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ORIGINAL ARTICLE

Control of an H1N1 outbreak in a correctional facility in central Taiwan

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Abstract *Background:* Controlling the outbreak of H1N1 in correctional facilities is difficult due to the inevitable close and prolonged contact between inmates. The current study reports an H1N1 outbreak in a correction facility and investigates the effectiveness of oseltamivir to control the spread of H1N1.
Methods: All 2690 inmates at the prison received medical service from a single hospital. A list of patients with a diagnosis of influenza was compiled based on medical diagnoses with respiratory symptoms during the outbreak period. The outbreak was then investigated using both chart review and questionnaires.
Results: In the 4-week outbreak period, 24.6% (663/2690) of inmates experienced influenza-associated symptoms, 50.5% (335/663) fulfilled the criteria for influenza-like illness (ILI) with fever, and the overall attack rate of ILI was 12.8%. Twelve inmates were admitted for complicated influenza, and three of them experienced respiratory failure. Oseltamivir was provided at the end of the 2nd week, and the effectiveness of oseltamivir in the 1004 inmates from seven major sections in the prison was analyzed. The ILI incidence rate reduced from 12.6 $\pm$ 4.1% between the 1st and 2nd weeks to 4.8 $\pm$ 2.4% between the 3rd and 4th weeks ($p = 0.018$) after the oseltamivir intervention. In the 878 uninfected inmates 47.0% (413/878) of inmates received prophylactic oseltamivir at the end of the 2nd week, the incidence of ILI was lower than those without prophylaxis (6.2% versus 2.4%; $p = 0.013$).

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Conclusion: H1N1 influenza spread rapidly in the correctional facility. The use of oseltamivir may be a practical intervention to control an H1N1 outbreak an enclosed environment such as this.

Introduction

Influenza A (H1N1) pdm09 virus, a novel swine-origin virus, caused pandemic influenza in 2009 and is still a major threat in close-contact settings.[1] Epidemiological studies of laboratory-confirmed cases of the 2009 pandemic influenza show that the clinical attack rate ranged from 5.4% to 20.6% for community outbreaks, a higher attack rate was found in close-contact settings, including military units, schools, nursing homes, and correctional facilities.[2–5] In the school setting the reported attack rate for H1N1 influenza outbreaks ranged from 35% to 60%; and close-contact and prolonged contact were undoubtedly the major risk factors.[6,7] Correctional facilities, which are characterized by inevitable close and prolonged contact between inmates, are extremely vulnerable to H1N1 influenza outbreaks. However, little is known about what practical measures can be applied to facilitate early control of an outbreak in a correctional facility.[8]

In Taiwan, 66,106 inmates were under correctional supervision in prisons, detention centers, and juvenile detention houses at the end of 2012, and up to 53.4% (35,329/66,106) of these inmates had begun their period of incarceration in 2012. However, the capacity of all correctional facilities in Taiwan was only 54,593, so the over-capacity rate reached 21.1% in 2012.[9] Therefore, these inmates were extremely vulnerable to an outbreak of communicable diseases because of the over-crowded living conditions and the limited health resources.

Early use of oseltamivir in H1N1-infected patients has been shown to reduce the viral load with earlier resolution of symptoms; postexposure prophylactic use of oseltamivir was also proved to decrease the household secondary attack rate from 26.1% to 0.6%.[10,11] However, the use of oseltamivir in controlling an outbreak in a close-contact setting, in particular, the coverage necessary to establish adequate herd immunity in an H1N1 outbreak remains unclear.[12,13] In the current study, the prolonged control of an H1N1 outbreak in a correctional facility is reported and an analysis of the efficacy of oseltamivir is presented.

Materials and methods

Setting

The correctional facility investigated in the present study is located in central Taiwan and is one of the major prisons in Taiwan with 2614 ± 130 per day (mean ± SD) male inmates in the past 5 years. There are 14 large sections with 150–160 inmates in each section. In Taiwan, all inmates have been enrolled in the National Health Insurance (NHI) program since January 01, 2013, and both inpatient and outpatient healthcare services in the prison are provided by a single hospital, Taichung Veterans General Hospital, Chia-Yi branch, a 600-bed teaching hospital. In detail, the study hospital provides daily medical outpatient services within the prison from Monday to Friday, and inmates with flu-like symptoms were assessed by doctors including two chest physicians and one infection specialist. Those who were admitted for complicated influenza were cared for by the same medical team. Thus, it was possible to enroll all cases involved in the H1N1 outbreak at the prison.

Case enrollment and definitions

This study was approved by the Institutional Review Board of Taichung Veterans General Hospital (SF13215). Outpatient visit diagnoses from February 25 to March 26, 2013 were reviewed and a list of patients with respiratory illness, defined using the International Classification of Diseases, 9th Revision, for upper and/or lower respiratory infection, influenza, fever, pneumonia, sore throat, pharyngitis, rhinorrhea, and cough, was compiled. Influenza-like illness (ILI) was defined as a fever (temperature of 100°F [37.8°C] or greater) as well as a cough and/or a sore throat in the absence of a known cause other than influenza, based on the definition described by Taiwan's Center for Disease Control (CDC). During the outbreak period, body temperature was routinely checked every day for all inmates, and all febrile cases were sent to the outpatient clinic for further evaluation. Therefore, all ILI cases during the outbreak were detected.

Complicated or severe influenza cases were also recorded during the outbreak period. Inmates with respiratory distress were transferred to the hospital by a prisoner escort officer, and were admitted if lung infiltration was found on the chest X-ray. All admitted inmates received standard medical care from a chest physician or an infectious disease specialist, and were all reported to the Taiwan CDC as complicated influenza. A nasopharyngeal swab was then collected and sent to the central laboratory of the Taiwan CDC for analysis by real-time reverse transcriptase-polymerase chain reaction (RT-PCR) to detect the swine-origin influenza A (H1N1) virus (A/swH1). Briefly, the WHO-recommended method included a panel of oligonucleotide primers and dual-labeled hydrolysis (Taqman) probes to be used in RT-PCR assays for the *in vitro* detection and characterization of the novel H1N1/2009 strain in respiratory specimens.[14]

Outbreak investigation

A questionnaire was administered to the 693 inmates enrolled in the study in order to analyze potential factors affecting the outbreak of H1N1. The content of the questionnaire was related to influenza-associated symptoms, comorbidities, and the use of oseltamivir. The questionnaire was administered by two trained nurses after consent was signed. Each questionnaire was taken within 20—25 minutes of explaining how to complete the survey to inmates, and any ambiguous responses were clarified by directly asking the participants. For the 30 inmates who had been released from the prison during the study period, medical charts were used instead. For the 12 complicated influenza patients, the influenza-associated data including demographic characteristics, serial chest X-rays, laboratory results, major comorbidities, complications, antibiotics, and results of RT-PCR for swine-origin influenza A (H1N1) virus (A/swH1) were recorded.

Statistics

Data were presented as frequencies (n) or percentages (%) for categorical factors and as means $\pm$ standard deviations for continuous factors. Differences between febrile and afebrile cases were evaluated using the Student t test. Multivariate logistical regression was used to identify risk factors associated with fever. Wilcoxon signed-rank test was used to test the difference before and after the use of the oseltamivir intervention. Chi-square test was conducted for efficacy of oseltamivir prophylaxis. Finally, survival function was utilized to plot cumulative frequency of the ILI cases. Statistical significance was set at $p < 0.05$, two-sided. All data were analyzed using SPSS version 16.0 (SPSS Inc., Chicago, IL, USA).

Results

Epidemiological description of the outbreak

From February 25 until March 1, 2013, an abrupt increase in the number of visits for respiratory illness was noted in the outpatient clinic in the investigated correctional facility. The reported H1N1 outbreak was confirmed by Taiwan CDC with the positive rapid influenza test conducted at the prison in the start of outbreak from eight random febrile inmates and the positive RT-PCR for A/swH1 from five inmates who were admitted for complicated influenza. Since all inmates received both inpatient and outpatient care by the study hospital, it was possible to confirm that there were no other febrile infectious diseases during the outbreak period. After the confirmation of an H1N1 influenza outbreak by Taiwan CDC, on March 5, the local public health bureau promptly provided free therapeutic oseltamivir (Tamiflu, Roche) 75 mg twice daily for 5 days for all symptomatic inmates. In addition, free prophylactic use of oseltamivir with oseltamivir 75 mg once daily for 10 days was also provided to inmates in all sections of the facility on March 11.

Influenza continued to spread for 4 weeks. Among 2690 inmates, a total of 663 experienced influenza-associated symptoms during the outbreak period, and 50.5% (335/663) fulfilled the definition of ILI with fever, with an overall ILI attack rate of 12.5%. In fact, the correctional facility worked in a quite different way from the healthcare facility. Acetaminophen (Scanol) was directly given, without medical prescription, to inmates who had influenza-like symptoms, by guard officers, and thus it is unsurprising that only 50.5% (335/663) of inmates with influenza-like symptom had fever. Nevertheless, these symptomatic inmates without fever are still part of the reported outbreak. Despite the therapeutic use of oseltamivir, the number of new cases remained high with 32.0 $\pm$ 7.3 new cases per day for ILI and 63.4 $\pm$ 16.5 new cases per day for respiratory illness in the first 2 weeks. The number of new cases dropped in the next 2 weeks with 5.7 $\pm$ 4.0 new cases per day for ILI and 11.9 $\pm$ 9.0 new cases per day for respiratory illness after the use of oseltamivir (Figure 1).

Characteristics of patients with influenza-associated symptoms

As shown in Table 1, ILI cases had more influenza-associated symptoms, including cough (91.9% versus 73.2%), rhinorrhea (69.3% versus 52.7%), and myalgia (72.8% versus 42.7%) compared to the afebrile patients. Previous studies identified age and obesity as poor prognostic factors in patients with H1N1 influenza for the development of complicated influenza, but these two factors did not appear to have an effect in this study since the mean age was 40.2 $\pm$ 9.9 and mean body-mass index was 23.6 $\pm$ 3.0.[15—17] However, this study found that the percentages of diabetes mellitus (9.0% versus 6.7%), asthma (9.0% versus 5.5%), and chronic obstructive pulmonary disease (5.7% versus 3.7%) appeared to be higher in ILI cases when compared with afebrile cases, though in the logistical regression analysis these correlations did not reach statistical significance. As expected there was an extremely high proportion of substance abuse in both febrile and afebrile inmates: 97.1% (644/663) were current smokers and 65.5% (434/663) had a history of illegal drug use. However, only 38.2% (253/663) of inmates accepted free therapeutic

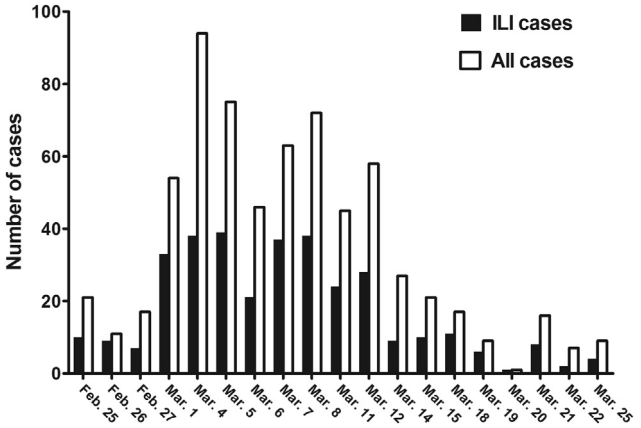

Figure 1. Epidemic curve of all cases with flu-like symptoms and cases that fulfilled the definition of influenza-like illness (ILI).

Table 1 Characteristics of patients presented with influenza symptoms with and without fever to a prison-based clinic.[a]

	Influenza-like illness[b]	Flu-like symptoms without fever	Total cases	*p*
	N = 335	*N* = 328	*N* = 663	
Symptom other than fever				
Cough	308 (91.9)	240 (73.2)	548 (82.7)	<0.01
Rhinorrhea	232 (69.3)	173 (52.7)	405 (61.1)	<0.01
Myalgia	244 (72.8)	140 (42.7)	384 (58.0)	<0.01
Medical co-morbidities				
Age (y)	39.8 ± 9.7	40.7 ± 10.1	40.2 ± 9.9	0.27
BMI	23.4 ± 2.9	23.7 ± 3.2	23.6 ± 3.0	0.25
Smoking				0.69
No smoking	9 (2.7)	10 (3.0)	19 (2.9)	
Smoking 0∼5 pieces per d	61 (18.2)	73 (22.3)	134 (20.2)	
Smoking 6∼10 pieces per d	249 (74.3)	229 (69.8)	478 (72.1)	
Smoking >10 pieces per d	16 (4.8)	16 (4.8)	32 (4.8)	
History of illegal drugs use	228 (68.1)	206 (62.8)	434 (65.5)	0.16
Hypertension	54 (16.1)	52 (15.9)	106 (16.0)	0.63
Diabetes mellitus	30 (9.0)	22 (6.7)	52 (7.8)	0.02
Asthma	30 (9.0)	18 (5.5)	48 (7.2)	<0.01
Chronic obstructive pulmonary disease	19 (5.7)	12 (3.7)	31 (4.7)	0.07
Hepatitis B virus carrier	37 (11.0)	26 (8.0)	63 (9.5)	0.26
Treatment				
Use of oseltamivir	165 (49.3)	88 (26.8)	253 (38.5)	<0.01
Interval from fever to oseltamivir (d)	4.2 ± 2.2	NA	NA	

BMI = body-mass index; NA = Not applicable.
[a] Data are presented as frequency (%) or mean ± standard deviation.
[b] Influenza-like illness, defined as fever (>38.0°C) with other respiratory symptoms.

oseltamivir and the average treatment delay was 4.2 ± 2.2 days (Table 1).

Complicated influenza cases

Twelve inmates were admitted for complicated influenza, defined by both influenza symptoms and lung infiltration on chest X-ray, their data are summarized in Table 2 and Figure 2. Nasal swabs were taken from all 12 cases for RT-PCR, and 41.7% (5/12) were positive for the H1N1 virus. The positive rate of RT-PCR was 80% (4/5) in inmates with complicated influenza admitted in the 1st week of the outbreak period; the 80% positive rate was similar to other reports using nasopharyngeal swabs for H1N1 RT-PCR.[18,19] The positive rate for RT-PCR was much lower after the 1st week (14.3%, 1/7) compared with high positive rate (80%, 4/5) in the 1st week. It is likely that the long interval between the immediate use of oseltamivir and sampling of nasal swabs may have led to the low positive rate of RT-PCR after the 1st week because oseltamivir was given immediately for all febrile inmates at emergency department after the awareness of the H1N1 outbreak.[20] The mean age was 44.3 ± 11.4 years, and the mean body mass index was 22.9 ± 2.3. There were a few underlying comorbidities including three patients with HIV (+) status and two patients with diabetes. All except two cases of complicated influenza were treated with oseltamivir and antibiotics. These two cases were both the earliest and most severe among the 12 cases. Case 1, a 65-year-old patient with well-controlled diabetes mellitus, was intubated on the 1st day of admission due to hypoxemia, and was extubated successfully on the 8th hospital day. Case 2, a 44-year-old patient without systemic disease, was intubated on the 1st day, and deteriorated rapidly with the development of septic shock and severe acute respiratory distress syndrome (Figure 2).

Efficacy of oseltamivir to reduce incidence of ILI

Low acceptance of oseltamivir was found in this study. Only 49.3% (165/335) of ILI cases received oseltamivir, whereas 26.8% (88/328) of inmates who experienced afebrile respiratory illness received oseltamivir. To find the general effectiveness of oseltamivir including the therapeutic effect and prophylactic effect, the ILI incidence of 1004 inmates in the seven major sections in which all inmates had quite similar living conditions was analyzed. The ILI incidence rate between Weeks 1–2 and Weeks 3–4 were compared among the 1004 inmates using the Wilcoxon signed-rank test, and found a reduction from 12.6 ± 4.1% to 4.8 ± 2.4% after the use of prophylactic oseltamivir, which was a statistically significant difference ($p = 0.018$) (Table 3). Furthermore, the cumulative ILI case proportion chart also showed a diminished rate of increase in ILI cases after the use of oseltamivir in these 1004 inmates (Figure 3). The study then moved to determine the effectiveness of prophylactic oseltamivir in these inmates. Of these 1004 inmates, 126 patients had ILI within the first 2 weeks. In the 878 uninfected inmates at the end of the 2nd week, 47.0% (413/878) of inmates received prophylactic oseltamivir.

Table 2 Characteristics of hospitalized patients during the outbreak of influenza.

Number	Date	WBC	CRP	Co-morbidities	Complication	Antimicrobial agents	Nasal swab[a]
		$10^3/\mu L$	mg/dL				
1	Mar 1	10,940	41.7		Respiratory failure[b]	Oseltamivir + Unasyn	Positive for A/swH1
2	Mar 3	14,790	16.9	DM	Respiratory failure[c]	Oseltamivir + Rocephin	Positive for A/swH1
3	Mar 6	10,420	0.1			Oseltamivir + Augmentin	
4	Mar 7	4630	4.3	HCV/HIV		Oseltamivir + Penicillin + Klaricid	Positive for A/swH1
5	Mar 7	10,360	14.5	HCV/HIV		Oseltamivir	Positive for A/swH1
6	Mar 11	30,080	27.5	Asthma	Respiratory failure[d]	Oseltamivir + Rocephin + Klaricid	
7	Mar 12	4500	1.3	HCV/HIV		Oseltamivir	
8	Mar 13	19,470	22.5	Hypertension		Oseltamivir	Positive for A/swH1
9	Mar 14	21,230	18.9	DM		Oseltamivir + Augmentin	
10	Mar 18	11,220	NA			Oseltamivir + Augmentin + Klaricid	
11	Mar 19	16,530	13.7			Oseltamivir + Augmentin + Klaricid	
12	Mar 19	7820	1.5			Oseltamivir + Augmentin	

CRP = C-reactive protein; DM = diabetes mellitus; HBV = Hepatitis B virus; HCV = Hepatitis C virus; HIV = human immunodeficiency virus; NA = not available; RT-PCR = real-time polymerase chain reaction; WBC = white blood counts.

[a] Nasal swab RT-PCR for A/swH1 (swine-origin influenza A (H1N1) virus).

[b] Case 1: Oxygenation failure postintubation on the 1st hospital day after successful weaning on the 8th hospital day.

[c] Case 2: Oxygenation failure postintubation on the 1st admission day complicated with acute respiratory distress syndrome after successful weaning on the 6th hospital day.

[d] Case 6: Ventilation failure ($PaCO_2$: 70 mmHg), recovered without intubation.

Importantly, other infection control measures, such as improvement of environmental sanitation and hand hygiene, were unrelated to the use of oseltamivir. Thus, the effectiveness of prophylactic oseltamivir can be determined by comparing the ILI incidence in the next 2 weeks between inmates with and without prophylactic oseltamivir. It was found that the incidence of ILI was statistically lower in inmates who received oseltamivir prophylaxis when compared with those without prophylaxis (6.2% versus 2.4%; $p = 0.013$) (Figure 4). Finally, only one inmate reported skin rash after taking oseltamivir, and thus the safety of oseltamivir appeared to be acceptable. Taken

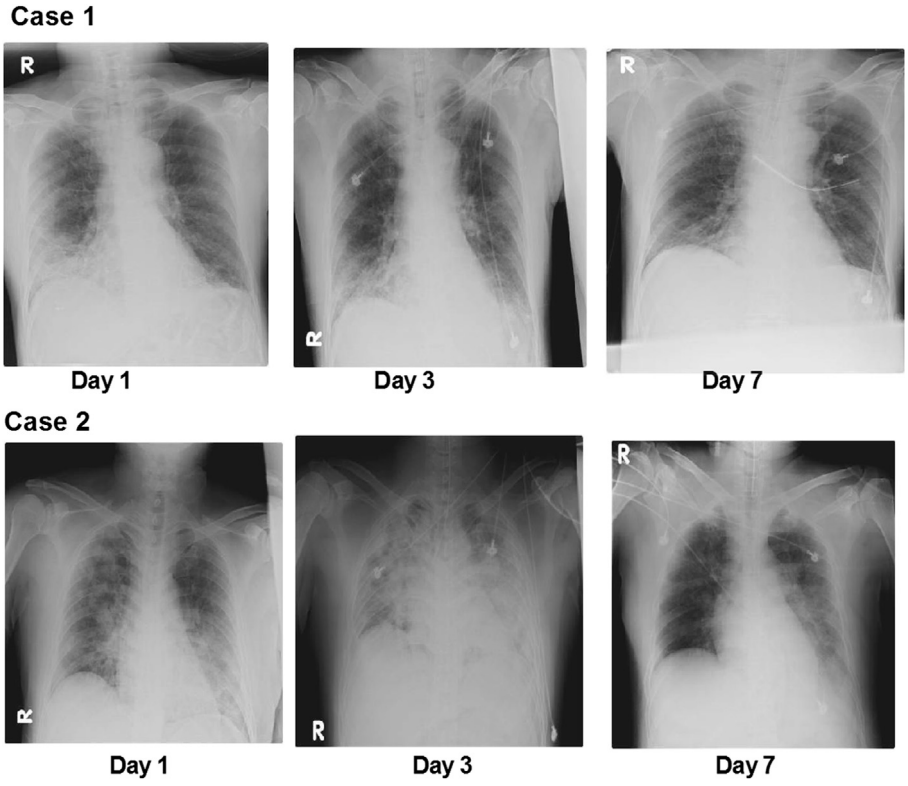

Figure 2. Serial chest-X rays of Case 1 and Case 2.

Table 3 The reduction of influenza-like illness incidence rate by preventive oseltamivir in 1004 individuals from seven sections.

	Preventive oseltamivir	Wk 1 ~ Wk 2		Wk 3 ~ Wk 4	
	coverage at wk 2	Not at risk	Incidence rate[a]	Not at risk	Incidence rate[a]
Section A	36.2% (55/152)	152	16.4% (25)	127	2.4% (3)
Section B	36.7% (62/169)	169	7.1% (12)	157	2.6% (4)
Section C	41.4% (70/169)	169	18.3% (31)	138	6.5% (9)
Section D	37.2% (51/137)	137	9.5% (13)	124	4.8% (6)
Section E	44.2% (72/163)	163	9.2% (15)	148	6.8% (10)
Section F	42.7% (67/157)	157	14.0% (22)	135	2.2% (3)
Section G	63.2% (36/57)	57	14.0% (8)	49	8.2% (4)
Average	41.1% (413/1004)		12.6%		4.8%*

* $p < 0.05$ determined using the Wilcoxon rank signed test.
[a] Data are presented as new influenza cases occurring within 2 weeks/cases at risk during the same period × 100%.

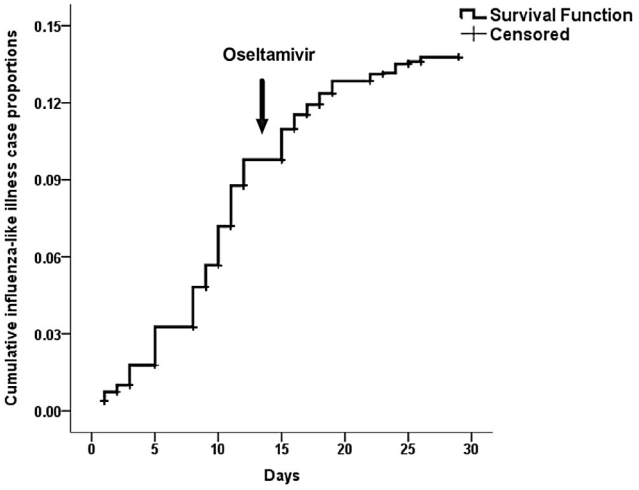

Figure 3. The change in slope of increased influenza-like illness cases after therapeutic and preventive oseltamivir in 1004 individuals from seven sections.

together, these results indicate that the use of therapeutic and prophylactic oseltamivir effectively reduced the ILI incidence rate.

Discussion

The H1N1 virus, which caused pandemic influenza in 2009, is still a threat in close-contact settings via aerosol transmission.[21] In this study, evidence of using oseltamivir to control an H1N1 outbreak in a prison by describing the magnitude of outbreak and analyzing the effectiveness of oseltamivir was provided. Study findings indicate that the use of oseltamivir, including therapeutic use and prophylactic use, reduced the ILI incidence rate.

Influenza spreads rapidly and extensively within populations living in a confined setting, which has a tremendous impact on the residents and disrupts daily activities.[22] A previous study of an influenza outbreak among Taiwanese military recruits showed a high attack rate of 57.7%.[3] A similarly high attack rate of 49.1% was reported in an H1N1 influenza outbreak on a Navy ship.[23] Inmates in correctional facilities, which tend to be over-crowded with prolonged close contact among inmates, are extremely vulnerable to outbreaks of H1N1 influenza. In the reported prison, the infection control measures only consisted of environmental disinfection, regular hand-washing with soap, and the use of oseltamivir. Other practical measures for H1N1 outbreak control, such as closing the facility or restricting common activities, are quite difficult to administer in correctional facilities[24,25]; therefore, early therapeutic antiviral treatment and chemoprophylaxis play a critical role in controlling an H1N1 outbreak in a correctional facility.

A long interval of up to 4.2 ± 2.2 days from the onset of fever to the use of oseltamivir was found in the present study. The delay of therapeutic oseltamivir largely reduced the beneficial effect of oseltamivir in the infected patients and lessened its capacity to break the transmission chain.[20] Although oseltamivir was provided freely, inmates only

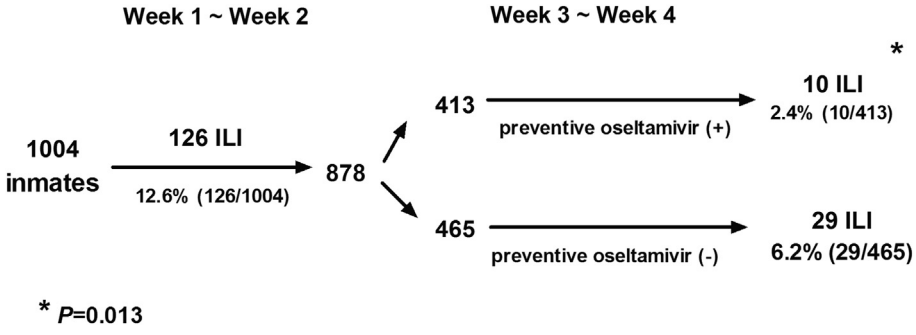

Figure 4. The efficacy of oseltamivir prophylaxis in reducing influenza-like illness (ILI) incidence in 878 uninfected inmates.

received the oseltamivir after they had attended a medical visit and had a prescription order. This system delay, not patient delay, pointed out the need of inter-departmental cooperation to ensure early control of an H1N1 outbreak in correctional facilities.[26] However, a sensitive and unresolved issue which exists globally is whether the ultimate responsibility for containing an influenza outbreak in a correctional facility lies with officials at the correctional facility, with public health officials, or with medical service providers.[27,28] Therefore, cross-department cooperation should be seen as the top priority in providing early treatment of symptomatic inmates in an outbreak of H1N1influenza.

In the present study, low acceptance of prophylactic oseltamivir was another problem in the H1N1 outbreak with only 41.1% (413/1004) of inmates in the seven major sections receiving prophylactic oseltamivir. In this study, the decision to take prophylactic oseltamivir was made by the inmates themselves immediately after a brief explanation given by a local public health official who was accompanied by a correctional facility official. Notably, both Case 1 and Case 2 were intubated immediately after they were sent to the hospital. The delayed detection of complicated influenza should be seen as a critical issue in dealing with an H1N1 influenza outbreak in prisons, but it is difficult for escort staff to identify complicated influenza cases early in the outbreak. Collectively, immediate cross-department coordination is urgently needed for early control of an H1N1 influenza outbreak in correctional facilities, which should include a comprehensive explanation of the need to use prophylactic oseltamivir, the timely use of therapeutic oseltamivir for febrile inmates, and the early detection of complicated influenza cases.

Herd protection to reduce the probability of transmission of communicable disease is not only important in influenza prevention by vaccination, but also plays a key role in the control of influenza outbreaks.[29] In this study, only 4.0% (104/2614) of inmates received the influenza vaccination in 2012, prophylactic oseltamivir was thus critical to establish herd immunity. Pedro Plans-Rubio[30] established a mathematical model to predict the herd immunity threshold for the 2009 pandemic H1N1 influenza, and found that the threshold and the prevalence of protected persons required to establish herd immunity depend on the effectiveness of prophylactic treatment, contact conditions in the setting, and the prevalence of persons already infected in the population. In this mathematical model with the high efficacy of prophylactic oseltamivir, 53—66% coverage was required to establish adequate herd immunity to interrupt the transmission chain of H1N1 influenza in correctional facilities where close contact among inmates is inevitable. In the current study, the overall protection coverage was 57.7%, comprising of vaccination in 4.0%, therapeutic approach for symptomatic inmates in 12.6 %, and prophylactic oseltamivir use in 41.1%.

This study has several limitations. First, this was a retrospective study in a in a real world setting without comparison, however, strong efforts were made to minimize recall bias. Second, the data of asymptomatic inmates were lacking, and inmates with minimal symptoms may not have been enrolled. However, it seems likely that all febrile cases were enrolled in this study due to the application of routine checks of body temperature twice a day during the outbreak period, the use of a single medical service provider, and full coverage by national health insurance among inmates. Third, not all symptomatic inmates received a rapid influenza test or nasal swab for RT-PCR in this real world setting.

In conclusion, by analyzing the data from the H1N1 outbreak in a prison this study provided the evidence that both early therapeutic and prophylactic oseltamivir are effective measures to control an influenza outbreak within a closed environment. In addition, good cross-department coordination is essential in controlling an H1N1 influenza outbreak in correctional facilities.

Conflicts of interest

The authors declare no conflicts of interest.

Acknowledgments

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