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# Effect of Time-Restricted Feeding on Insulin Sensitivity and Oxidative Stress in a Sample of Prediabetes Egyptian Patients

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## Abstract

*Background:* Time-restricted feeding (TRF) is a form of IF, with the daily limiting of food intake (≤10 hours), followed by a daily fast of at least (14 hours). TRF extends the daily fasting period between dinner and breakfast to the following morning; it can be practiced either with or without reducing calorie intake and losing weight.

*Aim of Study:* The current study aimed to assess the effect of time-restricted feeding on anthropometric measurements, vital data, insulin sensitivity, lipid profile, and oxidative stress in the TRF group compared to the habitual feeding group.

*Patients and Methods:* A Case-Control Study on 128 selected participants with prediabetes (HBA1c ≥5.7≤6.4%). Were divided into two groups. Group One time-restricted feeding (TRF) and Group Two (habitual feeding) for 12 weeks.

*Results:* Body weight, waist circumference, HbA1C, PPBG, TG, LDL, and body mass indexreduced in the TRF group in comparison to control group (after 12 weeks) (*p*-value 0.000**). Systolic Bp, diastolic BP, and pulse (*p*-value 0.764, 1.000), (*p*-value 0.769, 0.182) and (*p*-value 0.768, 0.321) respectively. Also HDL (*p*-value 0.519, 0.618) and CRP (*p*-value 0.718, 0.095). Regarding Fasting blood glucose and postprandial insulin after 6 weeks (*p*-value 0.015*). HOMA-IR and Fasting insulin after 12 weeks (*p*-value 0.014*, 0.010* respectively). Body weight, BMI and waist circumference (*p*-value 0.000**), HbA1C (*p* 0.000**, 0.006**), PPBG and TG (*p*-value 0.000**) and LDL (*p*-value 0.000**, 0.002**). Regarding Total cholesterol after 6 weeks (*p*-value 0.000**) and after 12 weeks (*p*-value 0.884). Urinary 8 Epi Prostaglandin F2 Alpha (EPA) after 6 weeks (*p*-value 0.225) and after 12 weeks (*p*-value 0.006**).

*Conclusion:* TRF might be beneficial for reducing anthropometric measurements, insulin sensitivity, lipid profile, and oxidative stress in prediabetes patients.

*Key Words: Time-restricted feeding – Insulin sensitivity – Oxidative stress – Prediabetes.*

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## Introduction

**TIME**-restricted feeding (TRF) is a form of IF, with the daily limiting of food intake (≤10 hours), followed by a daily fast of at least (14 hours). TRF extends the daily fasting period between dinner and breakfast to the following morning; it can be practiced either with or without reducing calorie intake and losing weight **[1].**

TRF reduces body weight, improves glycemic control, lowers insulin levels, prevents hyperlipidemia and improves inflammatory markers in rodents studies using feeding windows of 3-10 hr. report that **[2].**

Metabolic disorders such as elevated fasting hyperglycemia, hypertriglycedimia, hypertension and decreased high density lipoprotein cholesterol are cause of Insulin Resistance (IR). Continued IR can leads to type 2 diabetes (T2D) **[3].**

Insulin resistance, poor glucose tolerance, β-cell dysfunction have all been linked to oxidative stress **[4].**

TRF is a well-known method to lose weight and improve insulin sensitivity and oxidative stress. TRF also improves blood pressure, even without weight loss in human studies **[5].**

Our study aimed to assess the effect of TRF on anthropometric measurements, insulin sensitivity, lipid profile, and oxidative stress in prediabetes patients.

## Patients and Methods

A case Control Study that was performed on 128 selected participants with prediabetes (HBA1c ≥5.7≤6.4%). Age (18-65) years, at the Faculty of Medicine Ain Shams University, Egypt from

(April 2020 - February 2022).This protocol was approved by the Research Ethics Committee of the Faculty of Medicine; Ain Shams University (FWA 000017585). All patientswrote informed consent prior to participation in the study.

All Patients were evaluated for their eligibility in the present study. Inoutpatient clinic of the Internal Medicine and Diabetes Department. Inclusion criteria includes prediabetes.

(HBA1c ≥5.7≤6.4%), overweight, and obese (BMI ≥ 25).

*The patients who were excluded from the study having the following diseases:* Patients with any type of diabetes mellitus (HBA1c >6.4%), Patients with Chronic Heart Failure, Patients with chronic diseases on corticoids (asthma-rheumatoid arthritis-systemic lupus erythematosus... Etc.). Patients with a history of recent infection, Pregnancy or breastfeeding, Severe kidney disease, Severe liver disease, Patients with any diagnosed malignancy, or Treatment with a hypoglycemic agent, insulin sensitizer, or statins. The patients were classified into two groups:

Group One (TRF)consists of 64 prediabetes patients with an 8-hr eating period (12 pm-8 pm same day) and 16 hours of daily fasting from (8 pm the same day 12 pm the next day) for 6 weeks. Then they will return to normal habitual feeding for another 6 weeks. This group will eat 3 small meals during first 6 weeks of study.

- Breakfast (Loaf bread-100gm Bean Meds 0r boiled egg-Or 100gm cheese-cup of tea with ½ spoon sugar).
- Lunch (loaf bread or 100gm rice (5 spoons) - green salad - Piece of chicken (100g) or piece of meat (100g) - one fruit).
- Dinner (Loaf bread-100gm cheese or 2 yogurt-salad - cup of tea with ½ spoon sugar).

Group Two (habitual feeding)as a control group: consists of 64 age and sex-matched prediabetes patients with a 12-hr eating window (from 10 am-10 pm same day) and 12 hrs. Of daily fasting (from 10 pm the same day 10 am the next day) for 12 weeks.

This group will eat the same3 small meals during eating hours In addition to 2 snacks between meals.

- Breakfast (Loaf bread-100gm Bean Meds 0r boiled egg-Or 100gm cheese- cup of tea with ½ spoon sugar).
- Lunch (loaf bread or 100gm rice (5 spoons) - green salad - Piece of chicken (100g) or piece of meat (100g) - one fruit).
- Dinner (loaf bread-100gm cheese or 2 yogurt-salad-cup of tea with ½ spoon sugar).

*Snacks:*

(Half a Loaf of bread- cheese or egg – salad-fruit).

*Aim of 5 meals:*

To assess if there are any glycemic benefits in the habitual feeding groupwithout weight loss.

The patients weretold to continue their physical activity such as (walking-running) For 30 minutes daily during the study period.

The two study groups were followed up for 12 weeks and each patient had 3 visits:

*First visit:*

*Second visit (1.5 months after $^{1st}$ visit):*

Patients were reviewed about previous anthropometric parameters, lab investigations, and their compliance with time-restricted feeding.

*Third visit (1.5 months after $^{2nd}$ visit):*

Patients were reviewed about previous anthropometric parameters and lab investigations.

*Blood sampling:*

In the morning patients attended the outpatient clinic at hospital following overnight fasting (8-12 hours). Patients were permitted to sit for 10 min, and the patient's anthropometric parameters and vital data were assessed. Then (~10 ml) venous blood samples were collected.

*Anthropometric evaluation:*

Anthropometric measurements were evaluated for the selected patient, age (years), weight (kilograms), and height (centimeters), patients were barefoot. While patients were sitting blood pressure measured, following a 15-minute resting period. Body mass index (BMI) was calculated by using the following equation: weight (kg)/square meter of height ($m^2$) [6].

*Biochemical assays:*

Plasma glucose was assessed by the glucose oxidase method. Regarding Serum total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG) and LDL-C was calculated by the Friedewald formula [6]. Plasmainsulin (Fasting,postprandial) were analyzed using Enzyme-Linked Immunosorbent Assay (ELISA) kit. Homeostasis model assessment-insulin resistance (HOMA-IR) was computed according to the following formula: fasting glucose (millimoles/

liter) X fasting insulin (microunits/milliliter)/22.5 **[7]**. The ion exchange method was used to measure HbA1c%, CRP (latex agglutination-ELISA), and urinary 8-Epi Prostaglandin F2 Alpha (EPA) (oxidative stress marker) was analyzed using Enzyme-Linked Immunosorbent Assay (ELISA) kit.

*Adverse effects:*

The study participants were followed up by telephone and through personal interviews during the study period to assess their adherence to the study and report anyparticipant'scomplaints.

*Statistical analyses:*

The collected data were revised, coded, tabulated, and introduced to a PC using a statistical package for social sciences (IBM SPSS 20.0). Data were presented and suitable analysis was done according to the type of data obtained for each parameter. Continuous data were expressed as means ± SD, Independent sample *t*-test was used to assess the statistical significance of the difference of a parametric variable between two independent means of two study groups and Paired sample *t*-test was used to assess the statistical significance of the difference of a parametric variable between two means of one study group before and after the intervention.

The *p*-value was considered significant as the following: *p*-value >0.05: Non-significant (NS), *p*-value <0.05: Significant (S), and *p*-value <0.001: Highly significant (HS).

## Results

At first, 128 patients were included in our study after inclusion and exclusion criteria were set over a three-month.

*Baseline data of the participants in both groups:*

The Time-restricted feeding group (TRF) revealed no difference in anthropometric baseline data in comparison to habitual feeding group. This study included 128 Participants, 102 female, and 26 male. The mean age was (43.50 ± 8.49 vs 43.73 ± 9.90 years) in the TRF group and habitual feeding group, respectively (*p* - 0.886), mean body weight was (89.45±15.62 vs 92.00±16.21kg) *p*-value (0.367). Mean Height was (160.97±5.43 vs 161.58±6.29cm) *p*-value (0.559) and mean BMI was (35.00±6.01 vs 36.08±6.60kg/$m^2$) P-value (0.336). Mean Waist Circumference was (106.53± 11.11 vs 106.67±10.87cm) *p*-value (0.942) (Table 1).

The Time-restricted feeding group (TRF) showed no significant difference in baseline vital data compared to the habitual feeding group regarding mean diastolic Bp (80.86±5.81 vs 79.98±6.69 mmHg) *p*-value (0.431) and mean pulse (82.41±4.91 vs 82.73±5.74 bpm) (*p*-value 0.729), while mean systolic Bp was (120.00±14.80 vs 127.80±15.86 mmHg) with a highly significant difference in habitual feeding group compared to TRF group (*p*-value 0.005**). (Table 1).

Table (1): Mean baseline parameters Comparison in two groups.

| Parameters | Time restricted feeding (n = 64) | Habitual feeding (n = 64) | *p*-value |
|---|---|---|---|
| Age (years) | 43.50 ± 8.49 | 43.73±9.90 | 0.886 |
| Body weight (kg) | 89.45±15.62 | 92.00±16.21 | 0.367 |
| Height (cm) | 160.97±5.43 | 161.58±6.29 | 0.559 |
| BMI (kg/$m^2$) | 35.00±6.01 | 36.08±6.60 | 0.336 |
| Waist circumference(cm) | 106.53±11.11 | 106.67±10.87 | 0.942 |
| Systolic Bp (mmHg) | 120.00±14.80 | 127.80±15.86 | 0.005** |
| Diastolic Bp (mmHg) | 80.86±5.81 | 79.98±6.69 | 0.431 |
| Pulse (bpm) | 82.41±4.91 | 82.73± 5.74 | 0.729 |
| FBG (mg/dl) | 95.34±13.23 | 95.53±11.43 | 0.932 |
| PPBG (mg/dl) | 116.56±15.40 | 117.33±29.48 | 0.854 |
| F insulin (µIU/ml) | 12.87±8.47 | 13.90±8.98 | 0.506 |
| PP insulin (µIU/ml) | 43.85±24.16 | 34.90±26.48 | 0.048* |
| HBA1C (%) | 6.04±0.22 | 6.04±0.23 | 0.905 |
| HOMA-IR | 3.07±2.33 | 3.19±2.29 | 0.765 |
| T cholesterol (mg/dl) | 229.8±31.93 | 212.23±30.52 | 0.002** |
| TG (mg/dl) | 167.42±57.38 | 138.67±52.64 | 0.004** |
| HDL-C (mg/dl) | 44.19±5.92 | 47.55±8.93 | 0.013* |
| LDL-C (mg/dl) | 160.53±28.96 | 139.44±29.68 | 0.000** |
| CRP (mg/dl) | 7.37±8.03 | 8.72±6.63 | 0.304 |
| EPA (ng/L) | 3506.83±1532.08 | 3459.30±1608.52 | 0.864 |

Chi-square test.

Mean HOMA-IR was (3.07±2.33 vs 3.19±2.29) in TRF group and habitual feeding respectively *p*-value (0.765), mean PPBG was (116.56±15.40 vs 117.33±29.48 mg/dl) *p*-value (0.854), mean of F insulin was (12.87±8.47 vs 13.90±8.98µIU/ml) *p*-value (0.506), mean fasting blood glucose was (95.34±13.23 vs 95.53±11.43mg/dl) *p*-value(0.932), mean HBA1C (6.04±0.22 vs6.04±0.23%) *p*-value (0.905). While the Mean of PP insulin was (43.85 ±24.16 vs 34.90±26.48 µIU/ml) which was significantly different (*p*-value 0.048*). (Table 1).

Regarding Mean T cholesterol (229.8±31.93 vs 212.23±30.52mg/dl) there was a highly significant difference (*p*-value 0.002**). Mean TG (167.42±57.38 vs 138.67±52.64mg/dl) which was a highly significant difference (*p*-value 0.004**) mean HDL was (44.19±5.92 vs 47.55±8.93 mg/dl) with a significant difference (*p*-value 0.013*), mean LDL (160.53±28.96 vs 139.44±29.68mg/dl) which was highly significant difference (*p*-value 0.000**) and mean CRP (7.37±8.03 vs 8.72±6.63mg/L) with no significant difference between 2 groups (*p*-value 0.304). (Table 1).

The mean of urinary 8-Epi Prostaglandin F2 Alpha (EPA) was (3506.83±1532.08 vs 3459.30± 1608.52ng/L), with no statistically significant difference between 2 study groups' (*p*-value 0.864) (Table 1).

*Body weight, waist circumference and BMI:*

The mean (body weight) of both groups were significantly changed after 6 weeks from baseline (7.85±1.58 vs 3.22±1.30kg) (*p*-value 0.000**) andafter 12 weeks (4.88 ± 2.24 vs 2.14±2.34kg) (*p*-value 0.000**) (Table 3). Also, the TRF group showed a significant reduction in mean waist circumference by (5.48±1.58) in the TRF group vs (3.16±1.18cm) in the habitual feeding group post-intervention (1) and (2.28±1.23 vs 1.77±2.12cm) post-intervention (2) (*p*-value 0.000**) but reduction was greater in TRF group in comparison to habitual feeding group (Table 2).

BMIdecreased by (3.42±1.48 vs 1.48±1.52kg/$m^2$) post- intervention (1) and (2.28±1.23 vs 1.77 ± 2.12 kg/$m^2$) post- intervention (2) (*p*-value 0.000**) (Table 3).

*Vital data:*

After 12 weeks from baseline, the two study groupsshowed no statistically significant change in mean systolic Bp, diastolic BP, and pulse (*p*-value 0.764, 1.000), (*p*-value 0.769, 0.182) and (*p*-value 0.768, 0.321) respectively. (Tables 2,3).

*Glycemic control and HOMA-IR:*

There was a highly statistically significant change regarding postprandial glucose (PPBG)decreased by (−26, –15%) in TRF group in comparison to habitual feeding group, HbA1cdecreased by [−5 vs –3%], HOMA-IR decreased by [−44 vs -10%] and F insulin level decreased by [−37 vs -4%] (*p*-value 0.000**) after first 6 weeks of study from baseline, changes were higher in TRF group in comparison to habitual feeding group.While a significant change in the mean fasting blood glucose (FBG) decreased by (−7, –5%) and PP insulindecreased by (−30, –21%) (*p*-value 0.015*). After ending the next 6 weeks of study there was highly significantly differences in mean HbA1c, PPBG, PP insulin, and FBG (*p*-value 0.006**, 0.000**, 0.000**, and 0.001**) in TRF group more than habitual group, and a significant difference in HOMA-IR and F insulin (*p*-value 0.014*, 0.010*) in TRF group to habitual feeding group.

We observed increased of F insulin [1%] in the habitual feeding group post-intervention 2 (Tables 2,3).

*Lipid profile:*

After intervention for first 6 weeks of study, the TRF group show highly significant differences in Total Cholesterol, triglycerides, and LDL-cholesterol (*p*-value 0.000**) in comparison to habitual feeding group, and no significant difference in HDL-Cholesterol levels between the two groups (*p*-value 0.519). While after ending the next 6 weeks of study there was highly statistically significant differences between TG and LDL-C (*p*-value 0.000**, 0.002*) in TRF group to habitual feeding group, and no significant difference in TC and HDL-C levels in both groups (*p*-value 0.884, 0.618) (Table 2).

Our study reported that the TRF group had a greater reduction in T-cholesterol by [−10, –8 vs –6, -8 %] (*p*=0.000**, 0.884) compared to the habitual feeding group (Table 3).

The present study results revealed a reduction in triglyceride levels for both groups but a more significant reduction in the TRF group in comparison to the habitual feeding group [−18, –22 vs –4, –5%] (*p*-value 0.000**).

Our results revealed that the TRF group had a greater decrease in LDL cholesterol compared to the habitual feeding group [−13, –10 vs –6, –6%] (*p*=0.000**, 0.002*) post intervention (1, 2).

Regarding HDL-cholesterol there were no significant changes between the two groups, HDL levels decreased by (−2, –5%) in the TRF group vs (–3, –4%) in the habitual feeding group (*p*-value 0.519, 0.618), (Table 3).

Table (2): Changes in mean variables between two study groups from baselineand post intervention (1, 2).

| Variables | Mean post intervention (1) from baseline (group1 vs group 2) | 1st (6) weeks *p*-value | Mean post intervention (2) from baseline (group1 vs group 2) | 2nd (6) weeks *p*-value |
|---|---|---|---|---|
| Body weight(kg) | 7.58±1.58 vs 3.22±1.30 | 0.000** | 4.88±2.24 vs 2.14±2.34 | 0.000** |
| BMI (kg/m$^2$) | 3.42±1.48 vs 1.48±1.52 | 0.000** | 2.28±1.23 vs 1.77±2.12 | 0.000** |
| Waist circumference (cm) | 5.48±1.58 vs 3.16±1.18 | 0.000** | 2.80±2.76 vs 2.23±1.69 | 0.000** |
| Systolic Bp (mmHg) | 2.50±4.80 vs 2.80±6.27 | 0.764 | -.31±2.50 vs -.31±2.50 | 1.000 |
| Diastolic Bp (mmHg) | .78±2.58 vs .61±3.71 | 0.769 | .00±.00 vs -.23±1.39 | 0.182 |
| Pulse (bpm) | .78±2.58 vs .92±2.80 | 0.768 | -.09±.75 vs .00±.00 | 0.321 |
| FBG (mg/dl) | 7.08±6.15 vs 5.11±1.67 | 0.015* | 13.45±10.66 vs 7.31±10.45 | 0.001** |
| PPBG (mg/dl) | 29.70±16.59 vs 18.20±9.47 | 0.000** | 13.61±16.57 vs 2.88±11.21 | 0.000** |
| F insulin (µIU/ml) | 4.87±6.16 vs. 49±3.62 | 0.000** | 1.98±5.84 vs -.28±3.81 | 0.010* |
| PP insulin (µIU/ml) | 12.43±16.37 vs 6.98±6.42 | 0.015* | 17.62±18.79 vs 5.66 ± 6.09 | 0.000** |
| HBA1C (%) | .35±.17 vs. 20±.08 | 0.000** | .02±.32 vs .15±.19 | 0.006** |
| HOMA-IR | 1.33±1.78 vs. 32±.94 | 0.000** | .88±1.72 vs .26±1.05 | 0.014* |
| Total cholesterol (mg/dl) | 21.52±17.09 vs 12.80±7.32 | 0.000** | 17.34±19.17 vs 16.95±9.58 | 0.0884 |
| TG (mg/dl) | 30.14±19.65 vs 4.98±4.94 | 0.000** | 37.33±35.68 vs 7.03±9.29 | 0.000** |
| HDL-C (mg/dl) | 1.05±5.50 vs 1.50±1.35 | 0.519 | 2.39±5.25 vs 2.00±3.26 | 0.618 |
| LDL-C (mg/dl) | 20.54±16.05 vs 7.71±10.10 | 0.000** | 17.03±19.44 vs 8.21±11.30 | 0.002* |
| CRP (mg/dl) | .64±2.55 vs. 52±.88 | 0.718 | .26±2.73 vs .49±1.68 | 0.095 |
| EPA (ng/L) | 1062.48±553.87 vs 954.19±445.67 | 0.225 | 525.34±395.98 vs 353.78±286.93 | 0.006** |

Chi-square test.

Table (3): Differences between mean baseline and post intervention (1, 2) data in both groups.

| Variables (mean) | Baseline (TRF vs habitual) | 1st intervention (1st 6 weeks) | 2nd intervention (2nd 6 weeks) | Baseline-1st intervention % | Baseline-2nd intervention% |
|---|---|---|---|---|---|
| Weight (kg) | 89.45 vs 92.00 | 81.88 vs 88.78 | 84.57 vs 89.86 | ↓–8 vs 4 | ↓–5 vs 3 |
| BMI (kg/m$^2$) | 35.00 vs 36.08 | 31.58 vs 34.60 | 32.72 vs 34.31 | ↓–10 vs 3 | ↓–8 vs 3 |
| Waist Circumference (cm) | 106.53 vs 106.67 | 101.05 vs 103.52 | 103.73 vs 104.44 | ↓–5 vs 3 | ↓–3 vs 2 |
| Systolic BP (mmHg) | 120.00 vs 127.80 | 117.50 vs 125.00 | 120.31 vs 128.11 | ↓–2 vs 2 | 0 |
| Diastolic BP (mmHg) | 80.86 vs 79.98 | 80.08 vs 79.37 | 80.86 vs 80.22 | ↓–0.9 vs 0 | 0 |
| Pulse (bpm) | 82.41 vs 82.73 | 81.62 vs 81.81 | 82.50 vs 82.73 | ↓–1 vs 1 | 0 |
| HOMA-IR | 3.07 vs 3.19 | 1.74 vs 2.88 | 2.19 vs 2.93 | ↓–44vs 10 | ↓–30 vs 10 |
| EPA (ng/L) | 3506.83 vs 3459.30 | 2444.34 vs 2505.11 | 2981.48 vs 3105.52 | ↓–30 vs 27 | ↓–15 vs 10 |
| HbA1C (%) | 6.04 vs 6.04 | 5.69 vs 5.84 | 6.01 vs 5.89 | ↓–5 vs 3 | 0 |
| FBG (mg/dl) | 95.34 vs 95.53 | 88.27 vs 90.42 | 81.89 vs 88.22 | ↓–7 vs 5 | ↓ |
| PPBG (mg/dl) | 116.56 vs 117.33 | 86.86 vs 99.12 | 102.95 vs 114.45 | ↓–26 vs 15 | ↓ ! |
| F insulin (Uiu/ml) | 12.87 vs 13.90 | 8.00 vs 13.41 | 10.89 vs 14.19 | ↓–37 vs 4 | ↓ ↓–1 |
| Pp insulin (Uiu/ml) | 43.85 vs 34.90 | 31.42 vs 27.92 | 26.23 vs 29.24 | ↓–30 vs 21 | ↓ 5 |
| TG (mg/dl) | 167.42 vs 138.67 | 137.28 vs 133.69 | 130.09 vs 131.64 | ↓–18 vs 4 | ↓ |
| HDL (mg/dl) | 44.19 vs 47.55 | 43.14 vs 46.05 | 41.80 vs 45.55 | ↓–2 vs 3 | ↓ |
| LDL (mg/dl) | 160.53 vs 139.44 | 139.98 vs 131.73 | 143.50 vs 131.23 | ↓–13 vs 6 | ↓ |
| CRP (mg/dl) | 7.37 vs 8.72 | 6.73 vs 8.20 | 7.11 vs 7.78 | ↓–11 vs 5 | 0 vs 10 |

*Inflammatory and oxidative stress markers:*

Regarding CRP levels there was No significant difference between the two study groups after 12 weeks of study (*p*-value 0.718, 0.095) the decrease in CRP levels was higher in TRF group comparing to habitual feeding group after first 6 weeks of study [−11, 0 vs –5, 10%] while CRP levels reduced more in habitual feeding group to TRF group after ending the study.

Regarding EPA there was no significant difference between 2 study groups after first six weeks of study (*p*-value 0.225). While a highly significant difference after ending the study (*p*-value 0.006**) Reduction in EPA levels was higher in TRF group to habitual feeding group post intervention (1,2) (Table 2,3).

The present study showed that levels of 8 Epi Prostaglandin F2 Alpha (EPA) reductions was higher in the TRF group compared to the habitual feeding group. EPA levels decreased by [−30, –15 vs –27, –10 %] (*p*-value 0.225, 0.006**) from baseline (Table 3).

## *Discussion*

In our study,the effect of TRF on anthropometric measurements, vital data, indicators of glycemic control, insulin resistance, Inflammatory, oxidative stress markers, and lipid profile in prediabetes patients were analyzed.

The study results showed that the TRF group in prediabetes patients significantly improved anthropometric measurements, insulin sensitivity, lipid profile, and oxidative stress.

Our results showed a reduction in mean body weight in the TRF group compared to the habitual feeding group post- intervention ***[1]*** Which is Consistent with the results of some other research ***[8,9,10]***.

On the contrary, Lowe et al., reported no weight loss, with no significantly difference in control group ***[11]***.

Also, the TRF group showed a significant reduction in mean waist circumference in the TRF group vsthe habitual feeding group post- intervention ***[1]*** and post- intervention ***[2]***.

Our results in consistence with (Kesztyus et al.) They found adecrease in mean waist circumference in 40 Participants (−5.3±3.1cm) (*p*<0.001) ***[12]***.

And Cienfuegos S. et al., found that four-six-hoursTRF in 58 participants were highly statistically significant on BMI in TRF and control groups ***[13]***.

Our results showed non-significant reductions in mean systolic BP,diastolic BP and pulsein TRF group to habitual feeding groupafter 12 weeks from intervention.

Michael J. Wilkinson. Showed that TRF has a significant decrease in systolic and diastolic blood pressure [−4% −8%] respectively ***[14]*** which is Inconsistency with our results.

Our study results revealed a highly HOMA-IR significant reduction in the TRF group in comparison to habitual feeding study group [−44, 10%] post intervention 1 and [−30, 10%] post intervention 2. Jamshed et al., ***[15]*** supported our results, which found a significant HOMA-IR reduction (*p*<0.0001).

The studyresults showed a statistically significant decrease in Fasting blood glucose in both groups but more significant in the TRF group. PPBG and HbA1c decreased In the TRF group compared to the habitual feeding group. Which are in consistent with Antoni RRT et al. ***[16]*** who found decreased fasting plasma glucose concentration. Compared with controls who maintained habitual feeding patterns.

HbA1c reduced in the time-restricted feeding group compared to the control group over 12 weeks (*p*< 0.001) according to Che, T. et al. ***[17]*** which was consistent with our study.

Our results inconsistency with Carlson et al. ***[18]*** that found TRE with late eating was shown to increase fasting glucose. And TRF has no effect or worsened PP glucose levels.

The present study showed improvement in insulin levels in both groups but more in the TRF group than the habitual feeding group. F insulin decreased by (−37, –22%) in the TRF group vs (–4%) in the habitual feeding group while pp insulin decreased by [−30, –40 vs –21, –16%] in the TRF group in comparison to habitual feeding group.

We observed increased of F insulin [1%] in the habitual feeding group post-intervention 2.

Our results in consistent with Sutton et al., that found 5-weeks, randomizede TRF in prediabetes men, isocaloric and eucaloric controlled feeding reduced fasting insulin by (3.4±1.6mU/l) (*p*=0.05) and PP insulin levels (*p*≤0.01) ***[19]***.

Importantly, our results showed important improvement in lipid profile (TG, T-cholesterol, and LDL-cholesterol) which are cardiovascular disease risk markers.

Our study reported that the TRF group had a greater reduction in T-cholesterol.

A previous study by Wilkinson et al., ***[20]*** showed that 10 hrs. TRF decreased plasma cholesterol which was consistent with our study.

Gabel K et al. [21] found that eight hours TRF did notaffect plasma cholesterol levels between the 2 groups.

The present study results revealed a reduction in triglyceride levels for both groups but a more significant reduction in the TRF group in comparison to the habitual feeding group [−18, –22 vs –4, –5%].

Our results revealed that the TRF group had a greater decrease in LDL cholesterol compared to the habitual feeding group [−13, –10 vs –6, –6%].

Our results are In agreement with (Wilkinson et al., 2019), which found that Ten-hour TRF in 35 participants caused significant reductions in low-density lipoprotein cholesterol (LDL-C) (−11.94±19.01mg/dL (−11%), $p$=0.016).

Our results were incompatible with (Gabel K et al). Which found that eight hours of timerbestricted feeding did notaffect plasma LDL cholesterol compared to a matched historical control group.

Regarding HDL-cholesterol there were no significant changes between the two groups, HDL levels decreased by (−2, –5%) in the TRF group vs (–3, –4%) in the habitual feeding group.

Our results showed that TRF in group (1) and habitual feeding in group (2) had no significant effect on CRP levels, but reduction in CRP levels was higher in TRF group.

Our results were supported by (Sutton et al., 2018 and Wilkinson et al., 2020) who found that CRP concentrations did not change after 5–12 weeks of TRE.

Oxidative stress is defined as the increased generation of free radicals and impaired antioxidant defense it plays a leading role in the progression of DM and its complication [23].

Regarding oxidative stress, 8 Epi Prostaglandin F2 Alpha (EPA) is widely used as an oxidative stress biomarker [24].

8-iso-prostaglandin-F2α (8-iso-PGF2α), as one of the stable products of non-cyclooxygenase peroxidation of arachidonic acid, has proved to be the most available and reliable marker of lipid peroxidation in vivo and it appears more sensitive and specific than other markers of oxidative stress [25].

The present study showed that levels of 8 Epi Prostaglandin F2 Alpha (EPA) reduction was higher in the TRF group compared to the habitual feeding group. EPA levels decreased by [−30, –15 vs –27, –10%].

Our results were supported by (Cienfuegos et al., 2020) who measured oxidative stress markers and found significant decreases in oxidative markers after 5-8 weeks of TRF.

Several limitations of our research should be noted. Being a case-control study therefore causality could not be certainly determined. It is necessary to carry out a study with prospective nature in the future. Also, the time of intervention was short, and further follow-up is needed to observe the long-term results of TRF.

*Conclusion:*

TRF is helpful in reduction anthropometric measurements, improving glycemic control and insulin resistance in prediabetes. Also, TRF provides primary prevention of cardiovascular events in prediabetes by improving lipid profiles and improve oxidative stress markers.

*Availability of data:*

The data of this study finding are available upon request.

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# تأثير التغذية المقيدة زمنياً على حساسية الأنسولين والتأكسد فى عينه من المرضى المصريين الذين يعانون من خطورة الاصابه بداء السكرى

الهدف من الدراسه: تهدف الدراسة الحالية إلى تقييم تأثير التغذية المقيدة زمنيا على قياسات الجسم البشرى، البيانات الحيوية، حساسية الأنسولين، ملف الدهون والإجهاد التأكسدى فى مجموعة تطبق التغذيه المقيده زمنياً مقارنة بمجموعة تطبق التغذية المعتادة.

المرضى والطرق: تم إجراء دراسة الحالات والشواهد على ١٢٨ مشاركًا مختارًا يعانون من خطورة الاصابه بداء السكرى تتراوح نسبة السكر التراكمى لديهم بين (٥,٧-٦,٤ ٪) . تم تقسيمهم إلى مجموعتين .المجموعه الاولى تطبق التغذيه المقيده زمنيا لمدة ٦ اسابيع والمجموعه الثانيه تطبق نظام التغذيه المعتاده لمدة ١٢ اسبوع.

النتائج: انخفض وزن الجسم، محيط الخصر، ونسبة السكر التراكمى بالدم، السكر الفاطر، الدهون الثلاثيه، الكوليسترول منخفض الكثافه ومؤشر كتلة الجسم فى مجموعة التغذية المقيدة زمنياً مقارنة بالمجموعة الضابطة (بعد ١٢ أسبوعًا) من بداية الدراسه.

بعد ١٢ اسبوع من تطبيق الدراسه للمجموعتين لم يكن هناك اختلاف هام فى النتائج بين المجموعتين فيما يتعلق بضغط الدم الانقباضى، ضغط الدم الانبساطى والنبض. ايضاً نتائج البروتين الدهنى عالى الكثافه وبروتين سى التفاعلى لم يكن هناك اختلاف هام بين المجموعتين، بينما ظهر اختلاف هام فى النتائج بين المجموعتين فى مستوى السكر الصائم بالدم ونسبة الانسولين الفاطر بعد ٦ اسابيع من بداية الدراسه حيث انخفض اكثر في المجموعه الاولى مقارنة بالمجموعه الثانيه. فيما يتعلق بنتائج مقاومة الانسولين ونسبة الانسولين الصائم بالدم بعد ١٢ اسبوع من الدراسه كان هناك اختلاف هام بين المجموعتين وبمقارنة النتائج بين المجموعتين بعد ١٢ اسبوع من الدراسه كان هناك اختلاف واضح فيما يتعلق بوزن الجسم، مؤشر كتلة الجسم، محيط الخصر، السكر التراكمى، السكر الفاطر والبروتين الدهنى منخفض الكثافه.

فيما يتعلق بالكوليسترول الكلى، كان هناك اختلاف هام في النتائج بين المجموعتين بعد ٦ اسابيع من الدراسه حيث انخفضت في المجموعه الاولي مقارنة بالمجموعه الثانيه ولكن لم يكن هناك اختلاف فى النتائج بعد انتهاء الدراسه بين المجموعتين.

وبقياس نسبة ايزوبروستان الفا في البول (مؤشر حيوى للاجهاد التأكسدى) بعد ٦ اسابيع من الدراسه لم يكن هناك اختلاف هام فى النتائج بين المجموعتين. ولكن ظهر اختلاف هام فى نتائج ايزوبروستان الفا فى البول بعد ١٢ اسبوع فى المجموعه الاولى مقارنة بالمجموعه الثانيه.

الاستنتاج: تعتبر التغذيه المقيده زمنياً مفيده في تقليل قياسات الجسم (الوزن – مؤشر كتلة الجسم – محيط الخصر)، تحسن حساسية الانسولين، تحسن مستوى الكوليسترول والدهون بالدم ومفيده فى تحسن الاجهاد التأكسدى فى المرضى الذين يعانون من خطورة الاصابه بداء السكرى.