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Seasonal Variation in Stroke in the Hunter Region, Australia

A 5-Year Hospital-Based Study, 1995-2000

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Background and Purpose—Seasonal variation in stroke has long been recognized. To date, there are minimal published data on seasonal variations in rates of stroke and subsequent case fatality in the Southern Hemisphere. The aim of this study was to examine stroke seasonality through the use of data from a hospital-based stroke register in the Hunter Region of New South Wales, Australia.

Methods—From July 1, 1995, to June 30, 2000, 3803 stroke events were registered in residents of the Hunter Region, New South Wales, Australia. We analyzed the trend of seasonal and monthly stroke attack rates and case-fatality rates using Poisson regressions with age and sex as covariates.

Results—Stroke attack rates were highest in the winter and lowest in the summer. From February (summer) to July (winter), there was a significant trend in increasing stroke attack rates (rate ratio, 1.07; 95% confidence interval, 1.05 to 1.10; $P<0.001$). This increase was seen mainly in those ≥65 years of age. Case-fatality rates showed similar trends with a 1- to 2-month lag compared with attack rates.

Conclusions—There is an increase in stroke attack rates and case-fatality rate from summer to winter in the Hunter Region, Australia. These trends are similar to those found in the Northern Hemisphere. **(*Stroke*. 2003;34:1144-1150.)**

Key Words: case fatality rate ■ incidence ■ seasons ■ stroke

Seasonal variation in stroke incidence and mortality has been extensively evaluated in many countries of the Northern Hemisphere. Seasonal variation in stroke has been reported in Japan,[1] the United States,[2,3] Canada,[4] and the United Kingdom.[5] Most studies have reported a marked increase in both stroke mortality[2,5–8] and the rate of hospital presentations[1,3,9,10] in the winter. In contrast, no seasonal variation was demonstrated in studies from Yugoslavia[11] and Mexico.[12] Environmental and acquired factors are thought to have a role in this variation. However, our understanding of the specific triggers of these events is limited. Such an understanding may reveal novel links between vascular pathology and environmental factors.

To the best of our knowledge, few studies have been performed to evaluate seasonal variation in Australia or elsewhere in the Southern Hemisphere. More than 20 years ago, Christie[13] observed that stroke incidence was higher in the winter in Australia, and seasonal (winter and spring) peaks of subarachnoid hemorrhage have been demonstrated recently by Feigin et al.[14] These studies were performed in metropolitan areas and in specific stroke subtypes. Uncertainty exists about seasonal variation in other types of stroke. The Hunter Region is a typical coastal region of New South Wales, Australia. It has a population of 521 178 on the basis of the 1996 Australian National Census, with 71 615 (13.7%) ≥65 years of age. The purpose of the present study was to determine whether seasonal variations in stroke rates occur in the Hunter Region. The main hypothesis of this study was that there is a trend of increased stroke attack rates from summer (hottest month, February) to winter (coldest month, July).

Subjects and Methods

Case Ascertainment

The main source of data was hospital discharge statistics entered into the Hunter Region Heart and Stroke Register.[15] All hospitals (15 public, 7 private) in the Hunter Region contribute data to the register, which tracks all hospital stroke admissions in patients who are residents of the Hunter Region who are 20 to 85 years of age (population, 366 354). From July 1, 1995, to June 30, 1998, the discharge diagnoses of all the patients were coded under the World Health Organization's *International Classification of Diseases, 9th Revision* (ICD-9).[16] From July 1, 1998, to June 30, 2000, all patients

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were coded under ICD-10.[17] The data of patients with subarachnoid hemorrhage were not collected until after January 1, 1997.

All stroke patients were included in the Heart and Stroke Register if their primary discharge diagnoses were coded as stroke (ICD-9: 430, 431, 433, 434, 436; ICD-10: I60, I61, I63, I64). Stroke was then classified into 4 groups: (1) ischemic stroke (IS; ICD-9: 433, 434; ICD-10: I63), (2) intracerebral hemorrhage (ICH; ICD-9: 431; ICD-10: I61), (3), subarachnoid hemorrhage (SAH; ICD-9: 430; ICD-10: I60.9), and (4) unspecified stroke (UNSP; ICD-9: 436; ICD-10: I64).

Patients who died outside the hospital system with a death certificate diagnosis of stroke were also included in the study. Patients were excluded from the study if their usual residence was outside the Hunter Region. Two investigators (J.F., Y.W.) inspected all data to ensure that patients who transferred between hospitals were counted as only 1 admission.

Definitions

Seasons

The 4 seasons were defined on the basis of meteorological reports before the study: winter (June through August), spring (September through November), summer (December through February), and autumn (March through May).

Stroke Attack Rate

Monthly stroke attack rate was defined as the average number of strokes occurring in the study period per 100 000 population per month. The seasonal stroke attack rate was defined as the average number of strokes occurring in the study period per 100 000 population per season.

Case Fatality

The monthly 28-day and 12-month case-fatality rates were defined as the proportion of all patients deceased within the 28-day and 12-month periods, respectively, after stroke occurrence. For example, the patients admitted with stroke during September were followed up for 28 days, and the 28-day case-fatality rate in September was the proportion of these patients who died during follow-up. This included the patients who died before they reached hospitals.

Mortality Tracking

The Hunter Area Heart and Stroke Register receives mortality data monthly from the Register of Births, Deaths and Marriages of New South Wales, allowing identification of all deaths among residents of the region. These deaths are then registered to identify out-of-hospital mortality.

Statistical Analysis

Age, sex, and type-specific monthly stroke attack rates were calculated with 95% confidence intervals (CIs) using normal approximation for the Poisson distribution. Because there was no large variation from February (summer in Australia) to February (winter in Australia), the months with the highest and lowest attack rates were chosen as the 2 reference months. The trends in attack rates (from lowest to highest points or vice versa) were evaluated by the rate ratio (RR) from Poisson regression with period (month) used as a continuous variable in the Poisson regression model, adjusting for age and sex. The trends of 28-day and 12-month case-fatality rates were evaluated with the method described above. This measure indicates whether attack rates or case-fatality rates are generally increasing or decreasing over the period and, if so, to what extent. The fitness of the Poisson regression models was examined by a χ^2 goodness-of-fit test.[18]

All analyses were performed with the STATA data analysis system (release 7.0, Stata Corp).

Stroke Diagnostic Accuracy

An assessment of the accuracy of hospital discharge diagnosis coding was undertaken. One hundred medical records with a diagnosis of stroke were randomly selected from the principal teaching hospital of the Hunter Region. One author (Y.W.) reviewed each of these medical records while blinded to the ICD diagnosis and obtained a clinical diagnosis based on the World Health Organization (WHO) definition of stroke.[19] The clinical diagnosis from chart review was considered the gold standard. The diagnoses obtained from hospital discharge data were then compared with this to determine the accuracy of the hospital discharge coding. CT/MRI reports were checked to verify stroke subtype. Of the 100 randomly selected medical records, the discharge diagnosis was incorrectly classified in only 4 medical records, giving a coding accuracy of 96%. In the 4 cases with coding errors, patients actually suffered cerebral infarction, which was verified by CT scans, but were classified as UNSP. In the 100 cases of stroke, the diagnoses were verified by neuroimaging in 97 cases (97%), CT scans in 72 (72%) cases, and MRI scans in 17 cases (17%). Only 3 cases (3%) received neither CT nor MRI scan during hospital stay and were diagnosed completely according to the WHO definition of stroke.

Ethical Considerations

The method of data collection used by the Heart and Stroke Register was approved by the Hunter Area Research Ethics Committee and the Human Research Ethics Committee of the University of Newcastle.

Results

Overall, 3803 cases of stroke were recorded in the Heart and Stroke Register between July 1, 1995, and June 30, 2000. The mean$\pm$SD age of the patients was 71$\pm$12 years.

Attack Rates by Season and Month

The crude seasonal stroke attack rate was highest in winter (57 per 100 000 population; 95% CI, 50 to 65) and lowest in summer (48 per 100 000; 95% CI, 41 to 55). Table 1 shows the monthly attack rates for total stroke and the subtypes. Total stroke monthly attack rate was highest in July (the high-peak winter month; 20 per 100 000; 95% CI, 16 to 25) and lowest in February (the low-peak summer month; 13 per 100 000; 95% CI, 10 to 18). There was a strong trend of increasing attack rates from February to July (Figure 1). When Poisson regression adjusted for age and sex was used, this trend was highly significant (RR, 1.07; 95% CI, 1.05 to 1.10; $P<0.001$) (Table 2). The goodness-of-fit test has a value of $P=0.619$, suggesting that there is no evidence of lack of fit. There was also a statistically significant trend of decreasing stroke attack rates from August to January. The RR for the decrease in attack rates was 0.97 (95% CI, 0.95 to 0.99; $P=0.006$) (Table 2). The goodness-of-fit test, however, suggests that the model did not fit the data well ($P=0.016$).

The age-specific total stroke attack rates are shown in Figure 2. Poisson regression models were also fitted for each age category of total stroke (Table 3). Seasonal trends were not obvious within the younger patient groups (20 to 44, 45 to 54, and 55 to 64 years of age), probably because of smaller numbers. There was a significant or nearly significant trend of increasing and decreasing stroke attack rates in the older age categories (65 to 74 and 75 to 85 years of age). The probability values of the goodness-of-fit test for each Poisson regression model are shown in Table 3. Except for the age group of 65 to 74 years from July to January, which has a value of $P=0.002$, all the Poisson regression models fit the data reasonably well.

TABLE 1. Stroke Attack Rates and Case Fatalities in the Hunter Region, Australia, 1995 Through 2000

	Total, %	IS, %	ICH, %	SAH, %	UNSP, %
Stroke attack rate per 100 000 per month					
Summer					
Jan	16.1	6.9	1.9	0.7	6.6
Feb	13.3	6.6	1.4	0.6	4.7
Autumn					
Mar	15.6	8.2	1.8	0.2	5.4
Apr	15.3	7.0	2.0	0.7	5.7
May	17.5	7.7	2.0	0.8	7.0
Winter					
Jun	17.4	6.8	2.2	0.5	7.9
Jul	19.9	8.8	2.7	0.8	7.6
Aug	19.8	8.1	2.1	0.7	8.9
Spring					
Sep	17.4	6.6	2.6	0.6	7.6
Oct	19.5	7.4	2.4	0.9	8.8
Nov	17.4	6.8	2.4	0.7	7.5
Summer					
Dec	18.4	7.6	2.4	0.3	8.1
28-day case-fatality rate					
Summer					
Jan	26.9	19.8	48.6	61.5	24.2
Feb	30.0	20.8	52.0	36.4	35.6
Autumn					
Mar	23.9	18.7	39.4	25.0	26.5
Apr	27.0	17.2	44.4	53.8	29.8
May	29.3	18.4	51.4	46.7	32.8
Winter					
Jun	29.2	16.0	37.5	33.3	38.2
Jul	28.8	22.4	46.9	53.3	27.1
Aug	34.4	21.5	50.0	38.5	42.3
Spring					
Sep	34.8	19.8	55.3	54.5	39.3
Oct	35.5	26.5	43.2	68.8	37.7
Nov	29.5	19.4	45.5	69.2	29.7
Summer					
Dec	33.2	19.4	59.1	50.0	37.8
12-month case-fatality rate					
Summer					
Jan	37.1	31.7	57.1	69.2	33.3
Feb	42.0	35.0	60.0	45.5	46.0
Autumn					
Mar	32.3	29.3	48.5	25.0	31.6
Apr	38.4	32.0	52.8	53.8	39.4
May	37.1	29.8	51.4	46.7	39.8
Winter					
Jun	39.9	26.4	50.0	33.3	49.3
Jul	41.4	36.0	59.2	53.3	40.0
Aug	41.9	30.9	55.3	38.5	49.1
Spring					
Sep	43.6	28.9	61.7	72.7	47.9
Oct	42.5	36.0	47.7	75.0	43.2
Nov	35.7	25.8	52.3	69.2	36.2
Summer					
Dec	44.5	33.1	61.4	50.0	50.0

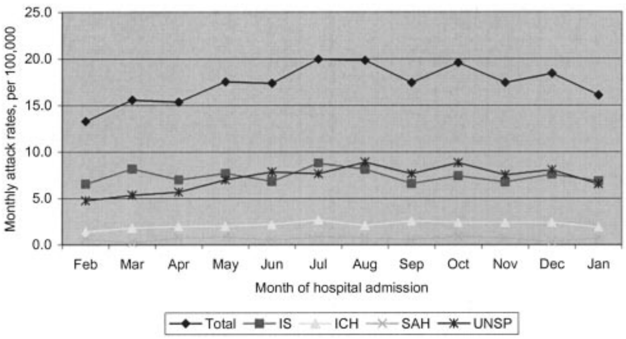

Figure 1. Monthly variation of stroke attack rates in the Hunter Region, Australia, 1995 through 2000.

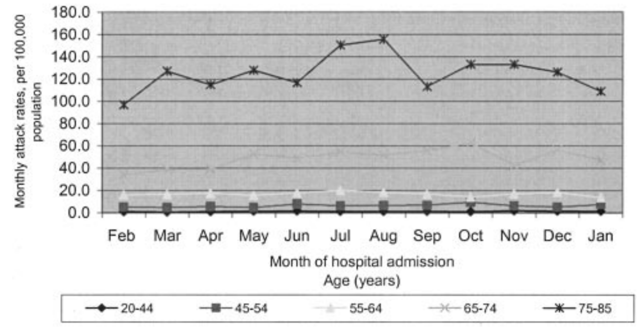

Figure 2. Age-specific monthly attack rates for men in the Hunter Region, Australia, 1995 through 2000.

Attack Rates in Subtypes of Stroke

Stroke attack rates for IS, ICH, SAH, and UNSP are shown in Table 1 and Figure 1. Besides UNSP, for which the attack rate was highest in August, all the other subtypes of stroke had peak attack rates in July. The numbers of stroke events in IS and UNSP were similar, however, with different distribution throughout the year (Table 2). The number of IS events was higher from February to July, whereas the number of UNSP events was higher from September to January.

Poisson regression models were also fitted to subtypes of stroke (Table 2). The same seasonal trends were seen for each subtype of stroke, although only some reached statistical significance. Goodness-of-fit tests suggest that the Poisson regression models for the subtypes of stroke had a very good fit for the data. IS showed a significant trend of decreasing attack rates from August to January (RR, 0.97; 95% CI, 0.95 to 0.99). ICH also showed a trend of increasing attack rates from February to July (RR, 1.12; 95% CI, 1.03 to 1.21); however, the number of patients was much smaller. UNSP showed a strong trend of increasing attack rates from February to August (RR, 1.11; 95% CI, 1.08 to 1.15) and decreasing attack rates from September to January (RR, 0.95; 95% CI, 0.90 to 0.99).

Case Fatality

The monthly variations for the 28-day and 12-month case-fatality rates are shown in Table 1 and Figure 3. Compared with those of stroke attack rates, the trend of case-fatality rates had a similar pattern but with a 1- to 2-month lag. After the lowest point of stroke attack rates in February, the 28-day case-fatality rate was lowest in March. After the peak of stroke attack rates in July, the 28-day case-fatality rate was highest in September. The trend of increasing case fatality from March to September was highly significant, with an RR of 1.52 (95% CI, 1.46 to 1.58; $P<0.001$). The trend of decreasing case fatality from October to the following February was also highly significant, with an RR of 0.76 (95% CI, 0.73 to 0.80; $P<0.001$). The 12-month case-fatality rate followed the same pattern as the 28-day case fatality. Poisson regression indicated a trend of increasing attack rate from

TABLE 2. Evaluation of Trends in Stroke Attack Rates in the Hunter Region, Australia, by Poisson Regression*

	Stroke, n	RR	95% CI	*P*	Goodness-of-Fit Test
Total					
Feb–Jul	1813	1.07	1.05–1.10	<0.001	0.619
Aug–Jan	1990	0.97	0.95–0.99	0.006	0.016
IS					
Feb–Jul	825	1.03	0.99–1.07	0.126	0.251
Aug–Jan	795	0.97	0.94–0.99	0.042	0.119
ICH					
Feb–Jul	220	1.12	1.03–1.21	0.006	0.422
Aug–Jan	252	0.97	0.92–1.03	0.355	0.235
SAH					
Feb–Jul	67	1.1	0.95–1.27	0.187	0.167
Aug–Jan	72	0.95	0.85–1.06	0.335	0.347
UNSP					
Feb–Aug	701	1.11	1.08–1.15	<0.001	0.170
Sep–Jan	871	0.95	0.90–0.99	0.037	0.450

*This table shows a summary of the results of the evaluation of trend in attack rates by Poisson regressions adjusted for age and sex. The reference population is 366 354 (20 to 85 years of age).

TABLE 3. Evaluation of Trends in Stroke Attack Rates in Different Age Categories in the Hunter Region, Australia, by Poisson Regression

Period	Age, y	Stroke	Population, n	RR	95% CI	*P*	Goodness-of-Fit Test
Feb–Jul	20–44	62	191 429	1.16	1.00–1.35	0.046	0.549
Jul–Jan		80	191 429	1.05	0.95–1.17	0.322	0.779
Feb–Jul	45–54	109	64 366	1.08	0.96–1.20	0.188	0.454
Jul–Jan		134	64 366	1.00	0.93–1.09	0.936	0.382
Feb–Jul	55–64	232	45 042	1.04	0.96–1.12	0.336	0.995
Jul–Jan		221	45 042	0.96	0.91–1.02	0.198	0.198
Feb–Jul	65–74	567	42 517	1.10	1.05–1.15	<0.001	0.559
Jul–Jan		670	42 517	0.98	0.95–1.02	0.325	0.002
Feb–Jul	75–85	843	23 000	1.06	1.02–1.11	0.003	0.317
Jul–Jan		885	23 000	0.95	0.93–0.98	0.003	0.488

*This table shows a summary of the results of the evaluation of trend of attack rates by Poisson regressions adjusted for sex.

March to September (RR, 1.08; 95% CI, 1.04 to 1.13; $P<0.001$) and a decreasing rate from October to February (RR, 0.95; 95% CI, 0.90 to 0.99; $P=0.028$). When the case fatalities for only hospital presentations were evaluated (excluding the patients who died before hospital admission), the 28-day and 12-month case fatalities showed similar trends (not shown). All the goodness-of-fit tests (not shown) suggest that the Poisson regression models fit the data well.

Discussion

The present study demonstrates a clear seasonal and monthly variation in the occurrence of all stroke events in both sexes. The stroke attack rate was highest in July (winter in Australia) and lowest in February (summer in Australia). This pattern seemed to hold for all age groups, although statistical significance was reached for those subgroups with the largest numbers, ie, ≥65 years of age.

Seasonal variation (peak stroke incidence in winter) has been found in many countries in the Northern Hemisphere.[20–22] However, stroke seasonal variations in countries of the Southern Hemisphere have received less attention. The relatively mild weather throughout the year in Australia may be the reason. The findings of the present study, together with another Australian study conducted 20 years ago,[23] strongly suggest the seasonality of stroke in Australia or even the Southern Hemisphere. This seasonality appeared to hold for all subtypes of strokes, although significance was again reached only in the groups with the largest numbers, ie, IS and UNSP. Point estimates for ICH and SAH also indicated the same seasonal patterns. This is congruent with the findings of an Australasian study of SAH rates,[14] although some other studies have not demonstrated seasonality with SAH.[1,22]

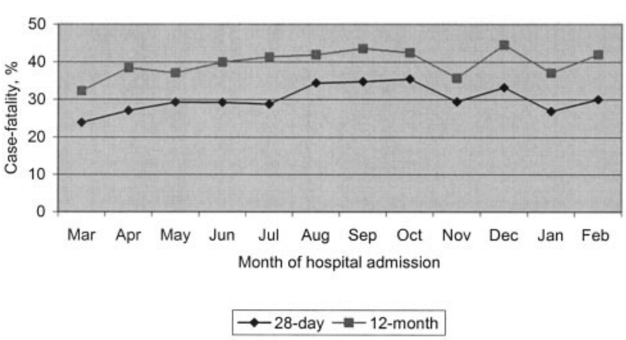

Figure 3. Monthly variation of case-fatality rates in the Hunter Region, Australia, 1995 through 2000.

The stroke attack rates appear to increase linearly from February to July, in which Poisson regression is an appropriate tool for analysis. From August to January, there were some slight variations in stroke attack rates, especially in the 65- to 74-year-old group. This could explain the lack of good fit in this age group and this period.

The biological reasons for the higher occurrence of strokes during the winter are not known, but several mechanisms may be suggested. First, the seasonal variation of blood pressure is well known, with blood pressure being higher in winter,[24] perhaps because of cold-induced peripheral blood vessel constriction.[24,25] Elevated blood pressure during the winter may be the trigger for ICH and IS. Second, total cholesterol and triglycerides tend to be higher in winter than in summer.[26] Third, and perhaps more important, plasma fibrinogen concentration and viscosity show considerable seasonal variation, at least in elderly persons,[27,28] and there is evidence that fibrinogen is a significant predictor of stroke.[29] Fourth, infection, particularly influenza epidemics and other respiratory tract infections,[30,31] may also play a role. Influenza may cause some complications in atherosclerotic disease and induce hypercoagulation.[32] In Australia, the peak influenza activity was coincident with the peak in stroke attack rates and case fatality, being highest in winter and early spring (July, August, and September).[33–35] Older people are more sensitive to environmental changes and are more likely to suffer from respiratory infection during winter. In our study and in others,[3,36,37] seasonality was strongest in those ≥65 years of age. Previous literature has reported that seasonal differences in cerebral infarction and myocardial infarction are greater in older than in younger age groups.[38–40]

The 28-day and 12-month case-fatality rates showed trends similar to those of the attack rates. However, it is interesting to note the time lag of 1 or 2 months between the surges of hospital presentations of stroke and case fatalities. The 28-day case-fatality rate was highest in September (spring in Australia), although hospital presentations were beginning to decline. It is noticeable that these trends were evident for both hospital presentations and total stroke events (including those who died outside the hospital system). This interesting phenomenon of case fatality may be explained by the higher prevalence of infection (eg, pneumonia and influenza epidemics) in winter and spring.[33–35,41] It has been demonstrated that recent infection is associated with a more severe post-stroke deficit[42] and higher mortality.[43] Several studies have concluded that the winter and spring excess of stroke mortality is due to an increase in patient case fatality as a result of superimposed acute respiratory illness.[5–7,44]

We acknowledge some caveats in our hospital-based study. One of the major limitations of the study is that we have not determined the proportion of patients who were treated outside the hospital system. The North East Melbourne Stroke Incidence Study (NEMESIS) study demonstrated that the proportion of patients treated outside the hospital system was relatively small (5%).[45] This is expected given the free public health system in Australia. To minimize this selection bias, we included the patients who died outside the hospital system.

The other potential limitation of hospital-based stroke registers using medical record coding is the possibility of coding errors. In the sample evaluated, however, the occurrence of coding errors was very low (4%). The reason is probably that the medical records in only 1 hospital were selected, and this hospital is the main tertiary referral hospital. The coding errors in other regional hospitals may be higher because some of these hospitals did not have access to CT and MRI. However, this is unlikely to change results substantially because it has been found that the positive predictive value of hospital coding is 90% in primary tertiary care hospitals and 80% in community hospitals.[46]

The hospital stroke attack rates reported in the present study may not be as accurate as stroke incidences reported from large community-based studies. However, community-based studies are very time and resource intensive. We suggest that hospital-based registers can still be used to monitor trends and hospitalization and are a low-cost method of obtaining local health services data. Because the Hunter Region is a typical coastal region in Australia and 90% of Australian population lives in the coastal areas, our study may be generalizable to other groups and locations and may reflect the hospital burden of stroke.

In conclusion, we noted a significant trend toward higher stroke attack rates in winter in the Hunter Region, Australia. The increase in attack rate was particularly prominent in the older population. The case-fatality rates changed 1 to 2 months after the change in stroke attack rates. The biological mechanisms for these variations remain uncertain but may be important in increasing our understanding of this important disease.

Acknowledgments

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