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SEASONALITY OF PNEUMONIA ADMISSIONS AND ITS ASSOCIATION WITH CLIMATE: AN EIGHT-YEAR NATIONWIDE POPULATION-BASED STUDY

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The aim of the study was to examine seasonal variability in monthly admissions for community-acquired pneumonia (CAP) in Taiwan. Our study sample comprised 477,541 pneumonia patients in Taiwan between 1998 and 2005, inclusive. Results showed a fairly consistent seasonal pattern of pneumonia admissions, regardless of sex and age, and for the groups combined. Seasonal trends showed a peak in hospitalizations from January through April, followed by a sharp decrease in May and a trough from August through October. The auto-regressive integrated moving average (ARIMA) test found significant seasonality for all age and sex groups and for the whole sample (all $p < 0.001$). After adjusting for seasonality, month, and trends, the ARIMA regression models revealed that the monthly pneumonia admissions rate was significantly associated with ambient temperature, for the total sample, for female groups, and for the 65–74 and ≥75 age groups (all $p < 0.01$). A 1°C decrease in ambient temperature was associated with roughly a 0.03 increase in monthly pneumonia admissions rate (per 10,000 people) for the entire sample. We conclude the monthly pneumonia admissions rate was significantly associated with seasonality, and was higher in periods with low ambient temperatures. (Author correspondence: henry11111@tmu.edu.tw)

Keywords Pneumonia, Seasonality, Ambient temperature, Climate

INTRODUCTION

Community-acquired pneumonia (CAP) is a common infectious illness that causes significant morbidity and mortality worldwide, despite improvements in antibiotic and supportive treatment (Bartlett & Mundy, 1995; Bartlett et al., 2000; Lieberman et al., 1996b; Mandell, 1995;

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Mandell et al., 2003). The reported incidence of radiographically confirmed CAP per year in different populations has varied between 1.3 and 11.6 cases/1,000 inhabitants (Almirall et al., 2000; Gutierrez et al., 2006; Jokinen et al., 1993; Macfarlane et al., 1993; Marrie et al., 1989; Marston et al., 1997; Ortqvist et al., 1990; Santos de Unamuno et al., 1998; Viegi et al., 2006; Woodhead et al., 1987). Approximately 20% of CAP patients require hospitalization (Oosterheert et al., 2003), and 10–35% of admitted patients require treatment in an intensive care unit (ICU) (Ewig et al., 1998; Moine et al., 1994). Reported mortality in such patients is between 20 and 50%. Pneumonia is the sixth most common cause of death in the United States (Bartlett et al., 2000). Similarly, it is the fourth leading cause of death in Taiwan (Taiwan Department of Health, 2009), placing a significant burden on the healthcare system.

Like other pulmonary diseases or cerebrovascular accidents (Lee et al., 2008; Lin et al., 2008; Tsai et al., 2007), seasonal variation in hospitalization rates for CAP (CAP-H) has long been observed by researchers, with the focus of much of the research being on mortality (Donaldson & Keatinge, 2002), specific sub-populations such as the very young (Muller-Pebody et al., 2002) and elderly (Nguyen-Van-Tam et al., 2001), or particular etiological agents (Dowell et al., 2003; Kim et al., 1996; Lieberman et al., 1996a). Studies consistently report distinct seasonal patterns, with peak mortality and morbidity occurring in the winter and troughs in the summer (Carrat & Valleron, 1995; Dowell et al., 2003; Saynajakangas et al., 2001). Variations in the seasonal timing of peaks and troughs by age and sex have also been reported (Crighton et al., 2004; Saynajakangas et al., 2001).

However, previous studies have frequently been characterized by a number of methodological limitations, including short time periods (Dowell et al., 2003; Lieberman et al., 1996a) and small clinical samples (Lieberman et al., 1996a, 1999). We believe that short study periods and small samples do not enable one to determine whether the seasonal variability found for an individual year is incidental or a phenomenon that occurs in other years as well. Moreover, many prior studies have tended to use CAP-H patient samples from selected hospitals, an approach that could clearly leads to selection bias due to variations in practice between hospitals, such as criteria for admissions and number of available beds (Lieberman et al., 1996a, 1999). Furthermore, the majority of population-based studies have also made no attempt to explore the relationship between climatic parameters and CAP-H (Crighton et al., 2004; Saynajakangas et al., 2001). Because previous studies have been mainly conducted in frigid and temperate regions of the world, their results are difficult to generalize to other regions. For example, the climate in tropical and subtropical regions has less extreme variation compared to the summer and winter swings in frigid or temperate zones.

In light of the above, the aim of the study was to examine the seasonal variability of CAP-H in Taiwan, which has a largely subtropical climate, using a time series analysis approach to assess an eight-year nationwide population database. This study set out to investigate the meteorological factors (i.e., ambient temperature, relative humidity, atmospheric pressure, rainfall, and total hours of sunshine) associated with CAP-H, according to age and sex groupings. We used nationwide hospital admissions records from 1998 to 2005, inclusive. To our knowledge, this is the largest and most complete nationwide population-based study to investigate the dependence of CAP-H admissions rates on meteorological conditions in tropical and subtropical regions.

METHODS

Hospitalization Data

This study used hospitalization data from 1998 to 2005 from the Taiwan National Health Insurance Research Database (NHIRD), published by the Taiwan National Health Research Institute. The NHIRD covers all hospitalization and medical benefit claims for about 98% of Taiwan's population of over 23 million, and it is plausibly the largest and most comprehensive population-based health database in the world. The NHIRD provides one primary diagnosis from the International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) and up to four secondary diagnoses for every hospitalization claim. As these were de-identified secondary data, released to the public for research purposes, after consulting with the director of the IRB of our university, the study was exempt from full review; nonetheless, it conforms to the international ethical standards of the journal (Portaluppi et al., 2008).

Study Sample

We selected all adult (≥18 yrs) inpatient claims between January 1998 and December 2005 with a principal admission diagnosis of pneumonia (ICD-9-CM codes 480–483.8, 485–486, and 487.0). We excluded readmissions within 30 days, as these were regarded as the same episode. Ultimately, our study sample comprised 477,541 cases of pneumonia patients for 1998–2005, inclusively.

Population Data

This study used population registry data in Taiwan to compute the monthly incidence of pneumonia per 10,000 people for the period from 1998–2005. For this study, we defined the monthly pneumonia incidence as

the proportion of the total monthly admissions for pneumonia as a fraction of the entire island's population. Population data were obtained from the Population Affairs Administration of the Ministry of the Interior, Taiwan.

Meteorological Data

We used meteorological data, including average monthly ambient temperature, relative humidity, atmospheric pressure, rainfall, hours of sunshine, and maximum and minimum temperatures, from 19 Taiwan Central Weather Bureau (CWB) observation stations. Although the CWB has 26 observation stations across the island, we discarded meteorological data from seven stations located in mountainous regions with very sparse population in order to more closely represent the conditions experienced by the majority of the population. The monthly mean values were then derived by averaging the monthly data from the remaining 19 stations. Because Taiwan is a relatively small island, with a total land area slightly less than 36,200 km^2, we could use monthly mean values for climatic data to explore its association with pneumonia admission rates.

Statistical Analysis

We used the Statistical Package for the Social Sciences (SPSS Statistics 17.0 for Windows, 2007, SPSS, Chicago, Illinois, USA) to perform the analysis. Monthly pneumonia admission rates/10,000 people were calculated over the 96-month span and categorized by sex and age groupings (of 18–64, 65–74, and ≥75 yrs). Seasonality is a general feature of time series patterns, so the seasonality of the pneumonia admission rates was evaluated using the ARIMA method (Auto-Regressive Integrated Moving Average), which describes a univariate time series as a function of its past values. In addition, a series of cross-correlations was used to reveal the association between climatic factors and monthly pneumonia admission rates. We also adopted the ARIMA regression method as a means of evaluating the associations between climatic parameters and monthly pneumonia admission rates, after adjusting for time-trend effect. The selection of the final parameters was based upon the lowest mean absolute percentage error or mean absolute error, allowing us to choose the best model from the family of ARIMA regression models. All p values of < 0.05 were considered statistically significant in this study.

RESULTS

Admission Rates

The number of admissions for pneumonia by year throughout the study period was 47,752 (1998), 55,554 (1999), 56,137 (2000), 60,063

(2001), 62,620 (2002), 56,795 (2003), 61,046 (2004), and 77,574 (2005). These figures correspond to annual admission rates of 31.58, 36.03, 35.76, 37.60, 38.56, 34.47, 36.53, and 45.84 per 10,000 people, respectively. Throughout the study period, the monthly pneumonia admission rates ranged from a low of 1.91/10,000 in November 1998 to a high of 5.64/10,000 in March 2005, with a mean of 3.27/10,000 and a standard deviation of 0.85/10,000. The mean monthly pneumonia admission rate for males was 3.95/10,000 and 2.57/10,000 for females. The mean monthly levels for the five climatic variables across the entire 8-yr study period were 23.12°C temperature, 78.43% relative humidity, 998.88 hPa atmospheric pressure, 183.73 mm rainfall, and 158.27 monthly hours of sunshine.

Table 1 summarizes the profile of the sampled cases. The mean length of stay for sampled admissions was 11.41 days (standard deviation ±13.02 days) and mean hospitalization costs were NT$65,548 (standard deviation ± NT$113,640). The average exchange rate in 2003 was US$1.00 = NT$ 33.50. In total, 60.91% of the admissions were male and 37.86% were ≥75 yrs of age. As for co-morbidities or complications, 19.51% had an additional diagnosis of essential hypertension, 15.32% diabetes, and 12.38% acute respiratory failure. In addition, 10.75% of patients admitted for pneumonia were diagnosed with stroke, 8.10%

TABLE 1 Pneumonia inpatients in Taiwan, 1998–2005 (n = 477,541)

Variable	n (%)
Sex	
Male	290,847 (60.91)
Female	186,694 (39.09)
Age group (yrs)	
18–64	193,924 (40.61)
65–74	102,805 (21.53)
≥75	180,812 (37.86)
Complications or co-morbidities*	
Essential hypertension	93,168 (19.51)
Diabetes	73,159 (15.32)
Acute respiratory failure	59,120 (12.38)
Stroke	51,336 (10.75)
Septicemia	38,681 (8.10)
Chronic airways obstruction, not elsewhere classified	36,627 (7.67)
Renal disease	32,855 (6.88)
Asthma	31,279 (6.55)
Pleurisy	29,130 (6.10)
Chronic bronchitis	25,501 (5.34)
Congestive heart failure	23,208 (4.86)
Anemia	20,916 (4.38)
Pulmonary tuberculosis	18,576 (3.89)
Malignant neoplasm of trachea, bronchus or lung	14,804 (3.10)
Gout	13,276 (2.78)
Fever	7,354 (1.54)

*Only present complications or co-morbidities occurring in over 1.5% of all cases are presented.

septicemia, 7.67% chronic airway obstruction, and 6.88% renal disease. Also, asthma was identified in 6.55% of the patients; 6.10% had pleurisy, 5.34% chronic bronchitis, and 4.86% congestive heart failure. In total, 17.5% of the sampled patients had more than one co-morbidity.

Seasonality

According to the Taiwan CWB, spring occurs in Taiwan from March to May, summer from June to August, autumn from September to November, and winter from December to February. Monthly variations in pneumonia admission rates for each sex group, each age group, and both sex groups combined are presented in Figures 1 and 2. A similar seasonal pattern of pneumonia admissions is apparent for both men and women, each age group, and all groups combined. Hospitalizations were most numerous between January through April, sharply decreased in May, and were least numerous between August through October. Then, an upward trend started in November and peaked again in January. The ARIMA test for seasonality found significance for all age and sex groups and for the whole sample (all $p < 0.001$).

Climatic Influences

Figure 3 depicts the variations of monthly mean ambient temperature, relative humidity, atmospheric pressure, rainfall, and sunshine hours, together with the corresponding monthly pneumonia admission rates. After adjusting for seasonality, month, and trends, the ARIMA regression models (results in Tables 2 and 3) revealed that the monthly pneumonia admissions rate was significantly associated with ambient

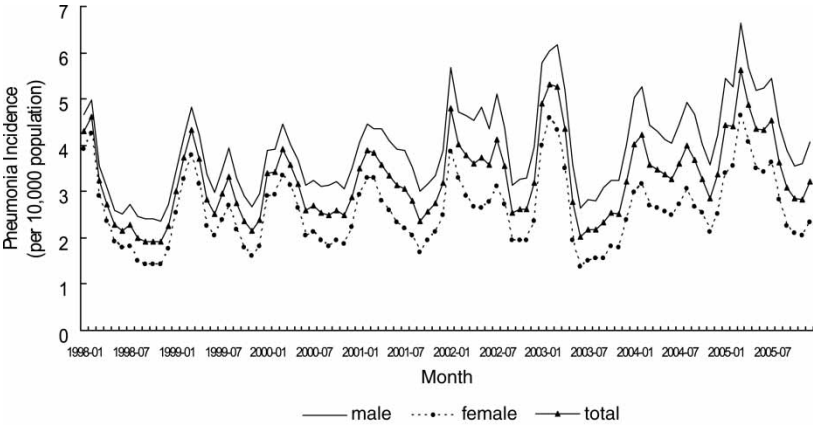

FIGURE 1 Monthly hospitalization rates (per 10,000) for pneumonia in Taiwan, by sex from 1998 to 2005.

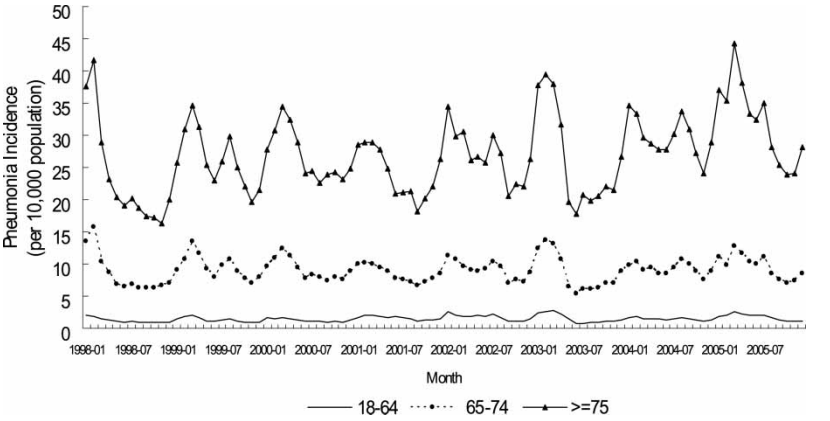

FIGURE 2 Monthly hospitalization rates (per 10,000) for pneumonia in Taiwan, by age, from 1998 to 2005.

temperature for the entire sample, the female group, and for the 65–74 and ≥75 age groups (all $p < 0.01$). Based on the model parameters in Table 2, we can roughly conclude that a 1°C decrease in ambient temperature is associated with a ~0.03 increase in the monthly pneumonia admissions rate (per 10,000 people) for the whole population.

DISCUSSION

This study used an 8-yr population-based dataset to examine seasonal variations in pneumonia admission rates and explore their association with weather conditions in Taiwan. Our results indicate that the monthly pneumonia admission rate was significantly associated with seasonality for all age and sex groups, and it was also significantly associated with ambient temperature for the total sample, females, and the 65–74 and ≥75 age groups.

In the present study, we found that the annual pneumonia admission rate for the year of 2005 was much higher than it was between 1998 and 2004. This could be due to the high rate of influenza occurring in 2005 in Taiwan. According to data released by the Taiwan Centers for Disease Control, the annual consultation rate for influenza-like illnesses reported by general practitioners was noticeably higher in year 2005 compared to previous years (1998 to 2004). We also found that hospitalizations peaked from January to April (late winter and early spring), and a trough appeared from August to October (late summer and early autumn) for all age and sex groups and for the whole sample. Findings from prior studies parallel our own, showing the peak month for hospitalizations for pneumonia to be January and the fewest admissions in August in southern Israel and England (Lieberman et al., 1996a; Nguyen-Van-Tam et al., 2001). Furthermore, the number of pneumonia admissions in winter and

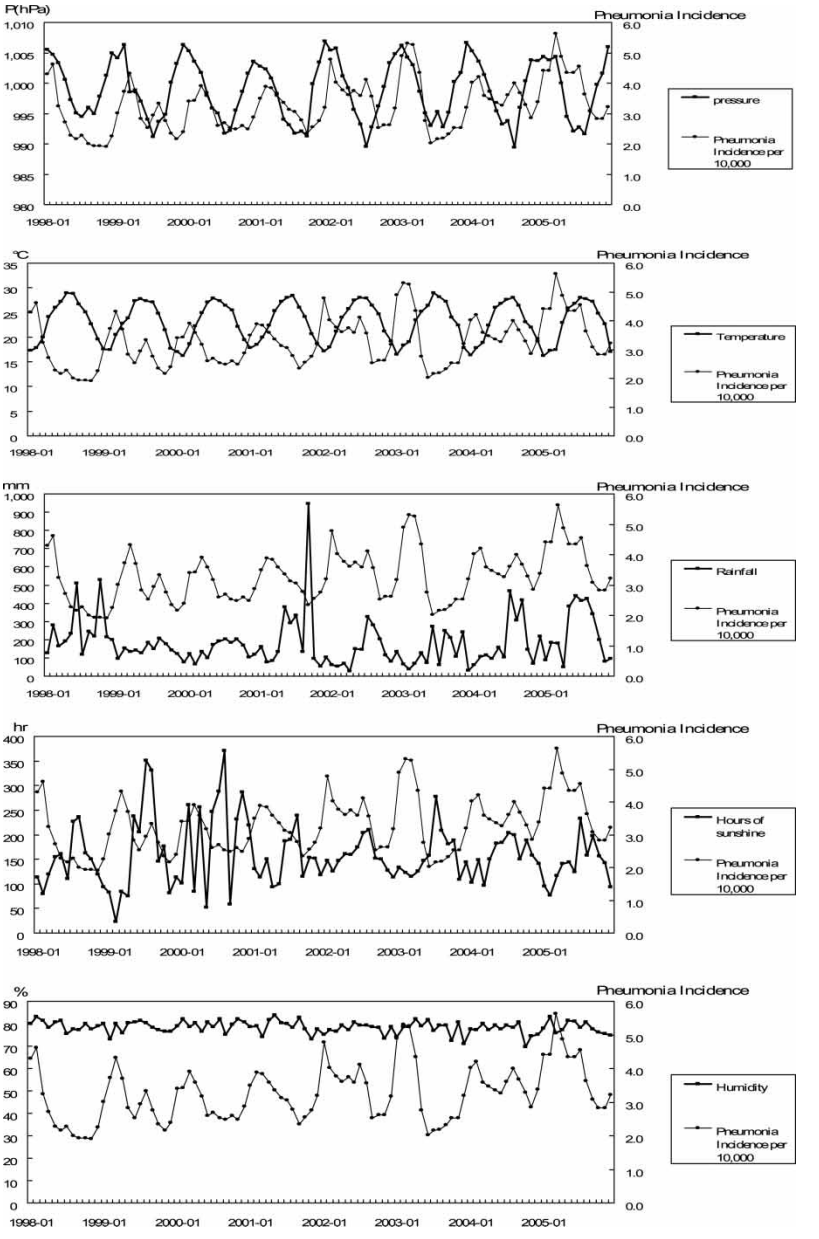

FIGURE 3 Mean monthly trends of climatic factors.

spring was significantly higher than in the summer and fall for all ages and each age group separately in the United States, Finland, Sweden, and France (Carrat & Valleron, 1995; Dowell et al., 2003; Ortqvist et al., 1990; Saynajakangas et al., 2001). The increased presence of circulating pathogens in the winter months may explain this pattern. Most studies show that the most frequent bacteria identified in pneumonia patients was

TABLE 2 ARIMA regression analysis by sex group

Independent variable	Sex group								
	Total			Male			Female		
	β	SE	t-value	B	SE	t-value	β	SE	t-value
Intercept	20.52	22.58	0.91	23.82	29.97	0.79	21.41	17.15	1.25
Atmospheric pressure	−0.02	0.02	−0.73	−0.02	0.03	−0.63	−0.02	0.02	−1.07
Ambient temperature	−0.03	0.01	−2.73†	−0.16	0.09	−1.78	−0.03	0.01	−3.37†
Relative humidity	0.01	0.05	0.28	−0.01	0.09	−0.17	0.03	0.04	0.80
Rainfall	0.01	0.01	1.26	0.01	0.00	1.10	0.01	0.01	1.32
Hours of sunshine	0.01	0.01	0.56	0.01	0.00	0.41	0.01	0.01	0.52
Trend	0.01	0.01	3.71‡	0.02	0.00	4.65‡	0.01	0.01	2.48*
January	1.18	0.18	6.61‡	1.20	0.21	5.71‡	1.14	0.16	7.31‡
February	1.37	0.23	6.05‡	1.35	0.25	5.34‡	1.37	0.21	6.65‡
March	1.30	0.25	5.16‡	1.35	0.28	4.78‡	1.24	0.23	5.39‡
April	0.78	0.33	2.35*	0.89	0.39	2.29*	0.67	0.29	2.29*
May	0.17	0.43	0.40	0.34	0.51	0.65	0.01	0.36	0.02
June	−0.17	0.50	−0.34	−0.04	0.61	−0.06	−0.30	0.42	−0.72
July	−0.06	0.56	−0.11	0.16	0.68	0.23	−0.27	0.47	−0.58
August	−0.22	0.55	−0.41	−0.03	0.67	−0.05	−0.40	0.46	−0.88
September	−0.56	0.48	−1.18	−0.42	0.58	−0.72	−0.70	0.40	−1.75
October	−0.56	0.36	−1.54	−0.50	0.44	−1.15	−0.60	0.31	−1.94
November	−0.53	0.21	−2.47	−0.53	0.26	−2.06	−0.51	0.18	−2.83†
AR1	0.47	0.13	3.63‡	0.49	0.14	3.43†	0.48	0.12	4.06‡
MA1	0.47	0.13	3.75‡	0.34	0.15	2.28*	0.57	0.11	5.36‡
Akaike info criterion (AIC)		0.94			1.25			0.67	
Schwarz criterion (SC)		1.48			1.79			1.20	
R^2		0.86			0.85			0.87	

*$p < 0.05$, †$p < 0.01$, ‡$p < 0.001$

Selection of the final parameters was based upon the lowest AIC and SC. Reference group = December.

Abbreviations: AR1 = autoregressive, lag 1; MA1 = moving average, lag 1.

Streptococcus pneumoniae (Diaz et al., 2007; Lauderdale et al., 2005). The occurrence of *Streptococcus pneumoniae* infection is related to seasons. In the Northern Hemisphere, pneumonia usually peaks between December through February. People with weaker immune systems are at higher risk than others for *Streptococcus pneumoniae* infection; therefore, the monthly pneumonia admission rate is higher in winter.

We also found the monthly pneumonia admissions rate was significantly higher at times of low ambient temperatures. In recent years, influenza viruses have been recognized as a potential common cause of pneumonia in adults (Jennings et al., 2008; Johnstone et al., 2008). One study reported that colder temperatures are associated with increased viral activity in subtropical regions of Brazil (Lowen et al., 2008). Shahid

TABLE 3 ARIMA regression analysis by age group

	Age group								
	18–64 yrs			65–74 yrs			≥ 75 yrs		
Independent variable	β	SE	t-value	B	SE	t-value	β	SE	t-value
Intercept	13.22	13.32	0.99	119.91	80.22	1.49	77.20	186.83	0.41
Atmospheric pressure	−0.01	0.01	−0.85	−0.11	0.08	−1.34	-0.04	0.18	-0.23
Ambient temperature	−0.05	0.04	−1.24	−0.02	0.01	−3.22†	-0.04	0.01	-3.06†
Relative humidity	0.03	0.03	1.00	−0.14	0.15	−0.91	-0.07	0.38	-0.19
Rainfall	0.01	0.01	1.40	0.01	0.01	0.57	0.01	0.01	0.93
Hours of sunshine	0.01	0.01	0.15	0.01	0.01	0.90	0.01	0.01	0.32
Trend	0.01	0.01	2.31*	0.01	0.01	0.69	0.08	0.28	2.99†
January	0.67	0.10	6.50‡	1.96	0.54	3.64‡	7.86	1.41	5.59‡
February	0.78	0.13	5.93‡	2.85	0.63	4.50‡	8.96	1.74	5.14‡
March	0.70	0.15	4.67‡	2.76	0.71	3.89‡	9.00	1.94	4.65‡
April	0.38	0.20	1.91	1.91	0.99	1.92	5.55	2.60	2.13*
May	0.06	0.25	0.22	0.20	1.32	0.15	1.44	3.38	0.43
June	−0.16	0.29	−0.55	−0.51	1.57	−0.32	-0.63	3.97	-0.16
July	−0.17	0.33	−0.54	0.12	1.77	0.07	1.06	4.46	0.24
August	−0.28	0.32	−0.89	−0.16	1.73	−0.09	0.35	4.37	0.08
September	−0.46	0.28	−1.66	-0.90	1.50	-0.60	-2.30	3.80	-0.61
October	−0.42	0.21	−1.98	−0.82	1.12	−0.73	−2.80	2.88	−0.97
November	−0.32	0.12	−2.63*	−0.98	0.66	−1.47	−3.54	1.69	−2.09*
AR1	0.56	0.12	4.62‡	0.52	0.14	3.71‡	0.46	0.13	3.44‡
MA1	0.43	0.13	3.24†	0.27	0.16	1.73	0.43	0.13	3.22‡
Akaike info criterion (AIC)		−0.13			3.12			5.05	
Schwarz criterion (SC)		0.41			3.66			5.59	
R^2		0.84			0.77			0.83	

*$p < 0.05$, †$p < 0.01$, ‡$p < 0.001$

Selection of the final parameters was based upon the lowest AIC and SC. Reference group: December.

Abbreviations: AR1 = autoregressive, lag 1; MA1 = moving average, lag 1.

et al. (2009) demonstrated that influenza virus lost infectivity after 30 min at 56°C, after 1 day at 28°C, but remained viable for more than 100 days at 4°C. This study shows that influenza viruses are more active in low ambient temperatures, which explains, at least in part, why the monthly pneumonia admission rate is higher in cold weather. In addition, seasonal difference in immunity function or crowding may also play a role in seasonality of pneumonia.

Prior studies documented that aging is associated with a higher risk of acquiring pneumonia caused by *Streptococcus pneumoniae* and influenza virus (Gutierrez et al., 2006; Muller-Pebody et al., 2002; Nguyen-Van-Tam et al., 2001). We found that the pneumonia admission rate of the ≥75 yrs age group was higher than other age groups. Weaker immune systems and the higher incidence of infection can explain the higher admissions rate for the ≥75 yrs age group. The World Health Organization states that vaccines are the only available tool to prevent pneumococcal infections. An increase in vaccine coverage from 50–60%

would have resulted in a 5% reduction of the number of deaths observed, with a vaccine effectiveness of 40%, whereas a 13% reduction could be expected for a vaccine effectiveness of 80% (Carrat & Valleron, 1995; Nguyen-Van-Tam et al., 2001).

The strength of our study lies in its longitudinal base and large population size, combined with the use of a comprehensive time-series analysis approach applied to the data of the age and sex subgroups. The method adopted was to fit the ARIMA models with the time series of the pneumonia admission rates; this is a method that has been widely used to examine the association between climate and the incidence of other diseases. The prior literature has noticeably documented the relationship between weather and pneumonia incidence rates using only univariate statistical analyses; however, given the high correlation between the meteorological parameters of each season, univariate analysis is not at all conducive to the identification of significant contributory factors. These results add significantly to our understanding of sex and age differences, as well as overall trends in pneumonia hospitalizations in a subtropical region of the Northern Hemisphere. Unlike prior studies that included participants from diverse ethnic groups, more than 98% of Taiwan's residents are of Chinese Han ethnicity. While the homogenous population may exempt our study from potential confounding by race, it also limits its generalizeability to other ethnic groups.

Several other limitations of this study deserve consideration. First, we were unable to analyze behavioral factors, such as smoking and heavy drinking, which were not available in the databases used. Studies have found that behavioral factors are significantly associated with different age and sex-specific models (Diaz et al., 2007; Ewig et al., 1998; Pereira & Escuder, 1998; Woodhead et al., 1987). Second, the initial clinical symptoms of pneumonia are similar to clinical symptoms of the common cold, which may mean patients delay seeking treatment for the disease. Our study cannot analyze the period between the onset of the clinical symptoms of pneumonia and the start of treatment (i.e., hospitalization date) for this disease. Despite these limitations, we found that the monthly pneumonia admissions rate was significantly associated with seasonality and was higher at times of low ambient temperature. Public heath authorities should provide health education for people preparing them for high pneumonia risk seasons, and they should also provide vaccines to reduce risk of community-acquired pneumonia in winter.

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