Epidemiological Analysis of Seasonal Influenza Epidemic in Taiwan in 2006/2007

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Abstract

To investigate severity of influenza epidemic in Taiwan in 2006/2007, we used disease surveillance results of the CDC, including reported cases of influenza from the Sentinel Physician Surveillance System, the School-based Infectious Disease Surveillance Reporting System, and Laboratory Surveillance System, and the cases of influenza with severe complications from the National Notifiable Disease Surveillance System from June 1, 2006 to June 30, 2007. The results showed that there were more cases of seasonal influenza in 2006/2007 than in 2005/2006. The peak happened in late 2006 and 2007, but cases started to increase in the 42nd week of 2006 in the School-based Infectious Disease Surveillance Reporting System, one month earlier than two other surveillance systems (cases in the Sentinel Physician Surveillance System increased since the 47th week of 2006, and numbers of viral isolation increased since the 48th week of 2006). The results of influenza virus isolation showed that 77.0% were influenza

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virus type B, and the major type was B/Malaysia/2506/2004. In this influenza season, 154 cases of influenza with severe complications were reported from the legal infectious disease system, and 34 were confirmed cases. The major viral type was also type B influenza virus. When Poisson distribution was used to estimate 95% confidence interval (95% CI) of the incidence of influenza with severe complications, it was 0.15 cases per one hundred thousand people per year (95%CI: 0.10-0.21). The incidence in northern Taiwan was 0.24 cases per one hundred thousand people per year (95% CI: 0.15-0.35), higher than other areas in Taiwan. The incidence among people between 0 and 9 years old was 0.51 cases per one hundred thousand people per year (95% CI: 0.27-0.88), higher than people of other ages. In summary, there are more cases of seasonal influenza in Taiwan in 2006/2007 than in 2005/2006, and the peak was between late 2006 and early 2007. The major viral type was type B, B/Malaysia/2506/2004.

Keywords: influenza, disease surveillance, influenza virus

Introduction

Influenza is an acute respiratory disease caused by influenza virus infection. The major transmission route is aerosol or direct contact with secretion from patients. People of all age groups can be infected [1,2]. Clinical symptoms of influenza virus infection include fever, headache, myalgia, malaise,rhinorrhea, sore throat, cough, etc [2-4]. In addition to characteristics of fast and widespread transmission, influenza can have severe complications, including viral pneumonia, encephalitis, encephalopathy, myocarditis, pericarditis, and death, especially in elders, children, immunocompromised and chronic patients [2,3]. According to WHO, three to five million people have influenza with severe complications each year globally, leading to death of 250-500 thousand people [4].

Influenza virus is a single strand RNA virus of the *Orthomyxoviridae*. Influenza virus is classified into type A and B, and subtyped according to the surface glycoprotein hemagglutinin (HA) and neuraminidase (NA) [1,2,5]. Influenza A virus can also be sub-typed according to surface HA antigens and NA antigens. There are 16 (H1-H16) HA antigen subtypes and 9 (N1-N9) NA antigen subtypes. Since influenza virus can mutate easily, they can generate new viruses via mutation and recombination. Antigenic drift is caused by accumulated point mutations [2,3,5]. Besides, antigenic shift can be caused by exchange of genetic fragments during replication, leading to generation of novel viruses. If humans have no immunity toward new viruses, global pandemic can happen [1,5].

Vaccination is the best way to prevent influenza. Since variation of viruses is very big, even though vaccines are administered every year, humans still cannot have immunity toward non-vaccine strains or novel strains [2,3]. Hence, highly efficient and real-time influenza surveillance system has become an important part of prevention. To effectively monitor the trend of influenza, the CDC has established multiple surveillance systems [6], including systems for influenza-like illness, influenza virus, and influenza with severe complications. In this study, we investigated epidemiological characteristics of the influenza season in 2006/2007 in Taiwan. We focused on analysis of influenza-like illness and influenza with severe complications, as well as results of virus isolation. We compared the results with two previous seasons in order to understand the trend of influenza epidemics and spreading for references of future disease prevention policies.

Materials and methods

In this study we used secondary data for analysis, using the data for the 2006/2007 influenza season in the National Disease Surveillance Systems (NDSS)

of the CDC [6]. We gathered data from July 1, 2006 to June 30, 2007, as well as data from 2004 to 2006, including influenza-like illness from multiple surveillance systems, isolation of influenza viruses and cases of influenza with severe complications, for statistical analysis to understand the trend of influenza infection.

1. Data sources

In this study, the data came from transmissible disease surveillance systems of the CDC, including:

(1) Sentinel Physician Surveillance System

(2) School-based Infectious Disease Surveillance Reporting System

(3) Laboratory Surveillance System

(4) National Notifiable Disease Surveillance System

Besides, demographic data of late 2006 came from Ministry of Interior Department of Statistics

2. Case definition

(1) Influenza-like illness: all the following criteria are required:

a. Sudden onset of symptoms, fever (ear temperature ≥ 38°C), and respiratory symptoms

b. Myalgia or headache, or severe malaise

c. Simple rhinorrhea, tonsillitis, and bronchitis should be ruled out

(2) Influenza with severe complications

Cases having influenza-like illness with the following complications that require admission or intensive care:

a. Pneumonia: viral pneumonia or respiratory distress syndrome

b. Encephalitis or encephalopathy: brain inflammation or edema with consciousness disturbance or other neurological abnormalities, including

Reye's syndrome.

c. Other severe secondary complications

Suspected cases having the above symptoms were reviewed and confirmed by the infectious disease consultants of the CDC.

3. Methods

In this study, we used the Sentinel Physician Surveillance System and the School-based Infectious Disease Surveillance Reporting System to analyze and compare distribution of influenza like symptoms. Statistics from Laboratory Surveillance System were then used to analyze relationships between epidemics of influenza-like illness and virus isolation. Besides, demographic data, clinical symptoms, diagnoses, and vaccination history of suspected cases of influenza with severe complications from the National Notifiable Disease Surveillance system were also analyzed.

4. Statistics

Microsoft Excel was used for statistical analysis and generation of figures. Besides, SAS was used for Poisson distribution calculation of 95% confidence interval of disease incidence (age and geographic areas).

Results

According to the Sentinel Physician Surveillance System (Fig. 1), in this flu season, cases of flu-like symptoms increased since the 47th week of 2006, and peaked at the 2nd week of 2007 (5.80%). As to the School-based Infectious Disease Surveillance Reporting System, the curve increased since the 42nd week of 2006, and peaked at the 52nd week (1.65%). Because of winter vacation, no data was reported between the 3rd and 9th week of 2007 from schools.

We compared epidemiological curves of the two surveillance systems during

the past years and found the trend to be similar (Fig. 1). Take the season of 2004/2005 for example; cases with flu-like symptoms increased since the 48th week of 2004 in the Sentinel Physician Surveillance System, and peaked in the 12th week of 2005 (6.08%). Cases with flu-like symptoms increased since the 47th week of 2007 in the School-based Infectious Disease Surveillance Reporting System (the winter vacation of schools was between the 2nd and the 9th week of 2005), and peaked in the 12th week of 2005 (1.28%). However, during the season of 2004/2005, another small epidemic surge occurred in the summer of 2005 besides the epidemics in the fall and the winter. Moreover, the flu season in 2005/2006 was flatter than two other seasons. Cases increased since the 47th week of 2005 in the Sentinel Physician Surveillance System, and peaked in the 10th week of 2006 (3.99%). In the School-based Infectious Disease Surveillance Reporting System, cases increased since the 47th week of 2005 (the winter vacation was between the 3rd and 8th week of 2006), and peaked in the 10th week of 2006 (0.78%).

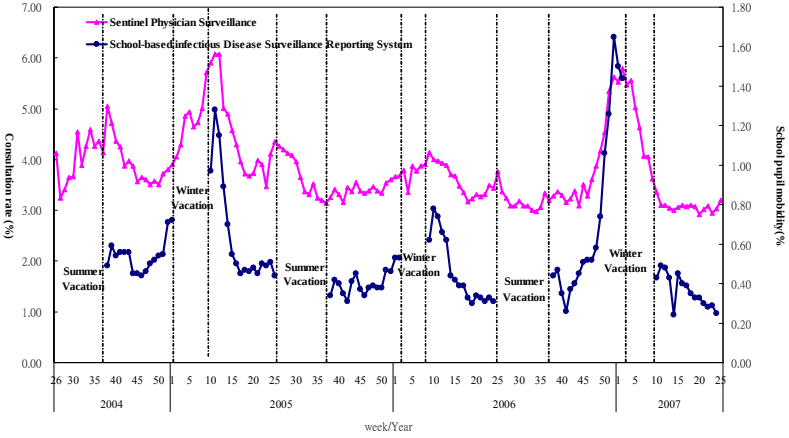

Figure 1. Comparsion between two ILI trend assessments, one was from the Sentinel Physician surveillance and another from School-based infectious disease surveillance reporting system

Epidemiology of influenza

According to surveillance data of virus contract laboratories, positive isolation increased late November in this flu season (Fig. 2), and peaked in Jan. 2007. The major strain was influenza type B. Positive cases of influenza A/H3 increase since Jan. 2007, and became the major strain in Feb. Compared with the two previous seasons, the major viral strain in the season of 2004/2005 was also influenza type B, and positive cases of influenza A/H3 increased since Apr.-Mar. of 2005. Influenza A/H1 was the major viral strain in the season of 2005/2006. Besides, the trend of positive cases of virus isolation was consistent with the curve of the Sentinel Physician Surveillance System; positive cases of virus isolation and cases of influenza-like illness increased since late Nov., and decreased since Jan. of the next year. As to the severity of the epidemic, this flu season and the one in 2004/2005 had more cases and increased more rapidly than the one in 2005/2006.

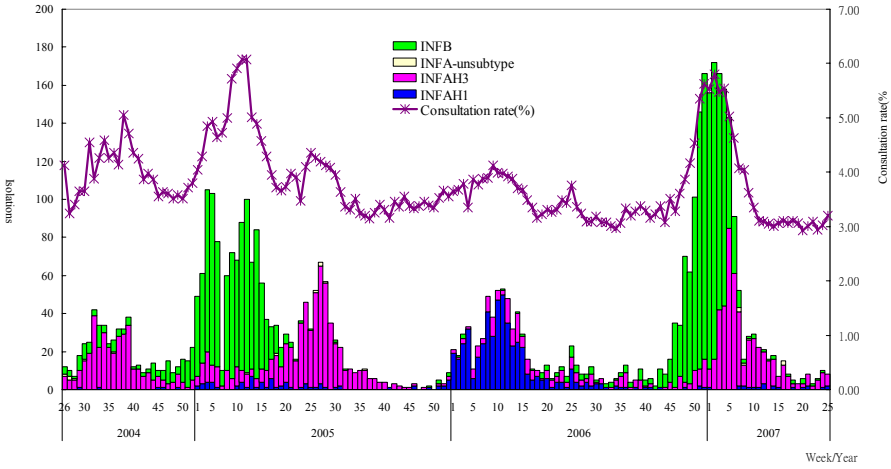

Figure 2. Comparison between Isolation of Influenza virus and ILI by the Sentinel Physician reporting system, 2006-2007 season

As to viral subtypes, according to virus isolation and subtyping of viruses by hemagglutination and sequencing in the National Influenza Center (Fig. 3), 23% were influenza type A, and 77% were type B. The main virus strain was B/Malaysia/2506/2004-like. The results of subtyping were as the following:

1 Type A/H1N1 virus:

A/H1N1 accounted for about 1.5% of the cases, including 57.1% of A/SolomonIsland/3/06 and 42.9% of A/NewCaledonia/20/99-like.

2. A/H3N2 virus

A/H3N2 accounted for about 21.5% of the cases, including 93.3% of A/Wisconsin/67/05 and 6.7% of A/Brisbane/10/07.

3. Type B virus

99.6% were the Victoria lineage, and the major viral strain was B/Malaysia/2506/2004. Only 0.4% were the Yamagata lineage, and the major viral strain was B/Shanghai/361/2002.

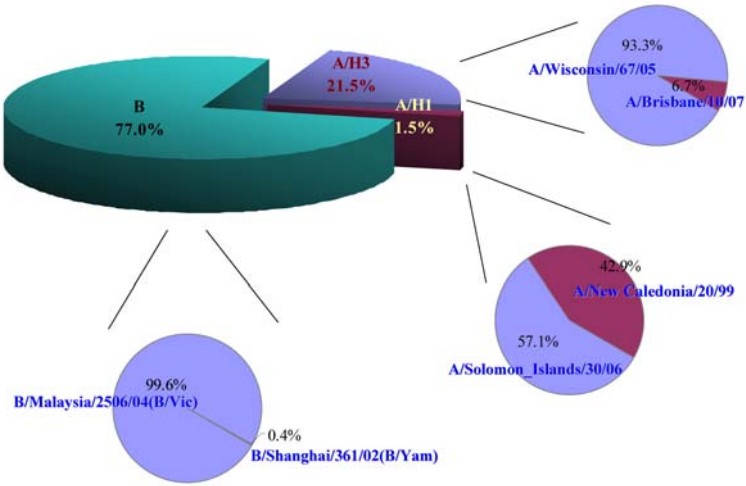

Figure 3. Isolate numbers and subtypes of influenza virus, Taiwan,2006-2007 season

Epidemiology of influenza with severe complications

According to the National Notifiable Disease Surveillance System of the CDC, 154 suspected cases of influenza with severe complications were reported, and 34 cases were confirmed by infectious disease consultants. Among the 34 confirmed cases of influenza with severe complications, the average age was 20 (median 12), and most cases were between 0 and 9 years old, followed by cases between 10 and 19 years old. As to clinical symptoms (Table 1), 85.3% cases had fever, followed by cough (55.9%), dyspnea or tachypnea (35.3%), myalgia (20.6%) and sore throat (17.7%). The most common clinical diagnosis was pneumonia (61.8%), followed by sepsis or shock (26.5%), encephalitis or meningitis (20.6%), and myocarditis or endocarditis (11.8%). As to virus examination results, throat swabs were gathered from confirmed cases by the reporting hospital, and examined by real-time polymerase chain reaction (RT-PCR). 29 cases (85.3%) were positive, and type B virus was the major strain (21 cases, 61.8%). 8 cases (23.6%) were A/H3. Besides, 97% of the cases did not have influenza vaccination in this flu season.

Table 1. Clinical Features of Severe Complicated Influenza Cases in Taiwan, 2006/2007 season

Clinical Feature		No of Case (%)*
.	Fever	29 (85.3)
	Cough	19 (55.9)
	Throat sore	6 (17.7)
	muscle aches	7 (20.6)
	Respiratory distress	12 (35.3)
	Diarrhea with fever	1 (2.9)
	Vomiting with fever	1 (2.9)
	Seizures	1 (2.9)
Diagnoses		
	Pneumonia	21 (61.8)
	Encephalopathy/Encephilitis	7 (20.6)
	Myocarditis/Pericarditis	4 (11.8)
	Sepsis/Shock	9 (26.5)

＊Multiple diagnoses in one case was possible.

Table 2 shows the analysis of incidence. Since the case numbers were low, we used Poisson distribution to estimate 95% CI of incidence of influenza with severe complications. The national incidence of influenza with severe complications was 0.15 cases per 100,000 people per year (95% CI: 0.10~0.21). The incidence was 0.24 cases per 100,000 people per year (95% CI: 0.15~0.35) in northern Taiwan, higher that other areas. The incidence was 0.12 cases per 100,000 people per year (95% CI: 0.05~0.25) in central Taiwan. The incidence was 0.51 cases per 100,000 people per year (95% CI: 0.27~0.88) among people between 0 and 9 years old, higher than other age groups. The incidence was 0.37 cases per 100,000 people per year (95% CI: 0.19~0.65) among people between 10 and 19 years old.

Table 2. Distribution of Cases and Incidence Rates with Geographic Location and Age Group among Severe Complicated Influenza cases in Taiwan, 2006-2007 season

		No. of cases (%)	Incidence rate per 100,000 (95% Confidence Interval)
Overall		34（100）	0.15（0.10～0.21）
Geographic regions			
	Northeast	24（70.59）	0.24（0.15～0.35）
	Midwest	7（20.59）	0.12（0.05～0.25）
	South	3（8.82）	0.05（0.01～0.14）
	West	0（0）	0（0～0.52）
Age group			
	0~9 yr	13（38.24）	0.51（0.27～0.88）
	10-19 yr	12（35.29）	0.37（0.19～0.65）
	20~29 yr	0（0）	0（0～0.08）
	30-39 yr	2（5.88）	0.05（0.01～0.20）
	40-49 yr	3（8.82）	0.08（0.02～0.23）
	50-59 yr	1（2.94）	0.03（0.001～0.19）
	60+ yr	3（8.82）	0.10（0.02～0.29）

Discussion and Suggestions

In summary, based on statistics of cases of influenza with severe complications, there were more reported and confirmed cases of seasonal influenza in 2006/2007 (154 and 34 cases, respectively) than in 2005/2006 (70 and 16 cases, respectively). Although results of each surveillance system were different because of monitoring subjects, goals and methods, the trends were consistent in time. However, in this flu season, cases in the School-based Infectious Disease Surveillance Reporting System increased since the 42nd week of 2006, in the Sentinel Physician Surveillance System, the 47th week of 2006, and in the virus contract lab, the 48th week of 2006. The School-based Infectious

Disease Surveillance Reporting System revealed the epidemic one month earlier than other two systems, suggesting that transmission between students ahead of transmission in the community. However, the peaks were all between late 2006 and early 2007.

As to the ages of cases of influenza with severe complications, most cases were between 0 and 9 years old, similar to the cases of pneumonia and influenza in 2002, when most cases seeking medical service or admitted were under 6 years old [7], and among them most were between 1 and 2 years old. Besides, surveillance results of the USA showed that people between 5 and 17 years old has the highest admission rates because of influenza than other age groups [3,8,9]. In New Zealand, people of age between 5 and 19 years old and between 20 and 34 years old have higher positive rates of influenza virus isolation and more cases of flu-like symptoms than people of other age groups [10]. Hence, infants/toddler and school age children are high risk groups of influenza infection and influenza with severe complications. They represent an important population in the design of disease prevention policies.

According to the influenza virus surveillance results in Taiwan, the major viral strain in this flu season was B/Malaysia and A/Wisconsin [16]. The variation of influenza viruses and protective effects of influenza vaccination were consistent with the vaccination suggestions from the WHO [4,16]. Monitoring of influenza viruses has become an important part of influenza prevention. Through monitoring of trends and mutations of key viral strains and analysis of epidemics in Taiwan and in other countries, we may predict epidemics in the future.

Analysis based on surveillance results and lacking of control groups were the main limitations of this study. Hence, we could not prove the relationship between viral strains and severe complications. Besides, sampling error may occur in the population of cases of influenza with severe complications. Although the data

were from reports of hospitals throughout the countries, the majority of reports were from medical centers in northern Taiwan. Moreover, clinicians of internal medicine or infectious disease might consider other respiratory diseases and report less. On the other hand, pediatricians might consider cases of upper respiratory diseases as influenza or influenza with severe complications during epidemics of influenza. Therefore, young patients dominate cases of influenza with severe complications.

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