ORIGINAL ARTICLE

Outbreak of Influenza Amongst Residential School Students in Malaysia

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Summary

In the months of July and August 2003, an outbreak of acute respiratory illness caused by influenza A virus occurred among students in seven residential schools situated in the northern part (Perak) of Peninsular Malaysia. Out of 4989 students, aged 13 to 18 years (mean = 15.9), 1419 (28%) were effected by influenza-like illness. All patients were treated as outpatients except for 36 students who required admission for high fever, severe coughing and shortness of breath. Abnormal chest X-ray findings were noted for those that required inpatient management.

Influenza A virus was isolated from 37 sputum specimens, 20 throat swabs and three nasal swab specimens from a total of 278 clinical samples obtained from 180 patients. Isolates from each of the outbreaks were sent to WHO Collaborating Centre for Reference and Research on Influenza, Melbourne, Australia for antigenic and genetic analysis. One school outbreak was due to influenza A (H1N1), A/New Caledonia/20/99-like virus while the other six school outbreaks were due to influenza A (H3N2) viruses which were A/Fujian/411/2002-like).

Key Words: Influenza A, Outbreak, Malaysia

Introduction

Influenza is a highly contagious, acute viral respiratory illness. Influenza viruses belong to the *Orthomyxoviridae* family and are classified as types A, B, and C based on the antigenic characteristics of their internal (nucleocapsid and matrix) proteins. Influenza type A viruses are further divided into a number of subtypes based on their haemagglutinin (HA) and neuraminidase (NA) surface antigens[1,2]. To date, 16 HA subtypes and nine NA subtypes have been identified. The hallmark of human influenza viruses is their ability to undergo antigenic changes that are responsible for epidemics of respiratory illness that occur almost every winter in temperate climates and which are often associated with increased rates of hospitalization and death[3,4]. Although influenza epidemics also occur in subtropical and tropical regions, disease patterns have been less well established[5]. Here, we report an outbreak of acute respiratory illness caused by influenza A virus among students in a number of residential schools in the northern part (Perak) of Peninsular Malaysia in the months of July and August, 2003.

The presence of acute onset of high fever (axillary temperature > 38°C) associated with dry cough and nasal congestion, with or without other symptoms (such as sore-throat, myalgia, headache) was used as the case definition for influenza like illness (ILI) in this outbreak investigation. During the ten-week period, seven residential schools in various parts of Perak were

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almost concurrently affected. Out of 4989 students aged 13 to 18 years (mean = 15.9), 1419 (28%) were affected by influenza-like illness. The total number of students and the respective proportion of students affected in each school are shown in Table I. Sekolah STAR Ipoh was the first school to be affected with the index case having onset of illness on 18th of July 2003. The index case in each respective school/institution is shown in Table I. The index cases of Sekolah STAR (Ipoh), Sekolah MRSM (Grik), Sekolah MRSM (Lenggong), and Sekolah Agama Al-Mizan (Telok Intan) apparently acquired the infection from their respective family members suffering similar illness (Table I). As all of the affected institutions were residential schools, an institutional quarantine was imposed for a period until a week after the last case, to limit the spread of illness in the community. All students were given symptomatic and supportive outpatient treatment except for 36 students who required hospitalized inpatient treatment for high fever, severe coughing and shortness of breath. Abnormal chest X-ray findings were noted for those who required inpatient management. No deaths occurred due to the illness or its accompanying complications.

A total of 278 clinical samples, consisting of 76 sputum specimens, 120 throat swabs, 35 nasal swabs and 47 blood specimens, were obtained from 180 patients with acute respiratory illness. Influenza A virus was isolated from 37 sputum specimens, 20 throat swabs and three nasal swab specimens. The identity of influenza A virus isolates were confirmed by indirect immunofluorescence assay using commercial respiratory virus typing monoclonal antibodies (Chemicon, USA) following virus isolation in MDCK cells. The preliminary subtyping of the influenza A viruses isolated in these outbreaks was performed by haemagglutination inhibition test using the WHO 2003 Influenza Reagent Kit which had reference anti-sera raised against the subtypes of influenza A viruses circulating at the time. Some viruses reacted to a lower titre with the A(H3N2) antisera suggesting they could be variants from the circulating A(H3) viruses. Virus isolates from each of the schools were further analysed by the WHO Collaborating Centre for Reference and Research on Influenza, Melbourne, Australia. Two of the isolates were identified as influenza A (H1N1) A/New Caledonia/20/99-like and the remainder were subtyped as A/Fujian/411/2002-like A(H3N2) viruses (Table I). Representative haemagglutination-inhibition (HI) test results are shown in Tables IIa and IIb. A(H1N1) viruses from the outbreaks reacted well with reference antisera indicating they were antigenically quite similar to previously circulating H1 viruses (Table IIa). The A(H3N2) viruses were mostly well inhibited with the panel of reference antisera however isolates from three of the schools did show reduced titres with A/Fujian-like antisera which might indicate some drift from the reference virus (Table IIb). The genetic analysis (based on sequence of the HA1 domain) of the outbreak strains of A(H1N1) and A(H3N2) viruses were also examined (Figures 1a and 1b). The two H1 isolates obtained from Int. Latihan Perindustrian school at Jelapang (A/Malaysia/1003/2003 and A/Malaysia/1004/2003) grouped phylogenetically with other A(H1) viruses obtained from Malaysia in 2003 and most closely to the reference virus A/Fujian/156/2000 (Figure 1a). The A(H3) isolates were phylogenetically similar to other Malaysian 2003 isolates and to A/Fujian/411/2002 although each school formed its own sub-branch (Figure 1b).

This report describes an outbreak of severe acute respiratory illness due to influenza A virus that occurred in a tropical country and led to the disruption of teaching at several schools over a ten-week period. In the past, the disease burden of influenza in sub-tropical and tropical countries has not been as well established as in temperate countries[5-8]. This lack of information on the disease burden of influenza in tropical countries has mainly been due to the less pronounced seasonality of influenza in tropical countries and the limited number of studies and laboratory-based respiratory disease surveillance that has been undertaken. However, several recent studies have now shown that the incidence of influenza in tropical and subtropical countries is significant, with increased incidence in the wet or cooler seasons, leading to extensive morbidity including hospitalization and in some cases death[5,9-12]. It is therefore important for all countries in tropical and subtropical regions to conduct systematic epidemiological studies on the morbidity and mortality as well as the socioeconomic burden due to influenza. The information derived from these studies will be critical to the future development and implementation of influenza vaccination policy and the use of anti-virals in the control of influenza epidemics[13].

Table I: The epidemiological features of influenza outbreak among students in seven schools in Perak, northern part of peninsular Malaysia

OB #	Name of school/institution	Number of students	Number (%) with ILI	Number of students hospitalised	Onset of illness in the index case	History of contact	Virus isolated
1	Sek. STAR, Ipoh	760	295 (39)	6	18/7/2003	Yes	A(H3)
2	Sek. Agama Al-Mizan, K. Kangsar	437	144 (33)	16	28/7/2003	Yes	A(H3)
3	Int. Latihan Perindustrian, Jelapang	780	101 (13)	-	6/8/2003	Unknown	A(H1)
4	Sek. MRSM, Lenggong	910	351 (39)	1	11/8/2003	Yes	A(H3)
5	Sek. Men. Sains, Teluk Intan	694	93 (13)	-	15/8/2003	Unknown	A(H3)
6	Sek. MRSM, Grik	712	361 (51)	12	16/8/2003	Yes	A(H3)
7	Sek. Men. Teknik, Grik	696	74 (11)	1	25/8/2003	Unknown	A(H3)
	Total	4989	1419 (28)	36			

Table IIa

REFERENCE ANTIGENS	OB #	Ferret antisera BAY/7	BEIJ/262	NC/20	AUCK/65	FUJI/156	ENG/51	Specimen date
A/BAYERN/7/99		**>2560**	<20	<20	<20	<20	<20	
A/BEIJING/262/95		<20	**640**	320	160	320	160	
A/NEW CALEDONIA/20/99		<20	80	**640**	320	640	160	
A/AUCKLAND/65/2000		<20	80	320	**320**	640	160	
A/FUJIAN/156/2000		<20	80	640	320	**640**	160	
A/ENGLAND/51/2002		<20	160	320	160	320	**320**	
TEST ANTIGENS								
A/MALAYSIA/1003/2003	3	<20	320	640	640	640	320	21.8.03
A/MALAYSIA/1004/2003	3	<20	320	640	320	640	160	21.8.03

Table IIb

REFERENCE ANTIGENS	OB #	Ferret antisera MOS/10	PAN/2007	FUJ/411	WYOM/3	AUCK/6	Specimen date
A/MOSCOW/10/99		**1280**	1280	160	320	320	
A/PANAMA/2007/99		<40	**640**	<40	<40	<20	
A/FUJIAN/411/2002		160	640	**>5120**	>5120	>2560	
A/WYOMING/3/2003		80	320	2560	**>5120**	1280	
A/AUCKLAND/6/2003		<40	<40	640	640	**640**	
TEST ANTIGENS							
A/MALAYSIA/1001/2003	2	80	<40	640	640	320	17.8.03
A/MALAYSIA/1002/2003	2	160	160	1280	2560	640	17.8.03
A/MALAYSIA/1009/2003	6	320	1280	>5120	>5120	640	26.8.03
A/MALAYSIA/1010/2003	6	160	640	>5120	>5120	1280	26.8.03
A/MALAYSIA/1011/2003	1	80	80	1280	1280	1280	13.8.03
A/MALAYSIA/1012/2003	1	80	160	2560	2560	2560	13.8.03
A/MALAYSIA/1013/2003	4	80	160	2560	2560	1280	22.8.03
A/MALAYSIA/1014/2003	4	80	80	2560	1280	1280	22.8.03
A/MALAYSIA/1015/2003	5	160	160	1280	1280	1280	25.8.03
A/MALAYSIA/1016/2003	5	80	80	640	640	640	25.8.03
A/MALAYSIA/1017/2003	7	80	40	320	320	160	22.9.03
A/MALAYSIA/1018/2003	7	80	80	320	320	320	22.9.03

Figure 1a
H1 (HA1)

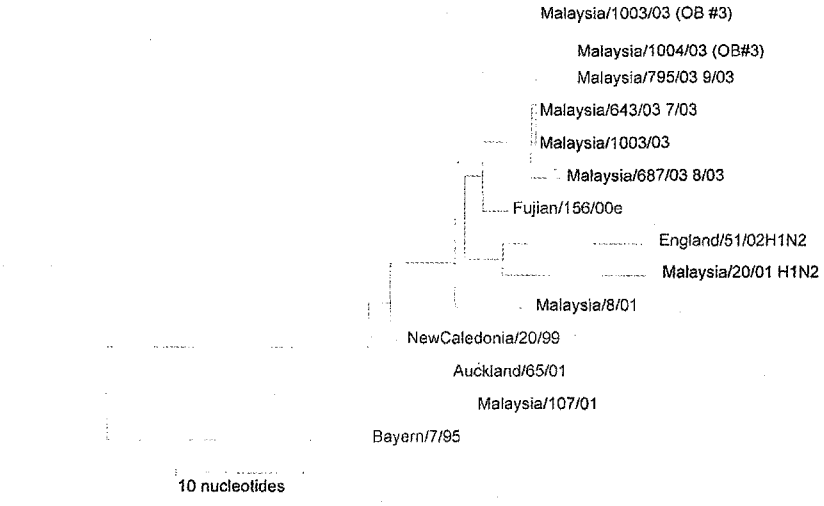

Figure 1b.
H3 (HA1)

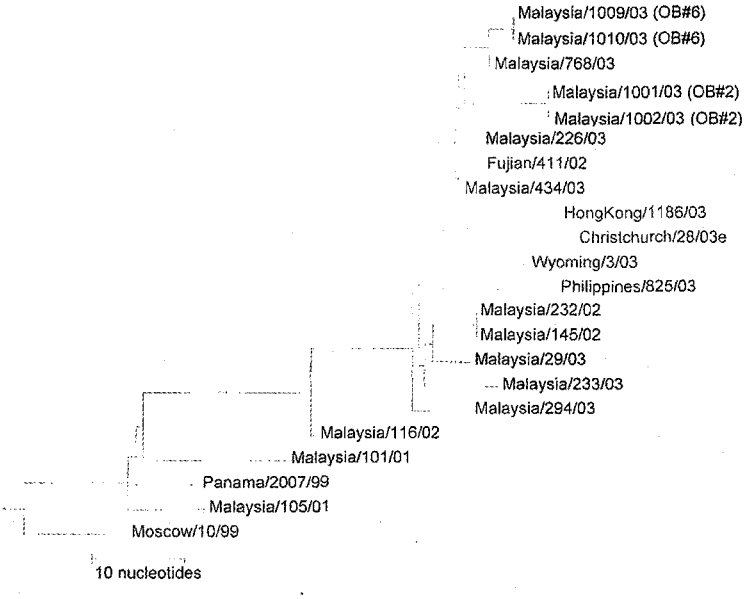

Fig. 1: Dendrograms of the HA1 domain of the H1 genes (1a) and the H3 genes (1b) from viruses isolated from the school outbreaks as well as other Malaysian and reference viruses. The outbreak from which the virus was obtained is indicated in the brackets at the end of the virus designation (eg OB #3, see Table I for details). Nucleotide sequences were analysed with PHYLIP using the maximum likelihood algorithm and drawn with Treeview. The horizontal bar indicates the percentage difference of the sequences based on nucleotides

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References

1. WHO Memorandum. A revised system of nomenclature for influenza viruses. Bull WHO 1980; 58: 585-91.
2. Murphy BR and Webster RG. Orthomyxoviruses. In: Fields BN, Knipe DM, Howley PM, etc. Fields Virology. 3rd edition. Philadelphia. Lippincott-Raven 1996; 1397-445.
3. Simonsen L. The global impact of influenza on morbidity and mortality. Vaccine 1999; 17: S3-S10.
4. Daly JM, Wood JM, Robertson JS. Co-circulation and divergence of human influenza viruses. In: Nicholson KG, Webster RG, Hay AJ, editors. Textbook of influenza. Oxford. Blackwell Science 1998; 168-77.
5. Shek LPC, Lee BW. Epidemiology and seaonality of respiratory tract virus infections in the tropics. Paediatr. Respir. Rev. 2003; 4: 105-11.
6. Menec VH, Black C, MacWilliam L and Aoki FY. The impact of influenza-associated respiratory illness on hospitalizations, physician visits, emergency room visits, and mortality. Can J Public Health 2003; 94: 59-63.
7. Chiu SS, Lau YL, Chan KH, Wong WH and Peiris JS. Influenza-related hospitalizations among children in Hong Kong. N Engl J Med 2002; 347: 2097-103.
8. Ng TP, Pwee KH, Niti M and Goh LG. Influenza in Singapore: assessing the burden of illness in the community. Ann Acad Med Singapore 2002; 31: 182-8.
9. Wong CM, Chan KP, Hedley AJ, Peiris JS. Influenza-associated mortality in Hong Kong. Clin. Infect. Dis 2004; 39: 1611-7.
10. Beckett CG, Kosasih H, Ma'roef C, Listiyaningsih E, Elyazar IRF, Wuryadi S, Yuwono D, McArdle JL, Corwin AL, Porter KR. Influenza surveillance in Indonesia: 1999-2003. Clin. Infect. Dis. 2004; 39; 443-49.
11. Simmerman JM, Thawatsupha P, Kingnate D, Fukuda F, Chasing A, Dowell SF. Influenza in Thailand: a case study for middle income countries. Vaccine 2004; 25: 182-7.
12. Berlioz-Arthaud A, Barr IG. Laboratory-based influenza surveillance in New Caledonia, 1999-2003. Trans R Soc Trop Med Hyg. 2005; 99: 290-300.
13. Szucs T. The socio-economic burden of influenza. J Antimicrob Chemother 1999; 44: 11-15.