INCIDENCE AND CLINICAL MANIFESTATIONS OF INFLUENZA IN NURSE ASSISTANT STUDENTS

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Abstract. A prospective study was conducted to find the incidence and clinical manifestations of influenza in 201 nurse assistant students of Faculty of Tropical Medicine during June 1998 to May 1999. There were 106 episodes of influenza-like illness (incidence 52.7%) of which only 33% were proven to be influenza (incidence 17.4%). Main clinical manifestations of influenza included headache, fever, malaise, myalgia, rhinorrhea, cough, and sore throat. We found that influenza could not be diagnosed solely by using clinical manifestations. Respiratory pathogenic bacteria were rarely isolated in patients with influenza-like illness and this led to our suggestion that routine pharyngeal culture and antibiotic therapy would not be helpful. Influenza vaccination of every nurse assistant student would be beneficial.

INTRODUCTION

Influenza is a common disease worldwide. It is caused by influenza viruses that infect the human respiratory tract. It is highly contagious and sometimes can cause pandemics due to antigenic shift, especially in influenza type A virus. Typical influenza illness is characterized by abrupt onset of fever, myalgia, sore throat, and cough (Stuart-Harris and Schild, 1976). These manifestations generally are mild and self limited in healthy people but may be severe or cause complications especially in elderly patients or those who have underlying chronic pulmonary or cardiovascular disorders. However, even mild influenza have an impact on health status as well as economic loss due to restricted activity of patients (Sullivan *et al*, 1993).

Nurse assistant students are at low risk of developing severe manifestations or complications from influenza. However, there are three important aspects in this population. Firstly, they study in the same lecture room and this crowded environment facilitates spread of influenza among them. Secondly, they have a high chance to get infection from their patients. Finally, once they are infected, they have a high chance to spread influenza virus to patients they are taking care of. Unfortunately there are no data on incidence and clinical manifestations of influenza in this population. These data are essential for consideration of the necessity and cost-benefit of influenza vaccination. We therefore studied the incidence and clinical manifestations of influenza in this population.

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MATERIALS AND METHODS

This was a prospective study. All 201 nurse assistant students of the Faculty of Tropical Medicine, Mahidol University, were studied from June 1998 to May 1999. These students had never received influenza vaccination before this study. An influenza-like illness (ILI) was defined as a respiratory illness which consisted of : (1) at least one of the following systemic symptoms: fever, headache, malaise, or myalgia plus (2) at least one of the following respiratory symptoms: rhinorrhea, cough, sore throat or hoarseness. Every studied subject who had ILI was asked to see any of the three investigating physicians within the first three days of illness. History taking and physical examination were done. Pharyngeal secretions were obtained for influenza and routine bacterial culture. The patients were also asked to record the duration and maximum severity of ILI symptoms. Fever was rated as mild (≥ 37.5ºC but < 38.5ºC), moderate (≥ 38.5ºC but < 40ºC), and severe (≥ 40ºC). The maximum severity of other symptoms

was classified into three grades: mild, aware of symptoms but easily tolerate; moderate, discomforting enough to interfere with normal daily activity or necessitating the patients to take medicine to relief the symptoms; and severe, disabling or necessitating sick leave. Bacterial culture was done at the Department of Microbiology and Immunology, Faculty of Tropical Medicine. Influenza virus was isolated at National Institute of Health, Ministry of Public Health by inoculating the specimens in Madin Darby Canine Kidney cells. The presence of influenza virus in cell culture was confirmed by immunofluorescence test. Subtyping of the virus was done by hemagglutination inhibition test. The patients were diagnosed as influenza if influenza virus was present in pharyngeal secretion; otherwise they were diagnosed as non-influenza ILI.

The data were analyzed by using descriptive statistics. Comparison of the severity of symptoms between patients who had influenza and those who had non-influenza ILI was done by using chi-square test or Fisher exact test as appropriate. A non-parametric test (Wilcoxon) was used for comparison of duration of symptoms between the two groups. This study was approved by the Ethics Committee, Faculty of Tropical Medicine, Mahidol University.

RESULTS

Among the 201 subjects, there were 29 males (14.4%) and 172 females (85.6%). Their ages ranged from 18 to 24 years (median 19 years). One hundred and six episodes of ILI (incidence 52.7%) occurred during the one-year period of study. Influenza virus was detected from pharyngeal secretion in 35 episodes (33.0%) which included 33 episodes of influenza A and 4 episodes of influ-

Table 1
Symptoms of influenza and non-influenza ILI.

Symptoms	Influenza (n=35)				Non-influenza ILI (n=71)			
	Absence (%)	Mild[b] (%)	Moderate[b] (%)	Severe[b] (%)	Absence (%)	Mild[b] (%)	Moderate[b] (%)	Severe[b] (%)
Headache	8 (22.9)	10 (28.6)	17 (48.6)	0	18 (25.4)	17 (23.9)	34 (47.9)	2 (2.8)
Fever	10 (28.6)	9 (25.7)	15 (42.9)	1(2.9)	32 (45.1)	9 (12.7)	27 (38.0)	3 (4.2)
Malaise[a]	11 (31.4)	14 (40.0)	9 (25.7)	1(2.9)	40 (56.3)	12 (16.9)	18 (25.4)	1 (1.4)
Myalgia	11 (31.4)	12 (34.3)	11 (31.4)	1(2.9)	26 (36.6)	16 (22.5)	29 (40.8)	0
Rhinorrhea[a]	5 (14.3)	16 (45.7)	14 (40.0)	0	25 (35.2)	10 (14.1)	35 (49.3)	1 (1.4)
Cough[a]	12 (34.3)	15 (42.9)	8 (22.9)	0	28 (39.4)	14 (19.7)	28 (39.4)	1 (1.4)
Sore throat	10 (28.6)	9 (25.7)	16 (45.7)	0	13 (18.3)	17 (23.9)	40 (56.3)	1 (1.4)
Hoarseness	23 (65.7)	7 (20.0)	5 (14.3)	0	46 (64.8)	15 (21.1)	10 (14.1)	0
Nausea, vomiting	27 (77.1)	6 (17.1)	2 (5.7)	0	65 (91.5)	2 (2.8)	4 (5.6)	0
Diarrhea	33 (94.3)	1 (2.9)	1 (2.9)	0	66 (93.0)	2 (2.8)	3 (4.2)	0
Abdominal pain	34 (97.1)	1 (2.9)	0	0	69 (97.2)	1 (1.4)	1 (1.4)	0
Dizziness	30 (85.7)	3 (8.6)	1 (2.9)	1(2.9)	64 (90.1)	2 (2.8)	5 (7.0)	0

[a]Statistically significant ($p < 0.05$)
[b]Maximum severity of the symptom

Table 2
Physical findings of influenza and non-influenza ILI.

Physical findings	Influenza (n = 35)		Non-influenza ILI (n = 71)	
	Absence (%)	Presence (%)	Absence (%)	Presence (%)
Inflamed nasal mucosa	19(54.3)	16(45.7)	42(59.2)	29(40.8)
Injected pharynx or tonsils	6(17.1)	29(82.9)	23(32.4)	48(67.6)
Pulmonary rhonchi	34(97.1)	1(2.9)	70(98.6)	1(1.4)

Table 3
Duration of symptoms (days) and number of patients (n) who had symptoms in influenza and non-influenza ILI.

Symptoms	Influenza (n = 35)			Non-influenza ILI (n = 71)		
	n	Range	Mode	n	Range	Mode
Headache	27	1-7	3	53	2-9	3
Fever	25	1-8	3	39	2-9	3
Malaise	24	1-9	3	31	1-9	3
Myalgia	24	1-7	3	45	1-9	3
Rhinorrhea	30	2-17	3	46	1-14	7
Cough	23	1-14	3	43	1-14	3
Sorethroat	25	2-9	5	58	1-9	3
Hoarseness	12	2-9	5	25	2-9	2
Nausea, vomiting	8	2-4	2	6	1-9	1
Diarrhea	2	2-5	2,5	5	1-3	1
Abdominal pain	1	2	2	2	2-3	2,3
Dizziness	5	2-5	2	7	2-5	2

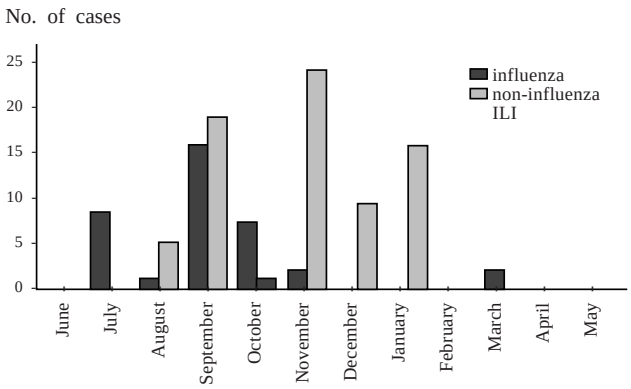

Fig 1–Number of cases by months of influenza and non-influenza ILI.

enza B. Co-infection of influenza A and B occurred in 2 episodes. Respiratory bacterial pathogens were found in only four episodes (3.8%) consisting of two episodes of *Klebsiella pneumoniae* and one episode each of *Enterobacter agglomerans* and *Streptococcus* group A. The incidence of influenza in nurse assistant students was 17.4% per year. Its peak incidence occurred in July through October while peak incidence of non-influenza ILI occurred in September through January (Fig 1).

Tables 1 and 2 show clinical manifestations of influenza compared to ILI due to other causes. Most of the symptoms were mild to moderate in severity. Most of these clinical manifestations were not significantly different in term of occurrence and maximum severity between both groups of the patients except malaise and rhinorrhea that occurred significantly more frequently in influenza and cough that tended to be more severe in non-influenza ILI.

Once the symptoms occurred, most of them subsided within three days and nearly all of them recovered within one week except cough and rhinorrhea that might last for two weeks. The duration of symptoms in influenza did not significantly differ from those in non-influenza ILI (Table 3).

DISCUSSION

We found that the incidence of influenza is surprisingly much higher than previous reports. In Thailand in 1996, the overall reported incidence of influenza was only 75.31 per 100,000 population while the highest incidence in one province was 486.65 per 100,000 population. (Ministry of Public Health, 1996). This high incidence in nurse assistant students was unlikely to be caused by influenza epidemics because there was no report of epidemics during the period of study. Furthermore, the influenza A viruses that we could isolate were Flu A/Sydney/05/97 H3N2 and FluA/Beijing/262/95 (H1N1). These influenza A subtypes had the same hemagglutinin (H) and neuraminidase (N) antigen as influenza A subtypes isolated in the previous years. In general, antigenic

drift of influenza A virus does not cause serious epidemics of the disease. The low incidence of influenza reported by the Ministry of Public Health may be because most health workers were not aware of influenza and most patients who suffered from influenza were vaguely diagnosed as upper respiratory tract infection. Another reason is that nurse assistant students studied in a crowded lecture room and thus facilitated transmission of influenza virus. This would result in a higher incidence of influenza among nurse assistant students than in the general population.

The clinical manifestations of influenza in nurse assistant students were the same as previous reports (Stuart-Harris and Schild, 1976; Sullivan *et al*, 1993). The relatively mild symptoms in our patients might be because the influenza A subtypes that infected our patients did not have significant antigenic difference from the previous year and thus our patients might have had partially cross protective immunity from previous minor, antigenically different, influenza virus infection. However, we did not prove this possibility. Other explanation is that all of our patients were healthy young adults who were at low risk of developing severe symptoms from influenza.

We found that influenza cannot be precisely differentiated from non-influenza ILI by using only clinical manifestations. This supports previous knowledge (Seppala *et al*, 1993; White and Fenner, 1994). By extrapolation of our study, we can predict that 33% of patients who come with clinical manifestations of ILI have influenza (95% confidence interval = 24-42%). However, this figure may differ from population to population and from time to time according to risks of exposure to influenza viruses and seasonal variation of the disease.

One interesting finding is that the incidence of bacterial infection in ILI was very low. This evidence suggests that antibiotic treatment as well as routine pharyngeal culture is not helpful in most of previously healthy patients who have ILI. While overuse of antibiotics in acute respiratory tract infection has been one of the important health problems in Thailand (Sunakorn *et al*, 1995), our finding will give a confidence to physicians to withhold prescribing antibiotics for previously healthy patients who have ILI without other definite evidence of bacterial infection.

Nurse assistant students should be vaccinated against influenza because they can transmit this illness to persons at high risk of having complication or severe manifestations from influenza. This agrees the Advisory Committee on Immunization Practice (ACIP) recommendation (1997). For other healthy adults, although influenza vaccination was found to be beneficail (Nichol *et al*, 1995), the recommendation for vaccination in this population is still controversial. In general, the recommendation on vaccination depends on its cost-benefit which varies with the cost and effectiveness of the vaccine as well as the incidence and severity of the disease. It is accepted that influenza vaccine is effective in preventing influenza if the infecting influenza virus is the same subtype as that contained in the vaccine (ACIP, 1997). In respect to the disease incidence and severity, although influenza viruses do not cause severe illness in healthy people, influenza vaccination is still beneficial if its incidence is high. If it is proven that the incidence of influenza is also high in other populations at risk, such as students or adults working in a crowded environment, influenza vaccination should be considered. Further studies should be done in other populations before deciding to give the vaccine. In addition, in considering the cost-benefit of influenza vaccination,we should be aware that the vaccination may not be cost-effective if there is antigenic drift or antigenic shift of influenza virus (Weingarten *et al*, 1988).

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