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Experience in Emergency Response to Epidemic of Infectious Disease Related to Climate Change and Natural Disaster-Typhoon Disaster as an Example

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Abstract

Several major natural disasters have occurred in this country during the past twenty years. For earthquake events, the most representative was the 921 earthquake in 1999, which have caused enormous damages to this country but allowed the governments to acquire a lot of experience in emergency response to post-disaster infectious disease control. Taiwan lies in the typhoon belt of the western Pacific and is devastated by typhoon in different scale in almost every year. The Typhoon Morakot in 2009 was the one that has caused the most serious injuries and deaths in the meteorological history of Taiwan and has severely destroyed southern Taiwan. The Typhoon Fanapi in 2010 also brought serious flooding and damages to Taiwan. In order to deal with the potential risk of the spread of infectious diseases likely to occur following natural disaster, Taiwan CDC has integrated relevant resources and has established operational procedures for this issue, which include two major parts: pre-disaster preparedness and post-disaster response and reconstruction, so that the spread of infectious disease after natural disaster could be effectively prevented.

Keywords: climate change, greenhouse effect, natural disaster, typhoon disaster, Typhoon Morakot

Introduction

Natural disaster is a distressing event caused by natural environment factors, such as atmospheric, geographical, and hydrographic change. The natural disasters commonly occurred include earthquake, volcanic eruption, landslide, tsunami, flood, and drought. The occurrence of natural disaster often poses serious threats to human health and social economy. Over the past twenty years, several million of human lives have been deprived and the daily activities and economy of at least billion population have been affected worldwide due to natural disasters [1]. In recent years, the occurrence of natural disasters caused by extreme weather, such as a hurricane or flood, has become more frequent in international community as a result of global warming, so the communicable disease control after natural disaster have received the highest attention from countries worldwide.

Since the late 20th century, the occurrence of the global warming and climate change resulted from greenhouse effect have become more obvious. The geographical location in the regions with tropic and sub-tropic climate and nearing the world's largest continent and ocean make Taiwan more vulnerable to attack by natural disaster resulted from greenhouse effect, leading to the frequent occurrence of extreme weather, such as typhoon and flash-rains. Because Taiwan has a very complicated geographical structure and unstable geological characteristics in mountain areas, a landslide and debris flow occurred following a heavy rain are commonly seen in these areas. Similarly, floods are also frequently found in densely populated plane or hill areas where the rainwater drainage is difficult. Based on the report, Natural Disaster Hotspots: A Global Risk Analysis, made by the World Bank in 2005, 73% of the land area and population in Taiwan simultaneously exposes to more than three natural disasters, including flood, drought, and earthquake, with the highest percentage in the world [2]. To effectively prevent and control epidemic probably occurred following natural disaster, the Center for Disease Control in Taiwan (Taiwan CDC) has compiled the Guideline for Emergency Response to Epidemic after Natural Disaster. This guideline has provided detail description on issues about stockpile of disinfectant and pesticide, and manpower training and scheduling, and established standard operation procedures for post-disaster epidemic prevention and control. In addition that the health authorities at different administrative levels should complete emergency preparedness in ordinary times by following the guideline, they should conducted various control activities, such as household disinfection, disease surveillance in disaster-affected areas and shelter center for displaced persons, and health education, after the natural disaster, to reduce the risk of post-disaster epidemic.

Effect of climate change on disease epidemic

The effect of climate change on disease epidemic can be discussed from three sides, human behavior, infectious agents, and vectors. Climate change has a direct effect to human behavior and these behaviors are highly associated with the spread of infectious disease. For example, a disease in one place may be introduced into a previously unaffected geographic place through seasonal employment and labor migration, and different living pattern between winter and summer can cause different epidemics. During the chilling winter months, most of the daily activities in people mainly occurred in a less-ventilated indoor area, leading that the infectious diseases of respiratory tract are more likely to occur in winter season. In contrast, countries in warm or cool regions have a relatively higher opportunity to occur gastrointestinal infectious diseases because warm climate implies that people may do their outdoor picnic activities more often than those in other regions. During hot summer season, the fact that people tend to consume ice products, cold drinks, and raw and cold foods has become an important factor causing the spread of intestinal infectious diseases [3].

The climate conditions, including temperature and humidity in the environment, are very important to pathogenic agents living outside human body. Most of pathogens, such as viruses, bacteria, and parasites, can proceed through their life cycle only when they are staying under a specific temperature. For example, the vector mosquitoes must live in an environment with temperature higher than 18℃ for *Plasmodium falciparum* to go through the reproduction cycle, while the warm environment more than 20℃ is advantageous to Japanese encephalitis virus to replicate. Although elevated environment temperature can promote the reproduction rates of pathogenic agents, the high temperature will also depress the activation of pathogenic agents when it is higher than the level that the agent can tolerate [4].

Climate change can affect vector mosquito mainly through three factors: temperature, humidity, and rainfalls. These factors may lead to the change of life cycle, population density, and inhabitation places of the mosquitoes. As a result, the seasons suitable for disease transmission become longer and the geographical areas affected by an epidemic are wider. To take dengue fever as an example, warm environment will increase the activities of mosquitoes, the external incubation period of dengue virus within mosquito will be shortened, and rainfalls will increase mosquito breeding sites and population of adult mosquito [5]. During the past decade, the dengue epidemic in southeastern Asia has become more and more serious from year to year. No matter it is in developed countries, such as Singapore, or in developing countries, such as Philippines, Indonesia, Thailand, and Vietnam. The distribution of Anopheles mosquito also gradually spread to higher altitude areas, leading to the expansion of geographical distribution of malaria [6]. Global climate change has made the geographical areas of tropical and sub-tropical regions become wider, and this has directly influenced the ecosystem of the animals and plants. As a result, the biological flora, the population and distribution of rodents capable of transmitting disease, and the distribution and population density of vector mosquito became changed, and these have further influence the status of global disease distribution.

Natural disaster and communicable diseases

After the natural disaster, because the residential environment was damaged and were lack of sanitary food and adequate drinking water, the affected residents were more prone to epidemic of the gastrointestinal infectious diseases. A large amount of floodwater submerging the land will make the environment be more suitable for vector mosquito and pathogens to reproduce. In addition, to make activities in the environment flooded with dirty muddy water and filth will largely elevate the opportunities of acquiring the infections of water-borne diseases, such as melioidosis and leptospirosis [7]. The communicable diseases associated with natural disaster can be divided into two categories as follows:

A. water-borne or food-borne diseases that are gastrointestinal diseases spread through fecal-oral route, including diarrhea (such as salmonella infection), typhoid/paratyphoid, shigellosis, cholera, and hepatitis A and E, as well as diseases transmitted through contact with contaminated water, such as melioidosis and leptospirosis [8];

B. vector-borne diseases that are diseases transmitted through mosquito bite, such as dengue fever, malaria, chikungunya fever, yellow fever, and Japanese encephalitis, as well as diseases spread through contact with infected excreta of rodents, such as hantavirus infection and leptospirosis.

Preparedness and emergency response to epidemic associated with natural disaster

The preparedness and emergency response plan can be divided into several stages. They are prevention and preparedness stages before natural disaster, for the purposes of being capable of effectively responding to emergency situations associated with natural disaster; and emergency response and restoration stages, with the aims of reducing damages potentially caused by natural disaster and shortening time duration for post-disaster restoration [9].

A. Emergency preparedness for disease control before natural disaster

a. Operation framework for epidemic associated with natural disaster

The central governments involved in the disease control after natural disaster include the Department of Health (DOH), Environmental Protection Administration (EPA), Council of Agriculture (COA), Ministry of Interior (MOI), and Ministry of Economic Affairs (MOEA). Among these agencies, the DOH is the competent authority for communicable disease control and is responsible for establishing Task Force for Communicable Disease Control following natural disaster. The activities of the Task Force for DOH are to have person to stay on duty in the Central Emergency Operation Center, to conduct close surveillance of epidemic and to perform disinfection for prevention of communicable disease in disaster-affected areas, and to implement health education. The activities for EPA are to supervise local governments to conduct environmental cleaning and disinfection in disaster-affected areas. The responsibilities for COA in the Task Force are to perform treatment of corpses of livestock or animals and to conduct disinfection of the livestock farm in the disaster-affected areas. The Public Health Bureau and the Environmental Protection Agency in local governments will have to conduct the activities related to communicable disease control under the supervision and instructions of the relevant ministries in the central government.

b. Preparation and management of disinfectants and disinfection equipments

Based on Article 5 of the Communicable Disease Control Act, local governments should keep stockpile of disinfectant and disinfection equipments but they can also request central government to provide supplies when necessary. This article has clearly regulated the individual responsibility and works for health authorities in local and central governments. In practice, health authorities in county governments are required to allocate appropriate budgets to purchase and maintain a sufficient amount of disinfectants at the usual time based on the self-evaluation on the frequency and risk of the occurrence of natural disaster in their administrative regions. Moreover, Taiwan CDC also has always stockpiled a certain amount of disinfectants and disinfection equipments at the Branch Offices, which can be supplied to county governments for emergency use based on their requests. The stockpiling items of disinfectant and disinfection equipments include phenolic disinfectants, bleaching solution (sodium hydrochloride solution), bleaching powder (calcium hydrochlorite powder), chlorine tablet, vehicle for disinfectant spraying, and support vehicles for emergency response activities. The amount of disinfectant to be stockpiled is determined based on the severity of natural disaster occurred in the past several years, and the management and emergency scheduling of the stockpiled disinfectants are worked out through the Communicable Disease Control Resource Management Information System. Taking the typhoon Fanapi in 2010 for example, before the typhoon season is coming, Taiwan CDC has already elevated the amount of stockpiled phenolic disinfectant up to 150,000 units (available for 150,000 households) based on the experience from typhoon Morakot in 2009. Therefore, when typhoon Fanapi struck southern Taiwan on 20 September, 2010, and caused severe floods in Kaohsiung County/City and Pingtung County, Taiwan CDC immediately conducted demand assessment for typhoon-affected areas and activated the disinfectant scheduling system on the same day, and, on 22 September, sent all the demanded disinfectant to the affected areas in response to the request of county governments, so that local governments could conduct household health education and disinfection immediately after flood water disappeared to prevent epidemic from occurring.

c. Establishment of communicable disease surveillance and notification system

Taiwan CDC has established a variety of communicable disease surveillance and notification information systems, including Notifiable Communicable Disease Surveillance System, Communicable Disease Investigation System, and Communicable Disease Business Objects Database. These systems were used to monitor and collect data on the occurrence of cases and clusters of infectious diseases nationwide at usual time, and the data collected were utilized as a basis for setting up the epidemic alert criteria and epidemic threshold values for each infectious diseases so that we can rapidly detect the epidemic status of infectious diseases occurred following the natural disaster.

d. Preparation and training of infectious disease control personnel

The quality and enforcement of communicable disease control and public health activities implemented following natural disaster were closely associated with factors of environmental conditions and size of the affected areas, number of residents affected, efficiency of transportation and telecommunication, and training and mobilization of public health personnel. When a severe natural disaster occurred, a surging capacity for public health and communicable disease control emergency must be timely provided. Therefore, health authorities in different levels of government should during normal times develop different name lists with the member's contact information for emergency response and set the mobilization priority of them in different stages of the natural disaster so that the necessary manpower can be rapidly mobilized and scheduled for post-disaster infectious disease control activities. Moreover, Taiwan CDC has been continually authorizing health bureaus of local governments every year to conduct evaluation on the post-disaster infectious disease epidemic status, risk of epidemic occurrence, and population at high risk of infection, and to perform the preparation and training of infectious disease control personnel for elevating the capacity of emergency response.

B. Emergency response to possible epidemic following natural disaster

a. Demand assessment and decision making on infectious disease control following natural disaster

The demand relating to infectious disease control following natural disaster may be changed from time to time, depending on the type of natural disaster and the severity of damage caused by the natural disaster. Generally speaking, except under very unusual conditions, the possibility of infectious disease epidemics occurring immediately after natural disasters is not very high. However, the evaluation and analysis on issues relating to infectious disease still should be rapidly administered at the appropriate time, for obtaining sufficient information to provide to decision-maker or leader as a basis for making policy, taking suitable emergency response actions, and preventing the occurrence of delayed-impact infectious disease. The key items to be evaluated for infectious disease control purpose include the number of affected household, severity of flooding, drink water supply and garbage collection, damage in health facilities (including electricity supply and vaccine maintenance), transportation and communication systems, demand for disinfectants, and the number, scale, and locations of shelters.

b. Surveillance of infectious diseases

Natural disaster may increase the risk of infectious disease epidemics in the affected areas, such as the flooded areas caused by typhoon. Except through the routinely operated communicable disease surveillance and notification systems, Taiwan CDC has conducted extra surveillance in the disaster-affected areas through the assistance of local health bureaus. For example, the local health bureaus will collect data on disease occurrence from clinics, hospitals, and temporary medical stations in the affected areas, as well as from shelter centers for displaced population, and send these data to the Taiwan CDC on a daily basis. Then, the Taiwan CDC will perform data integration and data analysis to update and closely monitor the occurrence of post-disaster disease infections so that the control measures can be carried out in no time. The data to be collected focus on the total number of patient visits for medical service, and number of patients for individual disease or symptom, such as respiratory tract diseases (including pneumonia, asthma, and cough), gastrointestinal diseases (including bloody diarrhea, watery diarrhea, nausea, and vomiting), skin diseases (including rash and scabies), and other diseases (including fever, jaundice, and acute conjunctivitis). In fact, fourteen infectious diseases that the flooding may result in as increase of their occurrence have been included into the disease list for extra surveillance by Taiwan CDC during the period immediately after Typhoon Morakot in 2009. These were cholera, typhoid, paratyphoid, shigellosis, amoebiasis, E. Coli O157:H7 hemorrhagic colitis, acute viral hepatitis A, dengue fever, Japanese encephalitis, severe enteroviral infections, epidemic meningococcal meningitis, leptospirosis, melioidosis, and tetanus. The occurrence of these diseases was compared with the baseline data that occurred during the same period in 2008. In addition, the novel influenza A (H1N1) infections, including mild cases, severe cases, and cluster infections, also have been the disease under close monitoring for Morakot-affected areas.

c. Environmental sanitation and disease control

1. Disinfection of household environment

Since natural disaster will usually damage the environmental sanitation system, to strengthen environmental disinfection for disaster-affected areas is a very important activity to health and environmental authorities in different levels of government in terms of avoiding worsening of environmental sanitation and preventing infectious disease from occurring. The waste transportation and environmental disinfection in public open areas are the responsibilities of the environmental authorities while the disinfection of household environment is the duties performed by health authorities. In practice, health authorities should teach residents in flood-affected regions to conduct household disinfections by following the three steps: removal of solid waste, cleaning environment, and disinfecting environment, and should encourage them to buy the commercial household chlorine bleach solution to conduct household environment disinfections by themselves. In case the residents are unable to obtain the disinfectants or are trapped in severely affected areas, the disinfectants necessary for household disinfection will be provided and distributed to them from the stockpiled disinfectants by local health authorities. When local governments do not have sufficient stockpiles to satisfy residents' demands, they can send request to the Taiwan CDC for supply or allocation of disinfectants. Based on statistics provided by health authorities of local governments in affected regions, a total of 304,354 houses in 14 counties were suffering from floods during the period of Typhoon Morakot. Based on requests raised by county governments, Taiwan CDC not only released stockpiled disinfectants but also emergently purchased another 460,000 bottles of disinfectants, and completed transportation and distribution of these to disaster-affected areas within one week after Morakot struck. In addition, Taiwan CDC dispatched vehicle for disinfectant spraying and persons to the affected areas to assist residents to conduct household disinfection as well as to perform health education.

2. Shelters and emergency settlement

The chaotic environment and garden will have to be cleaned and the living function and sanitation conditions must be restored within the shortest time period after natural disaster for effectively reducing the risk of infectious disease epidemic. In severely affected areas, displaced residents will definitely face conditions with worse environment sanitation from several days to several weeks or even several months. Therefore, they urgently need to be provided with a tentative settlement for residence or staying. A shelter or emergency settlement should satisfy the three primary conditions: safe environment, good and clean water supply, and environmental protection facilities and sanitary facilities. Following the establishment of shelter or emergency settlement by the Social Welfare Bureaus or the Civil Affairs Bureaus of county governments in affected areas, health authorities will set up emergency medical station at the center to provide residents in the shelter with primary medical services and will conduct surveillance on the occurrence of infectious disease and the activities of vectors. During the period of Typhoon Morakot, Taiwan CDC, in order to avoid occurrence of infectious diseases, has arranged staff visiting the shelters or emergency settlement, based on information provided by the Department of Social Affairs, Ministry of the Interior, to perform field investigation and monitoring, to provide different types of face mask and personal protective equipments, to educate residents about post-disaster infectious disease prevention and control, respiratory tract hygiene, and cough manner, and to install infrared temperature sensor monitor at large-sized settlement to check residents' health. In addition, Taiwan CDC has developed the Control Measures of Novel Influenza A (H1N1) at shelters to continually strengthen influenza control activities at the disaster-affected areas, including to perform monitoring and early response, to provide medical care service, to conduct infection control around the settlement areas, to loosen the requirements for disaster-affected residents about the use of antiviral drugs, and to give residents in shelters and settlements the first priority for seasonal influenza vaccine and novel influenza A (H1N1) vaccine. During the Typhoon Morakot time period, no significant clusters of infectious disease were identified at the shelters and settlements due to the implementation of various intervention measure made by health authorities at different levels of government.

3. Vaccine and reset of cold storage equipment

When natural disaster occurred and the vaccine cold storage equipment was unable to maintain at the required vaccine storage temperature due to power supply failure and equipment damage, the health units at different levels of government and the contract hospitals or clinics must conduct emergency response according to the Guideline on the Procedures and Measures of Emergency Response to Failed Vaccine Cold Storage Equipment. Immediately after the occurrence of natural disaster, the person in charge of vaccine management should inspect vaccine storage equipment and make record on the condition, operation, and temperature of the vaccine cold storage equipment, as well as on vaccine status and emergency response to equipment failure, and then send the records to the superior health authorities. The health units at different levels of government are responsible for collection and integration of information on vaccine damage and equipment failure in their administrative regions so that the equipment reparation and rebuilding, and vaccine allocation can be immediately conducted. When the facilities of vaccination service units were severely damaged due to natural disaster, an evaluation on vaccine items and target population vaccinated must be rapidly conducted, and a temporary vaccination station should be established as soon as possible so that the implementation of routine vaccination services could be continued. During the period of Typhoon Morakot, the damaged vaccines and failed equipments were found in 14 public health stations or contract clinics in Jiayi, Tainan, Kaohsiung, and Pingtung County. The Taiwan CDC was immediately dedicated to restoring the operation of vaccine cold storage equipment and vaccination information equipment and to allocating vaccine for the continuation of routine vaccination service. In addition, the health stations were required to check vaccination history of residents suffering from typhoon, reissue vaccination record book, and arrange and track children to complete the series of required vaccination.

4. Intervention for epidemic

Hospitals, clinics, or temporary medical stations are required to immediately notify local health authorities of any suspected cases or potential epidemic of infectious diseases so that the health authorities can conduct timely investigation on the status and causes of the disease occurrence and take necessary actions to effectively control the disease. These actions include to take specimens from the patients, contacts, and environment; to conduct environment disinfection; to send the patient to hospital for isolation; to perform health education to the patients and their contacts; and, then, to report to superior health authorities or to ask for assistance. After the natural disaster, a false epidemic occasionally might be reported at the disaster-affected areas. Therefore, health authorities should immediately have staff to investigate the purported epidemic other than the cases notified by hospitals, clinics, or temporary medical stations to understand the real situation, and make correct clarification of the investigation results to general public at an appropriate time. For example, a cluster of leptospirosis infection was reported from Wandan Township in Pingtung County following the Typhoon Morakot in 2009. On receiving the report of the cluster, Taiwan CDC immediately dispatched infectious disease control physicians to conduct field investigation and found that the cluster infection probably resulted from contaminated drinking water. After taking public health measure and disinfection intervention, the epidemic was soon under well control.

d. Health education and health information dissemination

Since natural disaster may make environment sanitation worse and result in the occurrence of infectious disease, health units at different levels of government should strengthen health education and health information dissemination to remind public of enforcing all health activities, including to take care of the drinking water, food, and environment sanitation to prevent gastrointestinal infection; to conduct household environmental disinfection; to clean up vector breeding sources to prevent dengue fever; to take protective measures to the hands and foots to avoid infection of leptospirosis and melioidosis; to take precautionary measures when drinking water supply was recovered from interruption; and to enforce respiratory tract hygiene and cough manner in densely populated shelters. In addition, Taiwan CDC will also create health education material over post-disaster environmental disinfection and infectious disease prevention and control and widely disseminate these materials through multimedia, such as newspaper, television, internet, and other electronic media. Moreover, a letter to medical practitioner was written and sent to physicians through email to remind them of the importance of staying alert on notification of infectious disease (especially those transmitted through contaminated water, such as melioidosis and leptospirosis) likely to occur in post-disaster conditions, and providing patients with pertinent treatment to reduce the occurrence of deaths.

Discussions

Except that the epidemic of water-borne, food-borne, and vector-borne disease that probably occurred at the early stages following natural disaster, such as typhoon or floods should be closely monitored and responded to as soon as possible, for a natural disaster causing devastating damage and, therefore, needing a longer post-disaster reconstruction period, the other public health activities for residents in shelter settings should be considered as an important part of the overall post-disaster disease control program. These activities including to provide sufficient living space, to offer primary health and medical services, to supply safe daily water, drinking water, and foods, to properly treat daily waste, to continually provide routine vaccination, and to keep on implementing the control of endemic infectious disease. In recent years, several natural disasters causing enormous damage have occurred in international community, such as earthquake in Wenchuan, China in 2009, in Haiti in 2010, and in Japan in 2011; Hurricane Katrina in the USA in 2005; tropical cyclone in Myanmar in 2008; and Typhoon Morakot in Taiwan in 2009. In the case of the Haiti earthquake, because water supply system and sanitary facilities in the hit regions were severely damaged and the reconstructions were going slowly, a total of more than four hundred thousand cholera cases, including five thousand deaths, have been reported during the one and a half year after the earthquake. In Myanmar, because of the worse health conditions following the strike of cyclone, residents in affected areas can only drink contaminated river water, leading that the gastrointestinal infectious disease, such as cholera, spread rapidly. In other countries, owing to the active intervention by the governments, a large-scale epidemic was rarely found. These cases indicate that the pre-disaster preparedness and post-disaster emergency response are very important.

Based on Climate Change 2007, the Fourth Assessment Report of the United Nations Intergovernmental Panel on Climate Change (IPCC), the frequency of disaster caused by climate change in countries worldwide will present an increasing tendency in the future and the damage incurred by the disasters will also appear at an enlarged scale. Although we have accumulated abundant experience in practices of and in response to post-disaster infectious disease control and have established enough capacity for post-disaster emergency response for future years (1-3 years), for the long term, the primary capacity for post-disaster will still need to be modified annually base on the scale of disaster occurred in the past years, viewing of the uncertainty of the speed of climate change and scale of extreme climate events. Since the scale of damages caused by natural disaster was changed largely from year to year and was unpredictable, health authorities will have to keep flexible in the plan of pre-disaster preparedness. To take the disinfectant as an example, the averaged amount of disinfectants used for post-disaster infectious disease control in recent years could be considered as the safe primary storage. However, in procurement of disinfectant, we should adopt the higher-than-average amount and make an open purchase contract with manufacture, to ensure having the priority of obtaining necessary disinfectants for emergency response. In addition, the source of a second-line disinfectants (for example, the commercial household bleach solutions could be a substitute of phenolic disinfectants in emergency situation) also should be planned in advance since it is important for emergency response to catastrophic damage from natural disaster.

Although Taiwan CDC has developed the Guideline for Emergency Response to Epidemic after Natural Disaster for health authorities at different level of governments to follow in planning and working for post-disaster infectious disease control, and the responsibilities for ministries in central governments involving emergency response to post-disaster epidemic control, such as DOH, EPA, COA, MOI, and MOEA have been clearly defined, the relevant ministries, in practice, still need to cooperate closely through the National Disaster Response Center (NDRC) in the process of exchanging emergency information, so as to elevate efficiency of emergency response. In addition, health authorities should actively participate in natural disaster prevention and rescue exercise organized by the NDRC or a higher level of government in the Executive Yuan, and should complete the establishment of cooperation channel and mechanism with other ministries.

Considering that the problems of global greenhouse gases are yet not well controlled, the climate change will probably proceed continually. The establishments of the model of risk assessment for post-disaster infectious disease occurrence and the model of predicting the spread of an infectious disease are issues that cannot be neglected under future extreme climate conditions. Although relevant researches on these issues currently have been emphasized in international communities, the results cannot be totally applied to this country due to the difference in climate conditions, geographical environments, social and economic conditions, and situations for developing prediction model. Therefore, we would like to see that relevant authorities, such as the DOH and the National Science Council, could conduct researches about the association of climate change and natural disaster with infectious disease occurrence, so that some important information suitable for the development of infectious disease control policy could be established for this country.

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Analysis of pdm-H1N1 Severe Complicated Influenza Cases in Eastern Region of Taiwan, 2008-2011

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Abstract

To understand the evolving features of the pandemic H1N1 (pdm-H1N1) severe complicated influenza cases (SCICs) in Eastern Region of Taiwan, we retrospectively reviewed those confirmed cases between April 2008 and March 2011, and categorized their date of onset into three periods, which were pre-, during, and post- pdm-H1N1 Influenza epidemic period (IEP) for April 2008 through March 2009, April 2009 through March 2010, and April 2010 through March 2011, correspondingly. In the pre-pdm-H1N1 IEP, there was only one SCIC. After the global outbreak of pdm-H1N1 influenza, the number of SCIC increased sharply to 104 and 195, and among them, 99 (95.2%) and 89 (45.6%) were seropositive for pdm-H1N1 influenza during and post pdm-H1N1 IEP, respectively. During both periods, there were six fatal SCICs (i.e. a mortality rate of $10.5/10^6$), which were 4.8 and 1.9 times, respectively, of the national rate in Taiwan. Among the 188 pdm-H1N1 SCICs confirmed during and post pdm-H1N1 IEP, all of them were hospitalized and 43 (22.9%) had underlying diseases. Among them, 27 were cared in intensive care units (ICUs) and the rest 161 cases admitted into general wards. These two hospitalized groups showed differential symptoms - 24 (88.9%), 21 (77.7%) and 18 (66.7%) cases hospitalized in ICUs showed pneumonia in X-ray, fever and difficulty breathing; and 147 (91.3%), 132 (82.0%), and 123 (76.4%) cases hospitalized in general wards showed fever, pneumonia in X-ray, and coughing, respectively. Death occurred in 11 pdm-H1N1 SCICs, of which eight were Hualien residents and three were Taitung residents, with a mean age of 54.7 (37 to 72) and 25.3 (22 to 30), respectively. Risk factors for SCIC mortality were underlying diseases in both counties. In addition to underlying diseases, SCIC deaths in Taitung County had additional risk factors of obesity and pregnancy, with body mass index between 34.7 and 50.7.

Keywords: pandemic H1N1 (pdm-H1N1) influenza, severe complicated influenza cases (SCIC), pdm-H1N1 Influenza epidemic period (IEP), risk factors

Introduction

Responding to the pandemic following the outbreak of pandemic H1N1/09 Influenza (pdm-H1N1) virus (A/California/7/2009 (H1N1)), which is a chimera novel influenza virus of recombination from swine-, avian- and human-origin influenza viruses, in Mexico that started around March and early April in 2009 [1], the Taiwan Centers for Disease Control (TCDC) promulgated pdm-H1N1 as a first category notifiable disease on April 27, 2009, and the Central Epidemic Command Center (CECC) was enacted in organizing pdm-H1N1 surveillance, resource allocation, and prevention and control.

Pdm-H1N1 influenza is an acute viral disease of the respiratory tract transmitted via aerosol or respiratory droplets [4] with an incubation period of 1.5 to 3 days [5]. About 8% to 32% of the patients infected with pdm-H1N1 influenza virus showed mild symptoms including fever, cough, sore throat, myalgia, fatigue, headache, and running nose. For adults, self-limited symptoms including diarrhea and vomiting were also observed. A review study of the first 100 hospitalized pdm-H1N1 influenza cases in Taiwan during July and August 2009 suggested that the major risk factors of pdm-H1N1 severe complicated influenza cases (SCIC) were underlying diseases, chronic lung diseases, a compromised immune system, cardiovascular diseases, pregnancy and diabetes mellitus [6-7].Among those hospitalized pdm-H1N1 severe complicated influenza cases, 70% had more than one underlying disease [8] and more than 60% of the mortality cases had underlying diseases [9].

As the pdm-H1N1 pandemic became less and less severe, the CECC was relieved off its duty on February 23, 2010. We retrospectively analyzed the severe complicated influenza cases during the pdm-H1N1 outbreak and found the mortality rate to be $10.5/10^6$ in Eastern Region of Taiwan, which was 4.8 times in comparison to the national rate of $2.2/10^6$ in Taiwan. This study elucidated the symptoms and signs, underlying diseases and risk factors of severe complicated influenza cases and its mortality cases in Eastern Region of Taiwan between April 1 2008 and March 31 2011.

Materials and Methods

A. Study object and period: Severe complicated influenza cases whose residence were in the Eastern Region of Taiwan (Hualien and Taitung Counties) reported between April 1, 2008 and March 31, 2011. Reported cases with neurologic diseases, asthma, chronic obstructive pulmonary disease, cardiovascular disease (excluding hypertension), diabetes mellitus, chronic anemia, liver diseases, cancer, immune diseases or chronic kidney diseases, and patients under treatments which might lead to immune suppression, were considered part of the high risk group with underlying diseases. SCIC mortality cases were also evaluated for underlying diseases, age, obesity, pregnancy and other relevant risk factors.

B. Data source: Reported severe complicated influenza cases whose residence were in the Eastern Region of Taiwan (Hualien and Taitung Counties) reported between April 1, 2008 and March 31, 2011 in the National Notifiable Disease Surveillance System (NDSS) database were downloaded and analyzed in Microsoft Excel®.

C. Influenza epidemic period: To elucidate the differences of risk factors and mortality rates attributable to severe complicated influenza cases among different pdm-H1N1 influenza epidemic periods (IEPs), we retrospectively reviewed those severe complicated influenza cases that were confirmed by a laboratory between April 2008 and March 2011, and categorized their date of onset into three periods, which were pre-, during, and post-pdm-H1N1 IEPs for April 2008 through March 2009, April 2009 through March 2010, and April 2010 through March 2011, correspondingly.

D. Definition and classification [11]

1. Clinical criteria of a severe complicated influenza case:

Suspected case is defined as development of one of the following conditions within four weeks of influenza-like illness:

a. Pulmonary complications that require hospitalization;
b. Neurological complications;
c. Myocarditis or Pericarditis;
d. Invasive bacterial infections;
e. Intensive care unit (ICU) admission or death.

2. Influenza-like illness:

Definition for the reporting of Influenza-like illness (should concurrently meet the following three conditions):

a. Sudden onset of disease, with fever (ear temperature ≧ 38℃) and respiratory tract symptoms;
b. One of the symptoms of muscle aches, headache, and extreme fatigue;
c. Simple running nose, tonsillitis and bronchitis should be excluded.

3. Definition of severe complicated influenza cases:

a. Exclusion criteria: reported severe complicated influenza case who did not meet the clinical criteria.
b. Probable case: reported severe complicated influenza cases that met the clinical criteria but tested negative.
c. Possible case: reported severe complicated influenza cases that met the clinical criteria who were living with or taking care of laboratory confirmed case(s) or had close contact with their body fluid or secretion of respiratory tract but tested negative.
d. Confirmed case: reported severe complicated influenza cases that met both the clinical criteria and tested positive.

E. Laboratory test: Throat swabs of severe complicated influenza cases tested positive for influenza virus reverse transcriptase polymerase chain reaction (RT-PCR) or influenza virus isolation in cell culture done by the Eastern Region Contract Laboratory of Taiwan Centers for Disease Control (TCDC).

F. Chart review of mortality cases: The local Bureau of Health collected medical charts and chest X-ray images or films of each reported severe complicated influenza mortality case who tested positive from relevant medical institutions. These records were subsequently passed onto Medical Officers of Taiwan Centers for Disease Control to identify their cause of death. Only case-patients whose causes of death attributable to infection of influenza viruses were defined as severe complicated influenza mortality cases.

Results

A. Analysis of severe complicated influenza cases in each pdm-H1N1 Influenza epidemic period (Figure and Table 1)

1. Pre- pdm-H1N1 Influenza epidemic period (IEP):

During this period, there were 18 reported severe complicated influenza cases. Among them, four and 13 were determined as excluded and probable cases, respectively.

Only one case tested positive for influenza virus AH1 and was determined as confirmed severe complicated influenza case.

2. pdm-H1N1 Influenza epidemic period (IEP):

There were 146 and 25 severe complicated influenza cases reported in Hualien and Taitung Counties, respectively. Among them, two, 63, two and 104 cases were determined as excluded, probable, possible and confirmed cases, respectively.

Among the 104 severe complicated influenza cases, 99 (95%), 4 (4%) and 1 (1%) tested positive for influenza virus pdm-H1N1, AH3 and B, respectively.The first pdm-H1N1 influenza positive case showed up in July 2009, and the pdm-H1N1 cases occurred from August through December in 2009, and peaked during September and October. As to the AH3 Influenza cases, the first cases appeared in August 2009, and August and September 2009 each saw the addition of two cases (Figure).

The geographic distribution of 104 severe complicated influenza cases were 95 and 9 cases in Hualien and Taitung Counties, respectively. In Hualien, the cases concentrated in Jian Township (36 cases), Hualien City (23 cases) and Sioulin Township (9 cases). In Taitung, the cases concentrated in Haiduan Township (3 cases), Taitung City (2 cases) and Beinan Township (2 cases). For the demographics, the sex ratio of severe complicated influenza cases during this period was 1.04:1 (M:F = 53:51). The age group showed a positive skew distribution, with 67 cases in age group 0 to 10, 21 cases in age group 11 to 30, 12 cases in age group 31-60 and four cases in age group 61-100.

Table 1. Analysis of pdm-H1N1 severe complicated influenza cases (SCICs) [a] in Eastern Region of Taiwan, 2008-2011

	Total cases (Hualien , Taitung) [b]			
	Pre-IEP [c]	During IEP	Post-IEP	Subtotal
Excluded	4 (4, 0)	2 (2, 0)	0 (0, 0)	6 (6, 0)
Probable	13 (13, 0)	63 (48, 15)	185 (160, 25)	262 (322, 40)
Possible	0	2 (2, 0)	0	2 (2, 0)
SCIC	1 (1, 0)	104 (95, 9)	195 (160, 35)	300 (256, 44)
Mortality cases attributable to SCIC	0	6 (3, 3)	6 (6, 0)	12 (9, 3)
Serotype [d] of SCIC				
AH1	1 (1, 0)	0	0	1 (1, 0)
AH3	0	4 (4, 0)	56 (47, 9)	60 (51, 9)
pdm-H1N1	0	99 (90, 9)	89 (64, 25)	188 (154, 34)
A (untyped)	0	0	1 (1/0)	1 (1/0)
B	0	1 (1, 0)	49 (48, 1)	50 (49/1)
(-)	17 (17, 0)	66 (50, 16)	195 (160, 35)	268 (227, 41)

Severe complicated influenza cases (SCICs) [a] in Eastern Region of Taiwan were analyzed by their status of laboratory examination and chart review and demonstrated in the form of [b] total cases (subtotal number of confirmed severe complicated influenza cases in Hualien , and in Taitung Counties). Each case was categorized into [c] pdm-H1N1 Influenza epidemic period (IEP) of pre-, during- and post- IEP by his/her date of onset. The serotype [c] of influenza virus of each SCIC was categorized as AH1 (influenza virus A H1N1), AH3 (influenza virus A H3N2), pdm-H1N1 (pandemic Influenza A H1N1), and A (untyped) (influenza virus A untyped), and (-) represents negative.

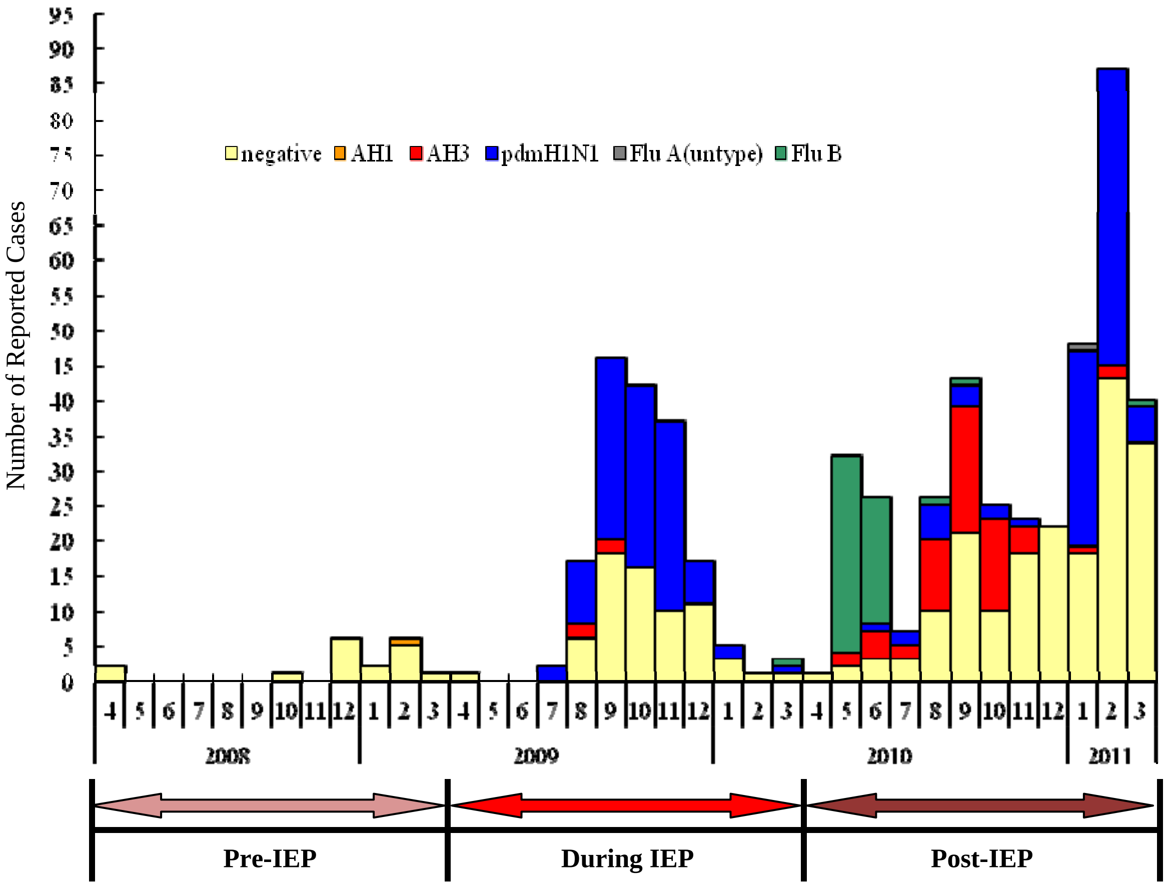

Figure. Laboratory Results of severe complicated influenza cases in Eastern Region of Taiwan, April 2008 - March 2011 (n = 569)

For the chart review of severe influenza mortality cases, six cases had their cause of death attributed to infection with the influenza virus, of which there were three cases each in Hualien and Taitung Counties. As a result, the mortality rate was 8.9 and 13.0 per million in Hualien and Taitung Counties, respectively. During the same period, the mortality rate averaged 2.2 per million across Taiwan and was 10.5 per million in the Eastern Region of Taiwan.

3. Post-pdm-H1N1 Influenza epidemic period (IEP):

There were 320 and 60 severe complicated influenza cases reported in Hualien and Taitung Counties, respectively. Among them, 185 and 195 cases were determined as probable and confirmed cases, respectively.

Among the 195 severe complicated influenza cases, 89 (45.6%), 56 (28.7%), 1 (0.5%) and 49 (25.1%) tested positive for influenza virus pdm-H1N1, AH3, A (untyped) and B, respectively. Both of the first Influenza AH3 and B positive cases showed up in May 2010, and peaked in September 2010. The first pdm-H1N1 influenza positive case showed up in June 2010, and the pdm-H1N1 cases occurred from June 2010 through March 2011, and peaked between June 2010 and February 2011 (Figure).

The geographic distributions of the 195 severe complicated influenza cases were 160 and 35 cases in Hualien and Taitung Counties, respectively. Most of the severe complicated influenza cases were distributed in urban areas, including 44 cases in Hualien City, 36 cases in Jian Township and 9 cases in Yuli Township. And most severe complicated influenza cases clustered in the rural areas of Taitung City (13 cases) and Beinan Township (3 cases) and in the mountainous region of Chenggong Township (3 cases).

For the demographics, the sex ratio of severe complicated influenza cases during this period was 1.5:1 (M:F = 117:78). The age distribution were 50 cases in age group 0 to 10, 37 cases in age group 11 to 30, 62 cases in age group 31-60 and 46 cases in age group 61-100.

For the review of severe influenza mortality cases, six cases had their cause of death attributed to infection with the influenza virus, of which there were six cases and zero case in Hualien and Taitung Counties, respectively. As a result, the mortality rate was 17.8 per million and 0 per million in Hualien and Taitung Counties, respectively. During the same period, the mortality rate was 3.5 per million across Taiwan and 10.5 per million in the Eastern Region of Taiwan.

B. Symptoms, underlying diseases and risk factors of pdm-H1N1 severe complicated influenza mortality cases in Eastern Region of Taiwan:

Between April 2008 and March 2011, there were 188 laboratory confirmed pdm-H1N1 severe complicated influenza cases, and all of these 188 cases were hospitalized. Among them, 161 pdm-H1N1 severe complicated influenza cases were hospitalized in general wards and all recovered, whereas the remaining 27 pdm-H1N1 severe complicated influenza cases required intensive care and 11 of those cared in ICU died. The major symptoms and signs of those pdm-H1N1 severe complicated influenza cases hospitalized in general wards were fever (91.3% (147/161)), pneumonia (82.0% (132/161)), and cough (76.4% (123/161)); 17.4% of these patients had underlying diseases including chronic lung diseases (28.6% (8/28)) and metabolism diseases (21.4% (6/28)). On the other hand, the major symptoms and signs of pdm-H1N1 severe complicated influenza cases who required intensive care were pneumonia (88.9% (24/27)), fever ((75.0% (21/28)), difficulty breathing (66.7% (18/27)); 55.6% of these patients had underlying diseases including metabolism diseases (33.3% (5/15) and kidney diseases (33.3% (5/15)) (Table 2).

C. Clinical manifestations and risk factors of severe complicated influenza mortality cases:

There were 12 severe complicated influenza mortality cases in Eastern Region of Taiwan between March 2008 and April 2011, of which six occurred during and six occurred post IED. Only one of the etiologic agents was influenza AH3, and the remaining 11 were all attributable to pdm-H1N1 influenza. The age distribution of these twelve severe complicated influenza mortality cases were 22 to 72. The three severe complicated influenza mortality cases who resided in Taitung County were all younger

Table 2. Analysis of Symptoms and Underlying Diseases of Severe Complicated Influenza Cases in Eastern Region of Taiwan, April 2008 - March 2011

Influenza Epidemic period [a]	During IEP (2009/4~2010/3)		Post-IEP (2010/4~2011/3)		Subtotal	
Ward [b] (Number)	General (86)	ICU (13)	General (75)	ICU (14)	General (161)	ICU (27)
Symptoms or signs						
Fever	90.7%(78/86)	76.9%(10/13)	92.0%(69/75)	78.6%(11/14)	91.3%(147/161)	77.7%(21/27)
Cough	81.4%(70/86)	53.8%(7/13)	70.7%(53/75)	14.3%(2/14)	76.4%(123/161)	33.3%(9/27)
Pneumonia (CXR)	86.0%(74/86)	92.3%(12/13)	77.3%(58/75)	85.7%(12/14)	82.0%(132/161)	88.9%(24/27)
Sore throat	33.7%(29/86)	23.1%(3/13)	30.7%(23/75)	14.3%(2/14)	32.3%(52/161)	18.5%(5/27)
Muscle pain	23.3%(20/86)	38.5% (5/13)	18.7%(14/75)	7.1%(1/14)	21.1%(34/161)	22.2%(6/27)
Short of breath	1.2%(1/86)	30.8%(4/13)	21.3%(16/75)	35.7%(5/14)	10.6%(17/161)	33.3%(9/27)
Difficulty breathing	4.7%(4/86)	84.6%(11/13)	13.3%(10/75)	50.0%(7/14)	8.7%(14/161)	66.7%(18/27)
Underlying disease	**4.7%(4/86)**	**76.9%(10/13)**	**32.0%(24/75)**	**35.7%(5/14)**	**17.4%(28/161)**	**55.6%(15/27)**
Mental illness	0	0	4.0%(3/75)	0	10.7%(3/28)	0
Cardiovascular disease	0	23.1%(3/13)	4.0%(3/75)	0	10.7%(3/28)	20.0%(3/15)
Neuromuscular diseases	0	0	0	0	0	0
Chronic lung diseases	0	0	10.7%(8/75)	7.1%(1/14)	28.6%(8/28)	6.7%(1/15)
Kidney diseases	2.3%(2/86)	15.4%(2/13)	0	21.4%(3/14)	7.1%(2/28)	33.3%(5/15)
Liver diseases	0	15.4%(2/13)	4.0%(3/75)	7.1%(1/14)	10.7%(3/28)	20.0%(3/15)
Metabolism diseases	2.3%(2/86)	23.1%(3/13)	5.3%(4/75)	14.3%(2/14)	21.4%(6/28)	33.3%(5/15)
Asthma	0	0	1.3%(1/75)	0	3.6%(1/28)	0
Cancer	0	0	5.3%(4/75)	0	14.3%(4/28)	0
Death (attributable to pdm-H1N1)	**0**	**6**	**0**	**5**	**0**	**11**

There were no pdm-H1N1 severe complicated influenza cases (SCICs) before the pdm-H1N1 influenza epidemic period [a] (IEP), thus we abridged the pre-pdm-H1N1 IEP in this analysis. Pdm-H1N1 severe complicated influenza cases who required intensive care to sustain their lives in intensive care units (ICUs) were analyzed versus those in general wards in this analysis.

than 30 years of age, whereas the remaining nine pdm-H1N1 severe complicated influenza mortality cases were residents of Hualien County and were all older than 31 years of age.

Among 12 pdm-H1N1 severe complicated influenza mortality cases, ten have underlying diseases, and the remaining two also had the risk factor of obesity or pregnancy. The major symptoms and signs were pneumonia (91.7% (11/12)), short of breath (75.0% (9/12)), difficulty breathing (66.7% (8/12)), fever (66.7% (8/12)), cough (41.7% (5/12)), sore throat (25.0% (3/12)) and muscle aches (25.0% (3/12)).

Nine pdm-H1N1 severe complicated influenza mortality cases received Tamiflu treatment, of which four were treated with Tamiflu 48 hours after onset. Only one pdm-H1N1 Severe complicated influenza mortality case had received influenza vaccination in the same influenza season (Table 3).

Discussion and conclusion

Severe complications from influenza were proclaimed as a category III communicable disease in Taiwan in 1999, and following the proclamation, the reporting and surveillance of severe complicated influenza cases were initiated in 2000. Each reported severe complicated influenza case required expert review with a rigorous and careful review process. The first reporting of a severe complicated influenza case in Eastern Region of Taiwan was in 2003. There had been only 13 severe complicated influenza cases reported in Eastern Region of Taiwan between 2000 and 2007, and only three were confirmed cases. All of these 13 cases resided in Hualien County. In 2007, the Taiwan Centers for Disease Control revised the diagnostic criteria for severe complicated influenza cases and incorporated these checking criteria into the National Notifiable Disease Surveillance System while terminating the review of paper records to simplify the reporting and reviewing process. There had been only 13 reported severe complicated influenza cases between 2000 and March 2008, of which eight and

Table 3. Analysis of Clinical Manifestations and Risk Factors of Severe Complicated Influenza Mortality Cases in Eastern Region of Taiwan, April 2008 - March 2011

No.	Age	Residence [a]	Gender	Date of onset	Date of death	Clinical manifestation [b]							Underlying diseases	Risk factors [c]	Test results	Initial Date of taking Tamiflu	Vaccine	Tribes [d]
						A	B	C	D	E	F	G						
1	24	T	M	2009/8/13	2009/8/21	V	V	V	V				N	BMI 37.9	Pdm-H1N1	2009/8/20	N	B
2	58	H	F	2009/ 9/5	2009/9/8	V		V	V	V	V	V	DM Heart disease	U	Pdm-H1N1	2009/9/7	N	--
3	22	T	F	2009/9/18	2009/9/20	V	V	V		V		V	N	BMI 34.7 P	Pdm-H1N1	None	N	B
4	45	H	M	2009/9/24	2009/10/1		V		V	V	V		DM Hypertension	U	Pdm-H1N1	2009/9/28	N	T
5	52	H	F	2009/10/8	2009/10/11		V	V	V	V			Liver diseases	U	Pdm-H1N1	2009/10/10	N	A
6	30	T	M	2009/12/8	2009/12/11	V	V	V	V				Liver cirrhosis Hypertension	BMI 50.7 U	Pdm-H1N1	None	N	B
7	37	H	M	2010/7/19	2010/7/26	V	V	V	V				Liver diseases	U	Pdm-H1N1	None	N	--
8	70	H	M	2010/7/31	2010/8/6	V	V		V				Lung diseases	U	AH3	2010/8/3	N	--
9	52	H	M	2010/10/20	2010/11/2	V	V		V	V			Cardiovascular disease	U	Pdm-H1N1	2010/10/25	N	--
10	52	H	M	2010/12/29	2011/1/9		V	V					Liver diseases	U	Pdm-H1N1	2011/1/1	N	--
11	54	H	M	2011/2/18	2011/2/19	V	V		V		V	V	Kidney disease	U	Pdm-H1N1	2011/2/18	N	--
12	72	H	M	2011/2/16	2011/2/23		V	V					DM	U	Pdm-H1N1	2011/2/21	Y	--

The residence [a] of mortality severe complicated influenza cases (ISCS) in Eastern Region of Taiwan were abbreviated as Hualien (H) and Taitung (T) County. The clinical manifestations [b] of each ISCS were expressed as A (fever), B (pneumonia), C (short of breath), D (difficulty breathing), E (cough), F (sore throat), and G (muscle pain). The major risk factors [c] of these mortality ISCSs were obesity (expressed in BMI), underlying disease (U) and pregnancy (P). Among these severe complicated influenza mortality cases, five were indigenous people in Taiwan, and they were from the Amis (A), Bunun (B) and Atayal (T) tribe, respectively.

five cases resided in Hualien and Taitung Counties, respectively. On the contrary, the number of cases reported increased to 18 during the pre-pdm-H1N1 IEP and sharply increased to 171 and 180 during- and post-pdm-H1N1 IEP, respectively. This dramatic increase in reporting might have been partially due to the simplified reporting process and the coverage of Tamiflu treatment under the national health insurance program during the H1N1 influence pandemic, which in turn led to an increase in the willingness to report and the sensitivity of the surveillance system to detect severe complicated influenza cases.

Serotypes of the influenza virus: An analysis of the virus serotypes isolated from 300 severe complicated influenza cases suggests the following: 1) The number of severe complicated influenza cases tremendously increased during the pdm-H1N1 IEP, and among all severe complicated influenza cases, 95.2% (99/104) were pdm-H1N1 severe complicated influenza cases. This phenomenon indicated a high attack rate and a high risk for developing severe complications from pdm-H1N1 influenza in a naïve community. 2) Although the proportion of pdm-H1N1 severe complicated influenza cases decreased from 95.2% (99/104) during pdm-H1N1 IEP to 45.6% (89/195) post pdm-H1N1 IEP, the other two serotypes, influenza B and AH3, led to 49 (25.1% (49/195)) and 60 (30.8% (60/195)) severe complicated influenza cases respectively, which made the rate of SCIC in the post-pandemic period 1.9 times higher than that during the pdm-H1N1 IEP; and 3) the pdm-H1N1 virus remained a threat to high risk groups with underlying diseases during the post pdm-H1N1 IEP, as data pointed to a trend of resurging numbers pdm-H1N1 severe complicated influenza cases from January to March 2011, which resulted in three additional fatal cases.

Symptoms, underlying diseases and risk factors of pdm-H1N1 severe complicated influenza mortality cases in Eastern Region of Taiwan: 1) Among the 188 pdm-H1N1 severe complicated influenza cases, 22.9% had underlying diseases. This general phenomenon of severe complicated influenza cases having underlying diseases was quite different from the 70% of hospitalized pdm-H1N1 severe complicated influenza cases having underlying disease as described in another study [8]. On the other hand, the statistic of 55.6% of the pdm-H1N1 severe complicated influenza cases that required intensive care having underlying diseases was similar to the previous report, indicating that the criteria for hospitalization in the general ward might be more relaxed in the Eastern Region of Taiwan. The top risk factors for severe complicated influenza cases were chronic lung disease (37%), a compromised immune system (17%) and heart diseases (17%) based on statistics from US CDC [7]. In our study, the top risk factors are metabolism diseases (18.5% (5/27)) and kidney diseases (18.5% (5/27)) for hospitalized cases requiring intensive care, and chronic lung diseases (5.0% (8/161)) and metabolism diseases (3.7% (6/161)) for cases hospitalized in general wards. The overall most frequently identified risk factors were metabolism diseases (5.9% (11/188)) and chronic lung diseases (4.8% (9/188)) among the 188 cases confirmed throughout the pre-, during-, and post-pdm-H1N1 IEP. 2) Obesity is a risk factor for modifying the lung mechanics, including increase in airway flow resistance and decrease in air exchange ability. Recent studies have demonstrated chronic airway inflammation in morbidly obese cases, and these factors affected the outcome of recovery from acute lung injury caused by infection with pdm-H1N1 influenza virus [12-13]. In addition, obesity significantly increased the risk of severe complications, severe infection and required intensive care [14]. Adiponectin, an anti-inflammatory adipokine, can partially explain the changed mechanism of inflammation and immune response in obese individuals who contracted the pdm-H1N1 influenza virus [15]. The concentration of adiponectin was lower in morbidly obese individuals than in the general population, which led to hyper immune response against pdm-H1N1 influenza virus infection and in turn resulted in cytokine storms and the septic shock syndrome [16]. In our study, the BMI of the three pdm-H1N1 severe complicated influenza mortality cases were all larger than 30. Although all cases were from the indigenous Beinan Tribe, we suggest that the risk factor leading to their death should be obesity; and 3) research indicates that pregnancy was one risk factor for having severe complications and for death from infection with the pdm-H1N1 influenza [18]. The concentration of adiponectin was also low in pregnant women [17], and thus pregnant women who contracted pdm-H1N1 influenza virus might have hyper immune response against pdm-H1N1 influenza infection, which would lead to cytokine storms and the septic shock syndrome [15]. Pregnant women showed increased risk in delivery complications, hospitalization, and death, especially in the first and second trimesters of pregnancy during the 2009 and 2010 pdm-H1N1 IEP [19]. Although mild to severe infections with pdm-H1N1 influenza might occur during all trimesters of pregnancy, most occurred in the last trimester. Based on an analysis of mortalities among pregnant women who contracted the pdm-H1N1 influenza virus [21], 7%, 27% and 64% occurred in the first, second and third trimester, respectively. The only one mortality among pregnancy woman in Eastern Region of Taiwan occurred on her third trimester. She suffered from the risk factors of both obesity and pregnancy. 4) Age: based on statistics from US CDC between April 2009 and April 2010, the age distribution of hospitalizations and mortalities from pdm-H1N1 influenza were highest among young adults aged 18-64, who accounted for 58.4% of hospitalizations and 76.74% of deaths [20]. In our study, the age distribution of hospitalizations from pdm-H1N1 influenza was highest in teenagers aged 0-17 (49.5% (93/188)) followed by young adults aged 18-64 (43.6% (82/188)), and it was lowest in elderly aged 65 years or above (6.9% (13/188). On the other hand, the age distribution of mortalities was highest among young adults aged 18-64 (90.9% (10/11)) from pdm-H1N1 influenza. This finding echoed the statistics of US CDC and demonstrated that age was a risk factor for mortality among pdm-H1N1 severe complicated influenza cases.

Chart review of mortality cases: 1) The number of severe influenza mortality cases were 3, 4 and 2 cases for year 2009, 2010 and 2011, in that order. All of the 9 mortality cases had underlying diseases with BMI between 19.8 and 31.3. The age distribution of these mortality cases was between 34 and 72 years of age. Only one of these cases contracted influenza AH3, and the remaining eight cases were pdm-H1N1 influenza positive. 2) All three severe influenza mortality cases occurred in 2009 with age distribution between 22 and 30. All these cases were from the indigenous Beinan Tribe without underlying diseases but were exposed to risk factors including obesity (BMI between 34.7 and 50.7) and pregnancy. One of these mortality cases was a pregnant woman in her third trimester (32 weeks) who refused to take Tamiflu because of concern over the side effect of Tamiflu on her fetus. The etiologic agents of these three cases were pdm-H1N1 influenza virus. 3) Only one 72 years old man of all the 12 severe complicated influenza mortality cases received influenza vaccination. 4) All mortality cases were exposed to risk factors for severe complications from influenza. 5) During the 2009 and 2010 influenza season, the mortality rate of Eastern Region of Taiwan was higher than the national average. In the 2009 influenza season, the mortality rate in Eastern Region of Taiwan was 10.5 per million (8.9 per million in Hualien County and 13.0 per million in Taitung County), which was 4.8 times the mortality rate of 2.2 per million across the whole country; whereas in the 2010 influenza season, the mortality rate in Eastern Region of Taiwan was 10.5 per million (17.8 per million in Hualien County and 0 per million in Taitung County), which was 1.9 times the mortality rate of 5.5 per million across the whole country.

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