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# Seasonality and First Ever Ischemic Stroke, In Sohag University Hospital, Sohag, Egypt

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**Abstract**
**Introduction:** *The effect of Seasonality on stroke has been reported in several regions worldwide. Nevertheless, there is inadequate data related to these phenomena in other areas. The aim of the present study was to investigate the possible effect of seasonality on first ever ischemic stroke (FEIS).*
**Patients and Methods:** *A total of 350 patients with first ever ischemic stroke (FEIS) admitted, within 24 hours of onset. Admission rates, risk factors, stroke severity, in hospital mortality and clinical and laboratory parameters on admission were compared in relation to different seasons.*
**Results:** *The admission rate for FEIS was highest in summer. Patients were more likely to be hypertensive during winter. The highest rate of cardiac diseases was found during winter. The most severe stroke was recorded during winter. Significantly, the highest value of leukocytic count and mean platelet volume and the lowest value of activated partial thromboplastin time were recorded during winter. The highest rates of in-hospital mortality were reported during winter.*
**Conclusion:** *Seasonality has a paramount effect on first ever ischemic stroke. Different risk factors have different influences on ischemic stroke in relation to seasonality.*
**Keywords:** *- acute cerebral infarction - ischemic stroke - risk factors - seasonal variation in ischemic stroke*

## Introduction

An impact of climate upon cerebrovascular risk is both biologically conceivable and confirmed by epidemiological studies. These associations are worthy as they could produce public health policies to help protect the susceptible from the increased death rates arising during tremendous cold and heat waves [(1)]. The effect of Seasonality on stroke has been reported in several regions worldwide. Nevertheless, there is inadequate data related to these phenomena in other areas [2]. Data are incongruous as some studies determined higher stroke incidence during winter and spring and lower incidence during summer and autumn on the other hand no differences could be found in other studies [3]. Numerous trigger factors, such as hypercoagulable state, acute infections, and cold induced hypertension, as well as seasonal variations in serum lipids and glucose were discussed as possible clarifications for seasonality in vascular diseases [3]. The aim of the present study was to investigate the possible effect of seasonality on stroke severity and acute Ischemic stroke (AIS) risk factors impact in Sohag Governorate.

## Patients and Methods

This is a descriptive study analyzing the relation between seasonality and first ever ischemic stroke (FEIS).The study was conducted in Sohag University Hospital. The Sohag Governorate extends from the southern edge of Assiut Governorate at latitude 26°57′N to the northern edge of Qena Governorate at latitude 26°07′N. It forms a part of the Nile Valley, lying 62 meters above the sea level. The River Nile length in this area is 125 km, and the width of the valley ranges between 16 and 20 km [4]. The Four seasons were defined as the following: winter (December through February) where the monthly temperature Ranging between 15˚c and 16.5˚c with a seasonal mean 16˚c, spring (March through May) where the monthly temperature Ranging between 19.7˚c and 29.3˚c with a seasonal mean 24.7˚c, summer (June through August)where the monthly temperature Ranging between 30.3˚c and 31.5˚c with aseasonal mean 30.8˚c, and autumn (September through November) where the monthly temperature Ranging between 26.4˚c and 28.6˚c with a seasonal mean 25.3˚c. Temperature variations in this region are greater than in the more northern parts of Egypt. Upper Egypt is characterized by an extreme desert climate [5].

We followed the World Health Organization definition of stroke [6]. Inclusion criteria included every consecutive patient aged 18 years and older with first ever ischemic stroke (FEIS) admitted, within 24 hours of onset, to Neurology Department, Sohag University Hospital. The study period was from the 21$^{st}$June 2011 to 20 June 2013. Exclusion criteria included; residence outside Sohag governorate, patients with a transient ischemic attack (an event lasting <24 hours), died within 24 hrs of admission, a previous history of stroke, the diagnosis of stroke is uncertain, and a major illness causing prolonged bed rest. According to the previous criteria among 187 cases with first ever ischemic stroke admitted to the hospital during summer only 126 cases were from Sohag, another 54 cases were also excluded as a result of being diagnosed as having haemorhagic stroke (43 cases), TIAs (one case), or recurrent ischemic stroke (9 cases). In autumn and spring among 127 and 120 admitted cases only 99 and 71cases were included respectively while the other cases were excluded due to either residence outside Sohag governorate or not meeting (FEIS) diagnosis. In winter also 54 cases only met our inclusion criteria from 121 admitted stroke cases. Subjects' data were registered and completed prospectively during their hospital stay up to discharge. Demographic and stroke risk factors were assessed. Hypertension was diagnosed if the patient was on antihypertensive medication on admission or in case of diastolic blood pressure (DBP) ≥ 90 mmHg and systolic blood pressure (SBP) ≥ 140 mmHg. Diabetes mellitus was diagnosed in patients with fasting blood glucose level above 125 mg/dl, with antidiabetics on admission or if a physician had previously made this diagnosis.

Hypercholesterolemia was diagnosed in patients with fasting cholesterol levels ≥ 200 mg/dl or LDL-cholesterol ≥140 mg/dl or with cholesterol-lowering medication on admission. On admission, the following clinical data were recorded: systolic and diastolic blood pressure, temperature, pulse rate, and complete medical and neurological examination. The severity of stroke was determined using the Canadian Stroke Scale (CSS). The in-hospital mortality was recorded. The following laboratory data were evaluated: blood sugar, serum creatinine, complete blood count, coagulation profile, lipid profile and liver functions test. CT brain was done for all patients, and MRI brain was done for some patients.

A specialist in physical geography (Dr M. Hegab) retrieved the meteorological data collected from the Egyptian Meteorological Authority on the day when each of the 350 acute ischemic strokes occurred.

## Statistical Analysis

Data were grouped, tabulated and statistically analyzed using the Statistical Package for the Social Sciences (SPSS version20). Descriptive statistics were used to compare the characteristics of each season. Continuous variables were expressed as mean (SD) or median (IQR), and categorical variables as percentages. Chi square test was used for detection of seasonal difference of categorical data while seasonal differences in the means of continuous measurements were tested by the One Way ANOVA test. A P-value of <0.05 was considered significant.

## Results

A total of 350 patients with FEIS were included in the study, of whom 213 (60.8%) were females and 137 (39.2%) were males. The mean age of the patients was 62.1 ± 13.7 years. For women the mean age was 61.4 ± 13.7 years and for men it was 63.21 ± 13.7 years. The weather parameters for the days included in this study are described in table 1.

Distribution of cases regarding demographic data and vascular risk factors in different seasons are shown in table 2. No significant seasonal difference was found regarding age or sex. Patients were more likely to be hypertensive during winter(P=0.011). Also highly significant seasonal difference was found for history of cardiac diseases (P=0.002) the highest rate was found during winter.

Clinical findings in different seasons were shown in table 3. Significant seasonal difference was found for diastolic blood pressure (P value =0.019) with lowest values in spring and highest in summer. Stroke severity on admission measured by the Canadian Stroke Scale revealed significant seasonal difference with the most severe stroke in winter and the least severe in autumn(p = 0.03).

Laboratory findings on admission in different seasons are shown in table 4. A highly significant seasonal differences was shown for leukocyte count on admission (p = 0.007), with highest values during winter. Mean platelet volume (MPV) revealed a significant seasonal variation with highest value during winter (p= 0.015). Also high statistically significant seasonal difference (p = 0.0008) was shown for activated partial thromboplastin time (aPTT) with the lowest value during winter.

Significant seasonal differences could be shown for in-hospital mortality, with highest rates during winter (29.6%) and lowest rates during spring (4.2%) (P= 0.001) (Figure 1).

**Table 1** Weather parameters for Sohag Governorate (from 21June 2011 to 20 June 2013)

| | Summer | Autumn | Winter | Spring |
|---|---|---|---|---|
| Average temperature | 32.68±1.8 | 24.35± 5.1 | 17.21 ± 4.07 | 30.04 ± 4.7 |
| Maximum temperature | 39.6 ± 2.03 | 31.6 ± 5.5 | 24.9 ± 4.9 | 37.5 ± 4.9 |
| Minimum temperature | 25.5 ± 1.9 | 17.4 ± 5.06 | 9.7 ± 3.6 | 21.8 ± 4.4 |
| Atmospheric pressure | 1005.6 ± 2.01 | 1013 ± 2.8 | 1016.54 ± 3.9 | 1009.4 ± 2.9 |
| Relative humidity | 1.83 ± 0.59 | 3.08 ± 1.03 | 3.21 ± 1.09 | 2.0 ± 2.2 |
| Precipitation | 0 | 0.02 ± 0.14 | 0 | 0.03 ± 0.167 |
| Vertical Visibility | 10 | 10 | 9.92 ± 0.26 | 9.9 ± 0.167 |
| Average wind velocity | 10.14 ± 2.6 | 7.3 ± 3.1 | 5.44 ± 2.5 | 8.2 ± 3.5 |
| Maximum wind velocity | 18.66 ± 4.6 | 15.0 ± 5.7 | 13.75 ± 6.9 | 15.82 ± 5.8 |

**Table 2:** Distribution of cases concerning demographic data and vascular risk factors in different seasons

| season | Summer | Autumn | Winter | Spring | Total | P-value |
|---|---|---|---|---|---|---|
| Cases *no. (%)* | 126 (36.00%) | 99 (28.29%) | 54 (15.43%) | 71 (20.29%) | 350(100%) | |
| Age *mean (SD)* | 62.21 (13.9) | 60.68 (13.9) | 62.72 (13.9) | 63.61 (13.1) | | 0.57 |
| Sex *no. (%)*<br>Female<br>Males | <br>78 (61.9%)<br>48(38.09%) | <br>54(54.54%)<br>45(45.45%) | <br>30(55.5%)<br>24 (44.5 %) | <br>42 (59.2%)<br>29 (40.8%) | <br>204(58.2%)<br>146(41.7%) | <br>0.49 |
| Hypertension *no. (%)* | 52 (41.27%) | 49 (49.49%) | 35 (64.81%) | 28 (39.44%) | 164(46.8%) | 0.011 |
| Diabetes mellitus *no. (%)* | 37 (29.37%) | 20 (20.20%) | 19 (35.19%) | 22 (30.99%) | 98(28%) | 0.480 |
| Cardiac disease *no. (%)* | 14(11.11%) | 20 (20.20%) | 21 (38.89%) | 9 (12.68%) | 64(18.28%) | 0.002 |
| Hyperlipidemia *no. (%)* | 27(21.4%) | 32 (32.3%) | 9 (16.6%) | 12 (16.9%) | 80(22.85%) | 0.051 |

**Table 3:** Seasonality and clinical findings on admission

| Season | Summer | Autumn | Winter | Spring | P-Value |
|---|---|---|---|---|---|
| Systolic BP, *M(SD)* | 143.8 (25.2) | 143.2 (23.4) | 144.1 (23.9) | 138.3 (20.8) | 0.347 |
| Diastolic BP, *M(SD)* | 87.60 (13.3) | 84.49 (11.1) | 86.60 (12.1) | 82.25 (11.5) | 0.019 |
| Clinical presentation | | | | | |
| Disturbed Consciousness, % | 31 (24.6%) | 23 (23.2%) | 21 (38.8%) | 13 (18.3) | 0.32 |
| Weakness, % | 105 (83.3%) | 82 (82.8%) | 47 (87.0%) | 57 (80.2%) | 0.56 |
| Speech Disturbances, % | 12 (9.5%) | 8 (8.1%) | 3 (5.5%) | 2 (2.8%) | 0.3 |
| GCS | 12.32 (3.2) | 12.96 (2.6) | 12.29 (2.6) | 12.70 (2.5) | 0.33 |
| Stroke severity (CSS) *M(SD)* | 5.9 (3.5) | 6.65 (3.5) | 4.96 (2.8) | 5.44 (3.3) | 0.03 |

*BP: blood pressure; M (SD): mean (standard deviation); GCS: Glasgow Coma Scale; CSS: Canadian Stroke Scale*

**Table 4:** Seasonality and laboratory findings on admission

| | Summer | Autumn | Winter | Spring | P-value |
|---|---|---|---|---|---|
| Blood sugar *M(SD)* | 152.61 (78.4) | 153.01(82.35) | 158.34 (89.12) | 158.85 (77.02) | 0.94 |
| Serum creatinine *M(SD)* | 1.36 (1.38) | 1.11 (0.53) | 1.44 (1.7) | 1.49 (1.8) | 0.17 |
| RBCs *M(SD)* | 5.02 (0.97) | 8.56 (34.75) | 4.72 (0.99) | 4.71 (0.84) | 0.49 |
| HGB *M(SD)* | 13.03 (1.97) | 12.93 (2.07) | 12.71 (2.7) | 12.42 (1.86) | 0. 23 |
| WBCs *M(SD)* | 10.51 (4.8) | 9.5 (5.2) | 12.5 (7.01) | 10.4 (5.8) | 0.007 |
| Platelet count *M(SD)* | 270.2 (90.63) | 269.0 (93.54) | 258.13 (67.7) | 260.45 (95.41) | 0.82 |
| MPV | 8.86 (2.18) | 8.19 (2.1) | 9.6 (1.97) | 8.98 (1.5) | 0.015 |
| INR *M(SD)* | 1.16 (0.24) | 1.23 (0.46) | 1.14 (0.12) | 1.18 (0.19) | 0.36 |
| aPTT *M(SD)* | 38.10 (9.6) | 35.39 (10.4) | 30.75 (4.9) | 35.22 (5.9) | 0.0008 |

*M (SD): mean (standard deviation); RBCs: red blood corpuscles; HGB; hemoglobin; WBCs: white blood corpuscles; MPV: mean platelet volume; INR: international normalization ratio; aPTT: activated partial thromboplastin time*

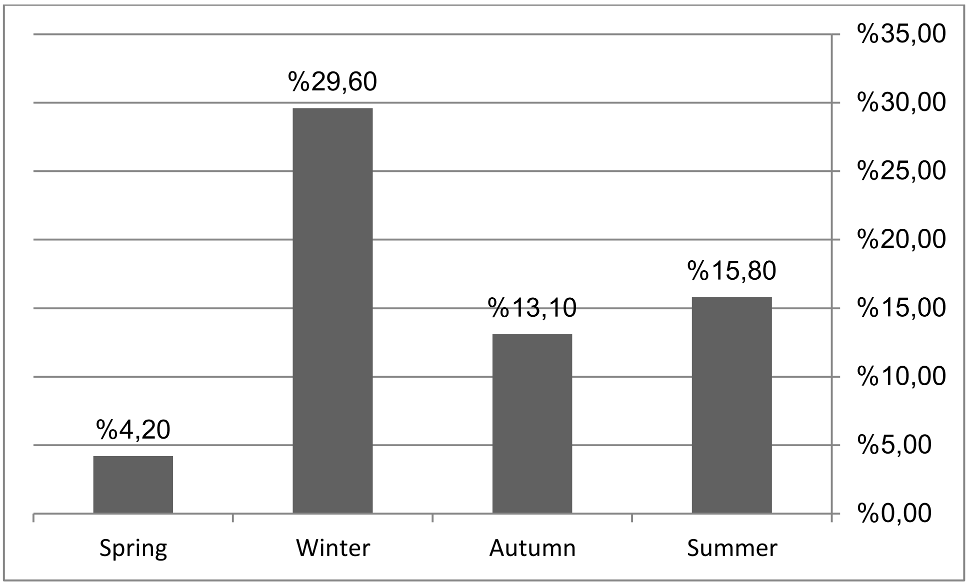


**Figure 1** seasonality and in hospital mortality

**Discussion**

We analyzed the effect of seasonality on FEIS. The admission rate for FEIS was highest in summer and lowest in winter. Our findings are consistent with several previous studies [7,8]. The possible biological explanations for these observations is that , in hot environment, the body needs to raise heat diffusion through thermoregulatory mechanisms, such as sweating, vasodilatation, and elevating heart rates; so, blood supply to the brain may be decreased and existing ischemia may be aggravated [9]. Blood viscosity and cholesterol levels may also be increased by dehydration on hot days, which in turn increases the likelihood of microvascular thrombosis and subsequent stroke [1].

On the other hand, our findings are not consistent with other studies, in which, the incidence of cerebrovascular stroke is significantly increased during winter [10, 11]. From the biological point of view, no obvious explanation for the higher rate of ischemic stroke in winter; in spite of this, numerous mechanisms have been suggested, cold exposure can lead to vasoconstriction, which increases arterial pressure , raised cholesterol and triglyceride levels in winter ; and significant seasonal variations (SVs) in fibrinogen levels and plasma viscosity , seasonal patterns of infections are assumed to affect the SVs of cerebrovascular stroke hospitalization and mortality [2].

In a multicenter hospital-based study, carried out in 24 centers, Chang et al [12] grouped these centers into "cold centers" and "warm centers" in accordance with whether their minimum mean temperature in any given month ever reached lower than 5°C or not. Such categorization could partially solve the controversy between previous studies; i.e. cold areas have higher incidence of ischemic stroke in winter and warm areas have higher incidence of ischemic stroke in summer [7,8,10,11].

Also vitamin D could solve another aspect of this controversy. Accumulating data implies that vitamin D deficiency is linked with increased risk of stroke. In northern countries at latitudes more than around 40°N (north of Madrid), sunlight is not adequately strong to activate synthesis of vitamin D in the skin from October to March [13]. We have a sunny winter and exposure to the sun is almost always better in winter than in summer as a tradition of our population, and this could explain the low rate of ischemic stroke admission in winter.

We have found SVs regarding the prevalence of hypertension, which was significantly lowest in spring and highest in winter. Also, we have found a SVs regarding DBP on admission, which was significantly lowest in spring and highest in summer and winter. This means that a better control of blood pressure occurring in spring, while winter and summer were associated with bad impact on blood pressure control. Seasonal effect on arterial blood pressure has been shown by various studies. A winter peak has been reported of both systolic and diastolic blood pressures, denoting seasonal effect on arterial blood pressure [14]. Recent data suggesting better control of blood pressure during summer in patients with hypertension support this thesis [15]. The above mentioned observations could be right for cold areas, in which summer is similar to the spring in our locality. however our finding of raised DBP on admission during summer in consistent with other studies that reported that, the DBP increased by 0.20 mmHg due to a 1°C increase in the ambient temperature [16]. Another study reported that an elevation in personal-level environmental temperature of 1° Celsius was associated with a 0.81–1.44 mm Hg and 0.59–0.83 mm Hg increase in systolic and diastolic BP, respectively [17].

The highest rate of cardiac diseases was found during winter and the lowest was found during summer. This could suggest that ischemic stroke secondary to cardiac disease is more likely to occur during winter. Winter peaks in cardiac events and stroke have been reported in different region of the world [2]. Fustinoni and colleagues found a marked SVs in the frequency of cases with AF, with a peak in winter and a valley in summer. They also reported that, low ambient temperatures enhancing sympathetic function by stimulation of central angiotensin or hypothalamic receptors for mineralocorticoids could cause episodes of AF [18].

In spite of the low rate of ischemic stroke admission in winter observed in our study; stroke severity and in hospital mortality are significantly higher in winter. Our findings are in agreement with Sheth and colleagues, who reported that patients who suffer a stroke in the winter have a substantially worse prognosis than patients who have a stroke at other times of the year, particularly if they are older [19]. Regarding stroke severity, our finding is consistent with Palm and colleagues who reported that stroke severity is higher in winter and autumn and lower in summer [3]. Contrary to this previous study we have found that stroke severity was lower in autumn. However this study was done in cold area, in which summer's climate is similar to autumn in our locality. Regarding our findings of the seasonal variation of in hospital mortality which was highest in winter, several previous studies reported increased stroke mortality in winter [3]. We did not asses the level of fibrinogen in our subjects, however two laboratory parameters in our study could suggest a SVs of hypercoagulability with peaks in winter; the first is aPTT which was significantly lower in winter and the second is MPV which was significantly higher in winter. Woodhouse and colleagues [20] reported that higher fibrinogen activity in winter provide further possible explanations for the marked seasonal variation in death from ischaemic heart disease and stroke.

The winter peak of leukocytic count found among our subjects suggests a SVs of infections during winter. This finding in agreement with previous studies which reported that, stroke risk temporally increases by acute infections, and these infections show characteristic SVs with higher incidence in winter and spring and lower incidence in summer.

Our study has a number of limitations. Being a hospital based, our study may be subjected to referral bias. Some of the risk factors such as fibrinogen level, infections and air pollution were not analyzed. Our subjects were not categorized into age groups as climatic factors have different impact on different age groups.

In conclusion seasonality has a paramount effect on first ever ischemic stroke. The highest rate of admission was found during summer, while the worst prognosis, including the highest rate of in-hospital mortality, was found during winter. Different risk factors have different influences on ischemic stroke in relation to seasonality. Further studies are needed to unmask the complex effect of seasonality on ischemic stroke.

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