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Field Epidemiology Training Program, Division of Epidemiology, Department of Disease Control, Ministry of Public Health, Tiwanond Road, Talad Kwan Subdistrict, Muang District, Nonthaburi 11000, Thailand

Tel: +662-5901734, Fax: +662-5918581, Email: osireditor@osirjournal.net

Website: <**http://www.osirjournal.net**>

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Field Epidemiology Training Program, Division of Epidemiology
Department of Disease Control, Ministry of Public Health, Thailand
Tel: +6625903894, Fax: +6625903845, Email: osireditor@osirjournal.net, http://www.osirjournal.net

Editorial

What can We Learn from the Response to COVID-19?

Wiwat Rojanapithayakorn, Chief Editor

For the past 2 and a half years, the whole world has been struggling with the pandemic spread of corona virus disease 2019 (COVID-19) up to the level that all sectors in the society are affected. It is unbelievable that all the cumulative wisdom on disease prevention and control over the past thousand years was unable to stop the pandemic. The combination of the high level of epidemiology knowledge, the advanced medical and health technology and the facilitative social support mechanism failed to win the fight against the virus. By mid of June 2022, over 540 million of cases and 6.3 million of deaths were reported. Not only the high level of morbidity and mortality caused by the disease, but much bigger social disturbances have also been observed in over hundreds of affected countries. The disease has caused massive and widespread social consequences, affecting socio-economic wellbeing of people around the world. The high magnitude of undesirable outcomes includes interference or interruption on population mobility, closures of various social functions including airports, schools and universities, hotel business, markets, department stores, business centers, factories, tourist industry and many others, resulting in severe negative impact on the economy and the big burden for the control of the outbreaks. The huge costs of vaccine, antiviral drugs, and protective devices were among the burden bearing by the national authorities. Most governments have been facing a dilemma between the strict epidemic control interventions and some relaxation to allow the return of various economic movements. It can be mentioned that in the past 100 years there was no other single infectious disease that was able to cause such enormous socio-economic and health consequences. The past 40 years of HIV/AIDS pandemic with over 35 million deaths had caused very insignificant socio-economic disturbances to the overall society compared to the COVID-19 pandemic.

Many experts are saying that the pandemic is currently downsizing. The number of deaths has dropped remarkably. This may not be due to the effective control, but probably to the change of the infectivity and the virulency of the corona virus, as there is still fluctuation in the number of cases reported. No matter what is the cause of the decline, most governments are paying more attention to transform the disease into a sporadic and an endemic illness. In Thailand, relaxing level of disease control is observed almost everywhere. The government has issued announcements to gradually resume social activities and functions toward the pre-pandemic routine.

What should the health sector, especially epidemiologists do from now on? Firstly, close monitoring of the disease is still very essential. Early signs of re-emerging should be reported to government and the public as soon as possible. Secondly, whether the epidemic situation is subsiding or recurring, epidemiologists should continue to generate lessons from the overall national and global response. A key question is: if we can travel back to the early 2020, based on our intelligence and wisdom gained from this 2-and-a-half-year response, are we going to react the same ways as what has already been done. There are numerous lessons from the situation and the national and global responses. For example, is it possible to prevent the massive spreading by "more strict" universal mask wearing and social distancing with limited interruption of daily social and economic function? Can the disease be controlled without huge investment? Studies on the benefit of every intervention should be very useful for making better decisions on the disease control, not only for the COVID-19—but also for any emerging infectious disease to come. Therefore, the future of disease control is in your hands.

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Field Epidemiology Training Program, Division of Epidemiology
Department of Disease Control, Ministry of Public Health, Thailand
Tel: +6625903894, Fax: +6625903845, Email: osireditor@osirjournal.net, http://www.osirjournal.net

An Outbreak of SARS-CoV-2 in a Garment Factory near the Thailand–Myanmar Border, Tak Province, Thailand, August–September 2021

Sein Hlyan Bo[1,2]*, Witaya Swaddiwudhipong[1], Rapeepong Suphanchaimat[1,3], Saran Sujinpram[1], Chanasan Sawangpol[1], Vanlaya Srethapranai[1]

1 International Field Epidemiology Training Programme, Division of Epidemiology, Department of Disease Control, Ministry of Public Health, Thailand

2 National Leprosy Control Program, Disease Control Unit, Department of Public Health, Ministry of Health, Myanmar

3 International Health Policy Program, Ministry of Public Health, Thailand

*Corresponding author email: seinhlyanbo@mohs.gov.mm, seinhlyanbo@gmail.com

Abstract

On 16 Sep 2021, Thailand's Division of Epidemiology, was notified of an outbreak of coronavirus disease 2019 (COVID-19) in a garment factory in Tak Province. An outbreak investigation was conducted to determine epidemiological characteristics of cases, identify risk factors associated with infection, and recommend appropriate preventive measures. A review of COVID-19 surveillance data and outbreak reports was performed. An active case finding was conducted among the factory workers. We interviewed the manager and workers of the factory and performed an environmental observation and conducted a case-control study. Logistic regression models were employed. Of 242 workers tested for severe acute respiratory syndrome coronavirus 2 by rapid antigen test kit, 90 (37.2%) were found positive. The attack rate was highest in the sewing department (47.4%) and among female workers (53.8%). The prevalence of asymptomatic infection was 15.6%. One case with pneumonia was found and there were no deaths. Working in the sewing department was a significant risk factor [adjusted odds ratio (OR) 3.15, 95% confidence interval (CI) 1.01–9.79] while mask wearing [adjusted OR 0.34, 95% CI 0.14–0.82] was a protective factor. Overcrowding and poorly ventilated conditions were observed in the workplace. Our investigation confirmed a COVID-19 outbreak in a garment factory. Reorienting the environment and strengthening individual protective measures, such as mandatory mask wearing and physical distancing amongst the workers, are recommended.

Keywords: COVID-19, outbreak, garment factory, sewing department, face mask

Introduction

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). People infected with the virus mainly experience mild to moderate respiratory illnesses.[1] Common symptoms are fever, cough, tiredness, and loss of taste. Around 15% of COVID-19 cases develop serious complications such as pneumonia and respiratory failure.[1,2]

Globally, as of 1 Oct 2021, there have been 233,503,524 confirmed cases and 4,777,503 deaths.[3] The study in Malaysia suggests that immediate action taken by the employer and the health officer to identify and investigate those who had close contact with the index case was important in preventing further transmission.[4] In Thailand, from 1 Jan 2020 to 1 Oct 2021, there were 1,615,229 confirmed cases of COVID-19 with 16,850 deaths.[5] An increasing trend was seen due to outbreaks in factories and business establishments.[4,6,7] Sporadic outbreaks in other places such as school and restaurant have also been reported.[8,9]

On 16 Sep 2021, Thailand's Department of Disease Control, Ministry of Public Health, was notified of an outbreak with about 50 COVID-19 suspected cases in a garment factory at Mae Sot District, which is a metropolitan district close to the Thai–Myanmar border in Tak Province. At the time of the investigation, the factory was functioning in containment mode under supervision of occupational health personnel. The investigation team, deputed from the Department of Disease Control, conducted an investigation from 18 to 22 Sep 2021. The objectives of the investigation were to: (i) describe the epidemiological characteristics of the outbreak, (ii) determine possible risk factors, and (iii) provide appropriate prevention and control measures in the factory.

Methods

Descriptive Study

The surveillance data on COVID-19 cases and outbreaks in 2021, as well as the preliminary outbreak report of the investigated factory, were reviewed. The medical records of all workers in the factory were examined.

The occupational health officer of Maesot General Hospital and the factory manager were interviewed. The factory manager was asked about the production chain, working nature and workers' behaviour during the COVID-19 pandemic.

Active Case Finding

An active case finding was conducted in the factory using the following case definitions. A probable case was worker that showed positive SARS-CoV-2 detection from an antigen test kit (ATK) from nasopharyngeal swab from 7 Aug to 3 Oct 2021 period, whereas a confirmed case was a probable case with laboratory confirmation by viral ribonucleic acid detection of SARS-CoV-2 by reverse transcription polymerase chain reaction (RT-PCR). Those eligible to undertake nasopharyngeal swab were workers in the investigated factory who had symptoms compatible with COVID-19, such as fever, cough, sore throat, runny nose and myalgia, or were asymptomatic but had a contact history with a probable/confirmed case from 7 Aug to 3 Oct 2021.

Laboratory Investigation

Nasopharyngeal samples collected from symptomatic workers or asymptomatic workers who had history of contact with probable or confirmed cases were tested for SARS-CoV-2 by ATK. Only the specimens from the patient with pneumonia referred to the hospital were re-examined by RT-PCR in accordance with the Thai national guideline on COVID-19 case management.[6]

Environmental Observation

Environmental conditions of the factory were observed to identify possible risk factors. Areas surrounding the factory, isolation area of the cases, and the quarantine area of the close contacts were observed to determine possible epidemiological linkage.

Analytical Study

An unmatched case-control study was carried out. Sample size calculation was applied using the formula for comparing two proportions with a case to control ratio equal to 1:1.[10] The sample size was adjusted to allow for a 10–20% rate of missing data. Cases were workers identified as either probable or confirmed cases. Controls were defined as workers who were identified as neither close contact with case nor having symptoms of COVID-19 in previous two weeks by questionnaire. We used the following parameters: alpha 0.05, power 80%, proportion of controls with exposure 65%, proportion of cases with exposure 88.1%, odds ratio (OR) 3.99. With these parameters, we required 55–60 cases and controls each. Finally, we were able to obtain 59 cases and 59 controls. A systematic random sampling technique was used to select participants. The median age of cases and non-cases were compared with the rank-sum test. Univariable and multivariable logistic regression models were employed to determine associated factors. Variables which were likely to be risk factors from literature with a *p*-value less than 0.05 from the univariable analysis were included in the multivariable analysis by rule of thumb. Crude OR, adjusted OR, and 95% confidence intervals (CI) were presented. Stata version 16 was used for data analysis.

Ethics

Participants provided consent verbally. Names of participants in this study were coded to ensure anonymity. This study was conducted as part of an emergency public health response. There were no invasive procedures in this investigation.

Results

Epidemiological Characteristics of the Outbreak

Among 242 factory workers, 90 met the case definition (89 probable cases and one confirmed case) resulting in an overall attack rate of 37.2%. Of the 90 cases, 68 (75.6%) were identified from the occupational health officers of the hospital between 30 August and 15 September and 22 (24.4%) were identified by active case finding by the factory. The aim of the investigation was to detect asymptomatic cases after passive screening. One case was admitted to hospital due to pneumonia and there were no deaths. During the investigation, the first case, a worker in the the sewing department, developed symptoms on 11 Aug 2021. The epidemic curve shown in Figure 1 depicts two peak infection periods, one from 31 August to 3 September, the other one from 13 to 20 September. A propagated curve pattern was seen after the report of the outbreak.

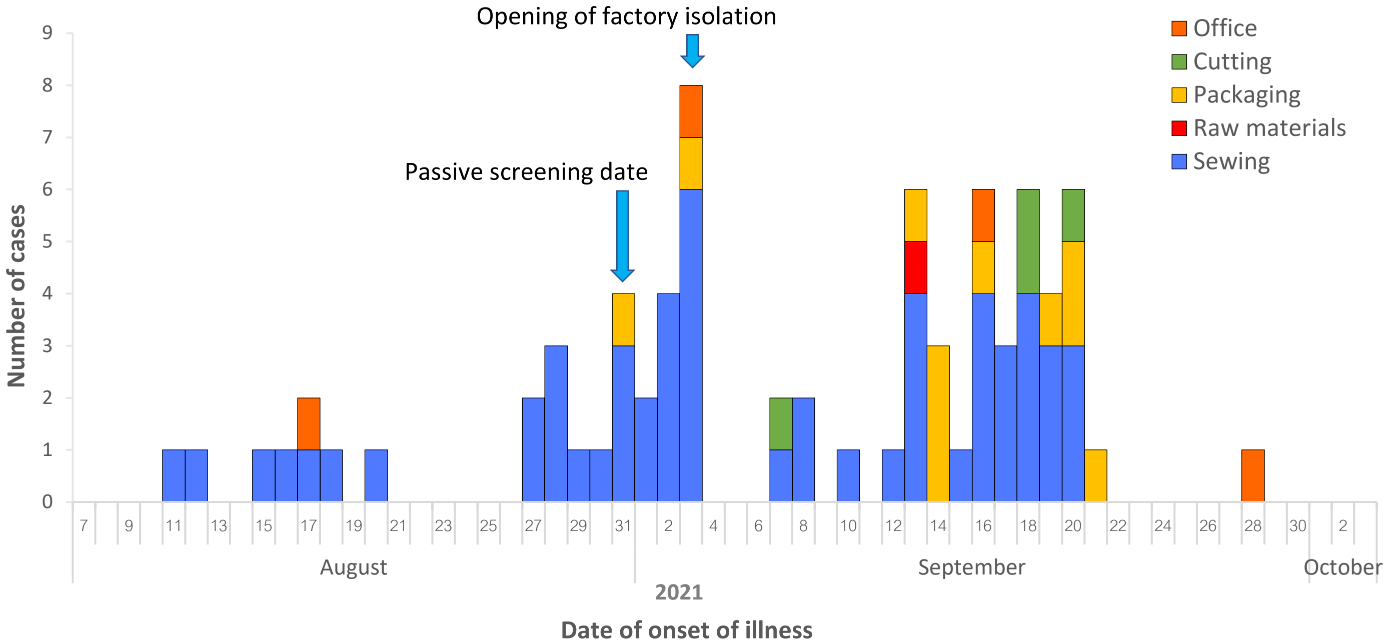

Figure 1. Epidemic curve of COVID-19 cases stratified by work department in the factory, August–September 2021 (only symptomatic cases are shown in the graph) (n=76)

The proportion of asymptomatic cases was 15.6%. Loss of smell and taste was the most common presenting symptom (45.6%), followed by fever (40.0%), runny nose (37.8%) and myalgia (36.7%) (Figure 2).

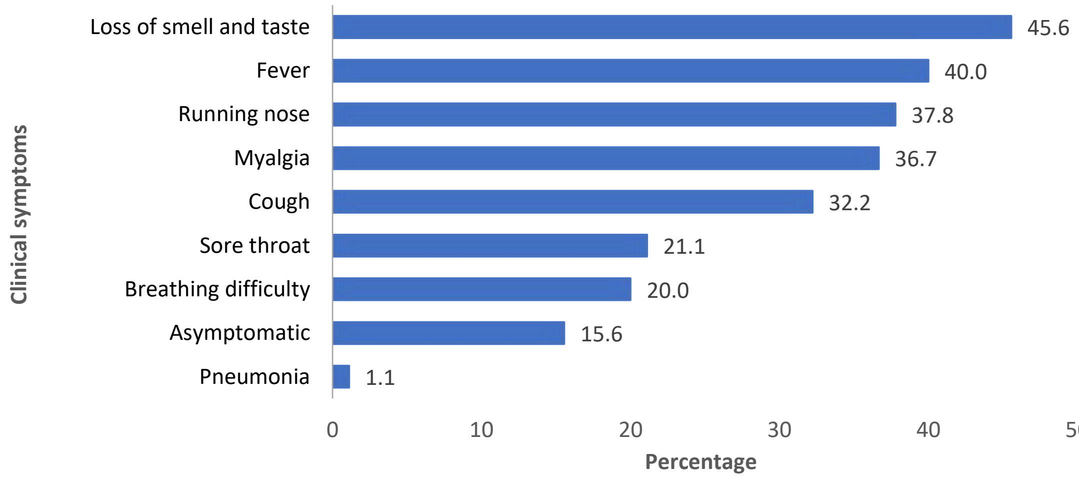

Figure 2. Percentage of COVID-19 cases by clinical symptoms (n=76)

The attack rate was highest in the sewing department (47.4%), followed by the raw materials department (28.6%) (Table 1).

The attack rates of COVID-19 stratified by gender, age group and nationality are shown in Table 2. The attack rate in female workers was about two times higher compared to male workers. Workers aged 25–35 years had the highest attack rate. Burmese were four times higher risk than Thais (Table 3).

Table 1. Number of cases and attack rate of COVID-19 by department of the factory, August–September 2021

Department	Number of cases	Number of workers	Attack rate (%)
Sewing	74	156	47.4
Raw materials	2	7	28.6
Packaging	7	33	21.2
Cutting	3	20	15.0
Office	4	26	15.4
Total	**90**	**242**	**37.2**

Table 2. Number of cases and attack rate of COVID-19 by gender, age, and nationality in the factory, August–September 2021 (n=90)

Characteristics	Number of cases	Total number of workers	Attack rate (%)	Prevalence ratio (95% CI)	*P*-value
Gender					
Female	57	106	53.8	2.22 (1.57–3.13)	<0.001
Male	33	136	24.3	Ref	
Age (years)					
<25	44	114	38.6	2.47 (1.07–5.71)	0.015
25–35	41	96	42.7	2.73 (1.18–6.32)	0.006
>35	5	32	15.6	Ref	
Nationality					
Burmese	85	191	44.5	4.54 (1.94–10.59)	<0.001
Thai	5	51	9.8	Ref	

Laboratory Findings

Of 242 factory workers that were tested by ATK, 90 (37.2%) were positive for COVID-19. Among these, one case (the pneumonia case) underwent RT-PCR due to the protocols of the factory and Maesot General Hospital.

Environmental Observation

The size of the factory building was very large with a high roof and multiple fans installed. It had a large open space with no partitions between working departments. Male and female restrooms were separated. The sewing department contained over 100 workers working less than one meter apart. It was the most crowded working place in the factory and poor air ventilation was observed. Hot and humid conditions were observed. There were about ten lines for working and each line contained about ten workers. The equipment for sewing procedures was not properly arranged. According to an interview with the factory manager, some workers did not wear a face mask properly during and after work. Hand washing stations with soap were provided.

The factory isolation area was a dormitory spread over two floors. Separate male and female restrooms were situated outside the dormitories. Each floor had 16 rooms. The lower floor was designated for the close contacts and the upper floor for the ATK-positive cases. The remaining workers were instructed to remain inside the factory separated from the isolation area. There was a telemedicine room for COVID-19 cases on the upper floor. The rooms in the isolation area were crowded and sanitation was poor. There was no physical barrier that separated between the floors. The restrooms for the isolation area were not adequate.

Case-Control Study

Fifty-nine cases and 59 controls were interviewed. The median age of the cases was 25.5 years and that of non-cases was 26.0 years (p-value 0.05). Based on the univariable analysis, working in the sewing department was a significant risk factor, and wearing mask, during and after work, were protective factors (Table 3).

Table 3. Univariable analysis on possible risk factors of COVID in the factory, August–September 2021

Factors	Cases (n=59) n (%)	Controls (n=59) n (%)	Crude OR (95% CI)	*P*-value
Works in the sewing department				
Yes	48 (81.4)	31 (52.5)	3.94 (1.72–9.05)	0.001
No	11 (18.6)	28 (47.5)	Ref	
Always wore a mask during work before the outbreak				
Yes	48 (82.8)	57 (96.6)	0.17 (0.04–0.81)	0.026
No	10 (17.2)	2 (3.4)	Ref	
Always wore a mask after work before the outbreak				
Yes	23 (39.7)	37 (62.7)	0.39 (0.18–0.82)	0.013
No	35 (60.3)	22 (37.3)	Ref	

Table 3. Univariable analysis on possible risk factors of COVID in the factory, August–September 2021 (cont.)

Factors	Cases (n=59) n (%)	Controls (n=59) n (%)	Crude OR (95% CI)	*P*-value
Stayed with a known COVID-19 patient in the same house				
Yes	4 (6.9)	8 (13.8)	0.46 (0.13–1.63)	0.231
No/not sure	54 (93.1)	50 (86.2)	Ref	
History of contact with a known COVID-19 patient in a nearby house				
Yes	7 (12.3)	15 (25.9)	0.40 (0.15–1.08)	0.069
No/not sure	50 (87.7)	43 (74.1)	Ref	
Dined with a known COVID-19 patient outside the factory				
Yes	6 (10.5)	7 (12.1)	0.86 (0.27–2.73)	0.794
No/not sure	51 (89.5)	51 (87.9)	Ref	
Dined with a known COVID-19 patient in the factory				
Yes	20 (35.1)	16 (27.1)	1.45 (0.66–3.20)	0.355
No/not sure	37 (64.9)	43 (72.9)	Ref	
Ever had a social gathering with a known COVID-19 patient outside the factory				
Yes	3 (5.3)	9 (15.3)	0.31 (0.08–1.21)	0.091
No/not sure	54 (94.7)	50 (84.7)	Ref	
Ever had a social gathering with a known COVID-19 patient in the factory				
Yes	13 (22.8)	9 (15.3)	1.64 (0.64–4.21)	0.302
No/not sure	44 (77.2)	50 (84.7)	Ref	
Smoked socially with a known COVID-19 patient				
Yes	4 (7.0)	3 (5.1)	1.41 (0.30–6.59)	0.663
No/not sure	53 (93.0)	56 (94.9)	Ref	
Worked with a known COVID-19 patient in the same department				
Yes	19 (33.3)	26 (44.1)	0.63 (0.29–1.35)	0.237
No/not sure	38 (66.7)	33 (55.9)	Ref	

The results of multiple logistic regression are presented in Table 4. Working in the sewing department (Adjusted OR 3.15, 95% CI 1.01–9.79) and mask-wearing after work (Adjusted OR 0.34, 95% CI 0.14–0.82) remained significant after adjusting for all other variables in Table 4.

Table 4. Associated factors based on multiple logistic regression model of COVID-19 cases in the factory, August–September 2021

Factors	Adjusted OR	95% CI	*P*-value
Female (Ref=male)	1.37	0.58–3.24	0.47
Incremental age (years)	0.96	0.89–1.04	0.33
Burmese nationality (Ref=Thai)	2.28	0.44–11.73	0.32
Worked in the sewing department (Ref=other department)	3.15	1.01–9.79	0.047
Always wore a mask during work (Ref=not always wearing mask)	0.17	0.03–1.03	0.053
Always wore a mask after work (Ref=not always wearing mask)	0.34	0.14–0.82	0.016

Discussion

This COVID-19 outbreak in a Thai factory near a border where many migrant workers were employed was characterized by a delay in outbreak detection and notification. We suspect that the delays occurred due to communication barriers as the majority of workers were Burmese who could not speak Thai and nearly all of the cases had mild or asymptomatic infection. Our investigation also detected some COVID-19 cases after the opening of the factory isolation unit. This might point to a possible flaw in isolating the cases and quarantining the contacts as supported by our observation that there were no physical barriers to separate the cases on the upper floor from the contacts on the lower floor.

This study reaffirms the belief that COVID-19 outbreaks commonly take place in factories where workers are stationed in close proximity with each other and there is poor air ventilation.[11–16] The United States (U.S.) Centers for Disease Control and Prevention recently reported COVID-19 infections among workers from 36 states.[15] In each state, the percentage of workers with COVID-19 ranged from 2.0%–43.5%.[15] Our study found that the attack rate of COVID-19 in the factory outbreak was 37.2%, similar to the U.S. Centers for Disease Control and Prevention report. The proportion of symptomatic infections was 84.4%, which is also similar to the figure of 83.2% in the U.S. study.[15]

It is well known that workers in high-density workplaces are at high risk for SARS-CoV-2 transmission.[11,13–16] The investigation of COVID-19 outbreaks in meat and poultry processing plants in Germany showed that employees who worked with a minimum distance of less than 1.5 meters had a higher chance of developing COVID-19 (adjusted OR 3.61; 95% CI 2.83–4 .6).[16] Hot and humid conditions and poor airflow was observed in the study factory, and these conditions can increase the spread of COVID-19.[15] We found that the highest attack rate occurred in the sewing department, the most crowded area in the factory. The case-control study indicated that working in the sewing department was a significant risk factor on univariable and multivariable analyses. Moreover, the factory manager also reported that some workers did not wear a mask during work because of the high temperature. Wearing a face mask is widely recommended to prevent transmission of SARS-CoV-2.[17,18] The World Health Organization recommends people to wear a properly fitted mask, especially when physical distancing is not possible or in poorly ventilated settings.[17] We found that the practice of always wearing a mask after work was a protective factor. We therefore encourage the continued use of a face mask among workers to prevent infection and to slow the transmission of SARS-CoV-2.

Limitations

According to the protocol of Maesot General Hospital's RT-PCR should be conducted only in a case with severe symptoms. In this outbreak, we found only one confirmed case. However, this finding should be interpreted with caution as the number of confirmed cases was driven by the testing protocol agreed by the factory and Maesot General Hospital. Additionally, we initially intended to collect the information on COVID-19 vaccine but as almost all workers in the factory had not been immunized, we decided to omit the vaccine history item from the questionnaire. In future outbreaks, questions about vaccination history should be included. There was a language barrier between the investigation team and many factory workers. Due to limited human resources, we asked health personnel at the hospital, who were not trained in interview techniques, to interview workers with the use of a translator. However, some misunderstandings may have occurred. Finally, information about the date of onset and some risk behaviours may have suffered from recall bias.

Recommendations

We recommended that the factory manager place a physical barrier such as a plastic partition to separate one worker from one another, particularly in the sewing department. The team discussed with the factory manager about a strict mandate on all workers to wear a properly fitted mask during and after work. Additionally, the surveillance and reporting systems in the factory should be strengthened to avoid delays in notification. The local occupational health team should regularly screen workers in the factory. The isolating area for the cases and the quarantine area for the contacts should be strictly separated, with close supervision by the factory manager, to reduce the risk of virus transmission from one area to another. We encourage the use of face masks among workers to reduce the risk of infection and to slow transmission of SARS-CoV-2.

Conclusion

This factory outbreak contained 89 probable cases and one confirmed case of COVID-19. Most of the cases had mild symptoms and there were no deaths. Working in the sewing department, where many persons worked close to each other, was a significant risk factor while mask wearing after work was a protective factor.

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Declaration of Conflicting Interests

All authors declare that there is no conflict of interest.

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References

1. World Health Organization. Coronavirus disease (COVID-19): overview [Internet]. Geneva: World Health Organization; [cited 2021 Oct 9]. <https://www.who.int/health-topics/coronavirus#tab=tab_1>

2. World Health Organization. Coronavirus disease (COVID-19): symptoms [Internet]. Geneva: World Health Organization; [cited 2021 Oct 9]. <https://www.who.int/health-topics/coronavirus#tab=tab_3>

3. World Health Organization. WHO coronavirus (COVID-19) dashboard [Internet]. Geneva: World Health Organization; [cited 2021 Oct 9]. <https://covid19.who.int/>

4. Shanmugam TS, Bakon SK, Mohamad ZA, Perumal AS, Rathakrishnan K, Nagalingam T, et al. An outbreak investigation of COVID-19 among furniture factory workers at Kuala Langat District, Selangor, Malaysia. OSIR. 2022Mar;15(1):15–9.

5. World Health Organization. WHO coronavirus (COVID-19) disease situation in Thailand [Internet]. Geneva: World Health Organization; [cited 2021 Oct 9]. <https://covid19.who.int/region/searo/country/th>

6. Emergency Operation Center, Department of Disease Control. The coronavirus disease 2019 situation: Thailand situation update [Internet]. Nonthaburi: Department of Disease Control, Ministry of Public Health; 2021 Sep 27 [cited 2021 Oct 9]. <https://ddc.moph.go.th/viralpneumonia/eng/file/situation/situation-no627-270964.pdf>

7. Lodz NA, Lin CZ, Hasani WSR, Ahmad NA, Ahmad FH, Rifin HM, et al. Cluster of COVID-19 cases in a workplace: the first cluster of a workplace-related outbreak in Malaysia, 2020. OSIR. 2022 Mar;15(1):7–14

8. Mae Sot General Hospital. The coronavirus disease 2019 situation in Mae Sot, 1 January–15 September 2021. Tak (TH): Mae Sot General Hospital, Ministry of Public Health; 2021.

9. Nittayasoot N, Samphao R, Poobua K, Suphanchaimat R. A cluster of Coronavirus Disease (COVID-19) cases linked to a restaurant during early local SARS-CoV-2 transmission in Thailand. OSIR. 2020 Jun;13(2):64–70.

10. Sullivan KM, Dean AG, Mir RA. OpenEpi: Sample Size Unmatched Case Control Study [Internet]. Atlanta: Rollins School of Public Health, Emory University; [updated 2013 Apr 6, cited 2021 Oct 31]. <https://www.openepi.com/SampleSize/SSCC.htm>

11. Gunther T, Czech-Sioli M, Indenbirken D, Robitaille A, Tenhaken P, Exner M, et al. SARS-CoV-2 outbreak investigation in a German meat processing plant. EMBO Mol Med. 2020 Dec 7;12(12):e13296. doi: 10.15252/emmm.202013296.

12. Baker MG, Peckham TK, Seixas NS. Estimating the burden of United States workers exposed to infection or disease: A key factor in containing risk of COVID-19 infection. PLoS One. 2020 Apr 28;15(4):e0232452.

13. Waltenburg MA, Victoroff T, Rose CE, Butterfield M, Jervis RH, Fedak KM, et al. Update: COVID-19 among workers in meat and poultry processing facilities–United States, April–May 2020. MMWR Morb Mortal Wkly Rep. 2020 Jul 10;69(27):887–92. doi: 10.15585/mmwr.mm6927e2.

14. Dyal JW, Grant MP, Broadwater K, Bjork A, Waltenburg MA, Gibbins JD, et al. COVID-19 among workers in meat and poultry processing facilities—19 States, April 2020. MMWR Morb Mortal Wkly Rep. 2020 May 8;69(18):557–61. doi: 10.15585/mmwr.mm6918e3.

15. Waltenburg MA, Rose CE, Victoroff T, Butterfield M, Dillaha JA, Heinzerling A, et al. Coronavirus disease among workers in food processing, food manufacturing, and agriculture workplaces. Emerg Infect Dis. 2021 Jan;27(1):243–9. doi: 10.3201/eid2701.203821.

16. Pokora R, Kutschbach S, Weigl M, Braun D, Epple A, Lorenz E, et al. Investigation of superspreading COVID-19 outbreak events in meat and poultry processing plants in Germany: A cross-sectional study. PLoS One. 2021 Jun 10;16(6):e0242456. doi: 10.1371/journal.pone.0242456.

17. World Health Organization. Coronavirus disease (COVID-19): prevention [Internet]. Geneva: World Health Organization; [cited 2021 Oct 9]. <https://www.who.int/health-topics/coronavirus#tab=tab_2>

18. Feng S, Shen C, Xia N, Song W, Fan M, Cowling BJ. Rational use of face masks in the COVID-19 pandemic. Lancet Respir Med. 2020 May;8(5):434–6. doi: 10.1016/S2213-2600(20)30134-X.

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Field Epidemiology Training Program, Division of Epidemiology
Department of Disease Control, Ministry of Public Health, Thailand
Tel: +6625903894, Fax: +6625903845, Email: osireditor@osirjournal.net, http://www.osirjournal.net

Effectiveness of the CoronaVac Vaccine on Symptomatic COVID-19 Infection, Severe Disease, ICU/semi-ICU Admission, and Mortality in Samut Sakhon Province: a Test-Negative Case-Control Study

Pornchanan Duriyaprapan[1]*, Anchalee Erjongmanee[2], Withoone Kittiphichai[3], Kanokwan Sengkhampha[4], Kunyanut Tuboonmar[5]

1 Hua Hin Hospital, Ministry of Public Health, Thailand

2 Samut Sakhon Provincial Health Office, Ministry of Public Health, Thailand

3 Samutsakhon Hospital, Ministry of Public Health, Thailand

4 Banphaeo General Hospital, Ministry of Public Health, Thailand

5 Krathumbaen Hospital, Ministry of Public Health, Thailand

*Corresponding author email: pornchanand@gmail.com

Abstract

A mass vaccination campaign with the inactivated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine, CoronaVac, was implemented in Thailand during the early months of the COVID-19 pandemic. As the Delta variant became the dominant strain in the country, we aimed to evaluate the real-world effectiveness of this particular vaccine among adults in Samut Sakhon Province, Thailand. A test-negative case-control study was conducted from 1 Jun to 31 Jul 2021 to evaluate the effectiveness of CoronaVac against symptomatic COVID-19 infection, severe disease, admission to intensive care unit (ICU)/semi-ICU and mortality. We estimated odds ratios using multiple logistic regression. Among 11,371 participants included in the study, 3,116 (27.4%) tested positive for COVID-19 and 3,333 (29.3%) completed two doses of vaccine. The adjusted vaccine effectiveness of two-dose CoronaVac was 65.8% (95% confidence interval (CI) 61.9–69.3) for the prevention of symptomatic infection, 71.8% (95% CI 58.5–81.6) for severe disease, 72.7% (95% CI 56.6–83.9) for ICU/semi-ICU admission and 86.7% (95% CI 34.8–99.3) for mortality. Results of this study demonstrate that CoronaVac had moderate effectiveness against symptomatic COVID-19 infection, while it was effective in preventing severe disease, ICU/semi-ICU admission and COVID-19 related deaths in a setting where the two variants were circulating.

Keywords: COVID-19, CoronaVac, vaccine effectiveness, test-negative study, Thailand

Introduction

Since the start of the coronavirus disease 2019 (COVID-19) pandemic, Thailand has recorded over 1 million confirmed cases and almost 10,000 COVID-19 related deaths.[1] In 2020, the government's nation-wide restrictive measures successfully contained the spread of the virus. However, during December 2020, a new outbreak, originating in a seafood market in Samut Sakhon Province, raised the total number of confirmed cases to over 20,000 within three months. Another outbreak, with the epicenter in Bangkok, followed in April 2021. The country's social environment, economy and healthcare system was severely affected despite considerable efforts at controlling the pandemic.

Apart from the lockdown strategy to restrict people's movement and other preventive measures, vaccination is another approach for combating the virus. CoronaVac (Sinovac), an inactivated vaccine developed in China, is known to be 50–65% effective against symptomatic COVID-19 infections based on studies from Brazil and China, while a study from Turkey reported a protective efficacy of 84%.[2–5] A preliminary report from Phuket in Thailand also showed promising results regarding the vaccine effectiveness among high-risk contacts.[6]

Although the first vaccination campaign was rolled out in early February 2021, initially focusing on healthcare workers in affected areas, the number of confirmed cases reached 10,000 cases per day with over 200 deaths per day. Moreover, concerns were raised over the effectiveness of the CoronaVac vaccine against the different COVID-19 variants circulating around the world, namely B1.117 (Alpha), B.1.351 (Beta) and B.1.617 (Delta). Thus, further studies assessing the vaccine efficacy are warranted to ensure public trust during the ongoing pandemic.

Samut Sakhon Province is a coastal province in central Thailand with a population of approximately 600,000. Over the past decade, the extensive industries in fisheries and seafood processing have brought in a large number of migrant workers from neighboring countries. Currently, it is estimated that over 250,000 migrant workers reside in this province. These characteristics, for example, high population density, dynamic population movement, migrant workers' living conditions, and limited access to healthcare services, pose several challenges in the management of the pandemic.

In light of the Ministry of Public Health's response to the latest COVID-19 outbreak in Samut Sakhon Province, the national policy in directing the vaccine and other resources to the areas of greatest need, combined with 'bubble and seal' measures at factories, effectively suppressed the spreading of the virus. In August 2021 the number of confirmed cases exceeded 50,000 and only 30% of the Sumat Sakhon Province population were vaccinated. A preliminary report found that the proportion of cases infected with the Delta-lineage had increased from 28% to 97% within two months.[7]

Since data regarding the effectiveness of the CoronaVac in Thailand are limited, we aimed to ascertain the real-world effectiveness of the vaccine against symptomatic COVID-19 infections and clinical outcomes of interest, namely severe disease, intensive care unit (ICU)/semi-ICU admissions and mortality among the adult population in Samut Sakhon Province, Thailand.

Methods

Study Population and Design

We conducted a retrospective test-negative case-control study. This type of study is widely used to estimate the effectiveness of influenza vaccines as it reduces bias from misclassification and differences in healthcare seeking behavior and access to testing between cases and controls.[8–10]

The study population consisted of residents of Samut Sakhon Province who attended an acute respiratory infection clinic between 1 Jun and 31 Jul 2021 in the three studied hospitals, namely Samutsakhon Hospital, Krathumbaen Hospital and Banphaeo General Hospital, and anyone who was categorized as a patient under investigation, defined by the Department of Disease Control, Ministry of Public Health, Thailand, as a person who had a body temperature ≥37.5 °C and/or any respiratory symptoms, for example, cough, runny nose, sore throat, anosmia, tachypnea, shortness of breath, or difficulty breathing, and with risk factors such as a history of living in an outbreak area or visiting a crowded public area within 14 days prior to symptom onset.[11]

Cases were participants who presented with symptoms of COVID-19 infection and tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by reverse transcription polymerase chain reaction (RT-PCR) within 10 days after symptom onset. Controls were persons who had symptoms compatible with COVID-19 infection but tested negative. We excluded persons who were vaccinated with other COVID-19 vaccines and those who tested positive for COVID-19 within the past six weeks. As the primary target group for the initial CoronaVac vaccination campaign in Samut Sakhon Province was Thai persons aged between 18–59 years, we accordingly excluded participants who were non-Thais and aged less than 18 or over 60 years and the data were collected from 1 Jul to 31 Aug 2021. To calculate a minimum sample size of cases in this study, the following formula was used:[12]

$$N = (z/d)^2 \, [1/A\,(1–A\,) + 1/CP_2\,(1–P_2)],$$

where C is the proportion of controls to cases, which was 1 (1:1 case-to-control ratio); P_2 is the vaccine coverage, which was 30% in the study population; A is the anticipated vaccine effectiveness, which was 60% according to a previous study, and d is the width of the confidence interval (CI). With 20% desired precision and z value of 1.96, the number of the cases and controls needed in this study was both 801.

Data Sources

Patient demographic data, clinical data and RT-PCR testing results were extracted from the hospitals' electronic medical record database. Additional data on COVID-19 patient registry and mortality data were collected from Samut Sakhon Provincial Health Office and the Office of Disease Prevention and Control Region 5 Ratchaburi. The COVID-19 vaccination registry data was retrieved from the Strategy and Planning Division of the Office of the Permanent Secretary, Ministry of Public Health. All of the data sources mentioned above were linked with the 13-digit national identification number.

Outcomes and Covariates

For vaccination status, we defined fully vaccinated individuals as those who received the second dose of vaccine for at least two weeks. The primary outcomes are RT-PCR confirmed symptomatic COVID-19 infection, severe COVID-19 disease (defined as severe pneumonia requiring oxygen therapy regardless of the type of oxygen delivery devices), admission to ICU/semi-ICU and COVID-19 related deaths. These clinical outcomes were assessed until the end of the study (31 Aug 2021) Covariates assumed to be associated with the risk of exposure to SARS-CoV-2 and likelihood of receiving a vaccine, including age and gender, were also recorded and included in the final model.

Statistical Analysis

Descriptive statistics were used to summarize frequency distribution, central tendency and variability of study samples. Chi-square and independent t-tests were used to determine the difference in all covariates between cases and controls. We used multiple logistic regression to estimate the odds of being fully vaccinated among all participants. The independent variables were vaccination status, age and gender. Age and gender were included in the multivariate model as they were potential confounders. The vaccine effectiveness was estimated by 1 minus the corresponding odds ratio and the 95% CI was obtained from the adjusted model and expressed as a percentage. Variables with a p-value <0.05 were considered significant. Statistical analysis was performed using R version 4.1.1 (Foundation for Statistical Computing, Vienna, Austria).[13]

Ethics

Ethical approval to conduct the study was obtained from the Research Ethics Committee of Samut Sakhon Provincial Health Office and permission was obtained from the three studied hospitals.

Funding

This research was supported by FETP-Outbreak response project (U.S. CDC/TUC Fund).

Results

Between 1 Jun and 31 Jul 2021, a total of 11,371 participants who had RT-PCR testing for SARS-CoV-2 at the three studied hospitals were included, of which 3,116 (27.4%) tested positive for COVID-19 and 8,255 (72.6%) tested negative. Figure 1 shows the study diagram and vaccination status (unvaccinated, vaccinated with one dose, or vaccinated with two doses) among cases and controls. Overall, 3,333 (29.3%) participants received 2 doses of the CoronaVac vaccine, 247 (2.2%) received 1 dose, and 7,791 (68.5%) were unvaccinated.

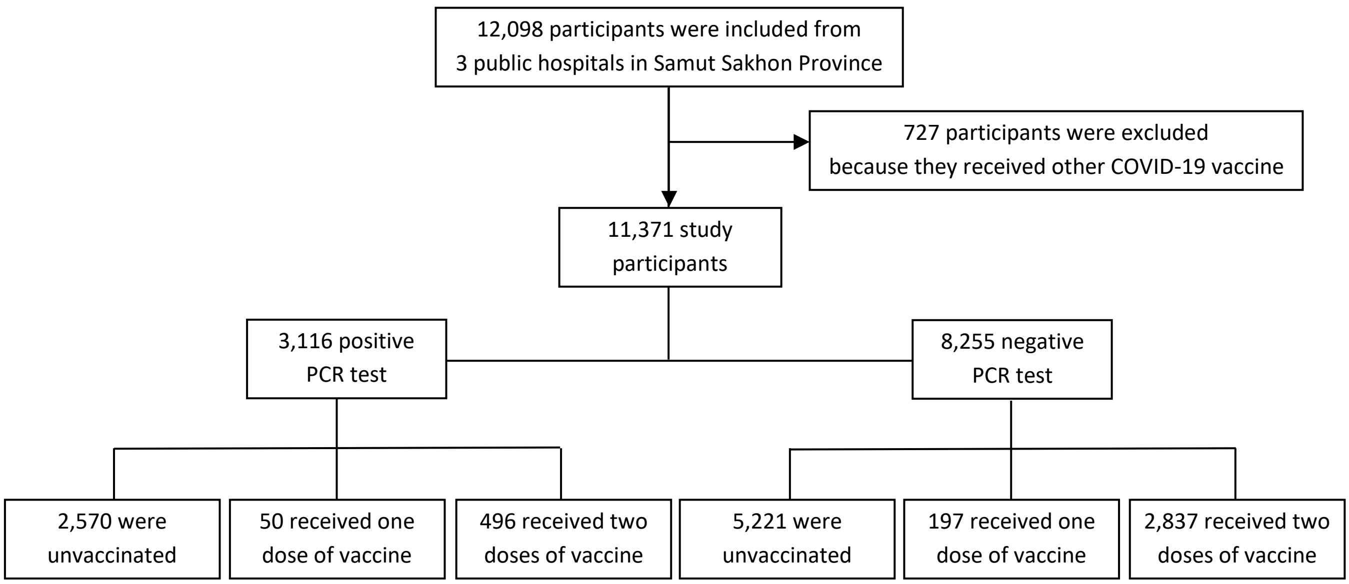

Figure 1. Flowchart of study population and vaccination status

Table 1 shows the demographic characteristics of the participants according to the RT-PCR test results and vaccination status. The mean age among those who tested positive and negative was 38.7 and 37.8 years, respectively. More than half of the participants were female among both cases (58.4%) and controls (58.1%) while almost three-quarters of the participants resided in Mueang Samut Sakhon District. The mean age and proportion residing in different districts were statistically different between cases and controls.

Results of the logistic regression analysis in which we estimated the vaccine effectiveness among fully immunized persons compared with unvaccinated individuals are shown in Table 2. The adjusted odds ratios obtained from the models were 0.34 (95% CI 0.31–0.38) for symptomatic infection, 0.28 (95% CI 0.18–0.42) for severe disease, 0.27 (95% CI 0.16–0.43) for ICU or semi-ICU admission, and 0.13 (95% CI 0.01–0.65) for COVID-19 related deaths. The adjusted vaccine effectiveness was 65.8% (95% CI 61.9–69.3) for the prevention of symptomatic infection, 71.8% (95% CI 58.5–81.6) for prevention of severe disease, 72.7% (95% CI 56.6–83.9) for the prevention of ICU/semi-ICU admission and 86.7% (95% CI 34.8–99.3) for the prevention of COVID-19 related deaths.

Table 1. Demographic characteristics of participants (n=11,371)

Characteristic	Cases	Controls	*P*-value	Unvaccinated	Vaccinated with one dose	Vaccinated with two doses
Total	**3,116**	**8,255**		**7,791**	**247**	**3,333**
Age, mean ± SD	38.7 ± 11.7	37.8 ± 11.5	<0.01	37.3 ± 11.8	37.9 ± 10.6	39.7 ± 10.9
Age group (years)						
18–29	870 (27.9)	2,477 (30.0)	<0.01	2,521 (32.4)	67 (27.1)	759 (22.8)
30–39	716 (23.0)	2,093 (25.4)		1,891 (24.3)	79 (32.0)	839 (25.2)
40–49	788 (25.3)	1,990 (24.1)		1,790 (23.0)	51 (20.6)	937 (28.1)
50–59	742 (23.8)	1,695 (20.5)		1,589 (20.4)	50 (20.2)	798 (23.9)
Gender						
Male	1,296 (41.6)	3,462 (41.9)	0.75	3,501 (44.9)	98 (39.7)	1,159 (34.8)
Female	1,820 (58.4)	4,793 (58.1)		4,290 (55.1)	149 (60.3)	2,174 (65.2)
District						
Krathum Baen	654 (21.0)	1,291 (15.6)	<0.01	1,524 (19.6)	28 (11.3)	393 (11.8)
Ban Phaeo	261 (8.4)	786 (9.5)		677 (8.7)	15 (6.1)	355 (10.7)
Mueang Samut Sakhon	2,201 (70.6)	6,178 (74.8)		5,590 (71.7)	204 (82.6)	2,585 (77.6)

Note: SD: standard deviation; Data are presented as frequency and percentage unless otherwise specified

Table 2. Effectiveness of CoronaVac against symptomatic infection, severe disease, ICU admission and COVID-19 related death

	Number of cases		Number of controls		Adjusted OR (95% CI)[a]	Effectiveness, % (95% CI)
	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated		
Symptomatic infection	486	2,570	2,780	5,221	0.34 (0.31–0.38)	65.8 (61.9–69.3)
Severe disease	27	204	3,239	7,587	0.28 (0.18–0.42)	71.8 (58.5–81.6)
ICU[b] admission	18	144	3,248	7,647	0.27 (0.16–0.43)	72.7 (56.6–83.9)
Confirmed deaths	1	16	3,265	7,775	0.13 (0.01–0.65)	86.7 (34.8–99.3)

Note: OR: odds ratio. CI: confidence interval. [a]Adjusted for age and gender. [b]Includes semi-ICU admissions

Discussion

Our study provides estimates of real-world effectiveness of the CoronaVac vaccine against symptomatic infection and clinical outcomes among those aged 18–59 years who had respiratory symptoms compatible with COVID-19 in Samut Sakhon Province, Thailand. The vaccine effectiveness of two-dose CoronaVac was 65.8% for symptomatic infection, 71.8% for severe disease, 72.7 for ICU/semi-ICU admission and 86.7% for COVID-19 related deaths. It was likely that the circulating variants in Samut Sakhon Province during the study period were mixing between the Alpha- and Delta-lineage viruses as the random sequenced samples demonstrated and increasing proportion of the Delta variant over time, although this could not be directly confirmed. Thus, the vaccine effectiveness reported in this study might not be specific to any particular variant. Our findings are consistent with estimates reported in other studies. The study of a prospective national cohort in Chile demonstrated a high efficacy of CoronaVac in preventing COVID-19 (65.9% [95% CI 65.2–66.6]), hospitalization (87.5% [95% CI 86.7–88.2]), ICU admission (90.3% [95% CI 89.1–91.4]) and COVID-19 related deaths (86.3% [95% CI 84.5–87.9]), while a randomized phase 3 clinical trial in Brazil among healthcare professionals showed a similar efficacy against symptomatic COVID-19 (50.7% [95% CI 36.0–62.0]), preventing the need for medical treatment (83.7% [95% CI 58.0–93.7]) and moderate/severe disease (100% [95% CI 56.4–100]).[3,13] Our results are somewhat lower than the estimates reported in a randomized phase 3 clinical trial in Turkey (83.5% [95% CI 65.4–92.1]) but significantly higher than the vaccine effectiveness reported in another study from Brazil (36.8% [95% CI 54.9–74.2]).[2,5] These differences in estimates are possibly owing to the dissimilar predominant viral lineage and various national policies on preventive measures implemented during the study period.

Despite the acceptable immunogenicity and safety profiles of CoronaVac, the effectiveness of the vaccine became highly questionable as the Delta variant has been the major variant circulating in Thailand.[15,16] Eventually, the Thai government decided to revoke the 2-dose CoronaVac schedule and endorse a mix-and-match vaccine combination for all Thai adults, known as the CoronaVac-AstraZeneca regimen. Moreover, concern over rapid immunity waning has been suggested by many studies.[17-19] Consequently, the Thailand Ministry of Public Health approved another type of COVID-19 vaccine, Pfizer and AstraZeneca, as a booster dose for every person who already completed 2 doses of CoronaVac, while the World Health Organization recommended a third dose specifically in persons aged over 60 years.[20] Thus, these mixed vaccine regimens are yet to be officially approved by World Health Organization and more evidence on immunogenicity and safety of combining different vaccines types against Delta variant is needed.

Our study has several limitations. First, our results may be subject to unmeasured confounding due to the nature of an observational study. Although we already included age and gender in the adjusted model, some potential confounders that might be associated with the risk of COVID-19 infection and acquiring severe disease, such as underlying medical condition, individual-level protective behavior, were not included. Second, throughout the study period, Thailand's fourth outbreak had severely affected the health system in Samut Sakhon Province. Given limited resources during the crisis (i.e., exceeding ICU/semi-ICU bed capacity, an increasing need for ventilators and medical personnel shortage), a number of patients were not admitted to hospital in a timely fashion and did not receive adequate treatment resulting in increased morbidity and mortality. Therefore, our estimates might not truly reflect the actual vaccine effectiveness. Lastly, our results may not be generalizable to those aged 60 years and above, and since our study population were relatively young and healthy, the need for ICU admission and mortality rate may be different from older and less healthy populations.

In conclusion, we found that the CoronaVac vaccine had moderate efficacy against symptomatic COVID-19 infection, while it was effective in preventing severe disease, ICU/semi-ICU admission and COVID-19 related deaths among Thai adults in a setting where the Delta and Alpha variants were circulating. Viral genetic mutation and waning immunity necessitates continued monitoring of vaccine effectiveness for inactivated SARS-CoV-2 vaccines.

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Suggested Citation

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References

1. Emergency Operations Center, Department of Disease Control. The Coronavirus Disease 2019 Situation: Thailand situation update on 23 August 2021. Nonthaburi: Department of Disease Control, Ministry of Public Health, Thailand; 2021 Aug 23 [cited 2021 Aug 31]. 3 p. <https://ddc.moph.go.th/viralpneumonia/eng/file/situation/situation-no592-230864.pdf>

2. Tanriover MD, Doganay HL, Akova M, Guner HR, Azap A, Akhan S, et al. Efficacy and safety of an inactivated whole-virion SARS-CoV-2 vaccine (CoronaVac): interim results of a double-blind, randomised, placebo-controlled, phase 3 trial in Turkey. Lancet. 2021 Jul 17:398(10296);213–22.

3. Jara A, Undurraga EA, Gonzalez C, Paredes F, Fontecilla T, Jara G, et al. Effectiveness of an Inactivated SARS-CoV-2 Vaccine in Chile. N Engl J Med. 2021 Sep 2;385(10):875–84.

4. Ranzani OT, Hitchings MDT, Dorion M, D'Agostini TL, de Paula RC, de Paula OFP, et al. Effectiveness of the CoronaVac vaccine in older adults during a gamma variant associated epidemic of COVID-19 in Brazil: test negative case-control study. BMJ. 2021 Aug 20;374:n2015. doi: 10.1136/bmj.n2015.

5. Hitchings MDT, Ranzani OT, Torres MSS, de Oliveira SB, Almiron M, Said R, et al. Effectiveness of CoronaVac among healthcare workers in the setting of high SARS-CoV-2 Gamma variant transmission in Manaus, Brazil: A test-negative case-control study. Lancet Reg Health Am. 2021 Sep;1:100025. doi: 10.1016/j.lana.2021.100025.

6. Phucharoen C, Sungkaew N, Sukontapol C, Laongpetch S, Kukiatkul K, Sawangpan K. Interim Estimates of Vaccine Effectiveness of CoronaVac among High Risk Contacts: An empirical study from Phuket. Phuket: Prince of Songkla University; 2021. 1–9 p.

7. Regional Medical Sciences Center 5 Samut Songkharm. Health Region 5 SARS-CoV-2 Genomic Surveillance: A Preliminary Report. Samut Songkharm (TH): Regional Medical Sciences Center 5 Samut Songkharm, Department of Medical Sciences, Ministry of Public Health; 2021.

8. Chua H, Feng S, Lewnard JA, Sullivan SG, Blyth CC, Lipsitch M, et al. The Use of Test-negative Controls to Monitor Vaccine Effectiveness: A Systematic Review of Methodology. Epidemiology. 2020 Jan;31(1): 43–64.

9. Lewnard JA, Patel MM, Jewell NP, Verani JR, Kobayashi M, Tenforde MW, et al. Theoretical Framework for Retrospective Studies of the Effectiveness of SARS-CoV-2 Vaccines. Epidemiology. 2021 Jul 1;32(4):508–17.

10. World Health Organization. Evaluation of COVID-19 vaccine effectiveness: Interim guidance [Internet]. Geneva: World Health Organization; 2021 Mar 17 [cited 2021 Aug 30]. 70 p. <https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccine_effectiveness-measurement-2021.1>

11. Department of Disease Control. Patient Under Investigation (PUI) Definition [Internet]. Nonthaburi: Department of Disease Control, Ministry of Public Health, Thailand: 2020 Jun 16 [updated 2020 Jun 23, cited 2021 Oct 1]. 2 p. <https://ddc.moph.go.th/viralpneumonia/eng/file/guidelines/g_surveillance_230620.pdf>

12. O'Neill RT. On sample sizes to estimate the protective efficacy of a vaccine. Stat Med. 1988 Dec;7(12):1279–88.

13. R Core Team. R: A Language and Environment for Statistical Computing [Internet]. Vienna (Austria): R Foundation for Statistical Computing; 2020 [cited 2021 Sep 10]. <https://www.R-project.org/>

14. Palacios R, Batista AP, Albuquerque CSN, Patino EG, Santos JDP, Conde MTRP, et al. Efficacy and safety of a COVID-19 inactivated vaccine in healthcare professionals in Brazil: the PROFISCOV Study. SSRN [Preprint]. 2021 Apr 14 [cited 2021 Sep 5]: [66 p.]. <https://ssrn.com/abstract=3822780>

15. Bueno SM, Abarca K, Gonzalez PA, Galvez NMS, Soto JA, Duarte LF, et al. Safety and Immunogenicity of an Inactivated SARS-CoV-2 Vaccine in a Subgroup of Healthy Adults in Chile. Clin Infect Dis. 2021 Sep 19:ciab823.

16. Zhang Y, Zeng G, Pan H, Li C, Hu Y, Chu K, et al. Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine in healthy adults aged 18-59 years: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial. Lancet Infect Dis. 2021 Feb;21(2):181–92 .

17. Hunsawong T, Fernandez S, Buathong R, Khadthasrima N, Rungrojchareonkit K, Lohachanakul J, et al. Limited and Short-Lasting Virus Neutralizing Titers Induced by Inactivated SARS-CoV-2 Vaccine. Emerg Infect Dis. 2021 Dec;27(12):3178–80.

18. Li M, Yang J, Wang L, Wu Q, Wu Z, Zheng W, et al. A booster dose is immunogenic and will be needed for older adults who have completed two doses vaccination with CoronaVac: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial. medRxiv [Preprint]. 2021 Aug 8 [cited 2021 Aug 31]. <https://doi.org/10.1101/2021.08.03.21261544>

19. Pan H, Wu Q, Zeng G, Yang J, Jiang D, Deng X, et al. Immunogenicity and safety of a third dose, and immune persistence of CoronaVac vaccine in healthy adults aged 18-59 years:

interim results from a double-blind, randomized, placebo-controlled phase 2 clinical trial. medRxiv [Preprint]. 2021 [cited 2021 Oct 10]. <https://doi.org/10.1101/2021.07.23.21261026>

20. World Health Organization. Interim recommendations for use of the inactivated COVID-19 vaccine, CoronaVac, developed by Sinovac: Interim guidance [Internet]. Geneva: World Health Organizaiton; 2021 May 24 [updated 2021 Oct 21, cited 2021 Dec 1]. <https://apps.who.int/iris/rest/bitstreams/1382254/retrieve>

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Department of Disease Control, Ministry of Public Health, Thailand
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Investigation of a Methemoglobinemia Outbreak Caused by Eating Sausages with High Concentrations of Nitrates and Nitrites in Trang Province, Thailand, January 2022

Choopong Sangsawang[1]*, Nalinee Chuaydamrong[1], Thawatchai Luankaew[2], Thidapon Thepparat[1], Nutjamee Leesahud[1]

1 Office of Disease Prevention and Control Region 12 Songkhla, Department of Disease Control, Ministry of Public Health, Thailand

2 Trang Provincial Health Office, Ministry of Public Health, Thailand

*Corresponding author email: sangsawangchoopong@gmail.com

Abstract

In late January 2022, a cluster of methemoglobinemia cases across five provinces of Thailand was notified to the regional public health authorities. A joint investigation was conducted aiming to describe characteristics of the outbreak in one of the provinces, traceback the suspected food, and recommend prevention and control measures. We conducted a cross-sectional descriptive study, interviewing the cases, reviewing their medical records, and interviewing their parents and treating physicians. An active case finding was conducted. A probable case was defined as a person who presented with acute central cyanosis with oxygen saturation less than 92% by pulse oximetry. Suspected food samples were collected for nitrates and nitrites testing. Three cases (2 males, 1 female) were identified and there was no death. Their ages ranged from 8–12 years. The sausages came from the same source and were found to have high concentrations of nitrates (1,270.8–1,690.0 mg/kg) and nitrites (3,554.5–3,776.2 mg/kg). The sausages were identified as a likely cause of the outbreak. Government regulation, product liability laws, and food safety concerns among food retailers and customers are important to reduce the impact of consuming unsafe foods.

Keywords: methemoglobinemia, sausages, nitrates, nitrites, Trang

Introduction

Methemoglobinemia is a rare disorder associated with oxidization of divalent ferro-iron of hemoglobin to ferri-iron of methemoglobin (MetHb), resulting in hypoxia due to impaired oxygen release to the tissue.[1–3] The normal level of MetHb in human blood is less than 1%. There is a direct correlation between MetHb levels and clinical signs and symptoms. Values less than 10% are associated with low pulse oximeter levels, alteration of the skin color and being asymptomatic. Values between 10–30% are associated with cyanosis, dark brown blood, and being asymptomatic and confused. Values between 30–50% are associated with dyspnea, dizziness, syncope, confusion, chest pain, palpitation, headache and fatigue. Values between 50–70% are associated with metabolic acidosis, arrhythmias, seizure, delirium and coma, while MetHb values above 70% are considered potentially lethal.[3–4] Acquired methemoglobinemia is mainly due to the exposure to oxidizing agents such as drugs or substances that cause oxidation of the hemoglobin.[3] There are numerous drugs that can cause methemoglobinemia including sulfonamides, dapsone, aniline derivatives, and nitrites. The most common causative drugs are benzocaine and lidocaine.[5–7] Nitrates and nitrites contaminating water supplies or used as preservatives in foods can also be triggering agents.[8] Among 62 food-related methemoglobinemia studies in which oxidizing agents were identified, nitrates and nitrites were the predominant suspected agent.[9]

During 28–30 Jan 2022, the situation awareness team of the Office of Prevention and Control Region 12 Songkhla (ODPC12) was notified of a cluster of methemoglobinemia cases in Kalase Subdistrict, Sikao District, Trang Province. Three cases were referred to Trang Provincial Hospital with acute central cyanosis and hypoxemia after all had eaten a particular type of sausage. During the same period, another five methemoglobinemia cases from Chiang Mai, Kanchanaburi, Saraburi and Phetchaburi Provinces were notified by the Ramathibodi Poison Center (RPC). A smoked chicken sausage purchased on the internet was the suspected cause of the outbreak. Staff from ODPC12 joined the Trang Provincial and District Health Offices to investigate the outbreak during 31 Jan–2 Feb 2022. The objectives were to verify the diagnosis, describe characteristics of the outbreak, traceback the suspected food, and recommend prevention and control measures.

Methods

ODPC12, in collaboration with Trang Provincial Health Office, Trang Hospital, Sikao District Health Office and Kalase Health Promotion Hospital, conducted a descriptive cross-sectional study. Face-to-face interviews were conducted with the cases, their parents and the treating physicians. Medical records of the cases and informal reports from the RPC were reviewed. Data collected included demographic characteristics, clinical history, treatment, outcomes, consumption of suspected food, and other potential risk factors. An active case finding was performed using a network of Trang Hospital's physicians and public health personnel using a software application (Line groups). Trang Provincial Health Office communicated an official order document including the active case finding guideline and a case definition to all hospitals and district health offices in Trang Province. A probable case of hemoglobinemia was defined as a person who visited a hospital or a health promotion hospital in Trang Province during 20 Jan–7 Feb 2022 and presented with acute central cyanosis and blood oxygen saturation less than 92% by pulse oximetry without cardiogenic, pulmonary or central nervous system causes and had at least one of the following two inclusion criteria: (i) blood drawn was chocolate-brown color; (ii) had history of consuming preserved food such as sausages or Vietnamese pork sausages within 4 hours before developing symptoms. A confirmed case was defined as a probable case who had a blood MetHb concentration exceeding 2%. Family members of the cases were interviewed eliciting demographic data, amount of suspected food consumption, and relevant clinical history.

Laboratory Study

Two of the three probable methemoglobinemia cases had available whole blood specimens in an EDTA tube. The specimens were collected on the date of onset and kept at a temperature of 2–8 °C. Measuring the methemoglobin concentration and confirming a diagnosis of methemoglobinemia was done by CO-oximetry at the Clinical Chemistry Laboratory Unit, Department of Pathology, Faculty of Medicine, Ramathibodi Hospital. Leftover sausages and those from the same lot eaten by the cases were collected for nitrates and nitrites testing at Trang Medical Science Center by high performance liquid chromatography technique.

Suspected foods were traced back after we performed in-depth interviews with the cases' parents, shopkeepers and a food dealer. Data collected consisted of the geographic distribution of sausage packages from the suspected lot, number of remaining packages in Trang Province, information of the source, and other potential risk factors. Multiple organizations from both the provincial and national level jointly conducted the investigation as the outbreak occurred in many regions of Thailand. We reported the results of our investigation to the Division of Epidemiology, Department of Disease Control and the Thai Food and Drug Administration (Thai FDA) in order for our results to be linked with other events and to broaden the search for the causative food source.

Results

Descriptive Epidemiology

Among the cluster of clinically suspected methemoglobinemia cases detected and notified by the RPC during 28–30 Jan 2022, eight were hospitalized and there were no deaths. Five were female and three were male, and their ages ranged from 1–12 years (median 7.5 years). The first case, from Kanchanaburi Province, developed symptoms on 20 Jan 2022 followed by a second case, from Trang Province, who developed symptoms on 26 Jan 2022. The last two cases, also from Trang Province, both developed symptoms on 29 January. The geographical distribution of cases by province is shown in Figure 1. All cases presented with acute central cyanosis and hypoxemia within 15 minutes to 2 hours (median 90 minutes) after eating packaged sausages. The range of oxygen saturation was 79–90% (median 85%). The packaging and labelling of the sausages varied by province. In Trang Province, the label on the package mentioned only the brand of the sausage, whereas in three other provinces, the label read "Smoked footlong chicken sausages, 1,000 grams". In one province, there was no label on the package.

Figure 1. Geographic distribution of reported cases of clinically suspected methemoglobinemia cases by province, 28–30 Jan 2022

In Trang Province, three patients from two separate families met the case definition; one confirmed case and two probable cases were epidemiologically linked and no additional cases were identified by the active case finding. The first case, a 12-year-old boy, developed symptoms on 26 Jan 2022 and the remaining two cases, an 8-year-old boy and a 9-year-old girl, developed symptoms on 29 Jan 2022 (Figure 2). The incubation periods ranged from 15 minutes to 1 hour. All cases developed acute central cyanosis, acute peripheral cyanosis, and nausea/vomiting. Other presenting symptoms are shown in Table 1. The level of oxygen saturation on arrival to the emergency room ranged from 79–90%. All cases were managed in the pediatric intensive care unit with 10–15 liters per minute (LPM) supplemental oxygen by a non-rebreather mask and other supportive care including fluid and electrolyte correction. The duration of hospital stay was 1–3 days and all three recovered.

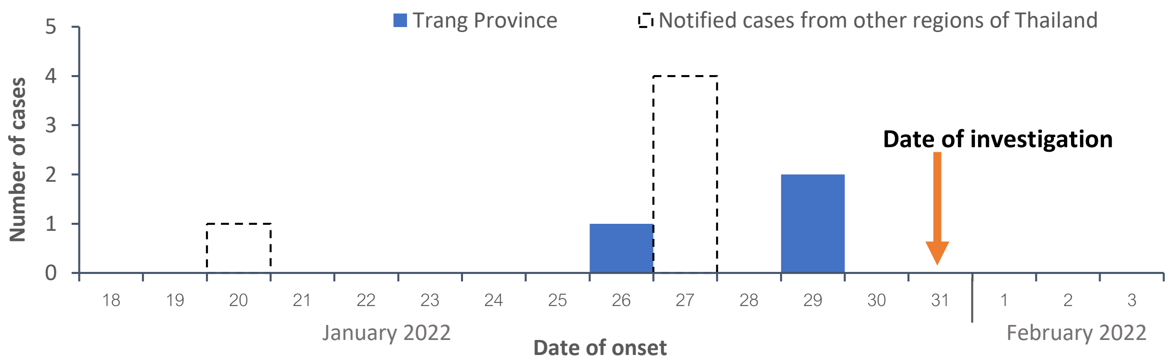

Figure 2. Number of methemoglobinemia cases by date of onset during 20 Jan–7 Feb 2022

Family 1: A 12- year-old boy with no underlying disease presented with acute central cyanosis, peripheral cyanosis, dizziness and weakness 30 minutes after eating 8 pieces of sausage. The boy's symptoms were noticed by his mother, who immediately took him to Sikao District Hospital. At the emergency room, his blood oxygen saturation was 79%. He received oxygen supplementation and was referred to Trang Provincial Hospital with the provisional diagnosis of acute central cyanosis, cause unspecified. His pulse oximetry showed that his blood oxygen saturation level was 86%. His blood was taken and showed a chocolate-brown color. He was promptly diagnosed with methemoglobinemia based on his clinical presentation and history of sausage consumption. The laboratory at Trang Provincial Hospital has no capability to test for MetHb. The RPC was consulted for a second opinion. The boy received

10–15 LPM of supplemental oxygen via a non-rebreather mask with close monitoring in the pediatric intensive care unit. On 28 Jan 2022, his clinical cyanosis recovered and his oxygen saturation level was 96% and he was discharged from the hospital. On interviewing the boy's mother, the consumed sausages were bought from a shop in the village and were fried before eating. The boy's mother had no symptoms after consuming only half of one sausage and neither did the boy's elder sister who ate one small piece.

Family 2: On 29 Jan 2022, an 8-year-old boy and his 9-year-old elder sister developed acute central cyanosis, peripheral cyanosis, chest pain, nausea/vomiting and dyspnea after eating 6 and 2 pieces of sausages, respectively. The boy's incubation period was 15 minutes while for the girl it was 1 hour. Both were with their mother when symptoms developed and they were promptly taken to Wangwiset District Hospital in Trang Province, blood oxygen saturation at room air of the boy and the girl was 85% and 90%, respectively. The attending physician consulted the RPC and referred the siblings to Trang Provincial Hospital. After receiving supplemental oxygen, their blood oxygen saturation was 90% and 95%, respectively. The provisional diagnosis was methemoglobinemia by clinical presentation, history of sausage consumption, and chocolate-brown blood color. Supportive treatment was given via 10–15 LPM of supplemental oxygen by a non-rebreather mask. Both recovered and were discharged on 31 Jan 2022. The suspected food was a sausage which was bought from a community market and fried before being served. The sausages were the same brand as those eaten by the first case but the characteristics of the sausages and the package label differed.

Table 1. Characteristics and clinical presentation of methemoglobinemia cases, Trang Province, 20 Jan–7 Feb 2022

Characteristics	Case 1 (family 1)	Case 2 (family 2)	Case 3 (family 2)
Type of case	Probable	Confirmed	Probable
Age (years) / gender	12 / male	8 / male	9 / female
Date of symptoms onset	26 Jan 2022	29 Jan 2022	29 Jan 2022
Time from ingestion to symptoms onset	30 minutes	15 minutes	1 hour
Implicated food	**Sausage brand X**	**Smoked sausage brand X**	**Smoked sausage brand X**
Sausages consumed (pieces)	8	6	2
Clinical presentation			
Acute central cyanosis	Yes	Yes	Yes
Acute peripheral cyanosis	Yes	Yes	Yes
Nausea/vomiting	Yes	Yes	Yes
Dizziness	Yes	No	Yes
Chest pain	No	Yes	No
Weakness	Yes	No	No
Facial pallor	Yes	No	No
Dyspnea	No	Yes	No
Oxygen saturation by pulse oximetry (%)			
At the first hospital (room air)	79	85	90
After administration of oxygen	86	90	95
Blood MetHb concentration (%)	**Not done**	**10.0**	**0.3**
Sample collection date	-	29 Jan 2022	29 Jan 2022
Laboratory receiving/testing date	-	2 Feb 2022	2 Feb 2022
Reporting date	-	3 Feb 2022	3 Feb 2022
Type of oxygen therapy	Oxygen 10–15 LPM by a non-rebreather mask		
Methylene blue prescribed	No	No	No
Outcome	Recovered	Recovered	Recovered

Note: First arterial blood gas results at the provincial hospital

Laboratory Results

Of these three cases, the two from the second family had leftover blood specimens available for collecting on the day of symptoms onset. The MetHb concentration of these two cases were 10.0% and 0.3% (Table 1). As shown in Table 2, there was a high concentration of nitrates and nitrites in sausages obtained from the same lot as those consumed by the first case and in leftover sausages uneaten by cases 2 and 3.

Table 2. Laboratory results of suspected foods in a methemoglobinemia outbreak, Trang Province, 20 Jan–7 Feb 2022

	Sample weight (g)	Sample collection date	Laboratory testing date	HPLC results (mg/kg)[a]	
				Nitrite[a]	Nitrate[b]
Case 1					
Leftover sausages	NA	NA	NA	NA	NA
The same lot of sausages	2,000	31 Jan 2022	31 Jan 2022	3,554.5	1,690.0
Cases 2 and 3					
Leftover sausages	100	31 Jan 2022	31 Jan 2022	3,776.2	1,270.8
The same lot of sausages	NA	NA	NA	NA	NA

Note: HPLC: High-performance liquid chromatography. NA: Not available. [a]Notification from the Ministry of Public Health in 2016: the maximum amount should not be more than 80 mg/kg. [b]Prohibited in all preserved meat products

Traceback of Suspected Food by Multi-Organizations

Figure 3 shows a flow diagram of the traceback process of the suspected sausages. The sausages consumed by the three cases in Trang Province came from the same source. The lot, consisting of 80 packs of sausages, were sent to a wholesale shop in Thungsong District, Nakhon Si Thammarat Province and then distributed to retailers in Sikao District. Fifty-two packs of sausages from this lot remained, 20 in the wholesale shop and 32 in the retail shops. Each pack weighed 500 grams and contained 12 sausages. This information was reported to the Thai FDA and the Division of Epidemiology, Department of Disease Control on 31 Jan 2022.

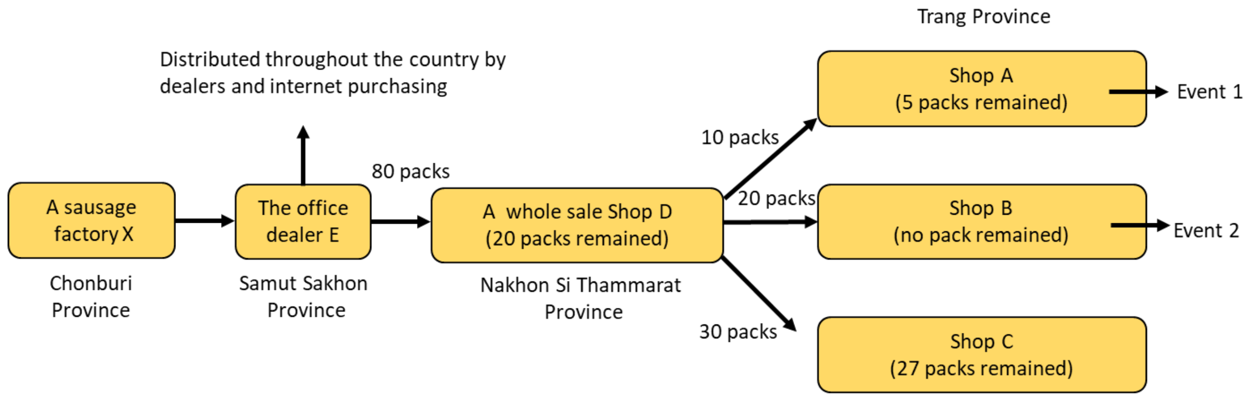

Figure 3. Traceback of suspected food in a methemoglobinemia outbreak, Trang Province, 20 Jan–7 Feb 2022

On 2 Feb 2022, the Thai FDA together with the Consumer Protection Police Division and the Division of Epidemiology, Department of Disease Control identified the production site, which was located in Chonburi Province. The site did not have a production license and the production process did not have a standard method of measurement of the chemical contents. Nitrates and nitrites were poured in manually and their amounts were not measured accurately.

Discussion

This study investigated a methemoglobinemia outbreak after cases had consumed packaged sausages with high nitrates and nitrites content. All cases were clinically diagnosed by their presentation of unexplained acute central cyanosis and hypoxemia with chocolate-brown colored blood and a history of sausage consumption. One case was confirmed with high blood MetHb concentration of 10% by CO-oximeter test, which is a non-invasive measurement method and gold standard for detecting the fraction of methemoglobin in the blood.[9] Due to clinical signs and symptoms of the cases including dizziness, dyspnea, chest pain and weakness, MetHb estimate levels may range from 30–50%. Delays in sending laboratory specimens may have resulted in a lower MetHb concentration than would have been detected had the specimens been sent sooner. MetHb is unstable as it can be converted enzymatically to hemoglobin and becomes oxyhemoglobin if measurement is delayed. A past study found that MetHb is stable for up to 2 hours in dipotassium EDTA, lithium heparin or potassium oxalate as anticoagulants.[10]

Methemoglobinemia is a rare but life-threatening condition. Severe methemoglobinemia is fatal due to persistent hypoxemic injury and multiple organ failure despite treatment with maximal ventilator support, especially when specific treatment such as methylene blue, ascorbic acid or blood transfusion is not delivered in time.[3,11–12] The severity depends on the MetHb level and access to appropriate treatment. A large systematic review of food-induced methemoglobinemia during 1936–2020 found that there were 568 cases with 35 deaths resulting in an overall case fatality rate of 6.2%. The majority of cases survived, even with severe methemoglobin levels of up to 89%, provided that methylene blue was administered.[9]

Most of the community and provincial hospitals in Thailand, including Trang Provincial hospital, have no capability to perform MetHb tests. Methemoglobinemia should be considered in cyanosis patients without cardiopulmonary disease who are unresponsive to oxygen therapy. A useful clinical sign is chocolate-brown colored blood. The attending doctor assessed the toxic severity by repeated evaluation of clinical hypoxemia and regular monitoring with pulse oximetry and arterial blood gas. The RPC in Thailand has consulting specialists available 24 hours a day and, during our investigation, gave the treating physician confidence in the diagnosis and treatment plan. Methylene blue from a nearby tertiary hospital was prepared and available for use if required. The recommendation for asymptomatic cases is regular monitoring without additional treatment. Oxygen supplementation should be added as needed.[3,13] The first-line treatment for symptomatic cases with a high MetHb level is methylene blue with a starting dose of 1–2 mg/kg of 1% methylene blue. Administration can be repeated up to a cumulative dose of 5.5 mg/kg if there is no response after 30 minutes. Ascorbic acid can be added as an adjunctive therapy. Patients who do not respond to first-line therapy should undergo blood transfusion or hyperbaric oxygen therapy. A high MetHb level is defined as a level more than 10–30%, with higher than 20% being the most reported level in the literature.[3]

Sodium nitrate and sodium nitrite are widely used to retard bacterial growth and to preserve the color of lean meat. Many previous studies reported that methemoglobinemia occurred after consumption of food containing high concentrations of nitrates or nitrites.[14–18] In 2016, the Ministry of Public Health prohibited the addition of nitrates in all preserved meat products and prohibited the addition of nitrites in smoked sausages. The maximum level of nitrites allowed to be added to preserved meat products, such as sausages, bologna, Chinese sausages (Kuncheing) or Northeastern Thai sausages, should not exceed 80 mg/kg of the product. The sausages produced at the factory in Chonburi contained 44–47 times more nitrites than the level allowed. Although the sausages from this lot were distributed to many customers in Trang, we could not identify additional cases by active case finding. Methemoglobinemia cases who have blood MetHb concentrations lower than 10% may be asymptomatic.[3] As the blood MetHb concentration is directly related to the amount of food consumed, those who consumed a small amount of sausage from the affected lot, for example the mother of the first case and the elder sister of the second case, reported no symptoms and therefore did not go to the hospital for further examination.

The suspected sausages came from the same source and were distributed to many provinces through dealers and internet purchases. This study presented many points needed for consideration concerning food safety. We found that the sausage factory did not have a production license and the production process did not have a standard method of measuring the chemical contents. The somewhat careless purchasing behavior of retailers and customers was also an important risk factor. Labels on food products should always be inspected to see if important information such as the serial number of the Thai FDA, date of manufacture and expiry date, name and location of the manufacturer, key ingredients and nutrition detail is included. None of this information was found on the packages of the suspected sausages. Recognition of the health dangers of unsafe food purchased on the internet is very important to the public's health.[19]

Public Health Actions and Recommendations

The Trang Provincial Health Office promptly communicated to the public about the risks of methemoglobinemia, advised them on their selection of sausages and preserved food that have the Thai FDA logo marked on the label with the ingredients and expiry date clearly visible. All remaining sausages from the same lot of suspected sausages in Trang were traced and prohibited to be sold. The shop owners were warned about the dangers of methemoglobinemia if these sausages were eaten and they agreed to return the remaining packs to the dealer to receive a refund. The Consumer Protection Group of Trang Provincial Health Office surveyed the preserved foods in the markets to assess the risk and give advice to the shop owners.

We notified the surveillance and rapid response team in Thungsong District, Nakhon Si Thammarat Province to conduct an active case finding in that area. The Division of Epidemiology, Department of Disease Control disseminated the surveillance information and investigation guidelines of methemoglobinemia to all local public health agencies throughout the country on 3 Feb 2022.

Regular monitoring of preserved foods in factories and markets according the Thai FDA guideline is needed to reduce the risk of excess chemicals in preserved foods. The government regulations must be enforced so that food factories follow standard operating procedures. Penalties must be given to factories that violate these regulations. Use of product liability laws also influences the practices of food businesses, and the consumer's right to seek compensation from the factory that allowed the food to become unsafe. Food retailers and customers should refuse products that fail to have standardized labels attached to the package. Regular monitoring of preserved foods in the factory and market according to the Thai FDA guideline.

Limitations

The patients' blood samples were taken on the date of symptom onset for other laboratories but the investigators could not promptly send the specimens to be examined for MetHb concentration. Therefore, the laboratory results may not accurately reflect the situation at the time of symptoms onset. In this outbreak investigation, we actively searched only symptomatic cases who visited a hospital or health promotion hospital, so the magnitude of the problem may be underestimated. Some asymptomatic or mild cases may have been missed.

Conclusions

Sausages with high nitrates and nitrites content were identified as the most likely cause of a hemoglobinemia outbreak in Trang Province in late January 2022. Three cases were identified with one having a laboratory confirmed methemoglobin level of 10%. All cases were children aged 8–12 years and all recovered after being treated with 10–15 liters/min of supplemental oxygen via non-rebreather mask. The high level of nitrates and nitrite concentration of the suspected sausages stemmed from the lack of standard operating procedures at the factory which produced the sausages. The factory also did not perform a proper measurement of the chemical contents of the sausages prior to distributing them to the wholesalers. Improved government regulations and product liability laws, and food safety concerns of food retailers and customers are important issues that can reduce the impact of consuming unsafe foods.

Acknowledgements

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Suggested Citation

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References

1. Prchal JT. Methemoglobinemia and Other Dyshemoglobinemias. In: Kaushansky K, Prchal JT, Burns LJ, Lichtman MA, Levi M, Linch DC. editors. Williams Hematology. 10th ed. New York: McGraw Hill; 2021.
2. Wright RO, Lewander WJ, Woolf AD. Methemoglobinemia: etiology, pharmacology, and clinical management. Ann Emerg Med. 1999;34(5):646–56.
3. Iolascon A, Bianchi P, Andolfo I, Russo R, Barcellini W, Fermo E, et al. Recommendations for diagnosis and treatment of methemoglobinemia. Am J Hematol. 2021 Dec 1;96(12):1666–78.
4. Skold A, Cosco DL, Klein R. Methemoglobinemia: pathogenesis, diagnosis, and management. South Med J. 2011;104(11):757–61.
5. McGuigan MA. Benzocaine-induced methemoglobinemia. Can Med Assoc J. 1981 Oct 15;125(8):816.
6. O'Donohue WJ Jr, Moss LM, Angelillo VA. Acute methemoglobinemia induced by topical benzocaine and lidocaine. Arch Intern Med. 1980 Nov;140(11):1508–9 .
7. Kane GC, Hoehn SM, Behrenbeck TR, Mulvagh SL. Benzocaine induced methemoglobinemia based on the Mayo Clinic experience from 28,478 transesophageal echocardiograms: incidence, outcomes, and predisposing factors. Arch Intern Med. 2007;167(18):1977–82.
8. Johnson CJ, Kross BC. Continuing importance of nitrate contamination of groundwater and wells in rural areas. Am J Ind Med. 1990;18(4):449–56.
9. McNulty R, Kuchi N, Xu E, Gunja N. Food-induced methemoglobinemia: A systematic review. J Food Sci [Internet]. 2022 Apr [cited 2022 Jun 11];87(4):1423–48. <https://ift.onlinelibrary.wiley.com/doi/full/10.1111/1750-3841.16090>

10. Lim SF, Tan IK. Quantitative determination of methaemoglobin and carboxyhaemoglobin by co-oximetry, and effect of anticoagulants. Ann Clin Biochem. 1999 Nov;36:774–6.

11. Mansouri A, Lurie A. Concise Review: Methemoglobinemia. Am J Hematol 1993; 42(1):7–12.

12. Sahu KK, Mishra A. Methemoglobinemia: Challenges in Diagnosis and Management. J Assoc Physicians India. 2019 Aug;67(8):94.

13. Beradai MA, Labib S, Boujraf S, Harandou M.Acute methemoglobinemia due to ingestion of MAHIA wine brandy. Ann Afr Med. 2016 Oct–Dec;15(4):207–9.

14. Chan T Y. Food-borne nitrates and nitrites as a cause of methemoglobinemia. Southeast Asian J Trop Med Public Health. 1996 Mar;27(1):189–92.

15. Siripanich S. Toxic effects of ingestion of nitrates and nitrites. Weekly Epidemiological Surveillance Report. 2012 Jun 15;43(23):353–6. Thai.

16. Greenberg M, Birnkrant WB, Schiftner JJ. Outbreak of sodium nitrite poisoning. Am J Public Health. 1944;35:1217–20.

17. Kaplan A, Smith C, Promnitz DA, Joffe BI, Seftel HC. Methemoglobinemia due to accidental sodium nitrite poisoning. S Afr med J. 1990 Mar 17;77(6):300–1.

18. Matteucci O, Diletti G, Prencipe V, Giannatale ED, Marconi MM, Migliorati G. Two case of Methemoglobinemia caused by suspected sodium nitrite poisoning. Vet Ital. 2008; 44(2):447–53.

19. Centers for Disease Control and Prevention. Severe methemoglobinemia and hemolytic anemia from Aniline purchased as 2C-E (4-ethyl-2,5-dimethoxyphenethylamine), a recreational drug, on the internet—Oregon, 2011. MMWR. 2012 Feb 10;61(5):85–8.

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Field Epidemiology Training Program, Division of Epidemiology
Department of Disease Control, Ministry of Public Health, Thailand
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An Intermittent Gastroenteritis Outbreak of Rotavirus Genotype G9P[8] in a Hotel in Songkhla Province, Thailand, April–May 2019

Choopong Sangsawang*, Sawanya Chantutanon, Laddawan Sukhum, Thidapon Thepparat

Office of Disease Prevention and Control Region 12 Songkhla, Department of Disease Control, Ministry of Public Health, Thailand

*Corresponding author email: sangsawangchoopong@gmail.com

Abstract

A series of acute gastroenteritis outbreaks occurred among participants of two seminars at a hotel in Songkhla Province during 26–29 Apr 2019 and 8–10 May 2019. Investigations were done to determine the causes of the outbreaks and recommend control measures. A case was defined as a participant who developed diarrhea, vomiting, nausea or abdominal pain between 26–30 April (Seminar 1) or 8–13 May (Seminar 2). Samples of the drinking and cooking water used during the seminars were taken and rectal swabs from cases and food handlers were collected for bacterial culture and viral reverse transcription polymerase chain reaction tests. A retrospective cohort study was conducted to identify risk factors. Of 349 participants interviewed, 237 were cases, giving an attack rate of 67.9%. The ages of the cases ranged from 11–57 years (median 15 years). The most common symptoms were watery diarrhea (94.1%), abdominal pain (81.0%) and nausea (57.8%). Rotavirus was detected in five cases, three food handlers and a sample of water used for cooking. All were of the same genotype G9P[8]. Implicated dishes included spicy seafood salad (adjusted odds ratio (AOR) 4.5, 95% confidence interval (CI) 1.7–11.8), shrimp in sauce (AOR 2.9, 95% CI 1.0-8.2), roast duck with vegetables (AOR 2.9, 95% CI 1.2–7.3) and water from a cooler (AOR 2.0, 95% CI 1.0–3.9). Contaminated water and infected food handlers were probable sources of cross-contamination. After the hotel's water system was repaired and the food handlers were educated on safe food handling practices and good personal hygiene, no other outbreaks associated with the hotel were reported.

Keywords: rotavirus, food poisoning outbreak, Songkhla

Introduction

Group A rotaviruses (RVA) are the most important cause of acute gastroenteritis in humans globally, especially among young children in developing countries.[1,2] Five genotypes (G1P[8], G2P[4], G3P[8], G4P[8], and G9P[8] represent over 90% of global human RVA.[3] A previous study showed that G9P[8] strains emerged and predominated in Ghana in the 4th quarter of 1999 and caused a severe rotavirus outbreak among children in Central Australia during 2001.[4,5] Rotavirus infection among adults has been associated with a wide spectrum of disease severity and manifestations. The illness most frequently begins 2–6 days after ingestion of the pathogen and continues for 1–4 days, with common symptoms including diarrhea, fever, headache, malaise, nausea, and cramping.[6] Clusters of rotavirus infections in adults most frequently occur in communities, and one of the largest outbreaks involved nearly 3,500 people in 1964 in an isolated area of Micronesi.[3,7] Outbreaks of rotavirus infection have also occurred in long-term healthcare facilities, particularly those with close living quarters; thus, compromised host immunity and multiple comorbid disorders might help facilitate the spread of infection.[8–13] The primary mode of transmission is the fecal-oral route usually through direct contact between people. However, since the virus is stable in the environment, transmission can also occur through ingestion of contaminated water or foods and contact with contaminated surfaces or objects.[14] The other most common causative agents of viral gastroenteritis in humans worldwide are noroviruses, adenoviruses, and astroviruses, most of which are transmitted via the fecal-oral route, including contaminated food and water and presenting symptoms include watery diarrhea, nausea, vomiting, fever, and abdominal pain.[15] Norovirus is a single stranded RNA virus belonging to the family *Caliciviridae.* The virus is transmitted by low doses and common symptoms include vomiting and diarrhea. Infections are more common in winter. Human adenoviruses are double strand viruses belonging to the family *Adenoviridae*. Serotypes 40 and 41 are the most remarkable pathogens associated with acute gastroenteritis. Human astroviruses are single-stranded RNA viruses belonging to the *Astroviridae* family. Diarrhea is common but milder than those caused by rotaviruses or noroviruses, and symptoms resolve spontaneously.[16–18]

A series of acute gastroenteritis outbreaks occurred among participants of two seminars held at a hotel in Songkhla Province on 26–29 April and 8–10 May 2019. On 29 April, the Office of Disease Prevention and Control was notified of the first cluster of acute gastroenteritis cases among participants of the first seminar. The first participant became ill with acute watery diarrhea, abdominal pain, nausea, and vomiting on 27 April. Most of the cases were adults who came from other provinces and planned to go home on that day. A joint investigation was initiated promptly on 29 April. A bacterial cause was suspected so rectal swabs were obtained from participants and sent for bacterial culture. All swabs were negative for a bacterial pathogen.

On 7–8 May, a second laboratory investigation was done to detect a possible viral pathogen. Rectal swabs from food handlers and water samples were collected and tested. During the process of investigation on 12 May, there was a notification of a second cluster of gastroenteritis cases among participants of a second seminar at the hotel with the same clinical presentation as the cases who attended the first seminar. Hence, a joint investigation was conducted during 29 Apr to 13 May 2019 to identify the causative agent, source of illness and recommend control and prevention measures.

Methods

A list of seminar participants was obtained from registration records. Face-to-face and telephone interviews with the participants of the two seminars were conducted. Respondents were interviewed about their demographics, clinical signs and symptoms, and food and water consumption while attending the seminars. A probable case was defined as a participant who had at least one of the following symptoms: diarrhea, vomiting, nausea, or abdominal pain and with an onset date between 26–30 April among participants of the first seminar or 8–13 May among participants of the second seminar. A confirmed case was defined as a probable case with a positive test result for rotavirus or norovirus by reverse transcription polymerase chain reaction (RT-PCR).

Separate retrospective cohort studies were conducted among participants of each seminar. All available participants were interviewed to classify their exposure to various food and drink during attending the seminars. The various food and drink consumed during 26–27 April for the first seminar and 8–9 May for the second seminar were included in the analysis. Those who met the probable case definition were designated as cases. A non-case was a participant who had no sign nor symptom during the same time period. Relative risk was used to demonstrate an association between eating a particular food or drink at the hotel and the risk of being ill.

Rectal swabs were obtained from 25 symptomatic cases who had a date of onset not more than 8 (first seminar) or 3 (second seminar) days before the collection. Rectal swabs were also obtained from all asymptomatic food handlers employed by the hotel during the seminar. Cary Blair transport media and universal transport media were used for bacterial and viral testing, respectively. Bacterial cultures were tested at Songkhla Hospital, Hatyai Hospital and Bamrasnaradura Infectious Diseases Institute. RT-PCR tests for rotavirus, adenovirus, astrovirus and norovirus were done at Bamrasnaradura Infectious Diseases Institute. Samples of cooking and drinking water and ice were collected for bacterial culture at the Regional Medical Science Center 12 Songkhla and viral RT-PCR for rotavirus, norovirus, adenovirus, astrovirus and sapovirus at the Neuroscience Centre for Research and Development. Positive specimens of rotavirus among humans were tested for genotypes by the conventional RT-PCR method at Neuroscience Centre for Research and Development.

We inspected the food and water sanitation facilities of the hotel. Food handlers who worked at the kitchen and the restaurant during the seminars were interviewed.

Descriptive statistics were presented by computing percentages, medians and ranges. The Chi-square test was used to compare the proportion of risk factors between exposed and non-exposed groups. Multiple logistic regression models were used for multivariate analysis. Variables with a p-value less than 0.2 from univariate analysis were included in the multivariate model. Adjusted odds ratios (AOR) and 95% confidence intervals (CI) were calculated. All probabilities were 2-tailed, and p-values <0.05 were considered significant. All analyses were conducted in Stata version 14.

Results

Epidemiologic Investigation

The affected hotel, located near Samila Beach in Songkhla Province, consists of 208 bedrooms. The first seminar included participants from the Nationwide Youth Network and was held during 26–29 Apr 2019. The second seminar contained students from the Science Match Ability program of a high school and was held during 8–10 May 2019. There were 447 participants of both seminars, of which 349 (78.1%) were interviewed. The attack rate was 67.9% (237/349). There were five confirmed rotavirus cases and two confirmed norovirus cases. The age of the cases ranged from 11–57 years (median 15 years) and 120 (50.6%) were female. Three (1.3%) were hospitalized and there were no deaths.

The first seminar consisted of 208 participants, of which 144 were interviewed and 96 were probable cases with no confirmed case giving an attack rate of 66.7%. One case was hospitalized. The ages of the cases ranged from 12 to 46 years (median 19 years). The sex-specific attack rates were 66.3% (57/86) among male and 67.2% (39/58) among female participants. Most (95%) cases were Thai nationals from 40 provinces and 5 (5.2%) were foreigners from India and Sri Lanka. Symptoms of illness were watery diarrhea (91.7%), abdominal pain (76.0%), nausea (56.3%), vomiting (42.7%), fever (39.6%) and mucous diarrhea (4.2%) (Figure 1). The first case developed symptoms on 27 April at 7 p.m. and as shown in Figure 2, the peak occurred on 28 April. The suspected meal was the welcome dinner on 26 April 2019, at 6 p.m. The median incubation period was 2 days (range 1–3 days).

The second seminar contained 239 participants and included teachers and students. Of 205 (85.8%) interviewees, 141 cases were identified (attack rate 68.7%) and 2 (1.4%) cases were hospitalized. The sex-specific attack rates were 67.4% (60/89) and 69.8% (81/116) among male and female participants, respectively. The ages of the cases ranged from 11 to 57 years (median 15 years). The attack rate among teachers and students was 53.3% (8/15) and 70.0% (133/190), respectively. Symptoms of illness were watery diarrhea (95.7%), abdominal pain (84.4%), nausea (58.9%), fever (55.3%), vomiting (37.6%) and mucous diarrhea (2.1%) (Figure 1). The first case developed symptoms on 8 May at 3 p.m. and as shown in Figure 2, the number of cases peaked on 10 May. The median incubation period from the first meal was 2 days (range 1–4 days).

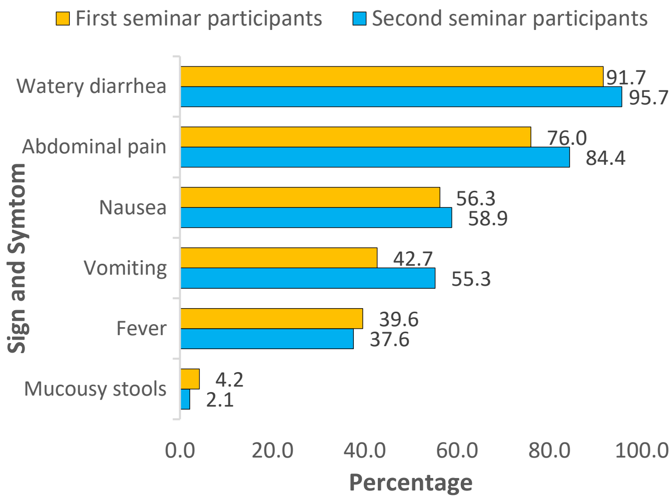

Figure 1. Signs and symptoms of acute gastroenteritis cases among the first seminar participants (n=96) and the second seminar participants (n=141), Songkhla Province, 26 Apr–13 May 2019

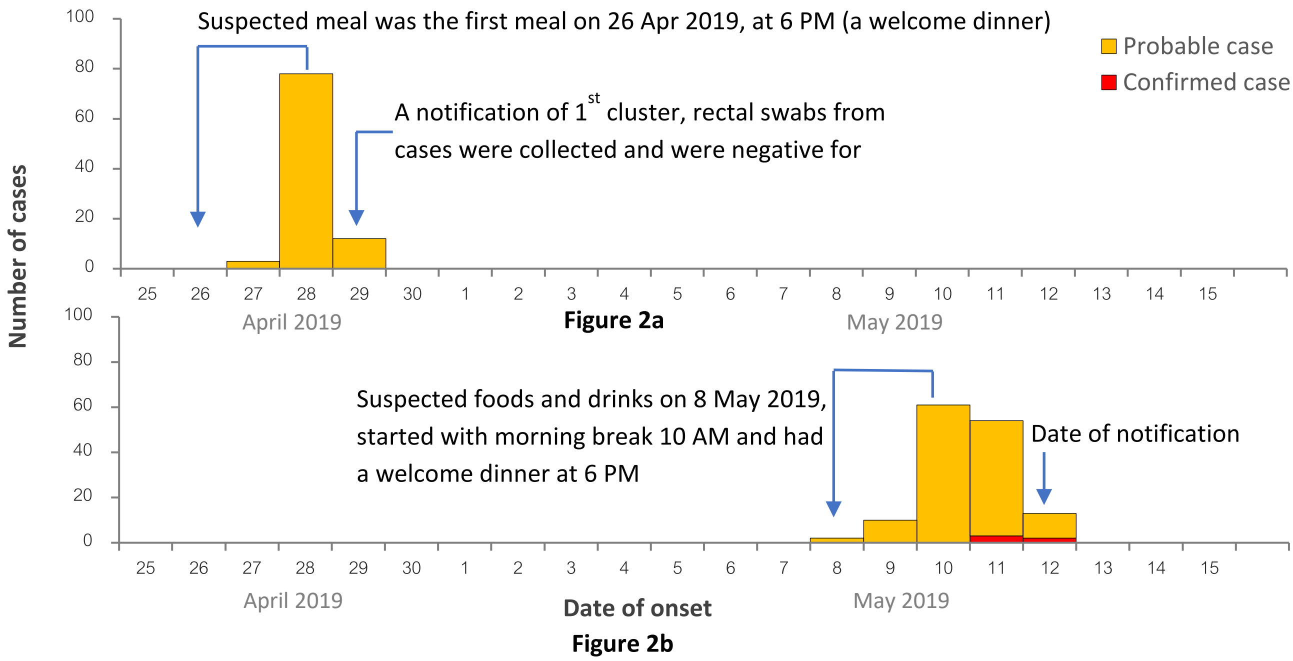

Figure 2. Number of gastroenteritis cases by date of onset among the first (Figure 2a, n=96) and second (Figure 2b, n=141) seminar participants, Songkhla Province, 26 Apr–13 May 2019

Retrospective Cohort Studies

A total of 144 interviewees from the first seminar and 205 interviewees from the second seminar were included in the analysis. Univariate analysis showed many food items were significantly associated with being a case for both seminars (Tables 1 and 2). On multivariate analysis, food items with an elevated risk for disease in the first seminar were the spicy seafood salad (AOR 4.5, 95% CI 1.7–11.8), shrimp in sauce (AOR 2.9, 95% CI 1.2–8.2), and roast duck with vegetables (AOR 2.9, 95% CI 1.2–7.3). In the second seminar, drinking water was the only significant risk factor (AOR 2.0, 95% CI 1.03–3.9).

Table 1. Risk factors in a gastroenteritis outbreak among the first seminar participants, Songkhla Province, 26–29 Apr 2019 (n=144)

Food items (date and time served)	Exposed		Non-exposed		Crude RR (95% CI)	Adjusted OR (95% CI)
	Case	Non-case	Case	Non-case		
26 April, 6 PM						
Spicy seafood salad	73	18	17	30	2.25 (1.52–3.33)[b]	4.51 (1.71–11.84)[b]
Shrimp in sauce	77	24	16	24	1.92 (1.29–2.85)[b]	2.91 (1.03–8.17)[b]
Roast duck with vegetables	62	18	30	30	1.57 (1.19–2.07)[b]	2.91 (1.16–7.28)[b]
Fried squid	52	18	44	30	1.24 (0.98–1.57)[a]	0.66 (0.40–1.10)
Fried mixed vegetables	25	8	65	40	1.28 (1.03–1.59)[b]	1.50 (0.73–3.08)
Chicken in sour soup	73	33	23	15	1.13 (0.85–1.51)	-
Candied pumpkin	37	12	55	36	1.27 (1.02–1.59)[b]	1.30 (0.49–3.46)
27 April, 10 AM–2 PM[c]						
Eclairs	32	13	59	35	1.17 (0.94–1.47)[a]	1.04 (0.63-1.70)
Fried mushroom with shrimp	54	19	37	29	1.34 (1.05–1.72)[b]	1.32 (0.51–3.41)
Fried snapper with celery	47	15	45	33	1.33 (1.06–1.68)[b]	1.02 (0.39–2.63)
Fried anise with shrimp	24	6	66	42	1.36 (1.10–1.68)[b]	2.08 (0.60–7.17)
Chicken in sour soup	72	33	24	15	1.11 (0.84–1.47)[a]	0.89 (0.57–1.39)

Note: CI: confidence interval. RR: relative risk. OR: odds ratio. [a]p-value <0.2 in univariate analysis. [b]p-value <0.05. [c]At the dinner on 27 April the participants did not eat together

Table 2. Risk factors in a gastroenteritis outbreak among the second seminar participants, Songkhla Province, 8–13 May 2019 (n=205)

Food items (date and time served)	Exposed		Non-exposed		Crude RR (95% CI)	Adjusted OR (95% CI)
	Case	Non-case	Case	Non-case		
Drinks during 8–9 May						
Water in a cooler	106	41	32	23	1.23 (0.96–1.58)[a]	1.98 (1.01–3.87)[b]
Juice	55	22	83	41	1.06 (0.88–1.28)	-
Food items by date and time						
8 May, 10–13 AM (not all participants attended this period)						
Steamed dumpling	53	29	14	8	1.01 (0.76–1.44)	-
Omelet	130	56	11	8	1.21 (0.78–1.81)	-
Sour soup with fish	43	27	25	10	0.86 (0.65–1.13)	-
8 May, 6 PM (welcome dinner)						
Spicy seafood salad	119	53	21	11	1.05 (0.80–1.38)	-
Roasted duck	124	48	16	16	1.44 (1.01–2.06)[b]	1.31 (0.83–2.06)
Fried squid	105	42	35	22	1.16 (0.92–1.46)[a]	0.96 (0.77–1.19)
Shrimp in sauce	122	54	18	10	1.07 (0.80–1.44)	-
Fried mixed vegetables	98	35	42	29	1.24 (1.00–1.54)[b]	1.28 (0.90–1.83)
Thai dessert	107	44	33	20	1.14 (0.90–1.45)	-
9 May, 10 AM–1 PM						
Boiled egg	89	43	46	20	0.96 (0.79–1.17)	-
Chicken in sour soup	115	50	20	13	1.15 (0.85–1.54)	-
Fried lettuce	104	40	31	23	1.25 (0.97–1.61)[a]	0.67 (0.40–1.02)
Mixed fruit	107	51	28	12	0.94 (0.76–1.21)	-

Note: CI: confidence interval. RR: relative risk. OR: odds ratio. [a]p-value <0.2 in univariate analysis. [b]p-value <0.05

Laboratory Results

A total of 21 fecal specimens from the cases were negative for bacterial pathogen. Five of nine (55.5%) rectal swabs from the cases on 13 May were positive for rotavirus and 2 (22.2%) samples were positive for norovirus. Rotavirus was also identified in fecal matter of 3 food handlers and 1 sample of water for cooking. The same genotype G9P[8] was confirmed among the cases and food handlers. Adenovirus was identified in fecal matter of a food handler and water for cooking and drinking. *Escherichia coli* and *Staphylococcus aureus* were also identified from samples of water for cooking and drinking (Table 3).

Table 3. Gastrointestinal pathogen isolates from gastroenteritis cases, asymptomatic food handlers and water samples from the study hotel, Songkhla Province, 26 Apr–13 May 2019

Source of isolates	Collection date	Bacterial culture		Viral RT-PCR	
		Number of isolates (samples)	Pathogen (n)	Number of isolates (samples)	Pathogen (n)
Symptomatic cases	28–29 April	0 (5)	-	Not collected	-
	7 May	Not collected	-	0 (4)	-
	13 May	0 (16)	-	7 (9)	Rotavirus, G9P[8] (3) Rotavirus, untyped (2) Norovirus (2)
Asymptomatic food handlers	8 May	1 (12)	*A. veronii* (1)	2 (11)	Rotavirus, G9P[8] (2)
	13 May	Not collected	-	2 (16)	Rotavirus (1) Adenovirus (1)
Water for cooking[a]	29 April	1 (1)	*E. coli* (1) *S. aureus* (1)	Not collected	-
	8 May	Not collected	-	1 (1)	Rotavirus (1) Adenovirus (1)
Drinking water[b]	29 April	1 (1)	*E. coli* (1) *S. aureus* (1)	Not collected	-
	8 May	Not collected	-	1 (1)	Adenovirus (1)

Note: [a]water from the retention system. [b]water from the water cooler near the seminar room

Environmental Investigation

The source of water for the hotel is tap water and a groundwater well which is located near a sewage pond. The water for cooking and drinking come from both water sources because the pipe system is interconnected. Water from the well goes through a filter system without any chlorination or other disinfection process (Figure 3). No chlorine was detected from water obtained from the end of the pipe.

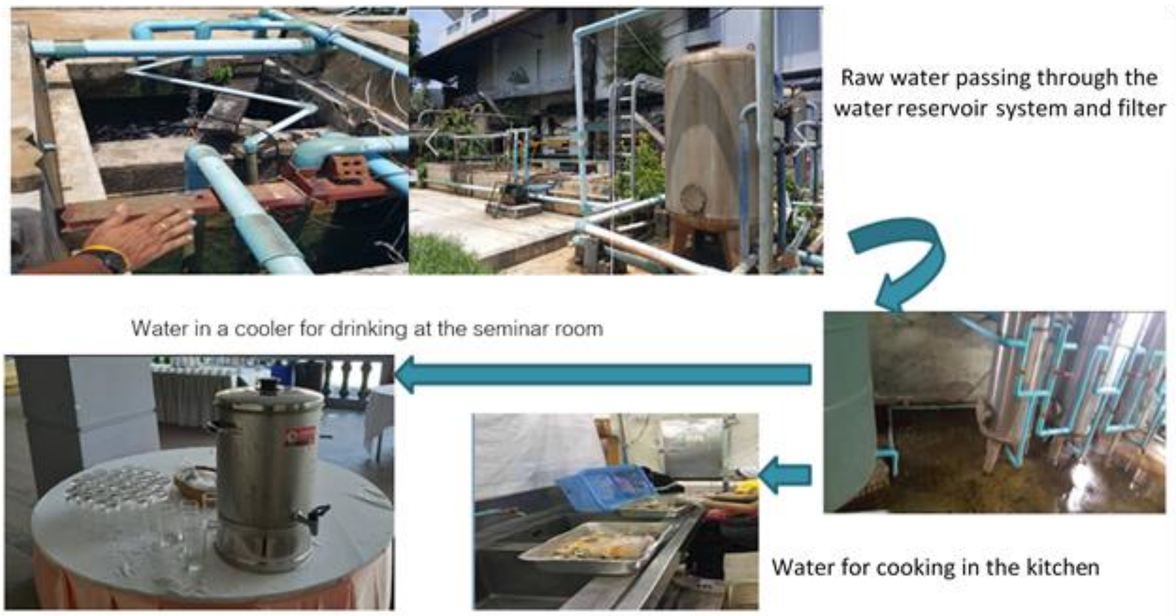

Figure 3. Trace back of the water for cooking and water in a cooler, a gastroenteritis outbreak, Songkhla Province, 26 Apr–13 May 2019

Discussion

Rotavirus and norovirus were considered as the probable causative agents of these acute gastroenteritis outbreaks with rotavirus as the main pathogen for the 2nd seminar. Rotavirus outbreaks among adults is not confined to geriatric populations. Many studies among healthy adults showed that the prevalence of symptoms among infected cases ranges from 22–50%.[7,19–23] We did not test for viral pathogens among asymptomatic participants, so our attack rate may be lower than the actual infection rate. A gastroenteritis outbreak investigation among adolescents and adults presenting with watery diarrhea, fever, nausea, and abdominal cramping should consider viral causes, including rotavirus and norovirus, in the differential diagnosis. Our report showed a delay in laboratory investigation for viral pathogens in the first cluster according to the contribution of viral pathogens that typically affect children is not recognized. Although the pathogen could not be confirmed from cases of the first cluster, due to the clinical presentation and the linkage of infected food handlers and contamination of water source, the same rotavirus infection is suspected to have caused both outbreaks.

The rotavirus G9P[8] strain was found during the outbreak and was implicated as the main pathogen. The G9P[8] strain was reported as a cause of the largest outbreak of rotavirus disease in Central Australian history in May 2001 when a total of 246 children with acute gastroenteritis arrived at the emergency department of the Alice Springs Hospital, of which 137 were hospitalized.[5] The severity of the cases in that study was higher than in our study probably because our population at risk were healthy adolescents and adults. The rotavirus surveillance project in Thailand during July 2001–June 2003 showed that the G9 serotype is predominant each year, while other identified rotavirus serotypes included G2, G4, G1, and G3.[31]

A spicy seafood salad, roast duck with vegetables, shrimp in sauce and drinking water from a cooler were the most likely sources of infection supported by laboratory confirmation of rotavirus detected in stool samples of food handlers and water for cooking which came from the same source as the drinking water. Many food items may have been contaminated with the pathogen by cross-contamination from infected food handlers or from the water used as an ingredient or for cleaning raw materials such as vegetables that were then added to the dishes without heating. Previous water and foodborne rotavirus outbreaks such as a waterborne outbreak of gastroenteritis in 1981 in Eagle-Vail and Avon, Colorado, United States in which severity of symptoms correlated with the amount of tap water consumed and foodborne rotavirus outbreaks reported in Japan and the United States.[25–27]

Groundwater can provide safe drinking water as long as the source is not polluted and the water is sufficiently treated. Public water systems often use a series of water treatment steps that include coagulation, flocculation, sedimentation, filtration, and disinfection. At the disinfection stage, chlorine, chloramines, ozone or other disinfectants are added to the water to destroy potential pathogens such as bacteria, viruses, and parasites.[28,29] The drinking water and water used for cooking at the affected hotel came from a groundwater well which was located near a sewage pond. We found many gastrointestinal pathogens including rotavirus, adenovirus, *Escherichia coli*, and *Staphylococcus aureus* in stool samples obtained from the food handlers and in the water supply, suggesting that the water source was contaminated with human feces. The most likely cause of contamination was leakage from the nearby sewage pond and/or deterioration of the water pipe system. There was no disinfection process on the water used for drinking and cooking.

Asymptomatic infection among food handlers was suspected to play an important role in disease transmission. Pathogens can be introduced into food from infected humans who handle the food without thoroughly washing their hands.[30] According to the standard of food safety, a food business should exclude employees who have a foodborne disease from handling food until a medical practitioner confirms that the employee no longer has the disease. However, among asymptomatic infected food handlers, good personal hygiene is important to prevent food contamination. Ready-to-eat food should not be handled with bare hands and food handlers are recommended to practice proper hand-washing after handling raw meat, before and after wearing gloves, going to the toilet, handling waste, and after cleaning food.[31]

Public Health Action and Recommendations

We recommend that hotel authorities improve the quality of their water for drinking and cooking as the first priority. Firstly, the hotel should provide bottled water from an external source for drinking and use only tap water that has passed the disinfection system for cooking by installing a new pipe. All food items and raw materials must be heat treated. The infected food handlers should be prevented from touching food until the test results show no infection. All surfaces and equipment in the kitchen should be disinfected with

1,000–5,000 ppm chlorine solution. The following steps should be included; new water pipes should be installed, tap water and well water should be separated, and an automatic chlorination system for well water should be added. Water for cooking and drinking should only come from tap water, and a new filter system should be installed by separating two sets of filters for cooking and drinking water.

After improving the hotel's water system, and providing health education to the food handlers to promote good personal hygiene, no further outbreaks were reported. To reduce the risk of developing large food-waterborne outbreaks in a hotel, it is important to show that materials, preparation process and food handling are safe and documentation should be kept. Food hygiene authorities should regularly visit hotels to inspect the food and water sanitation system and take random samples for laboratory analysis.[25]

Study Limitations

The investigators could not collect information from all participants, especially those who attended the first seminar, thus the analytic results may not reflect the whole cohort. Recall bias may have occurred by nature of the retrospective study and the large number of meals and food items consumed. We did not test for viral pathogens among asymptomatic participants and some participants may have developed the disease after the investigation had concluded.

Conclusion

An intermittent gastroenteritis outbreak at a Hotel in Songkhla Province during April to May 2019 was caused by mixed viral pathogens and rotavirus genotype G9P[8] was identified as the main pathogen. Cases were 237 participants of two seminars at the hotel and the attack rate was 67.9%. Contaminated water and infected food-handlers were important sources of cross- contamination. After the hotel's water system had been repaired and the food handlers were provided with health education to promote good personal hygiene, no further outbreaks were reported.

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Suggested Citation

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References

1. Kapikian AZ, Hoshino Y, Chanock RM. Rotaviruses, In: Knipe DM, Howley PM, Griffin DE, Lamb RA, Martin MA, Roizman B, Straus SE, Editors. Fields virology. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2001. p. 1787–834.
2. Tate JE, Burton AH, Boschi-Pinto C, Steele AD, Duque J, Parashar UD. 2008 estimate of worldwide rotavirus-associated mortality in children younger than 5 years before the introduction of universal rotavirus vaccination programmes: a systematic review and meta-analysis. Lancet Infect Dis. 2012;12(2):136–41.
3. Santos N, Hoshino Y. Global distribution of rotavirus serotypes/genotypes and its implication for the development and implementation of an effective rotavirus vaccine. Rev Med Virol. 2005 Jan–Feb;15(1):29–56.
4. Damanka SA, Agbemabiese CA, Dennis FE, Lartey BL, Adiku TK, Enweronu-Laryea CC, et al. Genetic analysis of Ghanaian G1P[8] and G9P[8] rotavirus A strains reveals the impact of P[8] VP4 gene polymorphism on P-genotyping. PLoS One [Internet]. 2019 Jun 26 [cited 2022 Apr 14];14(6):e0218790. <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0218790>
5. Kirkwood C, Bogdanovic-Sakran N, Barnes G, Bishop R. Rotavirus serotype G9P[8] and acute gastroenteritis outbreak in children, Northern Australia. Emerg Infect Dis. 2004 Sep;10(9):1593–600.
6. Anderson EJ, Weber SG. Rotavirus infection in adults. Lancet Infect Dis. 2004 Feb;4(2):91–9.
7. Bonsdorff CH, Hovi T, Makela P, Morttinen A. Rotavirus infections in adults in association with acute gastroenteritis. J Med Virol. 1978;2(1):21–8.
8. Foster SO, Palmer EL, Gary GW Jr, Martin ML, Herrmann KL, Beasley P, et al. Gastroenteritis due to rotavirus in an isolated Pacific island group: an epidemic of 3,439 cases. J Infect Dis. 1980 Jan;141(1):32–9.

9. Marrie TJ, Lee SH, Faulkner RS, Ethier J, Young CH. Rotavirus infection in a geriatric population. Arch Intern Med. 1982 Feb;142(2):313–6.

10. Cubitt WD, Holzel H. An outbreak of rotavirus infection in a long-stay ward of a geriatric hospital. J Clin Pathol. 1980 Mar;33(3):306–8.

11. Dupuis P, Beby A, Bourgoin A, Lussier-Bonneau MD, Agius G. Epidemic of viral gastroenteritis in an elderly community. Presse Med. 1995 Feb;24(7):356–8.

12. Abbas AM, Denton MD. An outbreak of rotavirus infection in a geriatric hospital. J Hosp Infect. 1987 Jan;9(1):76–80.

13. Lewis DC, Lightfoot NF, Cubitt WD, Wilson SA. Outbreaks of astrovirus type 1 and rotavirus gastroenteritis in a geriatric inpatient population. J Hosp Infect. 1989 Jul;14(1):9–14.

14. Division of Viral Disease, National Center for Immunization and Respiratory Diseases. Rotavirus [Internet]. Atlanta: Center for Disease Prevention and Control; 2021 Mar 26 [cited 2022 Apr 25]. <https://www.cdc.gov/rotavirus/clinical.html#>

15. Stuempfig ND, Seroy J. Viral gastroenteritis [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 [cited 2022 Apr 28]. <https://www.statpearls.com/ArticleLibrary/viewarticle/22095>

16. El Sayed Zaki M, Abo El Kheir N. Molecular study of astrovirus, adenovirus and norovirus in community acquired diarrhea in children: One Egyptian center study. Asian Pac J Trop Biomed. 2017 Nov;7(11):987–90.

17. Filho EP, da Costa Faria NR, Fialho AM, de Assis RS, Almeida MM, Rocha M, et al. Adenoviruses associated with acute gastroenteritis in hospitalized and community children up to 5 years old in Rio de Janeiro and Salvador, Brazil. J Med Microbiol. 2007 Mar;56(Pt 3):313–9.

18. Bosch A, Pinto RM, Guix S. Human astroviruses. Clin Microbiol Rev. 2014 Oct;27(4):1048–74.

19. Kapikian AZ, Wyatt RG, Levine MM, Yolken RH, Vankirk DH, Dolin R, et al. Oral administration of human rotavirus to volunteers: induction of illness and correlates of resistance. J Infect Dis. 1983 Jan;147(1):95–106.

20. Ward RL, Bernstein DI, Shukla R, Young EC, Sherwood JR, NcNeal MM, et al. Effects of antibody to rotavirus on protection of adults challenged with a human rotavirus. J Infect Dis. 1989 Jan;159(1):79–88.

21. Ward RL, Bernstein DI, Shukla R McNeal MM, Sherwood JR, Young EC, et al. Protection of adults rechallenged with a human rotavirus. J Infect Dis. 1990 Mar;161(3):440–5.

22. Ward RL, Bernstein DI, Young EC, Sherwood JR, Knowlton DR, Schiff GM. Human rotavirus studies in volunteers: determination of infectious dose and serological response to infection. J Infect Dis. 1986 Nov;154(5):871–80.

23. Middleton PJ, Abbott GD, Szymanski MT, Bortolussi R, Hamilton JR. Orbivirus acute gastroenteritis of infancy. Lancet. 1974 Jun;303(7869):1241–4.

24. Jiraphongsa C, Bresee JS, Pongsuwanna Y, Kluabwang P, Poonawagul U, Arporntip P, et al. Epidemiology and burden of rotavirus diarrhea in Thailand: results of sentinel surveillance. J Infect Dis. 2005 Sep 1;192 Suppl 1:S87–93.

25. Hopkins RS, Gaspard GB, Williams FP Jr, Karlin RJ, Cukor G, Blacklow NR. A community waterborne gastroenteritis outbreak: evidence for rotavirus as the agent. Am J Public Health. 1984 Mar;74(3):263–5.

26. Japan Ministry of Health and Welfare, National Institute of Infectious Diseases. An outbreak of group A rotavirus infection among adults from eating meals prepared at a restaurant, April 2000–Shimane. IASR. 2000;21:145.

27. Centers for Disease Prevention and Prevention. Foodborne Outbreak of group A rotavirus gastroenteritis among college students, District of Columbia, March–April 2000. MMWR [Internet]. 2000 Dec 22 [cited 2022 Apr 18];49(50):1131–3. <https://www.cdc.gov/mmwr/preview/mmwrhtml/mm4950a2.htm>

28. Safe Drinking Water Foundation. Groundwater [Internet]. Saskatoon (CA): Safe Drinking Water Foundation; 2021 [cited 2022 Apr 28]. <https://www.safewater.org/fact-sheets-1/2017/1/23/groundwater>

29. Center for Disease Prevention and Control. Water treatment [Internet]. Atlanta: Centers for Disease Prevention and Control; 2022 [cited 2022 Apr 28]. <https://www.cdc.gov/healthywater/drinking/public/water_treatment.html>

30. Minnesota Department of Health. Food contamination and foodborne Illness prevention [Internet]. Minnesota:Minnesota Department of Health; 2022 [cited 2022 Apr 28]. <https://www.health.state.mn.us/people/foodsafety/prevention.html2022>

31. Rentokil PCI. Food safety for hotels and restaurants [Internet]. West Sussex (GB): Rentokil initial plc; [cited 2022 Apr 28]. <https://www.rentokil-pestcontrolindia.com/hospitality/food-safety-for-the-hospitality-sector/>

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Field Epidemiology Training Program, Division of Epidemiology
Department of Disease Control, Ministry of Public Health, Thailand
Tel: +6625903894, Fax: +6625903845, Email: osireditor@osirjournal.net, http://www.osirjournal.net

The Grammar of Science: Are You Positive that Your Test is Positive?

Jaranit Kaewkungwal*

Mahidol University, Thailand

*Corresponding author email: jaranitk@biophics.org

In the era of coronavirus disease 2019 (COVID-19) pandemic, we all have heard or ever been tested with "antigen test kit" (ATK). The test tells whether a person tests positive or negative for COVID-19. If you test negative for COVID-19 using ATK, you are likely not to be infected, provided you do not have any symptoms. On the other hand, if you test positive, you are likely to be infected, provided you have any symptoms. So, do we use such test for diagnostic or screening? Are you sure that the negative and positive test results valid? Is it possible that you have false positive/negative result?

Diagnostic vs. Screening Test

Diagnostic and screening tests differ regarding their intended usage and whether a person shows symptomatic signs or not. On the pathway of natural history of disease, after a person gets infected with the disease, there typically are time gaps at different stages of disease status as shown in Figure 1. The tests could be used for detecting the diseases at different staging. Screening tests are usually intended for asymptomatic persons whereas diagnostic tests are intended for those showing symptoms in need of a diagnosis.[1,2]

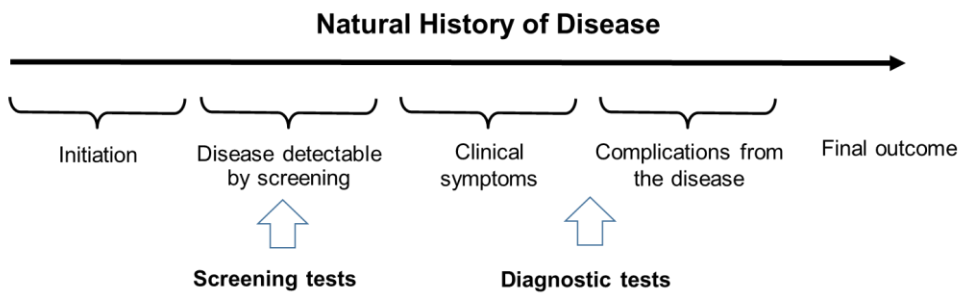


Figure 1. Screening and diagnostic tests at different stages of natural history of disease

The goal of screening is to detect disease as early as possible which is particularly useful for surveillance or reducing the risk of disease. Screening tests tend to be less invasive than diagnostic ones—and they are usually simpler to perform. ATK has become a quick tool for COVID-19 screening while other tests like RT-PCR tests are commonly used as diagnostic tests or confirmation tests. A positive result in a screening test usually requires a more accurate diagnostic test to confirm diagnosis.[3]

Validity and Efficacy of the Test

The screening or diagnostic test should have the ability to distinguish non-diseased and diseased persons. To do so, we need to compare the results of the test against some "gold standard" that establishes the true disease status. The gold standard may be a known test that provides a very accurate status but it may be more expensive and invasive or may take longer time to get the result. If there is no such gold standard, the assumed true disease status may be from the confirmed clinical signs and symptoms, or the acceptable consensus among experts. In some cases, the true disease status may be determined by following a certain group(s) of persons for a period of time to determine which patients ultimately develop the disease (Figure 2).[4–7]

The test is considered valid with two exquisitely qualifications. That is, the test is "sensitive" (true positive) when it gives high probability of detecting disease among diseased persons, and "specific" (true negative) when it gives high probability that those without the disease will have negative test result as shown in Figure 2.

The test is considered efficacious if it has favourable predictive qualification. The predictive value is the probability of having or not having disease according to test results. A positive predictive value (PPV) is the probability that the person has the disease when the test shows positive result while a negative predictive value (NPV) is the probability that the person does not have the disease when the test shows negative result.

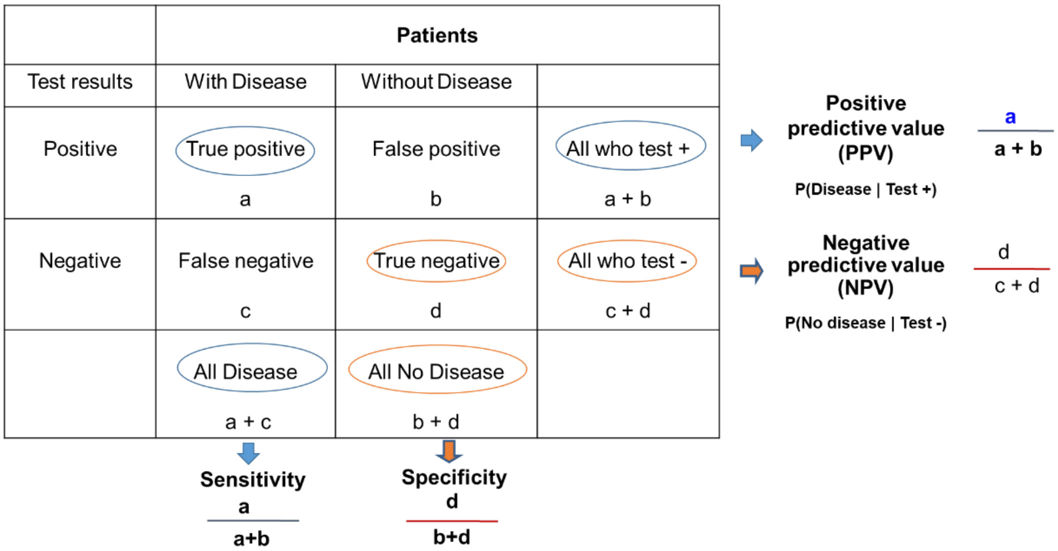


Figure 2. Sensitivity, specificity, positive predictive value and negative predictive value of a test

From the perspective of healthcare providers when we plan to use the test, we may prefer test with high sensitivity for screening purpose and the test with high specificity for confirmatory purpose. ***"If the person has the disease, how good that the test will show true positive result?" "If the person does not have the disease, how good that the test will confirm true negative result?"*** While sensitivity and specificity of a test are important considerations, predictive values are also important from the perspective of the patients. ***"If my test result is positive, what is the probability that I am truly positive?"***

While the values of sensitivity and specificity do not depend on the prevalence of the outcome in the population tested, the predictive values do. Given the same sensitivity and specificity, the PPV will increase and the NPV will decrease as the prevalence increases.[7] The relationships between these four terms are shown as follows.[8]

$$PPV = \frac{\text{Sensitivity x Prevalence}}{(\text{Sensitivity x Prevalence}) + (1\text{-Specificity})\text{x}(1\text{-Prevalence})}$$

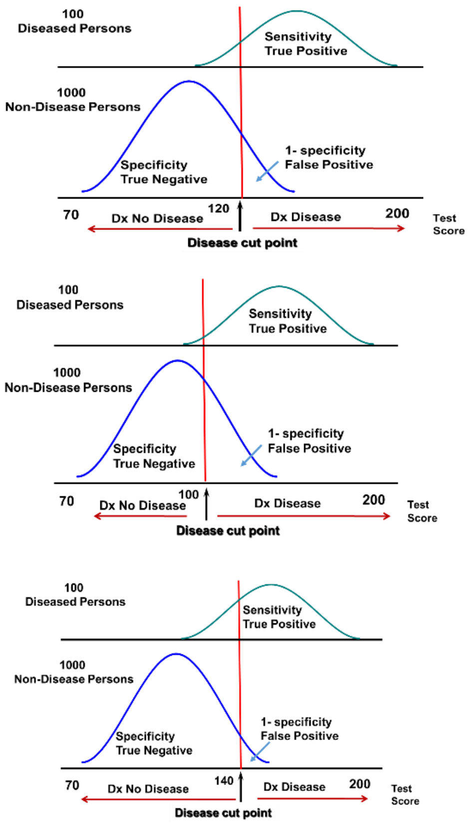
$$NPV = \frac{\text{Specificity x }(1\text{-Prevalence})}{[\text{Specificity x }(1\text{-Prevalence})] + [(1\text{-Sensitivity})\text{x Prevalence}]}$$

Cutoff Point for Test Score

While some test results are qualitative—"positive" or "negative"—as discussed above, some are quantitative score. For example, the result on ATK for COVID-19 tells you whether you are negative (one stripe) or positive (two stripes). If you use RT-PCR test, it usually gives the result as cycle threshold (Ct) which is a semi-quantitative value that can broadly categorize the concentration of viral genetic materials in a patient sample as low, medium or high.[9] In diabetes diagnosis, we may use blood sugar level two hours after the last meal, which is continuous value for decision making.[10] The latter approach usually requires setting up a cut-off point from continuous data. The cut-off will affect the sensitivity and specificity of the test. Upon varying selected cutoff values, if the sensitivity increases, the specificity will decrease and vice versa (Figure 3).

From varying cut-off points, a receiver operating characteristic curve (ROC curve) can be created representing a graphical plot that illustrates the diagnostic ability of a binary classifier outcome. The term "ROC" was originally developed for operators of military radar receivers starting in 1941. The ROC curve is created by plotting the true positive rate (sensitivity) against the false positive rate (1-specificity) at various threshold settings. The apex of the ROC curve, toward the upper left corner, represents a greater discriminatory ability of the test with high true-positive rate and low false-positive rate (Figure 3). It is important to note that ROC performance may change upon different conditions, such as patient populations and staging or severity levels of the disease. It has been suggested in a number of literature that we should explore and (if possible) pool the results of several studies that examined the same test in different situations, then generate averaged specificity and sensitivity and construct the ROC.[6,11,12]

The area under the ROC curve (AUC) is another indicator of the test's discriminatory power. When the test provides perfect performance (i.e., 100% sensitive and 100% specific), the AUC is 1.0. When the test has no discriminative value (i.e., 50% sensitive and 50% specific), the AUC is 0.5, representing by the area under a straight, diagonal line. In general, it is noted that an AUC ≤0.75 indicates that the test is not clinically useful, while an AUC >0.96 indicates excellent discriminatory ability.[13–15]



	Test Score	Sensitivity (%)	Specificity (%)	
	70	98.6	8.8	
	80	97.1	25.5	
Cut off	90	94.3	47.6	30.2% of non-disease persons are misdiagnosed as having disease
→	100	88.6	69.8	
Cut off	110	85.7	84.1	
→	120	71.4	92.5	
Cut off	130	64.3	96.9	42.9 % of true disease persons are not diagnosed
→	140	57.1	99.4	
	150	50.0	99.6	
	160	47.1	99.8	
	170	42.9	100.0	
	180	38.6	100.0	
	190	34.3	100.0	
	200	27.1	100.0	

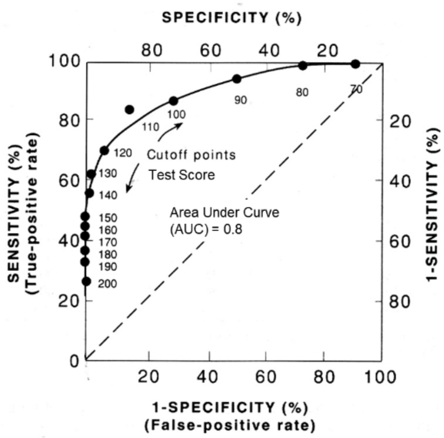


Figure 3. Sensitivity, specificity, receiver operating characteristic curve (ROC), and area under curve (AUC)

So, are You Positive that You Test Positive?

You can see now that the test kit could be used for different purposes–screening, diagnosis or confirmation. Many of those statistics related to the test kit depend on prevalence of the disease in the tested areas, characteristics of the tested populations, staging of the diseases, etc. Even though the test may not be perfect as it could not give 100% sensitivity and 100% specificity, or it does not show 100% correct predictive values, it is still useful in helping the clinician to estimate the probability that a person has disease. If your ATK test for COVID-19 shows positive, it may be true or false positive depending on the quality of the ATK itself. However, on the safe side, you should still follow the national practice guideline for COVID-19 case management.

Suggested Citation

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References

1. Sackett DL, Richardson WS, Rosenberg W, Haynes RB. Evidence Based Medicine. New York: Churchill Livingstone, 1997.
2. Machin D, Campbell MJ, Walters SJ. Medical Statistics: A Textbook for the Health Sciences. Chichester (UK): John Wiley & Sons, 2007.
3. Ruf M, Morgan O, Mackenzie K. Differences between screening and diagnostic tests and case finding [Internet]. Buckinghamshire (UK): HealthKnowledge; 2017 [cited 2022 Jun 25]. <https://www.healthknowledge.org.uk/public-health-textbook/disease-causation-diagnostic/2c-diagnosis-screening/screening-diagnostic-case-finding>
4. LaMorte WW. Screening for Disease: Test Validity [Internet]. Boston: School of Public Health, Boston University;[updated 2016 Jun 15, cited 2022 Jun 25]. <https://sphweb.bumc.bu.edu/otlt/mph-modules/ep/ep713_screening/EP713_Screening3.html>

5. Cardoso JR, Pereira LM, Iversen MD, Ramos AL. What is gold standard and what is ground truth? Dental Press J Orthod. 2014;19(5):27–30. doi:10.1590/2176-9451.19.5.027-030.ebo

6. Bachmann LM, Juni P, Reichenbach S, Ziswiler HR, Kessels AG, Vogelin E. Consequences of different diagnostic ‘gold standards’ in test accuracy research: Carpal Tunnel Syndrome as an example. Int J Epidemiol. 2005 Aug;34(4):953–5. <https://doi.org/10.1093/ije/dyi105>

7. Ford MP, Springman SR. Preanesthetic Evaluation: False-Positive Tests. In: Atlee JL, editor. Complications in Anesthesia. 2nd ed. Philadelphia: Saunders; 2007. p. 141-143.

8. Kanchanaraksa S, Johns Hopkins University. Evaluation of Diagnostic and Screening Tests: Validity and Reliability [Internet]. Baltimore (MD): Johns Hopkins University; 2008 [cited 2022 Jun 25]. <http://ocw.jhsph.edu/courses/fundepi/PDFs/lecture11.pdf>

9. Public Health England. Understanding cycle threshold (Ct) in SARS-CoV-2 RT-PCR: A guide for health protection teams. London: Public Health England; 2020 Oct [cited 2022 Jun 25]. 12 p. <https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/926410/Understanding_Cycle_Threshold__Ct__in_SARS-CoV-2_RT-PCR_.pdf>

10. International Diabetes Federation. A Guide to National Diabetes Programmes [Internet]. Belgium: International Diabetes Federation; 2010 [cited 2022 Jun 25]. 122 p. <https://www.worlddiabetesfoundation.org/sites/default/files/Guide-to-NDP_web.pdf>

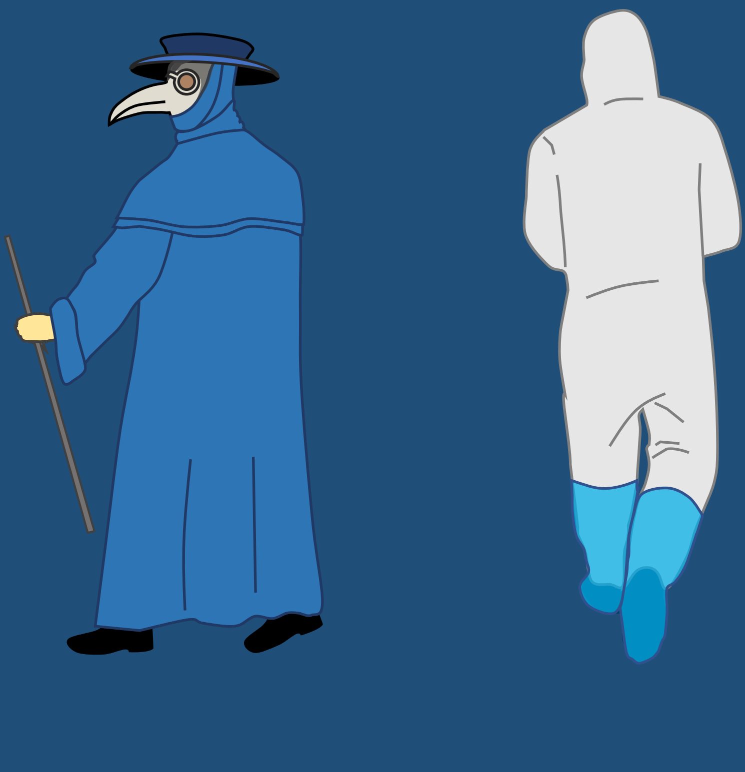
11. Florkowski CM. Sensitivity, specificity, receiver-operating characteristic (ROC) curves and likelihood ratios: communicating the performance of diagnostic tests. Clin Biochem Rev. 2008;29 Suppl 1(Suppl 1):S83-7.

12. Fan J, Upadhye S, Worster A. Understanding receiver operating characteristic (ROC) curves. Canadian Journal of Emergency Medicine. 2006;8(1):19–20. <https://doi.org/10.1017/S1481803500013336>

13. Zhu W, Zeng N, Wang N. Sensitivity, Specificity, Accuracy, Associated Confidence Interval and ROC Analysis with Practical SAS® Implementations [Internet]. SAS Conference Proceedings; 2010 Nov 14–17: Baltimore. [place unknown]: SAS Institute Inc; [cited 2022 Jun 25]. 9 p. <https://www.lexjansen.com/nesug/nesug10/hl/hl07.pdf>

14. Hanley JA, McNeil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. Radiology. 1982 Apr;143(1):29–36.

15. Whiting PF, Sterne JAC, Westwood ME, Bachmann LM, Harbord R, Egger M & Deeks JJ. Graphical presentation of diagnostic information. BMC Med Res Methodol. 2008 Apr 11;8:20.



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