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Multiple Disease Surveillance Systems against Pandemic (H1N1) Influenza in Taiwan

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Abstract

Taiwan announced pandemic (H1N1) influenza as a category 1 communicable disease as soon as H1N1 outbreaks occurred in USA and Mexico in April 2009. The Central Epidemic Commander Center (CECC) was launched to coordinate Ministries and Departments under the Executive Yuan for national policy making and communication. Subsequently, in light of World Health Organization's (WHO) declaration that the H1N1 epidemic could be mild, the CECC removed H1N1 influenza from category 1 communicable diseases and instructed that if a severe complicated H1N1 influenza case was reported, it should be dealt with according to regulations and control measures set up for category 4 communicable diseases. Although the majority of pandemic (H1N1) influenza cases would not become severe complicated cases, real-time monitoring of epidemic situation was crucial for communicable disease policy making. Hospitalization, Viral, Out Patient Department (OPD), and Mortality surveillance systems were adopted for disease surveillance. Hospitalization surveillance focused on severe complicated influenza cases in notifiable disease surveillance system and analyzed hospitalization, discharge, and prognosis for pandemic (H1N1) influenza severe complicated cases. Viral surveillance monitored the epidemic trend of novel H1N1 virus in the community via the virus typing of contracted viral laboratory system. OPD surveillance monitored physician visits due to influenza-like illness by using information from the Real-time Outbreak and Disease Surveillance System (RODS) in Emergency Rooms (ER) and OPD IC card database from the National Health Insurance. Mortality surveillance monitored real time moving average for four-week trends of pneumonia or influenza deaths in order to detect abnormal development in advance. Data from those surveillance systems were analyzed daily, and results from the analyses were published in "Taiwan Influenza Daily Report" and "Taiwan Influenza Express". Taiwan CDC expected to

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monitor the pandemic closely through multiple disease surveillance systems to provide references for making prevention and control policies so that appropriate measures could be implemented.

Keywords: pandemic (H1N1) influenza, severe complicated influenza cases, surveillance system

Introduction

In April, 2009, pandemic (H1N1) influenza outbreaks occurred in Mexico and USA. Due to the historical experience of the 1918 Spanish flu pandemic, health authorities around the world stood in combat readiness. Immediately after the World Health Organization (WHO) declared the case definitions of this novel flu on April 26, Taiwan CDC announced pandemic (H1N1) influenza as a category 1 communicable disease on April 27. The Central Epidemic Commander Center (CECC) was launched on April 28 to coordinate Ministries and Departments under the Executive Yuan for national policy making and communication. Although WHO raised the pandemic alert level to phase six on June 11, which was the highest pandemic alert level, WHO also emphasized that the H1N1 epidemic was likely to be mild. Consequently, on June 19, the CECC removed H1N1 influenza from category 1 communicable diseases and instructed that if a severe complicated H1N1 influenza case was reported, it should be dealt with according to regulations and control measures set up for category 4 communicable diseases [1, 2].

Pandemic (H1N1) influenza was a respiratory disease and could spread rapidly; Taiwan CDC integrated existing hospitalization, viral, OPD and mortality surveillance systems for the purpose of pandemic (H1N1) influenza surveillance. Taiwan CDC also published “Taiwan Influenza Daily Report” and weekly “Taiwan Influenza Express” for the public. The four major disease surveillance systems are introduced one by one in this article.

1. Hospitalization surveillance (Notifiable Disease Surveillance System)

Since 1971, Department of Health in Taiwan had conducted surveillance for some communicable diseases, and since 1993, a more comprehensive notifiable disease surveillance system had been developed. Beginning from July 1997, the surveillance systems has been incorporated under the Health Information Network (HIN) to save the costs of data transfer, shorten the duration of data collection and avoid repeated data entry. From July 2001, combined with more advanced information technology, the system has shifted to report via the Internet. For better integration

and comprehensiveness, in 2003 and 2006, more functions were designated for communicable disease control purposes in the system [3]. In 2009, all related surveillance systems were integrated to improve performance and establish single entry for reporting, which would in turn assist health officials promptly grasp all related information and increase the effectiveness of communicable diseases control.

Among those officially announced diseases throughout the years, influenza related surveillance has included "influenza," which was listed as a notifiable communicable disease on June 23, 1999 (surveillance terminated in December 2005), as well as "severe complicated influenza case" (listed on November 1999 and now as a category 4 communicable disease). After the SARS outbreaks in 2003, in response to the global effort in preparing and planning for emerging infectious diseases, Taiwan CDC announced the addition of "H5N1 influenza" as a notifiable communicable disease on December 29, 2004 (now as a category 1 communicable disease). On April 27, 2009, soon after pandemic (H1N1) influenza outbreaks occurred in Mexico and USA, Taiwan CDC added pandemic H1N1 influenza as a category 1 communicable disease; it was subsequently removed from that category on June 19, and if a severe complicated H1N1 influenza case was reported, it would instead be dealt with according to regulations and control measures set up for category 4 communicable diseases.

For those severe complicated influenza cases detected through the notifiable disease surveillance system, they could be to distinguished whether they are seasonal or pandemic H1N1 influenza by viral testing; furthermore, demographic information including patient age, sex and area of residence, as well as major symptoms, hospitalization status, hospitalization date, prognosis, underlying diseases, treatment measures (Extracorporeal Membrane Oxygenator, IVIG) could be gathered by local health authorities and monitored by CDC branch offices. Those data could help health officials grasp hospitalized cases status (Figure 1), recovered case number, underlying diseases in confirmed cases, and

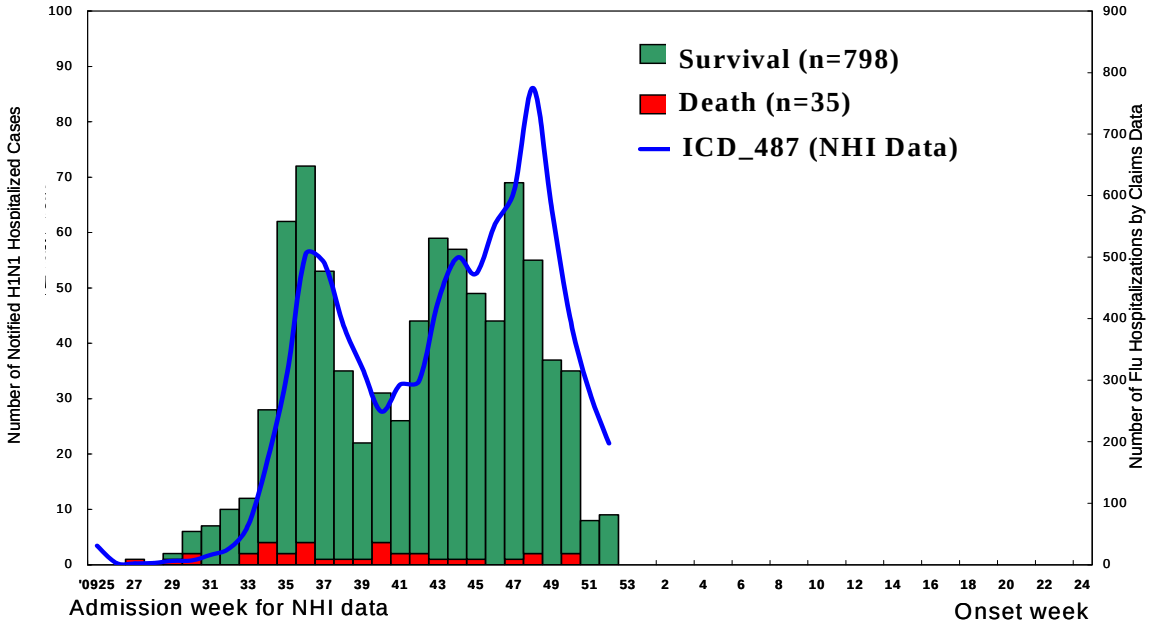

Figure 1: Number of H1N1 influenza hospitalized cases, by onset week—Taiwan, 2009

information about severity and risk factors. Such information could in turn serve as references for coordinating intensive care capacities around the nation and for health policy making.

2. Viral surveillance (Contract Laboratory Surveillance System)

Due to the difficulties associated with examination technology and shortage of equipment, there were few standard viral laboratories in Taiwan in early times. In 1998, when enterovirus outbreaks occurred, the need of virus exam tremendously increased. The outbreaks reflected shortages of those aforementioned capacities, lab manpower and exam volumes. Starting from March 1999, Taiwan CDC constructed a contract lab system for viral infectious diseases and devoted more effort to increasing exam abilities and professional education. In the beginning stages, there were only four contract labs for viral infectious diseases, and two quasi contract labs. In May 2000, a total of 11 labs were enrolled in the system.

The specimen came from sentinel physicians in the city or county of responsibility as well as from enterovirus and influenza-like cases detected during out-patient, hospitalization and emergency room services of the hospital where the contract lab is located. The number of specimen collection sentinel stations had expanded from 130 in the beginning phase to 240 stations now [3, 4]. In addition, contract labs also examined enteroviruses infection with severe complications cases in category 3 communicable diseases as well as severe complicated influenza cases in category 4 communicable diseases. The results and subtypes in turn served as references for confirming diagnoses.

In 2009, a total of 10 contract labs were enrolled in the surveillance system for viral infectious diseases. Their detailed information are as follows: 3 labs in the northern region, namely National Taiwan University Hospital (jurisdiction: Taipei City, Kinmen County, and Lienchiang County), Chang-Gung Memorial Hospital in Linkou (jurisdiction: Taoyuan County, Hsinchu City and Hsinchu County), and Tri-Service General Hospital (jurisdiction: Taipei County, Keelung County, Ilan County, and specimen from the military); 3 labs in the central region, namely China Medical University Hospital (jurisdiction: Miaoli County and Taichung City), Taichung Veterans General Hospital (jurisdiction: Taichung County and Nantou County), and Changhua Christian Hospital (jurisdiction: Yunlin County and Changhua County); 3 labs in the southern region, namely National Cheng Kung University Hospital (jurisdiction: Chiayi County, Chiayi City, Tainan County and Tainan City), Kaohsiung Medical University Chung-Ho Memorial Hospital (jurisdiction: Kaohsiung County, Pingtung County, and Penghu County), and Kaohsiung Veterans General Hospital (jurisdiction: Kaohsiung City); and 1 lab in the eastern region, namely Buddhist Tzu Chi General Hospital (jurisdiction: Hualien County and Taitung County).

The contract labs played an essential role for viral infectious disease control, and on average, the number of specimen collected monthly in 2008 was approximately 1,800; from historical experience, the volumes were relatively high from May to August (i.e. the

enterovirus season) and in December (i.e. the flu season) [4, 5] . Furthermore, to maintain lab capacity and exam quality, prior to the annual renewal of contracts, Taiwan CDC would evaluate the quality of each lab and its exam capacity.

In response to the H1N1 influenza pandemic and in order to monitor the epidemic situation in the community, contract labs collected specimen from cases of influenza like illness within 3 days of disease onset and increased the volume of specimen collection corresponding to the epidemic situation. Taiwan CDC was able to evaluate the development of pandemic H1N1 influenza in the community as well as major strains and virus activity by daily analyzing the specimen examination completion rates, positive rates and virus subtypes (Figure 2). Moreover, Taiwan CDC could estimate the case number of pandemic H1N1 influenza in the community and predict future epidemic trends based on the number of physician visits recorded under National Health Insurance IC card database.

In addition to monitor virus in the community from contract lab data, Taiwan CDC's own lab examined cases of drug-resistance against Oseltamivir and Adamantane to grasp whether and what resistant strains occurred in severe complicated influenza cases, cluster cases of influenza like illness, as well as mild influenza cases from July 1, 2009. Up till December 28, 2009. 7 cases of drug-resistant pandemic H1N1 influenza had been found among 825 strains; according to epidemiological investigation, there was no indication that such cases would develop into clusters or community epidemics.

3. Out-patient department surveillance (Real-time Outbreak and Disease Surveillance System combined with National Health Insurance IC Card Database)

In addition to adopting hospitalization

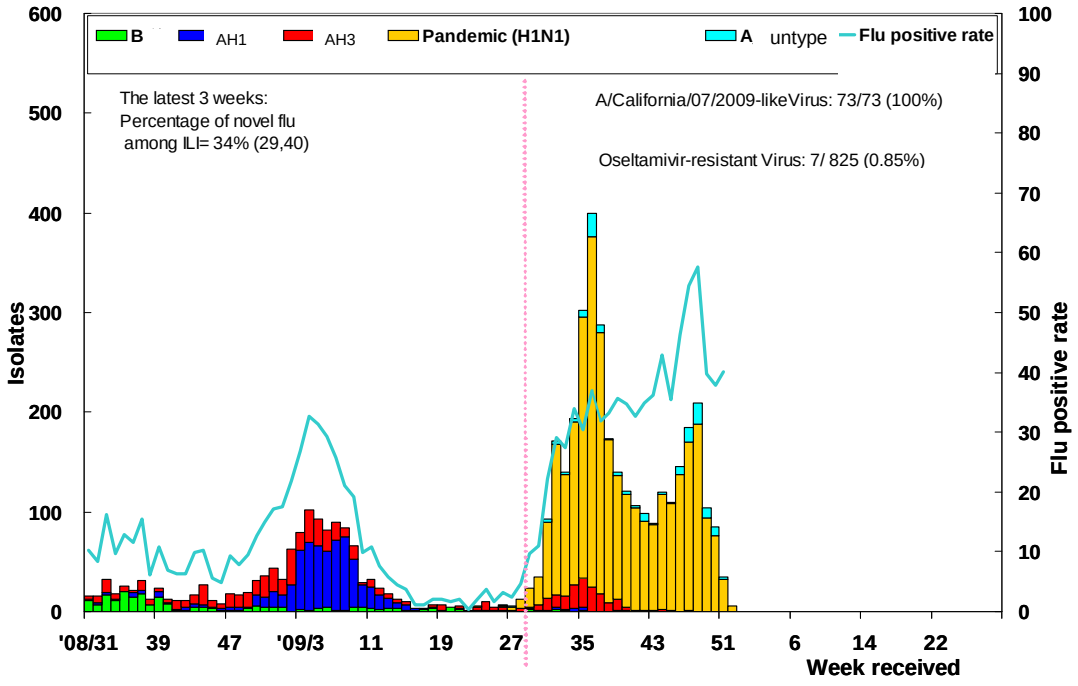

Figure 2. Trend of influenza like illness virus subtypes from contract labs for viral infectious diseases

and virus surveillance to track risk factors of pandemic H1N1 influenza severe complicated cases and virus activity in the community, Taiwan CDC also utilized Real-time Outbreak and Disease Surveillance System (RODS) and National Health Insurance IC Card Database to evaluate the epidemic situation of influenza-like illness mild cases. This multi-channel surveillance approach ensured that the epidemic would be monitored closely.

In September 1999, researchers at the University of Pittsburgh, USA, created the Real-time Outbreak and Disease Surveillance (RODS) system. It contributed basic results for disease outbreak detection from coded chief complaints from Emergency Room in real time. In the beginning stages, RODS demonstrated the feasibility of real-time data collection under a trusted broker arrangement in 13 counties in Western Pennsylvania; RODS surveillance covered the 2002 Winter Olympic Games in Utah State, also has won the recognition from Former U.S. President George Bush. The system was able to not only analyze clinical symptoms but also generate an alert if the signs were over the threshold; comparison with other communicable disease systems was also used to provide cross validation and to evaluate system sensitivity [6].

Taiwan CDC adopted RODS in 2004, and after planning, integration, and testing, the system had been in operation since November 2006. The system was aimed at physician visits in Emergency Rooms, and the main symptoms for monitoring included ICD 9 CM codes: influenza-like illness (respiratory syndrome), enterovirus (herpangina, and hand foot mouth disease), conjunctivitis, and acute diarrhea. So far, hospital emergency rooms enrollment had risen from a dozen in the beginning phase to more than 160 now, which included 80% of all ERs in Taiwan. Among those hospitals, 50% were district hospitals and 28% were regional hospitals; and the total number of reports ranged between 80,000 and 90,000 per week (7, 8). The system had connections with ERs and could automatically transfer ICD-9 codes and related information to the database of Taiwan CDC, and then this database would produce the statistical charts of physician visits by age, inhabit region or diseases, weekly or daily.

In addition to adopting RODS to obtain ER physician visit trends, Taiwan CDC cooperated with Bureau of National Health Insurance (BNHI) to derive physician visits due to communicable diseases related syndromes. Taiwan CDC ever collaborated with BNHI in the 2003 SARS outbreaks and monitored imported infectious diseases in 2006. During 2008 the enterovirus outbreak, BNHI transferred National Health Insurance IC Card Database to Taiwan CDC daily, and according to this information, Taiwan CDC was able to analyze symptoms and physician visits in out patient departments. Besides enterovirus, influenza-like illness and diarrhea were included. The results could be compared with the sentinel physician system to evaluate the system’s efficacy, performance and sensitivity. Information uploaded to the National Health Insurance IC Card Database included data entry date, physician visit date, jurisdiction city or county (name and code), OPD department, age group, hospital level, and diagnostic primary and secondary ICD 9 codes. Some limitations included that not every hospital uploaded primary and secondary codes or daily real time information. However, according to analysis results from April 2008 to December 2009, weekly trends of symptoms and diseases

corresponded to the RODS and the sentinel physician system (Figure 3). This suggested that the system was stable and could be used for estimation of epidemic situations.

So far, the epidemic of influenza-like illness could be determinated by coded ICD-9 influenza-like illness cases, which were supplied by daily RODS information and National Health Insurance IC Card Database (Figure 4). This could provide an estimation of next week's epidemic trend and an early alert for appropriate control measures to be implemented.

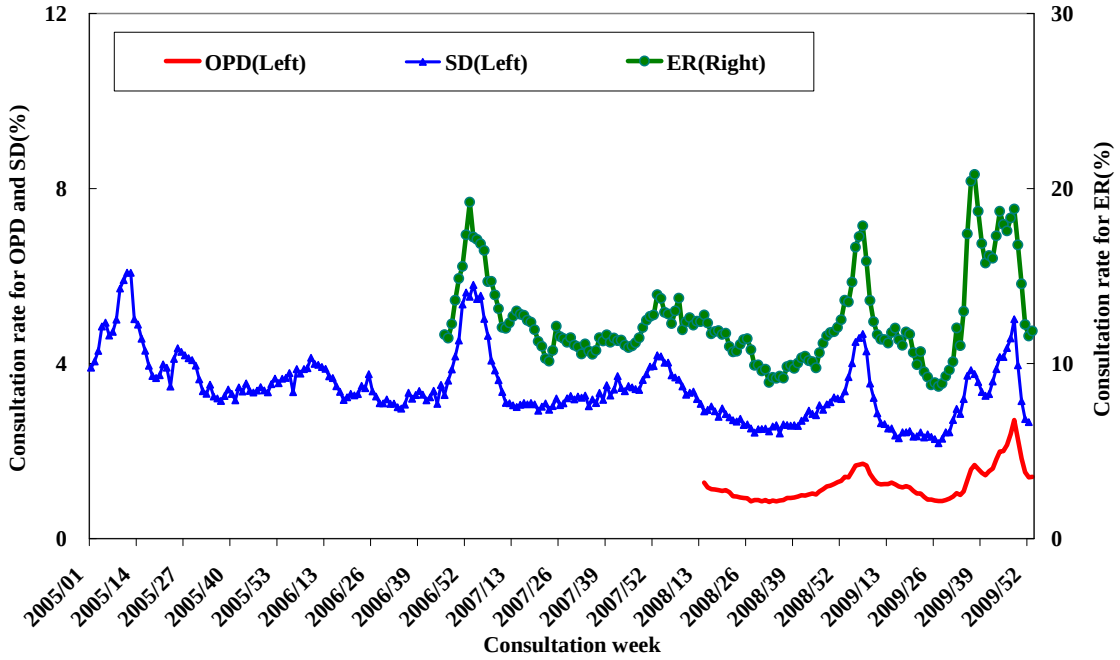

Figure 3. Physician visit trends of Influenza-like illness from RODS, National Health Insurance IC Card Database, and Sentinel Physician Surveillance

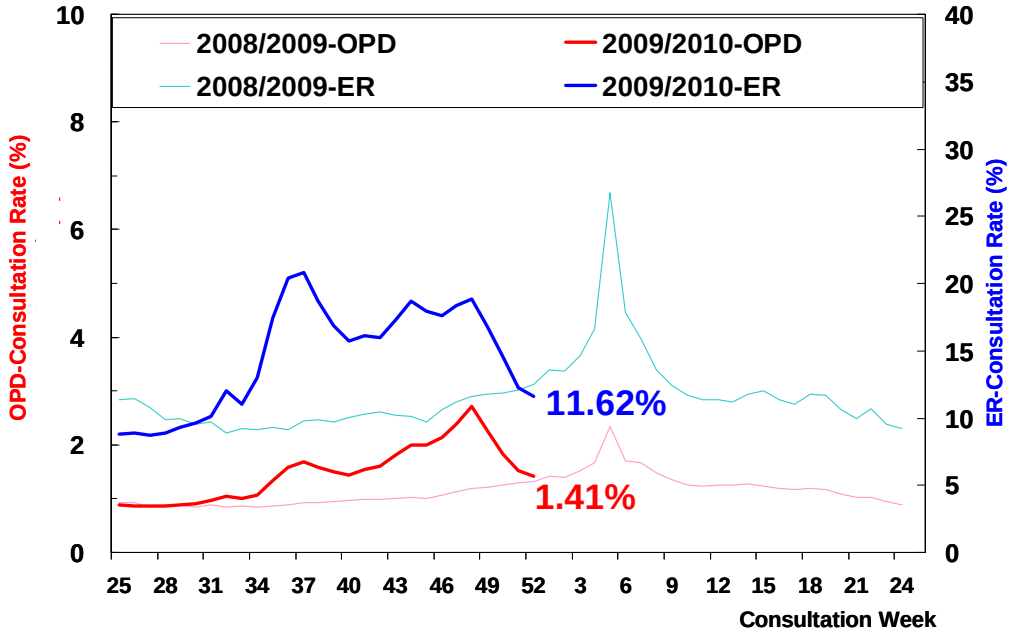

Figure 4. Physician visit trends of influenza-like illness from RODS and National Health Insurance IC Card Database—Taiwan, 2008-2010

4. Mortality Surveillance (real time surveillance system for mortality due to pneumonia and influenza)

Unlike the United States, Taiwan CDC did not construct an independent surveillance system to monitor deaths due to severe complicated influenza cases. However, Taiwan CDC had created columns for recording death information (such as date of death, cause of death and notes) in the Notifiable Disease Surveillance System. The information was maintained by local health authorities and recorded based on information in physician issued Death Certificates. To clarify whether direct causes of death were related to communicable diseases, Taiwan CDC had created a column for CDC medical officers to record their corroboration of cause of death after reviewing a case's medical chart or medical history abstract. In the current Notifiable Disease Surveillance System, if health officers in local health departments confirmed that a death was caused by influenza severe complicated syndromes, the system would send a mobile text message to related health officers for further investigation and clarification.

In addition to being able to obtain and analyze influenza severe complicated cases information from the Notifiable Disease Surveillance System, in response to pandemic H1N1 influenza and in order to monitor epidemic trends of pneumonia and deaths due to influenza, Taiwan CDC have collaborated with the Office of Statistics, Department of Health, to utilize the web death reporting system from April 2009 for the aforementioned trends. This collaboration provided real time surveillance of mortality that in turn served as a reference for deciding appropriate communicable disease control measures.

The web death reporting system in the Office of Statistics, Department of Health, recorded basic demographic information and cause of death for each case. Taiwan CDC utilized information on the week of death and the age at death and used the keywords "pneumonia, common cold, or influenza" to search the database in order to calculate death numbers due to pneumonia and influenza. Furthermore, to ensure data stability, the moving averages of the four weeks (including the present week) were used as standards for calculating weekly surveillance results (Figure 5). According to death reporting data from 2008 to 2009, death cases due to pneumonia and influenza rose from week 49 and achieved the highest number in week 6 in the next year. Two months later (approximately week 14), the epidemic became stable. The total epidemic lasted 18 weeks (week 47 to week 12 in the next year) determined by the average in the non-epidemic period; on average, the weekly death number due to pneumonia and influenza was 290, and highest volume of deaths, 373, occurred in week 5 of 2009. Taiwan CDC used 2008-2009 trends for reference to determine if there was an abnormal trend in mortality during 2009-2010.

Comparing to the number of deaths analyzed by the Department of Health, the number of the system was slightly higher; however, the trends were similar (Figure 6), and correlation coefficient was 0.85 ($p<0.0001$) [9]. Given that the statistics of causes of death was published by the Department of Health every June, the death trend surveillance was still necessary for the purpose of real time surveillance and early alert.

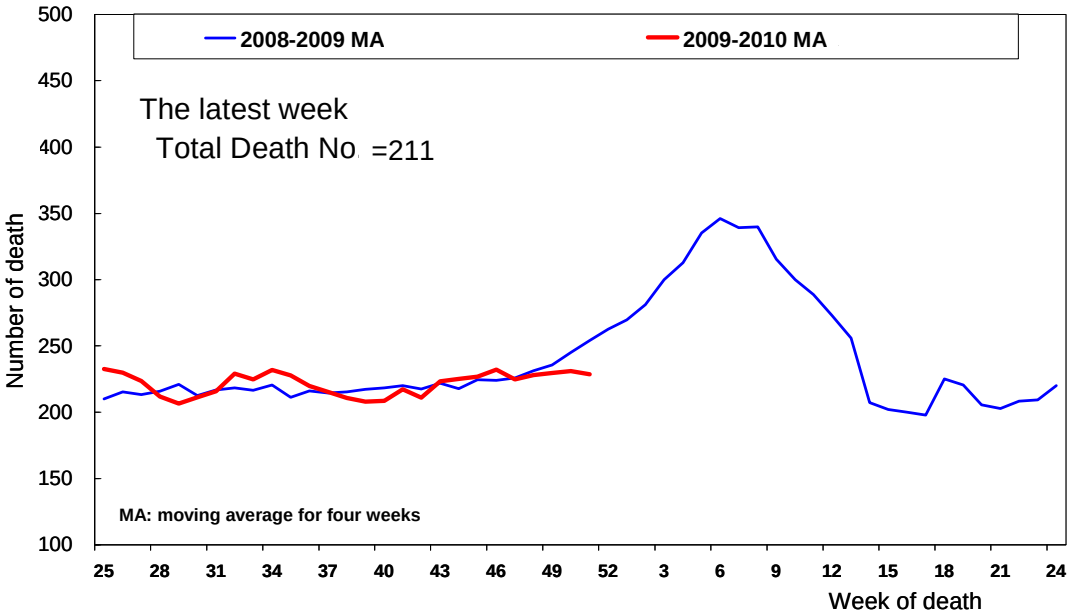

Figure 5. Real time mortality trends due to pneumonia and influenza in Taiwan

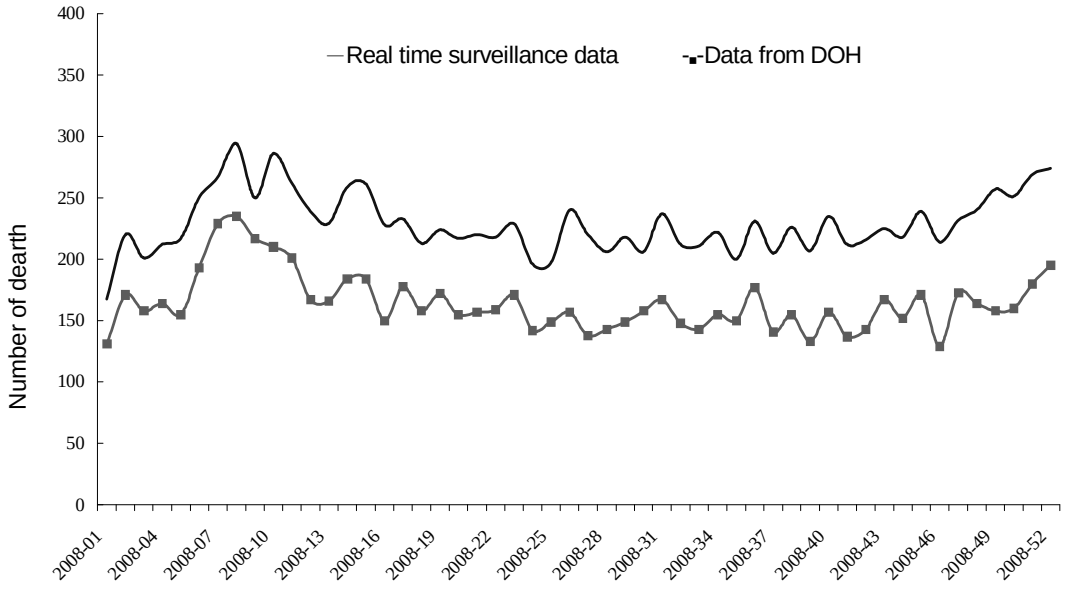

Figure 6.Comparison of trends of death due to pneumonia and influenza from the statistics of Department of Health and real time surveillance of mortality

Results and Discussion

The purpose of communicable disease surveillance systems was to promptly detect outbreaks or abnormal situations so that deaths, medical expenditure and social cost could be decreased through the adoption of appropriate response and control measures.

For pandemic H1N1 influenza surveillance, Taiwan CDC utilized different surveillance systems at different stages of the epidemic. In the beginning phase, under the strategy of "decisive battle outside the territory," quarantine as well as the existing communicable disease surveillance system were adopted to monitor imported passengers and related clusters events. For now, four major surveillance systems were utilized and were supported with school –base surveillance system, utilization rates of influenza vaccination and school closure statistics of

Ministry of Education to develop appropriate response measures to the influenza pandemic and set up strategies for vaccine administration. Furthermore, Taiwan CDC published Taiwan influenza Daily Report and complied detailed information from the four major surveillance systems and from sources of international communicable disease news for the Taiwan Influenza Express, which was published on the CDC's official website for the public to access.

Among the four major surveillance systems, all had the timeliness limits. Taking the Notifiable Disease Surveillance System as an example, for those pandemic H1N1 influenza severe complicated cases, the average length between reporting and a confirmed diagnosis was 2 days during the epidemic season. Ninety-four percent of the diagnoses were confirmed within 3 days, and very few cases would take a longer period to confirm, due to an initial rapid test result being negative but the result from pathogen isolation showing a positive diagnosis 14 days later. The average duration from onset to reporting was 3 days, and 75% of the cases were reported within 4 days from onset. It appeared that the course of the pandemic H1N1 influenza was changing rapidly, and if no appropriate therapy was given, it might take only three to four days for a case to deteriorate from disease onset to hospitalization. Regarding the contract lab surveillance system for viral infectious diseases, the length between specimen collection and completion of test (including virus isolation) would take two weeks. However, virus positive rate, two weeks before, used as references for policy-making did little to help in a critical situation. Therefore, the rate of positive results for pandemic H1N1 virus among samples tested in the prior three weeks was used as a reference. As for the National Health Insurance IC Card Database for out patient department surveillance, since not every hospital uploaded information daily, the numbers were likely to be more accurate on Thursday and Friday. As for the real time surveillance system for mortality due to pneumonia and influenza, since not every data were updated daily, statistics from the previous week might provide a more accurate representation. Given that each surveillance system had different targets, information sources and limitations, when monitoring outbreaks or emerging infectious diseases, adopting a single surveillance system might bias decision making due to delayed reporting or system errors.

For pandemic H1N1 influenza surveillance, the mode of adopting results from several surveillance system provided information for predicting further trends. Future studies should evaluate the overall effectiveness of communicable disease surveillance to provide a reference for responding to future outbreaks.

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Policy Review after the First Novel Influenza A (H1N1) Case in Kaohsiung-Pingtung Area

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Abstract

In order to prevent the second episode of pandemic novel influenza A (H1N1) and to respond timely to emerging infectious diseases, summing up the experiences in management of the first wave of confirmed cases is of paramount importance. In this article, we analyzed the first confirmed novel influenza A (H1N1) case in Kaohsiung-Pingtung area and discussed policies in prevention and control of the disease, including case reporting, case isolation, passengers list checking, specimen collection and testing, and the prescription of antiviral drugs.

Keywords: novel influenza A (H1N1), case analysis, policy for prevention and control of disease.

Introduction

Novel influenza A is an emerging infectious disease which originated from newly reassortant influenza A virus (H1N1) and was first recognized by the United States in April, 2009. This potentially fatal disease is transmitted from person to person, with fairly high infectivity [1, 2]. As of July 17, 2009, the worldwide cumulative number of cases and fatal cases had reached 120,000 and 700 respectively. In Taiwan, there were 93 confirmed cases; one of them was severe complicated influenza case [3]. Should a case be identified in a country, should it go out-of control, it will not only endanger lives, but can also cause community endemics, economics crisis, travel risks, and compromises in international relationship. Therefore, appropriate adaptive strategy is mandatory.

Lessons learnt from the past can guide us in the future. In this article, we reported the first confirmed case of novel influenza A in Kaohsiung-Pingtung area and shared our experience in the management, so that public

health agencies might be able to mitigate the possible dangers to individuals and society if respond accordingly.

Case Report

A. Basic information

Case A, a 21-year-old young lady, was an exchange student just coming back from the United States. She became ill on June 6, 2009 and was notified to the authorities for investigation on the next day. On June 8, 2009, she was tested H1N1 positive.

B. Course of disease

See table.

C. Control measures

a. Treatment and isolation of novel influenza A (H1N1) cases

After notification to the authority of the case, the doctor evaluated the patient's severity and performed influenza rapid test. The patient was allowed to go home because of her relatively mild symptoms and negative result of the rapid test. The public health center soon issued the Home Isolation Notification.

When the case was confirmed by contract laboratory, the commanding

Table Course of disease

Date	Course
Jan. 2~ May 15	A short-term exchange student to University of Wisconsin in USA.
May 15~ May 25	Vacation in New York.
May 25	Stayed in Wisconsin for one night.
May 26	Took a plane to Los Angeles.
May 26~ June 2	Visited Disneyland and Universal Studio when staying in Los Angeles.
June 2	Took a flight back to Taiwan at Pacific time 3:15pm at seat (xxD) and was accompanied by another student (seat: xxC). The passenger at seat xxG was coughing all the time.
June 3	Arrived in Taoyuan Airport at 8:20pm and was picked up by her father and uncle back to Kaohsiung.
June 4, 5	Stayed home because of jet lag.
June 6	Presented with itchy throat and cough since morning and visited a local clinic wearing a surgical mask. Due to her traveling history, transferal for further investigation was suggested. Patient declined due to mild symptoms and returned home to rest.
June 7	Visited ER in the morning wearing a surgical mask because of persisting symptoms. The hospital soon notified the authority and performed rapid test that turned out to be negative. Oseltamivir was prescribed and the patient was allowed to go home since her symptoms were mild. The patient had been to a convenient store before going home. The public health center issued Home Isolation Notification for the patient in the afternoon. The real-time PCR of swine flu performed in contract lab showed positive result. The specimen was sent to Research and Diagnostic Center of Taiwan CDC at 10:28pm. The patient was admitted into a hospital at 10pm and she started to take Oseltamivir that she got this morning. Close contacts were asked to take prophylactic Oseltamivir and perform health self- management.
June 8	Secondary tests by Research and Diagnostic Center of Taiwan CDC confirmed the positive result.
June 11, 12	Two RT-PCR tests of throat samples were negative. The patient was sent home.

officer soon assigned her to an isolation hospital for further treatment. The patient was admitted to the negative pressure isolation ward and started to take Oseltamivir. She was isolated until two consecutive real-time PCR negatives before she is eligible to be discharged on June 12.

b. Sample collection and the results of examination

Throat swab and serum specimen of the patient were collected at noon on June 7, when she was notified as an investigation case. The specimens were sent to a contract virology laboratory. At 5:30pm, the real-time PCR performed in contract laboratory was H1N1 positive. A colleague in Fifth Branch of Taiwan CDC then sent the samples to the Taiwan CDC Research and Diagnostic Center. These were confirmed as novel influenza A (H1N1). The patient became clear of symptoms on June 11 and her throat swabs on June 11 and June 12 were negative. She was discharged and her serum obtained during recovery period (day 15 of illness) was sent to Taiwan CDC laboratory as well.

c. Tracking the infection source

The patient was an exchange student at University of Wisconsin from January 2, 2009 to June 3, 2009. She had no relatives or friends who reported to have influenza-like illness.

She took a flight (seat xxD) with her friend (seat xxC) back to Taiwan at Pacific time 3:15pm on June 2, 2009. The plane arrived in Taoyuan Airport at Taiwan time 8:30pm on June 3, 2009. The time of flight is 17 hours. According to the statement of the patient, the passenger nearby (seat xxG), wearing a surgical mask, was coughing all the time.

According to the disease course and the incubation period of H1N1 influenza virus, this case was classified as an imported case. The source of infection might be in U.S. or on the airplane.

d. Follow-up of close contacts and prescription of prophylactic therapy

Total number of contacts was 12, including 2 clinic staff, 3 hospital staff in the emergency department, 2 workers in the convenient store, and 5 family members. But the 5 family members who were compatible with the definition of close contacts (close contact with definite H1N1 case within 2 meters and for at least 1 hour) remained asymptomatic. The commanding officer prescribed prophylactic medication and health self-management. The public health center educated all the other cases, issued Voluntary Quarantine Notification, and would offer medical assistance if anyone became symptomatic.

D. Following up

The patient tested negative on both June 11 and 12 and returned home. The 12 contacts were under health self-management until June 14, all were of good health.

Discussion and suggestion

A. Adequacy of notification criteria

Of the 642 symptomatic confirmed cases

in the United States identified between April 15 and May 5, 2009, 94% had fever, 92% had cough, 66% had sore throat, and 25% had diarrhea [2]. Among the 2009 confirmed cases found in Spain between April 24 and May 11, 2009, 96% had fever, 95% had cough, 41% had diarrhea [4]. The clinical presentations were similar in confirmed patients in the United Kingdom diagnosed between April 27 and May 11, 2009; 94% had fever, 82% had sore throat, and 28% had diarrhea [5]. Therefore, fever is the most common symptom while diarrhea is relatively unusual.

How to define notification criteria for an emerging infectious disease is always a difficult question. Stringent criteria may lead to delay in diagnosis and widespread of epidemic. Liberal policy, on the opposite end, may result in wasting of human resource, protective equipment, and medication.

Following WHO's lead, Taiwan CDC set up the notification criteria for the novel (H1N1) influenza as a category 1 communicable disease on April 27, 2009. Taiwan CDC defined a notifiable case as a patient with acute febrile respiratory illness (body temperature >38℃), from mild influenza-like disease to severe complicated with pneumonia, and compatible epidemiologic conditions [6]. However, in clinical practice, management should be highly individualized even if the case is not typical. In this case, the patient only presented with itchy throat and cough, which did not meet the criteria and might be overlooked. But the doctor still determined to report, Taiwan CDC respected the decision and provided testing and antiviral agents, to prevent the transmission of disease.

By June 11, 2009, WHO announced the scale of outbreak caused by pandemic influenza A (H1N1) had arisen to the highest phase 6 but with moderate severity. Taiwan had also downgraded it from category 1 communicable disease to category 4 on June 19, 2009, indicating that only severe cases are required to be reported [7]. Therefore, severity and infectivity of the disease, as well as social cost, are major determinants for modification of notification criteria.

B. Issues regarding case isolation

As a highly contagious emerging infectious disease, the severity of infection with 2009 pandemic H1N1 influenza was uncertain initially. To prevent transmission of the virus, a reported case should be isolated until the diagnosis could be excluded. The authorities need to consider where to isolate these reported cases, either at home or in a hospital. According to the management protocol for pandemic H1N1 influenza patients issued on May 4 by Taiwan CDC, doctors are allowed to decide whether the patient should be hospitalized or not, after thoroughly considering not only the clinical course, compliance and daily activity of the patient, but also the overall number of isolation beds and medical resources. For patients with minor illness but with higher risk for community spread based on the epidemiologic investigation, the attending physician or the local health bureaus should convince them to stay in the isolation wards until the results of laboratory examinations proved to be negative. Therefore, considering the life style of the reported case in this report, the availability of isolation beds, and the efficiency of the laboratory examination, the

case was isolated to prevent virus transmission in the community despite her symptoms were not very severe.

As the intensity of the pandemic arose, it was impossible to contain the disease. Considering the moderate severity of this influenza pandemic, which was not different from seasonal influenza, control measures against 2009 pandemic H1N1 influenza virus were adjusted following the example of seasonal influenza. Isolation was not necessary in suspected patients, while hand hygiene and respiratory etiquettes were still emphasized. Those with symptoms should stay at home instead of going to schools or work, keep away from their family members, and avoid close contacts with their friends [7, 8].

C. Issues regarding manifest investigation

The primary goal of manifest investigation is to closely follow up the case and close contacts. WHO have recommendations on contact tracing for confirmed cases of 2009 pandemic H1N1 influenza infection. Passengers sitting two rows before and after the case should be under investigation [9]. The infectious period of novel influenza H1N1 starts 1 day prior to development of symptoms and ends 7 days after becoming ill. The case in this report had stayed home one day before illness, so further tracking of passengers nearby was not necessary. Due to an incubation period of less than 7 days, the infection source was probably in the United States or on the plane. Since there is only one confirmed case on the plane, and her companions did not have any symptoms, the risk of transmission in the plane is believed to be very low, and it would be unnecessary to perform plane-wide manifest investigation.

D. Issues regarding examining the specimens

a. Novel influenza infection could not be excluded by using rapid influenza antigen test.

In this case, the result of the rapid test was negative, but the real-time PCR result was positive. Influenza rapid antigen test is a rapid diagnostic tool. The results could be available within 10 minutes after the specimen is taken from the patient’s nasopharynx. According to the study done by Ginocchio et al, they found the sensitivity and specificity for novel H1N1 virus to be 21.2% and 99.5% respectively, which meant the false negative rate was 78.8% and the false positive rate was 0.5% [10]. So if case notification was made according to the result of rapid test, some cases might be missed. At the present, the US CDC and Taiwan CDC use real-time RT-PCR as the standard procedure for confirming H1N1 cases [11].

b. The role of contract laboratories

To offer efficient and correct diagnosis, Taiwan CDC authorized 10 virology contract laboratories around the nation to examine obtained specimens by real-time PCR after quality assessment. The contract laboratories are required to send the very first positive specimen to the Research and Diagnostic Center to confirm the results. Once the capability and accuracy of contract labs were assured, they can perform examinations by themselves and email the results to

the CDC Research and Diagnostic Center, which will in turn release the results to health care providers. However, the discharge criteria included two negative throat swabs examined by CDC in Taipei, which led to significant delayed discharge of patients in southern Taiwan. Consequently, the patient had excessive suffering because of isolation; occupied wards and health resources had become a big waste. In conclusion, we could assign all confirmation tests to contract laboratories under reliable quality control.

E. Use anti-viral agents correctly

In the reported case, the attending physician prescribed the anti-viral drug for prophylaxis rather than for treatment. The patient did not take anti-viral drug until diagnosis was confirmed. These facts made us reconsider how good the adherence of a patient could be and what differences are there between prophylactic and therapeutic treatments.

According to recommendations from US CDC and Taiwan CDC, anti-viral drug such as neuraminidase (75mg of Oseltamivir twice per day for 5 days) should be given to confirmed cases and persons under investigation within 48 hours, since this prescription was proved to decrease mortality and shorten hospitalization [12]. As for close contacts of confirmed cases, prophylactic treatment could protect them from actual illness [13]. Therefore, the purpose was different in prophylactic and therapeutic treatment. Because treating patients timely is the key to avoid occurrence of severe complications, it is a major responsibility to clinical practitioners. We also considered the importance of patients' compliance. Doctors should explain to patients about the necessity of adherence and possible side effects of drugs. On the other hand, nursing staff in hospitals and public health centers should be responsible in urging hospitalized and home-care patients to take medications timely, to reduce the chances of other infections.

To date, 2009 pandemic influenza infection had spread throughout the world. Because of its moderate severity, the purposes of control measures are to prevent severe complications and outbreaks. Currently, therapeutic anti-viral drugs should be given to those patients with severe complicated influenza infections and probable cases of H5N1; prophylactic drugs should be given to contacts of probable cases, possible cases, and confirmed cases of H5N1. In addition, for patients with influenza-like illness but without dangerous signs, self-paid anti-viral drugs are not necessary and should be avoided to prevent emergence of resistant strains [14].

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