

Increase in Ischemic Stroke Incident Hospitalizations Among Bedouin Arabs During Ramadan Month

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Background—Previous studies have not shown any significant effect on stroke incidence during Ramadan. We aimed to investigate the association between ischemic stroke incident hospitalizations and Ramadan, accounting for seasonality and temperature.

Methods and Results—This retrospective cohort study included all patients admitted with acute ischemic stroke to Soroka University Medical Center from June 2012 to June 2016. We obtained daily mean temperatures and relative humidity rates from 2 monitoring stations in South Israel. We analyzed the association between stroke incidence and Ramadan month, adjusting for weekly temperature and seasonality using Poisson regression models. We compared the first versus the last Ramadan fortnight. We performed an effect specificity analysis by assessing stroke incidence in the non-Bedouin population. We identified 4727 cases of ischemic stroke, 564 cases of which were Bedouin Arabs. Fifty-one cases occurred during Ramadan. Ramadan was significantly associated with an increased risk for ischemic stroke (RR 1.48; 95% confidence interval, 1.04–2.09), mainly during the first fortnight (RR 1.73, 95% confidence interval, 1.13–2.66) when compared with non-Ramadan periods. Mean weekly temperatures and the summer season were not associated with stroke incidence among Bedouin Arabs (RR 0.98; 95% confidence interval, 0.82–1.18 and RR 0.77; confidence interval 0.56–1.06 accordingly). Such association was not observed in the non-Bedouin population.

Conclusion—The Ramadan month, particularly in its first 2 weeks, is an independent and ethnicity specific risk factor for ischemic stroke hospitalizations among the Bedouin Arab fasting population. (*J Am Heart Assoc.* 2018;7:e008018. DOI: 10.1161/JAHA.117.008018.)

Key Words: ethnicity • ischemic stroke • risk factor

Fasting, the act of willingly abstaining from food, drink, or both is practiced to some extent by most religions.¹ A month of daily fasting from *fajr* (dawn), until the *maghrib* (dusk) is an obligatory practice during the holy month of Ramadan² as well as refraining from sexual activity, smoking, and getting angry.³ Several physiological changes such as changes in circadian rhythm,⁴ serum lipid and glucose levels⁵ as well as renal function markers and hematocrit levels,⁶ have

been reported among observant Muslims during Ramadan. In addition, Ramadan has been associated with exacerbation of several medical conditions such as diabetes mellitus, migraines, and chronic kidney disease.⁷ Nevertheless, the effect of Ramadan on cardiovascular morbidity is not clear.^{8,9}

Ischemic stroke is one of the most prevalent causes for hospitalization and mortality in the Western world.^{10,11} Risk factors include medical conditions (hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation, sleep apnea, and others), lifestyle (smoking, physical activity),^{12,13} and environmental factors (air temperature and air pollution^{14–18}). Ramadan associated changes such as poor drug therapy compliance; reduced glycemic control, and dehydration may temporarily contribute to stroke risk, yet such an increased stroke risk during Ramadan has not been reported.^{19–22}

It is estimated that 23% of the world population is Muslim. The understanding of Ramadan-associated stroke morbidity may have profound impact on stroke prevention; therefore, we sought to evaluate stroke risk during Ramadan using the Bedouin Arabs who reside in the Negev region as a Muslim sample group and adjusting for the environmental factors.

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Clinical Perspective

What Is New?

- In a retrospective cohort study of stroke hospitalizations in a multicultural society, we demonstrated an increased risk for ischemic stroke hospitalization among Bedouin Arabs associated with the Ramadan fasting month (RR 1.47; 95% confidence interval, 1.04–2.09) and even more so during the first 2 weeks of the Ramadan month (RR 1.73; 95% confidence interval, 1.13–2.66).
- Non-Muslim population was not at an increased risk for stroke during the Ramadan month (RR 0.922; 95% confidence interval, 0.50–1.69).

What Are the Clinical Implications?

- Observant Muslims are at an increased risk to develop stroke during the Ramadan month.
- Further research is warranted to study the potential physiological mechanism with an aim of developing a prevention strategy in accordance with religious obligations.

Methods

All data, analytic methods, and study materials will be made available to other researchers for purposes of reproducing the results or replicating the procedure. The data that support the findings of this study are available from the corresponding author upon reasonable request.

Study Population

The study population comprised all patients admitted with ischemic stroke to Soroka University Medical Center (SUMC) between June 2012 to June 2016. SUMC is a 1000-bed tertiary care hospital and is the only hospital in the Southern Negev, serving a population of 700 000.²³ The Bedouin Arab population is the largest Muslim minority group in the south of Israel²⁴ and accounts for almost 20% of the entire population of the Negev area,²⁵ scattered across 18 homogeneous settlements, usually adjacent to non-Bedouin settlements. The Bedouin Arabs' demographic structure is characterized by a high birth rate, with a median age <18 years. Approximately 2% of the Bedouin Arab population are aged >65 years.²³ Bedouin Arab patients were identified according to address in the patient file. Universal health insurance coverage allows maximal availability of stroke services for the Bedouin Arab as well as the non-Bedouin communities.^{26,27} Several media campaigns conducted since 2010 in the region increased the awareness to stroke in the Bedouin Arab community in the Negev. Those factors allowed us to study all stroke events resulting in hospitalization in the Negev, with hardly any selection bias.

The Soroka Stroke Registry was approved by the SUMC ethics committee. Patient consent was waived by the committee because of the retrospective nature of this cohort analysis. All patients who presented with symptoms of stroke were examined by a neurologist upon admission, and stroke diagnosis was validated. Recorded data include demographic information such as address, sex, age at admission, stroke severity scales, and functionality scales (National Institutes of Health Stroke Scale, Functional Independence Measure, Modified Rankin Scale), vital signs at admission (heart rate, O₂ saturation rate, blood pressure, temperature) first laboratory test results at admission, and discharge *International Classification of Diseases, Ninth Revision (ICD-9)* diagnoses.

Using these data, we constructed weekly counts of stroke cases among the Bedouin Arab and non-Bedouin population in South Israel.

Meteorological Data

Daily mean temperatures and humidity rates were extracted from 2 meteorological stations in the south of Israel and averaged weekly over both stations. The Negev desert is characterized by a semi-arid climate with sporadic rainfall. Seasons were defined according to Alpert et al,²⁸ and annual Ramadan periods were identified according to the Muslim calendar. All Ramadan periods recorded in this study took place during the summer, with mean daily temperature of 79.52°F (±36.9°F) and mean humidity of 64.36% (±5.61). The Ramadan months and the adjacent preceding and following months were then further divided into fortnight periods.

Statistical Analysis

Data are expressed as mean±SD, median±interquartile range, or number and percentage. Patient characteristics according to ethnicity and later Ramadan/non-Ramadan were compared using independent t test and chi-square tests. First, we conducted hypothesis testing by using an interaction variable consisting of Ramadan and ethnicity on all patients. We then conducted Poisson regression for the weekly stroke incident hospitalizations in the Bedouin Arab population and we used negative binomial regression in the non-Bedouin population (Poisson distribution criteria was not fulfilled) to assess the association of Ramadan with ischemic stroke incidence. The model was adjusted for the mean temperature in the week preceding stroke, and for the summer season, as well sine and cosine functions of time. Incident hospitalizations were compared separately in each population—between the Ramadan months and the rest of the year, between the preceding months and all other non-Ramadan periods, and the months following Ramadan and all other non-Ramadan periods. We also compared the first fortnight and the last fortnight of Ramadan

with all non-Ramadan periods. We then repeated our models with the time stratified by fortnight intervals of the months before, during, and after Ramadan. Results are presented as relative risks and the 95% confidence intervals (CI). Data analysis was performed using IBM, SPSS, version 20. Two-sided P -value <0.05 was considered to be statistically significant.

Results

Study Population

The Soroka Stroke Registry included 5750 cases of incident hospitalization for cerebrovascular incident, 4727 (82%) of which are attributed to ischemic stroke. Among these were 564 incident hospitalizations of ischemic stroke among Bedouin Arabs, 51 (9%) of which occurred during the Ramadan months. Figure 1 presents patient population of Soroka Stroke Registry stratified by stroke type, ethnicity, and Ramadan timing.

Table 1 presents the baseline characteristics of ischemic stroke incident hospitalizations in the Soroka Stroke Registry, stratified by ethnicity (Bedouin Arabs and non-Bedouins). The Bedouin Arab patients were younger (66.9 ± 13.6 versus 73.1 ± 12.6 years, $P < 0.001$), included more males (59% versus 55.4%, $P = 0.106$), and were more likely to smoke (28.9% versus 21.1%, $P < 0.001$) than non-Bedouin patients. In addition, Bedouin Arabs had higher systolic blood pressure (147.2 ± 20.1 mm Hg versus 143 ± 19.2 mm Hg, $P < 0.001$) and higher serum glucose levels (193.5 ± 88.9 mg/dL versus

163.8 ± 72.6 mg/dL, $P < 0.001$). Non-Bedouins were more likely to be admitted with a previous diagnosis of dysrhythmia (15.2% versus 21.1%, $P < 0.001$). Fatality outcomes were similar between the two groups. Table 2 presents the baseline characteristics of ischemic stroke incident hospitalizations among Bedouin Arabs, stratified by Ramadan and non-Ramadan periods. The Ramadan periods are further divided into first and second fortnights of the Ramadan period. Demographic, clinical, laboratory findings, vital signs and fatality counts were similar between the groups, as well as between first and last fortnights of Ramadan.

Association Between Ischemic Stroke Incident Hospitalizations and Ramadan

First, we conducted hypothesis testing by assessing an interaction variable consisting of Ramadan and ethnicity in all patients using Poisson regression for the weekly stroke incident hospitalizations. Table 3 presents the multivariate analysis examining the association between ischemic stroke incident hospitalizations and Ramadan, adjusted for mean weekly temperatures, year, the summer season and seasonality. We first analyzed Ramadan periods as whole months, and then by comparing first and last fortnights of the Ramadan months to all other non-Ramadan periods. Humidity was not found to be significantly associated with incident stroke hospitalizations during univariate analysis and was therefore not included in multivariate analysis. Among Bedouin Arabs,

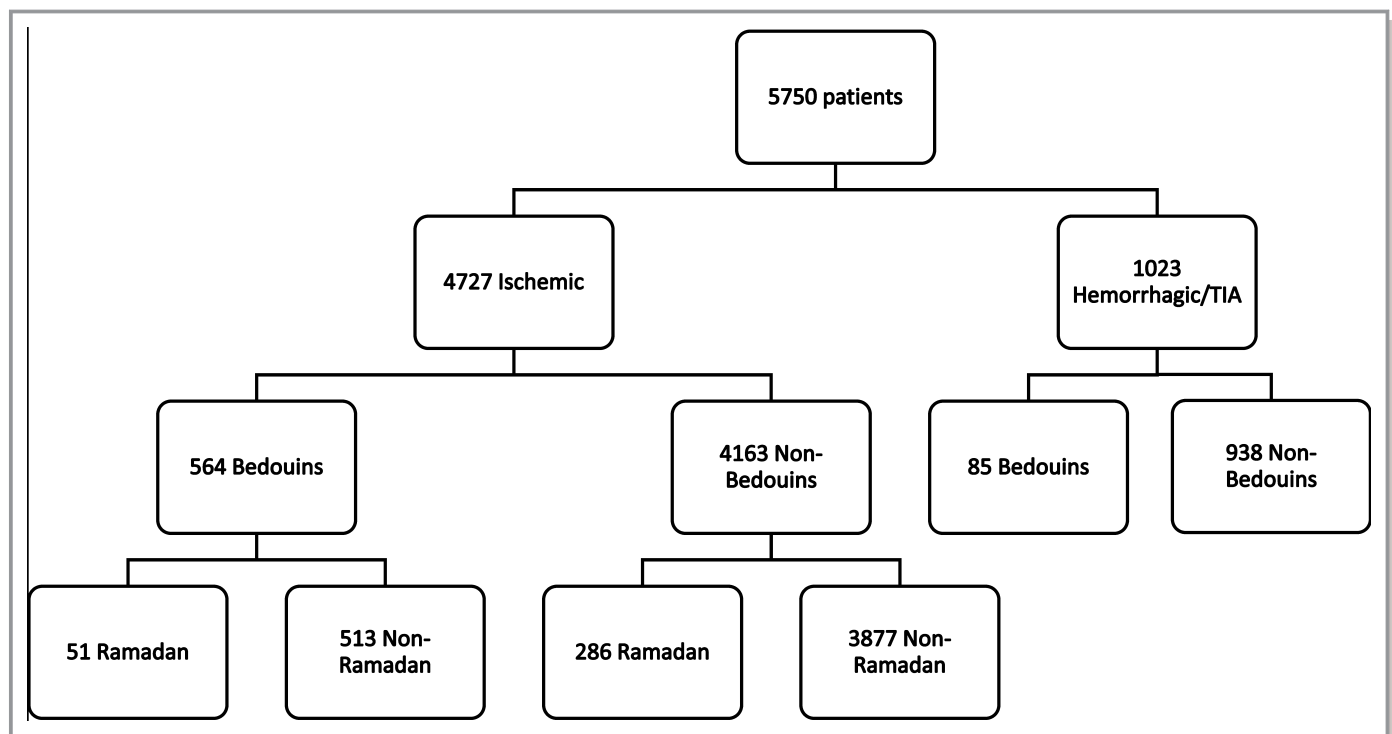


Figure 1. Flowchart detailing Soroka Stroke Registry data.

Table 1. Baseline Characteristics of Study Population

	Variable	Bedouin (n=564)	Non-Bedouin (n=4163)	P Value
Demographics	Sex-male, n (%)	333 (59)	2307 (55.4)	0.106
	Age at admission (y), mean±SD	66.9±13.6	73.1±12.6	<0.001
Medical history	Smoker, n (%)	134 (28.9)	751 (21.1)	<0.001
	Essential hypertension, n (%)	297 (52.7)	1851 (44.5)	<0.001
	Diabetes mellitus, n (%)	236 (41.8)	1217 (29.2)	<0.001
	Cardiac dysrhythmias, n (%)	86 (15.2)	902 (21.7)	<0.001
	Heart failure, n (%)	54 (9.6)	320 (7.7)	0.119
	Lipid metabolism disorder, n (%)	221 (39.2)	1207 (29)	<0.001
	Weight (kg), mean±SD	76.6±15.8	75.6±16.9	0.976
	Systolic (mm Hg) BP, mean±SD	147.2±20.1	143±19.2	<0.001
	Diastolic (mm Hg) BP, mean±SD	78.3±13.2	77.6±13.3	0.264
Laboratory results upon admission	Glucose (mg/dL), mean±SD	193.5±88.9	163.8±72.6	<0.001
	Cholesterol (mg/dL), mean±SD	173.7±43.5	171.9±45.9	0.494
	Triglycerides (mg/dL), mean±SD	163.6±102.8	141.8±88.5	<0.001
	HDL (mg/dL), mean±SD	39.6±9.9	44.2±12.4	<0.001
	LDL (calc. [mg/dL]), mean±SD	101.9±34.0	99.4±37.2	0.285
Stroke severity	NIHSS score, median (IQR)	4 (2–7)	4 (2–7)	0.839
	Minor (NIHSS 1–4), n (%)	137 (55.2)	1115 (56)	
	Moderate (NIHSS 5–15), n (%)	16.7 (37.9)	743 (37.3)	
	Moderate-to-severe (NIHSS 16–20), n (%)	16 (6.5)	113 (5.7)	
	Severe (NIHSS 21–42), n (%)	1 (0.4)	21 (1.1)	
Fatality	In-hospital fatality, n (%)	26 (4.6)	260 (6.2)	0.133

BP indicates blood pressure; HDL, high-density lipoprotein; IQR, interquartile range; LDL, low density lipoprotein; n, number of subjects; NIHSS, National Institute of Health (NIH) Stroke Scale.

results showed a significant increase in the risk of incident hospitalizations attributable to stroke during Ramadan (RR 1.47; 95% CI, 1.04–2.09), compared with the rest of the year. Specifically, this association may be attributed to the first fortnight of Ramadan, during which the association was even stronger (RR 1.73; 95% CI, 1.13–2.66) as opposed to the last fortnight of Ramadan, during which no significant association was found (RR 1.24; 95% CI, 0.77–1.73). Further analysis of the association between fortnight intervals of the months immediately preceding and following Ramadan and ischemic stroke incident hospitalizations among Bedouin Arabs showed no significance (Figure 2A).

Similar analysis performed on the non-Bedouin population indicated no significant association neither during Ramadan (RR 0.922 95% CI 0.50–1.69), nor in the months adjacent to Ramadan (Figure 2B).

Discussion

This retrospective cohort study of stroke hospitalizations of a multicultural society, demonstrated an increased risk for

ischemic stroke incident hospitalization among Bedouin Arabs associated with the Ramadan fasting month. This increased risk was found during the first 2 weeks of the Ramadan months. Because of the multicultural nature of our community, we had the opportunity to analyze a group of non-Muslims, showing specificity of the Ramadan effect while comparing each group to itself across several months. Ramadan was associated with stroke incident hospitalization risk only in the Bedouin Arab population and not in non-Bedouins. In addition, we found distinct differences in demographic characteristics among Bedouin Arabs compared with non-Bedouin stroke patients. Bedouin Arab patients were younger and with higher male predominance. Furthermore, we found higher prevalence of risk factors such as smoking, dyslipidemia, diabetes mellitus, and hypertension among Bedouin Arabs. These findings are similar to a previously published study comparing these ethnic groups in Israel.²⁹ The study, performed by the National Acute Stroke Israeli Survey Study Group, compared demographic and clinical characteristics of Arab and Jewish stroke patients and found higher rates of male sex, diabetes mellitus, and obesity among

Table 2. Baseline Characteristics of Bedouin Ischemic Stroke Patients During Ramadan and Non-Ramadan Periods

Variable	Ramadan			Non-Ramadan (n=513)	P Value*	
	First Fortnight (n=28)	Last Fortnight (n=23)	Total			
Demographics	Sex-male, n (%)	11 (39.3)	14 (60.9)	25 (49)	308 (60)	0.127
	Age at admission (y), mean±SD	68.3±13.5	69.5±14.3	68.8±13.7	66.7±13.6	0.295
Medical history	Smoker, n (%)	6 (21.4)	4 (17.4)	10 (23.3)	124 (29.5)	0.393
	Essential hypertension, n (%)	12 (42.9)	15 (65.2)	27 (52.9)	270 (52.6)	0.966
	Diabetes mellitus, n (%)	11 (39.3)	10 (43.5)	21 (41.2)	215 (41.9)	0.919
	Cardiac dysrhythmias, n (%)	5 (17.9)	5 (21.7)	10 (19.6)	76 (14.8)	0.364
	Heart failure, n (%)	2 (7.1)	6 (26.1)	8 (15.7)	46 (9)	0.132
	Lipid metabolism disorder, n (%)	4 (14.3)	11 (47.8)	15 (29.4)	206 (40.2)	0.134
	Weight (kg), mean±SD	74.5±15.2	74.5±10.9	74.3±13.3	75.7±16	0.579
	Systolic (mm Hg) BP, mean±SD	144.5±18.1	140.9±18.1	142.9±18	143±19.4	0.967
	Diastolic (mm Hg) BP, mean±SD	77.1±11.4	76±16.7	76.6±14	77.8±13.3	0.572
Laboratory results upon admission	Glucose (mg/dL), mean±SD	182.4±82.1	233.9±114.7	208.2±100.3	192.3±88	0.468
	Cholesterol (mg/dL), mean±SD	167.7±35.7	187.4±41.4	174±38	173.7±44	0.970
	Triglycerides (mg/dL), mean±SD	164.4±84.7	212.1±127.4	179.8±100.6	161.8±103.1	0.378
	HDL (mg/dL), mean±SD	38.2±8.5	38±9.1	38.2±8.5	39.8±10	0.415
	LDL (calc. [mg/dL]), mean±SD	100.9±27.3	116.6±44.4	105.5±33	101.6±34.2	0.594
Stroke severity	NIHSS score, median (IQR)	5 (3–15)	4 (2–8)	4 (3–12)	4 (2–7)	0.494
	Minor (NIHSS 1–4), n (%)			11 (47.8)	134 (53)	
	Moderate (NIHSS 5–15), n (%)			9 (39.1)	102 (40.3)	
	Moderate to severe (NIHSS 16–20), n (%)			3 (13)	15 (5.9)	
	Severe (NIHSS 21–42) n (%)			0	2 (0.8)	
Fatality	In-hospital fatality, n (%)	1 (3.6)	1 (4.3)	2 (3.9)	24 (4.7)	1

BP indicates blood pressure; HDL, high density lipoprotein; IQR, interquartile range; LDL, low density lipoprotein; n, number of subjects; NIHSS, National Institute of Health (NIH) Stroke Scale.

*P-values represent comparisons between all incident hospitalizations during the Ramadan period with all incident hospitalizations that occurred during the rest of the year among the Bedouin Arab population.

Arab patients, while dyslipidemia was more prevalent among Jewish patients. The authors did not find significant differences in cardiovascular disease, mortality, and stroke severity upon admission between the groups. These ethnic variations were similar to our findings and reflect the unique differences between various ethnicities in Israel, some of which may also be attributed to differences in socioeconomic status and education level. Because of the unique differences between the ethnic groups and the differences in sample size, we chose to compare the groups and examine the effect of Ramadan separately, similar to previously performed studies comparing ethnic differences in stroke.³⁰

Ramadan fasting affects multiple aspects of lifestyle (fluid and dietary intake, sleep patterns, smoking habits, physical activity), as well as compliance to medical therapy. Such alterations have the potential to induce cardiovascular events.^{7,31,32} However, several studies assessing the incidence of various cardiovascular outcomes failed to

demonstrate increased risk during Ramadan.^{9,20,33} Similarly, previous studies have failed to demonstrate increased stroke risk during Ramadan, comparing stroke admissions during the Ramadan to the previous month or to other months.^{19,20,22,34} The difference between our results and previous studies may be explained by several methodological factors.

Most of the previous studies compared heterogeneous groups of patients (both ischemic stroke and intracerebral hemorrhage),²⁰ and did not include a non-fasting group at the time of Ramadan.^{19,21,22}

Moreover, because of the lunar nature of the Muslim calendar, Ramadan occurs annually 11 days earlier in the Gregorian calendar, during different seasons and weather, making the generalizability of unadjusted study results limited. For example, during this study, Ramadan occurred during the summer, on July 20 to August 18, 2012, July 10 to August 7, 2013, June 29 to July 28, 2014, June 18 to July 17, 2015, and June 6 to July 6, 2016. Previous studies included data from

Table 3. The Association Between Ramadan and Ischemic Stroke

Model	Comparators	Bedouin Arabs		Non-Bedouins	
		RR (95% CI)	P Value	RR (95% CI)	P Value
Association between ischemic stroke and Ramadan	Non-Ramadan periods	Reference	0.028	Reference	0.794
	Ramadan	1.47 (1.04–2.09)		0.92 (0.50–1.69)	
Association between ischemic stroke and fortnight intervals of Ramadan	Non-Ramadan periods	Reference	0.011	Reference	0.748
	First fortnight of Ramadan	1.73 (1.13–2.66)	0.368	1.14 (0.50–2.60)	0.429
	Last fortnight of Ramadan	1.24 (0.77–1.98)		0.72 (0.33–1.59)	
Association between ischemic stroke and month before and after Ramadan	*Other non-Ramadan periods	Reference	0.894	Reference	0.539
	1 month before Ramadan	1.03 (0.65–1.63)	0.761	1.25 (0.61–2.55)	0.887
	1 month after Ramadan	0.93 (0.60–1.44)		1.04 (0.54–2.03)	

Table 3 shows the association between ischemic stroke and (1) Ramadan period, (2) Ramadan period divided into first and last fortnight, and (3) 1 month before and after Ramadan. All models were adjusted for weekly average temperature, year, summer season, and sine and cosine functions of time. CI indicates confidence interval.

*Ramadan periods were excluded from this analysis.

1991 (in which Ramadan began on March 28) to 2003 (October 27). All of the Ramadan periods in our study took place during the summer season, and therefore we adjusted accordingly—both to mean weekly temperatures and seasonality as well as to

the summer season specifically. We have used daily average humidity levels rather than day and night values; therefore, we can't fully address the possible interaction between humidity and Ramadan fast. Nevertheless, previous research from our institution has not indicated significance of humidity in multivariate models.³⁵

To our knowledge, this is the first time meteorological exposures were accounted for when assessing the association between Ramadan and ischemic stroke. Although Ramadan fasting minimally affects classical cardiovascular risk factors such as blood pressure and lipid profile,^{5,36} glycemic control is often disrupted in patients with diabetes mellitus.¹ During Ramadan, signs of dehydration, such as increased hematocrit, hemoglobin, and plasma osmolality were observed,⁶ probably because of a reduction of fluid intake, increasing blood viscosity and possibly contributing to the risk of thrombosis. The high risk during the first 2 weeks of the Ramadan may possibly be explained by habituation of homeostatic mechanisms to the changes in water and dietary consumption after the initial period of fast.³⁷ In addition, a previous study from our institution demonstrated a similar phenomenon of increasing frequency in renal colic admissions during the first fortnight of Ramadan.³⁸

Our study has several limitations. First, we identified Arab Bedouin patients using addresses from electronic medical records, which may have led to omission of Bedouin patients residing in non-Bedouin municipalities. In addition, inclusion of all cases admitted to SUMC may have led to inclusion of patients whose primary address is not in the Negev region, however resided in the region when stroke occurred. The additional limitation inherent to the ecological nature of our study is that we did not have information on the exact living conditions (such as air conditioning) or adherence to the fasting practice by an individual patient. Yet, the lack of information about adherence to the fast may have led to a bias toward null hypothesis attributable to misclassification of

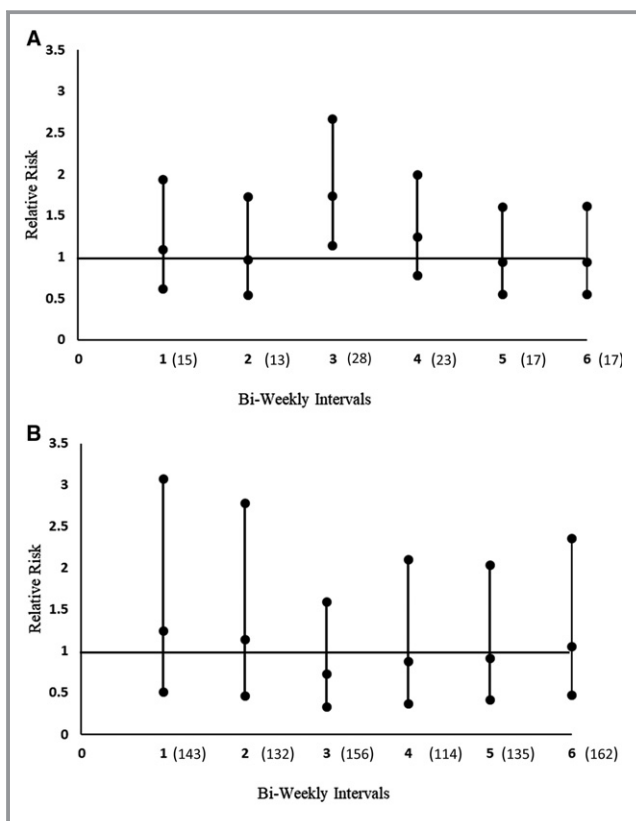


Figure 2. Forest plot depicting relative risk for stroke incidence before, during and after Ramadan, for Bedouin (A) and Non-Bedouin (B) patients, divided into bi-weekly intervals: intervals 1 to 2 are before Ramadan, intervals 3 to 4 are during Ramadan, and 5 to 6 are after Ramadan. Each Ramadan interval was compared with all other non-Ramadan weeks. Each non-Ramadan interval was compared with all other weeks excluding Ramadan period. Incident hospitalization counts are in parentheses.

the non-observers as being observers of the fast. Moreover, the small relative number of incident hospitalizations because of stroke in the Bedouin Arab population compared with non-Bedouin population may be explained by the fact that only $\approx 2\%$ of the Bedouin Arab population in the Negev is aged >65 years, compared with $\approx 10\%$ >65 years in the non-Bedouin population in the Negev. It is also important to note that as the only tertiary care facility in the Southern Israel, SUMC receives the majority of stroke cases in the entire Negev region, with little spillover to smaller hospitals.

The Ramadan fasting is an important religious and spiritual experience for observant Muslims. Health benefits of the fasting were even suggested by some.⁵ The increased risk for incident hospitalization because of stroke demonstrated by our study, suggests that research should be directed to identify evidence-based risk reduction strategies for fasting Muslims. Such strategies may include already identified glycemic control strategies,³⁹ hydration and nutrition before and after fasting, pharmacological risk reduction, sleep recommendations and others. Implementing these strategies may allow Muslims to safely observe the fast.

Conclusion

We have shown that the first 2 weeks of the Ramadan fast are associated with an increased risk of ischemic stroke. Further research is warranted to study the potential physiological mechanism with an aim of developing a prevention strategy in accordance with the religious obligations, in addition to validating this effect in other seasons as well.

Disclosures

None.

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