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Do Gender and Season Modify the Triggering Effect of Ambient Temperature on Ischemic Stroke?

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A B S T R A C T

Background: Ischemic stroke (IS) is a multifactorial disorder, a leading cause of long-term disability, and the second most common cause of death. Previous studies have examined the association between stroke and weather conditions with conflicting results. In this study we aimed to investigate the association between changes in ambient temperature and risk of IS onset.
Methods: We used a time-stratified case-crossover study design including all patients admitted to Soroka University Medical Center in southern Israel between 2012 and 2014 for IS. Exposure windows of 6, 12, 24, 48, 72, and 96 hours were examined. All patients were assessed and classified by a neurologist. Temperature (°C), and relative humidity (%) were obtained from monitoring stations located in Beer-Sheva.
Results: A total of 1,174 patients visited Soroka University Medical Center for admission for an IS during the study period. Among them, 56% were male, on average 69.8 ± 13.1 years old. IS incidence was associated with increase in temperature during the summer and autumn season over the 96 hours preceding symptoms onset; the odds ratio (OR) for an increase of 5°C was 3.10 (95% CI, 1.45–6.61) during the summer and 1.86 (95% CI, 1.15–2.99) in autumn. The association between temperature and stroke onset during the winter was negative (OR, 0.68; 95% CI, 0.48–0.97) for 96-hour moving average temperature exposure. Men were more sensitive to 96-hour exposure window temperature fluctuations (OR, 1.35; 95% CI, 1.01–1.80) than women (OR, 0.96; 95% CI, 0.68–1.36). We did not find any associations between IS onset and differences between the maximum and minimum measurements of temperature.
Conclusions: Our findings showed that short-term exposure to high temperatures is associated with a higher risk of IS in men but not in women. Further study is needed to validate this observation and to understand its pathophysiology.

Stroke is a multifactorial disorder and has become the leading cause of long-term disability and the second leading cause of death throughout the world (Lozano et al., 2013; Mozaffarian et al., 2015).

The Negev region (Israel) has hot and dry climate conditions with a negligible amount of rainfall through the entire year. Previous analysis performed in the Negev region in 1982 (Berginer, Goldsmith, Batz, Vardi, & Shapiro, 1989) showed that hot days are associated with increased stroke risk. Desertification and global warming trends pose significant global ecological and environmental problems (Schwartz, Parker, Glass, & Hu, 2006). According to the 2014 Fourth Assessment Report by the Intergovernmental Panel on Climate Change, the period from 1983 to 2012 was very likely the warmest 30-year period of the last 800 years (Pachauri et al., 2014). Thus, it is unclear whether the seasonal pattern of stroke occurrence would have changed during the last three decades.

Several previous studies have examined the association between ischemic stroke (IS) risk and weather conditions and found different results. Findings have included a higher risk associated with ambient temperature increase (Berginer et al., 1989), decrease (Mostofsky et al., 2014), or daily change in the minimum and maximum temperature (Goggins, Woo, Ho, Chan, & Chau, 2012; Kyobutungi, Grau, Stieglbauer, & Becher, 2005).

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Table 1
Clinical Characteristic of 1,174 Patients Hospitalized for Ischemic Stroke (2012–2014), by Sex

	All ($n = 1,174$)	Men ($n = 665$)	Women ($n = 509$)	p
Age (yrs)	69.8 ± 13.1	66.8 ± 12.7	73.8 ± 12.6	<.001
<54	162 (13.8)	120 (18.1)	42 (8.3)	<.001
55–64	223 (19.0)	161 (24.2)	62 (12.2)	
65–75	334 (28.5)	193 (29.1)	141 (27.7)	
≥75	454 (38.7)	190 (28.6)	264 (51.9)	
Atrial fibrillation	243 (25.0)	95 (17.2)	148 (35.1)	<.001
Hypertension	697 (59.6)	382 (57.6)	315 (62.3)	.109
Dyslipidemia	425 (36.4)	234 (35.3)	191 (36.5)	.388
Diabetes mellitus	415 (35.5)	235 (35.4)	180 (35.6)	.832
Beer-Sheva residents	592 (50.4)	322 (48.4)	270 (53.0)	.116
Seasons				
Summer	368 (31.3)	202 (30.4)	166 (32.6)	.413
Autumn	253 (21.6)	145 (21.8)	108 (21.25)	.809
Winter	333 (28.4)	176 (26.5)	157 (30.8)	.099
Spring	220 (18.7)	142 (21.1)	78 (15.3)	.009

Note: Values are n (%) or mean ±standard deviation.

Researchers have found associations to differ by age and sex subgroups (Guiraud, Amor, Mas, & Touze, 2010; Hong et al., 2003; Han, Yi, Kim, & Kim, 2015). A study from Japan (Ogata et al., 2004) found that stroke occurred most frequently during summer, but women were more likely to have a stroke during winter. A study from Seoul (Han et al., 2015), reported that an increase in monthly mean temperature was associated with higher risk for IS among elderly men.

The major limitation of most of these studies (Goggins et al., 2012; Berginer et al., 1989; Kyobutungi et al., 2005; Goggins et al., 2012; Han et al., 2015) was their reliance on nonvalidated administrative data, which does not provide information on stroke symptoms onset time.

Hypothesizing that exposure to high temperatures increases the risk of IS, we aimed to investigate the association between changes in ambient temperature and the risk of IS onset in general and in population subgroups in a prospective clinically validated cohort, documenting stroke symptom onset time.

Methods

Study Population

The study population comprised all patients admitted with IS to Soroka University Medical Center (SUMC) between October 2012 and October 2014. SUMC is a tertiary 1,000-bed hospital and the only medical center area serving a population of 700,000 in the Southern Negev in Israel. All patients were examined by a neurologist on admission, stroke diagnosis was validated and symptom onset was recorded. Patients younger than 18 years of age and patients demonstrating transient ischemic attacks or stroke mimics were excluded. Demographic and comorbidities data and stroke symptoms onset time were recorded prospectively.

Environmental Data

We obtained hourly meteorological data, including temperatures (°C) and relative humidity, from two monitoring stations located in the center of the largest city (Beer-Sheva) in the Negev area. The distance between the two monitor stations is 2 km. Seasons were defined according to Alpert's synoptic definition (Alpert, Osetinsky, Ziv, & Shafir, 2004), where winter and the summer each last approximately 4 months (3 months and 23 days), and the autumn and spring each last nearly a half of this period, 75 days and 61 days, respectively.

Statistical Analysis

We investigated the association between IS onset and temperature using a time stratified case-crossover analysis (Lumley & Levy, 2000; Maclure, 1991; Janes, Sheppard, & Lumley, 2005) This design samples only cases and compares each case's exposure during a time period just before the case-defining event (hazard period) with that subject's own exposure in other reference periods (control periods). We examined exposures by multiple windows of time: 6, 12, 24, 48, 72, 96, and 168 hours preceding each event. We calculated the moving average exposure according to those time units. We matched control days by same year, month, day, and hour of the day as the case day. For example, if the case occurred at 2 pm on January 1, 2013 (Tuesday), then the exposure window for that case was the 96 hours before 2 pm and the exposure windows for control days were 96 hours before 2 pm on all other Tuesdays in January of that year. This design has been shown to effectively control for seasonality, time trends, and chronic and slowly varying potential confounders (Schwartz, Zanobetti & Bateson, 2003).

We performed a regression analysis based on conditional logistic regression to obtain estimates of odds ratios (OR) and 95% confidence intervals (CI). We examined the impact of

Table 2
Descriptive Statistics for Weather Characteristics According to Seasons in Southern Israel, 2012–2014

Season	Variable	Mean ± SD	Median	Minimum	95% Percentile	Maximum
All	Temperature (°C)	19.1 ± 6.5	19.1	2.1	30.3	38.8
	Temperature (°F)	66.4 ± 43.7	66.4	35.8	86.5	101.8
	Relative humidity (%)	63.5 ± 18.6	65.0	5.0	88.0	100.0
Summer (May 31–Sep 22)	Temperature (°C)	25.4 ± 3.8	24.7	16.1	31.9	38.8
	Temperature (°F)	77.7 ± 38.8	76.5	60.9	89.4	101.8
	Relative humidity (%)	65.1 ± 17.6	68.0	9.0	85.0	97.0
Autumn (Sep 23–Dec 6)	Temperature (°C)	19.7 ± 4.6	19.7	6.0	27.7	36.2
	Temperature (°F)	67.5 ± 40.3	67.5	42.8	81.9	97.2
	Relative humidity (%)	64.1 ± 16.1	66.0	8.0	87.0	99.0
Winter (Dec 7–Mar 30)	Temperature (°C)	13.3 ± 4.4	12.9	2.1	21.9	33.8
	Temperature (°F)	55.9 ± 39.9	55.2	35.8	71.4	92.8
	Relative humidity (%)	64.8 ± 18.2	66.0	5.0	93.0	100
Spring (Mar 31–May 30)	Temperature (°C)	20.1 ± 5.3	19.3	7.9	30.4	36.1
	Temperature (°F)	68.2 ± 41.5	66.7	46.2	86.7	96.9
	Relative humidity (%)	56.9 ± 14.6	58.0	5.0	82.0	69.0