Metabolic alterations as a result of Ramadan fasting in non-insulin-dependent diabetes mellitus patients in relation to food intake

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ABSTRACT

Objectives: Diabetes is known to be associated with alterations in metabolic parameters. The aim of this study is to investigate whether Ramadan fasting can affect these metabolic parameters in non-insulin dependent diabetes mellitus (NIDDM) patients.

Methods: This study was conducted in the outpatient Clinic of Jordan University Hospital, Amman, Jordan in February of 1415 Hijra year (1995 Gregorian). Forty-four NIDDM male patients volunteered for this study. Patients fasted the month of Ramadan and few metabolic parameters were recorded. Body weight, fasting blood sugar (FBS), glycosylated hemoglobin (HbA1c), triglycerides (TG), total cholesterol (TC), low-density lipoprotein-cholesterol (LDL-C) and high density lipoprotein-cholesterol (HDL-C) were measured, before, at mid- and at the end- of Ramadan. Detailed energy intakes were also recorded. **Results:** Patients mean age were 52 ± 9 years (range 35-75). Patients showed a statistically significant reduction in their body weight, FBS, HbA1c, and TG levels by the end of Ramadan (1.57 kg, 31 mg/dl, 0.85%, and 35 mg/dl). Other parameters such as TC, LDL-C, HDL-C were not affected by Ramadan fasting. The total daily energy intake remained unchanged including the qualitative components of nutrients.

Conclusion: Muslim NIDDM patients showed a trend towards better glycemic control following Ramadan fasting. However, the pre-Ramadan existed dyslipidemia was sustained or even worsened following Ramadan fasting.

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 \mathbf{F} asting, the voluntary abstention from foods and drinks is a feature of many religions, and its putative health benefits have attracted both scientific and popular interest. In particular, the month of Ramadan is a unique model of intermittent fasting, and represents a great opportunity for scientific research due to its peculiar nature. Each year, during this month, faithful healthy adult Muslims must refrain from eating, drinking, smoking, and sexual relations from dawn to sunset. Data from the literature show that the relative risk for coronary artery disease in diabetic patients is age-matched non-diabetic greater than in

individuals.1 Diabetic patients with hypercholesterolemia usually demonstrate increased platelet aggregation, which predisposes them to clotting disorders. Good control of diabetes is the best way to prevent or delay its complication. In Jordan, the prevalence of diabetes is rising. Approximately 13.4% of Jordanian population are diabetics,² many of them insist on observing the fast. They hope to share the blessing of the holy month with other Muslims. Actually, non-insulin dependent diabetes mellitus (NIDDM) patients always confronted their physicians with complex ethical dilemmas during this month. Are they

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Received 19th June 2004. Accepted for publication in final form 25th July 2004.

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allowed to fast? Many doctors keep the option in the hands of their patients; whether to fast or refrain. In general, if a proper medication regimen is followed, stable and uncomplicated patients should be able to fast safely.3 Moreover, physicians encourage their overweight patients to fast, taking into consideration that in type II diabetes, obesity is associated with insulin resistance and therefore, weight loss can improve the action of insulin. It is logical to assume that in developing countries, the quality of glycemic control in diabetic patients is poor when compared to those in western countries. In addition, the prolonged daylight fasting and the "malfasting" practices during the month of Ramadan produce could undesirable biochemical consequences in NIDDM patients. In this regard, investigators have reported controversial results showing either improvement,⁴ impairment⁵⁻⁶ or no change^{3,7,8} due to Ramadan fasting (RF). Surprisingly, only few studies referring to RF in NIDDM have been published^{4,8} and none of them considered detailed food analysis. Therefore, this study is unique in term of discussing detailed food intake in diabetic patients choose to fast the month of Ramadan. We hope that our study can resolve, at least partially, some conflicting results reported in the literature regarding the advantages and limitations of RF in NIDDM patients.

Methods. Forty-four NIDDM male patients volunteered in this study with a mean age of 52 ± 9 years (range 35-75 years) and a body weight of 83 \pm 11.45 kg (range 63-108 kg) with a body mass index (BMI) (kg/m^2) of 27.87 \pm 3.24 (range 21.61-33.86). Six patients were current smokers. Patients with diabetes duration of at least one year were enrolled; average duration 8.37 ± 7.02 (range 1-27 years). Patients treated with a diet alone, oral hypoglycemic agents (OHA) or insulin were eligible. All patients enrolled expressed their willingness to fast and therefore, all of them were able to fast the entire month of Ramadan. All subjects signed informed consent forms, and the study was approved by the local ethics committee. All patients had to be free from clinically overt diabetic microvascular complications. Since women's fasting is interrupted during their menstrual period, male patients were only selected. The average fasting period was about 13 hours, starting approximately at 4:30 am (dawn) until 5:30 pm (sunset). The daytime temperature ranged between 5-15°C.

Volunteers reported to the clinic in the afternoon (14:00-15:00) of the sampling days after a minimum of 11 hours fasting (2-3 hours before the evening meal called "Iftar"). The pre-Ramadan samples were also drawn after 10-12 hours of overnight fasting. Three measurements were made for each patient: 1-2 days before Ramadan (pre-R), day 14th-15th (mid-R) and finally day 28th-29th of

Ramadan (end-R). A forearm vein was used for blood sampling. During the non-fasting periods (approximately from 5:30 pm to 4:30 am of the following day), patients allowed to eat and drink according to their own habits: based on their doctors' advice.

All patients completed a questionnaire providing data concerning their names, age, occupation, addresses, smoking habits, medical histories with emphasis on the family history of diabetes, medications, and life style (namely dietary habits and physical activity). Twenty-four hour recall regarding food intake was collected by dietitian. Charts and models were used to help estimate food portion sizes. Body weight was measured by a Testut scale (Bascule Type 295) with an accuracy of \pm 100 g. Subjects were weighed barefooted in light Standing height was measured once clothing. without shoes to the nearest 0.5 cm with the use of a stadiometer with the shoulders in relaxed position and arms hanging freely. Body mass index was calculated by dividing weight (kg) by squared height (m²). Patients were classified into 3 groups according to their initial BMI (normal "lean," BMI <25, n=10; overweight, BMI 25 to <30, n=20; and obese, BMI 30, n=14). Based on medication regimen, volunteers were also classified into 3 groups; diet alone (n=6), diet + OHA (n=30), or insulin (n=8).

Shortly after blood collection, sera and plasma were separated and stored in small aliquots at -20°C. Whole blood was also stored in 50 ml aliquots at -20°C. Stored samples were analyzed for glucose, total-cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and triglycerides (TG) by enzymatic methods using assay kits obtained from (Boehringer Mannheim GmbH Diagnostica). The percentage of glycosylated hemoglobin was determined by ion exchange chromatography using microcolumn kits obtained from Bio Systems. Low-density lipoprotein cholesterol (LDL-C) was obtained by calculation as follows:

LDL-C = TC - (HDL-C + TG/5)

Statistical methods. All data were presented as mean \pm SD in the text, and the figures unless indicated otherwise. Duplicate measurements of each pre-fasting, mid-fasting and end-fasting values were averaged for each subject. Data were statistically analyzed using the paired Student's t-test, and differences were considered significant whenever the p < 0.05.

Results. Fifty-eight patients were recruited, 44 completed the study and 2 withdrew. All patients expressed their willingness to fast and managed to do so without serious clinical complications. The main results are given in **Table 1**. Fasting blood

sugar (FBS), glycosylated hemoglobin A1c (HbA1c), and TG were significantly lowered after 15 days of fasting and remained low by the end-R. The decrease in FBS was $28 \pm 9 \text{ mg/dl}$ (p<0.05) by mid-R, which was maintained until the end of the month (31 \pm 9 mg/dl, *p*<0.05). Plasma TG levels were decreased by 13% (*p*<0.05) and 19% (*p*<0.05) after 2 weeks and 4 weeks of fasting respectively. Total cholesterol blood levels by mid-R (p>0.7) and end-R (p>0.6) were almost similar to pre-R values. Even for patients who lost 1 kg by the end of Ramadan (n=22), TC levels did not change (data not shown). Other lipid parameters, such as LDL-C, HDL-C, TC/HDL-C, and LDL-C/HDL-C were not significantly different among the 3 time points. Actually, LDL-C showed an increasing trend, however, it did not reach statistical significance (Table 1). In a second step, we classified our patients according to their initial BMI as shown in Table 1 into 3 groups; normal weight, overweight

Table 1 - Effects of Ramadan fasting on metabolic parameters in 44 non-insulin dependent diabetes mellitus patients in relation to initial body mass index.

Variables	Pre-Ramadan	Mid-Ramadan	End-Ramadan
All patients Weight (Kg) FBS (mg/dl) HbA1c (%) TG (mg/dl)	$\begin{array}{c} 83.01 \pm 11.45 \\ 176 \pm 73 \\ 9.83 \pm 2.13 \\ 192 \pm 107 \end{array}$	$\begin{array}{c} 82.47 \pm 11.41 * \\ 148 \pm 52 * \\ 8.90 \pm 1.93 * \\ 167 \pm 86 * \end{array}$	$\begin{array}{c} 81.44 \pm 10.96 * \\ 145 \pm 57 * \\ 8.98 \pm 2.12 * \\ 157 \pm 76 * \end{array}$
TC (mg/dl) LDL-C HDL-C	$\begin{array}{c} 225 \pm 51 \\ 152 \pm 50 \\ 35 \pm 7.6 \end{array}$	$\begin{array}{c} 226 \pm 47 \\ 160 \pm 45 \\ 35 \pm 8.7 \end{array}$	$\begin{array}{c} 223 \pm 50 \\ 157 \pm 45 \\ 36 \pm 9.0 \end{array}$
Normal weight Weight FBS (mg/dl) HbA1c (%) TG (mg/dl) TC (mg/dl) LDL-C	$\begin{array}{c} 69.45 \pm 3.64 \\ 148 \pm 58 \\ 9.11 \pm 2.32 \\ 185 \pm 119 \\ 216 \pm 48 \\ 140 \pm 48 \end{array}$	$\begin{array}{c} 68.81 \pm 4.27 \\ 141 \pm 51 \\ 8.67 \pm 1.32 \\ 146 \pm 87^* \\ 211 \pm 44 \\ 145 \pm 45 \end{array}$	$\begin{array}{c} 68.20 \pm 4.25 \\ 137 \pm 61 \\ 8.56 \pm 2.4 \\ 150 \pm 73 \\ 202 \pm 40 \\ 135 \pm 36 \end{array}$
Overweight Weight FBS (mg/dl) HbA1c (%) TG (mg/dl) TC (mg/dl) LDL-C	$\begin{array}{c} 80.89 \pm 6.76 \\ 169 \pm 60 \\ 10.16 \pm 2.17 \\ 188 \pm 88 \\ 229 \pm 56 \\ 157 \pm 52 \end{array}$	$\begin{array}{c} 80.36 \pm 6.57 * \\ 148 \pm 51 \\ 9.17 \pm 2.18 \\ 174 \pm 92 \\ 228 \pm 53 \\ 167 \pm 46 \end{array}$	$\begin{array}{c} 79.75 \pm 6.19 * \\ 138 \pm 49 * \\ 9.21 \pm 2.20 * \\ 150 \pm 63 * \\ 233 \pm 54 \\ 172 \pm 43 * \end{array}$
<i>Obese</i> Weight FBS (mg/dl) HbA1c (%) TG (mg/dl) TC (mg/dl) LDL-C	$\begin{array}{c} 95.72 \pm 5.91 \\ 206 \pm 90 \\ 9.86 \pm 1.99 \\ 203 \pm 126 \\ 225 \pm 48 \\ 153 \pm 52 \end{array}$	$\begin{array}{c} 95.24 \pm 5.38 \\ 153 \pm 56* \\ 8.71 \pm 2.02* \\ 175 \pm 82 \\ 236 \pm 41 \\ 163 \pm 46 \end{array}$	$\begin{array}{c} 94.22 \pm 4.27 \\ 158 \pm 65 \\ 8.93 \pm 1.94 \ast \\ 166 \pm 97 \\ 222 \pm 51 \\ 154 \pm 48 \end{array}$

*p<0.05 compared to pre-Ramadan values. Values are means ± SD, FBS - fasting blood sugar, HbA1c - glycosylated hemoglobin, TG - triglycerides, TC - total cholesterol, LDL-C - low-density lipoproteincholesterol, HDL-C - high-density lipoprotein-cholesterol and obese. Initially, obese patients started fasting with higher FBS ($206 \pm 90 \text{ mg/dl}$) when compared to lean patients (148 \pm 58 mg/dl). However. normal-weight patients failed to lower their FBS or HbA1c significantly at the end of Ramadan (Figure 1). It is worthmentioning that fructosamine results were inconsistent with the HbA1c results (data not Surprisingly, serum LDL-C levels in shown). overweight patients, increased from the baseline pre-R value of 157 ± 52 to 172 ± 43 mg/dl by the end of Ramadan (p < 0.05). When patients were classified according to their medication regimen, it has been found that the insulin-group patients benefited less when compared to the other 2 groups by fasting Ramadan (Table 2). Actually, their LDL-C levels were raised significantly by 9.7% (p < 0.05) after 2 weeks of fasting, but it returned back to almost baseline values by the end of Ramadan (Table 2). Patients on diet alone had the lowest pre-R TG levels (163 \pm 87 mg/dl), and were

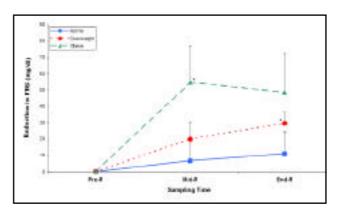
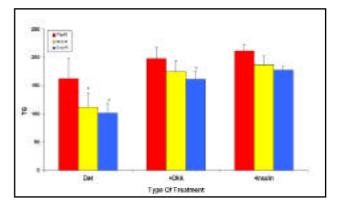
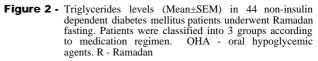


Figure 1 - Weight reduction (Mean±SEM) in 44 non-insulin dependent diabetes mellitus patients underwent Ramadan fasting. Patients were classified into 3 groups according to their initial body mass index. *Significant difference (p<0.05) from pre-Ramadan value. R - Ramadan, FBS - fasting blood sugar





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Table 2	- Effects of R	amadan fast	ing on me	tabolic par	ameters in 4	4
	non-insulin	dependent	diabetes	mellitus	patients	in
	relation to di	ifferent med	ication reg	giments.		

Variables	Pre-Ramadan	Mid-Ramadan	End-Ramadan
Diet alone FBS (mg/dl) HbA1c (%)	131 ± 44 8.83 ± 2.64	$117 \pm 38^{*}$ 8.33 ± 1.75	$118 \pm 34^{*}$ 9.00 ± 2.68
TG (mg/dl) TC (mg/dl) LDL-C	$\begin{array}{c} 163 \pm 87 \\ 205 \pm 47 \\ 135 \pm 37 \end{array}$	$\begin{array}{c} 114 \pm 63 * \\ 200 \pm 53 \\ 135 \pm 48 \end{array}$	$102 \pm 48^{*}$ 204 ± 52 147 ± 49
Diet + OHA FBS (mg/dl) HbA1c (%) TG (mg/dl) TC (mg/dl) LDL-C Diet + insulin FBS (mg/dl) HbA1c (%) TG (mg/dl) LDL-C	$\begin{array}{c} 188 \pm 80 \\ 10.25 \pm 1.88 \\ 197 \pm 123 \\ 222 \pm 49 \\ 148 \pm 51 \\ 172 \pm 50 \\ 9.00 \pm 2.58 \\ 213 \pm 34 \\ 252 \pm 56 \\ 177 \pm 57 \end{array}$	$\begin{array}{c} 158 \pm 48^{*} \\ 9.15 \pm 1.99^{*} \\ 177 \pm 96 \\ 223 \pm 43 \\ 156 \pm 43 \\ 140 \pm 69 \\ 8.43 \pm 2.07 \\ 189 \pm 38 \\ 262 \pm 48 \\ 194 \pm 51^{*} \end{array}$	$\begin{array}{c} 150\pm55^{*}\\ 9.00\pm2.21^{*}\\ 162\pm87^{*}\\ 218\pm48\\ 152\pm42\\ 150\pm77\\ 9.00\pm1.63\\ 180\pm22^{*}\\ 255\pm55\\ 180\pm53\\ \end{array}$
Values ar HbA1c - gi	.05 compared to p re means ± SD, Fl lycosylated hemog erol, LDL-C - lov OHA - oral hypog	BS - fasting blood globin, TG - trigh v-density lipoprot	sugar, ycerides,

able to reduce it significantly by the end of Ramadan (38%; p<0.05). The OHA group reduced their TG levels by 19% (p<0.05) while the insulin group reduced it by 16% (p<0.05) by the end of Ramadan (**Figure 2**). Overall, there were no statistically significant differences between the mean daily energy intake before Ramadan and at the end of the fasting month (1663 ± 703 versus 1631 ± 599 Kcal/day, **Table 3**). Similar conclusions were also observed regarding the mean daily intake of protein, fat, and carbohydrate content (**Table 4**).

Discussion. Usually, Jordanians have their main meal at lunch, while breakfast and dinner are In Ramadan, however, one usually light. good-sized meal is served immediately after sunset (Iftar) and one light meal just before dawn (Sahur). In addition to change in meal schedule, delicious foods are prepared during this month. Foods rich in animal proteins and fat are frequently consumed during Iftar, followed by sweetened deserts. Muslims, Unfortunately, many including Jordanians, convert this fasting month to a month of enjoyment of breaking fast and overeating. This practice, which defeats the concept of Ramadan, can cause health problems. Fortunately, in the last 10

 Table 3 - Food and calorie intake in 44 non-insulin dependent diabetes mellitus patients.

Variables	Pre-Ramadan	Mid-Ramadan	End-Ramadan
Protein (gm)	74 ± 31	67 ± 30	68 ± 25
Fat (gm)	47 ± 26	40 ± 21	44 ± 21
Carbohydrate (gm)	237 ± 117	222 ± 80	239 ± 98
Calories (Kcal)	1663 ± 703	1523 ± 546	1631 ± 599
	Values are me	ans \pm SD	

 Table 4
 The average food intake during Ramadan in 44 non-insulin dependent diabetes mellitus patients. Patients were classified according to their initial body weight.

Variables	Protein gm (%) n (%)	Fat gm (%) n (%)	Carbohydrate gm n (%)	Calories
Normal weight	64 (18.4)	35 (22.6)	206 (59)	1392
Overweight	62 (16.5)	38 (23)	225 (59.9)	1592
Obese	80 (17.1)	53 (25.9)	259 (55.9)	1857
All patients	67 (17.1)	42 (23.8)	231 (58.5)	1577

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days of the holy month, faster's appetite is relatively reduced⁹ and Muslims adhere more to the spirit of Ramadan, spending more time in religious activities (such as night Taraweeh prayer).

Most of the NIDDM patients assume that RF alters their carbohydrate and lipid profile in the desired way. Our findings support this view just partly, and emphasize in a small population that RF lowered body weight, FBS, HBA1c, and TG, but failed to induce significant change in TC, LDL, and HDL-cholesterol. The current research protocol pays a special attention towards energy intake and Therefore, that metabolic food composition. parameters are linked with detailed food intake in NIDDM patients during Ramadan. In the current study, the daily energy intake was slightly less than the reported energy intake in NIDDM patients living in Egypt.¹⁰ Nevertheless, our patients' food and energy intake during Ramadan were comparable to that before Ramadan. In other studies, energy intake was either reduced⁴ or increased during Ramadan.11 Carbohydrate contribution to the total energy intake was slightly above the recommended range of 50-55%.¹² This fact might reflect the traditional "fear" of subjects from suffering hypoglycemia during the day and being forced to break their fast. Fasting had a small but statistically significant impact on fasters' body weight. Surprisingly, obese type 2 diabetic Muslims failed to reduce their weight and TG significantly. In healthy Jordanians for instance, Takruri reported a more weight loss in overweight individuals when compared to normal or underweight subjects when fasting Ramadan.¹³ In the current study, we used different definition for the term "overweight". In addition, our volunteers were NIDDM patients and not normal individuals. It is clear that obese NIDDM patients are not taking this opportunity to improve their weight and metabolic parameters. The reason behind that would be multifactorial in nature. The fear of hypoglycemia is legitimate in this group of patients. Therefore, obese patients reduced their daily activity and consumed more calories.

Hemoglobin A1c reflects glycosylated hemoglobin levels and is reliable index of long-term (3 months) control of glucose in diabetic patients. Measuring HbA1c at one-month interval is not ideal to evaluate glycemic control. Therefore, in the current study, data regarding HbA1c must be interpreted with caution. Nevertheless, our study showed a significant decrease in HbA1c levels. Patients taking OHA have the greatest reduction in their HbA1c. In general, the reductions in FBS levels were more pronounced than in HBA1c levels. It seems likely that the day prior to blood sampling, patients started paying more attention to their blood glucose level. Nevertheless, the lower HbA1c may very well be due to a better control of glucose homeostasis in these patients. Other studies did not confirm a better glycemic control during Ramadan.¹⁴ Unfortunately, we did not follow the patients after the end of Ramadan, since the reduction of both FBS and HbA1c may not sustain when patients return to their usual dietary habits. The mechanism behind the improvement of glycemic control was not investigated in this study. It is logical to assume that weight reduction enhances insulin sensitivity. However, others have shown that weight reduction was not accompanied with better glycemic control following FR.⁴ It should be kept in mind that even if fasting does improve glycemic control, this will not necessarily result in a better metabolic control as other pathophysiologic parameters (such as gorging, malfasting, lack of exercise, abnormal sleeping pattern) might counterbalance this improvement.

Triglyceride levels decreased almost among all groups. Opposite to what was predicted, in the current study, blood cholesterol levels were not altered in a favorable way; it even showed a rising trend in the LDL-C levels. In agreement with our findings, other investigators have also shown an increase in serum LDL-C or TC concentrations in normal non-diabetic individuals5-6 as well as in diabetic patients⁸ following RF. All in all, although many studies have shown some improvement in lipid profile following RF,¹⁵ the evidence for a very marked degree of TC reduction is quite small. Yarahmadi et al⁸ postulated that lipid profile is unfavorably altered as a result of changes in both diet and biochemical response to starvation. It has been shown that when daily food intake is to be consumed in one large meal (gorging), an increase, instead of decreased cholesterol levels would be expected.^{6,16,17} The fact that our patient's energy intake was comparable before and during Ramadan supports this hypothesis.

In general, lifestyle during Ramadan become more sedentary and sleeping pattern is changed.¹⁸ Jordanian Muslims tend to stay up late watching TV with the family, playing cards, and some times they even smoke Hubble-bubble inside the so-called "Ramadan tents". In addition, most Muslim governments decrease working hours by 2-3 hours/day. If Muslims adhere to this new lifestyle, this month becomes an extra burden to NIDDM patients' health and therefore, some of the undesired reported effects of Ramadan can be explained. Collectively, lack of exercise, overeating, gorging, and change in sleeping pattern are components to what we name "malfasting practice".

The different results observed by other investigators would not argue against our findings. Actually, Ramadan, which is based upon a lunar calendar, can fall in any time of the year, and hence, the duration of the daily fasting span undergoes wide variations in relation to the season and latitude. In London, for example, fasting hours can be as short as 9 and half hours in winter or as long as 18 hours in summer.¹⁹ Therefore, fasting during summer may have more impact on the measured parameters. This can explain, at least partially, the variability of the results reported in the literature. Moreover, since RF is one of the 5 pillars of Islam, some Muslim investigators might be hesitant in publishing studies if their results contradict the beneficial effects of RF. beneficial effects of RF. Actually, our results showed that RF could be beneficial, but only if malfasting practices are avoided. The limitation of this study includes the small sample size, especially when patients were subgrouped and the inclusion of male volunteers only. Other limitation includes the lack of follow-up measurements one month after Ramadan. Thus, future research should be based on a representative sample of the general population and should include females too.

Finally, Muslims during Ramadan, especially obese NIDDM patients, are recommended to reduce their fat and energy intake by 300-400 Kcal/day, avoid gorging, keep some degree of physical activity (half-hour walking), and maintain regular sleeping pattern.²⁰

In conclusion, the results of this study showed that fasting in the month of Ramadan led to better glycemic effect but no change in the existed dyslipidemia in NIDDM patients. Ramadan should be observed properly specifically in obese patients. It is clear that more work should be carried out on RF to evaluate physiological and pathological changes in NIDDM patients.

Acknowledgment. This work was supported by grant No: 313/94-95 from the Deanship of Scientific Research of the University of Jordan. The authors thank Prof. Naif Abdullah (Department of Internal Medicine, University of Jordan) for providing the venue for this study. We also would like to thank Profs. Abdul-Azim Salhab, Munir Gharaybeh, and Dr. Faisal Mohammed for reviewing this MS. Also, we thank Mr. Mahmoud Al-Khateeb for his excellent technical work.

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