mild symptoms did not seek healthcare and were subsequently not detected as a case. Secondly, although levels of chemical pesticides in the water samples taken from GFS were found to be under the mandatory standard values, dilution of the chemicals may have occurred to some degree.

Conclusion

An acute gastroenteritis outbreak was detected in a rural area in Perak, Malaysia, that involved 25 cases with an attack rate of 2.85%. The possible source of this outbreak was water from a gravity feed system that was suspected to be contaminated by carbofuran. This hypothesis is based on epidemiological, clinical, and environmental findings, namely the mapping of cases, epidemic curve, and symptoms experienced by all cases, as well as the discovery of several empty containers of insecticide and nematicide containing carbofuran 3% w/w as its active ingredient nearby the river that supplies water to the GFS, although no laboratory analysis to detect the presence of carbofuran in the water was conducted. This acute gastrointestinal outbreak investigation shows the importance of not merely focusing on food but also on other possible sources of illness, including chemicals. This can help better understand these types of outbreaks and lead to a more proper intervention to control the outbreak and prevent its recurrence in the future.

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Conflicts of Interest

This research has no conflicts of interest.

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Implementation of Strategies to Prevent Mother-to-child Transmission of Hepatitis B Virus Infection, Thailand, 2016–2017

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Abstract

Mother-to-child transmission (MTCT) of hepatitis B virus can cause chronic liver disease. Thailand aimed to eliminate MTCT of hepatitis B virus by 2025. Strategies include hepatitis B surface antigen (HBsAg) screening for pregnant women, antiviral therapy for infected mother, hepatitis B birth dose vaccination (HepB-BD), HBV immunoglobulin (HBIG) administration and post-vaccination serologic testing (PVST) for infants born to HBsAg-positive mother. The objectives of this study were to assess the management of HBsAg-positive mothers and their infants. We reviewed medical records of HBsAg-positive pregnant women and their infants born during 1 Jan 2016–31 Dec 2017 at 14 hospitals in seven provinces to assess the percentage of women who were tested and treated for HBV and the percentage of infants born to them who received HepB-BD, HBIG and underwent PVST. All 69,303 pregnant women were screened for HBsAg and 1,179 (1.7%) were HBsAg positive. Of 1,179 HBsAg-positive women, 219 (18.6%) were tested for hepatitis B e-antigen (HBeAg) and 85 (38.8%) were HBeAg positive; 29 (2.5%) were tested for HBV DNA and 14 (48.3%) had viral load ≥200,000 IU/mL. Of 90 women eligible for antiviral therapy, 16 (17.8%) received treatment. Among 1,144 infants with available records, HepB-BD and HBIG coverage was 99.3% and 45.8%. Of 966 children with follow-up records, 12.2% underwent PVST and all were HBsAg negative. In conclusion, while the coverage of maternal HBsAg screening and infant HepB-BD was high, few women received follow-up testing and treatment. HBIG administration for infants was low and PVST rate still needed improvement.

Keywords: hepatitis B virus, hepatitis B infection, mother-to-child transmission, Thailand

Introduction

Approximately 296 million people worldwide are living with chronic hepatitis B virus (HBV) infection, which can lead to cirrhosis, liver cancer, and death.[1–3] HBV is transmitted through mother-to-child transmission (MTCT) and the likelihood of developing chronic HBV infection is up to 90%.[4,5] The highest risk of perinatal infection occurs when a pregnant woman with HBV infection has positive hepatitis B e-antigen (HBeAg) or has a high HBV DNA viral load.[6,7]

The foundation of prevention of HBV MTCT is universal HBV vaccination for the newborn within 24 hours of birth followed by two to three additional doses during infancy. Administration of HBV immunoglobulin (HBIG) to newborns of hepatitis B surface antigen (HBsAg)-positive mothers may provide an additional benefit to vaccination, especially when the mother is HBeAg positive.[5,8] Maternal screening to identify women at high risk of HBV transmission with additional antiviral treatment starting at 28–32 weeks gestational age until 4 weeks after delivery for certain HBV infected women, can decrease the risk of HBV transmission and has been recommended by the World Health Organization since July 2020.[8–10]

Thailand has the highest rate of hepatitis B causing hepatocellular carcinoma.[11] Since 1992, Thailand implemented universal HBV vaccination for all newborns and infants. The current vaccination schedule includes a hepatitis B vaccine birth dose (HepB-BD) within 24 hours of birth, and additional doses at two, four, and six months of age.[12] National coverage of HepB-BD and third dose hepatitis B vaccine have been >95% for the past decade.[13] Universal HBV vaccination has led to a significant reduction in the HBV prevalence in Thailand, with the seroprevalence of HBsAg among people born after vaccine introduction of 0.6% compared to 4.5% among those born prior to the introduction of the HBV vaccine.[12]

Standard practice for prevention of HBV MTCT in Thailand has also included universal maternal HBsAg screening and additional preventive measures for infants born to women with HBV infection. Infants born to HBV infected women should receive HepB-BD within 12 hours of birth followed by hepatitis B vaccine (HepB) at one, two, four, and six months of age as well as HBIG immediately after birth.[14]

In 2016, the World Health Organization announced that one of their goals was to eliminate HBV MTCT and reduce hepatitis B prevalence in children under 5 years to 0.1%. A HBV prevalence study in Thailand in 2016 indicated that the prevalence of HBV infection in children under 5 years in Thailand was 0.1%.[12] To achieve HBV MTCT elimination goal by 2025, Thailand launched a new strategy to eliminate MTCT of HBV in Thailand in 2018 which consists of four main indicators with the following minimum targets: 100% of pregnant women should be screened for HBsAg; 95% of pregnant women with a high risk HBV infection, as indicated by HBeAg positive or HBV DNA viral load ≥200,000 IU/mL, should be prescribed Tenofovir treatment; 90% of all infants should receive HepB-BD within 12 hours of birth; and 90% of all infants born to HBV infected mothers should receive HBIG within 7 days.[14,15] The strategy also recommends post-vaccination serologic testing (PVST) for children at 1 year of age, which consists of HBsAg and hepatitis B surface antibody testing.

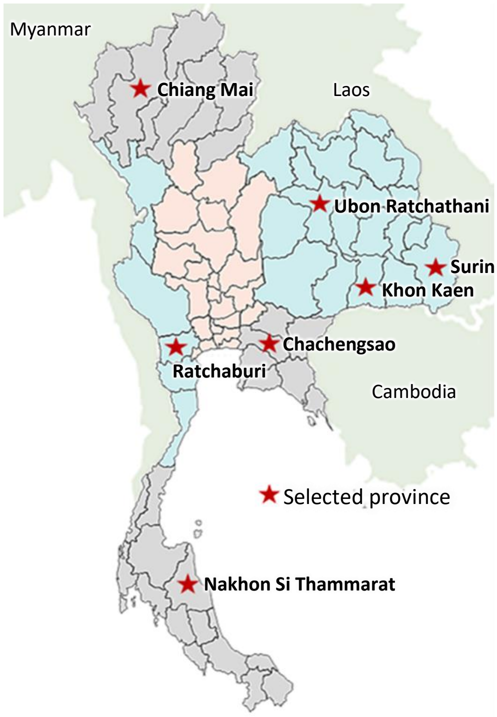
To support evidence-informed policy decision to strengthen the elimination of HBV MTCT, we conducted a survey to assess the management of HBsAg-positive mothers and their infants during 2016–2017, in an aim to identify gaps, challenges and opportunity for HBV MTCT in Thailand.

Methods

We conducted a retrospective survey to describe HBV MTCT practices in Thailand during 1 Jan 2016 to 31 Dec 2017.

Population and Sampling

We retrospectively reviewed medical records of pregnant women who gave birth during 2016–2017 and their infants in seven of the 77 provinces. These provinces are located in the Northern, North-eastern, Eastern, Western/Central and Southern regions of Thailand. Four of the seven provinces border Myanmar, Laos or Cambodia. From each province, one tertiary hospital and one district hospital was purposively selected (Figure 1).



The sites were distributed in seven out of the 77 provinces in Thailand, which are denoted by the stars. These seven provinces were Chiang Mai (Northern region), Ubon Ratchathani (North-eastern region), Surin (North-eastern region), Khon Kaen (North-eastern region), Chachoengsao (Easthern region), Ratchaburi (Central/Western region) and Nakhon Si Thammarat (Southern region).

Figure 1. Map of Thailand highlighting survey sites

Data Collection

At each hospital, we determined the total number of pregnant women and the number of HBsAg-positive pregnant women who delivered at the hospital during 1 Jan 2016 to 31 Dec 2017 by reviewing the labor room line list and hospital database. For women with a positive HBsAg result, we reviewed their medical records to abstract demographic, gravidity, lab results, and clinical management. For their infants, we abstracted demographic data, HepB-BD vaccination status, receipt of HBIG, and post-vaccination testing results.

Data Management and Analysis

We entered the data into Epidata version 3.1 (Odense, Denmark) or Microsoft Excel (Redmond, Washington, USA) using double data entry. We used Epi Info version 7.2.1.0 (Atlanta, Georgia, USA) and Microsoft Excel for data analysis. We conducted descriptive analyses to describe the prevalence of HBsAg among pregnant women and estimate the percentage of HBsAg-infected women who were tested for HBeAg and/or HBV DNA, were seen by an internist, and received anti-viral medication. Among infants born to HBsAg-positive women, we calculated the percentage of receiving timely HepB-BD vaccine (within 12 and 24 hours), total HepB-BD (received any time), HBIG, and post-vaccination testing with HBsAg and/or hepatitis B surface antibody.

Ethics

The survey was undertaken under the authority of the Thai Ministry of Public Health to conduct a review of medical records in government hospitals for program evaluation purposes. The participants' data remained confidential within the Ministry of Public Health.

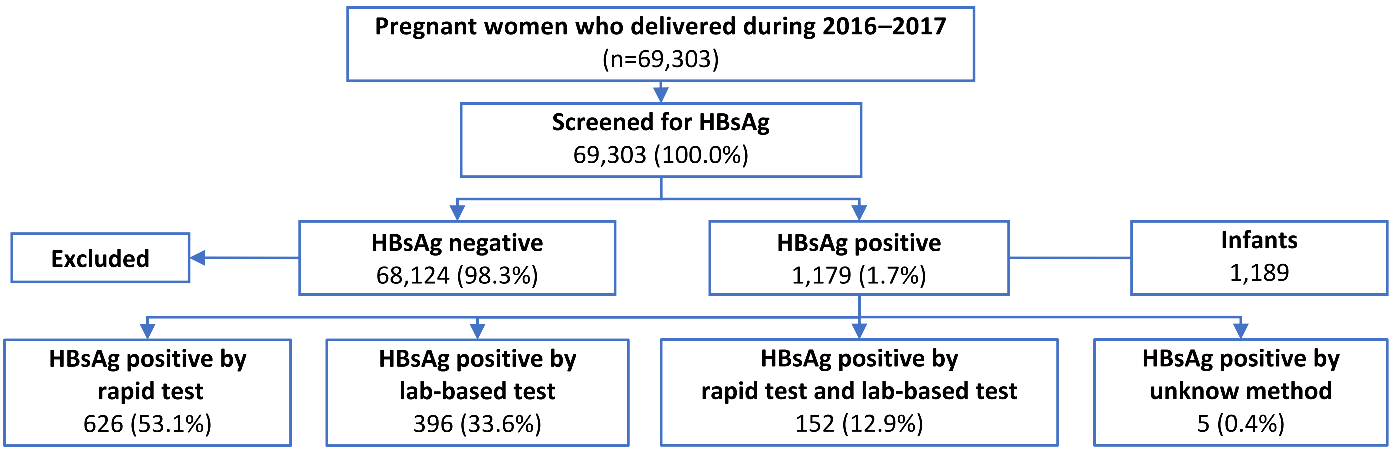
Results

General Characteristics of HBsAg-positive Women and Their Infants

We reviewed the records of 69,303 pregnant women who delivered in the selected hospitals during the survey period (Figure 2). All women were screened for HBsAg, and the HBsAg prevalence was 1.7% (n=1,179). The mean age of HBsAg-positive pregnant women was 30 years and most (81.0%) were Thai nationals (Table 1). Most women lived in the North-eastern region (44.4%) followed by the Northern region (26.2%). There were 1,189 infants (including 10 sets of twins) born to the 1,179 women who tested positive for HBsAg. Of the 1,189 infants, 585 (50.7%) were male. Among 1,180 infants with a recorded birth weight, 1,048 (88.8%) were normal (weight ≥2,500 grams). The mean birth weight was 3,032 grams. Among 1,173 infants with a record of gestational age, 1,036 (88.3%) were full term (gestational age ≥37 weeks).

Table 1. Characteristics of pregnant women who tested positive for HBsAg and infants at selected hospitals in Thailand, 2016–2017

Characteristic	n	%
Demographic data, n=1,179		
Mean age (years) =30	-	-
Nationality		
Thai	955	81.0
Myanmar	151	12.8
Lao	26	2.2
Other	24	2.0
Unknown	23	2.0
Region of residence		
North-eastern	523	44.4
Northern	309	26.2
Southern	115	9.8
Eastern	105	8.9
Western	87	7.4
Central	29	2.5
Other	7	0.6
Unknown	4	0.3
Gravidity		
1	358	30.4
2	447	37.9
≥3	355	30.1
Unknown	19	1.6
Demographic data of infants (n=1,189)		
Male (n=1,153)	585	50.7
Birth weight (grams) (n=1,180)		
Normal (≥2,500 g)	1,048	88.8
Low (<2,500 g)	132	11.2
Gestational age at birth (n=1,173)		
Term (≥37 weeks)	1,036	88.3
Preterm (<37 weeks)	137	11.7



HBsAg: Hepatitis B surface antigen. Of the 69,303 pregnant women delivered during 2016–2017 and all were screened for HBsAg. Among these, 1,179 (1.7%) were HBsAg positive. All of the HBsAg-positive women and their 1,189 infants (including 10 pairs of twins) were included in the review.

Figure 2. Participant flow diagram

Maternal HBV Diagnostic Testing

Of the 1,179 HBsAg-positive mothers, 626 (53.1%) were tested for HBsAg by RDT, 396 (33.6%) were diagnosed by a lab-based test (indirect ELISA or CMIA), 152 (12.9%) had both RDT and lab-based test, and 5 (0.4%) had and unknown testing method. Among the 132 women who received HBsAg testing at a district hospital, 117 (88.6%) were tested by RDT, 14 (0.6%) had a lab-based test, and 1 (0.8%) had both RDT and lab-based test. Among the 1,047 women who received HBsAg testing at a tertiary hospital, 509 (48.6%) were tested by RDT, 382 (36.5%) had a lab-basted test, 151 (14.4%) had both RDT and lab-based test, and 5 (0.5%) had an unknown testing method.

Women who were initially tested by an RDT should have had a confirmatory lab-based test; however, only 19.5% (152/778) of women diagnosed with HBsAg by an RDT had a confirmatory lab-based test.

Evaluation of Maternal HBV Risk Status and Treatment for Mothers at High Risk of Mother to Child Transmission

Of the 1,176 HBsAg-positive mothers whose medical records included a field for HBeAg results, 219 (18.6%) received HBeAg testing (Table 2). All but 4 of these women were tested for HBeAg in tertiary hospitals. By region, the proportion of women tested for HBeAg varied from 32.8% (North-eastern Region) to 1.0% (Eastern Region). Among the 219 women who had a test result for HBeAg, 85 (38.8%) were positive. The percentage of women who tested positive for HBeAg ranged from 64.3% (Northern Region) to 18.2% (Southern Region). Few women from the Central, Eastern and Western regions who were tested for HBeAg had either negative or missing results.

Table 2. Follow-up testing for pregnant women with HBV infection at selected tertiary hospitals, by region, Thailand, 2016–2017

Region	HBeAg tested			Positive HBeAg			HBV DNA viral load tested			Viral load ≥ 200,000 IU/mL		
	N	n	%	N	n	%	N	n	%	N	n	%
Northern	309	14	4.5	14	9	64.3	309	2	0.6	2	0	0.0
North-eastern	525	172	32.8	172	69	40.1	525	13	2.5	13	8	61.5
Central	28	1	3.6	1	0*	0.0	28	1	3.6	1	0*	0.0
Southern	115	11	9.6	11	2*	18.2	115	7	6.1	7	3*	42.9
Eastern	105	1	1.0	1	0*	0.0	105	1	1.0	1	0	0.0
Western	87	18	20.7	18	5*	27.8	87	5	5.7	5	3	60.0
Other country	7	2	28.6	2	0	0.0	7	0	0.0	-	-	-
Total	**1,176**	**219**	**18.6**	**219**	**85**	**38.8**	**1,176**	**29**	**2.5**	**29**	**14**	**48.3**

**Unknown results. HBV: hepatitis B virus. HBeAg: hepatitis B e-antigen. HBV DNA: hepatitis B deoxyribonucleic acid.*

Of the 1,176 HBsAg-positive mothers whose records included information on HBV DNA viral load testing, 29 (2.5%) had a test result. Of these, 14 (48.2%) had a viral load ≥200,000 IU/mL. None of the women who delivered in a district hospital were tested for HBV DNA viral load. Nine women were both HBeAg positive and had HBV DNA ≥200,000 IU/mL.

Among 1,176 HBsAg-positive women who had HBeAg or HBV DNA viral load testing, 90 (7.7%) were high-risk for HBV MTCT due to a viral load ≥200,000 IU/mL, presence of HBeAg, or both. Of these 90 women, 21 (23.3%) were seen by an internist for follow up of their HBV infection (Table 3). The percentage of high-risk women seen by an internist varied by region of residence, from 14.1% in the North-eastern region to 60.0% in the Southern and Western regions. Of the 21 women seen by an internist, 16 (76.2%) were prescribed an antiviral medication (lamivudine or tenofovir). There were six women with pre-existing HBV or HIV who were already receiving an antiviral medication from an internist at the time of their pregnancy. The percentage of high-risk women who received an antiviral medication varied from 60.0% in the Northern region to 100.0% in the Southern and Western regions.

Table 3. Management of pregnant women at high risk of mother to child transmission of HBV infection at selected tertiary hospitals in Thailand, 2016–2017

Region	High risk maternal status (HBeAg positive or viral load ≥200,000 IU/mL)			Referred to internist			Prescribed antiviral treatment		
	N	n	%	N	n	%	N	n	%
Northern	309	9	2.9	9	5	55.6	5	3	60.0
North-eastern	525	71	13.5	71	10	14.1	10	7	70.0
Central	28	0	0.0	-	-	-	-	-	-
Southern	115	5	4.3	5	3	60.0	3	3	100.0
Eastern	105	0	0.0	-	-	-	-	-	-
Western	87	5	5.7	5	3	60.0	3	3	100.0
Other country	7	0	0.0	-	-	-	-	-	-
Total	**1,176**	**90**	**7.7**	**90**	**21**	**23.3**	**21**	**16**	**76.2**

Management of Infants Born to HBsAg-positive Mothers

Records for 1,144 of the 1,189 infants (96.2%) were available for analysis. HepB-BD coverage was 99.3% overall, 99.2% for tertiary hospitals, and 100.0% for district hospitals (Table 4). HepB-BD coverage was 100.0% for all regions except for the Northern (97.8%) and North-eastern (99.8%) regions, where results were missing for 7/313 and 1/530 records, respectively. Among the 1,136 newborns who received HepB-BD, 1,104 (97.1%) received HepB-BD within 24 hours, as recommended by World Health Organization guidelines, and 32 (2.8%) were uncertain of HepB-BD administration time.[2] Among 1,104 newborns who received HepB-BD within 24 hours, 705 (63.8%) received it within 12 hours of birth.

Records for 1,106 infants included data on HBIG, of which 507 (45.8%) received HBIG. Of these, 499 (98.2%) received HBIG within the first day of life. The percentage of infants receiving HBIG varied by region and type of hospital. None of the infants in the Southern (n=114) or Eastern (n=109) regions received HBIG, whereas 457 of 526 (86.8%) infants in the North-eastern region received HBIG. Of the 526 infants in the North-eastern region, a higher proportion of infants received HBIG at a tertiary hospital (93.0%) than at a district hospital (54.2%). However, in the Northern region, fewer infants at a tertiary hospital (2.2%) received HBIG than at a district hospital (56.3%).

Table 4. Proportion of infants who received hepatitis B birth dose vaccination (n=1,144) and hepatitis B immune globulin (n=1,106) at selected hospitals, by region and type of hospital, Thailand, 2016–2017

Region	Hepatitis B birth dose vaccination									Hepatitis B immune globulin								
	Tertiary hospital			District hospital			Total			Tertiary hospital			District hospital			Total		
	N	n	%	N	n	%	N	n	%	N	n	%	N	n	%	N	n	%
Northern	278	271	97.5	35	35	100.0	313	306	97.8	272	6	2.2	32	18	56.3	304	24	7.9
North-eastern	446	445	99.8	84	84	100.0	530	529	99.8	443	412	93.0	83	45	54.2	526	457	86.9
Southern	106	106	100.0	5	5	100.0	111	111	100.0	109	0	0.0	5	0	0.0	114	0	0.0
Eastern	110	110	100.0	5	5	100.0	115	115	100.0	105	0	0.0	4	0	0.0	109	0	0.0
Western	72	72	100.0	3	3	100.0	75	75	100.0	50	25	50.0	3	1	33.3	53	26	49.1
Total	**1,012**	**1,004**	**99.2**	**132**	**132**	**100.0**	**1,144**	**1,136**	**99.3**	**979**	**443**	**45.3**	**127**	**64**	**50.4**	**1,106**	**507**	**45.8**

Post-vaccination Serologic Testing (PVST) for Children Born to HBsAg-positive Women

Of 966 children with HBsAg data, 118 (12.2%) were tested for HBsAg, and all had a negative test result. Of 960 children, 117 (12.2%) were tested for hepatitis B surface antibody. Out of the 117 children tested for hepatitis B surface antibody, 112 (95.7%) had a positive test result indicating immunity to HBV, one child was initially not immune but because immune after receiving an additional dose of HBV vaccine, and in four children, the result was missing.

Discussion

This study provided an overview of the practices to prevent MTCT of HBV in Thailand during 2016–2017, before nationwide introduction of Thailand's new strategy to eliminate MTCT of HBV. The purpose of the study was to report the baseline situation before implementation of the strategy to prevent MTCT of HBV in Thailand.

In this study, 100% of pregnant women were screened for HBsAg, which highlights the success of Thailand's maternal screening policy.[16] The maternal HBsAg prevalence of 1.7% indicates low HBV endemicity among pregnant women.[2] Despite the low HBsAg prevalence, only 18.6% of HBsAg-positive women received HBeAg and only 2.5% received HBV DNA viral load testing, with tests mostly provided by tertiary hospitals. These results are not unexpected because follow-up testing was not standard at the time and district hospitals in Thailand usually do not have the capacity to perform these tests. These results highlight key challenges for district hospitals; without these tests, pregnant women will need to be referred to tertiary hospitals for follow-up testing to ensure that those who are infected receive proper HBV treatment.

While only a small percentage of HBsAg-positive women received HBeAg or HBV DNA viral load testing, 38.8% of women who were tested for HBeAg were positive, and 48.3% of women who received HBV DNA viral load testing had levels ≥200,000 IU/mL. These women were at high risk of transmitting HBV to their infants; however, only 23.3% were referred to internists for evaluation and initiation of antiviral medication. These results suggested that there were many women at high risk of transmitting HBV to their infants who were missed by the health system. Due to limit availability of internists, allowing general practitioners to prescribe antiviral medication to HBsAg-positive women could increase the proportion of women on antiviral treatment and better prevent MTCT of HBV.

Thailand's immunization program has recommended universal, timely HepB-BD for all newborns to prevent MTCT of HBV for many decades.[12] In this survey, 99.3% of newborns received HepB-BD and 97.1% received HepB-BD within 24 hours of birth. The high HepB-BD coverage among the hospitals included in this survey are consistent with national HepB-BD coverage estimates.[13] Coverage of HepB-BD received within 12 hours of birth was lower at 63.8%; although this result may be underestimated because the time of receiving HepB-BD was missing for almost half of the newborns. Because Thailand's new strategy includes administration of HepB-BD within 12 hours for all infants, it will be important for the time of administration to be documented in the medical records so this indicator can be measured. Anecdotally, data collectors noted that some medical records did not include a field to record the time of vaccination, therefore we recommend that all medical record forms allow for complete HepB-BD documentation.

Although only 45.8% of eligible infants received HBIG, 97.1% of infants received the treatment within one day. There are a few possible reasons for the low HBIG coverage in this survey. First, only tertiary hospitals in Thailand stock HBIG, due to shortages, so infants born at district hospitals are less likely to receive the treatment. Second, some health facilities do not provide HBIG due to its high cost, while other health facilities charge parents for its use, and the parents may not be able to afford it. Third, none of the infants living in the Southern and Eastern regions received HBIG, possibly because health care workers do not offer this treatment to eligible newborn, as in some countries where lack of knowledge about indications for HBIG has led to missed opportunities to provide this treatment to eligible infants.[17] Under Thailand's new strategy to eliminate MTCT of HBV, 90% of infants born to HBsAg-positive mothers should receive HBIG, so the challenges noted above should be addressed to reach this target.

The percentage of children who received post-vaccination serologic testing coverage, which was not part of standard of care at the time of the survey, was low, with only 12.2% of children receiving hepatitis B surface antibody testing and 12.2% receiving HBsAg testing. To ensure that all children receive PVST at 12 months of age, it is important to ensure that health care workers and parents are aware of this new recommendation.

There were a few limitations in this survey. First, both provinces and health facilities were selected by convenience sampling and Bangkok was not included, thus the results may not be representative of the entire country. Second, the proportion of tertiary and district hospitals might not be representative of the current proportion of hospitals in each region nor the entire country. Third, the study was a retrospective medical record review and some of the data were incomplete. Some women could have received antenatal care and delivery care at different hospitals, thus the information in their records might be incomplete at the hospital included in the study.

Conclusion

Thailand has made tremendous progress towards HBV control with high HepB-BD and third dose hepatitis B vaccine coverage. In September 2019, Thailand was one of the first countries to be verified as having achieved HBV control through immunization in the World Health Organization South-East Asia Region.[18]

The next step towards HBV elimination is to eliminate MTCT of HBV, as recommended in Thailand's new 2018 guidelines. The HBsAg prevalence among pregnant women in this study was low; however, the proportion of HBsAg-positive women who received follow-up testing and antiviral treatment was low. Most infants born to an HBV infected mother received the hepatitis B vaccine but only half of them received HBIG. This study identified several key challenges that should be addressed as Thailand implements its new policy. First, women who are HBsAg-positive should receive follow-up laboratory testing and women with high-risk infection should be referred to clinicians for antiviral therapy. Second, district hospitals should increase the availability of HBIG and ensure that children receive PVST testing. Third, capacity building on HBV MTCT elimination should be done at all levels.

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Conflicts of Interest

The authors have no conflicts of interest to declare.

Author Contributions

SJ designed the survey protocol and oversaw survey implementation. NP planned the survey implementation procedures, created the data abstraction form, participated in data collection, analyzed the data, and drafted the manuscript. JC and NW facilitated survey implementation with local authorities. TR reviewed and revised the data abstraction form. AAM reviewed the results and drafted the manuscript.

Disclaimer

The findings and conclusions in this paper are those of the authors and do not necessarily reflect the position of the Centers for Disease Control and Prevention.

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An Investigation of the First Non-sexual Household-transmitted Mpox Cluster with Rapid Situation Analysis of Mpox Epidemic in Thailand

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Abstract

On 22 May 2023, the mpox cluster was reported in a household in Nonthaburi Province, Thailand. We investigated to confirm the outbreak and diagnoses, describe its possible linkage and source, and identify potential fomite transmission. We interviewed all cases, traced their contacts, and swabbed household surfaces for mpox. We conducted a rapid situation analysis of mpox cases in Thailand until July 2023. Three cases were confirmed within the same household involving five individuals. The first case was a sexually active male and the second case was his intimate partner. The third case was the mother of the second case. The first two cases reported no sexual activity after symptoms appeared. They both attended a shaving ceremony and engaged in activities without wearing face masks. The third case had direct contact with her son's droplets and rash and then developed symptoms, without rash and fever. No additional case was detected among participants of the ceremony. One of two other household members tested negative after developing symptom while the other was asymptomatic. Despite house cleaning with 70%-ethanol, before investigation, 18 of 27 environmental swabs tested positive, with cycle threshold values ≥30. Since situation analysis revealed no previously reported non-sexual household mpox transmission, this investigation confirmed its existence. Risk communication should address the plausibility of non-sexual transmission. Mpox symptom may occur without rash and fever, emphasizing the importance of testing suspected individuals and revising mpox investigation guidelines accordingly. Surface cleaning with 70%-ethanol may reduce fomite transmissibility.

Keywords: mpox, Thailand, household transmission

Introduction

Mpox is caused by the monkeypox virus (MPVX). It belongs to the *Orthopoxvirus*, same genus as smallpox. Human-to-human transmission occurs via droplet contact, direct contact with lesions, and indirect contact with contaminated fomites.[1] The secondary attack rate within households is less than 10%.[2] However, household secondary infections can spread across three waves, emphasizing timely outbreak investigations.[3] Although there is immunological cross-protection between mpox and smallpox,[1] the new global generation lacks this immunity because of the cessation of smallpox vaccination after the success of its eradication since 1979.[4]

The incubation period of mpox ranges from 5 to 21 days and around 10% of infected people are asymptomatic.[5] Symptoms start from the prodromal phase, characterized by fever, headache, lethargy, myalgia, and lymphadenopathy. A vesiculopustular rash appears following prodromal symptoms and lasts for 2–4 weeks. The infectious period starts from the prodromal phase until a new layer of skin has formed. Mpox is self-limited within 2–4 weeks. Severe illness and complications such as, pneumonia, and encephalitis, are rare.[4]

In 2022, a global-wide mpox outbreak occurred across 75 countries. The World Health Organization announced mpox as a Public Health Emergency of

International Concern on 23 Jul 2022.[3] The major route of transmission was sexual contact, with the majority of cases involving men who have sex with men (MSM).[1,4,6–8]

In Thailand, mpox is a communicable disease under surveillance by the Department of Disease Control (DDC). Every mpox case must be reported to the event-based surveillance (EBS) system. The first documented case of mpox in Thailand was on 18 Jul 2022.[9] At the time, Thailand's risk communication effort was primarily directed towards the lesbian, gay, bisexual, transgender, and queer or questioning communities. Additionally, there have been no previous documented case of household transmission of mpox via non-sexual routes nor any published study examining the mpox situation in Thailand. On 22 May 2023, a joint investigation team was notified by the Office of Disease Prevention and Control Region 4 Saraburi about the mpox cluster within a household in Bang Kruai District, Nonthaburi Province. Therefore, the outbreak investigation was conducted to confirm the outbreak and diagnoses, describe the epidemiological linkage, identify the possible source(s) of the outbreak, and potential risk of fomite transmission in the household. Moreover, we reviewed the mpox situation in Thailand to offer additional key insights into the context of the outbreak across the country.

Methods

Epidemiological Investigation and Contact Tracing

During 22–26 May 2023 we interviewed all confirmed cases, discussing demographic characteristics, clinical presentation, treatment, symptom onset, relationships, and shared activities with other cases, using a semi-structured questionnaire. We conducted contact tracing by interviewing confirmed cases to determine their potential exposure history. We interviewed the organizer of a shaving ceremony that case 1 attended to gather the ceremony details and any participant's illness history. Moreover, we developed an online questionnaire for symptom screening among ceremony-participants (details in the results section).

Our case definitions were as follows: a suspected case was an individual who was either suspected by a physician or in close contact with a confirmed mpox case between 1 and 21 Feb 2023 and developed one of the following symptoms: rash (including macules, papules, vesicles, pustules, or crusts), or fever along with associated symptoms including sore throat, headache, myalgia, back pain, or lymphadenopathy. A confirmed case was a suspected case with positive MPVX confirmation via real-time polymerase chain reaction (real-time PCR). Close contacts were individuals who had contact with a confirmed case from the beginning of the symptoms until the development of a scab including direct contact with a case's skin (either with or without lesion), mucosa, secretion, and surfaces such as clothes; or lived in the same house, or stayed overnight with a case for at least one night; or traveled with a case in the same vehicle within a distance of 1 meter; or shared a toilet with a case; or was involved with a case when having aerosol-generating activities. A discarded case was a suspected case with a negative test result on real-time PCR.

To confirm the diagnosis, a total of eight samples of lesion swabs, nasopharyngeal and throat swabs, and whole blood from all three confirmed cases and one discarded case were tested for MPVX by real-time PCR at Chulalongkorn or Bang Kruai Hospitals.

Environmental Study

To assess the risk of fomite transmission, we surveyed the affected household. We interviewed the cases about common touchpoints in their daily activities. Surface swabs from these touchpoints (n=27) were collected on 24 May 2023 after the house underwent cleaning with 70%-ethanol (details in results section). Samples were sent to the Bamrasnaradura Infectious Disease Institute for MPVX testing using real-time PCR. Positive samples with a cycle threshold (CT) value below 30 underwent further culture to assess virus viability.

Mpox Situation Analysis

To understand the mpox situation in Thailand, we reviewed confirmed case reports from the EBS system, up to 31 Jul 2023. Extracted data encompassed demographic characteristics, symptoms onset, treatment initiation date, notification dates, clinical presentations, HIV status, and reported risk behaviors.

Ethics

Since this study was part of routine DDC outbreak investigation, ethics approval was unnecessary.

Results

Epidemiological Investigation

We confirmed the diagnosis of the three mpox cases in Bang Kruai District, Nonthaburi Province. The first and second cases were male sexual partners. The third case was the mother of the second case. All lived in the same household, except for case 1 who lived elsewhere but often visited this house. This household also included two additional family members: the father of the second case (the husband of the third case) and a cousin of the second case.

The first case was a 27-year-old Indonesian-male. He was a dancer and was HIV-positive with a CD4 count >200 cells/mm^3 with undetectable viral load. He denied having multiple sexual partners. He lived alone in a condominium in Bang Phlat District, Bangkok. On 20 April, he performed dancing at a hotel in Sathon District, Bangkok, and had no physical contact with others. Between 25 and 29 April, he and his partner (case 2) spent time together at his condominium. They engaged in protected sex, using a condom, on 28 April. At that time, they had no symptoms and confirmed that they had no other sexual encounters. On 1 May he visited case 2's house, met their family, and stayed overnight. The next day, he participated in a shaving ceremony with case 2. On 3 May, he danced at a theater, denying close contact with others. During 4–8 May, he stayed at case 2's house and participated in various activities such as having dinner, without wearing a face mask. On 6 May, he developed headache, fatigue, and myalgia. Later, he developed fever and flank pain. On 9 May vesicles emerged on both arms, ankles, and the trunk, along with ulcers on the scrotum, penis, and perianal area. He then isolated at his condominium. He visited Chulalongkorn Hospital on 12 May and tested positive for MPVX. He reported no sexual activity after symptoms occurred.

The second case was a 25-year-old Thai-male. He had no underlying disease and denied multiple sexual partners. He stayed at his house in Bang Kruai District from 20 to 24 April, as he was recuperating from COVID-19. He visited the condominium of his partner (case 1) between 25 and 29 April and had shared activities, including intimacy, on 28 April. He returned to his house on 30 April. He took part in the shaving ceremony with case 1 on 2 May. From 4 to 13 May he stayed at his house. From 6 to 11 May, he experienced symptoms, starting with fever and cough on 6 May followed by headache and sore throat on 9 May. The rashes on his arms, head, trunk, and buttocks occurred on 11 May. He then isolated in his bedroom on 12 May. The next day, he visited case 1's condominium. On 14 May, he attended a polling station while wearing a face mask, long-sleeved shirt, and long-legged pants. He maintained social distance and had no close contacts. He visited Chulalongkorn Hospital on 15 May and tested positive for MPVX. As with case 1, he reported no sexual activity after symptoms occurred.

The third case was a 62-year-old retired Thai-female. She was the mother of the second case and lived in the same house. She underwent a smallpox vaccination during childhood. On 1 May, she had dinner with her son (case 2) and case 1 at her house in Bang Kruai District. Between 4–13 May she engaged in various activities such as having dinner with case 1 and case 2. She did not wear a face mask during these activities. She reported that her son coughed near her, without a face mask. On 11 May, she examined her son's rashes with her bare hands. On 12 May, she isolated in her bedroom. On 13 May, she experienced discomfort in her neck, followed by left cervical lymphadenopathy on 17 May and headache on 18 May. Note that she presented with neither fever nor rash. She visited Bang Kruai Hospital on 19 May and tested positive for MPVX.

Figure 1 shows a timeline of the shared activity among all cases.

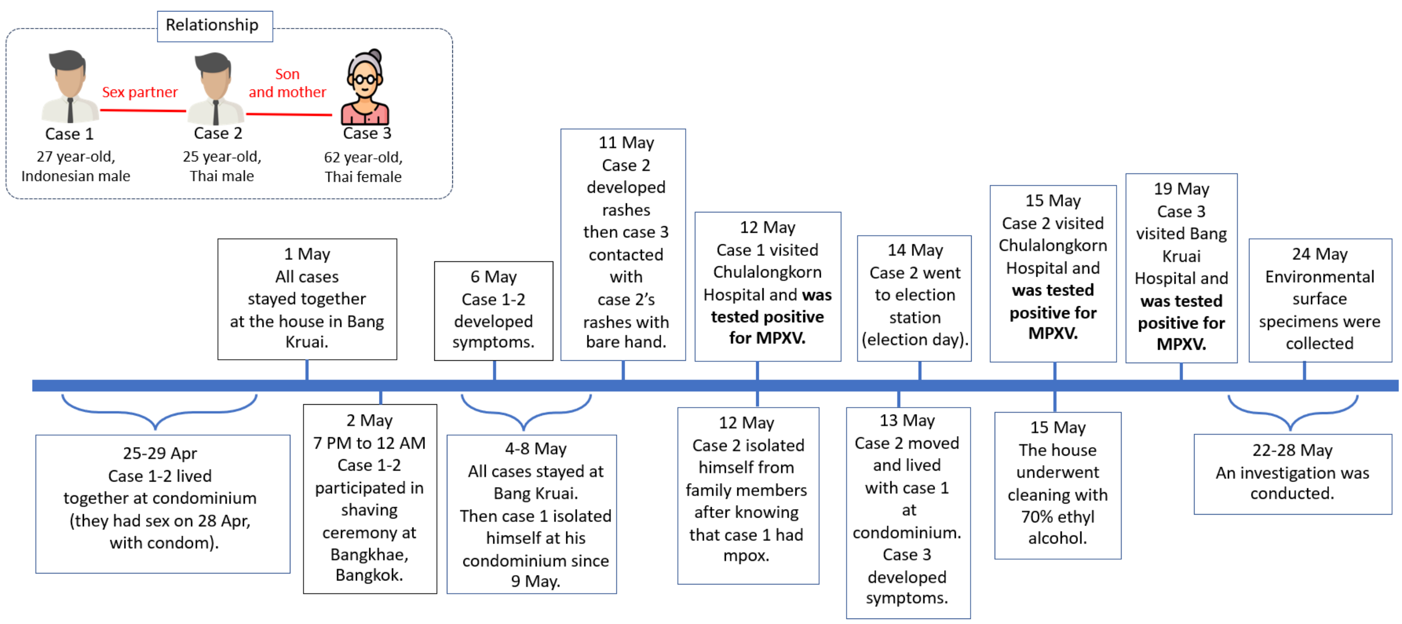

Figure 1. Summary of the shared activity and timeline among all mpox cases in Bang Kruai District, Nonthaburi Province, Thailand, 22–28 May 2023

Contact Tracing

The contact tracing revealed no additional case in case 1's condominium and the theater, where he performed on 3 May. We actively monitored the symptoms of the two other household contacts (the father and cousin of case 2) until 10 June. The father developed a nodule at the left index finger on 22 May, but his nasopharyngeal swab was negative for MPVX. The cousin was asymptomatic and was therefore not tested for MPVX.

The shaving ceremony is a tradition derived from Brahmanism to celebrate a boy's first haircut. This ceremony was held in Bang Khae District, Bangkok, on 2 May. There were about 100 participants who were primarily performers from several art institutions and reported to be from the LGBTQ+ community. The ceremony featured nine performances along with a self-serve dinner. Throughout the ceremony, there were close-contact behaviors such as handshakes and hugs among participants. Activities were conducted without face masks being worn. Shared toilet use was reported among participants. The ceremony-organizer stated that no additional mpox cases were reported by the participants. We developed an online questionnaire for ceremony-participants to record any symptoms and asked case 1 to help distribute the website address for this questionnaire on our behalf since we were not given the contact information of the ceremony-participants. However, only one individual responded, reporting no symptoms. Subsequent mpox cases reported to DDC after that were not linked to this ceremony.

Table 1 shows the laboratory findings for all cases. Case 3 had the highest CT value from nasopharyngeal and throat swab, still positive upon repeat testing seven days later.

Environmental Study

The affected household in Bang Kruai District is a three-storey-townhouse. The living room and kitchen are located on the first floor. Toilets are located on the second and third floors. There are various common touchpoints such as light switches, doorknobs, banisters, and faucets. Each family member occupies their own bedroom, with case 2 and case 3 residing on the third floor, the father on the second floor, and the cousin on the first floor. On 15 May, before our investigation, the house was cleaned with 70%-ethanol. Surface swabs yielded 18 positive samples out of 27, all with CT values exceeding 30. None were eligible for MPVX culture (Table 2).

Table 1. Laboratory results of all mpox cases in Bang Kruai District, Nonthaburi Province, 22–28 May 2023

	Case 1	Case 2	Case 3	
			1st test	2nd test
Onset date	6 May 23	6 May 23	13 May 23	
Test date	12 May 23	15 May 23	19 May 23	26 May 23
NPS & TS	Positive (CT 28.65)	Positive (CT 29.67)	Positive (CT 34.18)	Positive (CT 36.38)
Lesion swab	Positive (CT 14.34)	Positive (CT 18.31)	Not tested	Not tested
Whole blood	Weakly Positive (CT 35.28)	Negative	Not tested	Not tested

NPS & TS: nasopharyngeal swab and throat swab. CT: cycle threshold.

Table 2. Results of environmental surface swabs for testing the mpox virus at the household of mpox cases in Bang Kruai District, Nonthaburi Province, 24 May 2023

Floor	Touchpoint	Result	CT-value
First	Entrance doorknob	Positive (9/12)	37.75
	Toilet doorknob		36.96
	Light switches		35.52
	Toilet flush and seat cover		36.51
	Refrigerator door handle		36.13
	Table and stools		36.13
	Kitchenware		38.14
	Water filter machine		35.88
	Electric appliance switches		36.61
	Drainpipe	Negative	NA
	Faucet		
Second	Entrance door handle	Positive (2/7)	38.60
	Toilet doorknob		32.40
	Banister	Negative	NA
	Toilet flush and seat cover		
	Drainpipe		
	Shower		
	Light switch		
	Doorknob		
Third	Patient's room doorknob	Positive (7/8)	37.07
	Toilet doorknob		38.28
	Toilet flush and seat cover		35.80
	Drainpipe cover		38.16
	Light switches		34.38
	Electric appliance switches		33.75
	Banister		39.26
	Shower	Negative	NA

CT: cycle threshold. NA: not available.

Situation of Mpox in Thailand

As of 31 Jul 2023, there were 180 mpox confirmed cases (0.27 per 100,000 population). No death occurred. The median age of the cases was 35 years (interquartile range 29–40). About four-fifths of the cases (143/180) were identified as LGBTQ+ and approximately half (83/180) were HIV positive. Initial cases comprised individuals identifying as being male or female in approximately equal proportions. In March 2023 the number of LGBTQ+ cases started to increase. The number of mpox cases in Thailand reached its peak in mid-June 2023 (Figure 2). Of these 180 cases, 60% (108/180) provided a history of risk behaviors; 37% had multiple sex partners, and 33% had sexual intercourse with strangers (Figure 3). We did not find substantial evidence of mpox cases acquiring the disease within the household through non-sexual routes. The five most common mpox symptoms observed in Thailand were rash (97%), fever (73%), myalgia (44%), lymphadenopathy (42%), and sore throat (34%). Note that, we did not find any prior confirmed mpox cases without fever and rash simultaneously before this event. Mpox spanned 17 provinces, primarily concentrated within the Bangkok Metropolitan Area (Figure 4). The provinces with the five highest incidences were Bangkok, Phuket, Nonthaburi, Chonburi, and Nakhon Nayok (Table 3).

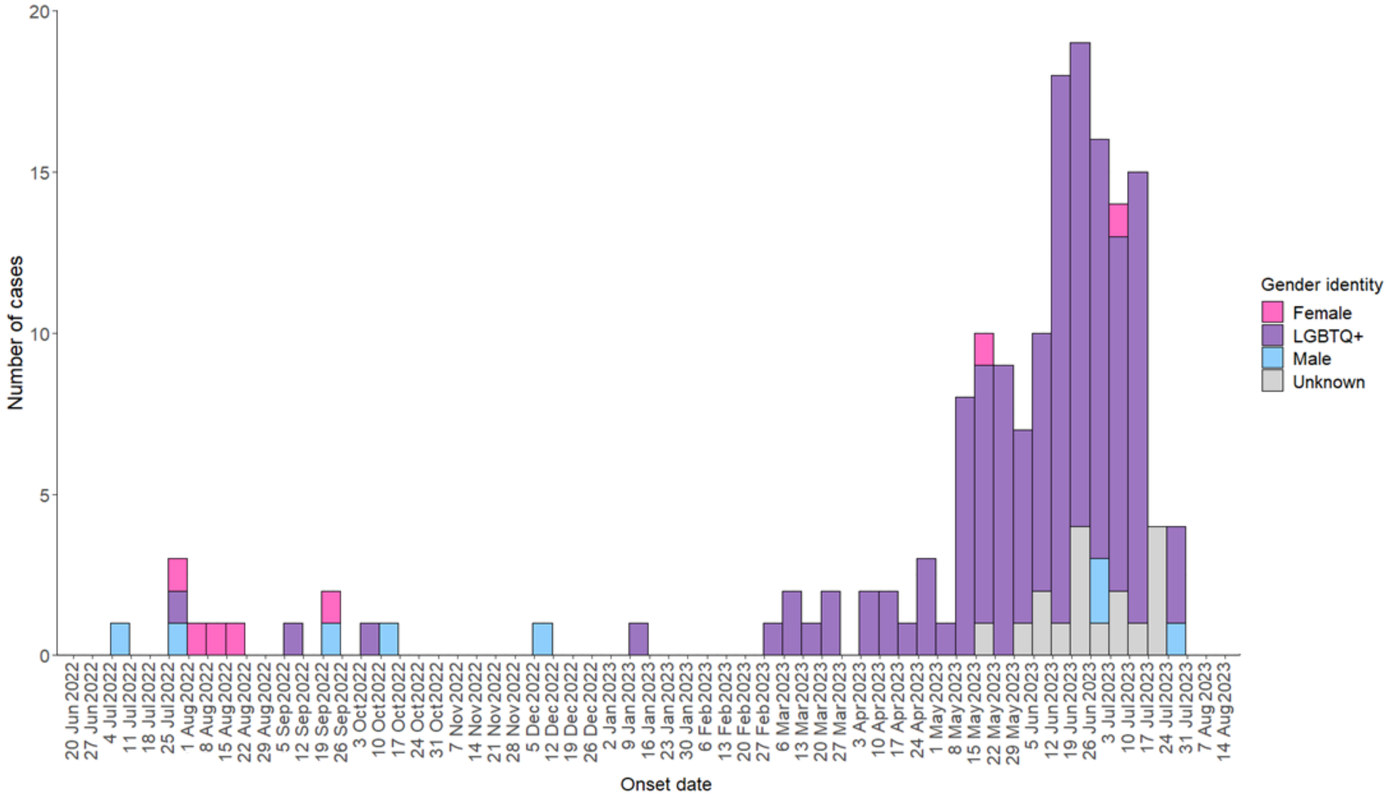

Figure 2. Number of weekly mpox cases in Thailand, 18 Jul 2022 to 31 Jul 2023, by gender identity (n=180)

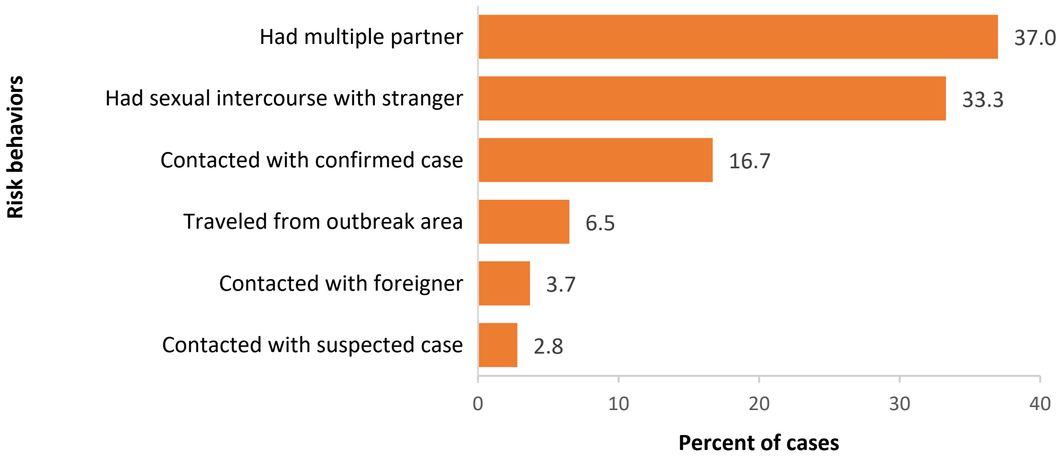

Figure 3. Risk behaviors among mpox cases (with availability of the information) in Thailand, 18 Jul 2022 to 31 Jul 2023 (n=108)

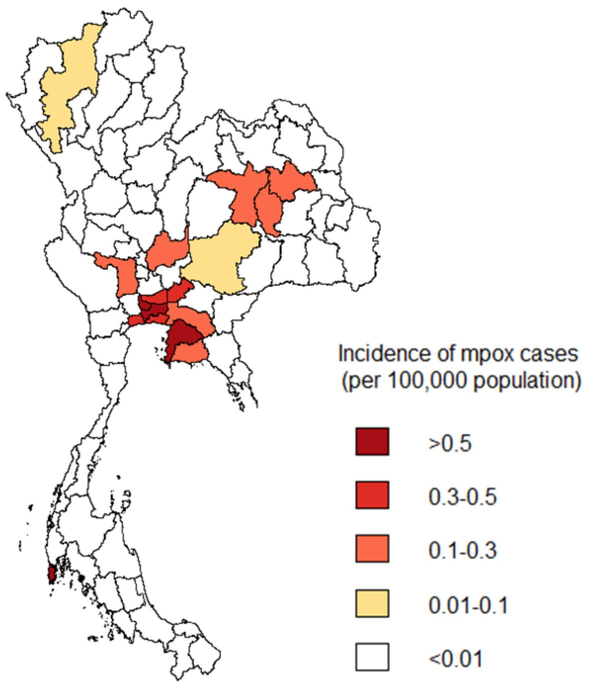

Figure 4. Incidence of mpox cases per 100,000 population in Thailand, 18 Jul 2022 to 31 Jul 2023, by province (n=180)

Table 3. Incidence of mpox cases per 100,000 population in Thailand, 18 Jul 2022 to 31 Jul 2023, by province (n=180)

Province	Number of cases	Incidence (per 100,000 population)
Bangkok	123	1.48
Phuket	7	1.33
Nonthaburi	13	0.97
Chon Buri	9	0.58
Nakhon Nayok	1	0.41
Samut Prakan	7	0.38
Samut Sakhon	3	0.34
Pathum Thani	4	0.30
Lop Buri	2	0.26
Kalasin	2	0.24
Maha Sarakham	2	0.24
Chachoengsao	1	0.14
Rayong	1	0.12
Suphan Buri	1	0.12
Khon Kaen	2	0.11
Chiang Mai	1	0.06
Nakhon Ratchasima	1	0.04

Action Taken

We provided health education on personal hygiene and environmental disinfection methods to all cases and household contacts. We monitored two household contacts for 21 days (until 10 Jun) from their last contact date with the cases. We conducted contact tracing and communicated the outbreak details to the organizer of the shaving ceremony. We urged him to disseminate outbreak information to the participants and encourage immediate reporting of any mpox symptoms.

Discussion

We confirmed the diagnosis of all cases through MPVX real-time PCR. The mpox outbreak was confirmed due to two reasons. First, this event was the first documented mpox cluster within Bang Kruai District. Second, a strong epidemiological linkage within a household was identified.

Case 3, had a history of close contact with her son's rashes and droplets. This observation confirmed the high plausibility of non-sexual transmission within a household beyond sexual transmission.[10] Our situational analysis did not reveal any evidence of this route of transmission within households before this investigation. So, this investigation was the first to document non-sexual transmission of mpox in Thailand, mirroring a similar occurrence in a hospital setting in the Republic of Congo.[11] Thailand risk communication should address the plausibility of non-sexual transmission. Even though, the likelihood of non-sexual transmission is low (4.6%).[2,12-14]

Case 3 exhibited no skin rash, consistent with our findings from the situation analysis, which indicated that approximately 3% of Thai-mpox cases had no rash. This aligns with a meta-analysis indicating that 5% of mpox cases manifest without rash.[2,15] Moreover, since case 3 did not exhibit any fever and rash, she does not meet the suspected case definition outlined in the mpox disease surveillance and investigation guidelines of the DDC.[16] And none of the previous mpox cases from our situation analysis lacked both rash and fever simultaneously. This might result in her not being tested, potentially increasing the risk of disease transmission to others. This observation emphasizes the importance for physicians to be vigilant towards nonspecific symptoms of suspected mpox patients and underscores the need for confirmed diagnoses by laboratory test. Additionally, the DDC should take this into account when revising the mpox disease surveillance and investigation guidelines regarding the criteria for diagnostic testing to ensure adequate sensitivity of case detection.

A significant portion (18/27) of the surface swabs from the household were positive for MPXV. Remarkably, these surfaces were cleaned with 70%-ethanol following the confirmation of mpox of case 2 who, together with the other affected cases, was isolated from the two non-affected family members. Despite these immediate measures, the persistence of MPXV on surfaces within the household was noteworthy.

However, all positive samples exhibited CT values that exceeded 30, which suggests that the virus was non-viable.[17] This aligns with previous studies indicating the ability of 70%-ethanol to mitigate the viability of the MPXV.[17,19–21] Thus, the fomite transmission in this household was unlikely during the investigation period. Hence, it is more likely that case 3 acquired the infection through direct contact with her son rather than through fomite transmission. Despite the low fomite transmissibility, case isolation is still recommended.[18] Additionally, the MPXV non-viability may not solely be attributed to the 70%-ethanol effect alone. The timing of our investigation, conducted two weeks after the onset of the first case, could have also influenced this finding.

Limitations

Limitations remain in this study. First, the cases appeared to be hesitant to reveal their exposure history, which led to difficulty in contact tracing. We tried to contact the shaving ceremony participants. However, we neither acquired full cooperation from the organizer nor received a full participant roster. This mirrors other mpox occurrences within LGBTQ+ communities and may be related to stigmatization.[22,23] Second, fomite transmission risk assessment relied on CT values obtained from specimens collected after the house was cleaned. So, caution must be taken when interpreting the fomite transmission risk. Third, the EBS contains unstructured data, leading to varying levels of detail provided by different reporters. Consequently, in our situation review, certain variables, such as gender identity were unavailable in some cases.

Recommendations

We recommend that direct contact with rash and droplet of mpox cases should be avoided. Risk communication in Thailand should address the plausibility of non-sexual transmission. Testing is recommended for symptomatic-contacts, even those presenting without rash. DDC should consider revising the mpox disease surveillance and investigation guideline to accommodate cases presenting without fever or rash concurrently. Moreover, it is crucial to promote rigorous hygiene and thorough environmental disinfection.

Conclusion

We confirmed the mpox outbreak within a household in Bang Kruai District. Disease transmission was observed through both sexual and non-sexual routes, emphasizing the importance of addressing the plausibility of non-sexual transmission in risk communication. Physicians should pay attention to nonspecific symptoms of mpox-contacts and confirm the diagnosis with laboratory tests. The mpox disease surveillance and investigation guideline should be revise to accommodate cases that present without fever or rash simultaneously. The environmental swabs revealed a large portion of specimens presenting with MPXV genetic, with CT values ≥30. This suggests a minimal risk of fomite transmission, potentially due to the effectiveness of 70%-ethanol.

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Investigation of Risk Factors for Lumpy Skin Disease and Prevention Practices in Dak Lak, Vietnam, 2021–2022

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Abstract

Lumpy skin disease is a transboundary animal disease primarily affecting cattle, and causing fever, anorexia, skin nodules, mastitis, swelling of peripheral lymph nodes, nasal discharge, watery eyes, and sometimes mortality. The disease was first detected in Vietnam in October 2020 and has spread to 55 out of 63 provinces with around 210,000 cattle and buffaloes infected. Dak Lak was one of the provinces seriously affected by the disease. A retrospective case-control study in three districts of the province was conducted to assess awareness of the disease among local livestock holders and to determine potential risk factors for disease transmission. A total of 276 holdings known to keep cattle or buffalo, including 138 cases (holdings that had at least one animal with clinical signs of the disease) and 138 controls (holdings with no clinically apparent infected animal), were investigated. The study revealed gaps in knowledge and practices among livestock holders on disease control with median scores of 8/20 for knowledge and 5/9 for practices. Vaccination against lumpy skin disease was the only risk factor significantly associated with disease transmission (adjusted odds ratio 0.39, 95% confidence interval 0.21–0.72). We recommend raising the awareness of livestock owners about the risk factors of lumpy skin disease and the importance of vaccination for better prevention and control of outbreaks.

Keywords: lumpy skin disease, case-control studies, vaccination, Vietnam

Introduction

Lumpy skin disease (LSD) is a transboundary infectious disease, mainly affecting cattle (breeds of *Bos taurus* and *Bos indicus*) and water buffalo (*Bubalus bubalis*). It is caused by a poxvirus of the genus *Capripoxvirus*, the family *Poxviridae.*[1] The lumpy skin disease virus (LSDV) is a double-stranded DNA virus having only one serotype but a close antigenic relationship to sheep pox and goat pox viruses.[2] According to the World Organisation for Animal Health, LSDV cannot infect humans, but some wildlife species such as springbok *(Antidorcas marsupialis),* eland *(Taurotragus oryx),* oryx *(Oryx gazelle),* Arabian oryx *(Oryx leucoryx),* guar *(Bos gaurus)*, mainland serow *(Capricornis sumtraensis)* and banteng *(Bos javanicus)* may be susceptible.[3] The disease is characterized by fever, anorexia, skin nodules, mastitis, swelling of peripheral lymph nodes, nasal discharge and watery eyes.[1,4] LSD can cause economic losses through reduced milk yield, damaged hides, low growth rate, costly treatment and control measures, and restricted animal trade. The morbidity rates exceed 85% while mortality rates are low (<3%).[5] The major route of transmission of the virus is by blood-sucking arthropod vectors such as mosquitoes, flies, and ticks or through injection with hypodermic needles contaminated with the virus.[6–9] Vaccination plays a crucial role in reducing the spread of disease in endemic areas; most commercially available vaccines are live-attenuated vaccines produced from the LSDV Neethling strain.[10]

The first outbreak of LSD was detected in Zambia in 1929. By the 1980s, the disease had spread across Africa.[11] In 1989, the disease was first reported outside

Africa in Israel.[12] In 2016, LSD spread into Russia and several South-East European countries.[13] LSD was initially observed in Bangladesh in 2019, followed by more than 20 other Asian countries.[14] According to the World Organisation for Animal Health, by December 2023 the disease was present in 85 countries and territories.

The Department of Animal Health of Vietnam reported the first LSD incursion in the country in October 2020. The disease quickly spread to 55 out of 63 provinces and affected more than 210,000 cattle and buffaloes. As of December 2022, 29,600 animals have been culled.

The first LSD outbreak in Dak Lak Province occurred in June 2021. The disease rapidly spread to all 15 districts in the province with 2,356 cattle and three buffaloes infected. The province culled 829 cattle and two buffaloes, and used 198,067 doses of LSD vaccine (Lumpyvac® attenuated live vaccine; Adiyaman, Turkey) to control the disease.

The objectives of this study are to assess the knowledge and control practices of livestock holders and to identify risk factors of LSD in holdings keeping cattle and/or buffalo in Dak Lak Province.

Materials and Methods

Study Design and Location

This case-control study was conducted in December 2022. Dataset collected was also used to assess LSD knowledge, control practices, and biosecurity measures among livestock holders.

The study was conducted in Krong Bong, Cu M'gar and Ea Sup Districts of Dak Lak Province (Figure 1). Dak Lak has an area of 1,307 km^2 and is in the central highlands of Vietnam with 15 districts and 184 communes (a subdistrict unit). There are 47 ethnic groups in Dak Lak, Kinh people (70%) constituting the majority. Other ethnic groups include Ede, Gia Rai, M'nong, Thai, Tay, and Nung. In 2021, there were approximately 1.9 million residents, 249,500 cattle and 29,200 buffaloes, according to Vietnam General Statistics Office.

Selection of Case and Control Holdings

A list of 13,399 livestock holdings including 283 holdings affected by LSD in the three study districts of Cu M'gar, Ea Sup and Krong Bong from June 2021 to October 2022 was obtained from the Dak Lak Sub-Department of Livestock Production and Animal Health. We selected 276 holdings keeping at least one cattle or buffalo (138 cases and 138 controls) which provided 80% power for detection of an odds ratio (OR) of 2.0 or greater for risk factors that were present in 30% of the control holdings when analyzing the data by unconditional logistic regression.

One LSD outbreak in each commune was confirmed by a real-time polymerase chain reaction assay. Cases were randomly selected from the available pool of holdings having at least one animal demonstrating typical nodular skin lesions of LSD in each district from June 2021 to October 2022. A control holding without clinical signs of LSD was also randomly selected from the same village that the case holding was recruited. In each holding, the livestock owner or the person taking care of the livestock was interviewed using a structured questionnaire form.

Questionnaire

A questionnaire was developed in Vietnamese to collect information about risk factors potentially associated with the occurrence of LSD and to describe the sociodemographic characteristics of livestock holdings in the study area. Data collected were also used to obtain information about LSD knowledge, control practices, and biosecurity measures to protect livestock owners.

The questionnaire consisted of four major sections: holding demographics, information on livestock keeping, knowledge about LSD, and control practices. Additional data on LSD features in each case holding was collected in a separate form. The questionnaire was administered by trained personnel through face-to-face interviews with livestock owners and a local communal animal health worker whenever possible. The questionnaire was pre-tested in five cattle holdings in Buon Ma Thuot City to ensure question clarity.

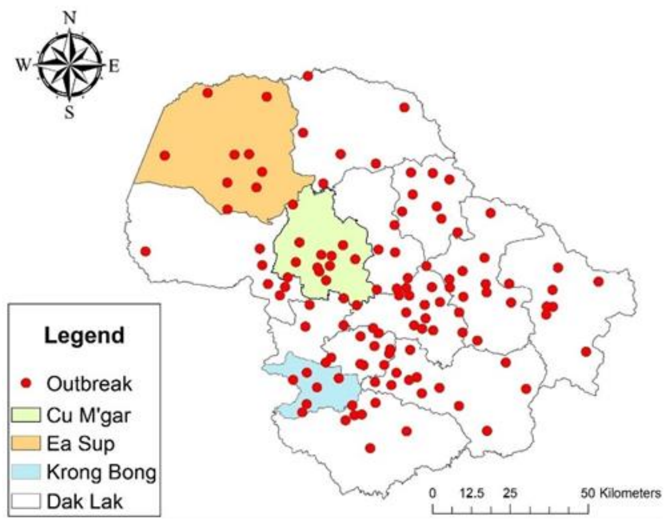

Figure 1. Lumpy skin disease outbreaks in Dak Lak Province, Vietnam, and the three study sites, June 2021–October 2022

Statistical Analysis

Data obtained from the questionnaires were recorded in KoboToolbox (Kobo, Inc.; Cambridge, MA, USA) then exported as a spreadsheet for subsequent analysis using STATA/SE 15.0 (Stata Corp LLC, College Station, TX, USA).

Spearman's rank correlation analysis was used to determine the relationship between knowledge and practices. The Mann–Whitney U test, Kruskal–Wallis test, and negative binomial regression were used to identify associations between demographic factors and knowledge and practice scores. Variables with a *p*-value less than 0.2 in univariable analysis were included in the mixed-effects negative binomial regression using menbreg in STATA/SE 15.0 with the district as a random effect.

For holding's LSD infection risk factor identification, the association of independent variables and outcomes was evaluated using a chi-square test in univariable analysis. Variables with a *p*-value lower than 0.25 and absolute correlation coefficient value (r-value) below 0.7 were included in the initial multivariable logistic regression model.[15,16] Variables changing more than 25% of coefficients of other variables were classified as confounding factors and included in the model if the affected variables were significant. Mixed-effects multivariable logistic regression models were built using meqrlogit in STATA/SE 15.0 with the village as a random effect. A stepwise backward manual elimination technique was used to identify significant predictors in the model. Factors with a *p*-value less than 0.05 were considered statistically significant.

Ethics

The study was approved by the Ethical Committee of the Institute of Malariology, Parasitology, and Entomology Quy Nhon–the Ministry of Health of Vietnam (No 1113/VSR-LSDT, 29 Nov 2022). The purpose of this study was explained to livestock holders by the investigators, and participants were only included in the study after their informed consent was given.

Results

Livestock Holder Demographics

Key demographic features of the survey respondents are summarized in Table 1. The majority of respondents were male (71.4%) and more than 79% were aged 31 to 60 years. Around two-thirds had graduated secondary school or higher. Most participants were involved in farming as their primary job with 31.2% describing themselves as "livestock holder". Over half of respondents belonged to the Kinh ethnic group (55.8%) followed by Ede (22.1%), and Gia Rai (2.2%). Most of the holdings (62%) kept less than 10 cattle and/or buffaloes.

Table 1. Social-demographic features of livestock holders

Variable	n (%)
Gender	
Male	197 (71.4)
Female	79 (28.6)
Age (years)	
18–30	14 (5.1)
31–45	79 (28.6)
46–60	140 (50.7)
>60	43 (15.6)
Education	
None	13 (4.7)
Primary school	64 (23.2)
Secondary school	103 (37.3)
High school	78 (28.3)
College/university	18 (6.5)
Occupation	
Livestock holder	86 (31.2)
Cultivation worker	124 (44.9)
Officer (local government staff)	14 (5.1)
Others	52 (18.8)
Ethnic group	
Kinh	154 (55.8)
Ede	61 (22.1)
Gia Rai	6 (2.2)
Other	55 (19.9)
Herd size (heads of cattle/buffalo)	
<10	171 (62.0)
10–29	80 (29.0)
30–59	20 (7.2)
≥60	5 (1.8)

LSD Awareness and Prevention among Livestock Holders

Knowledge among livestock holders about LSD is summarized in Table 2. In both cases and controls, a majority of respondents (82.6% and 79.7%, respectively) demonstrated awareness of LSD and its associated clinical signs including skin nodules, high fever, anorexia. However, a significantly higher proportion of respondents from cases did not know the causative agent of LSD compared to control (59.4% versus (vs) 47.1%, *p* 0.04). Both cases and controls exhibited knowledge of susceptible species, with similar awareness levels regarding cattle (73.9%) and buffalo (52.2% cases, 57.2% controls). Nevertheless, 22.5% of cases and 23.9% of controls could not identify any susceptible species. While the majority of respondents understood that LSD cannot be transmitted to humans (81.9% cases, 84.0% controls), a considerable proportion lacked knowledge regarding transmission routes (57.2% cases, 46.4% controls) and how infected cattle shed the virus (72.5% cases, 64.5% controls). To prevent LSD, vaccination was considered crucial by both cases and controls (75.4% vs 76.8%), followed by vector control (23.2% vs 31.9%), and implementing good biosecurity practices (5.1% vs 13.8%).

Table 2. Knowledge of livestock holders about lumpy skin disease in infected versus non-infected holdings

	Cases n (%)	Controls n (%)	*P*-value
Awareness of LSD			
Yes	114 (82.6)	110 (79.7)	0.538
No	24 (17.4)	28 (20.3)	
Clinical signs of LSD			
Subcutaneous hard nodule round shape, diameter 0.5–5 cm	98 (71.0)	96 (69.6)	0.792
High fever	62 (44.9)	57 (41.3)	0.543
Anorexia	57 (41.3)	40 (29.0)	0.031
Depression and reluctance to move	43 (31.2)	36 (26.1)	0.351
Enlarged anterior & inferior parotid lymph nodes	33 (23.9)	30 (21.7)	0.667
Rhinitis	25 (18.1)	25 (18.1)	1.000
Edema under the skin of the waist, neck and genitals	27 (19.6)	22 (15.9)	0.431
Conjunctivitis	17 (12.3)	18 (13.0)	0.856
Excessive salivation	13 (9.4)	18 (13.0)	0.339
Lactation reduction	13 (9.4)	9 (6.5)	0.373
Don't know any	24 (17.4)	31 (22.5)	0.291
The causative agent of LSD			
Virus	47 (34.1)	65 (47.1)	0.027
Parasite	8 (5.8)	6 (4.3)	0.583
Bacteria	2 (1.4)	3 (2.2)	0.651
Don't know	82 (59.4)	65 (47.1)	0.040
Domestic animal species can get LSD			
Cattle	102 (73.9)	102 (73.9)	0.918
Buffalo	72 (52.2)	79 (57.2)	0.434
Pig	3 (2.2)	3 (2.2)	0.992
Goat/sheep	2 (1.4)	2 (1.4)	0.994
Don't know	31 (22.5)	33 (23.9)	0.801
The infected animal can transmit the disease to humans			
Yes	25 (18.1)	22 (16.0)	0.631
No	113 (81.9)	116 (84.0)	
LSD vaccine availability for cattle & buffalo			
Yes	113 (81.9)	112 (81.2)	0.877
No	25 (18.1)	26 (18.8)	
List some routes of the disease transmission			
Through arthropod vectors such as flies, mosquitoes, ticks	52 (37.7)	67 (48.6)	0.068
Through nasal secretions, feces, urine, milk, meat	21 (15.2)	35 (25.4)	0.035
Through semen	11 (8.0)	20 (14.5)	0.084
Contaminated water	4 (2.9)	10 (7.2)	0.094
Don't know	79 (57.2)	64 (46.4)	0.071
How can an infected animal shed the virus?			
Scabs	25 (18.1)	37 (26.8)	0.094
Sperm	18 (13.0)	29 (21.0)	0.086
Nasal discharge	21 (15.2)	26 (18.8)	0.455
Milk	9 (6.5)	16 (11.6)	0.158
Urine	8 (5.8)	8 (5.8)	0.976
Don't know	100 (72.5)	89 (64.5)	0.105
What do you do to prevent the disease in your farm?			
Vaccinate the animal	104 (75.4)	106 (76.8)	0.777
Control arthropod vectors	32 (23.2)	44 (31.9)	0.105
Apply biosecurity in the farm	7 (5.1)	19 (13.8)	0.012
Don't know	30 (21.7)	31 (22.5)	0.885

Controls demonstrated a higher percentage of routine cleaning their livestock premises compared to case holdings (80.1% vs 71.0%), with statistical significance (p 0.033). As shown in Table 3, among controls, 43.5% disinfected their premises monthly, and (18.1%) disinfected weekly, whereas among cases, 37.0% disinfected monthly and 13.0% disinfected weekly. Regarding vector control, 48.6% of controls used insecticides significantly more than the case group (p 0.005). Moreover, most of control holdings (83.3%) vaccinated their animals against LSD more than case holdings (64.5%), with statistical significance (p <0.001). Participation in LSD surveillance programs over last two years was limited, with only 5.1% of cases, and 7.2% of controls involved.

Table 3. Practices of livestock holders for prevention of lumpy skin disease in infected versus non-infected holdings

	Cases n (%)	Controls n (%)	*P*-value
Prohibit visitor(s) coming into the farm			
Yes	34 (24.6)	48 (34.8)	0.065
No	104 (75.4)	90 (65.2)	
Clean the premise regularly	98 (71.0)	123 (89.1)	0.033
Daily basis	44 (31.9)	38 (27.5)	
Every 2–3 times/week	7 (5.1)	29 (21.0)	
Weekly	29 (21.0)	29 (21.0)	
Monthly	16 (11.6)	16 (11.6)	
Disinfect of the premises regularly	76 (55.1)	89 (64.5)	0.111
Daily basis	3 (2.2)	2 (1.4)	
Every 2–3 times/week	4 (2.9)	2 (1.4)	
Weekly	18 (13.0)	25 (18.1)	
Monthly	51 (37.0)	60 (43.5)	
Use of insecticides to control vectors	44 (31.9)	67 (48.6)	0.005
Monthly	5 (3.6)	5 (3.6)	
Quarterly	10 (7.2)	21 (15.2)	
Every 6 months	12 (8.7)	20 (14.5)	
Once per year	7 (5.1)	5 (3.6)	
Waste treatment at the farm	62 (44.9)	78 (56.5)	0.054
Biogas incubation	6 (4.3)	8 (5.8)	
Bio-heat incubation	34 (24.6)	52 (37.7)	
Probiotics	13 (9.4)	14 (10.1)	
LSD vaccination for the animal(s)	89 (64.5)	115 (83.3)	<0.001
Daily monitoring health status of livestock	118 (85.5)	120 (87.0)	0.727
Recording livestock entering/exiting the farm	27 (19.6)	43 (31.2)	0.026
Joined LSD surveillance program for last two years	7 (5.1)	10 (7.2)	0.451

Table 4 presents common practices in LSD infected holdings. Many (83.8%) of the livestock owners treated sick animals by themselves, and 64.6% reported the outbreaks to local veterinarians or authorities. More than half (56.2%) continued raising sick and healthy livestock together on the same premises, while 40% allowed sick animals to graze in community areas.

Table 4. Practices of livestock owners of LSD infected farms

Number of infected farms provided information (n=130)	Yes	%
The cattle/buffalo bitten by flies, mosquitoes, ticks within two weeks of symptoms onset	89	68.5
During one month before the LSD outbreak, there was close contact of animal(s) with infected animals from other farms	55	42.3
When your animal was suspected of having LSD		
Gave a treatment by yourself	109	83.8
Reported to local authorities/local vet	84	64.6
Sold sick animal(s)	15	11.5
Slaughtered	6	4.6
Did nothing	13	10.0
When your animals(s) got sick, did you quarantine them?		
Continued to raise sick animal(s) with healthy animals	73	56.2
Allowed sick animal(s) in the common grazing area	52	40.0
Isolated the infected animal(s) from healthy animals	42	32.3

Associations between Knowledge and Practices and Demographics

Table 5 presents associations between demographic factors and LSD knowledge and practices of livestock holders. The median (interquartile range) scores for knowledge and practices were 8±5 (range from 0–20) and 5±3 (ranging from 0–9), respectively. Correlation analysis showed a moderate positive correlation between knowledge and practices (Spearman's rho 0.45, *p* <0.001). Older age, Kinh ethnic group, higher education, and larger herd size were significantly associated with higher knowledge scores while district location and Ede ethnic group were significantly associated with practices (*p* <0.05). The Kinh ethnic group had both knowledge and practice scores significantly higher than the Ede ethnic group, but not for the practice score compared to the Gia Rai ethnic group. Importantly, those aged above 31 years had significantly higher knowledge scores than the younger respondents, but practice scores were not significantly different. In addition, those who graduated from a primary school or higher levels had significantly higher knowledge scores than those without any education, but their practice scores were not significantly different. The owners of holdings having more than 10 animals had significantly higher knowledge scores compared to those with less than 10 animals. However, the practice score was not significantly different between holdings containing different herd sizes. Gender and occupation were not significantly associated with knowledge and practices in the multivariable mixed-effects negative binomial regression analysis.

Table 5. Comparison of knowledge and practice scores with respect to demographics characteristics of study participants (n=275)

Variable	Knowledge			Practice		
	Median ± IQR	*P*-value (Univariable)	*P*-value (Multivariable)	Median ± IQR	*P*-value (Univariable)	*P*-value (Multivariable)
Overall score	**8 ± 5**			**5 ± 3**		
Gender*		**0.416**			**0.628**	
Male	8 ± 5		-	5 ± 3		
Female	8 ± 6			5 ± 3		
District†		**<0.001**	**NA**		**<0.001**	**NA**
Cu M'gar	7 ± 4			5 ± 2		
Ea Sup	10 ± 5			5 ± 2		
Krong Bong	6 ± 1			2 ± 1		
Age group (years) †		**0.035**			**0.099**	
18–30	1 ± 8		Ref.	5 ± 5		Ref.
31–45	8 ± 6		0.005	4 ± 3		0.372
46–60	8 ± 5		0.004	5 ± 3		0.997
>60	7 ± 4		0.003	4 ± 4		0.566
Ethnicity†		**<0.001**			**<0.001**	
Kinh	9 ± 5		Ref.	5 ± 2		Ref.
Ede	6 ± 6		<0.001	2 ± 2		<0.001
Gia Rai	1.5 ± 7		0.008	4 ± 2		0.082
Other	9 ± 10		0.047	5 ± 2		0.362
Level of education†		**<0.001**			**0.018**	
None	1 ± 6		Ref.	4 ± 3		Ref.
Primary school	7.5 ± 6		0.031	5 ± 3.5		0.883
Secondary	8 ± 5		0.006	4 ± 4		0.824
High school	9 ± 5		0.006	5 ± 3		0.531
College/ University	12 ± 9		0.001	5.5 ± 5		0.212
Occupation†		**0.037**			**<0.001**	
Livestock holder	9 ± 7		Ref.	5.5 ± 2		Ref.
Cultivator	7 ± 4		0.800	3.5 ± 3		0.092
Officer	7 ± 6		0.330	5 ± 3		0.304
Other	9 ± 10		0.359	5 ± 3		0.515
Herd size (head)		**<0.001**			**<0.001**	
<10	7 ± 5		Ref.	4 ± 4		Ref.
10–29	10 ± 5		<0.001	5.5 ± 2		0.065
30–59	12 ± 5.5		0.005	6 ± 3		0.124
≥60	17 ± 4		0.019	9 ± 2		0.051

**Mann–Whitney U test. †Kruskal–Wallis test. Ref.: reference. IQR: interquartile range. NA: not applicable.*

Univariable Analysis of Risk Factors

At the holding level, grazing practice, distance from the holding to grazing area, feeding animals mixed forage, cleaning practices, using insecticides, vaccination against LSD and recording livestock entering/exiting the holding were significantly associated with the occurrence of disease by univariable analysis (Table 6).

The odds of getting LSD among free grazing animals during the day time grazing was significantly higher than among fenced animals (OR 1.78, *p* 0.026). A significantly higher risk of LSD infection was seen in holdings located less than 100 meters from the grazing pasture compared to those more than 200 meters (OR 2.10, *p* 0.021). In contrast, a lower risk of getting the disease was seen in holdings where animals were fed with mixed forage (OR 0.43, *p* 0.026). A higher risk of getting LSD was seen at holdings not cleaning livestock premises frequently (OR 1.80, *p* 0.044), not using insecticides to control vectors (OR 2.02, *p* 0.005), having no LSD vaccination (OR 2.75, *p* <0.001), and holdings that did not record livestock entering/ exiting (OR 1.86, *p* 0.028).

There were no significant associations for district location, herd size, distance from the road or live animal market or another nearby farm, type of drinking water for livestock, breeding practice, whether the origin of the livestock was known or not, and waste treatment practice.

Table 6. Results from univariable analysis of factors associated with LSD infection

Exposure variable	Holdings surveyed	Holdings infected	OR (95% CI)	*P*-value
District				
Cu M'gar	81	42	Ref.	-
Ea Sup	140	68	0.88 (0.51–1.52)	0.638
Krong Bong	55	28	0.96 (0.48–1.91)	0.914
Herd size (head)				
<10	171	83	Ref.	-
10–29	80	44	1.29 (0.76–2.21)	0.340
30–59	20	9	0.87 (0.34–2.20)	0.765
≥60	5	2	0.71 (0.11–4.34)	0.708
Grazing practice				
Fenced	111	47	Ref.	-
Free in day time only	134	76	1.78 (1.07–2.97)	0.026
Free whole day	31	15	1.28 (0.57–2.84)	0.549
Distance to traffic road (meters)				
<100	115	59	Ref.	-
100–200	17	7	0.66 (0.24–1.87)	0.438
>200	142	70	0.92 (0.56–1.51)	0.749
Distance to live animal market (meters)				
<100	2	2	NA	-
100–200	10	6	1.49 (0.41–5.39)	0.545
>200	259	130	Ref.	-
Distance to lake or, pond (meters)				
<100	35	18	Ref.	
100–200	29	21	2.48 (0.87-7.08)	0.090
>200	197	90	0.79 (0.39-1.63)	0.531
Distance to closest farm (meters)				
<100	131	65	Ref.	
100–200	21	14	2.03 (0.77–5.36)	0.152
>200	106	52	0.98 (0.59–1.63)	0.931
Distance to grazing pasture (meters)				
<100	53	34	2.10 (1.12–3.95)	0.021
100–200	25	15	1.76 (0.75–4.12)	0.192
>200	187	86	Ref.	-
Distance to waste treatment area (meters)				
<100	5	1	Ref.	-
100–200	5	2	2.67 (0.16–45.10)	0.497
>200	248	126	4.13 (0.46–37.50)	0.207
Feeding animal with fresh grass				
No	12	5	Ref.	-
Yes	257	132	1.48 (0.46–4.78)	0.514

Table 6. Results from univariable analysis of factors associated with LSD infection (cont.)

Exposure variable	Holdings surveyed	Holdings infected	OR (95% CI)	*P*-value
Feeding animal with dry grass or straw				
No	29	18	Ref.	-
Yes	240	119	0.60 (0.27–1.33)	0.207
Feeding animal with silage feed				
No	242	126	Ref.	-
Yes	27	11	0.63 (0.28–1.42)	0.267
Feeding animal with mixed forage				
No	233	125	Ref.	-
Yes	36	12	0.43 (0.21–0.91)	0.026
Drinking water for livestock				
Drilling well	158	70	Ref.	-
Tap water	5	3	1.89 (0.31-11.60)	0.494
Pond/lake water	105	59	1.61 (0.98-2.65)	0.060
Breeding practice				
Artificial insemination	57	32	Ref.	-
From bull(s) in the holding	44	23	0.86 (0.39–1.88)	0.699
From bull(s) for hiring business	44	18	0.54 (0.24–1.20)	0.131
From bull(s) of another farm	2	1	0.78 (0.05–13.10)	0.864
From bull(s) in public grazing area	107	53	0.77 (0.40–1.46)	0.420
Origin of livestock breeds				
Known	123	62	Ref.	
Unknown	153	76	0.97 (0.60–1.56)	0.904
Quarantine area for new purchased cattle/buffalo				
No	210	112	Ref.	-
Yes	59	25	0.64 (0.36–1.15)	0.138
Floor type				
Cement	211	101	Ref.	-
Soil	63	36	1.45 (0.82–2.56)	0.198
Prohibiting visitor				
No	194	104	Ref.	-
Yes	82	34	0.61 (0.36–1.03)	0.066
Frequent cleaning				
No	64	39	1.80 (1.02–3.18)	0.044
Yes	211	98	Ref.	
Frequent disinfection				
No	111	62	Ref.	-
Yes	165	76	0.67 (0.42–1.09)	0.111
Using insecticides to control vectors				
No	165	94	2.02 (1.24–3.29)	0.005
Yes	111	44	Ref.	-
Waste treatment				
No	136	76	1.59 (0.99–2.56)	0.055
Yes	140	62	Ref.	
LSD vaccination				
No	72	49	2.75 (1.56–4.85)	<0.001
Yes	204	89	Ref.	-
Daily monitoring health status				
No	38	20	Ref.	-
Yes	238	118	0.88 (0.45–1.76)	0.727
Recording livestock entering/ exiting				
No	206	111	1.86 (1.07–3.24)	0.028
Yes	70	27	Ref.	-

LSD: lumpy skin disease. OR: odds ratio. CI: confidence interval. Ref.: reference. NA: not available.

Multivariable Analysis

Results of the multivariable analysis are shown in Table 7. Vaccination against LSD could significantly reduce risk of disease occurrence (adjusted OR 0.39, 95% confidence interval 0.21–0.72).

Table 7. Multivariable analysis of risk factors

Exposure variable*	Adjusted OR	95% CI	*P*-value
Distance to grazing pasture (meters)			
<100	Ref.		
100–200	1.13	0.41–3.13	0.813
>200	0.52	0.27–1.01	0.055
Using insecticides to control vectors			
Yes	0.61	0.36–1.04	0.070
LSD vaccination			
Yes	0.39	0.21–0.72	0.003
Recording livestock entering/ exiting			
Yes	0.60	0.33–1.10	0.098

*LSD: lumpy skin disease. Ref.: reference. OR: odds ratio. CI: confidence interval. *The final model includes five variables of "Distance from holding to grazing pasture", "Using insecticides to control vectors", "LSD vaccination", "Recording livestock entering/exiting holding" and "village".*

Discussion

LSD is an emerging disease in Southeast Asia and the region has become endemic.[7,18] Therefore, more research on LSD in the region is required.[18] Previous studies have recommended some preventive measures against LSD spreading such as restriction of livestock movement, vector control, culling infected animals and vaccination.[1,10,19] However, knowledge, practices and engagement of livestock holders would play an important role in the success of an animal disease control programme.

Our study identified gaps in LSD knowledge in livestock holders with the median scores of 8/20 for knowledge and 5/9 for control practices. We also found that livestock holders with higher education and those older than 31 years were more knowledgeable about animal diseases. Older people likely gained more knowledge from their experience of livestock keeping for many years. In fact, the youth prefer jobs in big cities while the elderly attach their employment to rural settlements.[20] In our study, we found that the respondents from larger-scale farms had significantly higher knowledge scores, but practice scores were not significantly different. Normally, when the farmers invest more in their livestock production, they should have better understanding of farm management, biosecurity and disease preventive measures. However, they were not ready to respond to the outbreak of new diseases such as LSD. The Kinh ethnic group had higher knowledge and better practices compared to the other ethnic groups. The ethnic minority groups in Dak Lak each has their own distinct language and traditions. The impact of language barriers on the knowledge process has been previously documented.[21] Therefore, communication of information on LSD to different ethnic groups should be made in their own language. Improving the literacy of minority ethnic groups and increasing their awareness of emerging infectious diseases should also be taken into consideration.

Non-infected holdings showed better practices in terms of cleaning, controlling vectors, recording livestock movement in and out of their holding, and vaccination against LSD in this study. Generally, better biosecurity practices by livestock farmers could mitigate disease transmission. Our study results also indicated that day time free-grazing and being close to the grazing area were significant risk factors. This finding is consistent with a study in Ethiopia showing that LSD occurrence was significantly associated with communal grazing.[22] Free grazing could facilitate transmission of LSDV through arthropod vectors. A recent study in Thailand reported that 95% of their livestock farms had at least one vector responsible for the disease.[23] Large herd size (exceeding 10 animals) was identified as a factor associated with LSD outbreaks in Kenya, while a study in Kazakhstan concluded that small herd size was significant.[24,25] However, we did not find a significant association between herd size and disease occurrence. Other risk factors from previous studies including district location, and type of drinking water of the livestock were not significant in our study.[26,27]

Vaccination was the only significantly associated factor in our study. Vaccination campaigns have been recommended for the prevention of LSD in both endemic or newly affected areas.[10] The live attenuated homologous vaccine (Neethling strain) used in Dak Lak has demonstrated high efficacy to eradicate LSD in Southeastern Europe.[28]

There were some limitations of our study. First, we did not observe the practices of the farmers directly. Second, we did not include season, climate or veterinary supervision as potential risk factors due to a time limitation. Third, we could only measure the knowledge and practices of the respondents after the outbreak occurred in their households or communities. Finally, livestock in the control holdings were not tested to confirm the absence of LSDV infection. However, clinical observation to confirm the absence of disease could be sufficient considering the infectiousness of LSDV.

Conclusion

Knowledge of LSD among livestock holders in Dak Lak province was low. A communication campaign on LSD prevention is recommended for livestock holders of all herd sizes, targeting minority ethnic communities such as Gia Rai and Ede. Application of the languages of different ethnic communities, literacy improvement for vulnerable groups, and more investment in LSD training for minority ethnic people are potential long-term solutions. Vaccination campaigns are needed to significantly reduce the risk of LSD transmission.

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Data Availability

All datasets supporting our findings are available from the corresponding author on reasonable request.

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Conflicts of Interest

The authors declare that they have no conflicts of interests.

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The Grammar of Science: Chance and Magnitude

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Statistical Significance (SS) vs. Effect Size (ES)

Most researchers are quite happy when they get statistically significant result (say, *p*-value <0.05). But statistical significance (SS) may or may not reflect clinical or practical importance. Compared to the standard treatment, your new treatment may increase statistically significant cure rate for five percent, but—is it good enough to change the treatment? Your innovative counseling program may reduce depression score of the patients with statistically significant at 3.6 score, but—is it a high enough score change? When your study result shows statistically significant relationship between the exposure(s) and the outcome variables—does mean it mean the exposure(s) have a substantial, negligible, or trivial impact on the outcome?

SS does not always provide all information about the magnitude or the meaningfulness of the effect or the relationship between variables.[1] On the other hand, effect size (ES) is the statistics that is helpful in determining whether the effect is practically meaningful in real-world applications.[2] ES will indicate not only the likely direction of the effect but also the magnitude of the effect whether it is important enough to care about.[3] A large effect size may reflect the practical importance of the research finding while a small effect size indicates limited practical applications.[4]

ES reflects the magnitude of differences found whereas SS examines whether the findings are likely to be due to chance.[5] SS can be affected due to large or small sample size but ES is independent of the sample size.[1,4,6] The relationship may change when sample size changes; and, simply increasing sample size may allow for easier rejection of the null hypothesis.[1] With a large sample size, the probability of getting small *p*-value will increase even with a very faint effect.[7] Unlike SS (with varying *p*-value), ES can be used to quantitatively compare the results of studies done in a different setting.[6]

Types of ES

It is noteworthy that much of the work regarding ES measures was developed as part of the meta-analysis, initiated by statistician and psychologist Jacob Cohen.[6,7] ES is the effect indicating the relationship between the variables of interest and thus derived from the objective of the analysis and the statistical procedure used to capture the effect it attempts to measure. However, it should be noted that ES is nonetheless a new statistic but rather amplifying the concept of statistical power, the probability that a test of significance will detect a deviation from the null hypothesis, should such a deviation exist.[7,8] In comparison between groups, ES could be calculated from the statistical testing methods, typically including: t-test, ANOVA, or chi-square test. In assessing the relationship between variables, ES could be estimated from the types of correlation or regression used in data analysis. Some ES measures are the known statistics regarding the correlation or strength of association between the two variables such as R-square (R^2) in linear regression, odds ratio (OR) in logistic regression and relative risk (RR) in Poisson regression. Table 1 summarizes different types of ES from literature.[1,6,7,9–15]

Table 1. Types of effect sizes

Statistical procedures	Objectives	Types of ES	Sizes of ES		
			Small	Medium	Large
Comparison between groups					
t-test	Difference between means with equal or unequal SD	Cohen's *d*	0.2	0.5	0.8
	Difference between means with equal sample size	Hedges' *g*	0.2	0.5	0.8
	Difference between means, compared with control group (typically assumed equal SD)	Glass's Δ	0.2	0.5	0.8
ANOVA	Difference among means	Cohen's *f* (extended Cohen's *d*)	0.14	0.39	0.59
	Eta-square, measure of degree that a model explains the data.	η^2 (equivalent to R^2)	0.01	0.06	0.14
	Eta-square measure for two-way factorial design	Partial η^2	0.01	0.06	0.14
	Correct the biasedness of Eta square measure	ω^2	0.01	0.06	0.14
	One-way MANOVA	Multivariate η^2	0.01	0.06	0.14
Chi-square	2 x 2 contingency table	Phi	0.1	0.3	0.5
	r x c contingency table (based on degree of freedom (df))	Cramer's V	0.1 (df=1), 0.07 (df=2), 0.06 (df=3)	0.3 (df=1), 0.21 (df=2), 0.17 (df=3)	0.5 (df=1), 0.35(df=2), 0.29 (df=3)
	r x c contingency table	Cohen's ω^2	0.1	0.3	0.5
Strength of associations between variables					
Correlation	Between continuous variables (normal distribution)	Pearson's r	0.1	0.3	0.5
	Between continuous variables (non-parametric)	Spearman's r	0.1	0.3	0.5
	Between dichotomous variable and continuous variable	Point-biserial r	0.1	0.3	0.5
Linear regression	Measure of degree that an outcome explained by the independent variable	R-square (R^2)	0.01	0.09	0.25
Logistic regression	Odds of outcome in one group vs another	Odds ratio (OR)	1.5	3.5	9
Poisson regression	Risk/chance of getting outcome in one group vs another	Risk ratio (RR)	1.5	3.5	9

Definitions and Formula of Different ES

The definitions and formula of different ES are briefly described as follow:

Cohen's *d*

Cohen's *d* is defined as a standardized difference, [$d = (\mu_1 - \mu_2)/\sigma$], between the two sample means (μ_1 and μ_2) and the common (pooled) standard deviation of the two comparison groups (σ).

Hedges' *g*

Hedges' *g* is the same as Cohen's d, [$g = (\mu_1 - \mu_2)/\sigma$], with the common (pooled) standard deviation (σ) weighted by standard deviation of each comparison group.

Glass' Δ

Glass' Δ is the same as Cohen's d, [$\Delta = (\mu_1 - \mu_2)/\sigma$], with the standard deviation (σ) of the control group.

Cohen's *f*

Cohen's *f* is an extended version of Cohen's *d*, [f= sqrt {[$\Sigma_{j=1,p}$ ($\mu_j - \mu)^2$/p] /σ^2}], where p is the number of groups, the numerator is an average difference of group means (μ_j) from the grand mean (μ) and denominator represents the common standard deviation (σ).

Eta Square

Eta square (η^2) is the same as the usual R squared (R^2) which represent a measure of degree that a model explains by the data, [$\eta^2 = SS_{effect} / SS_{total}$], where SS_{effect} represents variation of data due to group effect (between groups) and SS_{total} is the overall variation of the data of the dependent variable. Eta square can be converted into Cohen's *f* and vice versa, [f = sqrt ($\eta^2 / (1 - \eta^2)$)] or [$\eta^2 = f^2 / (1 + f^2)$].

Partial Eta Square

Partial eta square (η_p^2) is an extended version of η^2 used for a two-way factorial design, [$\eta_p^2 = SS_{effect} / (SS_{effect} + SS_{error})$], taking into consideration of SS_{error}, the residual variation of data fit in the model. Partial eta square can also be converted into Cohen's *f*, [f= sqrt {$\eta_p^2 / (1 - \eta_p^2)$}].

Omega Square

Omega square (ω^2) adjusts the η^2 (which is based on statistics from the sample) to population inference by accounting for variances of residual term (MS_{error}) in relation to sample sizes (i.e., degree of freedom – df_{effect}), [$\omega^2 = (SS_{effect} - df_{effect} MS_{error}) / (SS_{total} - MS_{error})$]. Omega square can be converted into Cohen's f, [$f \approx$ sqrt {$\omega^2 / (1 - \omega^2)$}].

Multivariate Eta Square

Multivariate eta square (η_m^2) is the η^2 for multivariate analysis of variance (MANOVA) with more than one dependent variables, [$\eta^2 = 1 - \Lambda^{1/s}$], where Λ is Wilk's lambda and s is equal to the number of levels of the factor minus 1 or the number of dependent variables, whichever is the smaller.

Phi

Phi (ϕ) is the ES for Chi-square test of 2x2 contingency table, [ϕ = sqrt(χ^2/ n)], where n is total number of observation.

Cramer's V

Cramer's V is the ES for Chi-square test of r x c contingency table, [V = sqrt (χ^2/(n(df))], where n is total number of observation, and df is degrees of freedom calculated by (r – 1)(c – 1).

Cohen's ω²

Cohen's ω^2 is the Chi-square test for *r* x *c* contingency table, [ω^2 = sqrt {Σ(observed proportion – expected proportion)^2 / (expected proportion)}]

Pearson's r

Pearson's r is the product-moment correlation for two continuous variables with normal distribution (X and Y) reflecting the ratio of covariance between the two variables and the variances of each variable, [r_{XY} = covariance (X,Y) / {sqrt (Variance X)(Variance Y)}]

Spearman's r

Spearman's r or Spearman's rho (ρ) is similar to the Pearson's r but it does not require normally distributed continuous-level data (interval or ratio). It can be used to analyze the association between variables of ordinal measurement levels as the calculation is based on ranks of the data, [$\rho = 1-(6\ \Sigma d^2 / n\ (n^2 - 1)$], where *d* is the difference between the two ranks of each observation, and n is the number of observations.

Point-biserial r

Point-biserial r is the correlation between a dichotomous variable and a continuous variable; r_{pb} is mathematically equivalent to the Pearson's r, [$r_{pb} \approx r_{XY}$].

R-square

R-square (R^2), so-called coefficient of determination, is the measure of degree that an outcome explained by the independent variable in Linear regression model, [$R^2 = 1 - (SS_{regression} / SS_{total})$], where $SS_{regression}$ represents the variation of the residuals or distance from the raw data and its predicted value in the model and SS_{total} is the variation of the distance all data from the mean value.

Odds Ratio

Odds ratio (OR) is the strength of association regarding odds of having the outcome (chance of having outcome vs. not having outcome) between the two comparison groups. OR can be calculated when performing Logistic regression, [OR = Odds_group1 / Odds_group2 = (a_1/b_1) / (a_2/b_2)] where a_1 and a_2 are the numbers of events (outcome), b_1 and b_2 are the number of non-events (no outcome) in the two groups.

Risk Ratio or Relative Risk

Risk ratio or relative risk (RR) is the strength of association regarding risk (chance) of having the outcome between the two comparison groups. RR can be calculated when performing Poisson regression, [RR = Risk_group1 / Risk_group2 = (a_1/n_1) / (a_2/n_2)] where a_1 and a_2 are the numbers of events (outcome), n_1 and n_2 are the number of observations in the two groups.

Sizes of ES

Let's look at the concept behind ES in an example of ES, Cohen's *d*, that is based on "normal distribution" of the data. A normal distribution is unimodal and symmetrically distributed with a bell-shaped curve with its mean and standard deviation (SD). The standard normal distribution, also called the z-distribution, is a special normal distribution where the mean=0 and the SD=1. Any normal distribution can be standardized by converting its values into z scores, [z-score = x−mean/SD].[16] As shown in Figure 1, z scores are corresponding to the SD and the area under the normal curve.

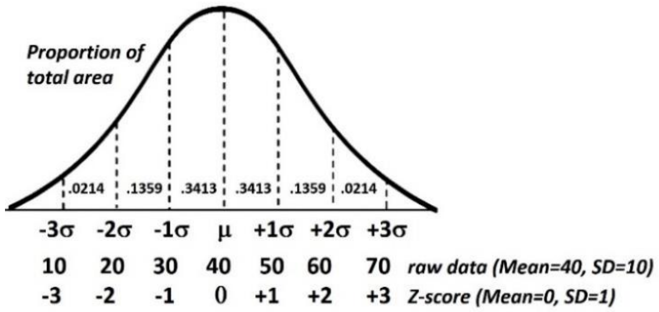

Figure 1. Normal distribution

Cohen's *d* is based on z-score distribution. In comparing two groups under the normal distribution concept, the ES (Cohen's *d*) is simply a measure of how far the difference between the two groups drifts away from the "true" difference between the groups as stated in the null hypothesis (H_0). Cohen suggested interpretation of effect sizes expressed as "small", "medium" and "large".[17] To depict the interpretation of sizes of ES at different cutoffs in a comparison of the mean scores between two groups, ES can be thought of as the average percentile of the mean of the treatment group [μ_2] relative to the mean of the control group [μ_1]. As shown in Figure 2, ES can be interpreted in terms of the percent of nonoverlap of the two groups.[12] Based on the normal distribution of the data of the two groups, the ES=0.0 indicates that the distribution of scores for the two group overlaps completely with one another, i.e., there is 0% of nonoverlap. With a small ES (Cohen's *d*=0.2), the distributions of the two groups overlap for 85%, or the nonoverlap of the two groups is 15%. With a medium ES (Cohen's *d*=0.5), the distributions of the two groups overlap for 67%, or the nonoverlap of the two groups is 33%. With a large ES (Cohen's *d*=0.8), the distributions of the two groups overlap for 53%, or the nonoverlap of the two groups is 47%. With a very large ES (Cohen's *d*=2.0), the distributions of the two groups overlap for 19%, or the nonoverlap of the two groups is 81%. When the means of the two groups are at farther distance, the ES and the nonoverlapping of the distributions of the two groups becomes larger. Nonoverlapping area is also related to the level of SS.

As noted in literature that ES is the difference between two conditions, the bigger the ES, the easier it is to tell the two conditions apart.[18] In comparison between the means of two groups, we may say that the bigger the ES, the farther between the means of the two groups. Several other types and sizes of ES have been proposed and recommended in literature as shown in Table 1.

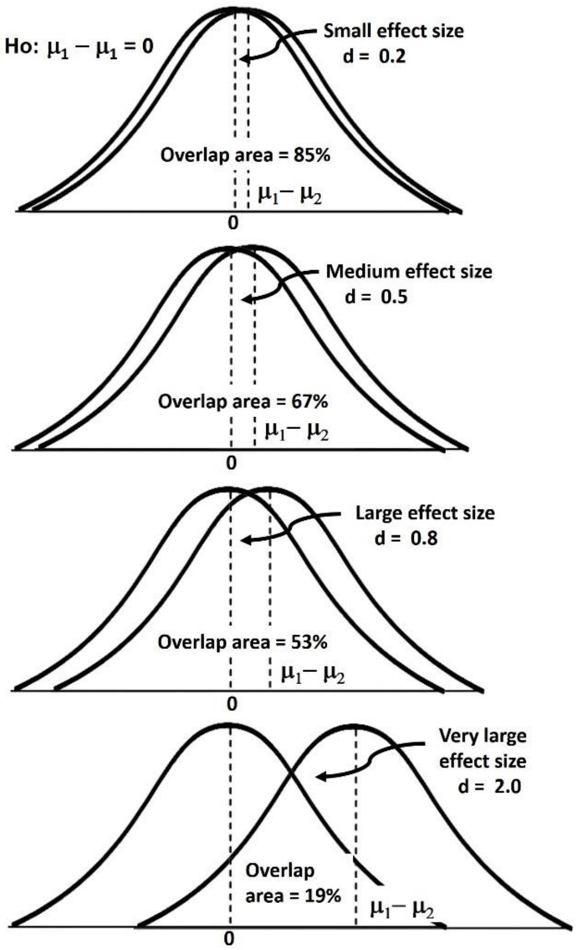

Figure 2. Effect sizes and overlap areas between two-group distributions

Calculating, Interpreting and Reporting the ES

It is recommended to calculate ES both before the study starts and after the study completes. Before starting the study, expected ES is typically a part of the sample size calculation formula to obtain the statistical power that could detect an effect of that size. After completing the study, the researchers can calculate and report actual ES of the study results.[4]

Interpreting the magnitude of ES started with Cohen who set "rules of thumb" to qualify the sizes of an effect as small, medium and large. The sizes or values of ES simply represent arbitrary cutoffs that are subject to interpretation.[1,2,12,15,17] Cohen acknowledged that the use of ES cutoffs is a certain risk in inherent in offering conventional operational definitions for power analysis.[12] It is recommended the use of these cutoffs only when there is no better frame of reference for practical importance, and one should make decision on the effect based on clinical or practical importance which requires domain knowledge.[3] The small or large effect may depend on the application and the context of use.

In testing hypothesis, you may have either negative or positive results. A bias in publishing study result may occur when the paper tends to get published only the one with "positive" outcome (statistically significant results) regardless to the size or magnitude of the outcome. Thus, it is suggested in literature that presenting the study results with both chance (SS) and magnitude (ES) would give a comprehensible picture of scientific achievement.[7] Presenting both SS and ES may reveal an apparent sizeable effect in the study result that is not significant. On the other hand, when the study results are statistically significant, ES may be used to determine whether it is practically important.[2] However, Cohen as well as some others also noted that researchers should report ES as a complement to standard SS testing but should not think that reporting ES is a mandatory requirement when writing up a paper.[1,3,17,19] ES is the abstract statistics that could be used to determine of what constitutes an effect of practical significance, but such interpretation depends on the context of the research and the judgment of the researcher.[1] Thus, one may decide to present ES with its unit in a clear manner and let the readers make the judgment on practical importance related to their own setting/application.[3,4,18] Moreover, ES is sometimes not easy to compute or to interpret. The main focus of the study is sometimes on the direction rather than magnitude of the effect; thus, one may decide to report only SS, and not necessarily ES.[3]

Conclusion

In conclusion, guidelines for calculating, reporting, and interpreting ES in literature are as follow: (1) choose the most suitable type of ES based on the purpose, design, and outcome(s) of the study, (2) be explicit about the type of ES that is used, (3) present the ES for all outcomes regardless of achieving positive or negative SS, (4) interpret effects in the context of the research settings and the study result application.[3,7,14,15,19]

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