ORIGINAL ARTICLE

Study of Beneficial Impact on Specific Biomarkers in Type 2 Diabetes During Ramadan Fasting (Unintentional Intermittent Fasting)

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Abstract

Background: Fasting during the holy month of Ramadan is observed by Muslims worldwide as it accounts for one of the five pillars of the religion Islam. We speculate the fasts observed during the month of Ramadan to be unintentional intermittent fasts, which may have health benefits.

Objective: The study was attempted to know the alterations in biomarkers viz. body weight (BW), body mass index (BMI), serum glycated haemoglobin (HbA1c), systolic and diastolic blood pressure (SBP and DBP) due to Ramadan IF on type 2 diabetes (T2D) patients of western India.

Methods: A total 50 patients of T2D were selected for above-mentioned biomarkers assessment immediately before the starting of fast followed by after 45 days.

Results: The present results indicated the beneficial impact on intermittent fasting among patients (baseline versus followed up) by detecting the alterations of above-mentioned biomarkers. In overall results (n=50), the BW (Kg) and BMI (Kg/m^2) values were significantly (P<0.001) decreased in followed-up patients (76.06 ± 15.41 and 27.45 ± 5.06) when compared to baseline value (77.26 ± **15.53** and 27.90 ± **5.**11) while the level of HbA1c (mmol/mol) was also significantly (P<0.05) decreased in followed-up patients (7.62 ± 0.99) when compared to baseline value (7.90 ± 1.24). But no significant changes in the values of SBP and DBP were observed.

Conclusions: In conclusion, this observational study revealed the reduction of body weight, BMI and serum HbA1c levels probably due to IF for the T2D patients during the holy month of Ramadan. Moreover, the IF can be utilized as a therapy along with other pharmacological therapies. It is suggested future research work with other important biomarkers, which can be easier for T2D therapy.

Background

In the Ramadan fasting, healthy adult Muslims must fast from dawn to sunset during the holy month of Ramadan. The people restrict fluid intake, cigarette smoking, and medications. Ramadan fasting is a common form of time-restricted feeding as Intermittent Fasting (IF). It encompasses a major shift from normal eating patterns to exclusive night eating. This religious practice leads to health benefit and causes normal functioning of several biomarkers.[4,9,10,14]

The people restrict to calorific or low energy diet, specific food types, etc.[26] In general, religious fasting depends upon continuous and intermittent and sometimes duration can vary from 1 to 200 days in which researchers observed the positive and negative health impacts .[4,9,10,14,15,21,26,29,31,32] Several research works have been revealed that the religious fasting has beneficial effects on body weight and glycemia, cardiometabolic risk markers, etc.[1,9,17,23,24,27]

Among several intermittent fasting, the Ramadan fasting duration is for 30 days, which revealed beneficial impacts on several biomarkers. In earlier studies it was observed a significant weight reduction due to Ramadan fasting.[28] It was also found a decreasing level of blood sugar, total cholesterol and other inflammatory markers viz. C-reactive protein, interleukin-6 and tumour necrosis factor-α, HbA1c, etc. due to Ramadan fasting.[2,11,17,18,25,35]

Among different glycaemic disorders, type 2 diabetes (T2D) is a well-known chronic disease, which is related to the epidemic of obesity that needs long-term medical therapy to prevent the development of its wide range of micro and macrovascular as well as neuropathic complications. These complications arise from the combination of resistance to insulin action, lower insulin secretion, and excessive or lower glucagon secretion.[12] On the other hand, it was reported by Salti et al.[29] that during the periods of fasting the risk factors in diabetics causing hypoglycaemia (sudden blood sugar lowering) and hyperglycaemia (sudden blood sugar increasing). It was suggested that people with diabetes who require insulin therapy are advised not to fast or who can fast appropriately monitor and adjust insulin delivery with the help of medical practitioner.[27] Another therapy is well-established that patients with T2D treated with biguanides or sulfonylureas who were stable and did not show complication in progressive comorbid pathology[16,29] Khalil et al. mentioned that insulin delivery should be rescheduled as per change in meal timing during fasting in Ramadan. Studies have shown that fasting blood sugar and postprandial (after a meal) blood sugar is decreased

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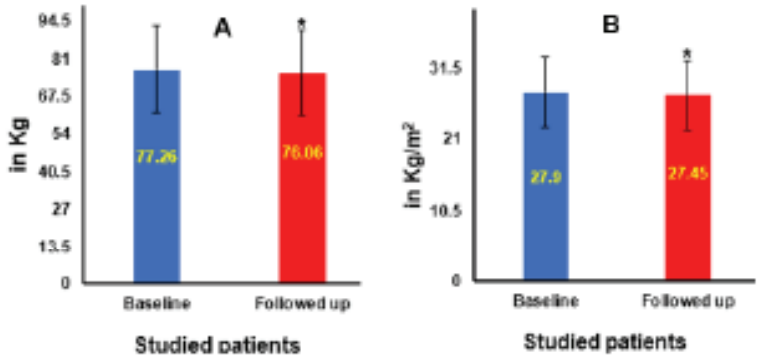

Fig. 1: A = BW (Kg) and B = BMI (Kg/m²) among patients (baseline compared to followed up) of T2D in intermittent fasting during the month of Ramadan (n = 50; *P<0.001)

among T2D patients during Ramadan. Overall glycaemic control appears to be improved during Ramadan.[3,27,33]

It was observed that major researchers have been found effect on individual biomarker or multiple markers such as body weight by using body mass index (BMI as Kg/m²) and glycaemic parameters such as fasting blood sugar (FBS as mg/dl) and/or post prandial sugar (PPS as mg/dl), glycated haemoglobin (HbA1c as mmol/mol), cardiometabolic risk markers as systolic blood pressure (SBP) and diastolic blood pressure (DBP) as mm/Hg, etc.[1,9,17,23,24,27] but comparative study between BMI, HbA1c, SBP and DBP during the religious fasting of baseline versus follow-up in the patients of western India are lacking.

Objectives

The present study was attempted to detect the changes in biomarkers with special reference to body weight (Kg), BMI (Kg/m²), serum HbA1c (mmol/mol), SBP and DBP (mm/Hg) due to intermittent fasting during Ramadan on T2D patients of western India.

Methods

Recruitment of patients

Consecutive patients were enrolled when they visited for pre-Ramadan counselling. A total of 50 patients of age groups (21-80years) were selected of which 25 were males and 25 were females. All the patients were studied in Dr. Kovil's Diabetes care Centre (Preventive Diabetes Centre and Diabetic Foot Clinic, Mumbai, India during the study period of 45 days.

Inclusion criteria

In present work, the patients were enrolled fulfilling the inclusion criteria such as Type 2 DM, age less than 80 years, observing Ramadan Fasts.

Exclusion criteria

In the present study, the exclusion criteria were Chronic kidney disease (CKD), Type 1 DM, pregnant women, patients on multiple dose of insulin and >80 years of age.

Study design

A total 50 patients were recruited for the prospective observational study. All patients were subjected to detailed history followed by general and systemic examination. The patients were categorized into insulin taking group (n=15) and non-insulin taking group (n=35), and sulfonylurea (Su) treated group (n=30) non-sulfonylurea (non-Sus) (DPP4 & Sglt2) treated groups (n=20). All the patients were selected for a baseline parameters body weight (Kg), BMI (Kg/m2), HbA1c (mmol/mol), SBP (mm/Hg) and DBP (mm/Hg) were estimated immediately before the starting of fast followed by after 45 days.

During the therapy as a part of Ramadan regime

All patients kept on background metformin therapy. Patients on insulin for once a day – insulin regime was kept at bedtime or pre-dinner. Patients on insulin twice a day – insulin regime was kept as 2/3rd in the evening and 1/3rd in the morning. Patients on sulfonylurea (Sus) twice a day- the dose was reduced to 1/2 for morning and same (regular) dose for night. Patients on Sus once a day – morning dose shifted to before dinner. Patients on Dpp4 and Sglt2 – dose remained the same.

Biomarkers assessment

All patients were assessed for biomarkers 10 days before observing Ramadan fasts and 1 week after the month of Ramadan as end of study assessment (followed up). The parameter body weight or BW (Kg) was measured using ultrasonic body weight analyser in baseline and followed up patients. A Body Mass Index, or BMI, is a measurement was used to detect height and weight of a patient. The BMI was calculated by using formula as per CDC (26) for baseline as well as followed up patients. The estimation of HbA1c (mmol/mol) was done using ALERE AFFINION™ which is a test based on spectral reflectance. The assay used here is boronate affinity. This parameter was estimated for baseline compared to followed up patients. The blood pressure was measured by using sphygmomanometer to detect SBP (mm/Hg) and DBP (mm/Hg) of studied patients for baseline compared to followed up.

Statistical analysis

The statistical analyses were done by using software (SPSS, version 20). The comparisons were expressed as number of patients and percentage of patients. All the variables were expressed as Mean ± Standard Deviation (M ± SD) and compared across the 2 groups Mann Whitney test and p value is <0.05 was considered as significant.

Results

The present results evaluated the impact on IF among patients (baseline versus followed up) of T2D by detecting the alterations of several biomarkers such as BMI (Kg/m²), serum HbA1c (mmol/mol), SBP and DBP (mm/Hg). In the gender distributions of patients, males 25 nos. (50.0%) and females 25 nos. (50.0%) were observed.

Among 50 patients of T2D, the BW (Kg) was significantly (P<0.001) decreased in the patients of followed up (76.06±15.41) when compared to baseline value (77.26±**15.53**) (Fig 1A). Among 50 patients of T2D, the BMI (Kg/m²) was decreased at a significant level of P<0.001 in the patients of followed up (27.45±5.06) when compared to baseline value (27.90±**5.**11) (Figure 1B). In case of serum biomarker as HbA1c (mmol/mol), in the patients of T2D, the level of HbA1c was significantly (P<0.05) slightly decreased in the patients of followed up (7.62±0.99) when compared to baseline value (7.90±1.24) (Figure 2).

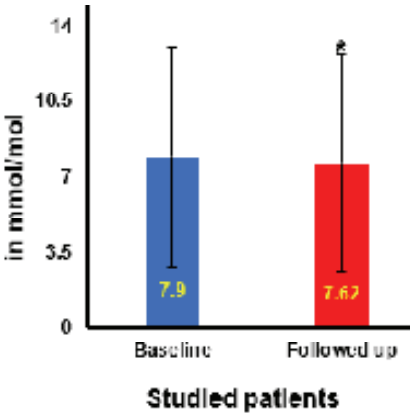

Fig. 2: HbA1c (%) of among patients (baseline compared to followed up) of T2D in intermittent fasting during the month of Ramadan (n = 50; *P<0.05)

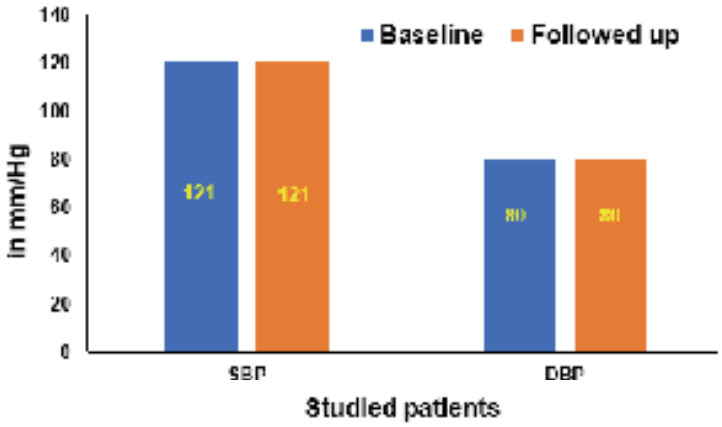

Fig. 3: SBP and DBP (mm/Hg) of among patients (baseline compared to followed up) of T2D in intermittent fasting during the month of Ramadan (n = 50; not significant)

In case of cardiac biomarker as SBP and DBP (mm/Hg), in the patients of T2D, the value of SBP and DBP did not show any change in the patients of followed up (121 and 80) when compared to baseline value (121 and 80) (Figure 3).

Table 1 describes the results for the patients of T2D on insulin therapy group and non-insulin therapy group in IF. For both baseline and followed-up BW (Kg), BMI (Kg/m^2) and the level of HbA1c (mmol/mol) non-insulin therapy values were decreased without significant change when compared to insulin therapy values. The change in weight, BMI and HbA1c values did not observe any significant differences when compared to non -insulin and insulin in baseline and followed up groups.

Table 2 evaluates the results for the patients of T2D as non-sulfonylurea treated group (DPPIV and SGLT2) and Sulfonylurea treated group in IF. In case of baseline and followed-up BW (Kg) as well as BMI (Kg/m^2), non-sus group values were decreased without significant change when compared to Sus group values. The baseline data for the level of HbA1c, it observed a decreasing trend at a significant level of P<0.005 for non-sus group value (7.33±1.27) when compared to Sus group value (8.27±1.09) while in the followed up data for HbA1c level, non-sus group value (7.18±0.85) was also decreased significantly (P<0.008) in comparison with sus group value (7.92±0.97). The change in weight and BMI values were observed a significant change at a level of P<0.001 when compared between non-Sus group and Sus group. Change HbA1c value did not show any significant differences whether the patients were on sus or non-sus drug therapy when compared between non-sus and Sus of baseline and followed up groups separately.

Table 1: Insulin versus non-insulin therapy among patients of T2D in IF (n = 50)

Parameters	Insulin			
	No (n = 35)	Yes (n = 15)	p Value	Significance
	M ± SD	M ± SD		
Baseline Weight (Kg)	74.85±15.00	82.88±15.80	0.088	NS
Follow-up Weight (Kg)	73.85±15.06	81.19±15.46	0.096	NS
Baseline BMI (Kg/m^2)	27.35±5.25	29.17±4.71	0.204	NS
Follow-up BMI (Kg/m^2)	26.96±5.19	28.59±4.69	0.276	NS
Baseline HbA1c (mmol/mol)	7.81±1.35	8.11±0.96	0.275	NS
Follow-up HbA1c (mmol/mol)	7.55±1.06	7.79±0.82	0.340	NS
Change in Weight	-1.00±1.54	-1.69±1.59	0.248	NS
Change in BMI	-0.39±0.55	-0.58±0.53	0.318	NS
Change in HbA1c	-0.25 ± 1.07	-0.32 ± 0.83	0.791	NS

M±SD = Mean ± Standard Deviation; NS = Not Significant

Table 2: Sus versus non-Sus therapy among patients of T2D in IF (n = 50)

Parameters	Sulfonylurea			
	No (n = 20)	Yes (n = 30)	p Value	Significance
	M ± SD	M ± SD		
Baseline Weight (Kg)	75.53±14.50	78.42±16.32	0.586	NS
Follow-up Weight (Kg)	73.40±14.07	77.83±16.23	0.384	NS
Baseline BMI (Kg/m^2)	27.15±4.89	28.40±5.28	0.368	NS
Follow-up BMI (Kg/m^2)	26.38±4.68	28.16±5.25	0.231	NS
Baseline HbA1c (mmol/mol)	7.33±1.27	8.27±1.09	0.005	S
Follow-up HbA1c (mmol/mol)	7.18±0.85	7.92±0.97	0.008	S
Change in Weight	-2.13±1.41	-0.60±1.38	0.001	S
Change in BMI	-0.76±0.49	-0.24±0.48	0.001	S
Change in HbA1c	-0.16 ± 0.95	-0.35 ± 1.04	0.372	NS

M±SD = Mean ± Standard Deviation; S = Significant; NS = Not Significant

Discussion

The present results clearly indicated the beneficial impact on IF of T2D patients. These important biomarkers such as BW, BMI and serum Hb1Ac level were significantly decreased (P<0.001 and P<0.05) in the followed-up patients in comparison with baseline value among the patients of T2D. But, cardiological parameters such as SBP and DBP were not varied between baseline and followed-up patients.

Generally, IF revealed low calorie restriction due to gap of 16:8 hrs diet intake. According to several researchers the IF is closely related for the improvement of cardiovascular and cerebrovascular functions, etc.[20,21,34] It was also known that reduced weight, waist circumference, HbA1c, etc. and risk of T2D due to the IF reported by many researchers.[5,21,30,34] The present

results for BW, similar observations were obtained that in the age groups of 18 to 58 years in which IF in Ramadan found statistically significant weight loss.[17,28,18] Hypertension is a common disease and can easily be known by the occurrence of systolic blood pressure (SBP) in the amount of 140 mmHg and more, or diastolic blood pressure (DBP) of 90 mmHg or more. The present results revealed as such no changes in the cardiovascular markers in intermittent fasting of the T2D patients.[6,34]

The patients who are not using a Sus or insulin, the risk is lower for hypoglycaemia and it is not recommended additional glucose monitoring during fasting. In patients on a sulfonylurea or insulin (either alone or in combination with any other antidiabetic medication), the risk factor of hypoglycaemia is higher.[34,35] The present study observed weight gain in patients on Insulin therapy compared to patients on sulfonylurea and non-sulfonylurea drug regime. The study also observed a significant weight and BMI reduction in patients who were on non-sulfonylurea (DPPIV and SGLT2) drug regime when compared to patients who were on sulfonylurea However, the biomarker serum HbA1c levels were decreased in all the patients of T2D in intermittent fasting, which has an evidence of previous study that reduction of HbA1c level prevent T2D.[34,35]

Conclusion

It is concluded from the present observational study that the overall reduction of body weight, BMI and serum HbA1c levels due to intermittent fasting (IF) during the holy month of Ramadan for the T2D patients is a suitable achievement in Western India. The present study observed significant reduction in weight, BMI and HbA1c values in patients on Non-Sulfonylurea (DPPIV and SGLT2) drug therapy compared to patients on insulin therapy as well as Sulfonylurea therapy where there was non-significant reduction in weight, BMI and Hba1c values. Moreover, the T2D patients are under antidiabetic medicines should be careful about hypoglycaemia in intermittent fasting. It is suggested future research work with other important biomarkers, which can be easier for T2D therapy.

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