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National Surveillance of Influenza A(H1N1)2009-Associated Encephalopathy — Japan, 2009–2010

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ABSTRACT

Background:

Influenza associated encephalopathy (IAE) is known as a rare but serious complication of influenza. IAE cases have been reported from Japan and other countries, although its pathogenesis is still unclear. IAE has been a notifiable disease as a part of acute encephalitis/encephalopathy surveillance system in Japan since 2004. Many IAE cases were reported during influenza A(H1N1)2009 pandemic. The main objective of this study is to describe epidemiological features of pandemic IAE.

Methods:

The first pandemic wave in Japan started in July, 2009 and waned in March, 2010, according to sentinel influenza surveillance. We described epidemiological features of the reported IAE cases from week 28 in 2009 to week 27 in 2010, and compared them with those of seasonal IAE in previous five seasons. We used the case definition of acute encephalitis/encephalopathy surveillance under Infectious Disease Control Law in Japan.

Results:

While the number of reported IAE cases during five seasons before pandemic was 246, 331 IAE cases were reported during the first pandemic wave. According to laboratory results, 322 of them were considered to be influenza A(H1N1)2009 associated encephalopathy. The median age of pandemic IAE and seasonal IAE was seven years (range, 0-72) and four years (range, 0-83) respectively ($p < 0.0001$, Mann-Whitney U test). Male patients account for 61% in pandemic, and 52% for seasonal influenza ($p = 0.047$, chi-square test). The case fatality rate (CFR) of pandemic IAE was 3.7%, which was significantly lower than that of seasonal IAE (13.2%, $p < 0.0001$, chi-square test). Although the greatest number of pandemic IAE cases was observed in 5-9 years of age, the number of cases per estimated number of ILI visit was peaked in 0-4 years of age.

Conclusions:

A number of IAE cases were reported in Japan during the first pandemic wave. Age and sex distributions were different from those of seasonal IAE. The CFR of pandemic IAE was lower than that of seasonal IAE. Surveillance of IAE in other countries would be helpful to understand this severe complication of influenza and a better epidemiological case definition is needed for data integration and comparison.

BACKGROUND

- Influenza-associated encephalopathy (IAE) is a serious complication of influenza and reported most frequently in Japan.
- Acute encephalitis/encephalopathy is a notifiable disease in Japan and IAE has been included in the case definition of it since March 2004.

METHODS

- To describe the epidemiologic characteristics of influenza A (H1N1) 2009-associated encephalopathy in comparison to seasonal IAE, national IAE and influenza-like illness (ILI) surveillance data from 2004–2005 to 2009–2010 seasons were summarized and analyzed.

- Data source: the National Epidemiological Surveillance of Infectious Diseases (NESID)

- Study periods: week 28, 2004–week 27, 2010

Case definition

Acute encephalitis / encephalopathy (Infectious Disease Control Law in Japan)

- 1) Clinically suspected encephalitis / encephalopathy AND
- 2) Disturbance of consciousness and admission with ≥ 24 hours of high fever or central nervous system symptom or infectious disease symptoms

Influenza-associated encephalopathy (IAE)

1) AND 2) + diagnosis of influenza

CONCLUSIONS

- Case fatality rate of influenza A (H1N1) 2009-associated encephalopathy was lower than that of seasonal IAE.
- One of the characteristic findings was the age distribution of the IAE cases.
- Further studies should include epidemiologic case definitions of IAE for a more accurate understanding of the epidemiologic status of IAE.

RESULTS

Table 1. Number of Reported Cases of IAE (Fatal Cases) in Japan, 2004–2010

| Dominant virus of epidemic | 2004-2005 | 2005-2006 | 2006-2007 | 2007-2008 | 2008-2009 | 2009-2010 |
|----------------------------|-------------|-----------|-------------|-----------|-------------|--------------------|
| | A (H3N2), B | A (H3N2) | A (H3N2), B | A (H1N1) | A (H1N1), B | A (H1N1) 2009 |
| A* | 19 (2) | 48 (6) | 31 (2) | 29 (6) | 42 (6) | 1 [§] (0) |
| B† | 30 (6) | 4 (1) | 7 (0) | 1 (0) | 7 (0) | 1 (0) |
| A (H1N1) 2009‡ | ... | ... | ... | ... | ... | 322 (12) |
| Unknown | 6 (2) | 0 | 5 (1) | 5 (0) | 5 (1) | 7 (0) |
| Total | 55 (10) | 52 (7) | 43 (3) | 35 (6) | 54 (7) | 331 (12) |

* Reported as influenza A from 28w in 2004 to 27w in 2009

† Reported as influenza B from 28w in 2004 to 27w in 2009

‡ Reported as influenza A (H1N1) 2009 or influenza A from 28w in 2009 to 13w in 2010

§ Reported as influenza A (H3N2) on 24w in 2010

Table 2. Characteristics of Reported IAE Cases in Japan, 2004–2010

| Virus Type | Reported Cases | Male (%) | p value | Median Age (Range) | p value | Fatal Cases (%) | p value |
|---------------|----------------|------------|--------------------|--------------------|---------------------|-----------------|---------------------|
| A | 170 | 94 (55.3) | 0.232 [†] | 4 (0-79) | <0.001 [‡] | 22 (12.9) | <0.001 [†] |
| B | 50 | 21 (42.0) | 0.012 [†] | 4 (0-83) | 0.006 [‡] | 7 (14.0) | 0.002 [†] |
| A (H1N1) 2009 | 322 | 196 (60.9) | ref | 7 (0-72) | ref | 12 (3.7) | ref |
| Unknown | 28 | 16 (57.1) | ... | 6 (1-52) | ... | 4 (14.3) | ... |
| Total | 570 | 327 (57.4) | ... | 6 (0-83) | ... | 45 (7.9) | ... |

* Statistically significant

† chi-square test

‡ Mann-Whitney test

Figure 1. Number of Cases of IAE in Japan, from week 28, 2004–week 27, 2010

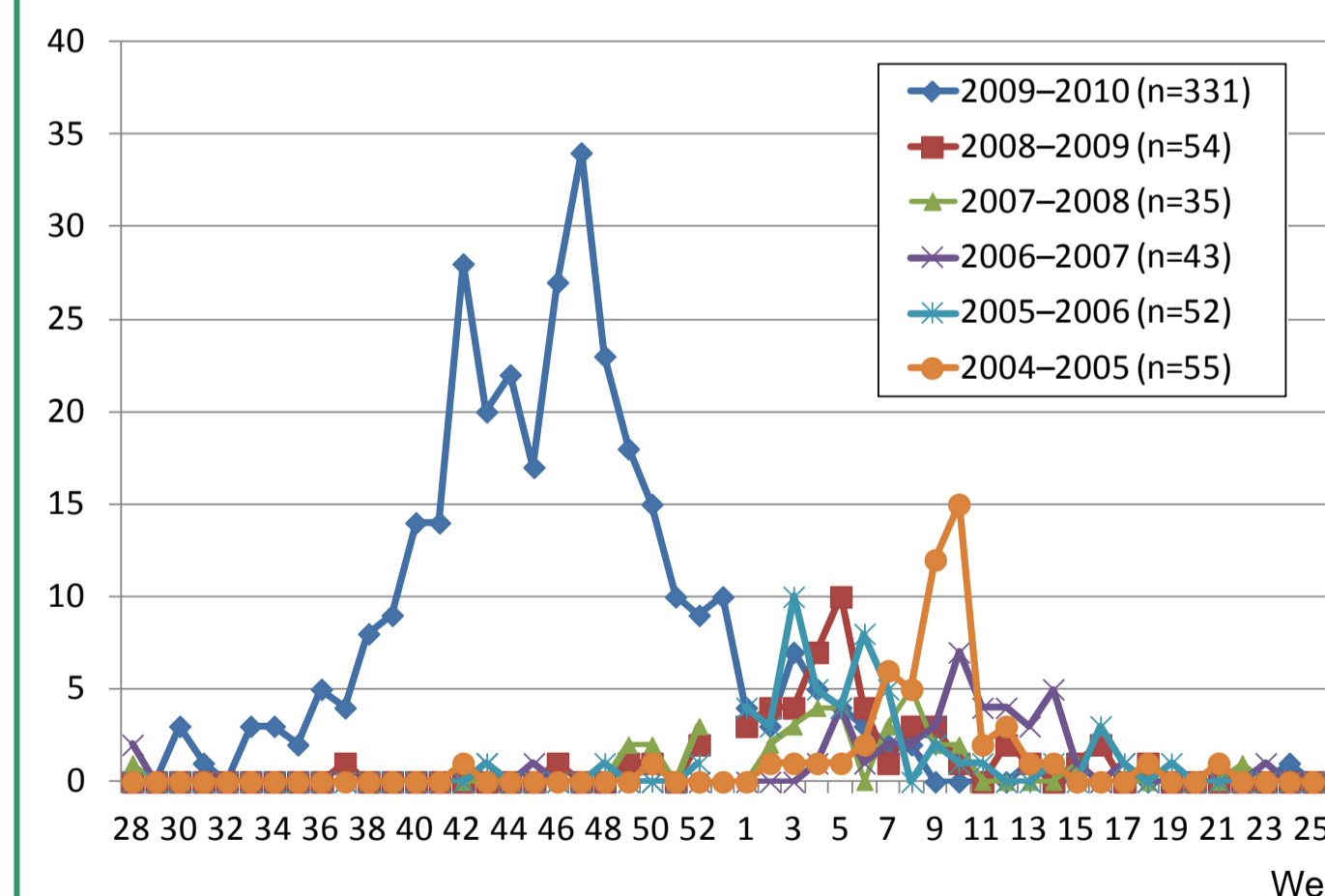


Figure 2. Number of influenza A-Associated Encephalopathy Cases per 1 Million Population by Age, 2004–2010

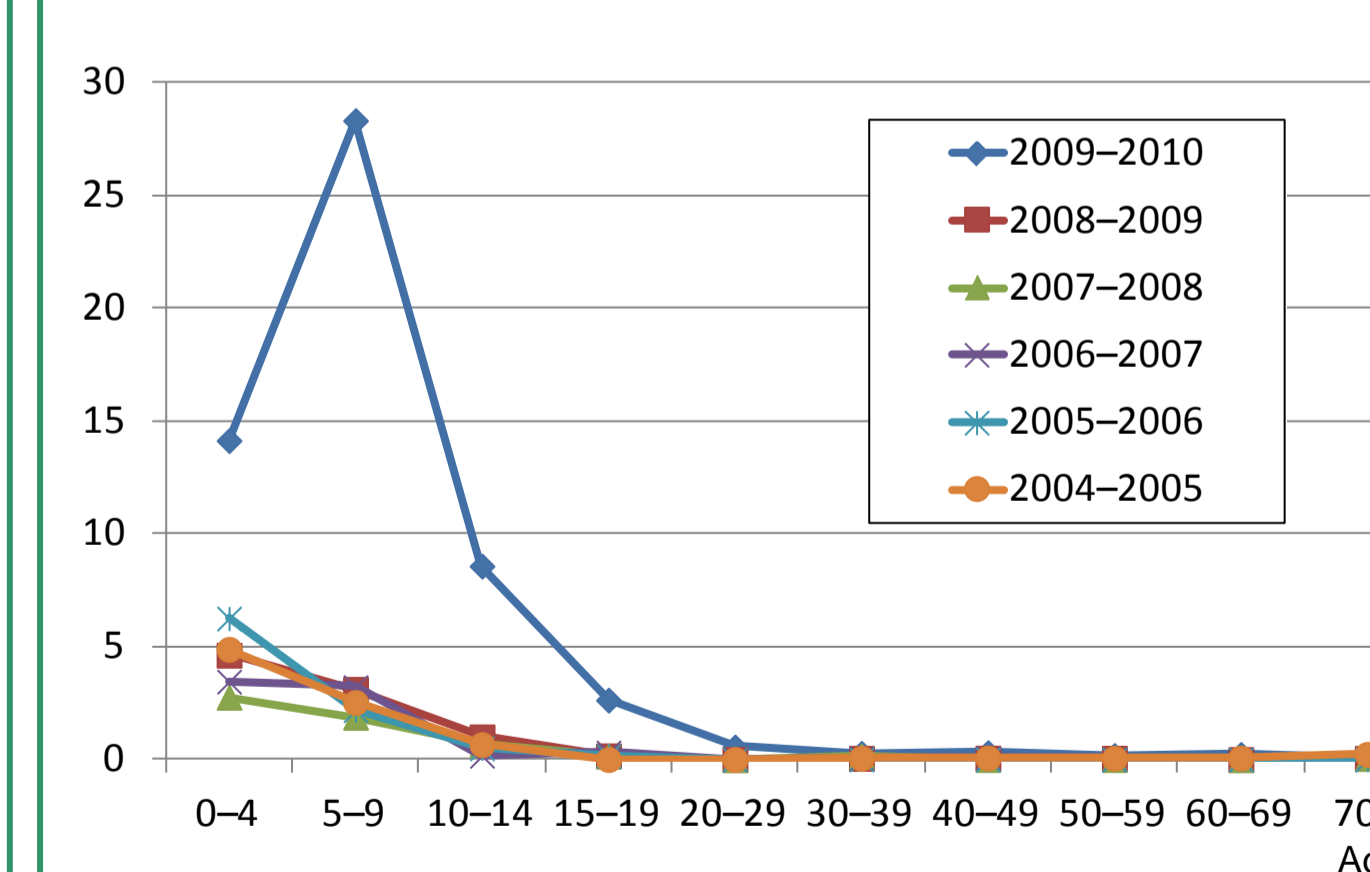
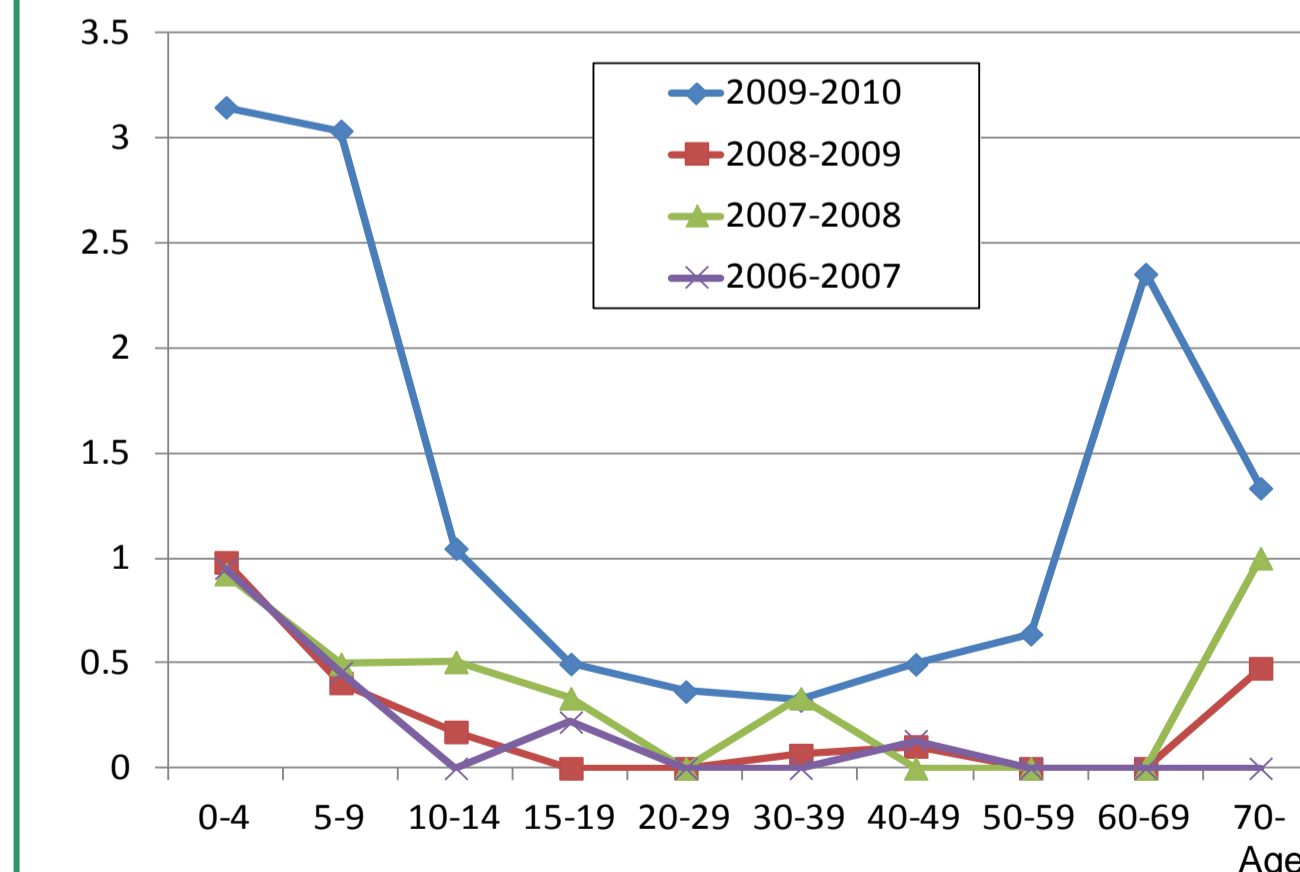


Figure 3. Number of Influenza A-Associated Encephalopathy Cases per 100 Thousand Estimated Number of Patient Visits by Age, 2006–2010



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