

## Effect of the Ramadan Fasting on the Variations of Certain Anthropometric and Biochemical Parameters in Type 2 Diabetic Patients Treated with Medications Mixture (Biguanides and Sulfamides)

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**Abstract:** The aim of this investigation is to follow (during and before the month of Ramadan fasting) the evolution of some parameters anthropometric and biochemical in men and the women suffering from the diabetes of the type 2, old from 45 to 55 years and treated with oral antidiabetics constituted of a mixture (Biguanides and Sulphamides). 84 patients of which (42 men and 42 women) were followed during two experimental periods: the 5 week before Ramadan (P1) and the 3rd week of fasting (P2). By comparison at the period before fasting, the Body Mass Index (BMI) remains practically stable ( $P>0.05$ ) during the Ramadan among the diabetic patients. However, the women recorded results of BMI significantly ( $P<0.01$ ) higher than those of the men. No relation between the variations of the levels of glucose, of glycosylated haemoglobin and the fasting of month of Ramadan was recorded during this experimental study. Also, during Ramadan the average content of plasma insulin recorded among diabetic women and men are significantly lower than during the non-fasting period. Concerning the lipidic parameters measured among all the studied population, the rates of plasmatic triglycerides and of HDL-c decreased significantly ( $P<0.01$ ) during the period of fasting by comparison at the period before fasting; on the contrary, rates of LDL-c and of cholesterol increased slightly ( $P>0.05$ ) during the month of Ramadan. In addition, during the two periods experimental, the women showed relatively high rates in LDL-c and cholesterol compared to the men ( $P<0.01$ ). As for proteinous compounds (protein and urea), their plasmatic rates remain practically stable ( $P>0, 05$ ) among the women and the men diabetic during all the periods experimental. The month of Ramadan seems not to exert of influence on glucidic and proteinic metabolisms. On the contrary, the metabolism of the lipids seems to be relatively affected among patients diabetic during this period of fasting.

**Key words:** Fasting • Month of Ramadan • Diabetes of the type 2 • Sulphamides • Biguanides

### INTRODUCTION

The Ramadan is the ninth month of the lunar calendar where all the Moslem must abstain daily of eat, drink and smoke from dawn to dusk. Its duration can take place at different moment from the year and varies approximately from 10 hour in winter at 18 hour in summer-time. The practices and the food behaviours of the populations are not similar during this month of fasting by comparison to the remainder of the year. These modifications are accompanied by changes of the rhythm of life and disturbances of the cycle of sleep.

The diabetes not dependant on insulin is the most known form of diabetes, it is often called diabetes of the age walls since it generally appears after 40 years and it results from a relative deficiency of the insulin secretion due to an increase in demand from the organization by increase in the fatty mass and reduction in the sensitivity of the cells to insulin [1,2]. This disease is characterized by disturbances of the metabolism especially glucidic than lipidic and can become manifest only when the environment supports a generous food contribution and a development of an obesity at the subjects [3-5]. In certain therapeutic treatments the recourse to the

medications mixture with the Sulphamides and the Biguanides proves to be necessary to the good maintenance of the health of the patients. The Biguanides act particularly on the liver and the muscles by supporting the use or the reserve of glucose. However, the Sulphamides can act primarily by stimulating the insulin secretion by the deficient pancreas and can be incidentally by a direct action on the liver and the muscle [6].

Few studies were undertaken on the biological modifications in particular lipidic during the Ramadan fasting in diabetes type 2 treated with oral antidiabetics.

## **MATERIALS AND METHODS**

**Patients:** The trial population comprised Muslim Women and men with Type 2 diabetes (according to WHO criteria) who practiced Ramadan fasting [7]. An explanatory session was given by the investigators in both French and Arabic languages and written consent was received from each willing participant. Four twenty four patients from 02 Regions (Chlef and Mascara) located in the West of Algeria participated in this study. Their ages ranged from 45 to 55 years (mean  $\pm$ SD =49.73 $\pm$ 3.33), had a Body Mass Index (BMI) of 27.395 $\pm$ 03.082 kg/m<sup>2</sup> (mean $\pm$ SD) and all the selected subjects are subjected to the treatment to antidiabetic consisted of a mixture of drugs containing Sulphamides and Biguanides.

Patients were excluded from the trial if they had cardiac disease (congestive heart failure, angina pectoris, previous myocardial infarction); impaired kidney or liver function; severe uncontrolled hypertension, severe diabetic complications; or had received therapy with insulin, other investigational drugs reduced lipidic catabolism such as oral contraception and corticosteroids within the 6 months. The study protocol was approved by the ethical committee hospitals of each region.

**Study Design:** The study was performed in September 2007, which coincided with the holy month of Ramadan. All participating patients were studied at the sixth week before the Ramadan and at the third week of Ramadan fasting. A 10 ml blood sample was withdrawn from 12 h fasting subjects by venipuncture into dry tubes for the pre-fasting period. To respect the 10–12 h fast in the pre-Ramadan period, the blood sampling during Ramadan must be done at 1300 h. Samples were allowed to clot and the serum centrifuged, divided into aliquots and stored at -18°C until analyzed. On both test days,

glucose, triglycerides, high-density lipoprotein cholesterol (HDL-c) and low density lipoprotein cholesterol (LDL-c) were measured from each of 168 blood samples. During Ramadan, the subjects slept uninterruptedly from 0200 h to 0800 h and their average sleep time was thus 1 h shorter during Ramadan than it had been during the control period. Daily working hours in Ramadan are from 0900 h to 1500 h; but on the a non-fasting day, work starts at 0800 h and finishes at 1700 h.

**Measurements:** Anthropometric measurements were performed on subjects in light clothing and without shoes. Height was measured to the nearest 0.5 cm and body weight was measured on a level balance calibrated daily and recorded to the nearest 0.1 kg. Body mass index (BMI) was calculated as weight (kg) divided by height (in m) squared [8]. Blood samples were drawn after at least 12 hours of fasting for determination of serum levels of glucose, Total cholesterol (Tot-c), high-density lipoprotein cholesterol (HDL-c) and triglycerides (TG) by enzymatic methods using Merck reagent kits and Elan 2000 autoanalyser. High density lipoprotein cholesterol (HDL-c) was measured in the supernatant after precipitation of apolipoprotein B-containing lipoproteins with dextran sulfate and magnesium chloride. LDL cholesterol was calculated with the Friedewald formula [ $LDL-c = Tot-C - (TG/5 + HDL-c)$ ] when triglycerides concentrations were <5.0 mmol/L; subjects with triglycerides levels >5.0 mmol/L were excluded [9]. Procedure for the separation and measurement of the percentage of HbA1c glucosylated haemoglobin in blood samples, in which a) a haemolysate is obtained from a blood sample, b) the said haemolysate is used to impregnate a weak cationic exchange resin c) a first buffer solution is passed through the resin to effect the selective elution of the glucosylated haemoglobins HbAla and HbAlb d) a second buffer solution is passed through the resin to effect the selective elution of the HbA1c glucosylated haemoglobin e) and if required the HbA1c content of the collected eluate is analysed and compared with the total haemoglobin present in the haemolysate [10]. To remove antibody-bound insulin, plasma was prepared immediately after venipuncture, mixed with an equal volume of 30% polyethylene glycol and centrifuged immediately [11]. Plasma free insulin was measured by radioimmuno assay [12]. Trained interviewers administered a structured questionnaire to collect information about age, medication and the consumed diet.

**Statistical Methods:** Data were analyzed using the StatBox 6.4 and are expressed as mean and Standard Deviation (SD). Parametric values were compared with one way ANOVA and Newman Keuls test. The level  $P < 0.05$  was considered as the cut-off value for significance.

## RESULTS

The results of the study have been summarised in (Table 1).

**Body Mass Index (BMI):** The diabetic patients showed a light increase ( $P > 0.05$ ) in BMI during the fasting period (26.86 Kg/m<sup>2</sup>) per comparison at the period before the Ramadan fasting (25.77 Kg/m<sup>2</sup>). However, the results

of BMI are significantly ( $P < 0.01$ ) higher in women (27.07 Kg/m<sup>2</sup>) than the men (25.56 Kg/m<sup>2</sup>).

### Blood Glucose and Glycosylated Haemoglobin (HbA1c):

Concerning the glucose level in the blood, the average values recorded vary insignificantly ( $P > 0.05$ ) from 1.67 to 1.73g/l at all studied patients. Apparently, the men indicate values relatively higher than women; 1.37 vs 1.67 g/l ( $P > 0.05$ ). Thus, before the fasting period the glycemia detected at the men is of 1.67 g/l whereas that of the women was of 1.78 g/l. On the other hand, during the Ramadan fasting the results were of 1.78 vs 1.68 g/l, respectively ( $P > 0.05$ ).

By comparison at the period before the Ramadan the rates of glycosylated haemoglobin (HbA1c) decreased

Table 1: Variations of the anthropometric and biochemical parameters in men and in women diabetics of type 2 during and before the month of Ramadan fasting

Parameters	Before the Ramadan		During the Ramadan		Periods (n=84)		Sex (n=84)				
	Men (n=42)	Women (n=42)	Men (n=42)	Women (n=42)	Before the Ramadan	During the Ramadan	Men	Women	F <sub>1</sub>	F <sub>2</sub>	IntF <sub>1</sub> XF <sub>2</sub>
BMI (Kg/m <sup>2</sup> )	25.315 <sup>b</sup> ±03.188	26.241 <sup>a</sup> ±03.104	25.015 <sup>b</sup> ±03.277	27.909 <sup>a</sup> ±03.209	25.778 ±03.146	26.862 ±03.243	25.565 <sup>b</sup> ±03.232	27.070 <sup>a</sup> ±03.156	NS	*	**
Glucose levels (g/l)	01.679 ±00.757	01.672 ±00.608	01.782 ±00.727	01.685 ±00.666	01.675 ±00.682	01.733 ±00.696	01.730 ±00.742	01.678 ±00.637	NS	NS	NS
HbA1c levels (%)	07.32 <sup>a</sup> ±00.83	07.66 <sup>a</sup> ±0.067	06.39 <sup>b</sup> ±00.85	07.93 <sup>a</sup> ±00.75	07.49 ±0.75	07.16 ±0.78	06.86 <sup>b</sup> ±00.83	07.80 <sup>a</sup> ±00.71	NS	**	**
Insulin levels (iu/ml)	10.90 ±2.19	12.24 ±4.21	8.58 ±1.55	8.27 ±2.99	11.57 <sup>a</sup> ±3.2	08.43 <sup>b</sup> ±2.28	9.74 ±1.81	10.26 ±3.48	*	NS	NS
Triglyceride levels (g/l)	01.280 <sup>a</sup> ±00.588	01.319 <sup>a</sup> ±00.461	01.180 <sup>b</sup> ±00.581	01.101 <sup>b</sup> ±00.467	01.299 <sup>a</sup> ±00.682	01.140 <sup>b</sup> ±00.996	01.230 ±00.742	1.210 ±00.637	**	NS	**
Cholesterol levels(g/l)	01.547 <sup>b</sup> ±00.427	01.880 <sup>a</sup> ±00.378	01.708 <sup>b</sup> ±00.509	01.889 <sup>a</sup> ±00.425	01.713 ±00.402	01.798 ±00.467	01.627 <sup>b</sup> ±00.468	01.884 <sup>a</sup> ±01.401	NS	**	**
HDL-c levels (g/l)	00.902 <sup>a</sup> ±00.668	00.821 <sup>a</sup> ±00.472	00.562 <sup>b</sup> ±00.138	00.624 <sup>b</sup> ±00.291	00.861 <sup>a</sup> ±00.580	00.593 <sup>b</sup> ±00.214	00.732 ±00.413	00.732 ±00.381	*	NS	**
LDL-c levels (g/l)	00.293 <sup>b</sup> ±00.744	00.779 <sup>a</sup> ±00.641	00.464 <sup>b</sup> ±00.426	00.958 <sup>a</sup> ±00.449	00.536 ±00.692	00.711 ±00.437	00.378 <sup>b</sup> ±00.585	00.868 <sup>a</sup> ±00.545	NS	**	**
VLDL-c levels (g/l)	00.178 ±00.254	00.246 ±00.619	00.161 ±00.184	00.146 ±00.098	00.212 ±00.436	00.153 ±00.141	00.169 ±00.219	00.196 ±00.358	NS	NS	NS
Protein levels (g/l)	81.670 <sup>a</sup> ±18.721	68.291 <sup>b</sup> ±21.244	81.008 <sup>a</sup> ±22.598	73.289 <sup>b</sup> ±16.371	74.980 ±19.982	77.148 ±19.484	81.339 <sup>a</sup> ±20.659	70.790 <sup>b</sup> ±18.807	NS	*	*
Creatinin levels (g/l)	08.086 <sup>a</sup> ±18.721	07.88 <sup>a</sup> ±21.244	09.355 <sup>b</sup> ±22.598	09.133 <sup>b</sup> ±16.371	07.983 <sup>a</sup> ±02.440	09.244 <sup>b</sup> ±01.862	08.720 ±02.227	08.506 ±02.075	**	NS	*
Urea levels(g/l)	00.360 <sup>a</sup> ±00.277	00.329 <sup>a</sup> ±00.149	00.326 <sup>b</sup> ±00.136	00.340 <sup>b</sup> ±00.190	00.344 <sup>a</sup> ±00.213	00.333 <sup>b</sup> ±00.163	00.343 ±00.206	00.334 ±00.169	NS	NS	**

F1: Factor period (before and During the Ramadan); F2: Factor sex (Men and women); Int: interaction between the studied factors (period and sex); NS: Non significant effect of the studied factor ; \*: Significant effect of the studied factor ; \*\*: Highly significant effect of the studied factor; a\*: Significant difference in comparison of the averages

slightly ( $P<0.05$ ) among patients diabetic during the last week of the month of Ramadan; from 7.32% to 6.39% in men and from 7.66% to 7.93% in women group.

**Insulin:** During the study, the insulin rates are significantly decreased ( $p<0.05$ ) during the fourth week of Ramadan to (8.58  $\mu\text{u/ml}$ ) in men and to 8.27  $\mu\text{u/ml}$  in women. On the other hand, the highest results are recorded during the period before the fasting of the month of Ramadan; 10.90  $\mu\text{u/ml}$  in men vs 12.24  $\mu\text{u/ml}$  in women.

**Lipidic Measurements:** In general, from period before the Ramadan to Ramadan fasting, the triglyceride level knows a significant reduction from 1.29 g/l to 1.14 g/l, on average ( $P<0.01$ ). During these both periods of the study (Pre-Ramadan and Ramadan fasting), the remarked values in plasmatic triglycerides (TG) at the subjects of male sex are comparable with those of female sex ( $p>0.05$ ); (1.23 g/l vs 1.21 g/l). Nevertheless, the level of TG noted among women at the first period before the fasting seems higher compared to men (1.31 g/l vs 1.28 g/l). This tendency is reversed at the second period of Ramadan where the high rate is announced at the men than the women; 1.18g/l against 1.10 g/l on average.

During both periods (Pre-Ramadan and Ramadan fasting) the plasmatic cholesterol concentrations remain identical at the subjects diabetic; 1.71g/l vs 1.79g/l, on average. Also, the lowest ( $P<0.01$ ) values are recorded at women (1.62 g/l on average) whereas the highest rates are recorded at the men (1.88 g/l on average). However, from the first period (P1) at the second period (P2) one attends a clear increase (from 1.54g/l to 1.88 g/l) in cholesterol levels among men; but the evolution noticed at the women seems to be stable and only varies (from 1.88 g/l to 1.88 g/l on average).

The rates of HLD-c show a significant reduction ( $p<0.05$ ) among diabetic patients during the Ramadan by comparison at the period before fasting; 0.86 g/l vs 0.59 g/l, on average. Moreover, the result observed at the men seems to be similar to those of the women; (0.73 g/l vs 0.72 g/l on average). However, from the first period before the fasting at the second period of the month of Ramadan the HLD-c reductions levels noted among patients are relatively more important at the men ( from 0.90 g/l to 0.56 g/l) than the women (from 0.82 g/l to 0.62 g/l).

Globally, during both experimental periods (Before and During the Ramadan) the rate of LDL-c varies slightly ( $P>0.05$ ) among all patients diabetic; nevertheless, the men showed low rates (0.37 g/l) comparatively at the women (0.86 g/l), ( $P<0.01$ ).

The variation of the plasmatic rate of VLDL-c noted during the two periods of the study is non significant ( $P>0.05$ ); 0.21 and 0.15 g/l on average, successively. Also, it appears that the concentrations recorded at women (0.19 g/l) are comparable with those of the men (0.16 g/l). At the first experimental period the average values of VLDL-c noted among the men and diabetic women are about (0.17 and 0.24 g/l) and decrease then insignificantly ( $P>0.05$ ) to (0.16 g/l and 0.14 g/l) respectively at the second period of fasting.

**Proteinous Measurements:** During the both experimental periods (P1 and P2) the plasmatic protein rates vary lightly (from 74.98 to 77.15 g/l) among patients ( $p>0.001$ ). The evolution of protein level during these two periods (P1 and P2) reveals a change non significant ( $P<0.01$ ) at the men (from 81.67 to 81.00 g/l); whereas among women it is noticed a light significant increase (from 68.29 g/l to 73.28g/l). Also, the values noted at the men (81.33 g/l) are significantly ( $p<0.005$ ) higher than those of the women (70.79 g/l).

Concerning the creatinin plasmatic, the rates low (7.98 g/l) noticed during the period before the fasting (P1) have tendency to increased significantly to (9.24 g/l) during the Ramadan (P2). The comparison of the creatinin values found at the male and female subjects (8.72 versus 8.50 g/l) does not indicate great differences ( $P>0.05$ ). However, at the 1st period before the fasting (P1) the results obtained among masculine subjects are generally higher (8.08 g/l) than those of the female sex (7.88 g/l); these values will increase notably (to 9.33 and 9.13 g/l, successively) during the Ramadan fasting (P2).

Finally, the level of the plasmatic urea noted during both periods under study (P1 and P2) remains comparable among men and the diabetic women ( $P>0.05$ ).

## DISCUSSION

**Body Mass Index (BMI):** The Ramadan fasting did not exert significant variations ( $P>0.05$ ) of the BMI at the diabetic patients. Nevertheless, the values recorded during the Ramadan are relatively high compared to the period before the fasting. Uysal *et al.*, Maislos *et al.* and Laajam [13-15] also observed a stability of the Quételet index (BMI) and the weight of the patients during the month of Ramadan [13-15]. However, other authors reported an increase [16,17] or a relative reduction in the BMI [18,19]. The reduction in the insulin concentration during the fasting can be an adaptive mechanism able to explain the maintenance of a normal weight at the subjects [20]. The light rise in the weight and thus of the BMI

noted during the fasting could be allotted to the consistency of the diet ingested during this period of abundance; but also undoubtedly to the reduced physical activity of the fasters whose the schedules of work during the Ramadan are often lowered from at least 1 hour by comparison in the other months of the year. In addition, Dattilo [21] and Dennis [22] reported that the reduction of the BMI is clearly associated to reduction in the cholesterol plasmatic concentrations. To this subject, it appears that the consumption of a food containing a low content of animal grease generates a substantial decrease of the cholesterol plasmatic accompanied by an ineluctable loss of body weight [23]. The women present an index of Quételet higher than those of men ( $P < 0.01$ ). This difference is probably due to the fact that the majority of the women of the studied population are sedentary and does not practise any profession except the domestic activity [24]. Also, the sick women by fear to have significant fluctuations of rates of glucose exert less physical activities which can generate considerable gains of weight during the period of fasting.

#### **Blood Glucose and Glycosylated Haemoglobin (HbA1c):**

According to the results obtained it seems that the fasting does not exert any significant effect ( $P > 0.05$ ) on the variations in levels of blood glucose by comparison at the period before the Ramadan fasting. Also, it was not detected any significant change in rate of blood glucose among the men and diabetic women ( $P > 0.05$ ). This confirms the remarks of Laajam and Nagra *et al.* [15,25] which suggested the existence of any relation between the variations of the glycaemia and the Ramadan fasting.

Nevertheless, other authors [26,27] observed a significant reduction in the glycaemia during the abstinence alimentary period of the month of Ramadan and explain it by the submission of the subjects to a hypocaloric diet. These controversial data can be due to a quantitative and qualitative food diversity consumed by the patients during the period of fasting; but also to the difference in the eating habit of the studied populations. Other factors such as the regular taking of medicines [28], the daily length of fasting, the individual variations in the quantity of blood glucose and the lack of physical exercise were also found to influence the outcome [27].

Avignon noted at the contrary an increase in levels of glucose during the fasting [29]. According to Clore *et al.* [30], this increase undoubtedly results from an activation of the gluconeogenesis. In addition, the significant rise in the circulating free fatty acids can contribute to the increase in the plasmatic

concentration of glucose newly formed particularly at the diabétiques ones showing an insulin resistance [31].

From the period before the fasting to Ramadan period, the results showed a significant reduction ( $P > 0.05$ ) of the rate of Glycosylated haemoglobin (HbA1c) among diabetic patients treated with the mixture of both medications formed of Biguanides and Sulphamides. Several studies have shown that serum HbA1c values [19,20,28,32-38] do not change during Ramadan fasting. In some cases HbA1c levels decrease during this month [33,39,40].

The reduction in the rate of Glycosylated haemoglobin (HbA1c) is a proof justifying the beneficial effect of the medicinal treatment taken during the fasting of Ramadan.

The Glycosylated haemoglobin results from nonenzymatic slowly and irreversible fixation of glucose (or other oses) on haemoglobin during all the lifespan of the red globules of blood. This denomination definitively replaced the unsuitable term of glycosylated haemoglobin; the glycosylation is an enzymatic mechanism of proteinic biosynthesis [41]. The HbA1c is henceforth recognized like the only reference dosage allowing to judge balance of the diet consumed by the diabetics, of therapeutic measurements to undertake and the necessity in certain situations to modify the treatment to reach the objectives recommended among the patients [41,42]. The rate of HbA1c is directly proportional to the concentration of glucose in blood. It is independent of the variations daily of the glycemia and is not affected by the physical exercise, the fasting or the recent ingestion of sugar. Its dosage among patients does not require 12 hours of fasting [41].

At the second period of the month of Ramadan one recorded a rather significant reduction in the rates of HbA1c which thus testify to the beneficial action of the medicinal treatment undertook by the patients particularly during the period of fasting. Each point gained on the reduction of HbA1c results in an unquestionable clinical benefit like suggested the majority of the preliminary studies [41]. The D.C.C.T (Diabetes control and complications trial), advances in the same order of ideas which each reduction in HbA1c decreases remarkably the risks of specific complications among the diabetic patients [42]. Also, the UKPDS [43] has noted clearly the clinical benefit which can bring back significantly each plasmatic reduction of 1% of HbA1c in terms of reduction of the risk of micro and macro vascular complications among the diabetics of type 2.

**Lipidic Measurements:** During the fasting the diabetics presented a highly significant reduction in the triglyceride rates than before the Ramadan period ( $P < 0.01$ ). At this subject, El Hazmi *et al.* [44] showed that the levels of triglycerides decrease at the first week of fasting and increase later towards the end of Ramadan. These observations are also advanced by other authors such as Sarrafzadeh *et al.* [45] and Yarahmadi *et al.* [20]. Afrasiabi *et al.* [46] explain the reduction in the rates of triglycerides during the month of Ramadan by the tendency of the volunteers to hypocaloric diet associated intense physical exercises during the fasting. These results contradict those of Nagra *et al.* [27] and Gumma *et al.* [47] which announced an increase of triglyceride levels consequently to the lipolytic effect considerable of fat tissues during the Ramadan fasting. The differences of triglyceride rates between the two studied sexes (male and female) is non significant ( $P > 0.05$ ). The same observation was reported by the study UKPDS [48] which suggests that triglyceride levels at the diabetics are often comparable between the men and the women.

During the both periods of the study (P1 and P2), the levels of cholesterol remains practically unchanged among patients ( $P > 0.05$ ). The same remarks are reported by Sarrafzadeh *et al.* [45]. On the other hand, other studies suggest either a reduction [17,47,49,50] or an increase [20] in rates of the cholesterol during the Ramadan fasting. Iacano and Daugherty [51] proved that the ingestion of the unsaturated fatty acids can reduce plasmatic total cholesterol particularly when their percentage is higher than 11% of total energy covering the food. These answers thus result, undoubtedly, of a difference in the eating habits and of the composition of the diet consumed during the period of fasting by studied populations. The absence of variation of the cholesterol rates could be also explained by the limited synthesis of endogenous cholesterol during the fasting [52]. In addition, the patients women show values significantly higher than those recorded at the men. According to Temizhan [53], the diet taken by the experimental subjects can undoubtedly be at the origin of these answers.

The rates of HDL-c decrease significantly ( $P < 0.05$ ) during the month of Ramadan. Avignon [29] and Leenen *et al.* [54] and found results similar and explain it to the slowing of hydrolysis metabolic of the VLDL<sub>c</sub> and on the other hand to the richness of the diet in carbohydrates which can to cause an appreciable reduction of the concentrations in lipoproteins plasmatic. The study of Yarahmadi *et al.* [20] realized at the diabetic of type 2 does not indicate any significant change of the HDL-c levels during the Ramadan. However,

Maislos *et al.* [14] indicate an increase in the rates of HDL-c during the fasting. The rise in the rate of HDL-c often coincides with the reduction in the rates of VLDL<sub>c</sub>; this supposes that the increased hepatic hydrolysis of the VLDL<sub>c</sub> supports an important synthesis of HDL<sub>c</sub> among these patients [55]. These beneficial changes in favour of the HDL<sub>c</sub> have summers also suggested by Latif *et al.* [56]. The rates of HDL-c noted at the experimental subjects (male and female) seem identical. According to Chapman [57] and Beucler [58], in generally, the non menopause women present higher values than the men and that is due certainly at the effect of the oestrogen's which can increase the levels of the HDL<sub>c</sub>. Apparently, majority of the women of this study arrived at the menopause; what explains the negligible effect of the oestrogen on the variations of the rates of HDL-c.

It seems that the month of Ramadan induces an increase in the plasmatic rate of LDL-c particularly among diabetic women. The studies of Yarahmadi *et al.* [20] and Nagra *et al.* [25] indicate also an increase in the rates of LDL-c during the fasting; whereas Fakhrazadeh *et al.* [50] report a reduction in these values. Streicher *et al.* [59] showed that the insulin which decreases during the fasting increases the expression of genes of the hepatic receivers of LDL-c. In addition, Keys [60], Matisson and Gundy [61] explained the diminutions of the levels of LDL-c during the fasting at the nature of the greases ingested by the patients whose composition noted during this period is richer in mono fatty acids unsaturated and in fatty acids poly unsaturated; on the other hand the saturated fatty acids are slightly represented. Thus, the high take of saturated fatty acids is at the probable origin of the rise in the rates of LDL-c noticed among our patients. Iacano and Daugherty [51] also confirmed that the ingestion of a diet rich in fatty acids poly unsaturated induced a notable reduction of the plasmatic levels of LDL-c.

However during the two experimental periods (P1 and P2), no significant variation ( $P < 0.01$ ) of the rates of VLDL<sub>c</sub> is not detected among patients diabetic. This corroborates the observations of Maislos *et al.* [62] which did not notice significant changes of the rates of the VLDL<sub>c</sub> during the Ramadan fasting. On the contrary, Fakhrazadeh *et al.* [50] and Jensen *et al.* [63] noted a highly significant reduction of the VLDL<sub>c</sub> who are partially hydrolyzed in periferic tissues showing a certain resistance to insulin by the action of the lipoproteins lipases while releasing from the free fatty acids (FFA) necessary to the synthesis of the glucose by gluconeogenesis.

**Proteinous Measurements:** From the 1st period before the fasting to the 2nd period of the Ramadan, the high rates ( $P<0.01$ ) of plasmatic proteins noticed in particular among diabetic women remain stable. According to Nagra *et al.* [25] the concentrations' of plasmatic proteins hardly vary during the fasting; on the contrary Norrelund [64] advance an increase in the protein levels at the subjects exposed to the growth hormone proceeding faculty to stimulate the muscular protein synthesis. The recorded results are undoubtedly in relation to the consumed diet whose composition is more consistent during the Ramadan by comparison at the other months of the year. These noted variations can possibly be due to a significant expression of certain hormones during the fasting as the glucagon which presents faculty to stimulate a more important mobilization of certain tissue components of which amino acids in order to compensate by gluconeogenesis the energy deficit recorded by the periferic tissues.

The creatin rates recorded at the diabetics during the fasting are relatively higher ( $P<0.01$ ) than before the period of Ramadan fasting. However the results noted respond to standard values admitted at a healthy subject; varying from 6 to 13 g/l. Lacour [65] indicates on this subject that levels of creatin in blood does not depend only on glomerular filtration; but also of the digestive absorption of meat products which probably increase modestly during the month of Ramadan. These results are certainly in relation with the differences in activities physical as well as the muscular mass of patients [65].

Finally, a light non significant reduction ( $P<0.05$ ) in the plasmatic urea rate is noted during the fasting. Nevertheless, Sulimani *et al.* [66] noticed a significant rise of the urea rate which results according to the same author from a bad glomerular filtration. Other authors explain the increase in the values among patients diabetic with the dehydration caused by the food restriction liquids during fasting period [67]. Indeed, according to Bonneau [68] the dehydration prolonged during fasting can induce a fall of the diuresis and in consequence can cause an increase in uraemia. Our results are probably due to the weak hepatic production of urea among diabetic patients who not presented a renal dysfunction during all experimental periods.

**Insulin:** The insulin rates decrease significantly ( $P<0.05$ ) in men and the diabetic women during the Ramadan compared to the period before the fasting. These results are in agreement with those advanced by Sadr *et al.* [69] and Al Arouj *et al.* [70]. Apparently, fasting plasma insulin and C-peptide levels do not change either [71]. According to a recent study, these two variables are

reported not to change in women but to decrease in men [20]. When bloods samples are taken at 4 h interval, the results show that plasma insulin level and C-peptide increase at 08:00 h and decrease later in the day [72]. Insulin resistance decrease in both genders during Ramadan, but this change is significant only in men [19].

The reduction in the insulin secretion is probably the most important phenomenon endocrinien during the food fasting. Its weak production accompanied by a notable secretion of glucagon during the month of Ramadan are undoubtedly the principal elements allowing the activation of the lipolysis, the startup of the gluconeogenesis and the muscular proteolysis [73,74]. Thus, during the prolonged fasting, the maintenance of a certain plasmatic insulin production undoubtedly avoids the exaggerated manifestation of certain metabolic reactions such as lipolysis and cetogenesis [75].

## CONCLUSION

During the Ramadan, none patients showed considerable variations in levels of plasmatic glucose being able to prevent it from fasting. This period of food restriction seems to deteriorate the level of the LDL .<sub>c</sub> which increases remarkably ( $P<0.01$ ) particularly among diabetic women. On the other hand, all the other lipidic and proteinic parameters measured among all patients were not affected by the fasting. In perspective, it would be extremely interesting to renew this expérimention while taking into account other biochemical parameters such as (apolipoproteins, glucagon, cortisol, thyroxin...) what allows certainly a good comprehension of the behavior metabolic among the diabetics of type 2 during fasting of the month of Ramadan .

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## REFERENCES

1. Fajans, S., G. Bell and K. Polonsky, 2001. Molecular mechanisms and clinical pathophysiology of maturity-onset diabetes of the young. N. Engl. J. Med., 345: 971-980.

2. Guillausseau, P.J., 2003. Diabète sucré de type 1 et 2 de l'enfant et de l'adulte. *La Revue du praticien*, 53(13) 1463-1471.
3. Bush, D., C. Jones, K. Bass, G. Walter, J. Bruza and P. Ouyang, 1998. Eshogen replacement reverses Dothelial dysfunction in post menopausal women. *Am. J. med.*, 104: 552-558.
4. Buysschaert, M., 2001. Diabétologie clinique. 2<sup>ème</sup> édition de boeck. Université de Belgique.
5. Belhadj, M., A. Daoud, S. Khalfa and R. Malek, 2005. Le diabète en Algérie. In *Présentation au deuxième congrès maghrébin d'Endocrinologie Diabétologie Nutrition*. Fèz, 24-27 novembre., pp: 34-40.
6. Gerard, S., 2000. Prise en charge du diabète de type 2 non insulino-dépendant. Edition Lavoisier.
7. World Health Organization and Expert Committee on Diabets, 1985. Report of WHO study group, Technical Report Series., no.727, 1-113.
8. Tchobrousky, G.M. and B. Guy-Grand, 1997. Nutrition, Métabolisme et diététique. 2<sup>ème</sup> édition Flammarion Médecine Paris.
9. Friedewald, W.I., R.I. Levy and D.S. Frederickson, 1972. Estimation of the concentration of low density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem.*, 18: 499-502.
10. Schnek, A.G. and W.A. Schroeder, 1961. The Relation between the Minor Components of Whole Normal Human Adult Hemoglobin as Isolated by Chromatography and Starch Block Electrophoresis. *J. Amer. Chem. Soc.* 83: 1472-1478.
11. Hanning, I., P.D. Home and K.G.M.M. Alberti, 1985. Measurement of free insulin concentration: The influence of the timing of extraction of insulin antibodies. *Diabetologia.*, 28: 831-835.
12. Soeldner, J.S. and D. Slone, 1965. Critical variables in the RIA of serum insulin using the double antibody technic. *Diabetes.*, 14: 771-779.
13. Uysal, B., M. Erdogan, G. Sahin, N. Kamel and G. Erdogan, 1998. Clinical and metabolic effects of fasting in 41 type 2 diabetic patients during Ramadan. *Diabetic Care.*, 21: 2033-20.
14. Maislos, M., Y. Abou Rabiah, I. Zuili, S. Iordash and S. Shany, 1998. Gorging and plasma HDL-Cholesterol concentrations: The Ramadan model. *Eur. J. Clin. Nutr.*, 52: 127-130.
15. Laajam, M.A., 2003. Ramadan fasting and non insulino-dependent diabetes: Effect on metabolic control. *J. Cool physicians Surg. Pak.*, 13: 329-332.
16. Rashad, A., 1992. The fasting of Ramadan. *BMJ.*, 304: 521-522.
17. Aldouni, A., N. Ghalim, A. Bensliman, F. Lecerf and R. Saile, 1998. Fasting during Ramadan induces a marked increase in high density lipoprotein cholesterol and decrease in low density lipoprotein cholesterol. *Ann. Nutr. Met.*, 41: 242-249.
18. Mafauzy, M., W.B. Mohammed, M.Y. Anum, A. Zulkifli and A.H. Ruhani, 1990. A study of fasting diabetic patients during the month of Ramadan. *Med. J. Malaysia.*, 45: 14-17.
19. Athar, S. and M. Habib, 1994. Management of stable typical 2 diabetes mellitus (NIDDM) during Islamic fasting in Ramadan. In: *The First International Congress one Health and Ramadan Casablanca, Morocco*, pp: 203-212 (Abstract).
20. Yarahmadi, S.H., B. Larijani, M.H. Bastanhagh, M. Pajouhi, R. Baradar Jalili, F. Zahedi, K. Zندهdeh and S. Akrami, 2003. Metabolic and clinical effects of Ramadan fasting in patients with type II diabetes. *J. Coll. Physicians Surg. Pak.*, 13: 329-332.
21. Dattilo, A., 1992. Effects of weight reduction on blood lipids and lipoproteins: ameta-analysis. *Am. J. Clin. Nutr.*, 56: 320-32.
22. Dennis, K., 1993. Differential effects of body fatness and body fat distribution on risk factors for cardiovascular disease in women impact of weight loss. *Arterioscler thromb.*, 13: 1487-1494.
23. Lichtenstein, A., 1994. Short-Term consumption of a low -fat diet beneficially affects plasma lipid concentrations only when accompanied by weight loss. *Arterioscler thromb.*, 14: 1751-1760.
24. Looker, H., W. Knowler and R. Hanson, 2001. Changes in BMI and weight before and after the development of type 2 diabetes. *Diabetes care.*, 24: 1917-1922.
25. Nagra, S., Z. Rahman, M. Javaria and A. Qadri, 1998. Study of some biochemical parameters in young women as affected by Ramadan fasting. *Int. J. Ramadan Fasting Res.*, 2: 1-5.
26. Nomani, M., M. Hallak, S. Nomani and I. Siddiqui, 1989. Changes in blood urea and glucose and their association with energie -contaning nutrients in men non hypo caloric diets during Ramadan fasting. *Am. Clin. Nutr.*, 49: 1141-1145.
27. Larijani, B., F. Zahedi, M. Sanjari, M. Amini, R. Jalili, H. Adibi and A. Vassigh, 2003. The effect of Ramadan fasting serum fasting serum glucose in healthy adult's. *Med. J. Malaysia.*, 48: 678-680.
28. Azizi, F. and B. Siahkolah, 2003. Ramadan fasting and diabetes mellitus. *Arch. Iranian Med.*, 22: 186-191.

29. Avignon, A., 2001. Athérosclérose: Physiologie, évaluation du risque cardiovasculaire et prévention nutritionnelle. *Cah. Nutr. Diet.*, 36: 2S88-2S94.
30. Clore, J., E. Post, J. Baily, J. Nestler and W. Blackard, 1992. Evidence for Increased liver glycogen in patients with non insulin-dependant diabetes mellitus after 3-days fast. *J. CLIN Endocrinal Metab.*, 74: 660-666.
31. Shepherd, P. and B. Kahn, 1999. Action of transporters-insulin of glucose implication for the insulin resistance and the diabetes mellitus. *N. Eng. J. Med.*, 341: 248-257.
32. Chandalia, H.B., A. Bhargav and V. Kataria, 1987. Dietary pattern during Ramadan fasting and effect on the metabolic control of diabetes. *Pratical Diabet.*, 4: 287-290.
33. Sulimani, R., M. Laajam, O. Al-Atlas, F.O. Famuyiwa, S. Bashi and M. Mekki, 1991. The effect of Ramadan fasting on diabetes control in type II diabetic patients. *Nutr. Res.*, 11: 261-264.
34. Al Hader, A.F. and A. Niazy, 1994. The effects of Ramadan fasting on certain biochemical parameters in normal subjects and in type II diabetic Patients. In: *The First International Congress on Ramadan and Health, Casablanca, Morocco, 1994*, pp: 26 (Abstract).
35. Belkhadir, J., H. El Ghomari, N. Klocker, A. Mikou, M. Naciri and M. Sabri, 1994. Muslims with not insulin dependant diabetes fasting during Ramadan; treatment with glibenclamide. *Br. Med. J.*, 307: 292-295.
36. Sulimani, R.A., 1997. Management of typical 2 diabetes with oral agent during Ramadan. In: *The congress of the diabetes mellitus during the holy month of Ramadan, Cairo, Egypt*, pp: 8 (Abstract).
37. Farad Bensenouci, S., F. Maillot and F. Lamiisse, 2002. Les risques du Ramadan chez les sujets Sains et les patients diabétiques. *Cahiers de Nutrition et diabétique.*, 37(2): 96-104.
38. Sari, R., M.K. Balci, S.H. Akbas and B. Avci, 2004. The effects of diet, sulfonylurea and Repaglinide therapy on clinical and metabolic parameters in type 2 diabetic patients during Ramadan. *Endocr. Res.*, 30(2): 169-177.
39. Mufauzy, M., W. Mohammed, M. Anum, A. Zulkifli and A. Ruhani, 1990. A study of the fasting diabetic patients during the month of Ramadan. *Med. J. Malaya.*, 45: 14-17.
40. Gustaviani, R., P. Soewondo, G. Semiardji and A.W. Sudoyo, 2004. The influence of calorie restriction during the Ramadan fast on serum fructosamine and the formation of beta hydroxybutirate in type 2 diabetes mellitus patients. *Acta. Med. Indones.*, 36: 136-141.
41. ANAES (Agence Nationale pour l'accréditation et l'évaluation en santé), 2000. Stratégie de prise en charge du patient diabétique de type 2 à l'exclusion de la prise en charge des complication. *Diabetes Metab.*, 26(5): 1-96.
42. Drouin, P., J.F. Blickle, B. Charbonnel, E. Eschwege, P.J. Guillausseau, P.F. Plouin, J.M. Daninos, N. Balarac and J.P. Sauvanet, 1999. Diagnostic et classification du diabète sucré; les nouveaux critères. *Rapport des experts de l'alfediam. diabetes and metabolism (paris).*, 25: 72-83.
43. UKPDS (UK Prospective Diabetes Study Group), 1998. Effect of intensive blood glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). *Lancet.*, 352: 854-65.
44. El-hazmi, M., F. Al-faleh and A. Al-mofleh, 1987. Effects of Ramadan fasting on the values of haematological and biochemical parameters. *Saudi Med. J.*, 8: 171-176.
45. Sarrafzadeh, N., M. Atashi, G. Nadri, S. Asgary, M. Fatehifar, M. Samarian and M. Zarei, 2000. The effect of fasting in Ramadan on the values and interrelation between biochemical, coagulation and haematological factors. *Annals of Saudi medicine.*, 20: 377-381.
46. Afrasiabi, A., S. Hassanzadeh, R. Sattarivand, M. Nouri and S. Mahbood, 2003. Effects of low fat and low caloric diet on plasma lipid levels in the fasting month of Ramadan. *Saud. Med. J.*, 24: 184-188.
47. Gumma, K., D. Mustafa, N. Mahmoud and A. Gader, 1978. The effects of fasting in Ramadan: Serum uric acid and lipid concentration. *Br. J. Nutr.*, 40: 573.
48. UKPDS (UK Prospective Diabetes Study Group), 1997. Prospective diabetes study 27. Plasma lipids and lipoproteins at diagnosis of NIDDM by age and sex. *Diabetes care.*, 20: 1683-1687.
49. Asgary, S., A. Aghaci, G. Nadri, R. kelishadi, M. Gharipou and S. Azali, 2000. Effects of Ramadan fasting on lipid per oxidation, Serum lipoprotein and fasting blood sugar. *Medical Journal of IAS.*, 13: 1-3.
50. Fakhrazadeh, H., B. Larijani, M. Sanjari, R. Baradr-Jalili and M. Amini, 2003. Effects of Ramadan fasting on clinical and biochemical parameters in healthy adults. *Annals of Saudi medicine*, 23: 223-226.
51. Iacano, J. and R. Doughery, 1991. Lack of effect of linoleic acid on the high density lipoprotein-cholesterol fraction of plasma lipoproteins. *Am. J. Clin.*, 13: 154-161.
52. Exton, J., J. Corbin and S. Harper, 1972. Control of gluconeogenesis in liver. *J. Biol. Chem.*, 247: 4992-5003.

53. Temizhan, A., O. Donderici, D. Oguz and B. Demirbas, 1999. Coronary heart disease events. *Int. J. Cardiol.*, 70: 179-53.
54. Leenen, R., Y. Vanderkooy, S. Meyboom, J. Scidell, P. Deurenbrg and J. Weststate, 1993. Relative effects of weight loss and dietary fat modification non serum lipid levels in the dietary treatment of obesity. *Lipid Res.*, 34: 599-604.
55. Basdevant, A., 1979. Diabète Sucré et hyperlipidémies. Reconnaître, comprendre, traiter le diabète sucré. 2eme ED ISEM maloine Canada, pp: 281-284.
56. Latif, A., M. Fharieba, H. Al-qussab and Q. Sartawi, 1994. Changes in serum lipid and electrolytes in type 2 diabetes mellitus during Ramadan on peptic ulcer complication. *Scand. J. Gastroenterol.*, 29: 603-606.
57. Chapman, M., 1982. Les lipoprotéines et le foie. *Gastroentérite Clin Biol.*, 6: 482-499.
58. Beucler, I., S. Salmon, E. Petit, M. Ayrault-Jarrier and J. Polonovski, 1986. Structure et métabolisme des lipoprotéines. *Am. Biol. Clin.*, 44: 531-534.
59. Streicher, R., J. Kotzka, D. Muller-wieland and G. Siemester, 1996. SREB-1 mediates activation of the low density lipoprotein receptor promoter by insulin-like growth factors-1. *J. Biol. Chem.*, 271: 7128-7133.
60. Keys, A., 1970. Coronary heart disease in sever counties. *The diet circulation.*, 41: 162-183.
61. Matisson, F. and S. Gundy, 1985. Comparison of effects of dietary saturated monosaturated and polyunsaturated fatty acids on plasma lipids and lipoprotein in man. *Lipid Res.*, 26: 164-202.
62. Maislos, M., N. Khamaysi, A. Assali, Y. Abourabiah, I. Zuili and S. Shany, 1993. Marked increase in plasma high density lipoprotein cholesterol after prolonged fasting during Ramadan. *Am. J. Clin. Nutr.*, 57: 640-642.
63. Jensen, M., V. Chadramouli, W. Schumann, K. Ekberg, S. Previs, S. Gupta and B. Landan, 2001. Source of blood glycerol during fasting. *Am. J. Physiol. endocrinal Metab.*, 281: 998-1004.
64. Norrelund, H., S. Nair, J. Jordensen, J. Christiansen and N. Moller, 2001. The protein retaining effects of growth hormone during fasting involve inhibition of muscle -protein breakdown. *Diabetes.*, 50: 96-104.
65. Lacour, B., 1992. Créatinine et fonction rénale. *Néphrologie.*, 13: 78-81.
66. Sulimani, RA., F.O. Famuyiwa and M.A. Laajam, 1998. Diabetes mellitus and Ramadan fasting: The need for a critical appraisal. *Diabetic Medicine.*, 5: 589-591.
67. Raza, H., M. Qureshi and W. Montague, 1994. Effects of Ramadan fasting on blood chemistry in healthy volunteers. *Emirates Med. J.*, 12: 27-33.
68. Bonneau, C., 2001. Valeurs sémiologiques des paramètres biochimiques urinaires. *Annales de Biologie Clinique.*, 59: 13-25.
69. Sadr, F., M. Afshar and S. Sarboluki, 2001. Effect of fasting on glucose, lipids, body weight and blood pressure among non-insulindependent diabetes Mellitus. In: *The Congress on Health and Ramadan, Tehran Iran, Iran J. Endocrinol Metab, Suppl (Autumn), Vol. 18.*
70. Al arouj, M., R. Bouguerra, J. Buse, S. Hafez, M. Hassanein, M. Ashraf ibrahim, F. Ismail-beigi, I. El-kebbi, O. Khatib, S. Kishawi, A. Al-madani, A.A. Mishal, M. Al-maskari, A. Ben Nakhi and K. Al-rubean, 2005. Recommendations for Management of Diabetes during Ramadan. *Re v i e w s/Commentaries/ADA Statements. Diabetes care*, september 2005., 28(9): 2305-2311.
71. Bagraic, N., V. Yumuk, T. Damci and M. Ozyazar, 1994. The effect of fasting on blood glucose fructosamine, insuline and C-peptide levels in Ramadan. In: *The First International Congress on Ramadan and Health, Casablanca, Morocco, 1994*, pp: 32 (Abstract).
72. Khatib, F.A. and Y.A. Shafagoj, 2004. Metabolic alterations as a result of Ramadan fasting in non-insulin-dependent diabetes mellitus patients in relation to food intake. *Saudi Med. J.*, 25: 1858-1863. (Abstract).
73. Barrè, H., J. Chatonnet, Y. Le Maho and J.L. Valatx, 2001. *Physiologie énergétique. Belin sciences Sup.*, 1-400.
74. Basdevant, A., M. Laville and E. Lerebours, 2007. *Traité de nutrition clinique de l'adulte. Flammarion Médecine Édition.*
75. Salti, I., E. Bernard, B. Detournay, M. Bianchi-Biscay, C. Le Brigand, Abdul Jabbar and On behalf of the epidiar study group, 2004. A population- based study of diabetes and its characteristics during the fasting month of Ramadan in 13 countries: resultts of the Epidemiology of Diabetes and Ramadan 1422/2001 (EPIDIAR) Study. *Diabetes Care.*, 27 (10): 2306-2311.