

# Advances in Acute Emerging Infectious Disease Symptom Monitoring

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**Abstract:** In recent years, the risk of acute emerging infectious diseases has increased significantly due to changes in environmental conditions and social factors, posing a serious threat to public health security and human health. The general susceptibility of the population and the unpredictability and increasing infectiousness of emerging infectious diseases reflect the inadequacy of the existing infectious disease surveillance system for timely detection and screening of emerging infectious diseases, often leading to a certain scale of epidemic outbreaks that seriously harm humans before being detected passively. This is a literature review on symptom surveillance of acute emerging infectious diseases at home and abroad, emphasizing on the subject matter and development of symptom surveillance of emerging infectious diseases, so as to provide a scientific basis for the establishment and improvement of symptom surveillance of acute emerging infectious diseases.

**Keywords:** Acute; Emerging infectious diseases; Symptom surveillance

**Online publication:** September 6, 2022

## 1. Introduction

An acute emerging infectious disease is a newly emerging infectious disease or an infectious disease that has emerged in the past but has not been identified to date and is now rapidly increasing in incidence. There are three broad categories of acute emerging infectious diseases: emerging infectious diseases caused by new pathogens and mutants; emerging infectious diseases where existing diseases are newly identified; and emerging infectious diseases where the infectious disease has caused new local epidemics <sup>[1]</sup>. At the end of the severe acute respiratory syndrome epidemic in July 2003, there were 8,098 cases and 774 deaths in 37 countries, with a mortality rate of 10% <sup>[2]</sup>. Since the widespread emergence of influenza A in 2004, spreading from Asia to Europe and Africa, with 16 countries reporting a mortality rate of 60% <sup>[3]</sup>, the World Health Organization (WHO) believes that the new coronavirus is a major cause of death. The World Health Organization now considers the new coronavirus pneumonia epidemic to be a global pandemic, with 16.83 million new confirmed cases and 9,084 deaths in a single day worldwide. The statistics above illustrate that acute emerging infectious diseases are more widespread and contagious, as well as spreading faster by more diverse routes, thus making prevention and treatment extremely difficult, while imposing a serious burden on the society <sup>[4,5]</sup>.

## 2. Symptoms of acute emerging infectious diseases

The emergence of acute emerging infectious diseases leads to sustained human-to-human transmission and human immunity, resulting in localized outbreaks that may rapidly progress into pandemics. Several

subtypes of avian influenza A that result in human morbidity have been identified in recent years. Initial symptoms of influenza A H5N1 and H7N9 include high fever and other flu-like symptoms, including cough and sore throat; patients may experience early onset of lower respiratory symptoms, including respiratory distress and hoarseness, as well as other early symptoms, including diarrhea, vomiting, abdominal pain, chest pain, and bleeding from the nose or gums. The incubation period for Ebola is 2–21 days, and most patients are clinically characterized by sudden onset of fever as the first symptom accompanied by other common early symptoms, including headache, vomiting, diarrhea, myalgia, rash, and vomiting. Gastrointestinal symptoms, which include abdominal pain, nausea, vomiting, and diarrhea two days after the initial symptoms, and a macular or maculopapular rash on day 5–7 of the illness are the common presentations [6]. The outbreak in Malaysia in 1998 was fatal. Nipah encephalitis was first identified in the 1998 outbreak of fatal encephalitis in Malaysia, and subsequently spread to other regions, including Bangladesh and India. The Bangladeshi strain is commonly characterized by respiratory symptoms with prodromal symptoms of sore throat, myalgia, fever, headache, and vomiting. Clinical features of the Middle East respiratory syndrome include flu-like symptoms, such as fever, cough, and shortness of breath, gastrointestinal symptoms, such as vomiting and diarrhea, severe pneumonia combined with acute respiratory distress syndrome, septic shock, diffuse intravascular coagulation disorder, and even multi-organ failure. The clinical presentation of severe acute respiratory syndrome usually begins with a high fever, along with headache and myalgia. A dry cough develops 2–7 days later in most patients. The clinical manifestations of Lassa fever include progressive fever, nausea, abdominal pain, sore throat, cough, conjunctivitis, buccal mucosal ulcers, exudative pharyngitis, and cervical adenopathy. Most cases are mild, but 20% of cases are severe [3]. Crimean-Congo hemorrhagic fever presents with non-specific signs and symptoms prior to the onset of the hemorrhagic syndrome in four phases: incubation, pre-hemorrhagic, hemorrhagic, and recovery. The incubation period is short and changes depending on the route of exposure. The initial symptoms that usually appear within a week are the same as those of other infectious diseases, which may include fever, chills, photophobia, myalgia, nausea, headache, and gastrointestinal symptoms [7,8]. In short, acute emerging infectious diseases are not common diseases. The main presenting symptom of the majority of acute emerging infectious diseases is fever. Other symptoms are mostly flu-like and gastrointestinal, such as nausea and vomiting, diarrhea, headache, cough, sore throat, abdominal pain, and myalgia.

### **3. Symptom surveillance**

#### **3.1. Infectious disease symptom surveillance abroad**

In the 1980s, Pasteur Institute in France proposed the combination of specific traditional indicators to predict influenza outbreaks. This surveillance method was in fact the prototype of symptom surveillance. In 1997, the United States (U.S.) Department of Defense launched the military infectious disease symptom surveillance to create a community-based disease early reporting system, in order to collect information on visits by military personnel and their families. In 1998, the United Kingdom developed a national real-time symptom surveillance system, using data from telemedicine triage systems, general practitioners (GPs), and emergency departments, to compare historical trends; it was used for early surveillance and to ensure mass gatherings [9]. In 1999, a real-time outbreak and disease surveillance system was developed in the U.S. to collect information on emergency patients and the status of over-the-counter drug sales in pharmacies [10]. The system has played an important role in the timely detection of infectious diseases and unusual epidemiological patterns [11,12]. Lazarus et al. studied automated records of approximately 250,000 health plan members in Boston from 1996–1999 and found that changes in the weekly incidence of lower respiratory tract infections from hospital databases followed the same trend as the national surveillance of deaths from pneumonia or influenza [13]. Symptom surveillance systems that were established in New York

City in 2001 to monitor emergency department visits were effective in the early detection of disease abnormalities in 39 participating emergency departments, where abnormal signs of respiratory and fever symptoms occurred at the peak of influenza A and B activity, while those of diarrhea and vomiting symptoms occurred during suspected norovirus and rotavirus transmission <sup>[14]</sup>. Symptom surveillance systems were established at 100 sites in the U.S. in 2003 <sup>[15]</sup>. From all these, it can be seen that symptom surveillance is growing at a rapid pace <sup>[16]</sup>.

### **3.2. Infectious disease symptom surveillance at home**

China's statutory infectious disease reporting surveillance system was established in 1950. Disease surveillance was in its infancy before 1978, when the infectious disease reporting system was focused on collecting passive data. From 1978 to 2002, China was in the exploratory period of surveillance, which consisted of active collection of population data in addition to infectious disease reporting to monitor, collect, analyze, and publish annual reports on a regular basis. In 1991, when the concept of symptom surveillance was still ambiguous, a surveillance system for acute flaccid paralysis was established with the request and assistance of the WHO in order to eradicate poliomyelitis; since 2003, after the outbreak of infectious atypical pneumonia, a direct reporting system for the network of public health emergencies was established and fully activated nationwide, and since then, special reporting information management systems for certain infectious diseases have been established and improved one after another. China's symptom surveillance systems include the influenza surveillance system, the acute flaccid paralysis surveillance system, the unexplained pneumonia surveillance system, the surveillance system for cases of severe respiratory infections, the surveillance system for five symptom clusters established after 2009 (febrile respiratory symptoms, diarrheal symptoms, fever with rash symptoms, fever with hemorrhagic symptoms, and encephalitis and meningitis symptoms), as well as the current new crown pneumonia outbreak with fever as the core. Xuzhou City, Jiangsu Province used its hospital outpatient diarrheal disease syndromes to establish an early warning system for early detection of peaks in the incidence of bacterial dysentery and other infectious diarrhea <sup>[17]</sup>. Taiwan China established Asia's first hospital emergency department-based real-time symptom surveillance system in 2004. This was the first time in Taiwan that information technology and data were used directly from hospitals to facilitate the operation of a surveillance system via a systematic approach to monitor influenza-like cases, respiratory symptoms, and the peak incidence of intestinal diseases. By analyzing the daily electronic data collected from the emergency department in 2004–2005, the detection of epidemic flu-like illnesses and respiratory syndrome illnesses with significantly higher total emergency visits during winter and summer peaks, weekends, and holidays than on weekdays was disclosed; the study also found an increase in gastrointestinal syndromes and an improving influenza preparedness as well as disease prevention and control in Taiwan <sup>[18]</sup>. In recent years, some regions have established school symptom surveillance systems with an aim to achieve early warning, as exemplified by Changning District's endeavor to gather data on the occurrence of illness-related absences and syndromes in primary and secondary schools and kindergartens at surveillance sites <sup>[19]</sup>. In 2009, Zhuhai started operating a school infectious disease symptom surveillance system, and Guan Tianji et al. retrospectively studied the surveillance data from 2015–2019 and evaluated the early warning effect of the system. The system functioned well, and the peaks of disease symptoms monitored were consistent with the those of corresponding infectious diseases in Zhuhai's schools <sup>[20]</sup>. Huang Chunping et al. studied the use of a fully launched smartphone-based school symptom surveillance system and the positive warning events in Hangzhou, with a citywide average usage rate and response rate of 54.65% and 70.68%, respectively, for automatic warnings among schools using this symptom surveillance system. Smartphones were used in the study to collect symptom monitoring information, which is a good solution to the shortcomings of traditional information collection, such as lagging and low coverage <sup>[21]</sup>.

#### 4. The use of symptom surveillance for acute emerging infectious diseases

Emerging infectious diseases have the same four phases as the average patient with an acute infectious disease: incubation, prodromal, symptomatic, and recovery. In symptom surveillance, data are collected from patients at the onset of the initial symptom. For instance, if a patient in the prodromal phase visits a pharmacy to purchase over-the-counter medication or takes time off work, the surveillance of abnormalities can be done by monitoring the pharmacy drug sales or the work absence data. When the patient's condition progresses to a point where symptoms become apparent, the patient may visit a healthcare facility; hence, through the complaint of symptoms, early warning can be detected, such as the early stages of an influenza epidemic, which can cause an increasing incidence of fever or flu-like symptoms in the population. The emergence of an emerging infectious disease is often accompanied by a range of similar symptoms. In a non-epidemic situation, the number of absences from school, sales of over-the-counter medication, emergency room visits, and other indicators collectively will reveal a certain normative curve. In the event of an epidemic, the curve breaks the norm and becomes abnormal. The symptom surveillance system detects and initiates epidemiological investigations and prevention through similar symptoms and unusual curves, thus moving the surveillance gates forward <sup>[22]</sup>. This will enable epidemiological investigation and control to be initiated in a timely manner.

Symptom surveillance systems are now widely used in a number of developed countries. While traditional symptom surveillance systems focus on known common infectious diseases, unknown and emerging infectious diseases that have evolved or are newly identified can also be monitored, which can be very effective in early warning. Since the 1999 West Nile virus outbreak in New York, which infected thousands of people, a city-wide mosquito surveillance system and sentinel surveillance of bird populations were established in the following year to understand the prevalence of West Nile virus infection; the results obtained from this surveillance advanced the implementation of control measures by four weeks <sup>[23]</sup>. Japan's prescription monitoring system, which has been reporting patients with influenza and chickenpox as well as the estimated number of people prescribed with certain drugs since 2009, estimates the number of patients based on the number of prescriptions with neuraminidase inhibitors, anti-herpes viral drugs, antibiotics, antipyretics, and cold medicines nationwide. The system also identifies diseases that are not being monitored, which may be new or re-emerging <sup>[24]</sup>. The primary results of a retrospective analysis by Wijngaard et al. in 2010, based on the Dutch Healthcare register's symptom data, showed that among three syndromes, respiratory syndromes were the most closely associated with laboratory pathogen counts, with respiratory syndromes being 0–5 weeks ahead of laboratory influenza virus counts, indicating more timely and sensitive syndromic surveillance; on the other hand, gastrointestinal syndrome counts were 1–2 weeks ahead of laboratory rotavirus counts, while 62% of variants reported in neurological syndromes were caused by known viruses, suggesting that a proportion of unknown viruses were causing meningitis <sup>[25]</sup>. In 2009, Chinese academics conducted a laboratory-based symptom surveillance of patients in nine sentinel hospitals in Guangxi and discovered new infections caused by rare pathogens <sup>[26]</sup>. In 2012, Shanghai initiated a comprehensive diarrheal disease surveillance, which not only assembled a large database of acute diarrheal cases and the changing patterns of diarrheal diseases, but also identified rare pathogens to provide clues to the outbreak <sup>[27]</sup>. In 2013, the first case of H7N9 human avian influenza infection was detected in Shanghai through the unexplained pneumonia surveillance system <sup>[28]</sup>. In the same year, the first human case of H10N8 avian influenza was detected in Jiangxi Province through the pneumonia of unknown etiology surveillance system, with its genes suggesting a newly identified reassortment virus <sup>[29]</sup>. In order to ensure effective symptom surveillance, it is important to proactively collect a substantial amount of data, analyze them, anticipate future situations, and establish a real-time symptom surveillance system so that the public can take early precautions to reduce the risk posed by infectious diseases.

Symptom surveillance is an emerging surveillance method that can promote early warning of acute emerging infectious diseases. The prodromal symptoms of acute emerging infectious diseases are non-specific, with fever as the main initiating symptom and flu-like and gastrointestinal symptoms overlapping each other as underlying symptoms. Early diagnosis is a challenge; hence, conventional surveillance based on laboratory and clinician-confirmed diagnostic information is falling behind. Symptom surveillance, on the other hand, enables the collection of data from the time a patient presents with prodromal symptoms and therefore early warning signs can be monitored several days earlier than conventional surveillance<sup>[30]</sup>. Research has been carried out on symptom monitoring systems in China, but the theory and practice behind these systems have not been fully developed. A complete electronic symptom monitoring early warning system that integrates mature traditional disease surveillance experience and data with symptom monitoring on a long-term, continuous basis is needed to enable rapid, continuous, and effective actions on symptom monitoring systems that can be used in practical emergency operations.

### Disclosure statement

The authors declare no conflict of interest.

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