

Review

Impact of religious Ramadan fasting on cardiovascular disease: a systematic review of the literature

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Abstract

Background:

Fasting during the month of Ramadan is a religious obligation that is practiced by millions of people around the world yet there is no clear scientific consensus on its effects on cardiovascular disease. This study was performed to inform physicians as well as patients of evidence based recommendations on this subject.

Aim:

The study was undertaken to assess: (1) any alteration in the incidence of acute cardiac illness during Ramadan fasting; (2) whether fasting during the month of Ramadan alters the clinical status of patients with stable cardiac disease; and (3) the impact of Ramadan fasting on cardiovascular risk factors in normal subjects, in patients with stable cardiac disease, metabolic syndrome, dyslipidemia, type 2 diabetes and systemic hypertension.

Study design:

Systematic review of the literature.

Method:

A Medline search of the English literature published between January 1980 and September 2012.

Results:

The incidence of acute cardiac illness during Ramadan fasting was similar to non-fasting days, although the timing of symptom onset may be different, with significant increase in events during the period of 'breaking fast' when compared to non-fasting days. The majority of patients with stable cardiac illness can undergo Ramadan fasting without any clinical deterioration. Body mass index, lipid profile, and blood pressure showed significant improvement in normal healthy subjects, patients with stable cardiac illness, metabolic syndrome, dyslipidemia and hypertension during Ramadan fasting. The lipid profile of diabetic patients deteriorated significantly during Ramadan fasting.

Conclusions:

Ramadan fasting is not associated with any change in incidence of acute cardiac illness and the majority of cardiac patients can fast without any difficulty. Improvement in lipid profile, especially 30% to 40% increment in high-density lipoprotein, as reported in some studies, appear promising. Diabetic patients should be carefully monitored during Ramadan fasting.

Introduction

The month of Ramadan is the ninth month in the Islamic lunar calendar, also called the Hijra. It is compulsory for all adult healthy Muslims to fast (absolute restriction of food, drink, smoking and sexual activity) from dawn to sunset

during the holy month. Muslim children worldwide grow up while they observe this religious phenomenon among family members and relatives and most of them start fasting by teenage or even before that. During the later years of life, when these people develop chronic diseases, fasting during the month of Ramadan becomes a concern. While religion exempts people with significant illness from the obligation of Ramadan fasting, Muslim patients usually have a strong motivation to continue the lifelong practice of fasting. This raises the general concern whether fasting is safe for them and the more specific question regarding what would be the precautions and outcome if these patients continue the month long fasting.

In this systematic review we attempted to analyze the change in incidence of cardiovascular disease during Ramadan fasting and to assess if there is any change in clinical status among patients with stable cardiac disease during Ramadan fasting. We also attempted to analyze the alteration in cardiovascular risk profile among healthy subjects, patients with stable cardiac disease, metabolic syndrome, dyslipidemia, type 2 diabetes mellitus and systemic hypertension during Ramadan fasting.

Method

A Medline search of the English literature published between 1980 and 2012 was performed using the heading 'Ramadan fasting' combined with 'acute coronary syndrome'; 'heart failure'; 'arrhythmia'; 'systemic hypertension'; 'metabolic syndrome'; 'diabetes'; 'lipids'. Local journals in Islamic countries and countries with prominent Muslim population were also searched using the same search criteria. Abstracts of identified papers were reviewed for appropriateness. Reference lists of articles were reviewed for additional papers. Data were extracted from original papers published in peer reviewed journals.

Case series, cohort study and randomized trials were considered appropriate if they assessed the incidence of acute coronary syndrome, congestive heart failure, cardiac arrhythmia or metabolic alteration in patients during Ramadan fasting. Studies with fewer than 10 subjects, unpublished abstracts lacking complete data, editorials and review articles were excluded. The data for incidence of acute coronary syndrome and heart failure were extracted in tables from the retrieved studies. Data for metabolic alteration in normal healthy subjects, patients with stable cardiac illness, metabolic syndrome, type 2 diabetes mellitus and systemic hypertension during Ramadan fasting were also extracted in tables from the retrieved studies. The studies included in this review were observational and case control studies. Meta-analysis was not possible because of the heterogeneous nature of included studies.

Results

Thirty-six studies met the criteria for inclusion of which 11 studies reported either the incidence or pattern of acute cardiac illness or stroke during the month of Ramadan or the clinical status of patients with known cardiac illness during the period. The remaining 25 studies reported the impact of Ramadan fasting on known cardiovascular risk factors in normal healthy adults as well as in patients with stable cardiac disease, metabolic syndrome, dyslipidemia, type 2 diabetes mellitus and systemic hypertension.

Impact of Ramadan fasting on incidence of acute cardiac illness

Table 1 enumerates the clinical studies which reported the incidence of acute cardiac illness as well as clinical status of cardiac patients during Ramadan fasting. Three retrospective cohort studies reported the incidence of acute coronary syndrome and acute decompensated heart failure during the month of Ramadan over 6 to 10 year periods^{1,2,3}. Previous studies done in our institution involving the analysis of clinical records of patients admitted for acute coronary syndrome or acute decompensated heart failure over a period of 10 years (1991 to 2001) reported that the incidence of acute coronary syndrome as well as hospitalizations for acute decompensated heart failure were similar during the month of Ramadan compared to other non-fasting days^{1,2}. Furthermore, it was noted that the incidence of acute decompensated heart failure in patients with a history of previous myocardial infarction was significantly lower ($p < 0.05$) during the month of Ramadan compared to other non-fasting days¹. In addition, a minimal non-significant increase in incidence of hospitalization for acute decompensated heart failure was noted in patients with type 2 diabetes mellitus¹.

The incidence of stroke is also not significantly affected by Ramadan fasting^{4,5,6}. Çomoğlu *et al.*⁶ reported that the incidence of hospitalization for ischemic and hemorrhagic stroke was similar during the month of Ramadan compared to other non-fasting days. However, in subgroup analysis it was noted that among patients with type 2 diabetes mellitus hospitalization for ischemic stroke was significantly higher during Ramadan compared to other non-fasting days, while hospitalization for hemorrhagic stroke was significantly lower among hypertensive patients during the month of Ramadan compared to the other non-fasting days.

Temizhan *et al.*³ analyzed the clinical records of patients who were admitted to the emergency department with acute coronary syndrome between 1991 and 1997 in Turkey. They reported that the number of patients hospitalized with acute coronary syndrome during Ramadan was

Table 1. Comparative incidence of acute cardiovascular illness during Ramadan fasting and usual non-fasting days.

Author(s)	Year	Place	Period of study	Type of study	Comparative incidence of acute cardiac illness or stroke
Temizhan <i>et al.</i> ³	1999	Turkey	1991 to 1997	Retrospective study of 1655 patients hospitalized with ACS during as well as 1 month before and after Ramadan between 1991 and 1997	The number of patients with ACS during Ramadan was significantly lower ($p=0.03$) as compared to 1 month before and after
Al Suwaidi <i>et al.</i> ¹	2004	Qatar	Jan 1991 to Dec 2001	Retrospective cohort study involving analysis of clinical records of 2160 patients admitted with CHF	Number of hospitalizations for CHF were similar during Ramadan compared to other days
Al Suwaidi <i>et al.</i> ²	2004	Qatar	Jan 1991 to Dec 2001	Retrospective cohort study involving analysis of clinical records of 8446 patients admitted with ACS	Number of hospitalizations for ACS were similar during Ramadan compared to other days
Chamshi-Pasha <i>et al.</i> ⁷	2004	Saudi Arabia	2004	Prospective observational study of 86 stable cardiac patients attending outpatient clinic	The clinical status of patients remained stable during Ramadan fasting
Al Suwaidi <i>et al.</i> ⁸	2005	Qatar, Kuwait, UAE, Bahrain	Oct 24 to Nov 24, 2003	Prospective observational study of 465 stable cardiac patients in 4 Gulf countries	The clinical status of patients remained stable during Ramadan fasting
Bener <i>et al.</i> ⁴	2006	Qatar	Jan 1991 to Dec 2003	Retrospective analysis of data of patients hospitalized for acute stroke over 13 years	The number of patients hospitalized for acute stroke was similar during Ramadan fasting compared to the non-fasting month before and after
Burazeri <i>et al.</i> ⁹	2008	Albania	2003 to 2006	A case control study which included 467 cases of consecutive non-fatal ACS compared with 1065 healthy controls	Incidence of ACS was inversely associated with religiosity. Association was strongest for regular Ramadan fasting
Khafaji <i>et al.</i> ¹⁰	2012	Qatar	NA	Prospective observational study of 56 stable cardiac patients	The clinical status of patients remained stable during Ramadan fasting

NA = data not available; CHF = congestive heart failure; ACS = acute coronary syndrome.

significantly lower ($p=0.03$) compared to other non-fasting days.

Burazeri *et al.*⁹ conducted a case control study in Tirana, Albania, a predominantly Muslim town, where the majority (67%) did not comply with Islamic rules. They reported that religiosity was inversely associated with the incidence of acute coronary syndrome. Moreover, on multivariable adjustments, regular fasting among Muslims was associated with significant reduction in the incidence of acute coronary syndrome as compared to non-observant Muslims (HR 0.28; 95% CI [0.13 to 0.58] $p<0.001$).

In a multicenter prospective follow up study, we recruited 465 stable cardiac patients attending cardiology outpatient clinics in Qatar, Kuwait, United Arab Emirates, Bahrain and Saudi Arabia before the month of Ramadan and they were followed up up to a month after Ramadan. Among them, 119 (25.6%) patients had congestive heart failure, 288 (62%) patients had angina, 22 (4.7%) patients had atrial fibrillation and 11 (2.4%) patients had prosthetic metallic valves. At the time of follow-up, we found that 91.2% could fast and only 6.7% felt worse while fasting in Ramadan. Of the studied subjects, 82.8% were compliant with cardiac medications and 68.8% were compliant with dietary instructions. We hospitalized 19 patients during Ramadan for cardiac reasons (unstable angina: 3, worsening heart failure: 8, MI: 2, uncontrolled hypertension: 2, subtherapeutic anticoagulation: 1, or arrhythmias: 2). We concluded that the effects of fasting during Ramadan on stable patients with cardiac disease are minimal. Most patients with stable cardiac disease can fast. These findings are consistent with a smaller scale study conducted in Saudi Arabia only⁷. However, the study design did not allow assessment of whether the incidence of hospitalization during Ramadan was different from non-Ramadan days. Above all, selection bias may have influenced the patients enrolled for the study.

We have previously shown that although the incidence of acute cardiovascular diseases is not significantly different during Ramadan when compared to the non-fasting days, there were significant variations in the timing of onset of symptoms with a peak that coincides with the time of breaking the fast and most probably attributed to food consumption, we concluded that our study emphasized the importance of the exogenous factors that are associated with fasting; namely, the changes in food intake and/or sleep timing, and their effects on the circadian rhythm of acute heart events¹¹.

Impact of Ramadan fasting on cardiovascular risk factors

Twenty-five clinical studies, conducted in different geographical regions, reported the changes in diet, body

weight/body mass index, blood pressure and lipid profile in normal healthy adults as well as in patients with stable cardiac disease, metabolic syndrome, dyslipidemia, systemic hypertension or type 2 diabetes mellitus during Ramadan fasting.

Table 2 enumerates the studies which reported the changes in diet, body weight, lipid profile and blood pressures in patients with stable cardiac disease or with multiple cardiovascular risk factors during Ramadan fasting. While one study reported unfavorable changes in the lipid profile¹⁰, the other three studies^{12–14} reported beneficial changes in the lipid profile, blood pressure and body mass index.

Table 3 summarizes the studies which reported the changes in diet, body weight, lipid profile and blood pressure during Ramadan fasting in normal healthy adults. Barkia *et al.*¹⁵ reported increased dietary intake of cholesterol during Ramadan and a subsequent increment in body mass index and worsening of lipid parameters in healthy Tunisian subjects. Ziaee *et al.*¹⁶ reported a decline in body mass index accompanied by worsened low-density lipoprotein (LDL) and high-density lipoprotein (HDL) levels in healthy Iranian subjects. All other studies reported improvement in lipid parameters along with decline or no change in body weight while two studies reported a decline in mean systolic and diastolic blood pressures among healthy subjects during Ramadan fasting^{17–25}.

Table 4 enumerates the studies which reported changes in dietary intake, body weight, lipid parameters and blood pressure among patients with metabolic syndrome or dyslipidemia. Sadiya *et al.*²⁶ reported 23% increased fat intake among patients with metabolic syndrome during Ramadan fasting but it was not accompanied by any change in lipid parameters. On the other hand, a significant reduction in body weight was noted ($p < 0.001$). Two other studies reported decreased fat intake, a decline in body mass index and a significant increase in HDL levels and an overall improvement in lipid parameters among patients with metabolic syndrome or dyslipidemia^{27,28}. A significant improvement in blood pressures was also noted among patients with metabolic syndrome²⁸. In the cohort of Akanji *et al.*²⁹ which comprised dyslipidemic patients, apo A1, apo A1/apo B and apo A1/HDL increased in all patients ($p < 0.001$), while patients with coexistent diabetes reflected significant increase in total cholesterol and apo B ($p < 0.05$).

Table 5 enumerates the studies which reported changes in lipid parameters during Ramadan fasting in patients with type 2 diabetes. Khatib and Shafagoj³⁰ reported decline in body weight, fasting blood sugar and serum triglyceride level while other lipid parameters remained unchanged in patients with type 2 diabetes mellitus during Ramadan fasting. Two studies reported a non-significant decline or an increase in body mass index,

accompanied by a significant worsening of lipid parameters during Ramadan fasting^{31,32}.

Table 6 summarizes three studies which evaluated the effect of Ramadan fasting on body weight, plasma lipids and 24 hour ambulatory blood pressure monitoring in hypertensive patients on combination therapy. One study reported a significant reduction in body weight but no change in ambulatory blood pressures while the other two studies reported a significant decline in daytime average systolic and diastolic blood pressures^{33–35}. A decline in plasma HDL level was reported in one study³⁶.

Inflammatory markers like interleukin-6 and C-reactive proteins as well as markers of intravascular coagulation like D-dimer, plasma homocysteine and plasminogen activator inhibitor type-1 levels declined significantly during Ramadan fasting in patients with stable cardiac illness and in healthy subjects^{12,13,22,24}.

Discussion

Fasting during the month of Ramadan constitutes one of the five pillars of Islam. The religious rules and guidelines governing the observation of Ramadan fasting is the same for Muslims all over the world. Muslims worldwide represent a diverse and heterogeneous population varying widely in terms of geographical distribution, language, life style, habits, customs, tradition, dietary habits and above all socioeconomic status which has a major influence on all other factors. Moreover, the already diverse dietary habits undergo further significant alteration during Ramadan fasting among the global Muslim population. Apart from the dietary changes, the amount and pattern of physical activity also undergo significant modification during Ramadan. These issues should be considered when the results of our systematic review are discussed.

To the best of our knowledge, until the time of preparing the manuscript for our systematic review, we did not get any study which reported adverse clinical outcomes in cardiac patients who underwent fasting during the month of Ramadan. On the contrary, a previous study done in our institution reported that the incidence of acute decompensated heart failure among patients of previous myocardial infarction was significantly lower during Ramadan¹. Temizhan *et al.*³ reported a significantly lower incidence of hospitalization for acute coronary syndrome during the month of Ramadan in Turkey while Burazeri *et al.*⁹ reported a 72% reduction in risk of acute coronary syndrome in Muslims who fasted regularly during Ramadan in Albania. Hunger is associated with suppression of sympathetic tone and has an overall protective effect on the heart³⁷. In addition, a restriction on smoking during Ramadan fasting may have an additive beneficial cardiac effect, which needs to be confirmed in clinical studies.

Table 2. Changes in body weight, lipids and blood pressure in patients with stable cardiac disease/multiple cardiovascular risk factors during Ramadan fasting.

Author(s)	Year	Place	Subjects (n)	Change in diet	Change in weight/BMI	Changes in lipids	Changes in blood pressure
Nematy <i>et al.</i> ¹²	2010	Iran	Stable cardiac patients (82)	NA	BMI 28.4 ± 4 vs 27.7 ± 4 kg/m ² (before Ramadan vs end Ramadan) <i>p</i> < 0.05	TC (193 ± 51 vs 184 ± 42 mg/dl), LDL (110 ± 41 vs 97 ± 32 mg/dl) VLDL (38 ± 14 vs 34 ± 17 mg/dl), HDL (43 ± 9 vs 48 ± 8 mg/dl) (before Ramadan vs end Ramadan) <i>p</i> < 0.05	SBP 133 ± 16 vs 130 ± 17 mmHg (before Ramadan vs end Ramadan) <i>p</i> < 0.05
Khafaji <i>et al.</i> ¹⁰	2012	Qatar	Stable cardiac patients (56)	None	None	LDL (3.31 ± 0.97 vs 3.59 ± 0.92 mmol/l; <i>p</i> = 0.022), HDL (1.05 ± 0.25 vs 1.12 ± 0.24; <i>p</i> = 0.012) (Ramadan vs pre-Ramadan)	NA
Ibrahim <i>et al.</i> ¹³	2011	Malaysia	Patients with multiple cardiovascular risk factors (76)	NA	BMI (27.65 kg/m ² vs 28.00 kg/m ² , <i>p</i> < 0.001) (pre-Ramadan vs end Ramadan)	LDL (3.24 mmol/L vs 3.19 mmol/L, <i>p</i> = 0.037), HDL (0.89 mmol/L vs 0.93 mmol/L; <i>p</i> = 0.34) (pre-Ramadan vs end Ramadan)	Mean SBP (136 mmHg vs 129 mmHg, <i>p</i> = 0.006), Mean DBP (78 mmHg vs 75 mmHg, <i>p</i> < 0.001) (pre-Ramadan vs end Ramadan)
Nematy <i>et al.</i> ¹⁴	2012	Iran	Stable cardiac patients; patients with metabolic syndrome or history of previous stroke (82)	None	BMI (28.4 ± 4, 27.7 ± 4 kg/m ² ; <i>p</i> < 0.001) (pre-Ramadan vs post-Ramadan)	TC (193.4 ± 51 vs 184.3 ± 42 mg/dl; <i>p</i> = 0.023), LDL (109.96 ± 46 vs 96.83 ± 35 mg/dl; <i>p</i> < 0.001), TG (224.8 ± 129 vs 182.9 ± 112 mg/dl; <i>p</i> < 0.001), VLDL (38.1 ± 14 vs 33.8 ± 17 mg/dl, <i>p</i> < 0.001), LDL/HDL (2.5 ± 0.8 vs 2.0 ± 0.6 mg/dl; <i>p</i> < 0.001), HDL (43.0 ± 9 vs 47.9 ± 8 mg/dl; <i>p</i> < 0.001) (pre-Ramadan vs post-Ramadan)	Mean SBP (132.9 ± 16 mmHg, 129.9 ± 17 mmHg, <i>p</i> = 0.03), Mean DBP (80.2 ± 9, 78.6 ± 11 mmHg, <i>p</i> = 0.14) (pre-Ramadan vs post-Ramadan)

NA = data not available; BMI = body mass index; TC = total cholesterol; TG = triglyceride; LDL = low density lipoprotein; VLDL = very low density lipoprotein; HDL = high density lipoprotein; SBP = systolic blood pressure; DBP = diastolic blood pressure.

Table 3. Changes in dietary intake, body mass index, lipid profile and blood pressures during Ramadan fasting in normal healthy adults.

Author(s)	Year	Place	Subjects (n)	Change in diet	Change in weight/ BMI	Changes in lipids	Changes in blood pressure
Matsios <i>et al.</i> ¹⁹	1993	Israel	Young healthy volunteers (24)	NA	BMI (14.6 ± 4.6 vs 24.8 ± 4.4 kg/m ²) (Ramadan vs post-Ramadan)	TC (4.02 ± 1.0 vs 3.88 ± 0.93 mmol/l; <i>p</i> = 0.1), LDL (2.52 ± 0.64 vs 2.57 ± 0.75 mmol/l; <i>p</i> = NS), VLDL (0.50 ± 0.28 vs 0.59 ± 0.25 mmol/l; <i>p</i> = NS), HDL (0.95 ± 0.26 vs 0.72 ± 0.20 mmol/l; <i>p</i> < 0.05), apolipoprotein A1 (1.89 ± 0.37 vs 1.51 ± 0.29 g/l; <i>p</i> < 0.0001), TC/HDL (4.41 ± 1.16 vs 5.66 ± 1.48; <i>p</i> < 0.001), LDL/HDL (2.80 ± 0.78 vs 3.81 ± 1.28; <i>p</i> < 0.001) (Ramadan vs post-Ramadan)	NA
Adlouni <i>et al.</i> ²¹	1997	Morocco	Healthy adult males (32)	Total caloric intake increased, carbohydrates increased 1.4%, proteins increased by 0.4% while fat decreased by 0.7%. Among fat, MUFA and PUFA increased while SFA intake decreased	Body weight (69.61 ± 10.83 vs 67.83 ± 10.73 kg; <i>p</i> < 0.001) pre-Ramadan vs end Ramadan	TC decreased by 7.9% (<i>p</i> < 0.001), TG decreased by 30% (<i>p</i> < 0.001), LDL decreased by 11% (<i>p</i> < 0.0001), HDL increased by 14.3% (<i>p</i> < 0.001)	NA
Adlouni <i>et al.</i> ²⁵	1998	Morocco	Healthy males (32)	Total caloric intake (2683.86 ± 785 vs 3210 ± 101.1 kcal/day; <i>p</i> < 0.05), carbohydrates (337.2 ± 109 vs 412.3 ± 13.7 g/day; <i>p</i> < 0.05), proteins (100 ± 27.4 vs 123.2 ± 24.4 g/day; <i>p</i> < 0.05) Daily intake of total fats was unchanged, but SFA (46.1 ± 3.7 vs 37.84 ± 1.7 g/day; <i>p</i> < 0.05), MUFA (38.7 ± 2.2 vs 56.96 vs 2.6 g/day; <i>p</i> < 0.05) (pre-Ramadan vs end Ramadan)	Body weight (69.61 ± 10.83 vs 67.83 ± 10.73 kg; <i>p</i> < 0.001) (pre-Ramadan vs end Ramadan)	Apo A1 (1.10 ± 0.33 vs 1.23 ± 0.29 g/l; <i>p</i> < 0.05), Apo B (0.95 ± 0.17 vs 0.86 ± 0.21 g/l; <i>p</i> < 0.05), LpAI (0.51 ± 0.16 vs 0.59 ± 0.11 g/l; <i>p</i> < 0.05) (pre-Ramadan vs end Ramadan)	NA
Rahman <i>et al.</i> ²³	2004	Bangladesh	Healthy males (20)	Total caloric intake was similar during Ramadan as well as before and afterwards. Fat intake was significantly higher during Ramadan (24.7 ± 3 vs 10.6 ± 1.4 g/day; <i>p</i> < 0.001)	BMI (24.20 ± 2.48 vs 23.44 ± 2.52 kg/m ² ; <i>p</i> < 0.05)	HDL increased significantly (38.14 ± 7.4 vs 46.71 ± 14.33 mg/dl; <i>p</i> < 0.05), while LDL, TG, and TC showed no significant change	Mean SBP (124.3 ± 13.9 vs 118 ± 10.8 mmHg; <i>p</i> < 0.05) Mean DBP (82.3 ± 11.4 vs 77.3 ± 10.6 mmHg; <i>p</i> < 0.05) (pre- and end Ramadan)
Saleh <i>et al.</i> ²⁰	2005	Kuwait	Healthy subjects (60)	NA	NA	In males, TC (4.91 ± 0.96 vs 4.75 ± 0.76 mmol/l; <i>p</i> < 0.05) and LDL (3.40 ± 0.82 vs 3.16 ± 0.78 mmol/l; <i>p</i> < 0.05). In females, HDL (1.27 ± 0.34 vs 1.32 ± 0.36 mmol/l; <i>p</i> < 0.05) atherogenic index (TC-HDL/HDL) reduced significantly in the study participants (3.78 ± 1.9 vs 3.4 ± 1.55; <i>p</i> < 0.01) (pre- and end Ramadan)	Mean BP (93.1 ± 9.0 vs 90.83 ± 9.83 mmHg, <i>p</i> = 0.13)

Aksungar <i>et al.</i> ²⁴	2005	Turkey	Healthy subjects (20)	NA	None	HDL (49 ± 15.25 vs 56 ± 16.31 mg/dl; <i>p</i> < 0.001) (pre- vs 3rd week of Ramadan)	NA
Ziaee <i>et al.</i> ¹⁶	2006	Iran	Healthy subjects (81)	None	BMI (21.2 ± 4.5 vs 21.4 ± 2.6 kg/m ² ; <i>p</i> = 0.48) (pre vs post Ramadan)	HDL (40.0 ± 9.9 vs 36.4 ± 8.4 mg/dl; <i>p</i> < 0.001), LDL (115.2 ± 26.2 vs 119.6 ± 27.9 mg/dl; <i>p</i> = 0.045) (pre- vs post Ramadan) TC, TG and VLDL remained unchanged	NA
Mansi and Anneh ¹⁸	2007	Jordan	Healthy male volunteers (42)	NA	Body weight (76.64 ± 9.53 vs 72.66 ± 9.2 kg; <i>p</i> < 0.05) (pre- vs end Ramadan)	TC (164.34 ± 28.24 vs 159.57 ± 19.5 mg/dl; <i>p</i> < 0.05), HDL (36.13 ± 6.42 vs 48.86 vs 12.34 mg/dl; <i>p</i> < 0.05) (pre- vs end Ramadan)	Mean SBP (126.32 ± 17.46 vs 112.41 ± 15 mmHg, <i>p</i> < 0.05) Mean DBP (84.53 ± 12.62 vs 76.5 ± 10.6 mmHg, <i>p</i> < 0.05)
Aksungar <i>et al.</i> ²²	2007	Turkey	Healthy subjects (40)	NA	None	No significant changes in TC, TG and LDL levels TC/HDL decreased in the fasting group	NA
Lamri-Serhadji <i>et al.</i> ¹⁷	2009	Algeria	Young healthy volunteers (46)	Total calories intake (13 MJ/day and 11 MJ/day vs 11 MJ/day and 9 MJ/day; <i>p</i> < 0.05) Carbohydrate intake (7.1 and 6.2 MJ/day vs 7.5 and 6.5 MJ/day; <i>p</i> < 0.05) in males and females respectively (pre- vs end Ramadan)	None	TC increased, while LDL decreased by 22% in females and 55% in males HDL increased by 1.4 times in both genders	NA
Barkia <i>et al.</i> ¹⁵	2011	Tunisia	Young healthy volunteers (25)	Total cholesterol (250.9 ± 125.2 vs 529.0 ± 147.3 mg/day; <i>p</i> < 0.001), PUFA (20.1 ± 11.3 vs 30.9 ± 8.7 g/day; <i>p</i> < 0.05), protein (12.2 ± 1.8 vs 15.6 ± 2.0%; <i>p</i> < 0.001) and vitamin E (6.7 ± 4.7 vs 9.6 ± 1.6 mg/day; <i>p</i> < 0.05) (pre- vs end Ramadan) intake increased during Ramadan while intake of carbohydrates decreased	Increased	TC (4.4 ± 0.5 vs 5.0 ± 0.7 mmol/l; <i>p</i> < 0.001), LDL (2.9 ± 0.5 vs 3.5 ± 0.8 mmol/l; <i>p</i> < 0.05) and Apo B (0.8 ± 0.2 vs 0.9 ± 0.1 mmol/l; <i>p</i> < 0.05) (pre- vs end Ramadan) increased during fasting	NA

NA = data not available; TC = total cholesterol; TG = triglycerides; LDL = low density lipoprotein; VLDL = very low density lipoprotein; HDL = high density lipoprotein; SFA = saturated fatty acids; MU = megajoule; MUFA = mono-unsaturated fatty acids; PUFA = poly-unsaturated fatty acids; Lp AI = Lipoprotein AI; BP = blood pressure; DBP = diastolic blood pressure.

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Table 4. Changes in dietary intake, BMI, lipid parameters and blood pressure in patients with metabolic syndrome or dyslipidemia.

Author(s)	Year	Place	Subjects (n)	Change in diet	Change in weight/BMI	Changes in lipids	Changes in blood pressure
Afrasiabi <i>et al.</i> ²⁷	2003	Iran	Patients with hyperlipidemia (28)	Total calories and fat intake was lower	BMI decreased significantly among subjects who fasted as compared to subjects who did not fast ($p < 0.05$)	Total cholesterol and triglycerides decreased while HDL increased significantly ($p < 0.05$) in fasting subjects. No change was noted in subjects who did not fast	NA
Akanji <i>et al.</i> ²⁹	2000	Kuwait	Patients with dyslipidemia	NA	None	Apo A-1, apo A-1/apo B and apo A-1/HDL ratios were increased in non-diabetic patients ($p < 0.001$). In diabetic patients, total cholesterol and apo B increased ($p < 0.05$) in addition to the changes seen in non-diabetics	NA
Shariatpanahi <i>et al.</i> ²⁸	2008	Iran	Males with metabolic syndrome (55)	Total caloric intake as well as intake of carbohydrate, fats and proteins were significantly lower	BMI reduced significantly (27.62 ± 3.39 vs 26.87 ± 3.36 kg/m ² ; $p < 0.001$)	HDL cholesterol increased (428.7 ± 54.5 vs 462.4 ± 55 mg/l; $p = 0.004$)	Mean systolic and diastolic blood pressures decreased ($p < 0.001$)
Sadiya <i>et al.</i> ²⁶	2011	Ajman	Patients with metabolic syndrome (19)	Protein intake was lower by 12% while fat intake increased by 23%. Total caloric intake was unchanged	Body weight (103.9 ± 29.8 vs 102.1 ± 29.0 kg, $p = 0.001$)	None	NA

NA = data not available; BMI = body mass index; HDL = high density lipoprotein.

Table 5. Changes in dietary intake, body weight/BMI and lipid parameters during Ramadan fasting in patients with type 2 diabetes.

Author(s)	Year	Place	Subjects (n)	Change in diet	Change in weight/BMI	Changes in lipids
Yarahmadi <i>et al.</i> ³²	2003	Iran	Patients with type 2 diabetes mellitus (57)	Daily cholesterol intake increased in all subjects	BMI increased in females ($p < 0.03$) but decreased in males ($p < 0.01$)	TC and LDL cholesterol increased significantly in all subjects
Khatib and Shafaghi ³⁰	2004	Jordan	Type 2 diabetes (44)	NA	Body weight (83.01 ± 11.45 vs 81.44 ± 10.96 kg; $p < 0.05$) (pre- vs end Ramadan)	TG decreased during end of Ramadan (192 ± 107 vs 157 ± 76 mg/dl, $p < 0.05$) (pre- vs end Ramadan) LDL, TC and HDL were not affected
Khaled <i>et al.</i> ³¹	2006	Algeria	Obese females with type 2 diabetes mellitus (60)	NA	Non-significant reduction in BMI	HDL decreased significantly (26.81%, $p < 0.001$) A significant increase in TC (13.85%, $p < 0.001$), TG (16.9%, $p < 0.003$) and LDL (22.39%, $p < 0.0001$) was noted

NA = data not available; BMI = body mass index; TC = total cholesterol; TG = triglyceride; LDL = low density lipoprotein; HDL = high density lipoprotein.

Table 6. Changes in body weight/BMI, lipids and 24 hour ambulatory blood pressure in treated hypertensive patients during Ramadan fasting.

Author(s)	Year	Place	Subjects	Change in diet	Change in weight/BMI	Changes in lipids	Changes in BP
Perk <i>et al.</i> ³³	2001	Israel	Hypertensives (17)	NA	Body weight decreased by 1.4 ± 1.6 kg, $p < 0.002$	NA	None
Khosropanah <i>et al.</i> ³⁴	2003	Iran	Hypertensives (21)	NA	NA	NA	The average daytime systolic and diastolic BP were significantly lower during Ramadan fasting ($p < 0.01$ and $p < 0.005$ respectively)
Akturk <i>et al.</i> ³⁵	2012	Turkey	Hypertensives (20)	NA	NA	NA	The mean daytime systolic and diastolic BP as well as the average systolic and diastolic BP were lower during Ramadan
Biyik <i>et al.</i> ³⁶	2012	Turkey	Hypertensives (20)	NA	NA	TC, LDL, VLDL, TG remained normal - A significant reduction in HDL cholesterol was noted (47.76 ± 16.93 vs 43.94 ± 12.96 mg/dl; $p = 0.014$) (pre- vs end Ramadan)	NA

NA = data not available; BMI = body mass index; BP = blood pressure; TC = total cholesterol; LDL = low density lipoprotein; TG = triglycerides; VLDL = very low density lipoprotein; HDL = high density lipoprotein.

Khafaji *et al.*¹⁰ reported a significant worsening of lipid parameters in stable cardiac patients during Ramadan fasting even though 90% of patients were compliant with dietary as well as medical recommendations and there was no significant change in weight during the study period. In this study, blood samples were collected between 9 am and 11 am during Ramadan as well as during the non-Ramadan days. During the two-meal schedule followed in Ramadan fasting, a big meal (suhour) is consumed during the pre-dawn period (around 3 am) which implies that blood samples were collected for estimation of lipid profile 6 to 8 hours after suhour, while the same was done more than 12 hours after dinner in non Ramadan days. As per National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III)³⁸ and European guidelines³⁹, blood for estimation of lipid profile should be collected after a fasting period of around 12 hours. This might be the reason for the lipid derangement noted in this study. In all other studies included in the analyses, blood extraction for lipid estimation was done after a fasting period of around 10 ± 2 hours. These studies reported a beneficial change in body weight, lipids and blood pressures during Ramadan fasting in patients with stable cardiac disease.

The most appropriate timing for blood extraction for estimation of lipid parameters in patients during Ramadan fasting is not known. The NCEP ATP III guideline recommends 9–12 hours fasting before blood extraction for lipid estimation³⁸. Further, NCEP ATP III guideline recommends an upright position for at least 5 minutes before blood extraction to avoid the effect of hemodilution and subsequent under-estimation of serum lipid levels^{38,40}. We believe that blood extraction after 9–12 hours fasting, preferably before the pre-dawn 'sahoor' would be the most appropriate time for lipid estimation because fluid deprivation associated with fasting during the daytime may result in hemoconcentration and subsequent over-estimation when samples are extracted during the late afternoon hours.

Barkia *et al.*¹⁵ reported that in Tunisian healthy subjects, the total dietary intake of cholesterol increased more than twice during Ramadan fasting and was accompanied by significant weight gain and worsening of lipid parameters. The blood levels of cholesterol and lipoproteins are a reflection of dietary fat intake⁴¹. Moreover, under circumstances of starvation, the body stores of fat tissues are utilized for energy production which manifests by derangements in lipid parameters⁴². When coupled with fluid restriction, the lipid derangements seen during starvation gets further aggravated⁴². In the cohort of Ziaee *et al.*¹⁶ which comprised healthy subjects, males had a mean body mass index of 23 kg/m^2 which decreased to 22 kg/m^2 while females had a mean body mass index of 21.9 kg/m^2 which declined to 20.9 kg/m^2 during Ramadan fasting. Dietary intake was similar during

Ramadan fasting and during the non-fasting days. Lipid parameters deteriorated in the study subjects, being more marked in females compared to males. The significant reduction in body mass index and blood sugar, while the subject's dietary intake were similar during Ramadan fasting and during the non-fasting days, suggests that the derangements in lipid parameters were probably secondary to ongoing starvation.

All other studies on healthy subjects reported a beneficial effect on lipid profile during Ramadan fasting, along with a decline or no change in body weight^{17–25}. Under normal circumstances, dietary modifications result in improvement of lipid profile only if associated with weight loss^{43,44}. The interesting finding of our systematic review are the studies which reported significant improvements in lipid profile, most notably 30% to 40% increase in HDL levels, even when there was no change in body weight among the subjects^{17,19,24}. Is it the change in feeding pattern during Ramadan fasting which gives rise to this substantial improvement in HDL level? This question needs to be addressed in properly designed clinical studies in the future.

Sadiya *et al.*²⁶ reported a 23% increase in dietary fat intake in a cohort of predominantly female subjects with metabolic syndrome, despite which there was no change in lipid profile while there was a significant decline in body weight during Ramadan fasting. The level of physical activity was higher among the subjects during the study which may be the reason why body weight and plasma lipids did not worsen. In the other studies, patients with metabolic syndrome as well as those with dyslipidemia showed a beneficial improvement in lipid profile, body mass index, dietary intake and blood pressures^{27–29}.

Patients with type 2 diabetes mellitus did not exhibit any significant improvement in lipid profile during Ramadan fasting. The diabetic subjects in the cohort of Khatib and Shafagoj³⁰ showed a significant reduction in body mass index and blood sugar during Ramadan fasting while a reduction in triglycerides was the only change noted in lipid parameters. Significant derangements in lipid parameters were noted in the other studies, even when Ramadan fasting was associated with a significant reduction in body weight^{29,31,32}. Small frequent meals are the hallmark of a diabetic diet and are associated with significant improvement in plasma lipid levels⁴⁵. During Ramadan fasting, an opposite dietary pattern is followed which might be the reason behind the derangement of lipid parameters reported. Secondly, insulin resistance in type 2 diabetes results in inefficient utilization of carbohydrates for energy production, as a result of which, fat is metabolized for energy production with subsequent increment in lipid components in blood – a situation similar to that seen during starvation⁴². However, as serum ketone levels were not measured in any of the studies, we can only speculate this as one of the possible explanations.

In view of increased incidence of ischemic stroke¹⁰ as well as a minimal non-significant increase in hospitalization for acute decompensated heart failure¹ during Ramadan fasting in patients with type 2 diabetes, these patients with type 2 diabetes mellitus should be closely monitored during Ramadan fasting. In our clinical practice, we observe that most diabetic patients increase carbohydrate intake and restrict physical activity during Ramadan fasting in apprehension of hypoglycemia. This practice should be discouraged and physical activity encouraged in an attempt to improve insulin sensitivity and the associated glucose metabolism, while avoiding fat catabolism for energy production and the subsequent abnormality in lipid profile.

Biyik *et al.*³⁶ reported a significant decline in HDL level, while other lipid parameters remained unchanged during Ramadan fasting in hypertensive patients on combination therapy. In the absence of data regarding dietary intake, weight change and the type of anti-hypertensive agents used, the reason for this decrease in high density lipoprotein level is difficult to interpret. However, further properly designed studies are required in this special patient group to evaluate this association. Other studies reported a significant improvement in daytime blood pressure in hypertensive patients on combination therapy during Ramadan fasting^{34,35}.

Limitations

Limitations of our systematic review relate to the limitations of the sources studied. Differences in definition and reporting of outcomes make comparison across studies difficult. The studies were done in different geographical locations where daylight hours and climatic conditions differed and the fasting was observed under different conditions. The number of studies in the different patient subgroups and the number of patients in these studies were few which limits our ability to draw firm conclusions.

Conclusion

On the basis of available evidence, we can conclude that fasting during the month of Ramadan does not increase the burden of acute cardiac illness. Patients with stable cardiac illness can fast during Ramadan provided that the recommended dietary and medication regimes are complied with. Cardiovascular risk factors reveal a trend towards improvement in healthy individuals and in patients with stable cardiac disease, metabolic syndrome, dyslipidemia and systemic hypertension, provided that an unhealthy dietary pattern is avoided. The improvement in plasma lipid levels, especially 30% to 40% improvement in HDL levels, as reported in some studies, appear promising and

should be explored further to gain insight into management of low HDL dyslipidemia.

Patients with type 2 diabetes mellitus failed to show any significant improvement in plasma lipid levels during Ramadan fasting even when a regime of proper diet and exercise is followed, while on the other hand, plasma lipids and other cardiovascular risk factors undergo significant deterioration when diet and exercise regime are not complied with. These patients should be counseled regarding the importance of strict adherence to diet and exercise regime during Ramadan fasting and should be closely monitored clinically.

Transparency

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