WEEKLY EPIDEMIOLOGICAL REPORT

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Clinical features of novel influenza A(H1N1): A preliminary analysis

The influenza pandemic 2009 is caused by a new strain of influenza virus that was clinically identified in April 2009. The new influenza virus strain is Novel influenza A (H1N1) virus. Mexico and America were the first countries to be affected with increasing numbers of cases being detected each day. On April 13, the first death attributable to novel influenza occurred in Oaxaca and the patient was found to be a diabetic woman who had suffered respiratory complications due to the influenza virus. Since it was a new strain of virus to which humans have not developed immunity, it was anticipated that a large number of people would be affected. The impact of the pandemic was to be determined by the virulence of the strain and the characteristics of the affected individuals. As this outbreak was new the characterization of the clinical course of the disease, its epidemiology and if they differ from that of the seasonal influenza had to be defined on data collected from case summaries from affected countries. Amidst these key uncertainties , concerns were increasing throughout the world and subsequently based on establishment of efficient sustained human to human transmission at the community and institutional levels in countries beyond WHO's Americas regions, pandemic was declared by raising the pandemic phasing to level 6 by the WHO.

Based on analysis of case summaries, a preliminary characterization of the clinical features of those who were diagnosed as having novel influenza A (H1N1) has been completed. The disease seems to manifest with many clinical features and the spectrum ranges from non febrile, mild upper respiratory tract illness to severe and fatal pneumonia. Most cases appear to have been uncomplicated, typical influenza like illness and recovered spontaneously. The most commonly reported symptoms include cough, fever, sore throat, malaise and headache. Fever has been absent in some outpatients and up to one in six surviving hospital patients. Some confirmed cases too did not have fever. It is likely that there are asymptomatic and very mild cases of infection as occurs with seasonal epidemics of influenza. A distinguished feature of this outbreak is observed gastrointestinal symptoms (nausea, vomiting and/or diarrhoea).These symptoms have occurred in up to 38% of outpatients in the United States. Some, but not all, countries reported cases that had diarrhoea. This initial finding requires further confirmation, and studies to determine if virus is shed in the faeces. If this is found, it could have significance for countries or situations in which there is inadequate sanitation.

Most cases of new influenza A (H1N1) infection seem to be mild and self-limited and do not require admission to hospital. However, severe illness and deaths have been reported in a small proportion of cases. In seasonal influenza, the overwhelming majority of severe morbidity and mortality occurs in persons of 65 years of age or more. However, with new influenza A (H1N1), a substantial proportion of the cases of severe illness and deaths have occurred among young and previously healthy adults. In addition, severe illness and deaths have also been reported in adults with underlying medical conditions including chronic lung or cardiovascular disease, diabetes, immuno-deficiencies and obesity. Moreover, pregnant women may be at increased risk of complications from new influenza A (H1N1). Severe illness has been reported in Mexico and the United States, in persons who were at risk for complications of seasonal influenza, such as the very young, women who were pregnant and persons with underlying medical conditions, as well as in healthy young adults.

It has been established that the virus is transmitted sufficiently easily from person-to-person to sustain institutional and community outbreaks and to spread regionally. In the United States and Mexico, community transmission has been widespread. Based on limited data, the secondary attack rate is estimated to be about 22%, but could be as high as 30% in some settings. As far as affected age groups are concerned, all age groups have been affected. However, most cases occur in younger age groups with a median age in the mid-20. Among 45 fatal cases in Mexico, 54% were among previously healthy people most of whom were aged 20–59 years.

Contents — **Page**

1.Leading Article - Clinical features of novel influenza A(h1n1) : A preliminary analysis	*1*
2. Surveillance of vaccine preventable diseases & AFP (10th May - 16th May 2009)	*3*
3. Summary of newly introduced notifiable diseases (10th May - 16th May 2009)	*3*
4. Laboratory surveillance of dengue fever (10th May - 16th May 2009)	*3*
5. Summary of selected notifiable diseases reported (10th May - 16th May 2009)	*4*

One was a pregnant woman at 34 weeks' of gestation. Case fatality ratios were lower in children and teenagers than in adults, for reasons still to be determined.

Approximately 2–5% of confirmed cases in the United States and Canada, as well as 6% in Mexico, had been admitted to hospitals. Among patients presenting with acute respiratory illness for care in Mexico, 13% were tested positive for new influenza A (H1N1) virus infection (about one-fifth have had seasonal influenza), of whom about 10% had been hospitalized and one-third of those hospitalized required mechanical ventilation. Mexico experienced a large number of persons over a short period of time seeking care and hospitalization for respiratory disease. However, health care systems of other affected countries had not experienced similar incidents to date. The principal reason for hospitalization of cases in Mexico and the United States was severe respiratory disease. In the Mexican experience, secondary bacterial pneumonia had occurred among hospitalized cases.

Almost one-half of the patients hospitalized in the United States, and 21 of 45 (46%) fatal cases in Mexico for whom data are available, have had underlying conditions, including pregnancy, asthma, other lung diseases, diabetes, morbid obesity, autoimmune disorders and associated immunosuppressive therapies, neurological disorders and cardiovascular disease. Among 20 pregnant women in the United States confirmed to have been infected with new influenza A (H1N1) virus, 3 required hospitalizations, 1 of whom died; this patient had started antiviral therapy 13 days after the onset of illness. Among 30 patients hospitalized in California, 64% had underlying conditions and 2 of 5 pregnant women developed complications, including spontaneous abortion and premature rupture of membranes. Diarrhoea has been uncommon in hospitalized cases.

Of those hospitalized in California, 15 of 25 (60%) tested had radiographic changes suggestive of pneumonia, including 10 with multi lobar infiltrates; 4 (13%) required mechanical ventilation. Both leukocytosis and leucopenia have been found in those hospitalized. In Mexico, many hospitalized patients had manifested lymphopenia, elevated aminotransferases, elevated lactate dehydrogenase (100% of 16 fatal cases) and, in some, very high levels of creatinine phosphokinase. Up to one-half of hospitalized patients had shown some degree of renal insufficiency, perhaps secondary to rhabdomyolysis and myoglobinuria, although other causes including hypotension, dehydration and hypoxia may be contributory. Acute myocarditis had been suspected in some patients, but encephalitis has not been described to date.

Rapidly progressive respiratory disease has accounted for most severe or fatal cases. In Mexico, the median time from onset of illness to hospitalization was 6 days (range, 1–20 days) in 45 fatal cases, compared with a median of 4 days in hospitalized cases in the United States. In fatal cases, the presenting manifestations have included fever, shortness of breath, myalgia, severe malaise, tachycardia, tachypnoea, low oxygen saturation and, sometimes, hypotension and cyanosis. Several patients experienced cardiopulmonary arrest shortly after arrival at hospital.

In Mexico, the clinical course has been notable for severe pneumonia, multifocal infiltrates including nodular alveolar and, less frequently, basilar opacities on chest radiographs, as well as rapid progression to acute respiratory distress syndrome (ARDS) and renal or multi-organ failure (24% of fatal cases). The median time from symptom onset to death was 10 days (range, 2–33 days).

At present, the virus is susceptible to oseltamivir (Tamiflu) and zanamivir (Relenza). In laboratory studies, there is no evidence so far that the virus has markers for human virulence that have been described for the 1918 H1N1 pandemic virus and avian influenza H5N1.

Few patients have had evidence of bacterial infection upon admission, but instances of empyema, necrotizing pneumonia and bacterial co-infection, as well as ventilator-associated pneumonias, had occurred. Some cases had received antibiotic treatment before hospitalization. In Mexico, bacterial co-infections were documented in 3 fatal cases. Preliminary studies utilizing molecular detection methods found two instances of co-infections (1 *Streptococcus pneumoniae*, 1 adenovirus) among 21 severe or fatal cases. Initial autopsy reports from Mexico indicate that the pathology was consistent with ARDS secondary to primary viral pneumonia, including diffuse alveolar damage, peribronchiolar and perivascular lymphocytic infiltrates, hyperplastic airway changes and bronchiolitis obliterans. Muscle biopsies performed in two cases showed skeletal muscle necrosis.

Analysis of data from affected countries has helped clinicians, epidemiologists and virologists all over the world. However, there are several important limitations about the data that must be considered by users. Countries are using different surveillance methods and case definitions to detect cases. This will influence information about clinical disease. For example, case detection focused in hospitals would be expected to preferentially detect cases of H1N1 infection with more severe disease. Conversely, detection and investigation of cases in the community setting may favour finding less severe illness.

Most countries are at an early stage of disease spread and have reported a small number of cases. The experience of Mexico and the United States suggest that only when and as more cases occur and infection spreads into the wider community can a more complete picture of the epidemiological and clinical characteristics of the H1N1 virus begin to be delineated. Caution must be exercised in interpreting information such as age as it may reflect patterns of travel or the occurrence of outbreaks in special settings such as schools. The early estimates of important epidemiological parameters such as incubation period and attack rate have been derived from a limited number of settings such as households and schools and may not be broadly generalizable. Although Mexico and the United States have reported deaths among persons with confirmed H1N1 infection, it is too early to get a reliable estimate of the case fatality ratio. Additional studies are needed to assess risk factors for infection with the H1N1 virus as well as the severity of illness.

The situation is expected to evolve over time and bears careful watching. Although illness to date has been mainly mild, as the number of cases and the geographic spread of the virus increase a fuller picture of the virus will emerge that will likely to include increased numbers of severe illness and deaths as occurs with seasonal influenza epidemics each year.

Sources :

World Health Organization. Weekly Epidemiological Record. 2009;21 (84):185-89. Available at : www.who.int/wer/2009/wer8421.pdf

World Health Organization. Summary report of a High-Level Consultation: new influenza A (H1N1) Geneva, 18 May 2009. Available at :www.who.int/csr/.../High_Level_consultation_18_May_2009.pdf

Editor wishes to thank Dr. Upekha Seneviratne for compiling this article.

Table 1: Vaccine-preventable Diseases & AFP

10th – 16th May 2009 (20th Week)

Disease	No. of Cases by Province									Number of cases during current week in 2009	Number of cases during same week in 2008	Total number of cases to date in 2009	Total number of cases to date in 2008	Difference between the number of cases to date in 2009 & 2008
	W	C	S	N	E	NW	NC	U	Sab					
Acute Flaccid Paralysis	01	00	00	00	00	00	01	00	00	01	01	27	34	-20.6%
Diphtheria	00	00	00	00	00	00	00	00	00	00	00	00	00	-
Measles	00	00	00	00	00	01	00	00	00	01	00	53	48	+10.4%
Tetanus	00	00	00	00	00	00	00	01 BD=1	00	01	01	11	14	-21.4%
Whooping Cough	01	00	00	00	00	00	00	00	00	01	02	25	16	+56.2%
Tuberculosis	09	43	86	01	03	52	29	08	00	231	320	3490	3460	+0.86%

Table 2: Newly Introduced Notifiable Disease

10th – 16th May 2009 (20th Week)

Disease	No. of Cases by Province									Number of cases during current week in 2009	Number of cases during same week in 2008	Total number of cases to date in 2009	Total number of cases to date in 2008	Difference between the number of cases to date in 2009 & 2008
	W	C	S	N	E	NW	NC	U	Sab					
Chickenpox	20	12	16	15	03	05	09	07	29	116	67	7249	2380	+204.5%
Meningitis	03 CB=2 GM=1	00	03 GL=2 MT=1	00	00	01 PU=1	01 AP=1	01 BD=1	01 KG=1	12	14	396	641	-38.2%
Mumps	02	03	04	07	01	00	05	03	05	30	25	728	989	-26.4%
Leishmaniasis	00	01 ML=1	06 HB=3 MT=3	00	00	00	02 AP=1 PO=1	00	00	09	Not available*	394	Not available*	-

Key to Table 1 & 2

Provinces: W: Western, C: Central, S: Southern, N: North, E: East, NC: North Central, NW: North Western, U: Uva, Sab: Sabaragamuwa.

DPDHS Divisions: CB: Colombo, GM: Gampaha, KL: Kalutara, KD: Kandy, ML: Matale, NE: Nuwara Eliya, GL: Galle, HB: Hambantota, MT: Matara, JF: Jaffna, KN: Killinochchi, MN: Mannar, VA: Vavuniya, MU: Mullaitivu, BT: Batticaloa, AM: Ampara, TR: Trincomalee, KM: Kalmunai, KR: Kurunegala, PU: Puttalam, AP: Anuradhapura, PO: Polonnaruwa, BD: Badulla, MO: Moneragala, RP: Ratnapura, KG: Kegalle.

Data Sources:

Weekly Return of Communicable Diseases: Diphtheria, Measles, Tetanus, Whooping Cough, Chickenpox, Meningitis, Mumps.

Special Surveillance: Acute Flaccid Paralysis.

Leishmaniasis is notifiable only after the General Circular No: 02/102/2008 issued on 23 September 2008.

Table 3: Laboratory Surveillance of Dengue Fever

10th – 16th May 2009 (20th Week)

Samples	Number tested	Number positive	Serotypes *				
			D1	D2	D3	D4	Negative
Number for current week	04	00	00	00	00	00	00
Total number to date in 2009	50	09	02	03	04	00	00

Sources: Genetic Laboratory, Asiri Surgical Hospital

* Not all positives are subjected to serotyping.

NA= Not Available.

Table 4: Selected notifiable diseases reported by Medical Officers of Health

10th – 16th May 2009 (20th Week)

DPDHS Division	Dengue Fever / DHF*		Dysentery		Encephalitis		Enteric Fever		Food Poisoning		Leptospirosis		Typhus Fever		Viral Hepatitis		Human Rabies		Returns Received Timely**
	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	%
Colombo	94	980	1	74	0	5	2	78	0	31	5	216	0	4	1	30	0	3	**85**
Gampaha	53	523	5	67	2	10	0	22	0	9	8	114	0	3	1	31	0	2	**79**
Kalutara	8	235	4	111	0	3	0	28	0	11	2	83	0	0	1	7	1	2	**67**
Kandy	80	876	6	151	0	3	1	15	0	52	8	93	6	65	1	19	0	0	**72**
Matale	9	269	1	45	0	2	0	16	0	5	4	198	0	2	0	6	0	2	**75**
Nuwara Eliya	5	36	24	187	0	0	6	83	6	28	0	20	1	30	1	26	0	0	**85**
Galle	12	59	8	78	0	7	0	1	4	12	5	76	0	2	0	6	0	3	**84**
Hambantota	87	261	2	32	0	6	1	3	0	5	8	38	2	33	0	8	0	0	**73**
Matara	45	269	4	141	0	2	0	4	6	14	3	75	1	63	1	8	0	0	**100**
Jaffna	0	8	0	49	0	3	1	85	0	22	0	0	2	102	0	18	0	2	**13**
Kilinochchi	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	**0**
Mannar	1	4	6	28	0	1	0	56	0	4	0	0	0	0	5	22	0	1	**50**
Vavuniya	0	4	0	417	0	2	0	21	0	2	0	2	0	0	0	191	0	0	**0**
Mullaitivu	0	0	0	2	0	0	0	1	0	0	0	0	0	0	0	0	0	0	**0**
Batticaloa	16	280	6	92	0	10	0	5	0	39	0	7	0	1	1	5	0	1	**55**
Ampara	0	37	0	24	0	0	0	5	0	4	0	7	0	0	0	4	0	0	**0**
Trincomalee	3	156	2	42	0	1	0	2	0	0	0	5	0	5	0	5	0	1	**30**
Kurunegala	44	374	1	70	1	5	2	27	0	1	0	44	1	43	1	30	0	4	**74**
Puttalam	8	81	2	53	00	6	1	44	0	0	1	42	0	22	0	6	0	1	**44**
Anuradhapura	7	204	0	33	0	3	0	3	0	2	0	67	1	26	1	8	1	1	**47**
Polonnaruwa	6	34	0	14	0	2	0	13	0	6	0	40	0	0	0	4	0	0	**71**
Badulla	1	41	6	107	0	2	1	21	3	18	0	36	1	36	4	95	0	1	**73**
Monaragala	1	18	2	22	0	0	0	9	0	7	0	10	0	36	2	23	0	1	**91**
Ratnapura	55	200	8	259	0	15	2	29	0	4	1	52	0	17	0	9	0	1	**78**
Kegalle	100	644	2	54	0	4	0	15	0	6	5	56	0	12	5	70	0	3	**73**
Kalmunai	2	94	2	60	0	1	0	5	0	1	0	2	0	1	0	7	0	0	**38**
SRI LANKA	**637**	**5687**	**92**	**2212**	**3**	**93**	**17**	**591**	**19**	**283**	**50**	**1283**	**15**	**503**	**25**	**638**	**2**	**29**	**65**

Source: Weekly Returns of Communicable Diseases (WRCD).
*Dengue Fever / DHF refers to Dengue Fever / Dengue Haemorrhagic Fever.
**Timely refers to returns received on or before 16 May, 2009 Total number of reporting units =311. Number of reporting units data provided for the current week: 201
A = Cases reported during the current week. B = Cumulative cases for the year.

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