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Original Article

Association of early annual peak influenza activity with El Niño southern oscillation in Japan

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Background Seasonality characterizing influenza epidemics suggests susceptibility to climate variation. El Niño southern oscillation (ENSO), which involves two extreme events, El Niño and La Niña, is well-known for its large effects on inter-annual climate variability. The influence of ENSO on several diseases has been described.

Objectives In this study, we attempt to analyze the possible influence of ENSO on the timing of the annual influenza activity peak using influenza-like illness report data in Japan during 1983–2007.

Materials Influenza surveillance data for 25 influenza epidemics, available under the National Epidemiological Surveillance of the Infectious Diseases, was used in this study. ENSO data were obtained from the Japan Meteorological Agency.

Results Influenza-like illness peak week varied largely during the study period, ranging between 4th and 11th weeks (middle of winter to early spring). The average of peak week during ENSO cycles (n = 11, average = 4·5 ± 0·9) was significantly earlier than in non-ENSO years (n = 14, average = 7·6 ± 2·9; P = 0·01), but there was no significant difference in the peak timing between hot (El Niño) and cold (La Niña) phases. Earlier peaks of influenza activity were observed in 16, out of 25, epidemics. These coincided with 10 (90·9%) out of 11 ENSO and 6 (85·7%) out of seven large-scale epidemics.

Conclusion Influenza activity peak occurred earlier in years associated with ENSO and/or large scale epidemics.

Keywords Annual peak, El Niño southern oscillation, influenza, influenza-like illness, Japan.

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Introduction

Annual influenza epidemics affect 10–20% of the population resulting in substantial mortality and morbidity worldwide. The incidence of influenza in temperate areas of the northern and southern Hemispheres is characterized by seasonal cycles with marked peaks in winter,[1] hence, suggesting a role for climate. However, the year round pattern of epidemics observed in tropical countries[2] implies non-uniformity in the factors governing epidemics. In addition, to environmental factors, such as temperature and humidity, fluctuations in host immune response throughout the year, seasonal changes in host behaviors, and overcrowding have also been implicated to play a role in seasonal variation.[3] Annual epidemics are attributed to the continuous evolution of influenza viruses resulting from point mutations in its antigenic determinants.[1] Despite the availability of extensive time series and developed surveillance systems, there is still a lack in the understanding of mechanisms underlying seasonality.

The influence of interannual climate changes on the incidences and trends of a range of water- and food-borne diseases caused by microbiological agents has been reported.[4–6] El Niño southern oscillation (ENSO), which is associated with two extreme events, El Niño (warm) and La Niña (cold), is the most well-studied climate phenomenon known to have the largest effect on periodic climate variability.[7,8] Thus, ENSO can serve as a marker to study the effect of climate variability on disease patterns.

Despite the strong seasonality, the timing of winter influenza epidemics changes from year to year. Influenza-like illness in Japan is mainly caused by influenza viruses and thus its incidence is highly representative of influenza activity.[9,10] In this study, we utilized influenza-like illness data from 25 epidemics to determine possible effect of ENSO on the timing of peak influenza activity.

Materials and methods

Influenza surveillance and data collection and analysis

Influenza-like illness report data were used as a marker of influenza activity.[9,10] Under the National Epidemiological Surveillance of Infectious Disease in Japan, clinically diagnosed influenza-like illness cases, defined as sudden fever ≥38°C, respiratory symptoms, and myalgia, are electronically reported on a weekly basis to the Infectious Disease Surveillance Center (IDSC) in the National Institute of Infectious Diseases, Tokyo. Reporting sentinels include pediatric and internal medicine clinics. The number of sentinels is decided on the basis of the size of population of the health center area where they serve. Ten percent of flu sentinels are appointed as laboratory diagnosis sentinels.

Influenza-like illness report data from 1983 through 2007 was obtained from the IDSC's webpage (http://idsc.nih.go.jp/index.html). The peak week for each influenza season was then defined as the week during which the most number of cases are reported. Large-scale epidemics were defined as those for which the peak was ≥38 cases per sentinel per week, which represents 70% of the largest peak observed during the study period, in 1994/1995. Data on circulating types and subtypes of influenza were also available from the IDSC.

Climate data

In Japan, ENSO cycles are identified using a 5 months moving average of the sea surface temperature anomalies. According to the definition of the Japan Meteorological Agency (JMA) El Niño events are associated with positive sea surface temperature anomalies (≥0·5°C), while La Niña events are associated with negative anomalies (≤–0·5°C). ENSO's data was obtained from the JMA's webpage (http://www.jma.go.jp/jma/index.html).

Statistical analyses

Statistical analyses were performed using Fisher's exact probability test (two-tailed) and Scheffe's multiple comparison method. Statistical significance was considered at $P < 0{\cdot}05$.

Results

We analyzed approximately 14·7 million influenza-like illness cases in Japan, which consist of weekly time series of disease incidence from 1983 through 2007, including 25 influenza seasons. Annual influenza seasons began between November and December, peaked between January and March, and returned to the baseline between April and June for the study period (Figure 1). The peak influenza-like illness activity varied between 4th to 10th weeks (late January and early March) during 1983–1994, between 4th and 5th weeks during 1995–2000, and ranged up to the 11th week (the middle of March) during 2001–2007.

Influenza A(H3N2) was dominantly circulating during the majority of seasons, followed by A(H1N1) and B. Large-scale epidemics were observed in seven seasons, namely the 1985/1986, 1989/1990, 1992/1993, 1994/1995 (largest), 1997/1998, 2002/2003 and 2004/2005 seasons. Major antigenic drift of A(H3N2) occurred in five of these epidemics (Figure 1). The average peak week for the study period was 6·2 (Figure 2). Early peak was observed in six of the large-scale epidemics (Figure 2).

Regarding ENSO, 10 episodes covering 11 influenza epidemics were identified during the study's period. The peak

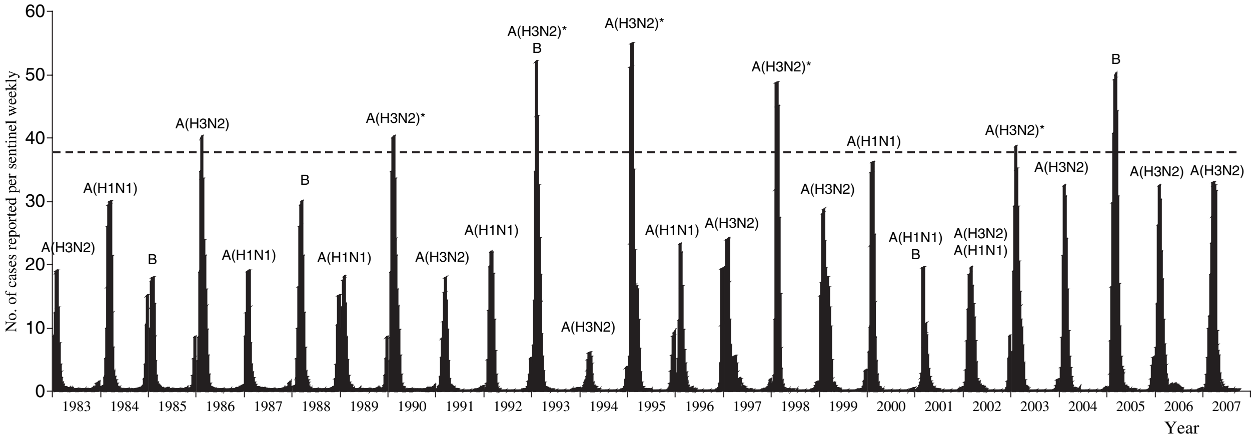

Figure 1. Weekly reported influenza-like illness cases per sentinel, 1983–2007. Data from Japan's Infectious Disease Surveillance Center. Dominant influenza types or subtypes circulating during each season are denoted on the top of the epidemic peak. Asterisks indicate a major antigenic drift in the A(H3N2). The dashed horizontal line indicates 38 cases per sentinel per week (representing 70% of the largest epidemic in 1994/1995). Epidemics with peak greater than 38 cases per sentinel per week were defined as large-scale epidemics.

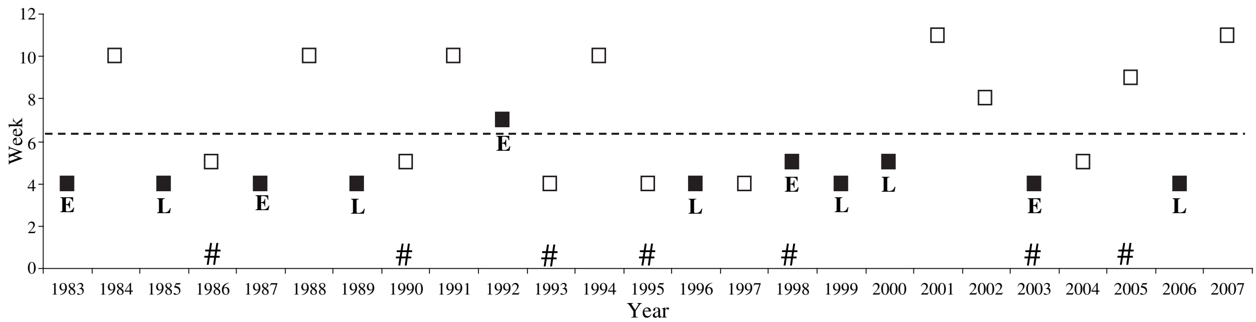

Figure 2. Yearly time series for peak week, defined as that during which the greatest number of influenza-like illness cases was reported, of influenza activity in Japan from 1983 to 2007 (data from Infectious Disease Surveillance Center). The dashed horizontal line, passing at 6·2, indicates the average peak week. # mark denotes a large-scale epidemic. Black boxes denote years during which El Niño southern oscillation (ENSO) episodes happened (E and L indicates El Niño and La Niña, respectively), while empty boxes resemble years with normal weather (non-ENSO years). ENSO data were obtained from Japan Meteorological Agency.

week of influenza epidemics was earlier than the average in 10 out of 11 ENSO years (90·9%) compared to 6/14 (42·9%) for non-ENSO years (P = 0·03 by Fisher's exact probability test, two-tailed). The average peak week for ENSO years, 4·5 ± 0·9 (n = 11), was significantly earlier than that for non-ENSO years (average = 7·6 ± 2·9, n = 14; P = 0·01 by Scheffe's multiple comparison method). No significant difference was found between the average peak weeks during El Niño (n = 5) and La Niña (n = 6) cycles, average = 4·8 ± 1·3 and 4·2 ± 0·4, respectively (P = 0·85 by Scheffe's method; Figure 2).

Discussion

Seasonality in disease incidence can often infer an association with weather factors and climate variability. We present here an evidence for a role of interannual climate variability on the temporal dynamics of influenza infections in Japan. The evidence is based on long-term time-series analyses of the relationships between peak influenza activity and ENSO as a major climate index.

El Niño southern oscillation arises from fluctuations in sea surface temperature of the tropical Eastern Pacific Ocean. It is well known for its wide-ranging and prominent consequences on weather around the world. It contributes to the likelihood of extreme weather events, such as strong winds, heavy rainfalls, and droughts.[8] The association between ENSO and cholera patterns in Bangladesh[11] and malaria epidemics in parts of South Asia and South America[12–14] were documented. Our data demonstrated that peak influenza-like illness activity occurred earlier in 16 out of 25 epidemics spanning 1983–2007. Early peaks were observed in 10 (90·9%) out of 11 ENSO and six (85·7%) out of seven large-scale epidemics (two of these occurred in ENSO cylces). Thus, we conclude that early peak influenza activity occurs in association with ENSO year or/and large-scale influenza epidemics.

Our observations demonstrated a strong association between the tendency to earlier peak activity and ENSO in Japan. The human response to weather fluctuations involved by ENSO, as inter-annual climate variability, may be different from their adaptation to usually experienced weather conditions. Changes in immunity, indoor crowding, and behavioral changes could set better conditions for virus transmission and consequently earlier peak influenza activity observed during ENSO cycles. Future studies on what factors of ENSO correlate mostly to influenza activity could provide better insight on such association.

Moreover, we demonstrated an association between early peak of influenza activity and large-scale epidemics mainly occurring because of a major antigenic drift of influenza A(H3N2), which dominantly circulated during these seasons. Although there was an exception in the 2004/2005 season in which influenza activity peaked late though being a large-scale epidemic. In this season, both influenza B and A(H3N2) were co-dominantly circulating and their peak overlapped, which could explain high incidence at peak. In a previous study, we similarly reported that the size of epidemic was correlated to the change in antigenicity and that large epidemics were mostly observed with new antigenic variants of influenza A(H3N2).[15] Furthermore, the greater the number of cases at peak week the shorter was the increasing-to-peak period. Thus, in case of a future pandemic we may expect large number of patients within short period, rapid speed of transmission, and early pandemic peak especially in winter season.

Viboud *et al.*[16] reported that higher morbidity impact of influenza was shown during cold phases of ENSO (La Niña) than in hot phases (El Niño). On the contrary, we found no significant difference in the incidence of influenza-like illness cases among the two phases. Nevertheless, higher incidence of influenza-like illness was found to be associated with a major drift in A(H3N2) (data not shown[15]).

Influenza's association with winter in temperate regions could be partly attributed to the direct influence of cold weather on virus survival or on the defense mechanisms of the upper respiratory tract.[17] We previously showed that influenza-like illness activity peaked first in western-central Japan rather than eastern Japan where the mean temperatures are lower,[15] suggesting a minor role of temperature in triggering peak activity. However, in tropical countries, temperature and humidity were considered to play an important role in driving the timing of influenza epidemics.[18] Different patterns and timings possessed by influenza epidemics in the tropics and temperate areas highlight both its susceptibility to trend modification in response to changing climate and the diversity of its driving factors.

The average peak week for the 25 influenza epidemics investigated in this study was in the winter season (6th week). Therefore, this is in line with the seasonality characterizing influenza epidemics. Yet, our data revealed that the peak of influenza activity was delayed until early spring during the 2000/2001 and 2006/2007 seasons. We have previously demonstrated a shift of peak rotavirus activity in Japan from winter to early spring, which could be related to global warming.[19] In contrast to the gradual shift observed in the case of rotavirus from 1983 through 2003, peak influenza activity showed a prompt shift to early spring during two seasons only. The extent to which global warming might affect the timing of influenza epidemics should be carefully followed up in future studies.

The importance of influenza as a human disease is well established, and concerns about future pandemics are clearly warranted.[2,20,21] Our study provides evidence of association between the timing of the peak influenza-like illness, as a marker of influenza activity, and ENSO and antigenic change of A(H3N2), both which can be forecasted half to 1 year ahead and can therefore serve as tools for predicting early peak activity, and consequently improve our preparedness for annual seasonal epidemics.

Finally, there are clear complexities in trying to understand relations between climate change and disease patterns. Knowing that climate change and ENSO effects on different locations of the globe are not uniform, our data remains specific to Japan. A global study of possible associations between climate change and influenza epidemics is essential. Better understanding of global influenza patterns is paramount to improving our control strategies and mitigating the disease burden.

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