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Outbreak detection of influenza-like illness in Prey Veng Province, Cambodia: a community-based surveillance

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ABSTRACT

On June 4, 2016, the Prey Veng Provincial Health Department reported a total of 107 patients with influenza-like illness (ILI) from Chakhlanh village to the Cambodian Ministry of Health. To confirm the outbreak and evaluate its clinical and epidemiological characteristics, the investigation team visited the village and reviewed the case-based surveillance (CBS) data on severe respiratory infection (SRI) and patients' records in health facilities. The team interviewed all households in the village from May 1 to June 5, 2016 and obtained the following data: age, medical history, date of onset, treatment, symptoms, and history of contact with patients or dead poultry. Nasal swab samples were collected from suspected ILI cases to test for influenza virus by RT-PCR. The investigation detected 498 suspected ILI cases, including 288 females. Although the incidence of suspected ILI cases who visited health centers was 63.0 per 1,000 persons per month, the attack rate was 27.1 per 100 population. The major age group was 5–14 years followed by 0–4 years. Major symptoms were cough, fever, runny nose, and headache. Six of seven nasal swab samples were positive for influenza A/H1N1 pdm09 virus. Most children with flu symptoms had contact with previous cases. This study showed that the ILI outbreak might be caused by seasonal influenza A/H1N1 pdm09 spread from person to person. Poor living conditions and poor hygiene and sanitation practices were environmental factors that caused the outbreak. As the CBS system was unable to identify this epidemic, it needs to be improved.

Keywords: Cambodia, community based surveillance, influenza A/H1N1 pdm09 virus, influenza-like illness

Abbreviations:
AET: Applied Epidemiology Training
CamEWARN: early warning and response system for Cambodia
CBS: case-based surveillance
CDC: Communicable Diseases Control Department
EBS: event-based surveillance
ILI: Influenza-like illness
MOH: Ministry of Health
SRI: severe respiratory infection

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INTRODUCTION

Epidemics of influenza are mainly classified into seasonal influenza and pandemic influenza. Pandemic influenza is a global outbreak caused by a new type of influenza virus A and occurs very rarely, such as the pandemic A (H1N1) in 2009. Seasonal influenza occurs annually, with a peak in the fall and winter, and influenza A and B viruses cause an epidemic of seasonal influenza.[1,2] Previous studies reported that seasonal influenza outbreaks occurred in specific restricted settings such as hospitals, schools, and long-term care centers.[3-5] Most influenza cases have relatively mild illness, and they resolve without any medical treatment. However, influenza viruses can cause serious complications, such as pneumonia and upper respiratory infections, or can worsen chronic medical conditions such as asthma, chronic cardiac, pulmonary, renal, metabolic, neurodevelopmental, liver, or hematologic diseases. It can also cause death in people with high risk for flu such as pregnant women, adults aged >65 years, children aged <5 years, and people with chronic medical conditions or immunosuppressive conditions.[2,6,7] Various control and prevention measures have been considered for mitigating the impact of influenza epidemics, including vaccination, antiviral medications, personal protective measures, and quarantine.[8-10]

In Cambodia, influenza is an endemic disease with a year-round activity, but its activity peaks during the rainy season, from June to November. Previous studies reported that influenza virus strains circulating across the country varied from year to year, but the predominant strains were type A, especially subtypes H1 and H3, and type B.[11-13] Southeast Asia is a hotspot of a novel influenza strain, where a new pandemic of influenza can occur. The Mekong Basin Disease Surveillance was established in 1991 for facilitating cooperative surveillance and control of infection diseases, including Cambodia, Laos, Myanmar, Thailand, Vietnam and a part of China.[14] To prevent a pandemic, Cambodia has been collaborating with neighboring countries and international organizations in sharing information and experiences, developing the guidelines and toolkits and preparing for a pandemic. A comprehensive plan for preventing, preparing and response to influenza pandemic was developed with the technical support from the World Health Organization (WHO) and the Centers for Disease Control and Prevention of the USA.[15] To monitor the trends of influenza infections and analyze the influenza virus strains in the country, the Communicable Diseases Control Department of the Cambodian Ministry of Health (CDC-MOH) developed three main surveillance systems: the early warning and response system for Cambodia (CamEWARN), influenza-like illness (ILI) surveillance, and severe acute respiratory infection (SARI) surveillance.[16,17] The CamEWARN is an integrated surveillance system that detects and responds in a timely manner to public health events. The ILI surveillance is performed at seven sentinel ILI sites to identify circulating strains of influenza viruses,[18] and the SARI surveillance is a hospital- and laboratory-based surveillance system with eight sentinel sites across the country.[16]

On June 4, 2016, the CDC-MOH and Applied Epidemiology Training (AET) were notified by the Rapid Response Team (RRT) from Prey Veng Provincial Health Department that 107 patients were diagnosed with ILI. Of 107 patients, 13 were referred to Neak Loeung Referral Hospital. The team of CDC staff, RRT, and AET trainees conducted a risk assessment on the ILI outbreak on June 5, 2016, and the outbreak investigation was conducted from June 5 to 7, 2016. The investigation aimed to describe the clinical and epidemiological characteristics of the outbreak, determine the sources of the outbreak, constitute some control and prevention measures, and provide some recommendations for preventing outbreaks in the future. This study reports the findings of this investigation.

MATERIALS AND METHODS

The CamEWARN surveillance and the alert threshold of diseases

The CamEWARN is divided into two main components: the case-based surveillance (CBS) and event-based surveillance (EBS). The CBS is based on a mandatory weekly reporting system, and an epidemiological week (epi-week) is used as the standardized method of counting weeks in the system. All public health facilities, including health centers and public hospitals, must report the number of cases encountered of the following seven epidemic-prone diseases and syndromes to the CDC-MOH: acute diarrhea, fever with rash, acute flaccid paralysis, severe respiratory infection (SRI), acute hemorrhagic fever, meningitis and encephalitis, and acute jaundice. To monitor disease trends and respond quickly to outbreaks, the number of cases encountered is compared with the alert thresholds of the diseases in every epi-week. The alert threshold is defined as 1.5-fold of the average number of cases in the same epi-weeks in the last 3 years. The EBS is a system that involves reporting of cases by directly calling the number 115 to notify or alert when there is an adverse public health event such as a suspected outbreak.

The investigation team for the outbreak of ILI

Based on the results of the EBS, the CDC-MOH and AET noted an ILI outbreak in Prey Veng Province on June 4, 2016 (epi-week 22). The investigation team, which consisted of the CDC-MOH staff, Prey Veng Provincial RRT, Neak Loeung operational district RRT, and AET trainees, visited Baboang Health Center, Peamro Health Center, Neak Loeung Referral Hospital, and several private clinics where ILI patients visited, as well as several public areas, such as shops, schools, and pagodas, from June 5 to 7.

Epidemiological investigation at health facilities

SRI, suspected ILI, and influenza cases were used in the outbreak investigation and were defined as follows. An SRI case was described as (1) an individual aged >5 years who had fever (≥38°C), with either cough or difficulty breathing or shortness of breath; (2) a child aged 1–5 years who had cough or difficulty breathing and a respiratory rate of >40/min; (3) an infant aged 2 months to 1 year who had cough or difficulty breathing and a respiratory rate of >50/min; and (4) an individual of all ages who showed evidence of pneumonia on chest X-ray. In this investigation, a "suspected ILI" case, which was described by modifying the definition of ILI in the surveillance, referred to a patient who presented either fever, malaise, headache, or myalgia, and experienced at least one of the following symptoms from May 1 to June 21, 2016 (epi-week: 18–25): cough, sore throat, and shortness of breath. An influenza case was defined as a patient whose nasal swab tested positive for influenza virus.

The investigation team found that most cases who visited Baboang Health Center and Peamro Health Center and those severe cases were transferred to the referral hospital. At the health centers, the investigators reviewed the CBS data of SRI cases and collected the following information from the medical logbooks: age, sex, and address. At the referral hospital, the investigation team queried the clinical symptoms of hospitalized cases and discussed with the physicians about the clinical signs, symptoms, laboratory results, and diagnosis. The team opened a mobile clinic for 3 days in Chakhlanh village, whose people were covered by the two health centers. The team set up the enhanced surveillance, which involved the daily reporting of suspected ILI cases and any unusual related events from the health centers, referral hospital, and two private clinics for 14 days (from June 8 to June 21, 2016).

Household survey

Chakhlanh village is covered by the two health centers. It had a population of 1,838 in 2016. We interviewed all households in the village using the standardized structured questionnaire, including demographic information, the date of onset and treatment, kind of treatment (antibiotics, oseltamivir phosphate (Tamiflu®)), duration of illness, clinical symptoms, history of travelling or joining any special events, and history of contact with patients or dead poultry from May 1 to June 5, 2016.

Laboratory investigation for influenza virus

The investigation team collected the nasal swabs from suspected ILI cases who were hospitalized or treated at home. The samples were stored in an ice box and sent to the National Public Health Laboratory to be tested for influenza virus using the standard real-time reverse transcription polymerase chain reaction algorithm.

Ethical issues

Approval of the national ethical review board was not required. This investigation was conducted as an emergency response to the outbreak. This study shows a report of the activities with no individual information.

RESULTS

The case-based surveillance data on severe respiratory infection at two health centers

The number of SRI cases and the alert threshold in 2016 are shown for Baboang Health Center (Fig. 1) and Peamro Health Center (Fig. 2), according to the CBS of CamEWARN. The two centers were not included in the sentinel site of the ILI surveillance. The number of SRI cases at Baboang Health Center was above the alert threshold in epi-week 7. However, the threshold in epi-week 7 was lower than other weeks around epi-week 7 and the number of cases was stable with approximately 11–14 cases around epi-week 7 (Fig. 1). The number of SRI cases at Peamro Health Center was under the alert threshold between epi-week 1 and epi-week 53, excluding epi-week 15 (61 cases) and epi-week 20 (59 cases) (Fig. 2). Although the number of cases in epi-week 23 (June 5–11) was under the alert threshold, it was much higher (104 cases) compared with that in epi-week 22.

Suspected influenza-like illness cases in Chakhlanh village

Among all 1,838 people in Chakhlanh village, 21 and 118 people were diagnosed as suspected ILI cases at Baboang Health Center and Peamro Health Center, respectively, from May 1 to June 5. The incidence of suspected ILI cases who accessed to health centers in the affected village was 63.0 per 1,000 person per month. The epidemic curve of the ILI outbreak was made by the household survey and enhanced surveillance in Chakhlanh village (Fig. 3). The investigation identified that there were 498 suspected ILI cases who had symptoms from May 1 to June 21 and that the index case was occurred on May 2. The number of cases dramatically increased from one on May 26 to 78 on June 2, then decreased greatly, especially after the investigation started on June 5, and reached to 3 on June 9. The surveillance on suspected ILI cases was enhanced at both health centers as well as the investigation. The number of cases per day was stable to be 3 or 4 from June 8 to 21, and the last case was reported on June 13 (Fig. 3).

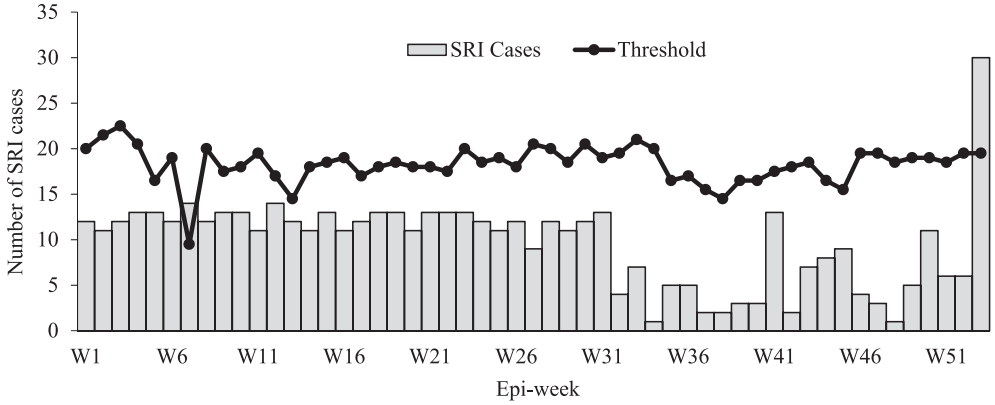

Fig. 1 Weekly report of severe respiratory infection cases at Baboang Health Center in 2016.
The number of severe respiratory infection (SRI) cases at Baboang Health Center was above the alert threshold in epi-week 7, but the number of cases was stable with approximately 11–14 cases around epi-week 7.

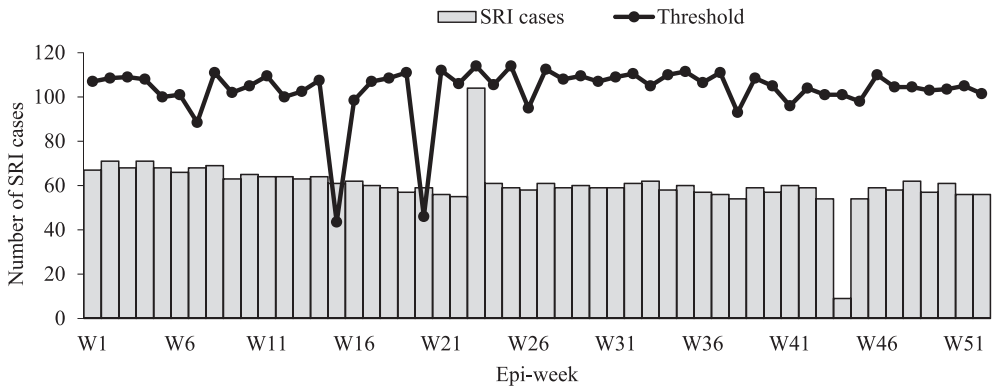

Fig. 2 Weekly report of severe respiratory infection cases at Peamro Health Center in 2016.
The number of severe respiratory infection (SRI) cases at Peamro Health Center was over the alert threshold only in epi-week 15 and epi-week 20. Although the number of cases in epi-week 23 (June 5–11) was under the alert threshold, it was much higher (104 cases) compared with that in epi-week 22.

Clinical and epidemiological characteristics of suspected influenza-like illness cases

Of all 498 suspected ILI cases, there were 210 males (42.2%) and 288 females (57.8%). No death was observed. It was found that 370 cases (74.3%) had contact history with one or more previous suspected ILI cases and that nine cases (1.8%) claimed that they had contact with dead poultry in their houses. Of 303 children under 14 years old with flu symptoms, 232 children (76.6%) had contacts with suspected ILI cases. Most cases (75.1%) reported to be treated with antibiotics, and no cases reported to have had a flu vaccine. The risk groups of flu were found as follows; 104 cases (20.9%) of children under 5 year of age, 16 cases (3.2%) of people aged above 65 year olds, seven cases (1.4%) with diabetes mellitus, six tuberculosis cases (1.2%), one case of chronic obstructive pulmonary diseases, and four pregnant cases (0.8%) (Table 1). The proportion of children under 14 years old was higher in male than female but there were

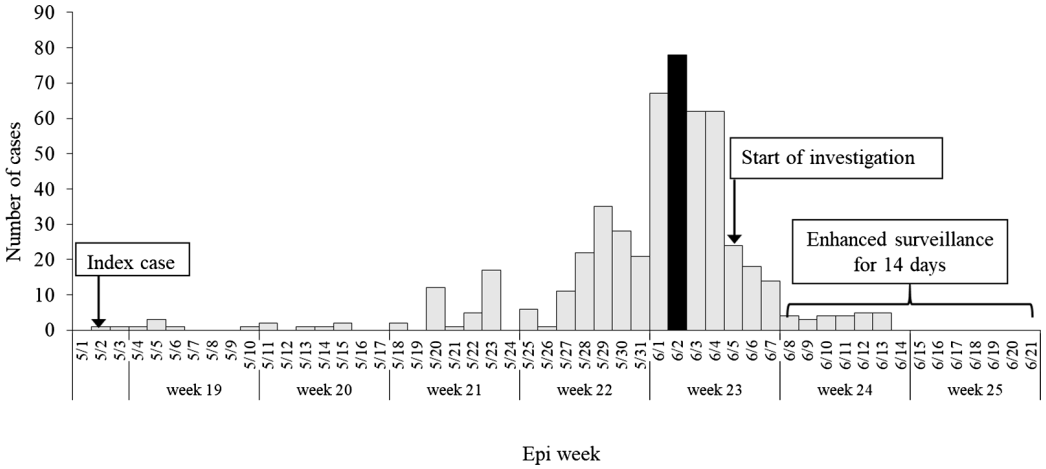

Fig. 3 Epidemic curve of suspected influenza-like-illness cases in Chakhlanh village from May 1 to June 21, 2016 (N=498).

The epidemic curve of the ILI outbreak was made by the household survey and enhanced surveillance and 498 people were identified as suspected ILI cases from May 1 to June 21. The index case was occurred on May 2 and the number of cases dramatically increased to 78 on June 2. The number of cases per day was stable to be 3 or 4 from June 8 to 21, and the last case was reported on June 13.

no differences in other characteristics between male and female. Symptoms of 498 cases were cough (89.8%), fever (87.6%), running nose (60.6%), headache (47.8%), sore throat (33.1%), and difficulty of breathing (12.7%).

The attack rate of suspected influenza-like illness

Table 2 shows the attack rate of suspected ILI by age groups. The number of suspected ILI cases was highest in the age group of 5–14 (40.0%), followed by the age groups of 0–4 (20.9%) and 25–49 (19.5%). However, the attack rate (per 100 population) was highest in the age group of 0–4 (61.2), followed by the groups of 5–14 (52.6) and 25–49 (17.3). For examination of the influenza virus, nasal-swab samples were collected from only seven suspected ILI cases, including six hospitalized cases and one case in the village because of the limited budget. Six of seven samples were positive for influenza A/H1N1 pdm09 virus. It was found that 44.3% (125/282) of students in 9 classes came to the primary school in the middle of the village although they had symptoms of flu after May 1, 2016.

Table 1 Demographic characteristics of suspected influenza-like illness cases in Chakhlanh village (N=498)

Characteristics	Male		Female		Total	
	n	(%)	n	(%)	N	(%)
Age (year)						
0–4	51	24.3	53	18.4	104	20.9
5–14	95	45.2	104	36.1	199	40.0
15–24	17	8.1	29	10.1	46	9.2
25–49	29	13.8	68	23.6	97	19.5
50–64	11	5.2	25	8.7	36	7.2
≥65	7	3.3	9	3.1	16	3.2
Contact history						
ILI case	153	72.8	217	75.3	370	74.3
Dead poultry	5	2.4	4	1.4	9	1.8
No contact	52	24.8	67	23.3	119	23.9
Treatment						
Antibiotics	165	78.5	209	72.6	374	75.1
Tamiflu®[1)]	1	0.5	0	0	1	0.2
No treatment	44	21.0	79	27.4	123	24.7
Influenza vaccination in the past year						
	0	0	0	0	0	0
Risk factor for influenza						
DM	3	1.4	4	1.4	7	1.4
TB	2	1.0	4	1.4	6	1.2
COPD	0	0	1	0.3	1	0.2
Pregnancy	0	0	4	1.4	4	0.8
≥65 year	7	3.3	9	3.1	16	3.2
< 5 year	51	24.3	53	18.4	104	20.9
No risk factor	147	70.0	213	74.0	360	72.3
Total	210	100	288	100	498	100

ILI, influenza-like illness; DM, diabetes mellitus; TB, tuberculosis; COPD, chronic obstructive pulmonary diseases.
[1)]Tamiflu®, oseltamivir phosphate.

Table 2 Attack rate of suspected influenza-like illness by age group in Chakhlanh Village from May 1 to June 5, 2016

Age group	Number of cases	Population	Attack rate (per 100 population)
0–4	104	170	61.2
5–14	199	378	52.6
15–24	46	408	11.3
25–49	97	562	17.3
50–64	36	217	16.6
≥ 65	16	103	15.5
Total	498	1,838	27.1

DISCUSSION

This investigation was conducted to describe the clinical and epidemiological characteristics of the ILI outbreak in Chakhlanh village. Prey Veng Province was not a sentinel site for ILI or SARI surveillance system; therefore, we were unable to check the influenza trend in the village. We focused on reviewing the number of SRI cases from epi-week 1 to 21 in 2016, which were reported through the CBS system to identify the trend of the ILI outbreak. The results showed that there was no potential alert of SRI outbreaks at the two health centers. Moreover, the investigation found that the reported numbers from two health centers in the surveillance system were not consistent with the number of cases in the medical registrations. These results suggest that the current situation of the CBS system may not be able to capture all outbreaks. This ILI outbreak was notified through the EBS system, suggesting that the EBS might be more sensitive than the CBS in some situations; however, previous studies in Cambodia revealed that the positive predictive value of the reports from the EBS was low because timely detection of outbreak or suspected event by 115 hotline (within 24 hours after occurring) was 33% (unpublished data).

There have been some reports on the quality of CBS and there are some reasons why the CBS cannot capture outbreaks. First, the CBS includes only public health facilities but not private health facilities. However, most Cambodian people seek the medical care at pharmacies or private health facilities due to the low quality of public health facilities.[19,20] Secondly, the number of cases which is reported to the CBS is often inconsistent with the number of registered cases in the medical logbooks, because the responsible staff for reporting mostly do not report the number of cases accurately. They do not count the cases in the books but report almost the same number of cases in every epi-week. It is just a bad behavior, although they always claim a burden with too much work. Thirdly, the system is collecting the total number of cases at health facilities but not in villages. When people of a village visit two health centers, the reports from health facilities cannot reflect the number of cases in the village. Therefore, the CBS system cannot capture any outbreak of infectious diseases in a community as well as the ILI outbreak in Chakhlanh village. Therefore, we recommend the following to improve the CBS system. First, the CDC-MOH staff who are responsible for the system should assess the quality of the system quarterly in order to identify the weak and strong points and improve the system in a timely manner. Second, the RRT at the provincial and operational levels should frequently conduct supervisory visits and spot checks in public hospitals and health centers to ensure that they report to the system timely and correctly. Finally, the RRT at the public hospital and health center levels must report the number of cases to the system consistent with the number of cases registered in the medical logbooks and based on the case definitions of the system.

From May 1 to June 21, 2016, a quarter of the population in the affected village were infected. However, the proportion of patients who visited the public health facilities was 63.0 per 1,000 persons per month and was considered low. There may be some reasons why most cases did not visit health facilities. First, they thought that a seasonal flu was only a mild disease or a disease that resolves on its own, based on their experiences. Second, there was poor provision of healthcare, the quality of public health facilities was low, and there was no private clinic in the village. Previous studies showed that people tended to visit private clinics rather than public health facilities due to the lower quality of public healthcare services in Cambodia.[20] It was also difficult during the investigation to collect data and information from private clinics in other villages of the province. It is common in Cambodia that physicians do not keep patients' medical records at private clinics. Nonetheless, they reported that most of their patients presented ILI signs and symptoms as what happened in the affected village.

The results of the investigation strongly support that the ILI outbreak in Chakhlanh village

was a seasonal influenza outbreak caused by an influenza A/H1N1 virus. The clinical signs and symptoms of suspected ILI cases were cough, fever, difficulty breathing, runny nose, and headache, which were consistent with those of seasonal influenza.[2] Based on the result of the laboratory investigation, most collected samples were positive for A/H1N1 pdm09. The data analysis of the ILI surveillance conducted by the CDC-MOH during the first semester of 2016 also illustrated that influenza A/H1N1 pdm09 had been the predominant circulating strains.[21] Moreover, the Global Influenza Surveillance and Response System of WHO in Southeast Asia showed that the activity of influenza A/H1N1 viruses was most frequently detected.[22]

Most patients reported taking antibiotics, which are considered to be an inappropriate treatment for viral infectious diseases. A previous Cambodian study showed that the proportions of antibiotics in all prescriptions at three health centers was high (60–81%) and all children who were 5 years old or younger with acute respiratory infections received antibiotics. Furthermore, the proportion of appropriate prescriptions for acute respiratory infection treatment was 45%.[23] According to the guidelines of the clinical management of human infection with pandemic (H1N1) 2009 by the WHO, antibiotics should be prescribed only in patients with suspected bacterial co-infection.[24] An antibiotics against *Staphylococcus aureus* (*S. aureus*) is recommended for severe cases, because staphylococcal pneumonia is frequently associated with influenza.[10,25,26] Overuse of antibiotics is a worldwide public health concern[27] because it is associated with antibiotics resistance[27,28] in not only specific microorganism but also other commensal bacteria and the bacterial pneumonia caused by methicillin-resistant *S. aureus* (MRSA) is recently a common cause of influenza-associated deaths in children.[10] Timely diagnosis of influenza infection might be helpful to reduce antibiotic use.[29] Moreover, none of the suspected ILI cases reported that they received an influenza vaccine because flu vaccination is not scheduled in the routine immunization program or is not prioritized in Cambodia.[30,31] The age group of 0–4 years showed the highest attack rate, and the ILI surveillance/CDC-MOH revealed that this age group had the highest proportion of ILI cases from January to June 2016 in the country.[18] To prevent deaths or outbreaks caused by an influenza virus, influenza vaccination should be considered for the high-risk group, especially children younger than 5 years old.[9,30]

The age group of 5–14 years showed the highest proportion of suspected ILI cases, and their attack rate was higher than 50%. In addition, the index case of the outbreak was a school student. The reasons why the attack rate of this age group was high may be because most of the children in this group were attending school and because they had multiple contacts with each other at their school without proper hygiene and sanitation practices. We observed that most students did not use facemasks, although we did not assess the students' practice of hygiene and sanitation. There were outbreaks that had similar findings with those reported in China and Vietnam.[3,32] Education on hygiene and sanitation was reported to be effective to reduce infectious diseases in Cambodia.[33] The analysis of eighteen cluster randomized controlled trials showed that hand hygiene interventions in educational settings may reduce respiratory infections.[34] Education on hygiene for children by caregivers at home may be effective, especially for pre-school children.[35] Education should include knowledge on hygiene, practice of hand washing and cleaning toilet for reducing influenza.[34-37] Another prevention method of ILI outbreak is that classes should be suspended temporarily when a certain proportion (e.g., >20%) of students in a class or in a school are absent from a school due to the infection.

The investigation team provided health education and disseminated the key messages and recommendations to people in the village during the seasonal influenza outbreak: (1) self-protective measures by hygienic practices (washing hands, wearing masks, and coughing etiquette), (2) keeping distance from sick people, and (3) seeking medical care at the early stage of infection. For severe cases, the team referred the patients to the referral hospital for symptomatic treatment

and Tamiflu® was provided for them. After the investigation, the enhanced surveillance for the outbreak was set up for 2 more weeks. It was recommended that public health facilities and all private clinics should continue ILI surveillance and report the number of suspected ILI cases every day. The provincial health department had to collaborate in the enhanced surveillance, seek for another outbreak in their territory, and report notifiable syndromes to the CDC-MOH early and timely.

There are some limitations in this investigation. First, the investigation was unable to identify the epidemiological links among all cases, although we obtained exposure histories for suspected ILI cases and influenza cases. Second, only seven specimens were obtained for testing due to limited budget, and most cases were not confirmed as influenza infections. However, 85.7% of the specimens were positive for influenza A/H1N1, and a criterion was used to identify 498 suspected ILI cases. These results suggest that the suspected ILI cases in the village might have been caused by influenza A/H1N1. The third limitation was that environmental factors were not quantitatively measured. In the village, the roads and some residential areas were dusty, dirty, and unclean. People were raising poultries and animals freely around their houses. People usually gathered in crowded areas, such as shops, pagoda, and school, although some of them had flu-like symptoms. All the people did not wear facemasks when they communicated with others or did not cover their mouths or noses when they coughed or sneezed. The team observed these conditions in the village but did not record them in a quantitative way.

In conclusion, this investigation showed that the ILI outbreak, reported by the EBS system, was caused by seasonal influenza A/H1N1 pdm09 spread from person to person. Suspected ILI cases were frequently reported in school children aged 5–14 years. Poor living conditions and poor hygiene and sanitation practices were among the environmental factors that might cause the outbreak. The EBS was effective in capturing this outbreak, although the CBS was unable to detect SRI, and ILI or SARI surveillance was not established in the province. These findings suggest that the CBS system needs to be improved to capture any outbreak in a timely manner and that vaccination for high-risk groups, especially children aged <5 years, and temporarily suspending classes at a school are strongly recommended to prevent outbreaks in the future.

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CONFLICTS OF INTEREST

The authors declared no conflicts of interest for this study.

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