Impacts of Ramadan on intensive care unit admission patterns and outcomes

Les impacts du Ramadan sur le profil des admissions en réanimation et leur pronostic

Imen Ben Saida^{1,2}, Hela Kallel¹, Sabrina Chaouch¹, Radhouane Toumi^{1,2}, Wafa Zarrougui^{1,2}, Mohamed Boussarsar^{1,2}

- 1- Hôpital Farhat Hached, 4000, Sousse, Tunisie / Université de Sousse, Faculté de Médecine de Sousse.
- 2- Laboratoire de recherche N°LR12SP09. Insuffisance cardiaque. Faculté de médecine de Sousse.

RÉSUMÉ

Introduction: Le jeûne du Ramadan est une obligation religieuse pour les musulmans adultes en bonne santé. Parmi les exemptés, plusieurs refusent cette permission et insistent pour jeûner. Ceci peut mettre en danger leurs vies et entrainer leur hospitalisation en unité de soin intensif (USI).

Objectif: Étudier les impacts du changement de mode de vie pendant le Ramadan sur le profil des admissions en USI et leur pronostic.

Méthodes: Il s'agissait d'une étude rétrospective menée dans une USI de l'hôpital universitaire Farhat HACHED (Sousse, Tunisie). Les patients admis pendant Chaaban (G1), Ramadan (G2) et Shawal (G3) durant 10 ans ont été inclus. Les caractéristiques démographiques, cliniques et le pronostic ont été comparés entre les groupes.

Résultats: Sept cent quarante-huit patients ont été inclus dans l'étude (G1=257; G2=230 et G3=261). Comparativement à Chaaban, durant Ramadan et Shawal, les pourcentages des patients, ayant un antécédent d'insuffisance rénale chronique (IRC) (respectivement, 2,3; 3,5 et 7,3%) et ceux hospitalisés pour un choc hypovolémique (respectivement, 1,6; 6,1 et 5,0%) étaient significativement plus élevés. Comparativement à Chaaban, durant Ramadan et Shawal, le pourcentage des patients ayant un rapport sodium/potassium urinaire inversé était significativement plus élevé (respectivement, 28,3; 48,7; 36,8%). Il n'y avait pas de différence significative concernant la durée du séjour et la mortalité entre les trois périodes.

Conclusion: Bien qu'il n'existait pas de différence dans le pronostic des patients admis en réanimation avant, durant ou après le Ramadan, il existait une augmentation significative des pourcentages des patients aux antécédents d'IRC, ceux admis pour choc hypovolémique et ceux ayant un rapport sodium/potassium urinaire inversé.

Mots-clés

Religion, alimentation, maladie aigue, exacerbations.

SUMMARY

Background: Ramadan fasting is a religious obligation for healthy adult Muslims. Even though those unable to fast are exempt, many individuals refuse this authorization and insist to fast. This may lead to life threatening conditions and an increase in intensive care unit (ICU) demand. **Aim:** To investigate the impacts of lifestyle changes during Ramadan on ICU admission patterns and outcomes.

Methods: It was a retrospective study carried out in the medical ICU of Farhat HACHED teaching hospital (Sousse, Tunisia). Patients who were admitted to the ICU during Ramadan (G2), Chaaban (G1), and Shawal (G3) over a period of 10 years were included. Demographic, clinical features and outcomes were compared.

Results: During the review period, 748 patients were included (G1=257; G2=230 and G3=261). Compared to Chaaban, during Ramadan and Shawal, the percentages of admitted patients with, chronic kidney disease (CKD) (2.3, 3.5 and 7.3%, respectively) and for hypovolemic shock (1.6, 6.1 and 5.0%, respectively) were significantly higher. Furthermore, compared to Chaaban, during Ramadan and Shawal, patients were more likely to have inverted urinary sodium to potassium ratio (28.3, 48.7, 36.8% respectively). There was no significant difference in length-of-stay nor in mortality between the three months' periods.

Conclusion: While there were no differences in any studied outcomes in patients admitted to ICU before, during or after Ramadan, there was a significant increase in patients presenting with past history of CKD, hypovolemic shock and inverted urinary sodium to potassium ratio.

Key words

Religion, diet, acute disease, exacerbation.

INTRODUCTION

Ramadan is the ninth month of the Islamic lunar calendar. Ramadan fasting (RF) is one of the five pillars of Islam. In this sacred month, Muslims must abstain from specific habits and behaviors such as eating, drinking and sexual relationships from dawn (al fair) to sunset (al maghrib) (1). During this holy month, the lifestyle habits of Muslims all over the world are markedly changed not only those who chose to fast but also those who do not (sleep deprivation and dietary changes)(2). In fact, RF can have harmful effects on the health of Muslim patients with acute or chronic medical conditions and may lead to an increase in the demand of intensive care unit (ICU) admission(1,3,4). Although acutely ill patients, pregnant women, travelers, frail elderly and patients with chronic diseases that can be adversely affected by RF are exempted, many insist to observe the fast(1). There are many studies related to the impacts of Ramadan on emergency department visits 5-7). However, to the best of the authors' knowledge, data on its impacts on ICU admissions patterns and on critically ill patients' outcomes are lacking. Documenting the physiological, biochemical and clinical changes on ICU admissions during the fasting month may be important to understand for care providers.

The aim of this retrospective study was to investigate whether Ramadan altered patient profiles and outcomes in medical ICU admissions.

PATIENTS AND METHODS

Study design

It was a retrospective cohort study carried out in a 9-bed medical ICU of Farhat HACHED teaching hospital (Sousse, Tunisia). The average number of ICU admissions is 260 per year and the overall mortality rate is approximately 35%. The main reason for admission is acute exacerbation of chronic obstructive pulmonary disease (COPD).

Population

Patients who were admitted to the ICU during the month of Ramadan, the preceding month (Chaaban), and the following month (Shawal) over a period of 10 years (2009-2018) were included. There were no exclusion criteria. Ramadan coincided with the summer season during the study period. The fasting duration was approximately 15-16 hours. The Average ambient temperature and humidity were 32°C and 62%, respectively.

Study protocol

Patients were divided according to the month of admission in relation to the month of Ramadan in three groups: group 1 : Chaaban, group 2 : Ramadan and group 3 : Shawal. Data were collected from medical patients' charts. Patients' charts were abstracted by well- trained residents. The data collected at ICU admission included basic demographics, past medical history, Charlson comorbidity index (CCI), reason for admission, the Simplified Acute Physiological Score (SAPSII). Were also collected physiological parameters (systolic and diastolic blood pressures, pulse rate), laboratory data (serum sodium, glucose, blood urea nitrogen, serum osmolality) and therapeutic interventions in the ICU (invasive ventilatory support and hemodynamic support with inotropic agents or vasopressors), mechanical ventilation duration, ventilator free days (VFD) and vasopressors free days (VPFD). Outcome information was recorded: length-of-stay in the ICU, vital status at discharge and 28-day mortality.

Applied definitions

-Obesity: defined by a body mass index ≥30kg/m2 (8).

-CCI: comorbidities and chronic disease burden calculated according to the scoring system established by Charlson et al.(9). Patients were divided into two groups: mild, with CCI score of 1-3; moderate or severe, with CCI score >3. -Mac Cabe (10): patients are classified according to their prognosis into three groups : 1 = Nonfatal (five years survival not affected by underlying disease); 2 = Ultimately fatal (not expected to survive more than five years) and 3 = Rapidly fatal (not expected to survive more than one year). -SAPSII Score (11): is made up of 17 variables, 12 physiological variables, age, type of admission (scheduled surgical, unscheduled surgical, or medical), and three variables related to underlying disease: acquired immunodeficiency syndrome, metastatic cancer, and hematological malignancy. It evaluates the severity of illness on admission and provides a reliable prediction of mortality. -VFD and VPFD defined, respectively as days alive and free from mechanical ventilation and days alive and free from vasopressors or inotropic agents within the ICU stay (12).

Statistical analysis

The Kolmogorov-Smirnov test was used to verify the normality of distribution of continuous variables. Descriptive statistics were computed for all study variables. Categorical data were expressed as numbers (%) and continuous ones as mean \pm standard deviation or as median (interquartile range 25-75), as appropriate. For categorical data, Fisher's exact or chi- square (χ 2) tests were used. For continuous variables, analysis of variance (ANOVA) or Kruskal-Wallis tests were used if the data were normally or non-normally distributed, respectively. Clinical and sociodemographic characteristics, severity of illness, diagnoses, laboratory tests and outcomes were examined and compared between the three months (Chaaban vs. Ramadan vs. Shawal). Significance threshold was set at 0.05. For variables found to be statistically different, differences between Chaaban vs. (Ramadan and Shawal) were checked. Data were analyzed using SPSS

RESULTS

A total of 748 patients were enrolled in the study. Two hundred fifty-seven (34.4%) were admitted during Chaaban, 230(30.7%) during Ramadan and the remaining 261(34.9%) during Shawal. Patients' characteristics are displayed in table1. Patients with chronic kidney disease (CKD) as an underling condition and hypovolemic shock as clinical presentation were more frequently to be admitted during Ramadan and Shawal vs. Chaaban. Biochemical parameters are displayed in table 2. Compared to Chaaban and Shawal, critically ill patients admitted to the ICU in Ramadan were more likely to have an inverted urinary sodium to potassium ratio. Table 3 outlines ICU course and outcomes for patients included in the present study. Its main results demonstrated no significant differences in invasive mechanical ventilation, inotropic and vasoactive agents use. Moreover, there were no statistically significant differences in length-of-stay or 28-day mortality between those admitted in ICU during Ramadan and the other two studied periods.

When the analysis was addressed to the pooled period of Ramadan and Shawal vs. Chaaban (Table 4), statistically significant differences remained regarding CKD, hypovolemic shock and inverted urinary sodium to potassium ratio.

Table 1 : Patients' demographic and clinical characteristics on ICU admission

Variables	All	Chaaban	Ramadan	Shawal	Р
	(n=748)	(n=257)	(n=230)	(n=261)	
Age	57[35-71]	55[30-68]	58[35-73]	58[40-72]	0.07
Male	438(58.6)	154(59.9)	125(54.3)	159(60.9)	0.29
Comorbidities					
Diabetes mellitus	183(24.5)	66(25.7)	55(23.9)	62(23.8)	0.85
Arterial hypertension	187 (25.0)	60(23.3)	65(28.3)	62(23.8)	0.38
COPD*	210 (28.1)	66 (25.7)	61 (26.5)	83 (31.8)	0.24
Obesity	34 (4.5)	9(3.5)	10(4.3)	15(5.7)	0.46
Coronaropathy	51 (6.8)	17(6.6)	20(8.7)	14(5.4)	0.34
Chronic heart failure	62 (8.3)	23(9.0)	19(8.3)	20(7.7)	0.86
Chronic kidney disease	33 (4.4)	6(2.3)	8(3.5)	19(7.3)	0.01
Epilepsy	31(4.2)	10(3.9)	8(3.5)	13(5.0)	0.68
CCI score >3	412(55.1)	128(49.8)	133(57.8)	151(57.9)	0.111
Mac Cabe score ≥2	298(41.0)	89(35.9)	102(45.5)	107(42.1)	0.09
SAPS II	30[20-42]	30[20-41]	30[22-45]	30[19-42]	0.547
Diagnosis on ICU admission					
Acute respiratory failure	408(54.5)	135(52.5)	131(57.0)	142(54.4)	0.61
Hypovolemic shock	31(4.1)	4(1.6)	14(6.1)	13(5.0)	0.03
Septic shock	33(4.4)	12(4.7)	8(3.5)	13(5.0)	0.69
Acute coronary syndrome	17(2.3)	7(2.7)	6(2.6)	4(1.5)	0.60
Decompensation of diabetes	43(5.7)	19(7.4)	9(3.9)	15(5.7)	0.25
Acute pulmonary edema Central nervous system	97(13.0)	35(13.6)	24(10.4)	38(14.6)	0.37
disorder	151(20.2)	46(17.9)	51(22.2)	54(20.7)	0.48
Stroke	22(2.9)	6(2.3)	10(4.3)	6(2.3)	0.31
Accidental pathology	34(4.5)	9(3.5)	13(5.7)	12(4.6)	0.52
BP on admission (mm Hg)					
Systolic BP	120[100-130]	120[100-140]	120[100-130]	120[100-130]	0.285
Diastolic BP	70[60-80]	70[60-80]	70[60-70]	70[60-80]	0.697
Mean BP Heart rate (beats/min)	83.3[70-93] 100[85-120]	83.0[73-96] 100[84-120]	83.3[70-93] 100[85-119]	83.3[70-96] 100[83-120]	0.81

Note. BP: blood pressure; CCI: Charlson comorbidity index; COPD: chronic obstructive pulmonary disease; ICU: intensive care unit; Mac Cabe score ≥2: ultimately or rapidly fatal prognosis; SAPS: Simplified Acute Physiology Score;

^{*}Data were Median (interquartile) for continuous variables and number (%) for categorical ones.

^{*}P: comparison between the three periods (Kruskal Wallis analysis of variance for continuous variables and chi square ($\chi 2$) test for categorical ones).

Table 2: Laboratory investigations on admission

Variable	All	Chaaban	Ramadan (n=230)	Shawal (n=261)	P
	(n=748)	(n=257)			
Serum glucose (mmol/L)	8.0[6-12]	7.8[6-11]	7.8[6-12]	8.0[6-13]	0.639
Blood urea (mmol/L)	7.2[5-13]	7.0[4-12]	7.5[5-12]	7.1[4-14]	0.595
Creatinine (µmol/L)	93[64-151]	88[65-157]	93[62-147]	98[68-152]	0.439
Serum sodium (mmol/L)	137[132-141]	138[134-142]	137[132-141]	138[13-140]	0.056
Serum potassium (mmol/L)	4[3-4]	4[3-4]	4[3-4]	4[3-4]	0.280
Osmolality (mmol/L)	292[283-303]	292[282-304]	281[283-300]	292[282-302]	0.710
Urinary sodium to potassium ratio	229 (37.7)	58(28.3)	94(48.7)	77(36.8)	0.000

Note.* Data were Median (interquartile) for continuous variables and number (%) for categorical ones.

Table 3: Patients' therapeutic characteristics and outcomes

Variable	All	Chaaban	Ramadan	Shawal	Р
	(n=748)	(n=257)	(n=230)	(n=261)	
In hospital Course					
IMV	479(64.0)	164(63.8)	145(63.0)	170(65.1)	0.887
Mean duration of IMV* (days)	2[0-5]	2[0-4]	1[0-5]	2[0-6]	0.330
Ventilator free days (days)	1[0-4]	1[0-4]	1[0-4]	1[0-3]	0.334
Vasopressor use	325(43.4)	106(41.2)	105(45.7)	114(43.7)	0.616
Mean duration of vasopressor use (days)	0 [0-2]	0[0-2]	0 [0-3]	0[0-2]	0.780
Vasopressor use free days (days)	3 [1-7]	3[1-5]	3[0-7]	4[1-8]	0.380
Length of ICU stay (days)	5[3-9]	5[3-8]	5[3-9]	5[3-11]	0.398
28-day mortality	258 (34.5)	77 (30.1)	86(37.4)	95(36.4)	0.176
Mortality	286(38.2)	91(35.4)	89(38.7)	106(40.6)	0.469

 $Note.\ ICU: intensive\ care\ unit;\ IMV:\ invasive\ mechanical\ ventilation.\ ^*Data\ were\ Median\ (interquartile)\ for\ continuous\ variables\ and\ number\ (\%)\ for\ categorical\ ones.$

Table 4: Differences between Chaaban vs (Ramadan and Shawal) regarding CKD as a comorbid condition, hypovolemic shock and inverted urinary ratio

Variable	Chaaban	Chaaban Ramadan and Shawal	
	(n=257)	(n=491)	
Past history of CKD	6(2.3)	27(5.5)	0.046
Hypovolemic shock as clinical presentation	4(1.6)	27(5.5)	0.010
Inverted urinary sodium to potassium ratio	58(28.3)	171(42.5)	0.001

Note. CKD: Chronic kidney disease; *Data were number (%).

DISCUSSION

The main findings of the present retrospective study were: i) There was no statistically significant difference in any of the studied outcomes between the two periods according to Ramadan; ii) Patients with CKD as an underling condition and hypovolemic shock as a clinical presentation were more frequently to be admitted during Ramadan and Shawal vs. Chaaban, and iii) Patients admitted during Ramadan and Shawal were more likely to have inverted urinary sodium to potassium ratio on admission than those admitted in Chaaban.

^{*}P: comparison between the three periods (Kruskal Wallis analysis of variance for continuous variables and chi-square (χ2) test for categorical ones).

^{*} P: comparison between the three periods (Kruskal Wallis analysis of variance for continuous variables and chi-square (χ 2) test for categorical ones).

^{*}p:x2 (chi-square) test

Study limitations

The present study had two main limitations. First, it was a retrospective study conducted in a single center. This retrospective design made the documentation regarding RF status lacking. However, this design can be considered adapted to such study and addressed the issue of lifestyle change rather than RF itself. Secondly, to better evaluate the effect of lifestyle changing during Ramadan, it may be comprehensive to include patients at mid or end of Ramadan, but it was assumed that Ramadan can affect patients with chronic conditions since its beginning and these effects could even be sustained beyond Ramadan. Future studies are needed to compare profiles and outcomes of ICU patients between the beginning, the mid and the end of Ramadan. To have a large sample, authors had to screen patients over a long period. This period was assumed not to be associated with significant changes in practices. Moreover, they rather compared the three periods within each year.

This study evaluated the impacts of Ramadan on admissions, frequency of specific diseases and outcomes of critically ill patients. To the best of the authors' knowledge, this issue has not been previously studied. The lunar year is 11 days shorter than the Gregorian year, so each lunar month moves 11 days earlier each year. It takes 33 years for the lunar months to complete a full cycle and return to the same season. In this 10-years period study, Ramadan was during the summer.

The effects of Ramadan on ICU admission patterns

In the present study, the only demonstrated differences between Ramadan and Shawal compared to Chaaban concerned CKD, hypovolemic shock and inverted urinary sodium to potassium ratio. A confounding factor between these three features could be the water deprivation. In fact, water deprivation may cause renal hypoperfusion and thus cause renal dysfunction and worsen existing renal impairment (13). These findings were consistent with those of Al Wakeel et al. (14) also who found a significant increase in serum creatinine and urea nitrogen, in a prospective study conducted in CKD and dialysis patients. Al Wakeel et al. also found that hemodialysis patients who insist to fast, developed hyperkaliemia, hyponatremia, hypertension and fluid overload. However, no adverse events requiring hospital admission were observed in this study. Dikme and Dikme(15) found an increase in sodium and potassium levels in Ramadan. In the present study, there were no differences in laboratory investigations on admission (eq: renal function tests and serum electrolytes levels). This could be explained by the small size of the subset of patients suffering from CKD (n=33). There were no observed effects of Ramadan on serum osmolality. Those results are in line with previous studies who reported no significant change of serum osmolality (16-18). The effect of Ramadan on osmolality is controversial (15). Ziaee et al. (19) reported an increase in serum osmolality after Ramadan but changes remain within normal range. In the present study, critically ill patients were more likely to have an inverted urinary sodium to potassium ratio during Ramadan and the subsequent month (Table 4). Urinary sodium to potassium ratio is often used as a surrogate marker of dehydration (20). In fact, water deprivation may cause an increase in antidiuretic and aldosterone secretion and thus a decrease in water and sodium excretion (21). Changes in dietary pattern and fluid restriction during Ramadan may have led to those modifications which can last up to one month later (22). Excessive thirst and hot climate during the summer may have played a role in dehydration (23).

There were also no differences in physiological parameters between the three groups. RF has been associated with catecholamine inhibition and thus decrease in blood pressure and heart rate (24–26). Other authors such as Sarraf-Zadegan et al. (27) reported that RF reduced both systolic and diastolic blood pressures. Some authors (28) reported a decrease in blood pressure regimen when comparing hypertensive patients before and after Ramadan. On the contrary and in line with this study, some authors reported no effect of RF on diastolic and systolic blood pressures in hypertensive patients. These discrepancies may be explained by different seasons when Ramadan occurred and different population habits (29).

The effects of Ramadan on some specific diseases

In agreement with previous reports evaluating the impact of RF on specific illnesses, there is no increased frequency of cardiovascular events and strokes (5–7,30). Moreover, there were no differences between Ramadan, previous and subsequent months regarding the incidence of congestive heart failure, acute coronary syndrome and stroke. Those results are consistent with the findings of Al Suwaidi (31) and Temizhan et al. (32) who found no differences regarding the incidences of acute coronary

syndrome, one month before Ramadan, during Ramadan and one month after Ramadan. Some authors (33,34) demonstrated that there is no change in hospitalizations for stroke during Ramadan compared with other months. Those results are similar to the findings of the present study. There was also no increase in the rate of severe metabolic complications of diabetic patients during Ramadan. Those results are in line with previous studies that suggested that patients with controlled diabetes could fast without harmful consequences (35-37). There was no increase of ICU admission of epileptic patients during Ramadan. In contrast, prior studies (38,39) found an increase of seizures in those patients. Those results were explained by modification in drug intake, sleep deprivation, emotional stress and long period of hunger. The rate of respiratory failure due to COPD exacerbations was comparable during Ramadan vs. Chaaban vs. Shawal. There was no significant effect of Ramadan on the incidence of severe COPD exacerbations. Indeed. some authors suggested that intermittent RF did not bring any changes in spirometric (40), inflammatory (41), and oxidant/antioxidant stress (42) data of stable COPD. Furthermore, using inhalers is permitted during RF which helps patients with COPD to have a good control of their disease (3).

The effects of Ramadan on outcomes of critically ill patients

In the present study, there were no differences in any studied outcomes in patients admitted to ICU before, during or after Ramadan. Those findings are in line with those of Elbarsha et al. (30) who evaluated the effects of Ramadan on hospital outcomes in diabetes patients admitted to medical ward, ICU and coronary care unit. They found no statistically significant difference in length-of-hospital-stay and in-hospital mortality between patients admitted during Ramadan compared to a non-fasting month. In a prospective study conducted in seven middle eastern countries, Salam et al. (25) demonstrated that the hospitalization of patients with acute heart failure in Ramadan was not associated with increased immediate or one-year mortality.

CONCLUSION

While Ramadan did not alter the outcomes of ICU patients, there was a significant increase in critically ill patients

presenting with past history of CKD, hypovolemic shock and inverted urinary sodium to potassium ratio during Ramadan and the subsequent month probably associated with water deprivation. Education of patients with chronic morbid conditions especially CKD, maintaining good habits and large hydration can be good solutions to ensure healthy fasting and to avoid the occurrence of serious illnesses during this holy month.

REFERENCES

- Abolaban H, Al-Moujahed A. Muslim patients in Ramadan: A review for primary care physicians. Avicenna J Med. 2017;7(3):81-7.
- Imtiaz S, Nasir K, Dhrolia MF, Hussain M, Abbas HN, Ahmad A. Mortality trend among hemodialysis patients during the islamic month of Ramadan: a 24 years retrospective study. J Coll Physicians Surg Pak. 2015;25(3):189-92.
- Beshyah S, Fathalla W, Saleh A, Al Kaddour A, Noshi M, Al Hateethi H, et al. Mini- symposium: Ramadan fasting and the medical patient: An overview for clinicians. Ibnosina J Med Biomed Sci. 2010;2(5):240.
- Beshyah S, Hajjaji I, Ibrahim W, Deeb A, El-Ghul A, Akkari K, et al. The year in Ramadan fasting research (2017): A narrative review. Ibnosina J Med Biomed Sci. 2018;10(2):39.
- Topacoglu H, Karcioglu O, Yuruktumen A, Kiran S, Cimrin AH, Ozucelik DN, et al. Impact of Ramadan on demographics and frequencies of disease-related visits in the emergency department: Impact of Ramadan. Int J Clin Pract. 2005;59(8):900-5.
- Pekdemir M, Ersel M, Yilmaz S, Uygun M. No significant alteration in admissions to emergency departments during Ramadan. J Emerg Med. 2010;38(2):253-6.
- Al Assaad RG, Bachir R, El Sayed MJ. Impact of Ramadan on emergency department visits and on medical emergencies. Eur J Emerg Med Off J Eur Soc Emerg Med. 2018;25(6):440-4.
- Tsai AG, Wadden TA. In the clinic: obesity. Ann Intern Med. 2013;159(5):ITC3.
- Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40(5):373-83.
- McCABE WR. Gram-negative bacteremia: I. etiology and ecology. Arch Intern Med. 1962;110(6):847.
- Le Gall JR, Loirat P, Alperovitch A, Glaser P, Granthil C, Mathieu D, et al. A simplified acute physiology score for ICU patients. Crit Care Med. 1984;12(11):975-7.
- Russell JA, Lee T, Singer J, De Backer D, Annane D. Days alive and free as an alternative to a mortality outcome in pivotal vasopressor and septic shock trials. J Crit Care. 2018;47:333-7.
- El-Wakil HS, Desoky I, Lotfy N, Adam AG. Fasting the month of Ramadan by Muslims: Could it be injurious to their kidneys? Saudi J Kidney Transpl. 2007;18(3):349-54.
- 14. Al Wakeel JS. Kidney function and metabolic profile of chronic

- kidney disease and hemodialysis patients during Ramadan fasting. Iran J Kidney Dis. 2014;8(4):321-8.
- Dikme O, Dikme O. Ramadan fasting and its influence on serum osmolality in emergency patients. J Emerg Med Crit Care. 2016;2(1):4.
- 16. Ünalacak M, Kara İH, Baltaci D, Erdem Ö, Bucaktepe PGE. Effects of Ramadan fasting on biochemical and hematological parameters and cytokines in healthy and obese individuals. Metab Syndr Relat Disord. 2011;9(2):157-61. 17. Hosseini SRA, Hejazi K. The effects of Ramadan fasting and physical activity on blood hematological-biochemical parameters. Iran J Basic Med Sci. 2013;16(7):5. 19
- Dewanti L, Watanabe C, Sulistiawati, Ohtsuka R. Unexpected changes in blood pressure and hematological parameters among fasting and nonfasting workers during Ramadan in Indonesia. Eur J Clin Nutr. 2006;60(7):877-81.
- Ziaee V, Yousefi R, Ahmadinejad Z, Shaikh H, Rezaei M, Behjati MJ. The effect of Ramadan fasting on serum osmolarity, some electrolytes and hematological parameters. Iran J Endocrinol Metab. 2007;9(1):47-53.
- Tam RK, Wong H, Plint A, Lepage N, Filler G. Comparison of clinical and biochemical markers of dehydration with the clinical dehydration scale in children: a case comparison trial. BMC Pediatr. 2014;14:149.
- 21. Gonçalves C, Abreu S, Padrão P, Pinho O, Graça P, Breda J, et al. Association between sodium excretion and hydration status by free water reserve: a cross-sectional analysis in adolescents. BMC Nutr. 2015;1(1):17.
- Chtourou H. Eds. Effects of Ramadan fasting on health and athletic performance. OMICS Group eBooks. Retrieved from https://www.esciencecentral.org/ebooks/ebookdetail/effectsof-ramadan-fasting-on-health-and-athletic-performance (last access: April 25th 2019).
- 23. Popkin BM, D'Anci KE, Rosenberg IH. Water, Hydration and Health. Nutr Rev. 2010;68(8):439-58.
- Stokholm KH, Breum L, Astrup A. Cardiac contractility, central haemodynamics and blood pressure regulation during semistarvation. Clin Physiol. 1991;11(6):513-23.
- Salam AM, Sulaiman K, Alsheikh-Ali AA, Singh R, Asaad N, Al-Qahtani A, et al. Acute heart failure presentations and outcomes during the fasting month of Ramadan: an observational report from seven Middle Eastern countries. Curr Med Res Opin. 2018;34(2):237-45.
- Fisler JS. Cardiac effects of starvation and semistarvation diets: safety and mechanisms of action. Am J Clin Nutr. 1992;56(1):230S-234S.
- 27. Sarraf-Zadegan N, Atashi M, Naderi GA, Baghai AM, Asgary S, Fatehifar MR, et al. The effect of fasting in Ramadan on the values and interrelations between biochemical, coagulation and hematological factors. Ann Saudi Med. 2000;20(5-6):377-81.
- M S, AH SA, SR S, KM B. Effect of Ramadan fasting on body weight, blood pressure and biochemical parameters in middle aged hypertensive subjects: an observational trial. J Clin Diagn Res. 2014;8(3):16-8.
- 29. Perk G, Ghanem J, Aamar S, Ben-Ishay D, Bursztyn M. The

- effect of the fast of Ramadan on ambulatory blood pressure in treated hypertensives. J Hum Hypertens. 2001;15:723–725.
- Elbarsha A, Elhemri M, Lawgaly SA, Rajab A, Almoghrabi B, Elmehdawi RR. Outcomes and hospital admission patterns in patients with diabetes during Ramadan versus a nonfasting period. Ann Saudi Med. 2018;38(5):344-51.
- 31. Al Suwaidi J. A population based study of Ramadan fasting and acute coronary syndromes. Heart. 2004;90(6):695-6.
- Temizhan A, Dönderici Ö, Ouz D, Demirbas B. Is there any effect of Ramadan fasting on acute coronary heart disease events? Int J Cardiol. 1999;70(2):149-53.
- Bener A, Hamad A, Fares, A, Al-Sayed HM, Al-Suwaidi, J. Is there any effect of Ramadan fasting on stroke incidence? Singapore Med J. 2006;404. 21
- Akhan G, Kutluhan S, Koyuncuoglu HR. Is there any change of stroke incidence during Ramadan? Acta Neurol Scand. 2000;101(4):259-61.
- 35. Benaji B, Mounib N, Roky R, Aadil N, Houti IE, Moussamih S, et al. Diabetes and Ramadan: review of the literature. Diabetes Res Clin Pract. 2006;73(2):117-25.
- Chandalia HB, Bhargav A, Kataria V. Dietary pattern during Ramadan fasting and its effect on the metabolic control of diabetes. Pract Diabetes Int. 1987;4(6):287-90.
- 37. Mafauzy M, Mohammed WB, Anum MY, Zulkifli A, Ruhani AH. A study of the fasting diabetic patients during the month of Ramadan. Med J Malaysia. 1990;45(1):14-7.
- 38. Gomceli YB, Kutlu G, Cavdar L, Inan LE. Does the seizure frequency increase in Ramadan? Seizure. 2008;17(8):671-6.
- Abdou A, El Fatatry A, Sad Allah H, Abd Elhakeem N. Effect of Ramadan fasting on seizure control in epileptic patients. Neurology. 2015;84(14 Supplement):P6.296.
- Zouari H, Latiri I, Mahjoub M, Boussarsar M, Benzarti M, Abdelghani A, et al. The Effects of Ramadan intermittent fasting (RIF) on spirometric data of stable COPD Patients: a pilot study. Am J Mens Health. 2018;12(2):359-69.
- 41. Rejeb H, Ben Khelifa M, Ben Abdallah J, Mrad S, Ben Rejeb M, Hayouni A, et al. The effects of Ramadan-fasting (RF) on inflammatory and hematological indices of stable chronic obstructive pulmonary disease (COPD) male patients: a pilot study. Am J Mens Health. 2018;12(6):2089-103.
- 42. Mrad S, Rejeb H, Abdallah J, Graiet H, Khelifa M, Abed A, et al. The impacts of Ramadan intermittent fasting on oxidant/ antioxidant stress biomarkers of stable chronic obstructive pulmonary disease male patients. Am J Mens Health. 2019;13(3):1557988319848281.