Ramadan Fasting And Cardiac Biomarkers In Patients With Multiple Cardiovascular Disease Risk Factors

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Citation

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Abstract

Objectives:
The study was aimed to evaluate the effect of fasting during Ramadan on cardiovascular bio-markers [high sensitive C - reactive protein (hs-CRP), plasminogen activator inhibitor type-1 (PAI-1)] with other conventional cardiovascular risk factors like diabetes (DM), hypertension (HPT) and dyslipidaemia before, during and after Ramadan of the subjects under study.
Methodology:
It was a prospective cohort study with 76 subjects (41 males and 35 females) who were observed before during and after Ramadan.).At each visit anthropometric parameters were measured including the body weight, body mass index (BMI) and blood pressure. Blood was analyzed for metabolic index [fasting blood glucose (FBG), glycosylated hemoglobin A1c (HbA1c) and fasting serum lipids], hs-CRP and PAI-1.More than 50% of the subjects under study had 4 risk factors such as DM, HPT, dyslipidaemia and either family history of CAD or smoking.
Results:
A significant reduction of hs-CRP and PAI-1 was observed during Ramadan compared to pre-Ramadan ($p < 0.001$ and 0.031). The reduction of PAI-1 levels was continued till post-Ramadan ($p = 0.005$). A rebound in the levels of hs-CRP was observed in post-Ramadan compared to Ramadan ($p < 0.001$).Significant ($p<.001$) reduction of the body weight, BMI, systolic and diastolic blood pressure was observed during Ramadan compared to pre-Ramadan and post-Ramadan. LDL-C levels were reduced during and post-Ramadan, ($p = 0.037$ and $p = 0.030$), however, no significant effect on triglyceride and total cholesterol was found throughout the study.
Conclusion:
The practice of fasting during the month of Ramadan by the people with multiple CVD risks might be cardio-protective as it resulted in the lowering of both hs-CRP and PAI-1. However this benefit is short-lived as the hs-CRP rebound a month later. Ramadan fasting practice was found to give short-term benefit against cardiovascular diseases among the patients with multiple cardiovascular risks factors.

INTRODUCTION

Ramadan fasting is one of the five pillars of Islam observed by the Muslim adults worldwide[1]. Fasting Muslims abstain from food, liquids, tobacco, sexual activity and medication (oral, inhaler or injection) from sunrise to sunset. Food and fluid are consumed at night and the frequency and quantity of meals, sleep duration and daily physical activity are reduced. The effects of fasting in Ramadan on the body are classified to physical (e.g. weight loss), metabolic (fuel stores, glucose), mineral (potassium, uric acid), hormonal (thyroid hormone, growth hormone), psychological adaptations[2]. Previous studies described the weight loss of 1.1 kg in females and 4.4 kg in males during Ramadan.[3] The Ramadan fasting also influenced lipid profile with variable results in healthy subjects[4].A previous study showed that the cholesterol level (HDL and total cholesterol) decreased in the first few days of fasting while some other studies showed no change [5] or reduction of cholesterol level during fasting.[6]

Several studies in a type 2 diabetes population showed that Ramadan fasting did not alter any biochemical parameters.[7] While other studies showed that there was either an increase or a decrease in certain biochemical (blood sugar, HbA1c) parameters during Ramadan.[8]

Fasting during Ramadan may have negative repercussions on cardiac patients; the obligation that the daily calorie

intake has to be taken in one or two meals instead of three to five is a considerable effort. Furthermore the obligation to perform heavy physical worship (long time prayer at night) after the break of fast can be strenuous on the cardiovascular system. The drug schedule during the daytime is changed due to fasting, which may have an effect on cardiac patients. Data on incidence of acute coronary syndrome (ACS) during fasting Ramadan are scarce and conflicting, Gumaa et al. based on clinical observations, reported an increase in complaints of angina pectoris during Ramadan[9]. However, other investigators have found no negative impact of fasting on ACS[10], stroke[11], or hospital admissions for heart failure during Ramadan.[12] The present study was therefore aimed at to determine the effect of Ramadan fasting on surrogate cardiovascular biomarkers (hs-CRP, PAI-1) in patients with multiple CVD risk factors and also to assess the effect of Ramadan fasting on body weight, blood pressure, fasting lipids (FSL) and fasting blood sugar (FBS) and HbA1c.

MATERIALS AND METHODS

Study population: Patients were recruited from the endocrine and cardiology clinics of the University Kebangsaan Malaysia Medical Centre (UKMMC)during Ramadan above the age of 40 and possessing two of the following CVD risk factors were included in the study.

- Hypertension (HPT) (systolic Bp >160, diastolic Bp >110).
- Diabetes Mellitus (DM) with (HbA1c >7 %).
- Dyslipidemia (LDL >2.7 mmol/l, HDL <1.0 mmol/l).
- Current smokers.
- First degree family history of premature CVD (male younger than 55 years and female younger than 65 years considered)
- Obesity (BMI >27.5 kg/m2)(Asian Pacific guidelines for the management of obesity)

Study protocol: This is a prospective observational study, which was conducted at UKMMC on 2 occasions during the fasting months of Ramadan in the year 2008 and 2009. During the 2 study periods a total of 121 patients were recruited, however, only 94 were examined at the first visit that was a week before the onset of Ramadan. The others were excluded due to various reasons (history of pre-existing CVD e.g. IHD, MI, CVA, other concurrent inflammatory disorders e.g. Rheumatoid disease or intercurrent infections and those if fasting endanger their health e.g. DM with frequent hypoglycemia, etc.). The second visit at the 3 th week of Ramadan only managed to screen 88 subjects while others were unable to continue fasting or did not turn up. During the last visit, which was a month after Ramadan, 76 subjects were available. Patients were recruited after obtaining their consent for the present study. At each visit anthropometric parameters were measured including the body weight, height, body mass index (BMI) and blood pressure (BP). An amount of 10milliliters of fasting venous blood was drawn at each visit and storedin separate plain tubes. The blood samples were analyzed for the following:

Fasting blood glucose (FBG) and Glycosylated hemoglobin A1c (HbA1c).

Fasting serum lipids (FSL) consisting of:

- Triglyceride (TG)
- Total cholesterol(TC)
- HDL-cholesterol(HDL-C)
- LDL-cholesterol (LDL-C)
- hs-CRP and PAI-1

Anthropometric variables: Body weight was measured during all visits by using a digital weighing scale (SECA, British-Indicators Ltd., U.K). The body weight was recorded in kilograms to the nearest 0.1 kilogram (kg). Subjects were weighed barefoot in very light clothing. Height was measured without shoes using a standard stadiometer. It was recorded in centimeter to the nearest 0.5 centimeter (cm) with the shoulder in relaxed position and arms hanging freely. BMI was calculated by dividing the weight in kilograms by the square of the height in metres (kg/m^2). BMI (kg/m^2) = body weight (kg) / height (m^2). In this regard Body Mass Index (BMI) classification of the Asia Pacific guidelines for the management of obesity was followed.[13]

BP was measured with the use of an automatic BP monitor (Omron M4-1; Omron Healthcare Europe BV, Hoofdorp, Netherland), in seated position, 10 minutes after resting. The reading was taken using an appropriate cuff on the right arm. Two reading were recorded in mmHg and the average of the 2 readings was recorded.

Biochemical assays: Sera for the all assays were obtained by centrifugation at 3500 rpm for 10 minutes at room temperature and stored at -20 C until assayed. All the samples were assayed in a batch analysis to avoid inter assay variation.

Fasting blood sugar (FBS) was measured by the Hexokinase enzymatic method. HbA1c concentration was measured after hemolysis of the EDTA anti-coagulated whole blood specimen by the COBAS INTEGRA 800 (I800) system (Roche Diagnostic, Basel Switzerland). The concentration of HbA1c was determined by high performance liquid chromatography (HPLC) with Boronate Affinity method using PDQ from PRIMUS CORP. The quality control (QC) samples were 4.5 – 5.5% for low level and 9.8 – 10.8% for high level.

Flinders Sensitive Line (FSL) including TC, plasma TG and HDL-C were analyzed by the COBAS Integra Cholesterol Gen.2 cassette contained diagnostic reagent system for the quantitative determination of TC, TG and HDL-C respectively. Cholesterol assays were measured by enzymatic and calorimetric methods Measurement of LDL-C was calculated by using the equation of Friedewald[14]: (LDL-C) = (TC - (TG/5 + HDL-C).

High sensitivity C-reactive protein (hs-CRP) assay: The assay was done with the collected sera by Demeditec Diagnostic Systems Laboratories inc. (DE-961CRP01H) Germany, C-Reactive Protein Enzyme-Linked immunosorbent Assay (ELISA) kit. The normal adult range was between 254-16104 ng/ml (0.0254 – 1.6104 mg/dl). The coefficient of variation ranges between 2.1 to 3.9%.

Plasminogen activator inhibitor type-1 (PAI-1):Sera was analysedfor PAI-1 by an enzyme-linked immunosorbent assay for the quantitative detection of human PAI-1, ELISA kit (BMS2033) Vienna, Australia.

Statistical analysis:Data was entered and analyzed using the Statistical Package for the Social Science (SPSS) version 16. Statistical significance was set at p value of less than 0.05 ($p<0.05$).

Ethics and funding: This study was approved by the Ethic and Clinical Research Committee, Faculty of Medicine, UKM project code (FF-221-2008). This research was funded by the research grant from the Faculty of Medicine UKM.

RESULTS

Response rate: A total of 121 subjects were screened during the 2 study periods of Ramadan in the year 2008 and 2009. At end of Ramadan 2009 only 76 subjects retained in the study.Majority of the variables were normally distributed, hence the mean and standard deviation (SD) were used.

Socio-demographic characteristics: Forty-one patients were males (53.9%) and 35 were females (46.1%). The mean age of the patients was 54.68 ± 8.34 (SD) years, with a range of 40 to 78 years. All of them were Malays (Muslims)

Clinical and biochemical characteristics of the subjects: There was reduction in the BP, LDL-C, TG, weight, BMI, PAI-1 and hs-CRP in Ramadan compared to pre-Ramadan (pre-R) and post-Ramadan (post-R)(table-1). The reduction in PAI-1 and LDL-C levels continued even post-Ramadan period. On the other hand, there was an increase in hs-CRP, HDL-C, FBS and HbA1c even post-R.

There was a significant reduction in LDL-C in and post-R as well as pre and post-R with (3.24 mmol/L vs. 3.19 mmol/L, $p = 0.037$ and 3.19 mmol/L vs. 3.01 mmol/L, $p = 0.030$) respectively. There was a significant increase in HDL-C pre-R, Ramadan and post-R (0.89 mmol/L vs. 0.93 mmol/L vs. 1.12 mmol/L, $p=0.034$, < 0.001 and < 0.001) respectively. There was a significant increase in HbA1c pre, Ramadan and post-R (7.79% vs.8.06% vs. 8.53%, $p= 0.002$, 0.002 and < 0.001) respectively. There was no significant difference in FBS, TG and TC throughout the study period ($p > 0.05$).

A significant difference was observed in systolic blood pressure (SBP) of post-R compared to the period during Ramadan, (136mmHg vs. 129mmHg, $p = 0.006$). There was a significant reduction in diastolic blood pressure (DBP) in Ramadan compared to pre-R (78. mmHg vs. 75mmHg, $p < 0.001$), as well as reduction in DBP post-R compared to pre-R (75.25mmHg vs. 78.33 mmHg, $p= 0.021$).

Figure 1

Table-1: Comparison of clinical and biochemical characteristics of subjects during Ramadan, pre-R and post-R

Characteristics	pre-R	Ramadan	post-R
Blood Pressure			
SBP	132.46 (18.02)[a]	129.78(17.95)[a]	136.64(17.69)[a]
DBP	78.33 (9.89)[a]	75.32(10.26)[a]	75.25(10.26)[a]
Anthropometric measurements			
*WT	72.00 (12.40)	71.00(12.87)	72.00(13.90)
BMI	28.00 (5.80)	27.65(6.08)	27.95(6.43)
FBS	8.25(3.24)[a]	8.51(3.25)[a]	8.05(2.87)[a]
HbA1c	7.79(1.74)[a]	8.06(1.72)[a]	8.54(2.13)[a]
Fasting serum lipid			
LDL-C	3.24(0.85)[a]	3.19(0.89)[a]	3.01(0.64)[a]
TG	1.96 (0.9)1.80(0.93)	1.88(0.98)	
HDL-C	0.89(0.26)[a]	0.93(0.25)[a]	1.12 (0.26)[a]
T-Chol	5.02(0.79)[a]	5.04(0.83)[a]	5.02(0.68)[a]
Cardiovascular biomarkers			
hs-CRP	1.35(1.87)	0.93(1.46)	1.50(2.30)
PAI-1	57.85 (42.76)	40.63(33.77)37.00(35.97)	

[a]Data is normally distributed, mean (±SD) *WT: Weight

Figure 2

Table-2: Risk factors changes during Ramadan, pre-R and post-R

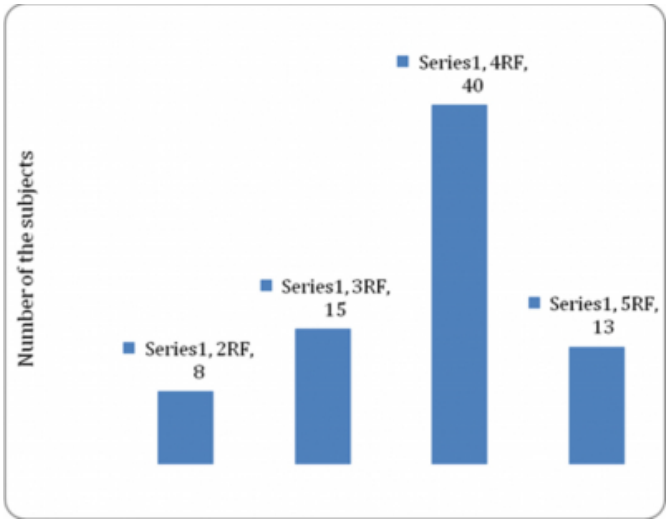
Variables	pre-R*	Ramadan*	p value#	Ramadan*	post-R*	p value#
LDL(mmol/L)	3.24	3.19	0.51	3.19	3.01	**0.037**
HDL(mmol/L)	0.89	0.93	**0.034**	0.93	1.12	**<0.001**
HbA1c %	7.79	8.06	**0.002**	8.06	8.53	**0.002**
Systolic Blood Pressure(SBP) mmHg	132.46	129.77	0.053	129.77	136.64	**0.006**
Diastolic Blood Pressure(DBP) mmHg	78.33	75.32	**<0.001**	75.32	75.25	0.752

*Mean value
p significant at < 0.05
using Paired samples t-Test

The majority of the subjects had two or more traditional risks factor for CAD, and 40 subjects of them (52.6 %) had 4 risk factors such as DM, HPT, dyslipidaemia, family history of CAD or smoking. (Fig.1).

Figure 3

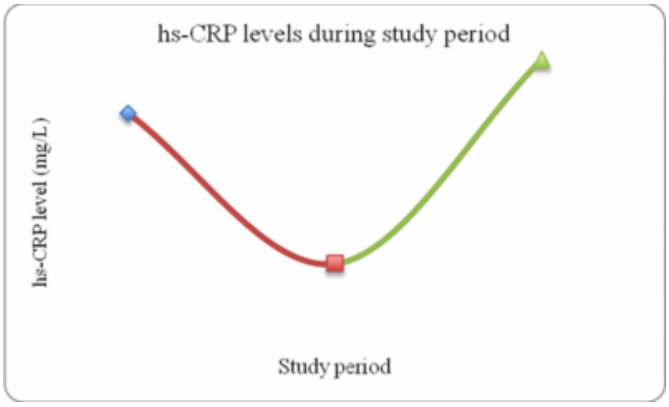
Fig. 1: Shows the cardiac risk factors among study population



There was a significant reduction in hs-CRP during Ramadan compared to the period pre-R (0.93mg/L vs. 1.35 mg/L, p<0.001). The hs-CRP post-R increased significantly compared to the period during Ramadan (1.50 vs. 0.93 mg/L, p <0.001). However, there was no significant change in hs-CRP pre-R and post-R (p = 0.464) (Fig.2).

Figure 4

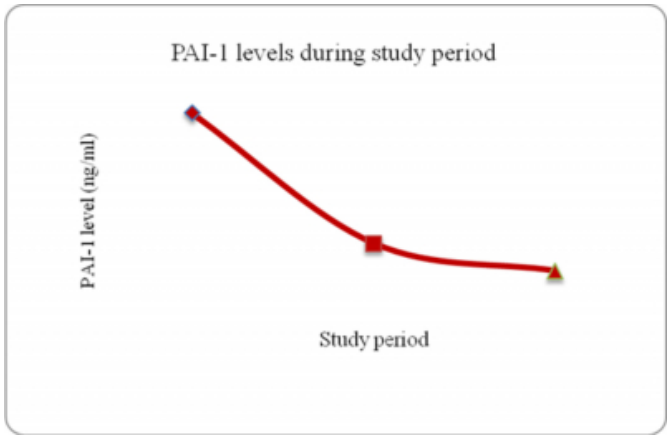
Fig.2: Shows the series of hs-CRP levels pre-R, Ramadan and post- R.



There was a significant reduction in PAI-1 during Ramadan compared to pre-R (57.85 vs. 40.63 ng/ml, p = 0.031), as well as significant reduction in PAI pre-R and post-R (57.85 vs. 37.00 ng/ml, p = 005). However, there was no difference of PAI during Ramadan compared to post-R (p = 0.366) (Fig.3).

Figure 5

Fig3: Shows the series of PAI-1 levels pre-R, Ramadan and post- R.



Difference in weight between male and female were observed, however, it was statistically significant only at pre-R (p=0.036). There was a significant reduction in female body weight during Ramadan compared to pre-R (70.50kg vs. 71.85kg, p <0.001) and post-R (70.00kg, p=0.003) respectively. Male patients had significant weight reduction during Ramadan compared to pre-R (71.00 kg vs. 72.95 kg, p <0.001). However, their weight was significantly increased post-R compared to Ramadan (72.50kg vs. 71.00kg, p <0.001).There was significant difference in BMI during Ramadan compared to pre-R (27.65 kg/m^2 vs.28.00 kg/m^2, p <0.001) and post-R respectively (27.65 kg/m^2 vs. 27.95 kg/m^2, p < 0.001).

Females had significantly higher hs-CRP levels pre-R and during Ramadan compared to males (1.69mg/L vs. 0.81 mg/L, p = 0.010 mg/L and 1.39 vs. 0.53 mg/L, p= 0.036) respectively. However hs-CRP level was not significantly different between the genders post-R (p = 0.058). PAI-1 was not significant throughout the study period (Table 3).

Non-diabetic patients had significantly higher hs-CRP level pre-R than diabetic patients (1.82 mg/L vs. 1.23 mg/L, p = 0.035). However there was no significant difference in hs-CRP level in and post-R between the two groups (Table 4).

Figure 6

Table-3: Cardiovascular biomarkers by gender

Variable	Male	Female	Mann-Whitney	p value
hs-CRP_1	0.81	**1.69**	453.500	**0.010**
hs-CRP_2	0.53	**1.39**	499.500	**0.036**
hs-CRP_3	1.30	2.23	409.00	0.058
$PAI\text{-}1_1$	54.54	60.16	669.00	0.766
$PAI\text{-}1_2$	40.63	42.04	633.00	0.496
$PAI\text{-}1_3$	32.66	39.80	422.500	0.119

hs-CRP_1, hs-CRP_2 and hs-CRP_3 refer to hs-CRP pre-R, Ramadan and post-R, respectively, $PAI\text{-}1_1$, $PAI\text{-}1_2$ and $PAI\text{-}1_3$ refer to PAI pre-R, Ramadan and post-R, respectively.
p significant at < 0.05

Figure 7

Table-4: Cardiovascular biomarkers compared between diabetic and non-diabetic patients

Variables	Diabetic	Non-Diabetic	Mann-Whitney	p value
hs-CRP_1	1.24	1.83	272.00	**0.035**
hs-CRP_2	0.67	1.37	303.00	0.092
hs-CRP_3	1.36	2.08	279.00	0.156
$PAI\text{-}1_1$	55.85	44.11	342.00	0.250
$PAI\text{-}1_2$	38.57	49.31	329.00	0.183
$PAI\text{-}1_3$	38.87	35.87	356.00	0.906

hs-CRP_1, hs-CRP_2 and hs-CRP_3 refer to hs-CRP pre-R, Ramadan and post-R, respectively, $PAI\text{-}1_1$, $PAI\text{-}1_2$ and $PAI\text{-}1_3$ refer to PAI pre-R, Ramadan and post-R, respectively.
p significant at < 0.05

There was an increase of HbA1c among diabetes population at pre-R, Ramadan and post-R (7.85% vs. 8.00% vs. 8.60%, p=0.001, 0.009 and < 0.001) respectively. There was significant reduction in hs-CRP in Ramadan compared to pre-R (0.66 vs. 1.24mg/L, p <0.001). The hs-CRP post-R was significantly increased compared to Ramadan (1.36mg/L vs. 0.66 mg/L, p <0.001). However, no significant difference was observed in hs-CRP pre-R and post-R (p= 0.485). A significant reduction was observed in PAI-1 among the diabetic patients in Ramadan compared to pre-R (57.85ng/ml vs. 38.89 ng/ml, p = 0.010) as well as significant reduction in PAI-1 pre-R and post-R (58.57ng/ml vs. 38.02 ng/ml, p = 005). However, there was no difference in PAI in Ramadan and post-R (p= 0.855).

There was positive correlation between hs-CRP and PAI among diabetic patients before Ramadan (r = 0.313, p=

0.014). There was no correlation between the hs-CRP and HbA1c and between PAI-1 and hbA1c pre-R.

DISCUSSION

Coronary artery disease (CAD) is the leading cause of cardiovascular mortality worldwide with > 4.5 million deaths occurring in the developing countries alone. Despite a recent decline in developed countries, both CAD mortality and the prevalence of CAD and its risk factors continue to rise rapidly in developing countries.[15] The patho-physiology of CAD remains a complex process involving inflammatory, haemostatic and vascular reactions. Inflammation plays a major role in atherothrombosis, and measurement of inflammatory markers such as hs-CRP may provide a novel method for detecting individuals at high risk of plaque rupture[16]. Several large-scale prospective studies demonstrate that hs-CRP is a strong independent predictor of future MI and stroke among apparently healthy men and women and that the addition of hs-CRP to standard lipid screening may improve global risk prediction among those with high as well as low cholesterol levels.[16]

The aim of this study was to determine the effect or the influence of fasting during the month of Ramadan on surrogate cardiovascular markers using hs-CRP which can predict the global cardiovascular risk as well as using PAI-1 which can predict the risk of atherosclerotic plaque thrombosis in high risk population.

In our study, we had managed to recruit 76 subjects who were a high risk group for CAD; there were 41 (53.9%) males and 35 (46.1%) females with mean age of 54.68 years. All of them were Malay, the majority of subjects had two or more traditional risk factors for CAD, and more than 50% of them had 4 risk factors such as DM, HPT, dyslipidaemia and either family history of CAD or smoking. In our study, 81.6% of them were diabetic, 75%, were hypertensive, 73.7% had dyslipidaemia, 30% of them had family history (first degree relative) of CAD and only 11% were smokers. This reflected the high risk of our study population with no prior history of CAD.

The major finding of the present study in fasting subjects is that hs-CRP and PAI-1 were significantly decreased during Ramadan compared to the period before Ramadan ($p < 0.001$ and 0.031 respectively). hs-CRP is an acute phase inflammatory protein that can predict the global cardiovascular risk.[16] Levels at less than 1mg/L, 1 to 3mg/L and more than 3mg/L can determine low, moderate and high risk groups for CVD.[17] These levels were measured before, during and after Ramadan and there were significant differences. The percentage of subjects with moderate and high risk before Ramadan reduced from 43.06% to 33.3% in the moderate risk group and 20.83% to 12.5% in the high risk group, this reductions were significant in the 2 groups ($p < 0.001$), as a result Ramadan fasting conveys a protection for this kind of patients as evidenced by reduction in their hs-CRP levels. Furthermore the percentage of low risk population who had a low level of hs-CRP before Ramadan was 36.11%, which increased during Ramadan to 54.2%. This can be easily explained by the addition of subjects from the moderate and high risk groups before Ramadan as their hs-CRP levels became lower during Ramadan. On the other hand the hs-CRP levels had significantly increased again after Ramadan ($p < 0.001$). Hence, the effect of Ramadan was not sustained the end of fasting (Fig. 3).

This finding was similarly seen by Fehime et al.[18] who evaluated the influence of prolonged intermittent fasting in a model like Ramadan on inflammatory markers such as CRP, homocysteine and TC- /HDL-C ratio in 40 healthy subjects. He found significant low levels of these markers in the fasting group during Ramadan ($p < 0.001$). The changes in the meal schedule during Ramadan may beneficially affect inflammatory markers. Recent studies demonstrated that fasting has anti-inflammatory, antiplatelet, and mild anticoagulant effects[19] although our study was not aimed to measure the above factors. Each of these effects has been shown to decrease cardiovascular risk, since these beneficial effects are combined during fasting, a decrease in cardiovascular risk can be expected[20].

A study by Lindmark et al[21] evaluated the pattern of immunologic and procoagulant between female and male patients with acute coronary syndrome. They found women had higher levels of CRP as well as platelet-leukocyte complex than men regardless of the severity of the disease, indicating differences in pathogenetic mechanisms.

The level of hs-CRP was also elevated more among non-diabetic patients before, during and after Ramadan however this was only significant before Ramadan ($p = 0.035$). Previous studies had evaluated interrelationships between CRP and metabolic syndrome, which is comprised of waist circumference, dyslipidaemia, abnormal glucose tolerance and BP[22] it showed that metabolic syndrome is associated with increased levels of CRP (36). CRP is considered as important biomarker in metabolic syndrome has been proved[23]

Lowering hs-CRP by lipid lowering agents like statins had shown a beneficial effect on cardiovascular risk in many previous studies (37-39) Ankur et al[24] found a greater reduction in hs-CRP up to 22-40% in patients with acute coronary syndrome treated with atorvastatin for 4 weeks. This beneficial effect was independent of statin effects on cholesterol. In the most recent trial "Jupiter trial"[25] using rosuvastatin in group of subjects with low cholesterol, which was stopped early due to decrease risk of primary endpoint of first major cardiovascular events? We assumed that statin therapy in most of our diabetic patients (73.7%) might have reduced their hs-CRP levels compared to the non-diabetic patients. Fasting in the month of Ramadan had significantly reduced hs-CRP levels as shown in our study. This result will have beneficial effect on cardiovascular patients. However, the present study in relation to antihypertensive medication was not performed.

In the present study, hs-CRP had a positive correlation with PAI-1 before and after Ramadan ($p = 0.025$ and $p = 0,005$). Hence Ramadan fasting was able to bring their levels to the low range which may bring protective effects.

In our study we were able to demonstrate that Ramadan fasting significantly reduced PAI-1 levels compared to the period before Ramadan ($p = 0.031$). There was significant reduction in PAI before and after Ramadan ($p = 005$). However there was no difference in PAI during and after Ramadan ($p = 0.366$) (Fig.4). The exact reason for such result of PAI has yet to be studied.

In our study PAI-1 had positive correlation in addition to hs-CRP to BMI, TC-, FBS and HbA1c before and after Ramadan but not during Ramadan ($p = 0.004$, 0.045, 0.024 and 0.010) respectively. On the other hand PAI did not show any correlation with triglyceride, LDL-C and HDL-C. In contrast to other studies plasma triglycerides and very low density lipoprotein (VLDL) were positively correlated with PAI-1 antigen, PAI-1 activity, and t-PA antigen[26]

The effect of fasting on body weight and BMI had been reported before with variable results. In our study, there were significant weight and BMI reductions during Ramadan ($p < 0.001$). The median difference before and during Ramadan in terms of body weight between males and females were 1.95 kg in male and 1.35 kg in female. Many other studies have reported weight lossduring the month of Ramadan[5]. Kamal et al[27] showed the mean difference between pre- Ramadan and Ramadan body weights of 2.2 kg in male and 1.2 kg in female. In our study hs-CRP had positive correlation with body weight and BMI during and post-Ramadan ($r = 0.379$, $p = 0.001$, $r = 0.447$, $p < 0.001$) respectively. Previous studies had shown similar results[28]. Heilbronn et al[28] studied the effect of weight loss on CRP in 83 healthy obese women. They found CRP was lowered in proportion to weight loss. It is assumed that weight loss during Ramadan contributed to the reduction in the hs-CRP.

In our study in addition to the weight reduction we also found significant reduction in LDL-C levels during and after Ramadan ($p = 0.037$ and $p = 0.030$) respectively. However, there was no effect on total cholesterol and triglyceride levels before, mid and after Ramadan. Other major finding is that HDL-C level was significantly raised during and after Ramadan ($p < 0.001$) which was more obvious among females than male patients before, mid and after Ramadan ($p = 0.002$).These improvement in lipid profiles during Ramadan due to the shift in the dietary composition from fat, protein to carbohydrate, people consumes more sweets, dates and drinks. The effect of Ramadan on lipid metabolism had been reported with variable results. Several studies reported decrease in TC, TG and LDL-C levels[29], Hallak et al[3] showed that by the end of Ramadan there was a reduction in body weight, triglyceride and HDL-C, with a non significant increase in total cholesterol and LDL-C. Saleh et al[29]found an increase in HDL-C in women compared to their pre-fasting level although the difference was not statistically significant. However in our study the increase in HDL-C was statistically significant.

Other positive finding in our study is that hs-CRP had a positive correlation with HbA1c during and after Ramadan ($r = 0.259$, $p = 0.044$ and $r = 0.312$, $p = 0.024$), however there were no correlation with the level of fasting plasma glucose. On sub analysis among diabetic population, we noted significant increase of their HbA1c by the end of the study ($p < 0.001$).

Previous studies had demonstrated the benefit of experimental supplemented fasting on the metabolic control of diabetes.[30] Ramadan fasting could be considered as an ideal hypo-caloric diet for the obese type 2 patients however the benefits of Ramadan fasting would only occur in patients who maintained their appropriate diet[30]

Previous studies showed that serum HbA1c values did not change during Ramadan fasting.[31] In some cases, HbA1c levels decreased during the month[32]. Among diabetic patients we found a significant reduction in PAI-1 during and after Ramadan ($p = 0.010$ and $p = 0.005$) respectively and on

performing the correlation test we found a positive correlation between hs-CRP and PAI-1 before and after Ramadan ($r = 0.313$, $p = 0.014$ and $r = 0.334$, $p = 0.016$).

In our study we also found no hypoglycemia episodes among the diabetes population and their fasting plasma glucose was not significantly different throughout the study period. The risk of hypoglycemia could increased during Ramadan because of daytime fasting and has been reported in both types 1 and 2 patients.[32] However, in type 2 diabetic patients Ramadan fasting has been reported not to alter glycaemia[7]

In our study diastolic blood pressure had shown significant reduction during Ramadan compared to the period before Ramadan ($p < 0.001$), together with reduction after Ramadan compared to before Ramadan ($p = 0.021$). However there was no significant difference in DBP between after Ramadan and during Ramadan ($p > 0.05$). Perk et.al.[33] had found no difference between mean blood pressure in 17 subjects before and during Ramadan and the neutral effect of Ramadan on BP was attributed to the effect of weight loss. However in others (46) this was attributed to life style changes during Ramadan and the effect control of BP with long-acting anti-hypertensive.

Ramadan fasting among subject with multiple CVD risks had beneficial effect on surrogate cardiovascular bio-marker, hs-CRP and PAI-1 which significantly reduced during Ramadan compared to pre-Ramadan.

The ritual of fasting in the holy month of Ramadan among subjects with multiple CVD risks may offer CVD protective benefit by lowering both hs-CRP and PAI-1. Though the benefit is short-lived, however, it could be maintained controlling food intake and changing lifestyle in favor of healthy living that practiced during Ramadan.

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