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Seasonal and Monthly Variation in Stroke and its Subtypes–10 Year Hospital-Based Study

Ahmad Bahonar[1], Alireza Khosravi[2], Fariborz Khorvash[1], Mohammadreza Maracy[3], Mohammad Saadatnia[1]

[1]Isfahan Neurosciences Research Center, Alzahra Hospital, Isfahan University of Medical Sciences, Isfahan, Iran.

[2]Isfahan Cardiovascular Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran.

[3]Department of Epidemiology &Biostatistics, School of Health, Isfahan University of Medical Sciences, Isfahan, Iran

Corresponding author:
Mohammad Saadatnia, Isfahan Neurosciences Research Center, Alzahra Hospital, Isfahan University of Medical Sciences, Isfahan, Iran.
Tel: +98 (0)31 36201250, Fax: +98 (0)311 36201250, E-mail: mosaadatnia@yahoo.com

ABSTRACT

Background and Objectives: there is no evidence of long-term studies of seasonal variations in stroke in Iran. Hence, the aim of this study was to determine the seasonal and monthly variation of 28-day mortality in Isfahan, Iran. **Methods:** From 2003 to 2013, In a Hospital-based retrospective study which was conducted by Isfahan Cardiovascular Research Center(ICRC), 24186 cases with first-ever stroke were recruited. Multinomial logistic regression was used to calculate odds ratios (OR) with 95% confidence intervals (CI) for seasonal and monthly 28-day mortality for stroke in general and three subtypes of stroke including intracranial hemorrhage (ICH), ischemic (IS) and subarachnoid hemorrhage (SAH). **Results:** In this study, unadjusted and adjusted odds ratios of seasonal 28-day mortality of stroke was highest in the winter and lowest in the summer. Although, differences were not statistically significant. For total and IS stroke, the unadjusted 28-day mortality ratio (UMR) was significant in February (1.19, 95% CI 1.00 -1.42, P= 0.04) as compared to March. Whereas after adjusted, for total stroke, 28-day mortality was significantly lowest in May (0.746, 95% CI 0.575-0.97, p=0.029), june (0.777, 95% CI 0.60-0.99, p=0.49) and july (0.771, 95% CI 0.59-0.99 p=0.049) as compared to March. The AMR between months were not significant in SAH and IS. **Conclusion:** Our findings demonstrate clear obvious monthly variation of 28-day mortality of stroke and its subtypes in Isfahan but no seasonal variations were observed.

Keywords: intracranial hemorrhage, ischemic, subarachnoid hemorrhage, mortality.

1. INTRODUCTION

Stroke is one of the main leading cause of 28-day mortality and disability in world (1). Evidence from epidemiological studies on the stroke and its subtypes have indicated association with biological (2) , physiological (3), socioeconomic status (4) and environmental factors (5). Over the last three decades, seasonal and monthly variation in the incidence and mortality stroke have been widely investigated in different geographical and climatic conditions (6-8). Nevertheless, findings in many cases are variable and sometimes contradictory. Numerous studies have demonstrated that stroke occurs often during the coldest months in winter and spring. Conversely, others found that the highest incidence and mortality of stroke occurs in summer and autumn as the warmest season of the year whereas, some studies revealed no seasonal and monthly variations in incidence and mortality of stroke. Seasonal variations among stroke subtypes have also been demonstrated by a few studies (6, 9, 10).

Data from an Iranian study indicate high stroke incidence and 28-day mortality in a metropolitan city of Iran, so that the age-adjusted hospital admission rate of stroke was increasing from 84.16 to 103.23/100,000 between 2000 and 2003, however the rate of 28-day case fatality had no changes (10). Nevertheless, despite such a high incidence of stroke, to our knowledge, no comprehensive studies have been performed about seasonal and monthly variation in stroke and its subtypes in Iran.

Therefore, in the current study, we investigated the seasonal and monthly variations of incidence

and 28-day mortality of stroke using the data base of a hospital-based stroke registry from Isfahan cardiovascular research center(ICRC) surveillence unit with over a 10-year period in rural and urban areas of Isfahan province, Iran. Isfahan as one of the metropolitan cities is located in the center of Iran and has an arid cool climate with hot summer and cool winter (11).

We also sought to examine seasonal and monthly variability in the incidence and 28-day mortality of the three subtypes of stroke including intracranial hemorrhage (ICH), ischemic (IS) and subarachnoid hemorrhage (SAH).

2. METHODS

In a Hospital-based retrospective study which was conducted by ICRC (a WHO Collaborating center), 24186 cases with first-ever stroke who admitted to eight hospital were recruited. The data were analyzed for this study by Isfahan neuroscience research center. All the necessary information included age, sex, date of admission, date of deaths both in and outside of hospital were recorded. Strokes, according to WHO definition, were diagnosed (12) and classified into three subtypes, IS (ischemic), ICH (intracranial hemorrhage) and SAH (subarachnoid hemorrhage) (13). Four seasons including spring (March, April and May), summer (June, July and August), autumn (September, October and November) and winter (December, January and February) were considered in this analysis.

Statistical Methods

Characteristic	Type of stroke No. (%)			
	IS	ICH	SAH	total
	N(%)	N(%)	N(%)	
	18413 (80.2)	4329 (17.9)	569 (2)	23311
Mean age ± SD, yr	70.6 ±14.5	66.9 ±14.7	55.9 ±16.3	69.5 ±14.8
Age group (yr)	N(%)	N(%)	N(%)	
‹45	806 (61.9)	351 (26.9)	144 (11.1)	1301
45-65	4828 (74.5)	1397 (%21.6)	256 (3.9)	6481
›65	12791 (82.4)	2586 (16.6)	171 (1.1)	15548
gender				
Men	9378 (79.2)	2191 (18.2)	264 (2.2)	11833
women	9047 (78.7)	2143 (18.6)	307 (2.7)	11497
Cardiovascular risk factors				
TIA (yes)	5031 (84.2)	894(14.9)	47(0.8)	5972
Diabetes(yes)	6208(86.5)	910(12.7)	62(0.9)	7180
Elevated blood pressure(yes)	12071(78.2)	3102(20.1)	268(1.7)	15441
Hearth attack(yes)	6926(85.1)	1119(13.7)	97(1.2)	8142
Hyperlipidemia(yes)	3367(84.2)	582 (14.5)	50 (1.2)	3999
Cigarette(yes)	1502 (80.8)	282 (15.2)	74 (3.9)	1858

Table 1 . Characteristics of stroke patients in Isfahan province,Iran, 2003 - 2013.

Data Characteristics of stroke patients were presented mean ± standard deviation for age and number (percentage) for other variables. Binary logistic regression was used to calculate odds ratios (OR) with 95% confidence intervals (CI) for seasonal and monthly 28-day mortality of stroke in total as well as ICH, SAH and IS Separately. OR were estimated for seasonal models with spring as a reference and for monthly models with March as a reference.

A significance level of 0.05 was considered statistically significant. All statistical analysis was performed using SPSS for Windows, version 19.0 (SPSS Inc, Chicago, IL).

	28-day mortality				
		Unadjusted Odds ratio (95% CI)	p	Adjusted Odds ratio (95% CI)*	p
Stroke					
	Spring	1 (Reference)		1 (Reference)	
	Summer	0.959 (0.879-1.048)	0.356	0.955 (0.827-1.102)	0.528
	Autumn	1.015 (0.931- 1.106)	0.742	1.049 (0.912-1.208)	0.501
	Winter	1.089 (0.994-1.194)	0.067	1.150 (0.991-1.334)	0.065
SAH					
	Spring	1 (Reference)		1 (Reference)	
	Summer	0.881 (0.520-1.492)	0.638	0.802 (0.410-1.568)	0.519
	Autumn	0.775 (0.471-1.276)	0.316	0.628 (0.336-1.1777)	0.147
	Winter	0.879 (0.497-1.555)	0.658	0.708 (0.348-1.442)	0.341
ICH					
	Spring	1(Reference)		1(Reference)	
	Summer	1.009 (0.833-1.223)	0.924	0.894 (0.647-1.236)	0.499
	Autumn	1.062 (0.884-1.277)	0.520	1.055 (0.774-1.440)	0.734
	Winter	1.088 (0.899-1.318)	0.384	1.088 (0.791-1.495)	0.605
IS					
	Spring	1(Reference)		1 (Reference)	
	Summer	0.984 (0.848-1.059)	0.343	0.913 (0.764-1.092)	0.319
	Autumn	0.972 (0.870-1.085)	0.613	0.946 (0.793-1.130)	0.542
	Winter	1.007 (0.895-1.133)	0.912	0.971 (0.802-1.176)	0.765

Table 2. Odds ratios for 28-day mortality of stroke and its subtype in summer, autumn, and winter setting spring as a reference ICH = intracranial hemorrhage, IS = ischemic stroke, SAH = subarachnoid hemorrhage *Adjusted for age, sex, living area and Cardiovascular risk factors including TIA, Diabetes, Elevated blood pressure, Hearth attack, Hyperlipidemia and Cigarette.

3. RESULTS

Demographic Characteristics and risk factor of study patients by stroke subtypes are presented in Table 1. Of the 23311 stroke patients studied (men, 11833; women, 11497), 18413 (80.2%) had IS stroke, 4329 (17.9%) had ICH stroke and 569 (2%) had SAH stroke. The mean ±standard deviation age of all patients were 69.46±14.87 years that IS stroke patients had the highest mean age (70.56 ±14.47). Most of the patients were in the age group of 65 years and above. Among the Cardiovascular risk factors, blood pressure had greater proportion than others risk factor.

The unadjusted and adjusted odds ratios (% 95 CI) for the 28-day mortality of stroke and its subtype in summer, autumn and winter (spring as a reference) are presented in Table 2. The unadjusted odds ratios of seasonal 28-day mortality of stroke was highest

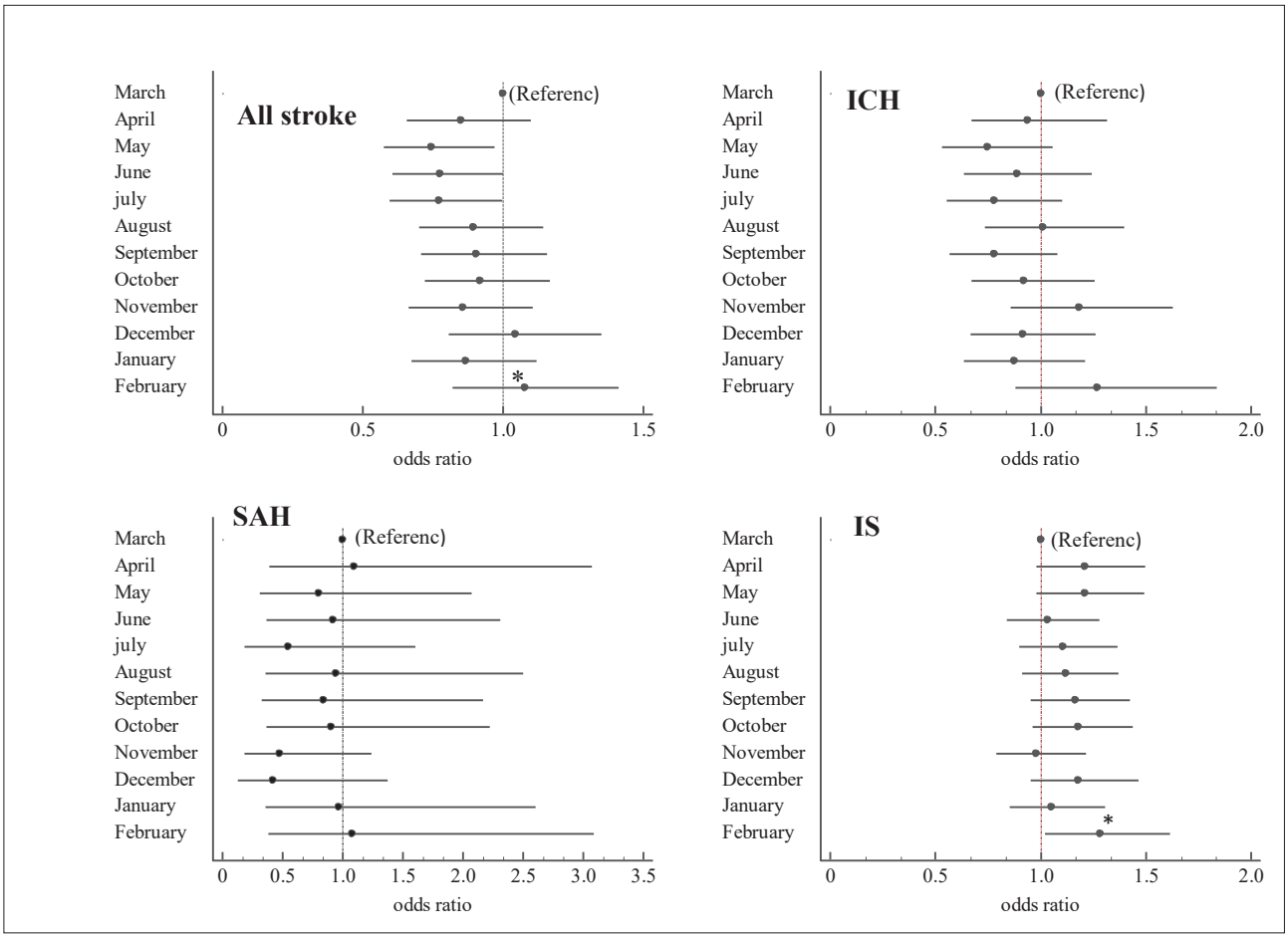

Figure 1. Unadjusted Odds ratios with 95% confidence intervals for monthly 28-day mortality of stroke in general and ICH (intracranial hemorrhage), IS (ischemic stroke) and SAH (subarachnoid hemorrhage). An asterisk indicates statistical significance compared to March as a reference

in the winter (1.089; 95% CI, 0.994-1.194) and lowest in the summer (0.959; 95% CI, 0.879-1.048). After adjusted for age, sex, living area and Cardiovascular risk factors, the highest OR was observed in the winter (1.150; 95% CI, 0.991-1.334) and lowest in the summer (0.955; 95% CI, 0.827-1.102). However, No significant association was found between seasonality and 28-day mortality of stroke. The OR for the 28-day mortality of SAH stroke was higher in spring than in any other season, whereas in IS and ICH stroke, OR was highest in winter. but the differences was not statistically significant (P>0.05).

The unadjusted Odds Ratio and 95% Confidence Interval of monthly variations for 28-day mortality of total stroke and its subtype with March as a reference are shown in Figure 1.

For total stroke, The unadjusted 28-day mortality ratio (UMR) was only significant in February (1.19, 95% CI 1.00 -1.42, P= 0.04) as compared to March. The lowest UMR of total stroke was seen in May)0.92, 95% CI 0.789 -1.089, P= 0.357). The UMR of ICH and SAH showed no significant variation by Months (p>0.05). For IS, the UMR was only significantly higher in February (1.28, 95% CI 1.021-1.614, P= 0.03) than in March.

Figure 2 shows adjusted 28-day mortality ratio (AMR) with 95% confidence intervals for monthly incidence of total stroke and its subtype with March as a reference. For total stroke, the AMR was significantly lowest in May (0.746, 95% CI 0.575-0.97, p=0.029), June (0.777, 95% CI 0.60-0.99, p=0.49) and July (0.771, 95% CI 0.59-0.99 p=0.049) as compared to March. The highest AMR for all strok types was observed in February (1.077, 95% CI 0.821-1.41), although not statistically significant (p=0.59). For ICH, the AMR was significantly lowest in july (0.502, 95% CI 0.283- 0.891, p=0.018) and may (0.543, 95% CI 0.30- 0.984 p=0.044) as compared to March. The AMR between months were not significant in SAH and IS.

4. DISCUSSION

In this study, we investigated monthly and seasonal variations in the 28-day mortality of stroke and three main subtypes, in more than 20,000 stroke patients registered in the Surveillence unit in ICRC between 2003 and 2013. To our knowledge, this is the largest study of monthly and seasonal patterns of stroke so far conducted in Iran.

The present study showed monthly variation in 28-day mortality of all stroke and some its subtypes, but no seasonal variations were observed. Nevertheless, it seems odds of the strokes 28-day mortality were highest in winter and lowest in summer. In accordance with our finding, several studies found that the mortality of stroke was highest in winter and lowest in summer (7, 14-18).

The weather in Isfahan follows distinct seasons. Mean temperatures between 2003 and 2013 in Isfahan for winter were 4.99 C°which was the coldest season of the year. It's somewhat well documented that cardiovascular diseases

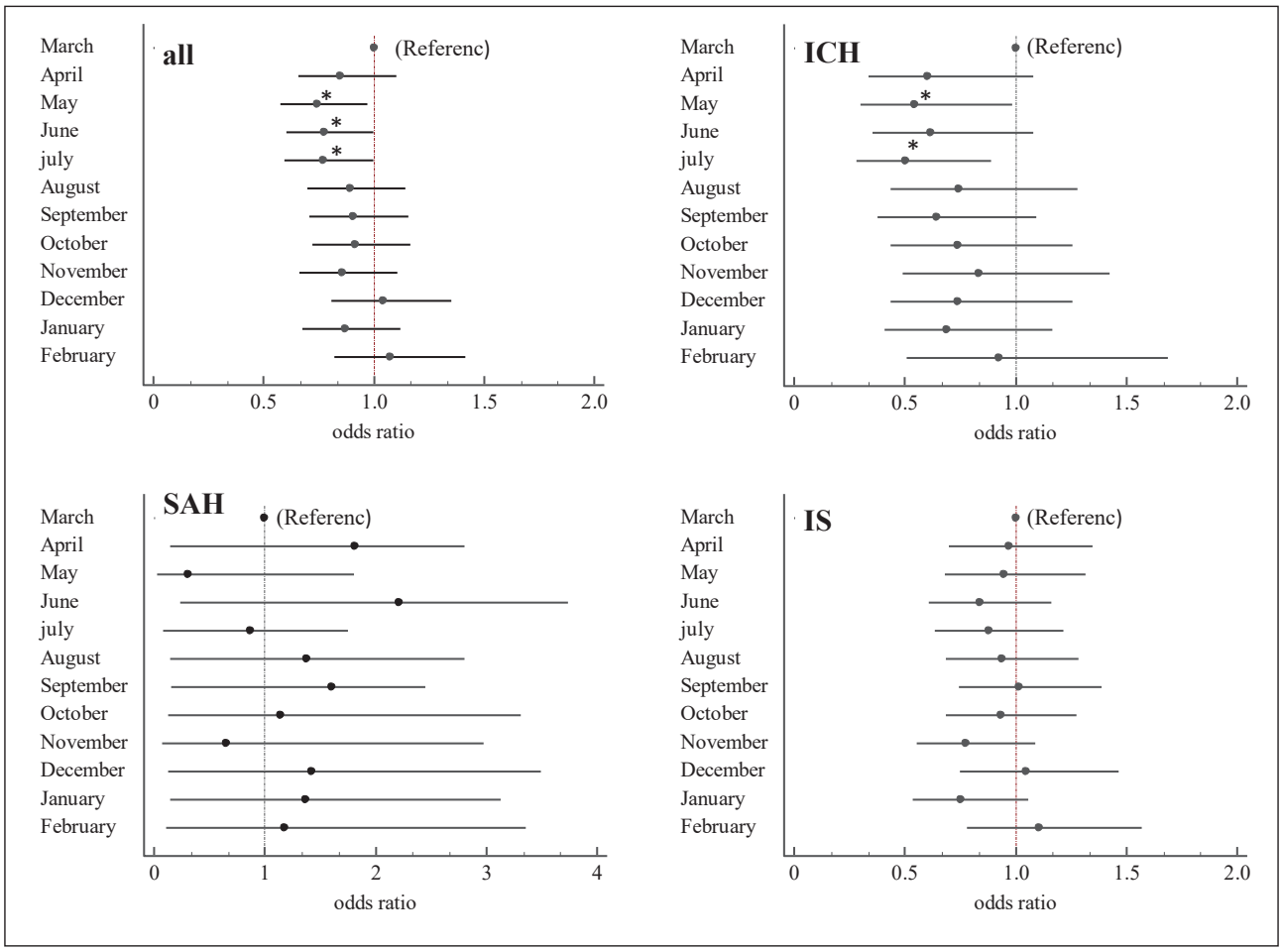

Figure 2. Adjusted Odds ratios with 95% confidence intervals for monthly 28-day mortality of stroke in general and ICH (intracranial hemorrhage), IS (ischemic stroke) and SAH (subarachnoid hemorrhage) An asterisk indicates statistical significance compared to March as a reference

rises during winter (19). it is assumed that cold weather played an important role in the occurrence of this phenomenon. A study in 21 countries showed that Rates of coronary events during winter was increased about 10% (20). Increased blood pressure (6, 21), incidence of influenza and other respiratory disease (16), decreased physical activity (22) and increased cholesterol and triglyceride (23) has been considered to be the likely main reasons for high incidence and mortality of stroke in the winter.

Although the difference was not statistically significant, the stroke subtypes showed somewhat similar seasonal pattern with the peak 28-day mortality in winter/spring and the lowest in summer. Apart from statistical significance, (24) showed that the 30 day mortality of IS was higher in winter and the lowest in the summer. Several studies found a seasonal variation in the mortality of subtypes of stroke with varied and sometimes contradictory results (16, 17, 25-27). Similar to our results, some studies demonstrate that no significant seasonal variation were observed among stroke subtypes (IS, ICH and SAH) (9, 18, 28, 29).

Unadjusted monthly 28-day mortality in all and IS stroke showed highest significant odds ratios only for February compared to March as a reference. Our finding is similar to most studies that have reported a higher 28-day mortality for stroke in winter months. (24) in a study found a higher 30-day mortality was in the winter month. Similar findings were reported by (7) with peak in December to March. after adjusting for age, gender and Cardiovascular risk factors, 28-day mortality in all and ICH stroke showed lowest significant odds ratios for summer months. overall, Cold temperatures can significantly change rheological and hemostatic parameters (7). For example, a study showed that plasma viscosity, red blood cell deformability, whole blood viscosity, hemoglobin, hematocrit, mean corpuscular volume, platelet count, alpha 1-glycoprotein, fibrinogen, plasminogen activator inhibitor-1, LDL cholesterol and triglyceride levels were significantly higher during cold months with an inverse pattern with summer peaks for HDL and cortisol (30). Other studies have shown similar seasonal variability in Hematological parameters. with winter peaks (31). These factors may be lead to a higher mortality in cold months and lowest mortality in warm months.

5. CONCLUSION

The present study showed monthly variation in 28-day mortality of all stroke and some its subtypes, but no seasonal variations were observed.

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