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A Review of Ramadan Fasting and Diabetes Mellitus: Controversies regarding the Effects of Ramadan Fasting on Diabetic Patients

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ABSTRACT

Although several studies have investigated the effects of Ramadan fasting on diabetic patients, the exact impacts on diabetes control have not been well elucidated yet. There are neither precise quantitative criteria nor clear guidelines regarding Ramadan fasting for diabetic patients. This review aimed to discuss the results of previous studies. The neglected points in performed studies should be considered in the design and interpretation of future research related to Ramadan fasting in diabetic patients.

A thorough research was carried out on the internet, using the following keywords: "Ramadan", "Ramadan fasting", "Islamic fasting", "fasting in Ramadan", and "fasting", in combination with words such as "diabetes mellitus", "hyperglycemia", "hypoglycemia", and "diabetic ketoacidosis". Databases including PubMed, Google Scholar, and some regional databases were searched in order to find related articles (cross-sectional, descriptive-analytical, cohort, clinical trial, and review studies), published during 1957-2013.

The obtained data showed that Ramadan fasting could be non-risky for partially controlled diabetic patients. However, the safety of Ramadan fasting for diabetic patients with different blood glucose levels and complications is not yet determined. Many deficiencies and limitations are observed in the related studies such as the heterogeneity of participants including differences in lifestyle and circadian rhythm changes. Therefore, well controlled studies need to be performed to evaluate factors affecting blood glucose level during Ramadan fasting.

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Introduction

Several studies have investigated the effects of Ramadan fasting on variations in blood glucose level. However, there is still a great deal of controversy regarding the risks of fasting, necessary changes in medication use, and appropriate dietary intake in diabetic patients. In this paper, we attempted to disclose the effects of Ramadan fasting on various aspects of diabetes and discuss the possible contributing factors.

Materials and Methods

A thorough research was carried out on the internet, using the following keywords: "Ramadan", "Ramadan fasting", "Islamic fasting", "fasting in Ramadan", and "fasting", in combination with words such as "diabetes mellitus", "hyperglycemia", "hypoglycemia", and "diabetic ketoacidosis". Databases including PubMed, Google Scholar, and some regional databases were searched in order to find related articles (e.g., cross-sectional, descriptive-analytical, cohort, clinical trial, and review articles), published during 1957-2013.

Variations of dietary intake in diabetic patients during Ramadan

The key to the management of diabetes mellitus is an appropriate and balanced diet; therefore, any dietary variations can affect disease control. Ramadan fasting is associated with unavoidable changes in dietary patterns and food intake. In some studies, reduced calorie intake of about 300 kcal per day has been reported in type 2 diabetic patients (1, 2).

In a study conducted in Algeria on 276 obese

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diabetic patients, a significant decrement of 335 kcal in daily energy intake was observed (3). This study revealed that the frequency of food intake decreased during Ramadan. Overall, 77%, 14%, and a low proportion of total daily energy came from Iftar (evening meal), Sahar (pre-dawn meal), and dinner (usually consumed a few hours after Iftar), respectively. On the other hand, in other months of the year, the highest amount of calorie was consumed during lunch (>35%) and dinner (30%) (3). Also, calories from carbohydrates and dietary fibers decreased and levels of protein, saturated fat, trans fatty acids, and cholesterol increased during this month (3).

Inconsistent with the previous study, low calorie and fat intake, as well as increased carbohydrate intake, has been reported in other articles (4). In a population-based study, physical activity level, food intake, sleep duration, and fluid intake did not change in more than 50% of the subjects. Moreover, the amount of food intake did not change in 51% and 56% of type 1 and type 2 diabetic patients, respectively. However, an increase in food intake was reported in 20% and 18% of patients, and a decrease in 23% and 30% of type 1 and type 2 diabetic patients, respectively (5).

Anthropometric changes in diabetic patients during Ramadan

In articles investigating the effects of Ramadan fasting on diabetic patients, no changes (5-14), decrease (1, 3, 5, 15-17), or even increase in body weight (18) have been reported. In a previous study, a significant reduction in body weight (up to 3 kg) was observed in obese individuals; however, these patients gained weight gradually after the end of Ramadan. Also, no significant changes of waist circumference or waist-to-hip ratio were observed (3).

Furthermore, a mean of 0.8 kg/m^2 decrease in body mass index (BMI) was reported by reducing calorie intake by 300 Kcal/day. The weight loss induced by Ramadan fasting in diabetic patients was associated with reduced energy intake and meal frequency (2). In some studies, body weight and BMI remained unchanged (5, 13, 19), while others reported an increase in body weight, although the weight gain was insignificant (20). In these studies, weight gain was associated with reduced physical activity and increased fat, sugar, and total energy intake (20).

Moreover, a study showed that basal metabolism decreases during Ramadan (19). Since the decrease in basal metabolism reduces the need for energy in the body, weight gain may still occur even by keeping the energy intake unchanged. Most diabetic patients reduce their physical activity due to the fear of hypoglycemia during Ramadan (11, 21). Reduced physical activity not only does not inhibit weight loss as an effect of Ramadan fasting, but also leads to weight gain.

Variations of glycemia in diabetic patients during Ramadan

Fasting in healthy subjects may contribute to an increase in insulin action, which leads to increased glucose uptake by tissues (22). Animal studies have shown that hunger can lead to a 7-fold increase in insulin sensitivity (23) and may reduce the incidence of diabetes (24). In some studies, a slight reduction (25-28) or variation (29) in blood glucose was reported.

Typically, in the month of Ramadan, fasting blood glucose level slightly decreases in the first few days, although it returns to the pre-Ramadan level in the second decade of this month (30). However, in a study, an average of 20-25% reduction in salivary glucose was observed in the first 10 days, followed by a decline in the next 10 days and an increase on day 29. This increment within the last 10 days of Ramadan was not similar to the normal level of salivary glucose in other months of the year (31).

Some studies have shown that fasting has no adverse effects on serum glucose in diabetic patients (1, 6-8, 11-13, 32-38). Ramadan fasting induces a significant decrease in fasting blood glucose (1-3, 15, 28, 34, 39-44), glycated hemoglobin (HbA1c) (3, 15, 28, 40-42, 45), and serum fructosamine, without producing beta-butyrate (2). The reduction in serum fructosamine may be due to decreased energy intake (1, 2). In fact, fructosamine level determines the blood glucose level over the over the past 2-3 weeks and can be a better indicator of the effects of fasting, compared to HbA1c (46).

In a previous article, blood glucose measurements before Iftar and Sahar and 2 hours after these meals showed no changes within the 1^{st}, 2^{nd}, 3^{rd}, and 4^{th} weeks of fasting.

However, after the end of Ramadan, glucose concentration gradually increased (2); this increment was accompanied by an increase in food intake. In fact, one of the causes of fructosamine increase after the end of Ramadan may be an increase in carbohydrate intake on Eid al-Fitr (Feast of Breaking the Fast) and the following days (20).

Variations in blood glucose level could be related to the type of consumed foods, compliance with medications, and individual differences in the regulation of energy metabolism (47). The conflicts between the obtained results could be due to differences in the dietary patterns of different subjects (47). Also, blood glucose level during Ramadan fasting was higher in diabetic patients, referring to medical centers. During Ramadan, the number of patients referring to medical centers was lower than other months of the year, which could be one of the causes of hyperglycemia in fasting individuals.

The acute complications of Ramadan fasting in diabetic patients

Hyperglycemia and diabetic ketoacidosis

Hyperglycemia is one of the potential complications associated with fasting. This condition could be caused by a reduction in drug dosage, increased food intake especially carbohydrate, and decreased physical activity (5). If glycemic control is poor, the production of ketone bodies will be accelerated due to lower liver glycogen levels. Therefore, in some studies, fasting has also led to diabetic ketoacidosis (5, 48).

Diabetic patients (especially type 1 diabetic patients) are at a potential risk of diabetic ketoacidosis if their blood glucose is poorly controlled before Ramadan (5). In those with relatively proper control of blood glucose, ketone bodies do not increase during Ramadan fasting (47). However, a significant change in the incidence of hyperglycemia in type 2 diabetic patients has been reported.

In a study, hospitalization due to hyperglycemia in patients with type 1 and type 2 diabetes mellitus was respectively 3 and 5 times more than the pre-Ramadan period; drug dose reduction was noted as the main reason for this increment (5). Generally, hyperglycemia may be caused by an adverse reaction to dose reduction, which aimed to prevent hypoglycemia. In a previous study, patients with increased food intake experienced higher frequencies of severe hyperglycemia (5).

Hypoglycemia

Reduced calorie intake during Ramadan fasting may contribute to hypoglycemia. The majority of diabetic patients do not consult their physicians to adjust their medication doses in Ramadan (5); this may be one of the causes of hypoglycemia (5, 13, 45, 49, 50). However, in some studies, no increased incidence of hypoglycemia has been reported (1, 6, 9, 11, 33, 34, 41, 51-53). Also, in type 1 diabetic patients, due to a decrease in glucagon and epinephrine responses to hypoglycemia, the risk of hypoglycemia increased during Ramadan (54).

Symptoms of hypoglycemia may be present at different blood glucose levels. In some patients, symptoms of hypoglycemia have been reported in a glucose concentration of 60-80 mg/dl, while in some cases, these symptoms have been even recorded at concentrations higher than 80 mg/dl. However, this difference was influenced by the compliance of individuals with low blood glucose and also the degree of their metabolic control (2).

According to a previous study, variation in the incidence of hypoglycemia in type 2 diabetes was significant, and the frequency of hypoglycemia and hyperglycemia increased, compared to a year before Ramadan (5). However, the increased incidence of severe hypoglycemia and hyperglycemia in patients with type 2 diabetes was statistically significant; in fact, the increased risk of hypoglycemia was related to a change in subjects' medication dosage and physical activity (5).

In the mentioned study, fasting increased the risk of severe hypoglycemia (defined as hospitalization due to hypoglycemia) 4.7 times in type 1 diabetic patients and about 7.5 times in individuals with type 2 diabetes. The lower estimated incidence of hypoglycemia may be probably due to excluding non-hospitalized patients.

In the aforementioned study, the prevalence of severe hypoglycemia was higher in patients with changes in hypoglycemic agents or insulin level and those with major changes in their lifestyle (5). Factors that may increase the risk of hypoglycemia during Ramadan included

geographical location (e.g., Indonesia, Malaysia, and Saudi Arabia), body weight <70 kg, waist circumference < 90 cm, insulin therapy, and prior history of hypoglycemia before Ramadan (22). A 4-fold increase in the incidence of hypoglycemia in diabetic patients, who had not been trained about fasting, was observed, whereas individuals, who had participated in educational programs, showed lower weight loss and reduced incidence of hypoglycemia (16).

Dehydration and thrombosis

Restriction of fluid intake during prolonged fasting can lead to dehydration. Hot climates, severe physical activities, and conditions leading to excessive sweating intensify dehydration. Hyperglycemia can cause osmotic diuresis and imbalance in electrolyte and blood volume. Moreover, in patients, who are already suffering from autonomic neuropathy, orthostatic hypotension may occur. Cardiac arrest, falls, injuries, and bone fractures may occur due to the effects of dehydration and low blood pressure. Also, dehydration can enhance blood clotting in patients with diabetes (55), and increased blood viscosity due to dehydration may increase the risk of thrombosis (56, 57).

Oral medications

Sulfonylureas

Those receiving multiple sulfonylureas often face problems during Ramadan fasting. Theoretically, use of long-acting sulfonylureas with afternoon and Iftar meals better controls blood glucose (58, 59). In a study, receiving 60 mg of gliclazide (modified-release type) at Iftar led to a decrease in fasting blood glucose. Therefore, this medication could be used during Ramadan without disrupting the blood glucose level in diabetic patients (60).

In another investigation, patients receiving glibenclamide at Sahar and Iftar experienced increased blood glucose and weight gain; in addition, hypoglycemia occurred in 4% of these participants (33). Ramadan fasting in patients under glimepiride monotherapy (receiving the same typical dosage at Iftar) led to a 0.3% reduction in HbA1c; however, 5% of patients experienced hypoglycemia (41). In fact, glyburide (glibenclamide) might be more significantly associated with the risk of hypoglycemia, compared to the second generation of sulfonylureas, particularly gliclazide, glimepiride, and glipizide (58, 61).

Biguanides (Metformin)

In a study conducted on patients with well-controlled type 2 diabetes, fasting and postprandial blood glucose levels decreased during Ramadan fasting, while serum insulin level increased; however, all the changes were within the normal range (39). In fact, medications, inducing sensitivity to insulin, are associated with a lower risk of hypoglycemia during fasting, compared to drugs elevating insulin secretion (62). Therefore, the risk of acute hypoglycemia is lower in patients receiving only metformin.

Thiazolidinediones and α-glucosidase inhibitors

An important issue concerning the use of glitazones during Ramadan fasting is that it takes 2-4 weeks until these medications affect the blood glucose. Thus, it is not possible to quickly replace these medications with other glucose-lowering agents (63). Patients using α-glucosidase inhibitors or thiazolidinediones such as glitazone are at a lower risk, and according to specialists' advice, their medication dosage does not need to be altered (54).

Meglitinides (repaglinide)

According to a previous study, serum fructosamine level decreased more significantly in patients using repaglinide, compared to those taking glibenclamide in Ramadan (17, 33). There was no significant difference in terms of glycemia between patients receiving single-dose glimepiride along with gliclazide and those taking repaglinide twice a day. Nevertheless, hypoglycemia was reported in patients receiving repaglinide (6). It seems that repaglinide is an appropriate choice for diabetic patients using sulfonylureas (6, 17, 33, 41).

As a previous study indicated, Ramadan fasting does not result in any changes in fasting or postprandial blood glucose, HbA1c, or serum fructosamine in three groups taking glimepiride at sunset (maximum dosage of 8 mg), repaglinide at dawn and sunset (maximum dose of 4 mg during each meal), and insulin glargine at 22 p.m. On the other hand, 2-h postprandial blood glucose was higher in non-fasting

patients, compared to fasting individuals; however, the effects of all 3 prescriptions were similar (20), and the risk of hypoglycemia did not change in these patients. It should be mentioned that the type and dosage of evaluated medications had been modified six months prior to the study (20).

Dipeptidyl peptidase-4 (DPP-4) inhibitor

In a study on type 2 diabetic patients with HbA1c higher than 8.5%, adding 50 mg of vildagliptin (twice a day) to the normal treatment with metformin improved hyperglycemia, without increasing the risk of hypoglycemia; however, this effect was not observed by adding 160 mg of gliclazide (twice a day) to the normal treatment (64).

Vildagliptin prevents the rapid degradation of glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic peptide, elevates the plasma concentration of the active forms of these hormones, and increases the sensitivity of pancreatic cells to glucose (65). Vildagliptin together with metformin, sulfonylureas, and thiazolidinediones reduces the incidence of hypoglycemia (66, 67); therefore, vildagliptin may be a better agent than sulphonylurea (68, 69).

GLP-1 receptor agonists

Compared to sulphonylurea, liraglutide (GLP-1 receptor agonist) may be more effective in combination with metformin in managing glycemia and severe hypoglycaemia (70).

Insulin therapy

Type 1 diabetes

Some type 1 diabetic patients opt to fast during Ramadan, and most of these patients change their insulin dosage immediately before, during, and some days after Ramadan. However, few studies have been conducted on the safety or efficacy of different insulin regimens in fasting patients with type 1 diabetes. In a study conducted on 15 patients receiving insulin glargine and rapid-acting insulin, all subjects, even those with some degrees of neuropathy, retinopathy, and nephropathy, tolerated fasting without facing any problems, and their mean daily blood glucose decreased during Ramadan (71).

In a study, glycosylated hemoglobin slightly improved in patients with type 1 diabetes using insulin pump, and there was a 5-50% reduction in insulin need in 50% of cases (52). In addition, insulin lispro, aspart, or lispro mix 25 could control blood glucose through lowering the frequency of hypoglycemia (72). It seems that if patients are given the necessary instructions about adjusting their insulin dosage [e.g., using analog insulin instead of neutral protamine hagedorn (NPH) and regular insulin and avoiding fasting in case of blood glucose drop], fasting would have fewer untoward effects on type 1 diabetic patients (73).

Type 2 diabetes

In a previous study, use of insulin glargine, together with glimepiride at sunset, led to a decrease in fasting blood glucose and HbA1c. However, the incidence of hypoglycemia increased, particularly in patients with low body weight and waist circumference. Blood glucose level > 120 mg/dl had a protective effect against hypoglycemia (45). Insulin lispro, aspart, and lispro mix 25 were associated with a lower incidence of hypoglycemia. Furthermore, using rapid-acting insulin analogs instead of regular insulin before meals resulted in a lower incidence of hypoglycemia and reduced the elevation of postprandial blood glucose (74, 75).

Combination of insulin lispro and Neutral Protamine Lispro (NPL) with a 50:50 ratio during Iftar and regular insulin along with NPH with a 30:70 ratio at Sahar led to the improvement of blood glucose and lowered the incidence of hypoglycemia; however, regular insulin and NPH with a ratio of 30:70 (used twice a day) did not have the same effects (76).

Evidence shows that hypoglycemia and hyperglycemia are preventable by training patients, holding educational programs (16, 77), adjusting medication dosages, modifying patients' lifestyle, self-monitoring of blood glucose, and novel therapeutic strategies (5, 16, 72, 78-83). Also, acute complications of fasting can be mitigated through the medical evaluation of patients before Ramadan and patient follow-up during and after this month (16).

Currently, no information is available regarding the effect of fasting on the mortality rate of diabetic patients and the interactive effect of fasting on chronic complications of diabetes. Based on the available data, it is hardly possible to demonstrate the innocuousness of

fasting regarding glycemic control and the severity of complications. Therefore, conducting well-controlled studies is necessary for determining the effects of Ramadan fasting on diabetic patients.

What should be considered in the design and interpretation of studies related to the effects of Ramadan fasting on diabetic patients?

Changes in sleep and circadian patterns (e.g., changes in peak cortisol level) (84-86), physical activity (87-89), body weight (20, 89-94), dietary patterns (3), daily calorie intake (1-3, 5, 89, 94), macronutrient proportion (3-5, 95), and glycemic index (96, 97) during Ramadan fasting can all affect glycemic control.

Differences in the dietary patterns of various populations, the season in which Ramadan falls, and fasting duration all encumber interpreting and comparing the results of different studies. Therefore, it is essential to consider these factors in designing and evaluating these findings. Moreover, there is a time difference in blood sampling between Ramadan and other months of the year; therefore, comparison of hematological parameters, without considering these factors, may be controversial.

During Ramadan, fasting blood sampling is performed right before sunset, while in other months, blood sampling should be done early in the morning, usually at 8:00 a.m. (8). Since serum cortisol concentrations, which are dependent on circadian rhythm (99), may affect blood glucose (98), it is not possible to compare these concentrations.

Seasonal differences in fasting duration and temperature, depending on the geographic location, may affect blood glucose level. Therefore, it does not seem reasonable to compare studies conducted in different seasons. Moreover, time intervals between meals in different seasons are among the most important factors affecting glycemia (100, 101).

Changes in dietary patterns, consumption of special foods during Ramadan (102) in different populations, and individual differences could result in discrepancies between the results of different studies regarding blood glucose and other biochemical parameters. During fasting, meal frequency and dietary fiber intake (from whole grains, fruits, and vegetables) may reduce in some cases and disrupt blood glucose control.

Changes and variations in dietary carbohydrate also lead to contradictory results. For instance, increasing carbohydrate intake at each meal without adjusting oral medication or insulin dosage would lead to increased blood glucose. Also, patient's reaction to insulin injection may vary in different hours of the day (103, 104). Differences between individuals in consuming foods with a wide range of glycemic indices also affect postprandial blood glucose (105). Moreover, the increase in glycemic load (especially during Iftar) for overcoming low blood glucose (induced by fasting) can increase postprandial blood glucose and disrupt glycemic control.

In most diabetic patients, consumption of high glycemic-index foods (e.g., dates) increases, especially during Iftar (106). Weight loss in overweight or obese people decreases insulin resistance and consequently lowers blood glucose concentration (107, 108). Studies have shown that reduced daily calorie intake may decrease the blood glucose level, even if it does not result in significant weight loss (109). Therefore, a slight increase or reduction in calorie intake, without significant changes in body weight, can lead to a change in blood glucose, which is often overlooked in the interpretation of the results.

Typically, patients are advised to increase the number of their daily meals and consume about 3-5 carbohydrate servings at each meal and 1-2 servings during snacks (109). If fasting diabetic patients take only two main meals during the day, they might receive their carbohydrate snacks as two main meals, especially during Iftar; this would lead to a rise in postprandial blood glucose.

A factor influencing the number of meals in Ramadan fasting may be the season in which Ramadan falls. Since time interval between sunset and bedtime reduces in summer, the number of meals and time interval between breaking the fast and late-night snack decrease; this reduced time interval may affect glycemic control (110). Conversely, the time interval between sunset and bedtime increases in winter, and therefore, there is more free time to consume snacks. The effect of these factors on glycemic control has not been analyzed in studies conducted in different seasons.

Additionally, some people tend to eat a light meal at Iftar, followed by a large meal like

dinner (which can vary among individuals) (87, 111). Thus, individual differences in meal frequency contribute to the inconsistency of the results.

An appropriate liquid intake is essential for maintaining body water, normal osmolality of body liquids, and excretion of excess glucose. In Ramadan fasting, liquid consumption is restricted to the time interval between Iftar and Sahar, and partial dehydration occurs during Ramadan fasting (112). Dehydration may increase serum glucose concentration (113). Thus, differences in liquid consumption, the season of Ramadan, ambient temperature, and lifestyle could lead to contradictory results in different studies.

Furthermore, in most studies, changes in physical activity and their effects on blood glucose level have been ignored in the interpretation of the results. Even though a decrease in physical activity has been reported in Ramadan (89, 114), it may not be true in all cases.

Conclusion

As the results indicated, fasting could be non-risky in patients with partially controlled diabetes and type 2 diabetic individuals, using oral glucose-lowering agents. Based on the obtained findings and considering several confounding factors, which were ignored in the analysis of the results, we cannot determine the exact effect of Ramadan fasting on metabolic control; also, we cannot assure the safety of fasting for different patients. Presently, there are neither precise quantitative criteria (covering medication, diet, and physical activity) nor clear guidelines regarding Ramadan fasting for diabetic patients. Therefore, well controlled studies should be conducted by considering all the factors affecting blood glucose in this period. However, based on clinical experience, the following points need to be considered:

1. All diabetic patients, who decide to fast, should be evaluated 2-3 months before Ramadan by a physician regarding the safety and complications of fasting and be informed about the necessary changes and required trainings.
2. Currently, Ramadan fasting is allowed in stable type 2 diabetic patients (normal or overweight), who are educable and use oral glucose-lowering agents.
3. Patients at high risk of fasting complications include insulin-treated patients, uncontrolled diabetic patients, breastfeeding mothers, patients experiencing unawareness hypoglycemia, gestation, the elderly, hypoglycemic individuals, patients affected by disease complications, non-educable patients, and those living alone.
4. It is necessary to educate patients with regard to symptoms of hypoglycemia, hyperglycemia, and loss of body water. Patients should be also trained about the measures, which need to be taken in these circumstances.
5. In addition to drugs, adjusting the dietary intake and physical activity (regarding its duration and intensity) should be considered.
6. Experts forbid fasting in patients with fasting blood sugar < 70 or > 200 mg/dl. Fasting should be stopped in case the blood glucose level exceeds 250-300 or drops to < 60-70 mg/dl.

References

1. Mafauzy M, Mohammed WB, Anum MY, Zulkifli A, Ruhani AH. A study of the fasting diabetic patients during the month of Ramadan. Med J Malaysia. 1990;45(1):14-7.
2. Gustaviani R, Soewondo P, Semiardji G, Sudoyo AW. 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. 2004;36(3):136-41.
3. Khaled BM, Belbraouet S. Effect of Ramadan fasting on anthropometric parameters and food consumption in 276 type 2 diabetic obese women. Int J Diabetes Dev Ctries. 2009;29(2):62-8.
4. Chandalia HB, Bhargav A, Kataria V. dietary pattern during Ramadan fasting and effect on the metabolic control of diabetes. Practical Diabet. 1987;4:287-90.
5. Salti I, Benard E, Detournay B, Bianchi-Biscay M, Le Brigand C, Voinet C, et al. A population-based study of diabetes and its characteristics during the fasting month of Ramadan in 13 countries: results of the epidemiology of diabetes and Ramadan 1422/2001 (EPIDIAR) study. Diabetes Care. 2004;27(10):2306-11.
6. Sari R, Balci MK, Akbas SH, Avci B. The effects of diet, sulfonylurea, and Repaglinide therapy on

clinical and metabolic parameters in type 2 diabetic patients during Ramadan. Endocr Res. 2004;30(2):169-77.
7. Bouguerra R, Belkadhi A, Jabrane J, Hamzaoui J, Maatki C, Ben Rayana MC, et al. [Metabolic effects of the month of Ramadan fasting on type 2 diabetes]. East Mediterr Health J. 2003;9(5-6):1099-108.
8. Ait saada D, Selselet attou G, Belkacemi L, Ait chabane O, Italhi M, Bekada AMA, et al. Effect of Ramadan fasting on glucose, glycosylated haemoglobin, insulin, lipids and proteinous concentrations in women with non-insulin dependent diabetes mellitus. African Journal of Biotechnology. 2010;9(1):87-94.
9. AlAlwan I, Al Banyan A. effects of Ramadan fasting on children with type 1 diabetes. IJDM. 2010;2:127-9.
10. Bakiner O, Ertorer ME, Bozkirli E, Tutuncu NB, Demirag NG. Repaglinide plus single-dose insulin glargine: a safe regimen for low-risk type 2 diabetic patients who insist on fasting in Ramadan. Acta Diabetol. 2009;46(1):63-5.
11. Laajam MA. Ramadan fasting and non-insulin-dependent diabetes: effect on metabolic control. East Afr Med J. 1990;67(10):732-6.
12. Sulimani R, lLaajam O, Al-Alas O, Famuyiwa FO, Bashi S, Mekki M. The effect of ramadan fasting on diabetes control in type II diabetic patients nutr res. 1991;11:261-64.
13. Uysal AR, Erdogan MF, Sahin G, Kamel N, Erdogan G. Clinical and metabolic effects of fasting in 41 type 2 diabetic patients during Ramadan. Diabetes Care. 1998;21(11):2033-4.
14. Maislos M, Abou-Rabiah Y, Zuili I, Iordash S, Shany S. Gorging and plasma HDL-cholesterol--the Ramadan model. Eur J Clin Nutr. 1998;52(2):127-30.
15. Khatib FA, Shafagoj YA. Metabolic alterations as a result of Ramadan fasting in non-insulin-dependent diabetes mellitus patients in relation to food intake. Saudi Med J. 2004;25(12):1858-63.
16. Bravis V, Hui E, Salih S, Mehar S, Hassanein M, Devendra D. Ramadan Education and Awareness in Diabetes (READ) programme for Muslims with Type 2 diabetes who fast during Ramadan. Diabet Med. 2010;27(3):327-31.
17. Mafauzy M. Repaglinide versus glibenclamide treatment of Type 2 diabetes during Ramadan fasting. Diabetes Res Clin Pract. 2002;58(1):45-53.
18. Vasan S, Mong PY, Grossman A. Interaction of prion protein with small highly structured RNAs: detection and characterization of PrP-oligomers. Neurochem Res. 2006;31(5):629-37.
19. Khoshniat M, Baradaran B, Najmi F, Shadman Z, Heshmat R. Effect of Ramadan fasting on resting energy expenduture in diabetic patients. diabetes and lipid. 2012;11(3):255-61.
20. Cesur M, Corapcioglu D, Gursoy A, Gonen S, Ozduman M, Emral R, et al. A comparison of glycemic effects of glimepiride, repaglinide, and insulin glargine in type 2 diabetes mellitus during Ramadan fasting. Diabetes Res Clin Pract. 2007;75(2):141-7.
21. Afifi ZE. Daily practices, study performance and health during the Ramadan fast. J R Soc Health. 1997;117(4):231-5.
22. Halberg N, Henriksen M, Soderhamn N, Stallknecht B, Ploug T, Schjerling P, et al. Effect of intermittent fasting and refeeding on insulin action in healthy men. J Appl Physiol. 2005;99(6):2128-36.
23. Anson RM, Guo Z, de Cabo R, Iyun T, Rios M, Hagepanos A, et al. Intermittent fasting dissociates beneficial effects of dietary restriction on glucose metabolism and neuronal resistance to injury from calorie intake. Proc Natl Acad Sci U S A. 2003;100(10):6216-20.
24. Pedersen CR, Hagemann I, Bock T, Buschard K. Intermittent feeding and fasting reduces diabetes incidence in BB rats. Autoimmunity. 1999;30(4):243-50.
25. Scott TG. the effect of Muslim fast of Ramadan on routine laboratory investigation King Abdulaziz Med J. 1981;1:23-35.
26. 26. Temizhan A, Tandogan I, Donderici O, Demirbas B. The effects of Ramadan fasting on blood lipid levels. Am J Med. 2000;109(4):341-2.
27. Larijani B, Zahedi F, Sanjari M, Amini MR, Jalili RB, Adibi H, et al. The effect of Ramadan fasting on fasting serum glucose in healthy adults. Med J Malaysia. 2003;58(5):678-80.
28. Bener A, Yousafzai MT. Effect of Ramadan fasting on diabetes mellitus: a population-based study in Qatar. J Egypt Public Health Assoc. 2014;89(2):47-52.
29. Khogheer Y. Ramadan fasting state of controls. Ann Saudi Med. 1987;7(1):5-6.
30. Azizi F, Rasouli HA. Serum Glucose, Bilirubin, calcium, phosphorus, protein and albumin concentrations during Ramadan. Medical Journal of the Islamic Republic of Iran. 1987;1:38-41.
31. Sariri R, Varasteh A, Erfani A. Alternations in salivary glucose during ramadan fasting. Health 2010;2(7):769-72.
32. Yarahmadi S, Larijani B, Bastanhagh MH, Pajouhi M, Baradar Jalili R, Zahedi F, et al. Metabolic and clinical effects of Ramadan fasting in patients with type II diabetes. J Coll Physicians Surg Pak. 2003;13(6):329-32.
33. Belkhadir J, el Ghomari H, Klocker N, Mikou A, Nasciri M, Sabri M. Muslims with non-insulin dependent diabetes fasting during Ramadan:

treatment with glibenclamide. BMJ. 1993;307(6899):292-5.
34. Katibi IA, Akande AA, Bojuwoye BJ, Okesina AB. Blood sugar control among fasting Muslims with type 2 diabetes mellitus in Ilorin. Niger J Med. 2001;10(3):132-4.
35. Akanji AO, Mojiminiyi OA, Abdella N. Beneficial changes in serum apo A-1 and its ratio to apo B and HDL in stable hyperlipidaemic subjects after Ramadan fasting in Kuwait. Eur J Clin Nutr. 2000;54(6):508-13.
36. Ramadan J, Telahoun G, Al-Zaid NS, Barac-Nieto M. Responses to exercise, fluid, and energy balances during Ramadan in sedentary and active males. Nutrition. 1999;15(10):735-9.
37. Karatoprak C, Yolbas S, Cakirca M, Cinar A, Zorlu M, Kiskac M, et al. The effects of long term fasting in Ramadan on glucose regulation in type 2 diabetes mellitus. European review for medical and pharmacological sciences. 2013;17(18):2512-6.
38. Sahin SB, Ayaz T, Ozyurt N, Ilkkilic K, Kirvar A, Sezgin H. The impact of fasting during Ramadan on the glycemic control of patients with type 2 diabetes mellitus. Exp Clin Endocrinol Diabetes. 2013;121(9):531-4.
39. M'Guil M, Ragala MA, El Guessabi L, Fellat S, Chraibi A, Chabraoui L, et al. Is Ramadan fasting safe in type 2 diabetic patients in view of the lack of significant effect of fasting on clinical and biochemical parameters, blood pressure, and glycemic control? Clin Exp Hypertens. 2008;30(5):339-57.
40. Jamal sS. Effects of ramadan fasting on glycemic control in Type 2 Diabetes Mellites. J Postgrad Med Inst 2008;22(1):17-20.
41. The efficacy and safety of glimepiride in the management of type 2 diabetes in Muslim patients during Ramadan. Diabetes Care. 2005;28(2):421-2.
42. Khaled BM, Bendahmane M, Belbraouet S. Ramadan fasting induces modifications of certain serum components in obese women with type 2 diabetes. Saudi Med J. 2006;27(1):23-6.
43. Bouguerra R, Jabrane J, Maatki C, Ben Salem L, Hamzaoui J, El Kadhi A, et al. [Ramadan fasting in type 2 diabetes mellitus]. Ann Endocrinol (Paris). 2006;67(1):54-9.
44. Al-Shafei AI. Ramadan fasting ameliorates oxidative stress and improves glycemic control and lipid profile in diabetic patients. Eur J Nutr. 2014;53(7):1475-81.
45. Salti I. Efficacy and safety of insulin glargine and glimepiride in subjects with Type 2 diabetes before, during and after the period of fasting in Ramadan. Diabet Med. 2009;26(12):1255-61.
46. Goldstein DE, Little RR, Lorenz RA, Malone JI, Nathan D, Peterson CM. Tests of glycemia in diabetes. Diabetes Care. 1995;18(6):896-909.
47. Azizi F, Siahkolah B. Ramadan fasting and diabetes mellitus. Int J Ramadan Fasting Res. 1998;2:8-17.
48. Friedrich I, Levy Y. [Diabetic ketoacidosis during the Ramadan fast]. Harefuah. 2000;138(1):19-21, 86.
49. Salman H, Abdallah MA, Abanamy MA, al Howasi M. Ramadan fasting in diabetic children in Riyadh. Diabet Med. 1992;9(6):583-4.
50. Al-Khawari M, Al-Ruwayeh A, Al-Doub K, Allgrove J. Adolescents on basal-bolus insulin can fast during Ramadan. Pediatr Diabetes. 2010;11(2):96-100.
51. Ahmadani MY, Riaz M, Fawwad A, Hydrie MZ, Hakeem R, Basit A. Glycaemic trend during Ramadan in fasting diabetic subjects: a study from Pakistan. Pak J Biol Sci. 2008;11(16):2044-7.
52. Benbarka MM, Khalil AB, Beshyah SA, Marjei S, Awad SA. Insulin pump therapy in Moslem patients with type 1 diabetes during Ramadan fasting: an observational report. Diabetes Technol Ther. 2010;12(4):287-90.
53. Hawli YMA, zantout MS, Azar ST. adjusting the basal insulin regimen of patients with type 1 diabetes mellitus receiving insulin pump therapy during the Ramadan fast: a case series in adolescents and adults. Current Therapeutic Research. 2009;70(1):29-34.
54. Al-Arouj M, Assaad-Khalil S, Buse J, Fahdil I, Fahmy M, Hafez S, et al. Recommendations for management of diabetes during Ramadan: update 2010. Diabetes Care. 2010;33(8):1895-902.
55. Beckman JA, Creager MA, Libby P. Diabetes and atherosclerosis: epidemiology, pathophysiology, and management. JAMA. 2002;287(19):2570-81.
56. Akhan G, Kutluhan S, Koyuncuoglu HR. Is there any change of stroke incidence during Ramadan? Acta Neurol Scand. 2000;101(4):259-61.
57. Alghadyan AA. Retinal vein occlusion in Saudi Arabia: possible role of dehydration. Ann Ophthalmol. 1993;25(10):394-8.
58. Schernthaner G, Grimaldi A, Di Mario U, Drzewoski J, Kempler P, Kvapil M, et al. GUIDE study: double-blind comparison of once-daily gliclazide MR and glimepiride in type 2 diabetic patients. Eur J Clin Invest. 2004;34(8):535-42.
59. Guillausseau PJ, Greb W. 24-hour glycemic profile in type 2 diabetic patients treated with gliclazide modified release once daily. Diabetes Metab. 2001;27(2 Pt 1):133-7.
60. Zargar AH, Siraj M, Jawa AA, Hasan M, Mahtab H. Maintenance of glycaemic control with the evening administration of a long acting

sulphonylurea in male type 2 diabetic patients undertaking the Ramadan fast. Int J Clin Pract. 2010;64(8):1090-4.
61. Rendell M. The role of sulphonylureas in the management of type 2 diabetes mellitus. Drugs. 2004;64(12):1339-58.
62. Kinzer CW, Tucker HS. The arylsulfonylurea drugs which produce hypoglycemia: their use in the treatment of diabetes mellitus. Va Med Mon (1918). 1957;84(9):455-80. Epub 1957/09/01.
63. Retnakaran R, Zinman B. Thiazolidinediones and clinical outcomes in type 2 diabetes. Lancet. 2009;373(9681):2088-90.
64. Devendra D, Gohel B, Bravis V, Hui E, Salih S, Mehar S, et al. Vildagliptin therapy and hypoglycaemia in Muslim type 2 diabetes patients during Ramadan. Int J Clin Pract. 2009;63(10):1446-50.
65. Ahren B, Foley JE. The islet enhancer vildagliptin: mechanisms of improved glucose metabolism. Int J Clin Pract Suppl. 2008(159):8-14.
66. Garber AJ, Sharma MD. Update: vildagliptin for the treatment of Type 2 diabetes. Expert Opin Investig Drugs. 2008;17(1):105-13.
67. Ferrannini E, Fonseca V, Zinman B, Matthews D, Ahren B, Byiers S, et al. Fifty-two-week efficacy and safety of vildagliptin vs. glimepiride in patients with type 2 diabetes mellitus inadequately controlled on metformin monotherapy. Diabetes Obes Metab. 2009;11(2):157-66.
68. Malha LP, Taan G, Zantout MS, Azar ST. Glycemic effects of vildagliptin in patients with type 2 diabetes before, during and after the period of fasting in Ramadan. Therapeutic advances in endocrinology and metabolism. 2014;5(1):3-9.
69. Shete A, Shaikh A, Nayeem KJ, Rodrigues L, Ali MS, Shah P, et al. Vildagliptin vs sulfonylurea in Indian Muslim diabetes patients fasting during Ramadan. World journal of diabetes. 2013;4(6):358-64.
70. Brady EM, Davies MJ, Gray LJ, Saeed MA, Smith D, Hanif W, et al. A randomized controlled trial comparing the GLP-1 receptor agonist liraglutide to a sulphonylurea as add on to metformin in patients with established type 2 diabetes during Ramadan: the Treat 4 Ramadan Trial. Diabetes Obes Metab. 2014;16(6):527-36.
71. Mucha GT, Merkel S, Thomas W, Bantle JP. Fasting and insulin glargine in individuals with type 1 diabetes. Diabetes Care. 2004;27(5):1209-10.
72. Kadiri A, Al-Nakhi A, El-Ghazali S, Jabbar A, Al Arouj M, Akram J, et al. Treatment of type 1 diabetes with insulin lispro during Ramadan. Diabetes Metab. 2001;27(4 Pt 1):482-6.
73. Reiter J, Wexler ID, Shehadeh N, Tzur A, Zangen D. Type 1 diabetes and prolonged fasting. Diabet Med. 2007;24(4):436-9.
74. Mattoo V, Milicevic Z, Malone JK, Schwarzenhofer M, Ekangaki A, Levitt LK, et al. A comparison of insulin lispro Mix25 and human insulin 30/70 in the treatment of type 2 diabetes during Ramadan. Diabetes Res Clin Pract. 2003;59(2):137-43.
75. Akram J, De Verga V. Insulin lispro (Lys(B28), Pro(B29) in the treatment of diabetes during the fasting month of Ramadan. Ramadan Study Group. Diabet Med. 1999;16(10):861-6.
76. Hui E, Bravis V, Salih S, Hassanein M, Devendra D. Comparison of Humalog Mix 50 with human insulin Mix 30 in type 2 diabetes patients during Ramadan. Int J Clin Pract. 2010;64(8):1095-9.
77. Hassanein M, Bravis V, Hui E, Devendra D. Ramadan-focused education and awareness in type 2 diabetes. Diabetologia. 2009;52(2):367-8.
78. Benaji B, Mounib N, Roky R, Aadil N, Houti IE, Moussamih S, et al. Diabetes and Ramadan: review of the literature. Diabetes Res Clin Pract. 2006;73(2):117-25.
79. Kassem HS, Zantout MS, Azar ST. Insulin therapy during Ramadan fast for Type 1 diabetes patients. J Endocrinol Invest. 2005;28(9):802-5.
80. Al-Arouj M, Bouguerra R, Buse J, Hafez S, Hassanein M, Ibrahim MA, et al. Recommendations for management of diabetes during Ramadan. Diabetes Care. 2005;28(9):2305-11.
81. Patel P, mirakhur A, karim mAE-M, El-Matty. ANA, Al Ghafri D. type 2 diabetes and its characteristics during Ramadan in Dhahira region. Oman Med J. 2007;22:16-23.
82. Kobeissy A, Zantout MS, Azar ST. Suggested insulin regimens for patients with type 1 diabetes mellitus who wish to fast during the month of Ramadan. Clin Ther. 2008;30(8):1408-15.
83. Beshyah S, Benbarka M, sherif I. practical management of diabetes during Ramadan fast. Libyan J Med. 2007(071008):185-9.
84. Van Cauter EV, Polonsky KS, Blackman JD, Roland D, Sturis J, Byrne MM, et al. Abnormal temporal patterns of glucose tolerance in obesity: relationship to sleep-related growth hormone secretion and circadian cortisol rhythmicity. J Clin Endocrinol Metab. 1994;79(6):1797-805.
85. Jialal I, Joubert SM. Cortisol, glucagon and growth hormone responses to oral glucose in non-insulin-dependent diabetes in the young. S Afr Med J. 1982;62(16):549-52.
86. Drejer J, Hendriksen C, Nielsen LM, Binder C, Hagen C, Kehlet H. Diurnal variations in plasma prolactin, growth hormone, cortisol and blood

glucose in labile diabetes mellitus. Clin Endocrinol (Oxf). 1977;6(1):57-64.
87. Karaagaoglu N, Yucecan S. Some behavioural changes observed among fasting subjects, their nutritional habits and energy expenditure in Ramadan. Int J Food Sci Nutr. 2000;51(2):125-34.
88. Leiper JB, Molla AM. Effects on health of fluid restriction during fasting in Ramadan. Eur J Clin Nutr. 2003;57 Suppl 2:S30-8.
89. Al-Hourani HM, Atoum MF. Body composition, nutrient intake and physical activity patterns in young women during Ramadan. Singapore Med J. 2007;48(10):906-10.
90. Vasan S, Thomas N, Bharani, Ameen M, Abraham S, Job V, et al. A double-blind, randomized, multicenter study evaluating the effects of pioglitazone in fasting Muslim subjects during Ramadan. Int J Diabetes Dev Ctries. 2006;26:70-6.
91. Husain R, Duncan MT, Cheah SH, Ch'ng SL. Effects of fasting in Ramadan on tropical Asiatic Moslems. Br J Nutr. 1987;58(1):41-8.
92. Sulimani RA, Famuyiwa FO, Laajam MA. Diabetes mellitus and Ramadan fasting: the need for a critical appraisal. Diabet Med. 1988;5(6):589-91.
93. Sweileh N, Schnitzler A, Hunter GR, Davis B. Body composition and energy metabolism in resting and exercising muslims during Ramadan fast. J Sports Med Phys Fitness. 1992;32(2):156-63.
94. Frost G, Pirani S. Meal frequency and nutritional intake during Ramadan: a pilot study. Hum Nutr Appl Nutr. 1987;41(1):47-50.
95. Gharbi M, Akrout M, Zouari B. [Food intake during and outside Ramadan]. East Mediterr Health J. 2003;9(1-2):131-40.
96. Gellar L, Nansel TR. High and low glycemic index mixed meals and blood glucose in youth with type 2 diabetes or impaired glucose tolerance. J Pediatr. 2009;154(3):455-8.
97. Nansel TR, Gellar L, McGill A. Effect of varying glycemic index meals on blood glucose control assessed with continuous glucose monitoring in youth with type 1 diabetes on basal-bolus insulin regimens. Diabetes Care. 2008;31(4):695-7.
98. Tabata I, Atomi Y, Miyashita M. Blood glucose concentration dependent ACTH and cortisol responses to prolonged exercise. Clin Physiol. 1984;4(4):299-307.
99. Orth DN, Island DP, Liddle GW. Experimental alteration of the circadian rhythm in plasma cortisol (17-OHCS) concentration in man. J Clin Endocrinol Metab. 1967;27(4):549-55.
100. Sacko M, De Clercq D, Behnke JM, Gilbert FS, Dorny P, Vercruysse J. Comparison of the efficacy of mebendazole, albendazole and pyrantel in treatment of human hookworm infections in the southern region of Mali, West Africa. Trans R Soc Trop Med Hyg. 1999;93(2):195-203.
101. MacGillivray MH, Mills BJ, Voorhess ML. Meal intolerance in type 1 diabetes mellitus: influence of time interval between insulin therapy and meal intake. J Med. 1984;15(5-6):417-35.
102. Shadman Z, Poorsoltan N, Akhoundan M, Larijani B, Soleymanzadeh M, akhgar Zhand C, et al. Ramadan major dietary patterns in Tehran, Iran. Iran Red Crescent Med J. 2014;ahead of print.
103. Rewers M, Dmochowski K, Walczak M. Diurnal variation in carbohydrate tolerance to mixed meal in insulin-dependent diabetic adolescents during continuous intravenous insulin infusion (CIVII). Endokrynol Pol. 1985;36(1):1-7.
104. Diaz VA, Mainous AG, 3rd, Koopman RJ, Geesey ME. Are ethnic differences in insulin sensitivity explained by variation in carbohydrate intake? Diabetologia. 2005;48(7):1264-8.
105. Schafer G, Schenk U, Ritzel U, Ramadori G, Leonhardt U. Comparison of the effects of dried peas with those of potatoes in mixed meals on postprandial glucose and insulin concentrations in patients with type 2 diabetes. Am J Clin Nutr. 2003;78(1):99-103.
106. Alberti H, Boudriga N, Nabli M. Lower attendance rates and higher fasting glucose levels in the month of Ramadan in patients with diabetes in a Muslim country. Diabet Med. 2008;25(5):637-8.
107. Even moderate weight loss can lower your heart risk. Research shows that strength training and aerobic exercise can help sedentary seniors decrease their risk for insulin resistance. Heart Advis. 2009;12(5):3.
108. Yoshida Y, Hashimoto N, Tokuyama Y, Kitagawa H, Takahashi K, Yagui K, et al. Effects of weight loss in obese subjects with normal fasting plasma glucose or impaired glucose tolerance on insulin release and insulin resistance according to a minimal model analysis. Metabolism. 2004;53(9):1095-100.
109. Franz MJ. medical nutrition therapy for diabetes mellitus and hypoglycemia of nondiabetic origin. 12 ed. Mahan LK, Escott-Stump S, editors. Philadelphia: WB Saunders; 2008.
110. Wolever TM, Jenkins DJ, Ocana AM, Rao VA, Collier GR. Second-meal effect: low-glycemic-index foods eaten at dinner improve subsequent breakfast glycemic response. Am J Clin Nutr. 1988;48(4):1041-7.

111. Lamri-Senhadji MY, El Kebir B, Belleville J, Bouchenak M. Assessment of dietary consumption and time-course of changes in serum lipids and lipoproteins before, during and after Ramadan in young Algerian adults. Singapore Med J. 2009;50(3):288-94.
112. Roky R, Houti I, Moussamih S, Qotbi S, Aadil N. Physiological and chronobiological changes during Ramadan intermittent fasting. Ann Nutr Metab. 2004;48(4):296-303.
113. Buonocore CM, Robinson AG. The diagnosis and management of diabetes insipidus during medical emergencies. Endocrinol Metab Clin North Am. 1993;22(2):411-23.
114. Haghdoost AA, Poorranjbar M. The interaction between physical activity and fasting on the serum lipid profile during Ramadan. Singapore Med J. 2009;50(9):897-901.