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Original Article

A Seasonal Model to Simulate Influenza Oscillation in Tokyo

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SUMMARY: The purpose of our study was to establish a seasonal model to simulate the oscillation of the number of influenza cases with weather conditions and calendar months in Tokyo, Japan, during the winter season. Surveillance data for influenza in Tokyo was retrieved from the Infectious Agents Surveillance Report, published by the National Institute of Infectious Diseases in Japan. We obtained data for 86 parameters of weather conditions from the Meteorological Agency. The best-fit model was built by multiple regression with stepwise analysis. The reported number of patients with influenza per week was significantly increased with fewer days of maximum temperature ≥10°C per week (T10) and more days of relative humidity <60% per week (S60), adjusted by calendar month, average temperature, and vapor pressure. Annual oscillation of the number of reported influenza cases at the start, peak, and end weeks almost exactly matched the model, although peak levels for each oscillation did not always match. However, this model showed that 81% of the variation among the observed number of influenza cases was explained by a linear relationship with the seasonal parameters utilized. The validity of this model applied to data from 1999 to 2002, showing a 75% correlation. Using this model, if the number of days with both T10 and S60 increased by one per week, the number of influenza cases was simulated to decrease by approximately half. These results suggest that most of the oscillation in the number of influenza cases may be explained using a seasonal model that can simulate the impact of global warming.

INTRODUCTION

Death due to influenza and pneumonia ranks as one of the leading causes of mortality, even in developed countries (1,2). In fact, the influenza season causes significant negative impact on total mortality and morbidity (3-6). Considerable year-to-year variability exists in influenza morbidity and its related mortality, particularly for the youngest and oldest age groups (7), which is dependent mainly on levels of immunity against prevalent influenza in the general population, alteration of antigens on influenza virus, and population dynamics. However, this variability may also be synchronized with yearly differences in climate conditions, suggested by strong seasonal and latitudinal differences in the incidence of influenza. We therefore investigated the association between incidence of influenza and climate conditions in order to establish a seasonal model to simulate future influenza epidemics.

PATIENTS AND METHODS

In Tokyo, an average of 129 clinics was used as sentinel points between 1987 and 1997. The number of sentinel points increased to 250 after 1999. Almost all of these points were pediatric clinics. Thus, patients reported to have influenza were mainly less than 15 years old. Pediatricians at the sentinel points diagnosed influenza or influenza-like disease by typical clinical symptoms, with or without laboratory tests. They reported the number of patients with influenza to the nearby health center on a weekly basis. The number of cases was totaled for Tokyo during the same week. We then retrieved the surveillance data from the Infectious Agents Surveillance Report published by the National Institute of Infectious Diseases in Japan (8).

From the Meteorological Agency we obtained weekly measurements of 86 kinds of weather parameters (Appendix I). We collected data for one-week periods prior to the reported cases of influenza.

Multiple regression analysis and model building was performed using STATA 7.0 software (STATA Corporation, College Station, Tex., USA).

RESULTS

Simple associations between vapor pressure/average temperature and the reported number of influenza cases in Tokyo are shown in Figure 1. The reported number of influenza cases increased sharply when the vapor pressure and temperature decreased below the threshold of 8 hPa and 10°C, respectively. In order to determine the relationship between the reported number of influenza cases and all weather parameters as well as calendar months, the best-fit model was built by multiple regression analysis with a stepwise approach. Significance testing was done using 86 weather parameters and 12 months as dummy variables. Only two weather parameters remained significantly correlated with the number of influenza cases. Days per week of maximum temperature greater than or equal to 10°C (T10) was negatively correlated, whereas days per week of average relative humidity less than 60% (S60) had a positive association, after adjusting for calendar month, vapor pressure, and average temperature per week (Table 1). This model implied that 72% of the variation among the observed number of influenza cases was explained by its linear relationship with these weather parameters and calendar months.

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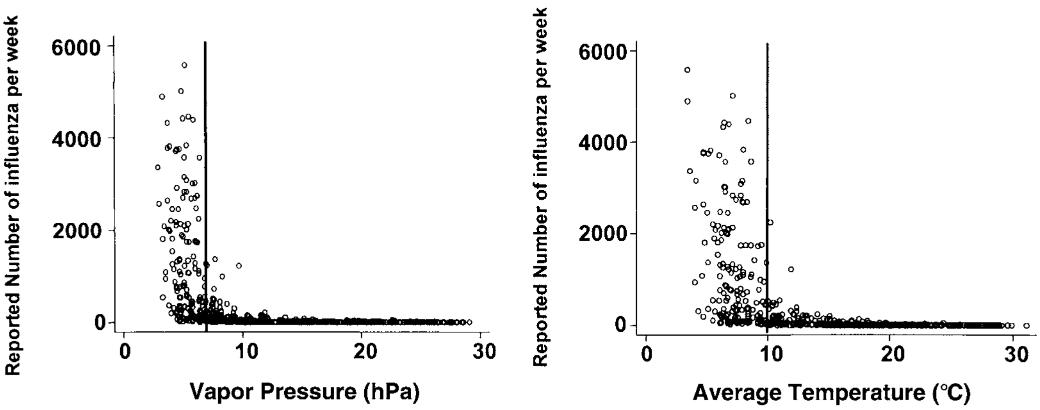

Fig. 1. Relationship between reported number of influenza cases per week and vapor pressure (left) or average temperature (right) 1 week prior in Tokyo.

Table 1. Weather parameters associated with number of patients with influenza[3]

	Coefficient	t[4]	*P*[5]	95% CI[6]
T10[1]	−153.9	−4.09	0.000	−227.9 to −80.0
S60[2]	96.43	3.27	0.001	38.5 to 154.3

[1] Days per week of maximum temperature ≥10°C.
[2] Days per week of average relative humidity <60%.
[3] Coefficients are adjusted for calendar month, average temperature of the week, and average vapor pressure.
[4] t distribution.
[5] percentile of the t distribution (*P* value).
[6] 95% confidence interval.

A regression equation was formulated using the coefficients of variables created by multiple regression analysis (Appendix II). With this equation, the number of influenza cases was calculated and compared to the observed number of influenza cases from 1987 to 1997. The annual oscillation of calculated influenza cases at the start, peak, and end weeks almost exactly matched the reported cases (Fig. 2). When the calculated numbers were squared and both the reported and calculated number of patients with influenza were transformed by natural logarithm, the correlation coefficient was 0.81 (Fig. 3).

The validity of this seasonal model was examined using data gathered between March 1999 and February 2002. The calculated peaks occurred within 2 weeks of the observed peaks and the calculated number of peaks approximated the observed number of peaks in 2000 and 2002, but not in 2001 (Fig. 4). The correlation coefficient remained relatively high (0.75, $P = 0.00001$) when both reported and calculated numbers were transformed by natural logarithm (Fig. 5).

With this model we simulated the impact of global warming on the incidence of influenza (Fig. 6). According to our model, when the number of days at T10 is increased by one and the number of days at S60 is decreased by one, then the number of influenza cases should decrease by 48%. Moreover, when the parameters changed by 2 days, influenza cases should decrease by 60%. For a change of 3 days, the decrease in influenza cases should be 70%.

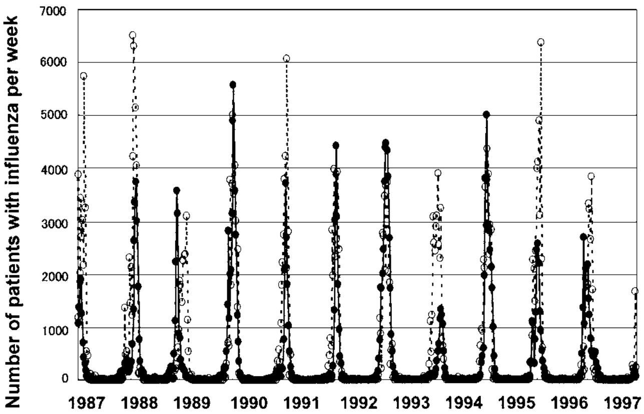

Fig. 2. Comparison of epidemic curves of weekly reported and calculated numbers in Tokyo between 1987 and 1997, based on the seasonal model. Solid lines show observed data and dotted lines show calculated data.

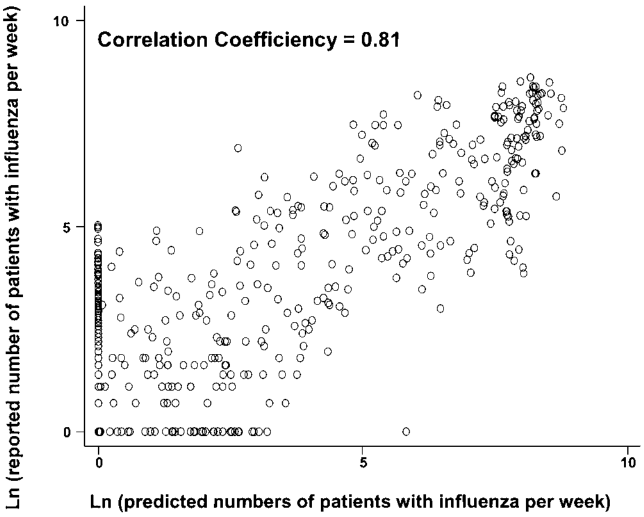

Fig. 3. Correlation between calculated number of patients with influenza per week transformed by natural logarithm and reported number of patients with influenza per week transformed by natural logarithm from 1987 to 1997.

DISCUSSION

In this study, we examined important weather parameters that might affect an influenza epidemic. The seasonal variability of some infectious diseases is quite clear, but only a few studies of the relation between infectious disease and climate have been reported in the literature (9,10). We found that temperature and humidity/vapor pressure were important

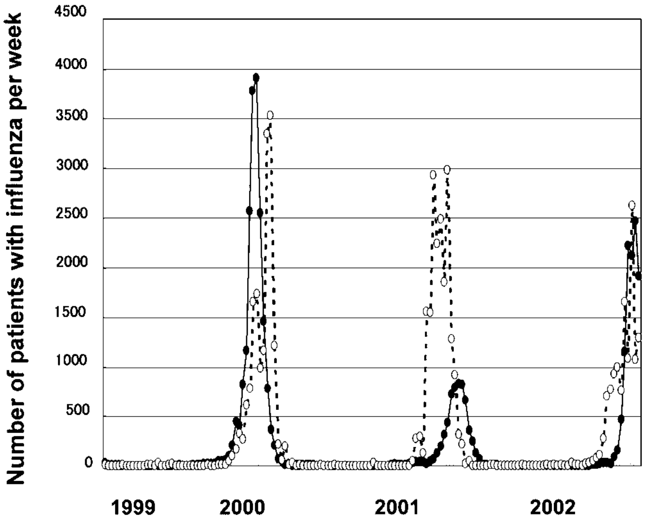

Fig. 4. Comparison of epidemic curves in Tokyo between March 1999 and February 2002 of weekly reported and calculated numbers, based on the model built by data between 1987 and 1997. Solid lines show observed data and dotted lines show calculated data, by seasonal model.

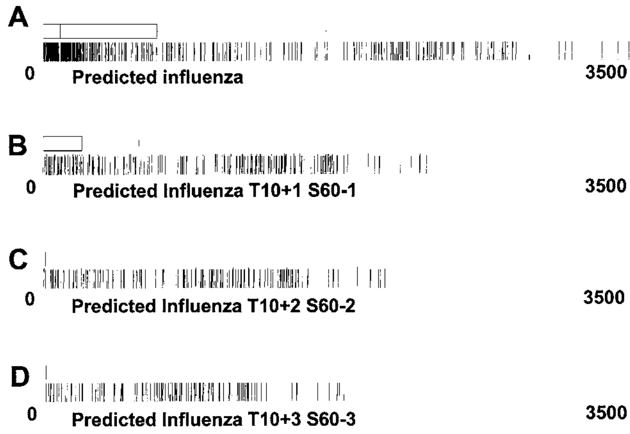

Fig. 6. Simulation for incidence of influenza by seasonal model. A: Calculated number of patients with influenza based on weather parameters between 1987 and 1997. B: Simulation of changes in warmer weather, with 1 more day of maximum temperature more than 10°C per week (T10) and 1 less day of average relative humidity less than 60% per week (S60). C: Simulation of changes in warmer weather, with 2 more days of T10 and 2 less days of S60. D: Simulation of changes in warmer weather, with 3 more days of T10 and 3 less days of S60. Number of days was no more than 7 days per week.

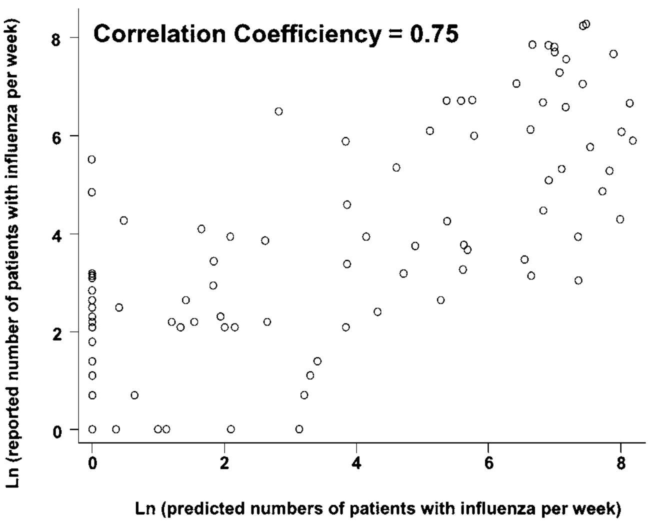

Fig. 5. Correlation between calculated number of patients with influenza per week transformed by natural logarithm and reported number of patients with influenza per week transformed by natural logarithm, between March 1999 and February 2002.

factors, particularly for T10 and S60. We have applied this model-building procedure to other prefectures in Japan (data not shown). Temperature and humidity related parameters, as suggested by Shoji (11), were also important in other prefectures, but exact formulation was different in each prefecture. Thus, the seasonal model for Tokyo may not be used for other prefectures in Japan.

Increase in air temperature has been demonstrated to alter the secondary structure and destabilize the trimeric form of hemagglutinin (HA) protein (12), which is important in initiating viral infection. However, few previous reports have suggested that air temperature and/or humidity alter the infectivity of influenza virus in vitro.

In our model, the correlation coefficient between the reported and calculated numbers of patients with influenza was 0.72. When the calculated numbers were squared, the correlation coefficient was increased to 0.81. Hamer postulated that the course of an epidemic depends on the rate of contact between susceptible and infectious individuals (13). This has been extensively studied by Anderson and May as the SEIR (susceptible/exposed/infectious/removed) model (14-16). We initially applied the SEIR model to influenza oscillation, but it was no more efficient than our model. In fact, the SEIR model has not been used to study influenza epidemics. In our model, most of the observed number of cases of influenza were explained by seasonal variability, including weather conditions and calendar months, suggesting that the variability of influenza may be more dependent on the season than on population dynamics. However, if information regarding immunity and vaccination against influenza were included in the model, its accuracy in calculating the incidence of influenza might be enhanced. Recently, Mugglin et al. demonstrated, using hierarchical statistical modelling, how an influenza epidemic can spread in space and time (17). Our model, however, focused on a broad area of Tokyo and ignored regional spread in time.

We retrieved surveillance data between 1987 and 1997. Recently, after the study period, prompt testing for influenza has been introduced in order to help primary care physicians and pediatricians in the clinical management of patients suspected of having influenza. In addition, new antiviral medications are now available for children as well as for adults in Japan. Influenza vaccine has also been re-considered to raise the number of shot for children and older generation. Therefore, the seasonal model that we have established may need to be modified using recent surveillance data. However, this study suggested, at least in part, cheaper ways of preventing epidemics in daily life; for example, maintaining a warmer and more humid indoor environment.

Evidence for global warming (18,19) may be inferred by the increase in heat-related deaths in Tokyo (20). In contrast, the number of patients with influenza may decrease if winters get warmer. Our study simulated how much increased temperature/humidity would decrease the calculated number of patients with influenza in Tokyo. Judging from our model, in a warmer winter, the number of patients with influenza could decrease dramatically.

In conclusion, most of the oscillations in the number of influenza cases were explained by our seasonal model. This kind of tool may enable us to simulate the impact of global warming on the incidence of influenza.

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APPENDIX

Appendix I. List of weather parameters and their means and min/max between 1987 and 1997

No.	Weather parameter average of the week	No.	Weather parameter average of the week
1	Average temperature of the day	44	Days of Ave temperature <5°C
2	Difference between Maximum and Minimum temperature of the day	45	Days of Ave temperature <10°C
		46	Days of Ave temperature <15°C
3	Days of Max temperature ≥0°C	47	Days of Ave temperature <20°C
4	Days of Max temperature ≥5°C	48	Days of Ave temperature <25°C
5	Days of Max temperature ≥10°C	49	Days of Ave temperature <30°C
6	Days of Max temperature ≥15°C	50	Days of Ave temperature <35°C
7	Days of Max temperature ≥20°C	51	Relative humidity
8	Days of Max temperature ≥25°C	52	Days of relative humidity ≥10%
9	Days of Max temperature ≥30°C	53	Days of relative humidity ≥20%
10	Days of Max temperature ≥35°C	54	Days of relative humidity ≥30%
11	Days of Min temperature ≥−5°C	55	Days of relative humidity ≥40%
12	Days of Min temperature ≥0°C	56	Days of relative humidity ≥50%
13	Days of Min temperature ≥5°C	57	Days of relative humidity ≥60%
14	Days of Min temperature ≥10°C	58	Days of relative humidity ≥70%
15	Days of Min temperature ≥15°C	59	Days of relative humidity ≥80%
16	Days of Min temperature ≥20°C	60	Days of relative humidity ≥90%
17	Days of Min temperature ≥25°C	61	Days of relative humidity <10%
18	Days of Min temperature ≥30°C	62	Days of relative humidity <20%
19	Days of Max temperature <0°C	63	Days of relative humidity <30%
20	Days of Max temperature <5°C	64	Days of relative humidity <40%
21	Days of Max temperature <10°C	65	Days of relative humidity <50%
22	Days of Max temperature <15°C	66	Days of relative humidity <60%
23	Days of Max temperature <20°C	67	Days of relative humidity <70%
24	Days of Max temperature <25°C	68	Days of relative humidity <80%
25	Days of Max temperature <30°C	69	Days of relative humidity <90%
26	Days of Max temperature <35°C	70	Station atmospheric pressure
27	Days of Min temperature <−5°C	71	Sea level atmospheric pressure
28	Days of Min temperature <0°C	72	Vapor pressure
29	Days of Min temperature <5°C	73	Days of Max wind speed ≥10 m/s
30	Days of Min temperature <10°C	74	Days of Max wind speed ≥25 m/s
31	Days of Min temperature <15°C	75	Days of Max wind speed ≥29 m/s
32	Days of Min temperature <20°C	76	Wind speed
33	Days of Min temperature <25°C	77	Cloud cover
34	Days of Min temperature <30°C	78	Days of Ave cloud cover <2.5
35	Days of Ave temperature ≥0°C	79	Days of Ave cloud cover ≥7.5
36	Days of Ave temperature ≥5°C	80	Days of Ave cloud cover <1.5
37	Days of Ave temperature ≥10°C	81	Days of Ave cloud cover ≥8.5
38	Days of Ave temperature ≥15°C	82	Duration of sunshine
39	Days of Ave temperature ≥20°C	83	Number of sunless days
40	Days of Ave temperature ≥25°C	84	Rate of sunshine
41	Days of Ave temperature ≥30°C	85	Mean flux of global solar radiation
42	Days of Ave temperature ≥35°C	86	Amount of precipitation
43	Days of Ave temperature <0°C		

Appendix II. Equation to calculate number of patients with influenza per week in Tokyo (= y)

y = − 62.02656 × (average temperature) − 554.4254 × (May) − 153.9496 × (days of Max temperature ≥10°C) − 657.1146 × (March) − 538.1663 × (June) + 63.1698 × (vapor pressure) − 571.9622 × (September) − 692.6898 × (April) + 96.43405 × (days of relative humidity <60%) − 714.7947 × (November) + 310.7671 × (February) − 596.2406 × (October) − 585.4984 × (July) − 599.8336 × (August) − 516.6195 × (December) + 1719.898

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