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Research Article

Prescription Surveillance and Polymerase Chain Reaction Testing to Identify Pathogens during Outbreaks of Infection

Hiroaki Sugiura,[1] Tsuguto Fujimoto,[2] Tamie Sugawara,[2] Nozomu Hanaoka,[2] Masami Konagaya,[2] Kiyoshi Kikuchi,[3] Eisuke Hanada,[4] Nobuhiko Okabe,[2,5] and Yasushi Ohkusa[2]

[1] *Sugiura Clinic, 2-8-3 Imaichi-Kita, Honmachi, Shimane, Izumo 693-0002, Japan*
[2] *Infectious Disease Surveillance Center, National Institute of Infectious Diseases, Shinjuku, Tokyo 162-8640, Japan*
[3] *Shimane Prefectural Central Hospital, Shimane, Izumo 693-8555, Japan*
[4] *Shimane University Hospital, Shimane, Izumo 693-8501, Japan*
[5] *Kawasaki City Health Institute of Public Health, Kanagawa, Kawasaki 210-0834, Japan*

Correspondence should be addressed to Hiroaki Sugiura; tomomaric@smn.enjoy.ne.jp

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Syndromic surveillance, including prescription surveillance, offers a rapid method for the early detection of agents of bioterrorism and emerging infectious diseases. However, it has the disadvantage of not considering definitive diagnoses. Here, we attempted to definitively diagnose pathogens using polymerase chain reaction (PCR) immediately after the prescription surveillance system detected an outbreak. Specimens were collected from 50 patients with respiratory infections. PCR was used to identify the pathogens, which included 14 types of common respiratory viruses and *Mycoplasma pneumoniae*. Infectious agents including *M. pneumoniae*, respiratory syncytial virus (RSV), rhinovirus, enterovirus, and parainfluenza virus were detected in 54% of patients. For the rapid RSV diagnosis kit, sensitivity was 80% and specificity was 85%. For the rapid adenovirus diagnosis kit, no positive results were obtained; therefore, sensitivity could not be calculated and specificity was 100%. Many patients were found to be treated for upper respiratory tract infections without the diagnosis of a specific pathogen. In Japan, an outbreak of *M. pneumoniae* infection began in 2011, and our results suggested that this outbreak may have included false-positive cases. By combining syndromic surveillance and PCR, we were able to rapidly and accurately identify causative pathogens during a recent respiratory infection outbreak.

1. Introduction

Japanese traditional surveillance is based on definitive diagnosis and is enforced by the infection control laws in Japan for the early detection of agents of bioterrorism and outbreaks of emerging infectious diseases. After the infectious disease is diagnosed at sentinel medical institutions, at least 10 days are required until it is announced nationwide. Therefore, a major fault of this surveillance system is the delay in disseminating information.

A surveillance system that can identify the early stages of an outbreak of infectious disease is necessary. Therefore, syndromic surveillance systems have been implemented in many countries since 1995 [1]. Syndromic surveillance monitors changes in the number of patients according to symptoms such as fever, vomiting, diarrhea, and rash for further investigations. Information regarding the identification of local infectious disease outbreaks, such as school absenteeism, emergency room visits, and prescriptions of therapeutic drug against infectious diseases, are also subjects of the survey [2]. Syndromic surveillance can offer a rapid method to detect an outbreak of infection compared with traditional surveillance; such surveillance systems are currently used worldwide [3, 4].

In some cases, an infectious outbreak can be detected on the same or the following day. Although syndromic surveillance provides rapid results, it has the disadvantage that

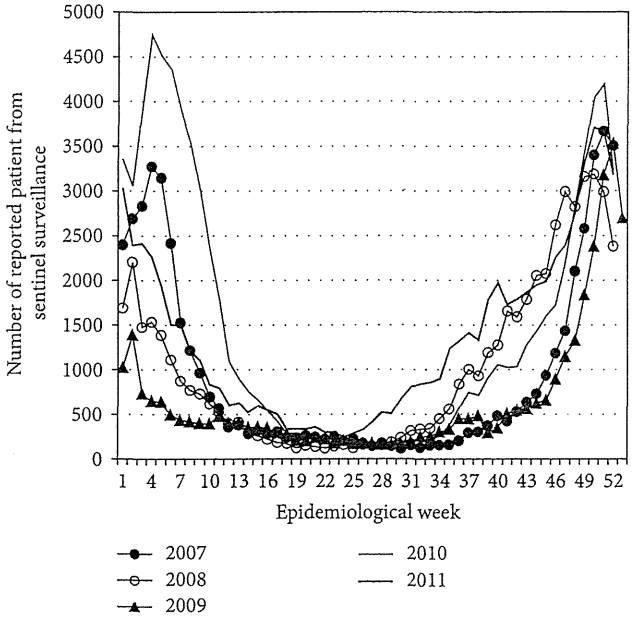

FIGURE 1: Number of reported RSV cases from sentinel medical institutions in Japan. There are approximately 500 sentinel medical institutions in Japan, which are selected from those equipped with departments of pediatrics and internal medicine and with more than 300 beds.

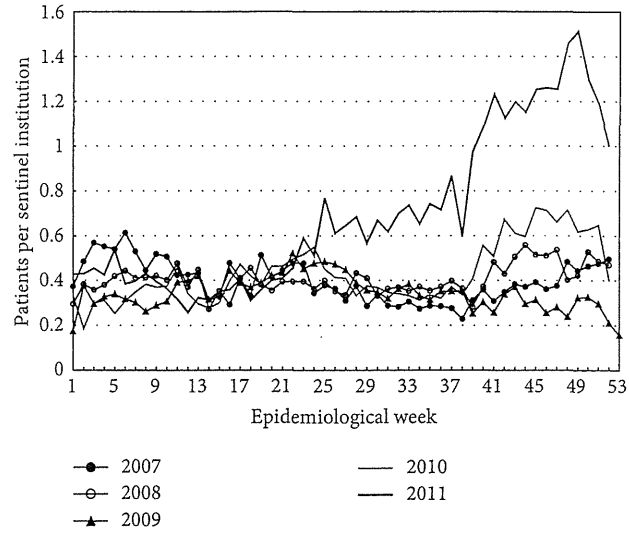

FIGURE 2: Patients per sentinel medical institution reporting *M. pneumoniae* infections.

definitive diagnoses are not considered. In other words, in general, its specificity may be lower than that of traditional surveillance systems. Laboratory testing performed on all symptomatic patients can yield a very high specificity, but is cost prohibitive, whereas laboratory testing on selected patients for syndromic surveillance can detect some specific aberrations at a lower cost, thereby overcoming the shortcomings of both systems. The current study highlights an example to further analyze this possibility.

In the fall of 2011, the number of patients with symptoms of upper respiratory tract infections markedly increased in Japan. Infectious disease weekly reports (IDWRs) (http://www.nih.go.jp/niid/ja/idwr.html in Japanese), which constitute the traditional and official Japanese sentinel surveillance system, reported a higher incidence of respiratory syncytial virus (RSV) (Figure 1) and *M. pneumoniae* infections (Figure 2). A primary feature of *M. pneumoniae* respiratory infections is the degree of the symptom worsening from mild upper respiratory tract inflammation to pneumonia. *M. pneumoniae* infection is associated with exanthem, hemolytic anemia, gastrointestinal damage, arthritis, and various neurological symptoms [5].

Outbreaks of *M. pneumoniae* persisted throughout June 2012, although it is unclear why this organism has continued to be responsible for such a widespread national outbreak in Japan since the fall of 2011 [6]. Koike et al. [7] detected only 40 patients (14.5%) among 275 suspected cases of *M. pneumoniae* infection from 2006 to 2008 in Japan. A clinical diagnosis of *M. pneumoniae* infection is difficult without laboratory confirmation. In many sentinel hospitals, the *M. pneumoniae*-specific IgM antibody rapid detection test is used, but during screening, a positive result in the test does not always indicate acute infection by this organism. We suspect that the outbreak of *M. pneumoniae* infection included false-positive cases [7, 8].

IDWRs are very important for clinicians, enabling them to identify the seasonal prevalence of known diseases. However, these reports become available after a minimum of 10 days following patient examinations. Therefore, traditional and official surveillance systems have the distinct disadvantage of being slow and are limited to reporting pathogens chosen in advance.

In the fall of 2011, by monitoring the increase in the number of combination cold medications (active ingredients: salicylamide, acetaminophen, anhydrous caffeine, and promethazine methylene disalicylate) prescribed since 2009, the prescription surveillance system detected an increase in the number of patients with symptoms of upper respiratory tract infections. On September 26, 2011, we noticed the first unusual peak and began to carefully monitor the real-time prescription surveillance system and observed a second peak on October 3, 2011 (Figure 3). However, monitoring prescriptions for combination cold medications does not lead to the identification of the pathogens responsible for the illnesses being treated. Thus, we conducted pathogen identification using the PCR method after being alerted by the prescription surveillance system on October 4, 2011 (the following day).

The purpose of the present study was to evaluate whether the PCR method triggered by the results of the prescription surveillance system can rapidly and accurately identify causative pathogens of local outbreaks of infection. Our results allowed for earlier diagnoses at medical facilities and the dissemination of this information among other institutions to avoid inappropriate use of antibiotics and instigate measures against the spread of infectious diseases.

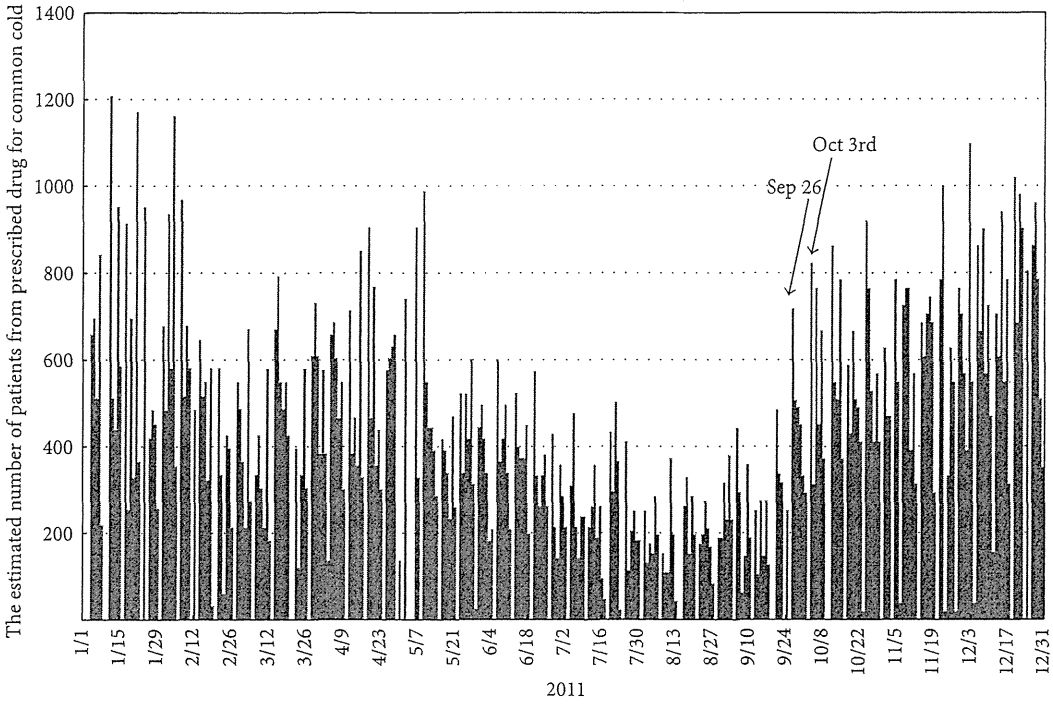

FIGURE 3: Combination cold medication prescriptions recorded by the prescription surveillance system over time. On September 26, 2011, we noticed an unusual peak and then carefully monitored the real-time prescription surveillance and found a second peak on October 3, 2011. We confirmed this abnormality and began this study on the following day (October 4, 2011).

2. Materials and Methods

2.1. Prescription Surveillance. Although very common in the US and other countries, there is no nationwide syndromic surveillance system to electronically monitor medical records in Japan. Because of the low prevalence of electronic medical records and a restrictive privacy policy, we perform prescription surveillance nationwide for syndromic surveillance by monitoring the number of prescriptions for certain types of drugs such as anti-influenza medications.

There are approximately 45,000 pharmacies that deliver almost half of the prescribed drugs nationwide and almost all record prescriptions electronically. The prescription surveillance system was developed by the Infectious Disease Surveillance Center of the National Institute of Infectious Diseases in collaboration with EM Systems Co. Ltd. (Osaka, Japan), a leading provider of prescription surveillance used by pharmacies through the Application Server Provider (ASP) system. The ASP system is very useful for syndromic surveillance because data transfer is unnecessary. Thus, it can dramatically decrease costs and maintain a high level of confidentially. Its widespread use started in April 2009, and approximately 6,300 (13%) Japanese pharmacies actively participated in the program as of October 2011.

The ASP system tracks prescription information, but patient symptoms and diagnoses are not recorded. Categories of syndromic surveillance include the type of prescribed drugs. Currently, the syndromic surveillance system monitors several types of drugs, including those for relief of fever and pain due to common colds, as well as antiviral agents, anti-influenza medications (except amantadine), and anti-varicella zoster virus (VZV) drugs. The surveillance of the last two is also classified by age: <15, 16–64, and >65 years. Data collection and analysis are automatically performed every night, and the results are available on the home page of a secure internet site early the next morning.

Monitoring the usage of anti-influenza and anti-VZV drugs is particularly useful for early detection of outbreaks of infection because these drugs are used only to treat specific viral infections.

2.2. Clinical Samples. Between October 4 and 28, 2011, 50 patients were included in the present study who either presented at a single clinic with a chief complaint of respiratory symptoms or fever or were suspected of having respiratory tract infections after being identified through the syndromic prescription surveillance system. In Japan, a rapid diagnosis kit suitable for use at outpatient clinics is currently available, and the costs are covered by the national health insurance program. The tests allow for rapid detection of infections caused by the influenza virus, RSV, and adenovirus. A total of 18 pharyngeal swabs to screen for adenovirus infections and 32 nasal swabs to screen for RSV and influenza viral infections (rapid RSV) were collected [9]. Viruses were extracted from the swabs using immunochromatography (IC) kits with approximately 500 μL of a mucolytic agent provided by the manufacturer. After the assay, approximately 200 μL of the agent remained in the IC-kit tubes. This medical waste was transferred to universal transport medium (359C; Copan Italia S.p.A, Brescia, Italy) and analyzed using

Table 1: Hyper-PCR primers.

Pathogen	Primer	Base sequence (5′-3′)	Polarity	Reference
RSV-A	RSA-F	TGC AAG CAG AAA TGG AAC AAG T	+	[14]
106 bp	RSA-R	AAT AAT GAT GCT TTT GGG TTG TTC A	−	
RSV-B	RSB-F	GATGGCTCTTAGCAAAGTCAAGTTAA	+	[15]
104 bp	RSB-R	TGTCAATATTATCTCCTGTACTACGTTGAA	−	
Parainfluenza 1	PIS1+	CCGGTAATTTCTCATACCTATG	+	[16]
317 bp	PIS1−	CCTTGGAGCGGAGTTGTTAAG	−	
Parainfluenza 3	Para3.1	CTCGAGGTTGTCAGGATATAG	+	[16]
189 bp	Para3.2	CTTTGGGAGTTGAACACAGTT	−	
Rhinovirus	SRHI-1-NIID	CGGGTAGCTTCCACCACCAGCCCTT	+	[16]
549 bp	SRHI-2	GGGACCAACTACTTTGGGTGTCCGTGT	−	
Enterovirus	entR1	ATTGTCACCATAAGCAGCCA	+	[17]
172 bp	entE2	CCTCCGGCCCCTGAATG	−	
H1N1 2009	swH1-F2	TCATGCGAACAATTCAACA	+	Present study
127 bp	swH1-R2	TGGGGCTACCCCTCTTAGTTTG	−	

real-time polymerase chain reaction (PCR) [10] and Hyper-PCR [11], which is a faster technique compared with the previously available PCR applications. Thus, we used Hyper-PCR for the applicable pathogens. The CycleavePCR respiratory infection-pathogenic virus detection kit (Takara Bio, Shiga, Japan) was used to detect 11 types of viruses: human RSV types A and B, human parainfluenza virus types 1–3, human metapneumovirus, influenza A and B viruses, human adenovirus, human bocavirus, and human rhinovirus. The Thermal Cycler Dice Real Time System II MRQ (Takara Bio) was used to detect and identify the 11 types of viruses detected by the CycleavePCR kit [10]. Hyper-PCR [11] was performed using the One Step SYBR High Speed RT-PCR Kit (Hyper-PCR) (Takara) to detect RSV types A, B, human parainfluenza virus types 1, 3, human rhinovirus, enterovirus, and influenza A (H1N1) 2009 (primers are listed in Table 1) using the Hyper-PCR MK IV PCR system (Trust Medical, Hyogo, Japan). The accuracy of the Hyper-PCR methods was confirmed by comparison with other conventional PCR methods. Conventional PCR was used to detect *M. pneumoniae* [12]. In addition, the presence of coronavirus infection was tested in patients from whom no infectious agents were detected [13].

3. Ethical Considerations

This study only collected anonymous information that cannot be associated with individual patients. Patient samples were collected during the course of medical care provided at the participating facilities, and all examinations and testing for pathogens occurred at the request of the medical facilities for the purposes of diagnosis and treatment. This study used only existing medical records and documents, and oral informed consent was obtained from all patients.

4. Results

After testing the specimens, we provided the results to a medical institution within 4 days including the conveyance period. The 50 patients tested in this study included 2 infants (1 male and 1 female, aged <1 year), 25 children (12 males and 13 females, aged 1–6 years), 10 elementary school pupils (6 males and 4 females, aged 7–12 years), 4 minors (2 males and 2 females, aged 13–18 years), 8 adults (3 males and 5 females, aged >18 years), and 1 patient (age unavailable).

Table 2 lists the pathogens detected by the PCR analysis stratified by age in the 27 patients. In children, enterovirus, rhinoviruses, RSV, and parainfluenza viruses were detected, whereas *M. pneumoniae* was detected only in elementary school pupils and minors. In the remaining 23 patients, no pathogens were detected. These 23 patients were also found to be negative for coronavirus.

PCR was used to obtain definitive viral diagnoses via rapid RSV and adenovirus diagnosis kits, and the sensitivity and specificity were calculated for these test kits. For the rapid RSV diagnosis kit, sensitivity was 80% and specificity was 85%. For the rapid adenovirus diagnosis kit, no positive results were obtained; therefore, sensitivity could not be calculated and specificity was 100%.

RSV infections were detected using the rapid diagnosis kit, but rhinovirus, enterovirus, and parainfluenza virus infections were not. The causative pathogens were unknown in many patients, although they were nevertheless treated for upper respiratory tract infections.

Evaluation of the incidence of various symptoms in patients infected with different pathogens showed that rhinoviruses were detected in nasal swab specimens more often than other viruses and patients with rhinovirus infections were less likely to present with fever (Table 3).

All RSV-positive patients were children, 80% of whom presented with coughing. All patients who were tested using the rapid adenovirus detection kit showed negative results. However, all these patients also tested negative for adenovirus using sensitive PCR tests. Thus, adenovirus was not considered to be the causative organism of this suspected outbreak.

Table 2: Numbers of pathogens detected by PCR according to age.

	Infants	Children	Elementary school pupil	Minor (junior high school student or older)	Adult
Enterovirus	0	2	1	0	1
Mycoplasma pneumoniae	0	0	1	1	0
Parainfluenza 1	0	2	0	0	1
Rhinovirus	2	9	0	0	1
Rhinovirus + parainfluenza 1	0	1	0	0	0
Rhinovirus + RSV-A	0	1	0	0	0
Rhinovirus + RSV-A and RSV-B	0	1	0	0	0
RSV-A	0	2	0	0	0
RSV-B	0	1	0	0	0

Table 3: Incidences of symptoms detected in infections according to individual pathogens ($n = 50$).

	Number of infections	Fever	Headache	Nasal discharge	Pharyngeal pain	Cough
Mycoplasma pneumoniae	2	0%	0%	0%	50%	100%
Enterovirus	4	67%	25%	75%	25%	25%
Parainfluenza 1	3	33%	33%	33%	0%	67%
Rhinovirus + parainfluenza 1	1	0%	0%	0%	0%	100%
Rhinovirus	12	20%	0%	67%	0%	83%
Rhinovirus + RSV-A	1	0%	0%	100%	0%	100%
Rhinovirus + RSV-A + RSV-B	1	100%	0%	100%	0%	100%
RSV-A	2	100%	0%	100%	0%	100%
RSV-B	1	100%	0%	0%	0%	0%
None	23	21%	13%	57%	30%	35%

5. Discussion

Here, we examined a combination of syndromic surveillance and PCR testing and showed the potential to identify pathogens during the early stage of an outbreak of respiratory infections. In the future, it would be desirable to develop an *M. pneumoniae* diagnosis kit that can diagnose pathogens from nasal or pharyngeal swabs at outpatient clinics or the bedside of patients.

In Japan, two official pathogen surveillance methods have been conducted under the infection control laws: sentinel pathogen surveillance and active surveillance. The official pathogenic surveillance has been conducted at sentinel medical institutions regardless of outbreaks. On the other hand, in patients with serious diseases, active pathogenic surveillance has sometimes been conducted on the basis of notifications by medical institutions. However, active surveillance is conducted only when an infection spreads widely enough to cause serious problems in a particular region and the surveillance of pathogens may not be timely enough to mount a response to control outbreaks. Pathogenic surveillance for all patients with signs of an infection would detect agents of bioterrorism and emerging infectious diseases; however, the cost would be prohibitive. Therefore, system coordination to perform pathogen surveillance based on early detection of outbreaks is necessary. The scheme proposed by the present study uses PCR testing triggered by detection alerts from syndromic surveillance systems. In general, syndromic surveillance offers earlier detection of infectious diseases than traditional surveillance. Moreover, if the pathogen remains unknown following bedside testing using several rapid tests or other typical examinations, the proposed scheme requires the collection of specimens as soon as possible and sending them to a laboratory for definitive diagnoses. However, it takes a few days to transfer the specimens and a few extra days for the information of the identified pathogen to be shared among medical facilities, public health centers, and local governments in the involved areas. In the proposed scheme, we can use pathogenic information to control ongoing outbreaks and, hopefully, decrease the number of potential infections.

Thus far, syndromic surveillance with pathogenic testing has been conducted by collecting samples from patients receiving telephone consultations [18] and those receiving emergency department consultations [19]. Syndromic surveillance using electronic medical records has been combined with testing for the influenza virus [20]. However, these systems have focused only on rapid testing and are mainly used for influenza monitoring [20, 21]. Therefore, syndromic surveillance trials for nonspecific pathogens using PCR for undiagnosed infectious diseases, similar to the present study, have not been performed before.

In the present study, an outbreak was detected by routine syndromic surveillance, in which samples were regionally collected for PCR analysis. These tests for viral infections allowed for differentiation between bacterial and viral infections, thus facilitating treatment without the unnecessary use of antibiotics. Although the present laboratory tests cannot be performed for all individual clinical diagnoses, the

results were immediately made available to clinicians for the treatment of other patients with similar symptoms.

The symptoms reported in the present study were rather mild; therefore, no patient required hospitalization, and no further testing was performed in undiagnosed patients. However, if severe cases were to occur, careful identification of pathogens would be desirable. Rhinoviruses were detected in nasal swab specimens more frequently than other viruses. Therefore, it is likely that children who present with nasal discharge and mild fever may be reservoirs for rhinoviruses [22]. Testing for respiratory viral infections in emergency room outpatients by PCR analysis showed that the most frequently detected viruses were picornaviruses, including rhinoviruses [23]. When children present with coughing as the main symptom, RSV should be considered as the most likely pathogen.

The finding that *M. pneumoniae* infection was not detected in infants and children, but rather in elementary school pupils and minors, was consistent with reports that *M. pneumoniae* may often cause asymptomatic infections before the age of 5 years, after which immunity decreases as children become susceptible to symptomatic *M. pneumoniae* infections [5].

In Japan, nationwide outbreaks of *M. pneumoniae* began in 2011 and continued as of January 2012, during which time *M. pneumonia*, rhinovirus, enterovirus, parainfluenza virus, and RSV have been identified. Our results suggested that this outbreak may include false-positive cases and subsequent inappropriate prescriptions of antibiotics.

An increased frequency of macrolide-resistant *M. pneumoniae* became widely reported in the Japanese media in the fall of 2011 [24]. Therefore, this news may have induced an abnormal increase in the number of patients (Figure 2). The rapid test available in Japan for *M. pneumoniae* uses sera samples [25]. Although general clinics may outsource *M. pneumoniae* antibody testing and cold hemagglutinin testing, blood testing is usually not performed in cases of mild pediatric illnesses.

In the future, it would be desirable to develop *M. pneumoniae* diagnostic kits using nasal or pharyngeal swabs at outpatient clinics or bedside. Until such kits for the diagnoses of *M. pneumoniae* and other infectious diseases are developed, syndromic surveillance with PCR testing offers a useful countermeasure against infectious outbreaks. In this study, we could not detect single infectious agents that explained the outbreaks; however, our results excluded *M. pneumoniae*.

The present study was limited to a single clinic. Therefore, further studies involving more facilities should be undertaken. It is also necessary to develop a network and sample transportation system among the facilities partaking in the syndromic surveillance system and to adequately staff laboratories with experienced technicians.

Syndromic surveillance data has been mathematically or statistically analyzed in many studies. However, when an abnormal value is reported by syndromic surveillance, there are many cases in which the pathogens cannot be identified by the calculations introduced in these articles.

6. Conclusion

When *M. pneumoniae* and RSV infections were prevalent nationwide during the fall of 2011, we observed an abnormal increase in common cold prescriptions through the Japanese surveillance system and were able to evaluate the incidence of various pathogens via PCR testing.

Authors' Contribution

The authors contributed equally to this paper.

Acknowledgment

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Original Paper

Real-time Prescription Surveillance and its Application to Monitoring Seasonal Influenza Activity in Japan

Tamie Sugawara[1], PhD; Yasushi Ohkusa[1], PhD; Yoko Ibuka[2], PhD; Hirokazu Kawanohara[3], BS; Kiyosu Taniguchi[1], PhD, MD; Nobuhiko Okabe[1], PhD, MD

[1]National Institute of Infectious Diseases, Infectious Disease Surveillance Center, Tokyo, Japan

[2]Hitotsubashi University, Tokyo, Japan

[3]EM Systems Co., Ltd, Tokyo, Japan

Corresponding Author:
Tamie Sugawara, PhD
National Institute of Infectious Diseases
Infectious Disease Surveillance Center
1-23-1Toyama
Shinjuku
Tokyo, 162-8640
Japan
Phone: 81 3 5285 1111
Fax: 81 3 5285 1129
Email: tammy@nih.go.jp

Abstract

Background: Real-time surveillance is fundamental for effective control of disease outbreaks, but the official sentinel surveillance in Japan collects information related to disease activity only weekly and updates it with a 1-week time lag.

Objective: To report on a prescription surveillance system using electronic records related to prescription drugs that was started in 2008 in Japan, and to evaluate the surveillance system for monitoring influenza activity during the 2009–2010 and 2010–2011 influenza seasons.

Methods: We developed an automatic surveillance system using electronic records of prescription drug purchases collected from 5275 pharmacies through the application service provider's medical claims service. We then applied the system to monitoring influenza activity during the 2009–2010 and 2010–2011 influenza seasons. The surveillance system collected information related to drugs and patients directly and automatically from the electronic prescription record system, and estimated the number of influenza cases based on the number of prescriptions of anti-influenza virus medication. Then it shared the information related to influenza activity through the Internet with the public on a daily basis.

Results: During the 2009–2010 influenza season, the number of influenza patients estimated by the prescription surveillance system between the 28th week of 2009 and the 12th week of 2010 was 9,234,289. In the 2010–2011 influenza season, the number of influenza patients between the 36th week of 2010 and the 12th week of 2011 was 7,153,437. The estimated number of influenza cases was highly correlated with that predicted by the official sentinel surveillance ($r = .992$, $P < .001$ for 2009–2010; $r = .972$, $P < .001$ for 2010–2011), indicating that the prescription surveillance system produced a good approximation of activity patterns.

Conclusions: Our prescription surveillance system presents great potential for monitoring influenza activity and for providing early detection of infectious disease outbreaks.

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KEYWORDS

Surveillance; influenza; real-time surveillance; prescriptions; pharmacy; anti-influenza virus; automatic surveillance; early response

Introduction

In Japan, the official sentinel surveillance reports the number of influenza patients per health care provider after collecting information from approximately 5000 clinics and hospitals. The intensity of influenza activity is assessed according to the number of influenza patients per clinic or hospital. Influenza is regarded as highly active if the ratio exceeds 1. In 2009, the number of patients per clinic or hospital approached 1 in the 32nd week, earlier than in any of the preceding 10 years, mainly because of the influenza pandemic A (H1N1), which started in April 2009 [1]. Accordingly, the vast majority of the reported cases were H1N1 novel influenza [1]. The number of influenza patients per health care provider declined below 1 in the 13th week of 2010. The total number of weeks during which influenza was highly active was 29, a longer active period than in any of the prior 10 years. In 2010, the reported number of influenza patients per clinic or hospital exceeded 1 in the 50th week [2]; a second peak week was detected in March 2011. Because of these irregular patterns of influenza activity, it is necessary that both policy makers and clinicians follow influenza activity closely to implement effective control of an influenza outbreak throughout the year.

Syndromic surveillance is a useful tool for seasonal influenza monitoring [3]. In Japan, the official sentinel surveillance of infectious diseases is implemented by the National Institute of Infectious Diseases. It reports the estimated number of influenza patients weekly as the *Infectious Diseases Weekly Report* [2]. The official sentinel surveillance collects the number of influenza cases from approximately 5000 hospitals and clinics all over the country and then estimates the number of influenza patients based on the reported cases [4]. The entire process of collecting information from health care providers, estimating the number of clinical influenza cases, and reporting them to the public usually takes 7–10 days. Furthermore, the cases are reported by health care providers as a weekly aggregate number. Some diseases spread rapidly, and the weekly aggregates might not provide sufficiently detailed information reflecting the complete character of disease activity. In addition, the official sentinel surveillance updates influenza activity less frequently during major holidays. In Japan, seasonal influenza activity usually starts to become active during the New Year holidays. Constant monitoring and reporting of activity during that period is necessary.

Syndromic surveillance is in widespread use for monitoring diseases, but usage of prescription drug sales as a source of information is fairly limited. In the United States, the most common source of syndromic surveillance reported by health officials is emergency department visits (84%), followed by outpatient clinic visits (49%) and over-the-counter medication sales (44%); less than 10% of health departments reported prescription medications as a source [3]. In the context of influenza, emergency department surveillance is used to monitor the impact of influenza by age [5]. For more rapid feedback, the Web recently has become a powerful tool for syndromic surveillance [6]. For example, health surveillance using a Web-based self-reporting daily questionnaire is applied to monitor influenza activities [7]. Google Flu Trends, a Web-based surveillance, tracks the rate of influenza using query logs [8]. In addition to monitoring disease activities, syndromic surveillance helps monitor bioterrorism-related disease [9] or health consequences of natural events [10].

Real-time information related to influenza activity is fundamentally important for better preparation of countermeasures against a sudden increase of influenza activity. Therefore, daily updates of influenza activity are indispensable for improved understanding and control of an influenza epidemic. We developed an automatic real-time prescription surveillance system with the collaboration of EM Systems Co. Ltd. (Tokyo, Japan) to provide timely information related to a disease outbreak. We applied the surveillance system to monitor influenza activity during the 2009–2010 and 2010–2011 influenza seasons to examine the magnitude and trajectory of an outbreak more closely and to share that information with public health authorities, as well as participating pharmacies.

We used prescription drug purchase data for surveillance of influenza activity for three reasons. First, prescribing anti-influenza drugs such as oseltamivir or zanamivir is a common clinical practice for diagnosed influenza cases in Japan. Japan has the highest annual level of oseltamivir usage in the world [11]. Therefore, prescription drugs can serve as a good indicator of the overall number of influenza patients. Physicians often perform rapid influenza diagnostic tests on patients who have a fever or report other influenza-like symptoms. If the test result is positive or, alternatively, if the physician clinically diagnoses influenza even when the test result is negative, then anti-influenza drugs are often prescribed. This contrasts to practices in some other developed countries, where anti-influenza drugs are recommended for those who are at high risk [12-14] or who have severe conditions from influenza infections [13,14]. In such circumstances, surveillance of prescriptions of anti-influenza drugs would trace influenza patients with severe symptoms [15].

Second, many pharmacies have adopted the electronic prescription record system (EPRS), which enables automatic, continuous, and constant information collection, and real-time analysis of prescriptions and patients. In Japan, the utilization rate of the EPRS among pharmacies was 99.0% in 2009 [16]. Japan also has a high rate of outpatient or office-based clinician visits in cases where people feel ill [17], partly because of the universal health insurance system. Therefore, one might infer that the number of influenza patients collected through the EPRS would closely approximate the number of symptomatic influenza patients.

Third, in contrast to the United States or Taiwan [18], in Japan electronic medical record (EMR) systems are not yet well established. In the United States, surveillance for influenza activity is based on data on outpatient visits along with data related to sales of over-the-counter drugs, school absenteeism, and ambulatory care encounters [3,9,19-21]. Surveillance for influenza activity using the EMR has been intensively discussed and widely applied [22-24]. By contrast, the Survey of Medical Institutions by the Ministry of Health, Labour and Welfare in Japan showed that the share of health care providers using EMRs

was just over 10% in 2008, or 948 hospitals (10.8% of all hospitals) and 12,939 clinics (13.1% of all clinics) [25].

We developed the surveillance system to collect the number of prescriptions together with patients' characteristics from the EPRS automatically, to analyze the data simultaneously to estimate the number of influenza cases, and then to provide real-time information of influenza activity to health care providers and policy makers. The system was tested for a limited time at the G8 Summit meeting in Toyako, Hokkaido in July 2008 for 1 month [26]. The present report summarizes details of our prescription surveillance system and presents an evaluation of its performance in the first two influenza seasons, those of 2009–2010 and 2010–2011, since the start of the nationwide operation of the system. The evaluation of surveillance performance, particularly outbreak detection performance, is challenging and few studies conduct such analyses [27]. A study showed that weekly variation in visits for lower respiratory tract infections approximated the national mortality data for pneumonia and influenza [28]. Similarly, our retrospective evaluation analyzed how closely the estimates of influenza cases followed the trajectory of influenza epidemics reported by two other sources.

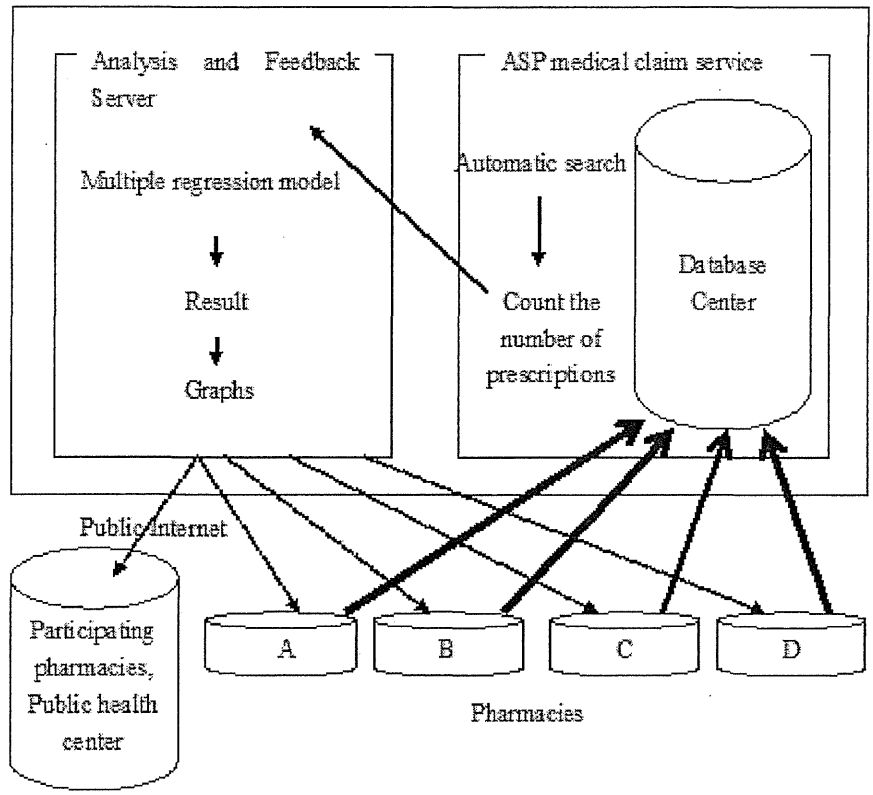
Methods

Prescription Surveillance

We started collecting and analyzing data related to prescriptions automatically through the application service provider of the EPRS in April 2009 (Figure 1 [29]). As of March 2011, the number of participating pharmacies was 5275. In the application service provider, data related to prescriptions from all participating pharmacies were collected and deposited in a single server, making the data collection secure, efficient, and nearly cost-free. Medications covered by the surveillance system included drugs for relief of fever and pain, drugs for common colds, antibiotics, and antiviral drugs including anti-influenza virus drugs and antivaricella-zoster virus drugs. The current study specifically addressed prescriptions for anti-influenza virus medication. The neuraminidase inhibitors oseltamivir, zanamivir, and laninamivir were included, but amantadine was excluded because it is not commonly prescribed for influenza in Japan.

The original prescriptions contain information related to patients' sociodemographic and social security information, as well as the health care providers' information. The automatic surveillance system aggregated the number of prescriptions for each type of drug and provided tabulations by age and by geography at both national and prefectural levels. The number of influenza patients was then estimated from the aggregated number of prescriptions for anti-influenza drugs by adjusting the number of prescriptions for anti-influenza drugs with the proportion of participating pharmacies and of prescriptions purchased through pharmacies. The analysis and estimation were conducted overnight and the report of the analysis was sent automatically at 7:00 AM on the next day to the registered recipients, including participating pharmacies and public health authorities. In addition, figures showing the number of prescriptions for each type of drug and of the estimated number of patients were created and posted on the website for public access.

Figure 1. Prescription surveillance. Pharmacies A–D use the application service provider's (ASP) medical claims service. All data are stored in a central database. The surveillance system automatically counts oseltamivir, zanamivir, and laninamivir prescriptions at the data center. The information is analyzed using multiple regression models. The results are presented as figures and tables and feedback to participating pharmacies as well as public health authorities.



Performance Evaluation

We evaluated our surveillance system from two perspectives for the 2009–2010 and 2010–2011 influenza seasons. First, we compared the estimated number of influenza patients with the estimates provided by the official sentinel surveillance [2]. The official sentinel surveillance estimates the number of influenza patients based on the number of influenza patients reported by 5000 health care providers, including 3000 pediatricians, in Japan. We chose the evaluation period to include the period when influenza activity was high for the 2009–2010 influenza season. The epidemiological threshold of seasonal influenza activity is determined by the number of influenza patients per hospital or clinic. If the ratio is equal to or greater than 1 based on the official sentinel surveillance, activity is *high* by the definition that is accepted and widely used throughout Japan [2]. This corresponds to the period between the 28th week of 2009 (the week starting on July 6, 2009) and the 12th week of 2010 (the week starting on March 21, 2010) for the 2009–2010 influenza season. For the 2010–2011 season, the performance was evaluated between the 36th week of 2010 (the week starting on September 6, 2010) and the 12th week of 2011 (the week starting on March 21, 2011). Second, for the 2009–2010 influenza season, we also compared our estimates with the number of influenza patients estimated by the Gifu Medical Association, where the total number of influenza patients in the prefecture was calculated and reported publicly [29]. The number of influenza patients in Gifu Prefecture was surveyed during November 16–22, 2009 by the local public health authority as a response to the A/H1N1 influenza pandemic. A survey questionnaire asking for the number of influenza patients who visited health care providers was sent to all hospitals and clinics located within the prefecture (total of 1677 health providers); 1033 providers responded to the survey (response rate 61.6%) [29].

The Internal Review Board at the National Institute of Infectious Diseases approved the current study (approval number 57, "Development and application of real-time surveillance system to monitor syndromic and symptomatic cases using electronic record system").

Results

For the 2009–2010 influenza season, the total number of influenza patients estimated by the prescription surveillance system between the 28th week of 2009 and the 12th week of 2010 was 9,234,289 (Table 1). The largest number of influenza patients, 234,519, was reported on November 24, 2009. For the 2010–2011 influenza season, the number of influenza patients between the 36th week of 2010 and the 12th week of 2011 was 7,153,437 (Table 1). The largest number of influenza patients, 230,288, was reported on January 24, 2011. The official sentinel

surveillance estimated the total number of patients for the same periods as 20,660,000 (95% confidence interval 20,460,000–20,860,000) for the 2009–2010 and 13,680,000 (95% confidence interval 13,350,000–14,010,000) for the 2010–2011 influenza seasons [2], indicating that the sentinel estimates were approximately double our estimates.

Table 1. Number of influenza cases estimated by the prescription surveillance, the official sentinel surveillance, and the Gifu Medical Association in Gifu Prefecture, 2009–2010 and 2010–2011 influenza seasons[a]

	2009–2010 influenza season: July 6, 2009–March 28, 2010 (28th week 2009–12th week 2010)	2010–2011 influenza season: September 6, 2010–March 27, 2011 (36th week 2010–12th week 2011)
Estimate by the prescription surveillance	9,234,289	7,153,437
Estimate by the official sentinel surveillance	20,660,000	13,680,000
Adjusted estimation by the survey in Gifu Prefecture	9,931,200	Not applicable[b]

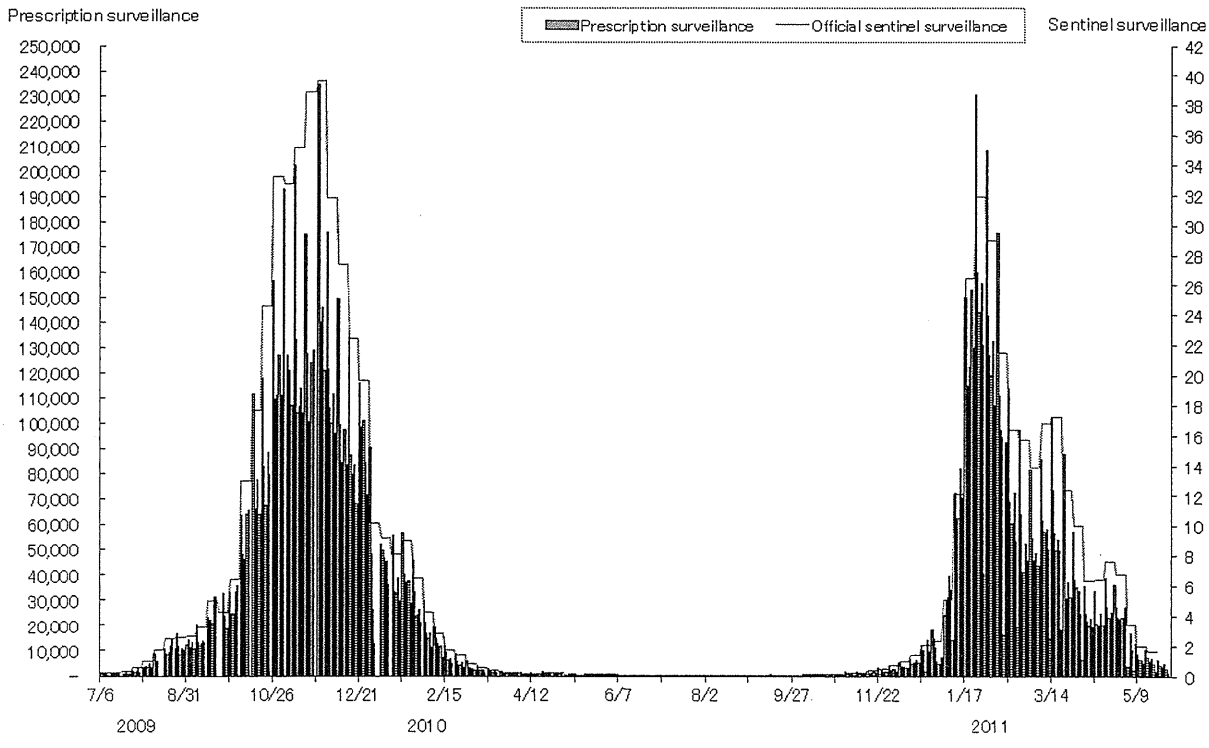
[a] Sources: the official sentinel surveillance [2]; Kawai et al [29].

[b] Adjusted estimation by the survey in Gifu Prefecture is shown only for the 2009–2010 influenza season because the data are available only for that year.

Pearson correlation coefficient (r) of time-series data on influenza patients between our estimates and the official sentinel estimate was .992 ($P < .001$) for the 2009–2010 influenza season, and .972 ($P < .001$) for the 2010–2011 influenza season (see Figure 2). A similar analysis was conducted at the prefecture level. The correlation was.950 or greater in 33 prefectures, .900–.949 in 5 prefectures, and .770–.899 in 8 prefectures. The correlation was the lowest in Akita Prefecture ($r = .689$).

The estimated number of influenza cases in the 2009–2010 influenza season was also compared with that ascertained from the survey of the number of influenza patients at all clinics and hospitals conducted in Gifu Prefecture. The estimated number from the survey collection in the prefecture based on the prescription surveillance was 127,568, whereas the number of influenza cases reported by the survey conducted by Gifu Medical Association was 132,474. The official sentinel surveillance estimated the number as 277,890.

Figure 2. Number of influenza cases, 2009–2011, estimated by the prescription surveillance and reported by the official sentinel surveillance. The estimated number of influenza cases by prescription surveillance was calculated based on the number of oseltamivir, zanamivir, and laninamivir prescriptions adjusted by the proportion of participating pharmacies and extramural dispensing percentage. See text for details. The reported number by the official sentinel surveillance shows the number of influenza patients per clinic or hospital, calculated with the reported number of influenza patients from 5000 sentinel clinics and hospitals.



Discussion

Our analyses showed that the time-series pattern of influenza activity reported by the prescription surveillance system in the first two influenza seasons was highly correlated with the pattern reported by the official sentinel surveillance, showing that pharmacy surveillance can be a good indicator of influenza activity in Japan. Although the estimated number of influenza patients was double that of the official sentinel surveillance, it was close to the estimate by Gifu Prefecture, where the total number of influenza patients was collected in a survey.

The significance of our prescription surveillance is threefold. First, the syndromic surveillance system collected, analyzed, and reported data related to influenza patients simultaneously. Therefore, clinicians and policy makers were able to obtain the estimated number of influenza patients of the previous day. This meant that the estimates were available 1 week ahead of those reported by the official sentinel surveillance, enabling predictions of influenza activity for the immediately following week. This was particularly important at the outset of a seasonal epidemic, when the trajectory of a quickly spreading disease would have changed. Though the Google Flu Trends tool, another real-time surveillance, has been shown to perform well in the United States [8] and European countries [30], the results may be sensitive to variations in patients' behavior across countries.

Second, our prescription surveillance was national and observed regional variations in influenza activity at the prefecture level, although the precision of surveillance varied somewhat between prefectures. This provided helpful information to public health services to plan for the allocation of medical, pharmaceutical, and human resources for influenza control, shifting limited resources to the most affected regions.

Third, our surveillance runs constantly, maintaining the method of counting and estimating influenza cases at all times, and thus we were able to obtain the complete trajectory of the influenza pandemic in the 2009–2010 season. Initially during the pandemic, the law required hospitals and clinics to report all influenza cases, but that practice was terminated on July 24, 2009, after which activity was tracked only by the official sentinel surveillance.

Our surveillance system also promises great potential for future application to the early detection of an infectious disease outbreak or bioterrorism attack, which could happen potentially anywhere at any time. When we started operating a prescription surveillance system in 2009, all other surveillance systems running in Japan covered only specific regions of the country for practical reasons [31]. Furthermore, because influenza outbreaks do not necessarily occur during winter, the time that is covered by the sentinel surveillance, continuous monitoring of influenza activity is necessary to detect outbreaks early in their course. Our automatic prescription surveillance system uses the same standard for detection of a disease outbreak and runs continuously, providing an important complementary role in support of existing surveillance systems in Japan.

If EMRs were widely kept, then information related to influenza patients could be collected even faster and possibly more accurately. However, the share of health care providers that have adopted the EMR system was slightly above 10%. Under such circumstances, purchases of anti-influenza drugs can serve as an alternative indicator of influenza activity.

Limitations to this study exist. First, the total number of influenza cases was estimated as almost half of the estimate based on the official sentinel surveillance, although it approximated estimates based on a survey collecting the total number of influenza cases in Gifu Prefecture. One reason for this gap might lie in the choice of health care providers participating in the official sentinel surveillance. The sentinel health care providers have, on average, a larger number of patients than others, potentially resulting in an overestimation of the overall number of influenza patients. Second, anti-influenza drugs are also prescribed for prophylaxis in addition to treatment, which might engender overestimation of the total number of influenza cases. However, in Japan the preventive usage of oseltamivir is limited to household members of influenza patients who are 65 years or older or who are high-risk individuals [32]. Third, the prophylactic usage of anti-influenza drugs for health care providers and for the public was most intensive at the beginning of the H1N1 pandemic outbreak. We did not include those prescriptions in our surveillance data because they were not prescribed through health care providers. Fourth, 60% of the prescriptions were purchased through pharmacies in 2008. The other prescriptions were purchased directly through health care providers and were not included in our surveillance [33]. This is still much higher than the rate of adoption of the EMR system in hospitals and clinics. Fifth, the participation rate of pharmacies is low, particularly in certain areas. If the number of participating pharmacies were increased, then estimating influenza cases would be possible even for smaller geographical units.

Despite these limitations, pharmacy surveillance provided an approximation of the trend of influenza activity in the first two influenza seasons after the start of its nationwide operation. It provided both clinicians and policy makers with helpful real-time information related to influenza activity. Our pharmacy surveillance system has great potential for detection as well as for monitoring of infectious disease outbreaks in the population and in cases of significant political or cultural events.

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Conflicts of Interest

None declared.

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Abbreviations

EMR: electronic medical record
EPRS: electronic prescription record system

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投稿

佐賀県におけるインフルエンザ年齢構成の検討

大日 康史＊1　菅原 民枝＊1　谷口 清州＊2　岡部 信彦＊3
森屋 一雄＊7　嘉村 明子＊8　山口 邦彦＊9　永尾 一恵＊7
末次 稔＊6　古川 次男＊4　平子 哲夫＊5

目的　インフルエンザ対策は公衆衛生上重要な対策のひとつであり，インフルエンザ患者数を推定することは，政策決定をする上で必須である。薬局サーベイランスによるインフルエンザ推定患者数と発生動向調査のインフルエンザ報告数の相関は高く，薬局サーベイランスはリアルタイムな情報として2009年からインフルエンザ流行時に活用されているが，年齢構成の検討は行われていなかった。そこで本研究の目的は，薬局参加率の最も高い佐賀県において年齢構成の情報を加えることで，今後のインフルエンザ対策に役立てることとした。

方法　薬局サーベイランスの抗インフルエンザウイルス薬の処方数による推定患者数と発生動向調査のインフルエンザ患者数の年齢構成を比較する。年齢構成は発生動向調査に従い，0～4歳，5～9，10～14，15～19，20～29，30～39，40～49，50～59，60～69，70歳以上とした。データ期間は，2010年36週（9月6日～12日）～2011年35週（8月26日～9月4日）の1年間とした。

結果　佐賀県の薬局サーベイランスの疫学曲線は，2011年第3週（1月17日～23日）がピークで17週（4月25日～5月1日）に2度目のピークがあった。年齢群別では5～9歳が最も多く15.8%，次いで30歳代が15.6%であった。15歳未満は38.8%で，20～49歳が40.4%であった。同県の発生動向調査の疫学曲線も2011年第3週がピークで17週に2度目のピークがあった。年齢群別では5～9歳が34.7%，次いで0～4歳が25.7%であった。15歳未満は77.2%で，20～49歳が14.3%であった。発生動向調査と薬局サーベイランスによるグラフのパターンは同じで，ピークのタイミングも同じであった。発生動向調査と薬局サーベイランスを週単位で相関をみたところ，相関係数は，0.962と強い相関を示した。

結論　インフルエンザ患者数の年齢構成は，2つの調査で大きな違いがみられた。インフルエンザが小児と成人の両方で流行する場合には動向は似るが，成人のみで流行が起こると，現在の発生動向調査ではとらえられない可能性があることが示唆された。薬局サーベイランスでは，すべての医療機関から処方せんを受けつけており，また面分業も広がっているので，特定の年齢に偏る可能性は医療機関より低い。勤労世代の罹患状況を迅速に把握することは，各企業等の事業継続計画（BCP）を運用するうえで重要であると考えられた。

キーワード　インフルエンザ，発生動向調査，薬局サーベイランス，処方せん，年齢構成

Ⅰ 緒　　言

インフルエンザは，2009年に発生した「新型」も含めて毎年流行を繰り返しており，例年多くの感染者と一万人ほどの超過死亡を生じさせている公衆衛生上重要な疾患である。また，

＊1 国立感染症研究所感染症情報センター主任研究官　＊2 同室長　＊3 同センター長
＊4 佐賀県健康福祉本部副本部長　＊5 同本部長　＊6 同健康増進課副課長
＊7 同感染症・新型インフルエンザ対策推進担当係長　＊8 同技師　＊9 同主任獣医師

来たるべき「鳥インフルエンザ」由来の病原性の高い新型インフルエンザの発生に備えて，季節性インフルエンザにおいても対策は必要不可欠である。2009年に発生した「新型」での大きな教訓は，事実上，「季節性」インフルエンザ対策として毎年行っていることしか「新型」対策としても有効でなかったということである。つまり，平時にできないことは非常時にもできない，非常時にできることは平時に淡々と行っていることのみ，ということである。その意味からも，平時において「季節性」インフルエンザ対策を進めることは，将来の「新型」に対する確実な備えになると思われる。

インフルエンザ対策での医療体制では，受診者数や重症者数に応じて医療従事者やベッドなどの限られた医療資源を効率よく配分することが重要である。その配分を考える際には，患者数を推計することがまず必要となる。しかし，発生動向調査は定点医療機関による抽出調査で，受診者数が推計されているが，推計が過大であるという指摘もあり[1)2)]，各自治体では全数調査などの取り組みも行われてきた[3)]。

一方で，薬局サーベイランスは国立感染症研究所感染症情報センターが2009年4月に本格運用を開始した。抗インフルエンザウイルス薬等の処方件数を迅速に把握し，翌日朝には情報共有され，発生動向調査を補完している。薬局サーベイランスによるインフルエンザ推定患者数と発生動向調査のインフルエンザ報告数の相関は高く，2009年のインフルエンザ（H1N1）2009流行時には行政の対策において活用された[2)]。また2010／2011シーズンの患者動向の把握では，年末年始からの流行開始状況であったことから，発生動向調査よりも先行した情報としてインフルエンザ対策に役立てられた[4)]。薬局サーベイランスは，全国で6,000薬局（約13%，2011年10月末現在）が参加しており，中でも佐賀県は最も参加率の高い県であり，188薬局（37.52%）が参加している。こうした特性もあり，佐賀県においても薬局サーベイランスの活用が行動計画[4)]に明記されている。

抗インフルエンザウイルス薬においては処方と診断が一致しており，参加薬局数も多く精度が高いことから[5)]，これまで発生動向調査だけであった患者数の推計が薬局サーベイランスからでも可能になった。しかしインフルエンザ対策において薬局サーベイランスによる推定患者数の情報は活用されてきたものの，年齢構成の検討は行われてこなかった。そこで本研究では，年齢構成の情報を加えることで，今後のインフルエンザ対策に役立てることを目的としている。

Ⅱ 方　法

（1） 対象と期間

薬局サーベイランスの対象薬剤は，解熱鎮痛薬，総合感冒薬，抗菌薬，抗インフルエンザウイルス薬，アシクロビル製剤である。院外処方せんをASP型（Application Service Provider）で記録している薬局から昨日分の対象薬剤の処方件数を自動集計し，推定患者数を算出している。

薬局サーベイランスの抗インフルエンザウイルス薬の処方数と発生動向調査のインフルエンザ患者数を年齢構成でのデータで比較する。年齢構成は，発生動向調査に合わせて0～4歳，5～9，10～14，15～19，20～29，30～39，40～49，50～59，60～69，70歳以上とした。

データ期間は，2010年36週（9月6日～12日）～2011年35週（8月26日～9月4日）の1年間とした。

（2） 倫理的配慮

本研究は，観察研究であるために疫学研究に関する倫理指針（平成14年6月17日）文部科学省／厚生労働省／告示第二号では，患者の同意は必要ではないとされている。さらに，医療・介護関係事業者における個人情報の適切な取り扱いのためのガイドライン（平成16年12月厚生労働省）は学術研究を対象外としているために，本研究は該当しない。なお，本研究は国立感染症研究所医学研究倫理審査を受け，承認されている（受付番号57「電子カルテ遠隔検索システムを用いた症候群及び疾患別リアルタイム・

サーベイランス・システム構築のための基礎的研究」)。

Ⅲ 結　　果

佐賀県の薬局サーベイランスによるインフルエンザ推定患者数の推移を図1で示す。2011年第3週（1月17日～23日）がピークで17週（4月25日～5月1日）に2度目のピークがあった。推定患者数は，期間中69,632人であった。推定患者数のうち，5～9歳は15.8%（11,002人），次いで30歳代が15.6%，10～14歳が14.7%，20歳代が14.5%，40歳代が10.3%，0～4歳が8.3%であった。15歳未満は38.8%，20～49歳が40.4%で，20～49歳のほうが15歳未満よりも高い割合であった。

佐賀県の発生動向調査のインフルエンザ報告数を図2に示す。第3週（1月17日～23日）がピークで，17週（4月25日～5月1日）に2度目のピークがあった。期間中13,812人の報告があった。報告された患者数のうち，5～9歳が34.7%（4,791人）と最も多く，次いで0～4歳が25.7%，10～14歳が16.8%であった。15歳未満は77.2%であった。20歳代5.0%，30歳代5.7%，40歳代が3.6%で，20歳～49歳が14.3%であった。

図1　薬局サーベイランスによる佐賀県のインフルエンザ推計患者数の推移

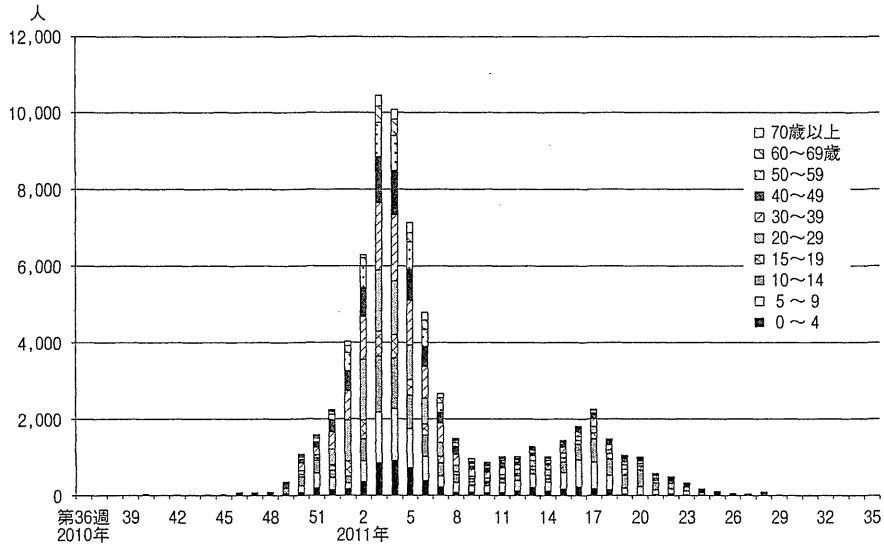
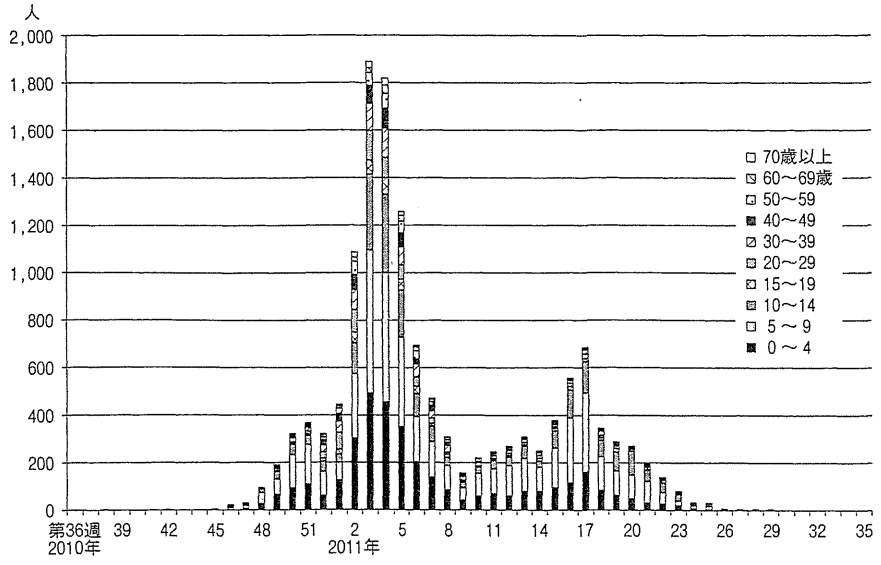


図2　発生動向調査による佐賀県のインフルエンザ推計患者数の推移



発生動向調査と薬局サーベイランスによるグラフのパターンは同じで，ピークのタイミングも同じであった。発生動向調査と薬局サーベイランスを週単位で相関をみたところ，相関係数は，0.962と強い相関を示した。

それぞれの年齢構成は，薬局サーベイランスでは15歳未満は38.8%だが，発生動向調査では77.2%となり，大きな違いがみられた（図3）。

Ⅳ 考　　察

薬局サーベイランスは，発生動向調査より早期に情報をとらえることができる点で，特にインフルエンザ対策では有用とされてきた。現在の発生動向調査では，インフルエンザは小児科定点3,000医療機関と内科定点

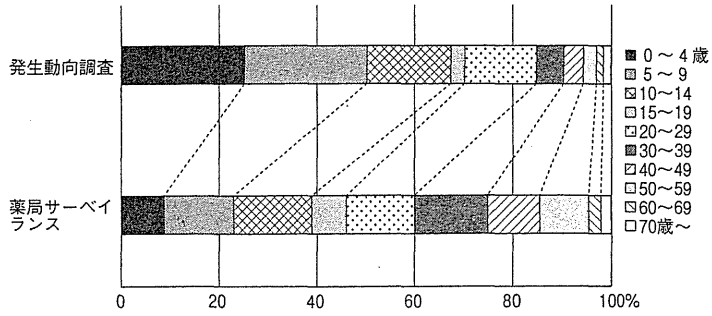
2,000医療機関から報告を受けている。インフルエンザ患者数の把握において，5歳未満の子どもの罹患を把握することはインフルエンザ脳症対策のためにも意義がある。しかし，発生動向調査は，小児科重視の定点設定になっているので，成人の罹患が多いと年齢構成が歪む。もし成人のみで流行が起こると，現在の発生動向調査ではとらえられない可能性がある。公衆衛生対策上，最も重要な高齢者（そもそも罹患率が低いのでとらえにくい）も定点ではほとんどわからない。

本研究により，これまでインフルエンザ対策で用いる資料として，発生動向調査の年齢別報告数しかなかった状況に比べ，薬局サーベイランスによって年齢構成の検討ができることが示唆された。薬局サーベイランスでは，20歳代，30歳代をとらえていたが，発生動向調査では少ない頻度でしかとらえていなかった。薬局サーベイランスはシステム設計上，すべての医療機関から処方せんを受けつけており，また面分業も広がっているので，特定の年齢に偏る可能性は医療機関より低いと考えられ[6]，より正しい年齢分布を反映していると考えられるが，発生動向調査は定点の設計の段階で，年齢分布がゆがんでいる可能性が高いためである。2010／2011インフルエンザシーズンは，2009／2010シーズンの影響を受け，20歳代，30歳代の罹患が多かったとおもわれる。

本研究による年齢構成の検討の結果，仮に薬局サーベイランスが真の年齢分布を示しているとして，発生動向調査をそれに合わせるためには，定点の選択が完全にランダムだとすると内科定点数を増やすことによって是正が可能である。

年齢区分を単純に小児（15歳未満）と成人（15歳以上）として，年齢分布の歪みを是正するのに必要な成人患者数は，現在の発生動向調査での患者数をA人とすると，小児での患者数は0.772×A人，成人の患者数は（1－0.772）×A人である。ここで内科定点を2倍に増やすと成人の患者数は（1－0.772）×A×2人になる。この時の患者総数は0.772×A＋（1－0.772）×A×2であるので，小児の患者数の割合は0.772×A／(0.772×A＋(1－0.772)×A×2）となる。分子分母でAを整理すると0.772／(0.772＋(1－0.772)×2）である。一般に内科定点をB倍に増やせば，小児の患者数の割合は0.772／(0.772＋(1－0.772)×B）となる。したがって，小児の患者数の割合が薬局サーベイランスと同じ0.388にするためには0.772／(0.772＋(1－0.772)×内科定点の拡充率）＝0.388を満たす。これを解くと，薬局サーベイランスと年齢分布が同じになる内科定点の拡充率は，(0.722／0.388－0.722)／(1－0.772)＝4.0965，つまり内科定点を約4倍にすることが必要となる。逆に言うと1／4.0965＝0.2441，つまり現在の内科定点は望ましい定点数の24％程度であると言えよう。

図3　発生動向調査と薬局サーベイランスの年齢構成比較



逆に薬局サーベイランスでは，小児より成人に偏っている可能性がある。しかし，薬局は原則的にすべての医療機関から処方せんを受けつけており，また佐賀県では地域に密着した医薬分業（平成22年度処方せん受け取り率74.6％）も広く行われているので，医療機関よりは特定の年齢に偏る可能性は低いと考えられる。

病原性の高い新型インフルエンザ発生時の対策として，勤労世代（15～65歳まで）の罹患頻度は，各企業等の事業継続計画（BCP：Business Continuity Planning）を運用するうえで，迅速に把握すべきデータであると考えられる。

本研究により，インフルエンザ患者数について年齢別のデータによって検討することが可能となり，こうした検討はシーズンごとの検討が