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Effects of Short-Term (20-Day) Alternate-Day Modified Fasting and Time-Restricted Feeding on Fasting Glucose and IGF-1 in Obese Young Women

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Abstract: Background: Obesity is a metabolic condition that may impair insulin sensitivity and disrupt glucose homeostasis. Since insulin and glucose affect insulin-like growth factor-1 (IGF-1), disruptions in this axis may elevate the risk of chronic diseases. Intermittent fasting (IF) modulates metabolic parameters, but the impacts on glucose regulation and IGF-1 remain underexplored. This study aimed to assess the short-term effects of two IF types, time-restricted feeding (TRF) and alternate-day modified fasting (ADMF), on fasting blood glucose (FBG) and IGF-1 in obese young women. **Methods:** A quasi-experimental pre-test post-test control group design was conducted over 20 days. The 31 subjects were allocated into: ADMF (n=10), TRF (n =11), and control (n=10). After excluding dropouts and outliers, the final sample consisted of 22 subjects (ADMF=7, TRF=8, Control=7). FBG and IGF-1 serum were measured pre- and post-intervention. **Results:** The FBG post-intervention significantly increased in TRF (p=0.001) and ADMF (p=0.036) groups, but not in controls. Only the TRF group showed a significant reduction in IGF-1 levels (p<0.001). Nevertheless, the ADMF group exhibited substantial decreases in body weight (p=0.047) and visceral fat (p=0.017). **Conclusions**: A 20-day IF in obese young women induced distinct metabolic effects: TRF lowered IGF-1, ADMF reduced adiposity, and both regimens increased FBG. These findings suggest that early changes in glucose regulation are highly dependent on the specific dietary regimen used. Specifically, TRF predominantly influences endocrine regulation (IGF-1 axis), while ADMF favors adiposity reduction. The concurrent rise in FBG may reflect a transient shift in glucose homeostasis during the early stages of fasting.

Keywords: intermittent fasting; TRF; ADMF; IGF-1; FBG; obesity; prediabetes

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1. Introduction

Obesity has become a primary global health concern. In 2022, 890 million adults were living with obesity, along with 160 million adolescents aged 5–19. The prevalence is consistently higher in women than in men [1,2]. Elevated body mass index (BMI) is associated with increased risk and earlier onset of various non-communicable diseases [3]. Obesity is closely related to the emergence of insulin resistance, a key feature of prediabetes and type 2 diabetes mellitus (T2DM) [4]. It is estimated that up to 70% of individuals with prediabetes will eventually progress to T2DM without appropriate intervention [5]. Notably, recent epidemiological trends indicate a growing burden of prediabetes among young adults, driven by sedentary lifestyles, poor dietary habits, and increased adiposity [6] . In this population, early glycemic deterioration is often overlooked due to the absence of overt symptoms, yet it is during this window that preventive interventions are most effective [7].

In obesity, elevated free fatty acids and pro-inflammatory cytokines induce chronic, low-grade inflammation, which impairs insulin sensitivity in skeletal muscle, hepatic tissue, and adipose tissue. This progressive deterioration leads to insulin resistance accompanied by hyperglycemia and compensatory hyperinsulinemia, both of which are hallmark features of type 2 diabetes [8]. In obese individuals, chronic hyperinsulinemia and hypernutrition may promote elevated insulin growth factor-1 (IGF-1) production [9,10]. The IGF-1 plays important anabolic roles in growth and metabolism; persistently elevated levels have been associated with increased risk of carcinogenesis and cellular senescence escape [11,12]. Thus, obesity and diabetes are linked to a higher possibility of certain types of cancer and other age-related diseases [13,14]. Since the energy surplus due to an imbalance between caloric consumption and energy expenditure facilitates the onset of obesity, modifying dietary patterns remains a key component in its overall nutritional management [8].

Intermittent fasting (IF) is a meal pattern modification that alternates periods of eating and fasting [15]. This method has shown benefits in obesity and diabetes by lowering body weight, enhancing glycemic indicators, and reducing growth factors [16–18]. The two most widely studied IF methods are time-restricted feeding (TRF), which limits daily calorie consumption to a specific timeframe (usually 6–8 hours), and alternate-day modified fasting (ADMF), where individuals alternate between fasting days with around 25% of their caloric intake and unrestricted eating days [19]. Intermittent fasting (IF) influences fasting blood glucose (FBG) and IGF-1 levels through multiple mechanisms. TRF improves glycemic control by aligning food intake with the circadian rhythm, enhancing glucose tolerance, insulin sensitivity, and promoting a shift toward fat oxidation [20–22]. In contrast, prolonged fasting in ADMF induces a more robust metabolic switch, improving glucose and lipid profiles, reducing pro-inflammatory cytokines, and promoting greater fat loss without compromising lean mass [15,23–25]. However, the effects of IF in glycemic control remain inconsistent across different populations, as they are influenced by age, health status, and fasting duration [26–28]. In short-term IF, the glucose homeostasis may be affected by insulin and counter-regulatory hormones dynamics [29–33]. Regarding IGF-1, intermittent fasting may lower its levels by increasing IGFBP-1, which consequently reduces IGF-1 bioactivity and bioavailability. Moreover, the downregulation of hepatic GH-signalling components, such as GHR and STAT5, during fasting may induce GH resistance and impair IGF-1 synthesis [26,34–36]. Moreover, a decrease in insulin availability during fasting may downregulate IGF-1 production, which then impacts glucose regulation due to their shared metabolic pathways. Nevertheless, the precise mechanisms underlying increased FBG and decreased IGF-1 during TRF and ADMF require further investigation.

The present study aimed to assess the short-term effects of two intermittent fasting (IF) regimens—time-restricted feeding (TRF) and alternate-day modified fasting (ADMF)—on FBG and IGF-1 levels. Given the limited evidence on short-term endocrine responses to these fasting regimens, we formulated an exploratory hypothesis that both interventions would elicit changes in fasting glucose and IGF-1, without specifying a directional difference between the two interventions. Furthermore, this study specifically focused on a metabolically vulnerable population, namely young women with obesity, as most existing IF studies have been conducted in heterogeneous age groups or individuals with chronic metabolic conditions [30,32,37–39]. Investigating this population is of particular importance, given that women exhibit the highest global prevalence of obesity and that early intervention during this stage may prevent progression to prediabetes, type 2 diabetes mellitus (T2DM), and other obesity-related chronic diseases [2,7].

2. Materials and Methods

2.1 Study Design

A pretest–posttest control group design was employed in this quasi-experimental investigation. Initially, thirty-three women were assessed for eligibility. Two subjects were excluded because they did not meet the inclusion criteria, leaving thirty-one eligible subjects. The thirty-one subjects, based on their scheduling feasibility, were allocated equally into three groups: Control, TRF, and ADMF. Over the 20-day intervention period, subject retention varied across groups. No subjects were lost to follow-up in the Control or TRF groups, whereas one subject was lost in the ADMF group. In terms of discontinuations, none occurred in the Control or ADMF groups, but two subjects discontinued in the TRF group. Following the intervention, several data points were excluded as outliers, specifically three in the Control group, two in the ADMF group, and one in the TRF group. A final sample of 22 subjects was included in the analysis (Control, n = 7; TRF, n = 8; ADMF, n = 7). Figure 1 illustrates the research workflow.

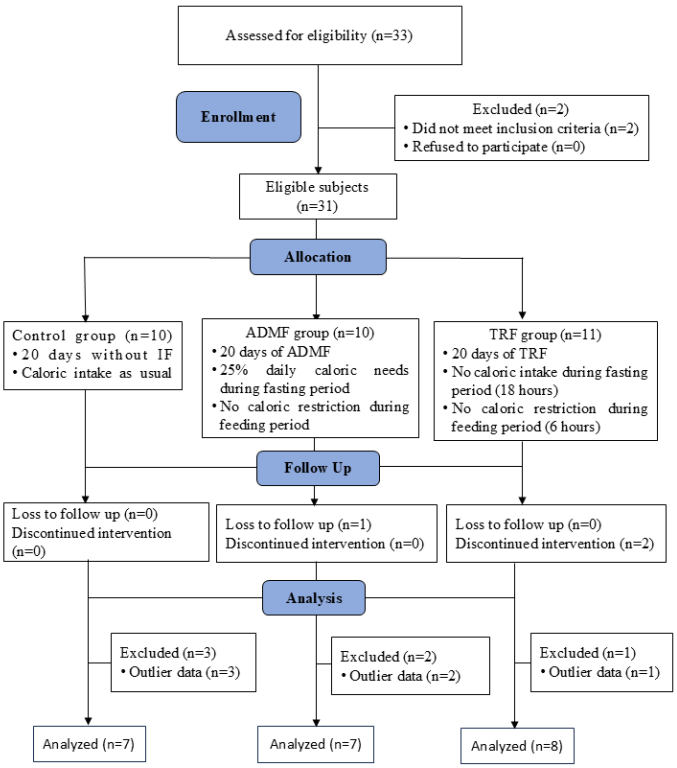

Figure 1. Research workflow. ADMF, Alternate Day Modified Fasting; TRF, Time-Restricted Feeding.

Outcome assessments included FBG and serum IGF-1, which were measured at baseline (pretest) and on day 20 (posttest). Anthropometric and body-composition variables were collected at the same time points to provide complementary information on metabolic and physiological changes. Subjects were excluded from the study if they were absent during the screening, pre-test, or post-test sessions, or if they developed a severe illness that prevented adherence to at least 80% of the prescribed fasting intervention. Baseline (pre-test) data were collected before the initiation of the fasting protocol, while post-test data were obtained one day after the final fasting session. All assessments at both time points were conducted directly by the research team to maintain consistency and ensure measurement accuracy. This research was approved by the Faculty of Medicine Ethics Committee, Airlangga University (No. 36/EC/KEPK/FKUA/2024). All subjects granted informed consent before data collection commenced.

2.2. Subject Characteristics

This study involved female young adults aged 18–25 years who met the inclusion criteria and provided informed consent before enrollment. The inclusion criteria were: (1) BMI ≥ 25 kg/m² based on the WHO Asia–Pacific classification; (2) body fat percentage > 30%; (3) nondiabetic status, defined as fasting blood glucose (FBG) < 126 mg/dL; (4) normal blood pressure (systolic < 120 mmHg and diastolic < 80 mmHg); and (5) haemoglobin (Hb) ≥ 12 g/dL.

Participants were excluded if they: (1) were diagnosed with chronic conditions such as gastritis, diabetes mellitus, hypertension, cardiovascular or endocrine disease; (2) had a history of malignancy or smoking; (3) reported regular intake of medications or supplements known to affect glucose metabolism, lipid metabolism, appetite, or hormonal balance; or (4) consumed alcohol, as all subjects were required to maintain complete abstinence.

Dropout criteria included: (1) failure to follow the researcher's instructions or absence during the screening, pre-test, or post-test assessments; (2) development of a severe illness during the study that prevented continuation of the intervention; or (3) completion of less than 80% of the total prescribed fasting days during the intervention period.

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2.3 Intermittent Fasting Protocol

This study employed two IF regimens: time-restricted feeding (TRF) and alternate-day modified fasting (ADMF). TRF followed an 18:6 schedule, in which subjects fasted for 18 hours and consumed their daily caloric intake within the remaining 6-hour eating periods [40,41]. This TRF group adhered to an 18-hour daily fast, starting at 08:00 p.m. and ending at 02:00 p.m. the following day. During the eating period, from 02:00 p.m. to 08:00 p.m., subjects could consume food ad libitum.

The ADMF group followed a 24-hour fasting protocol on alternating days, receiving less than 25% of their daily caloric requirements, as calculated using the Harris-Benedict formula [42–44]. A designated catering service provided meals on fasting days. The menu composition, food types, and preparation methods were standardized across participants to maintain consistency in dietary quality. Only the portion sizes differed, as they were individually adjusted to ensure that total caloric intake on fasting days did not exceed 25% of each participant's calculated daily energy requirement. On non-fasting days, the subjects had unrestricted access to food. Both of them are allowed to have plain water in the fasting period. The control group continued their usual eating patterns. Before the study began, they received standardized guidance to ensure accurate and consistent recording. During the intervention, subjects were instructed to document their daily food intake using an estimated food record method. Dietary logs, including portion size, timing, and

food type, were monitored by the research team through daily submissions in both individual and group-specific WhatsApp channels to enhance adherence tracking.

2.4 Outcomes Measurement

2.4.1. Body Composition Assessment

This study evaluated anthropometric data, including body weight (kg) and body mass index (BMI), as well as metabolic measures such as body fat percentage (%), visceral fat mass (level), and skeletal muscle mass (%). All measures were conducted utilizing a body composition monitor (Omron HBF-375 Karada Scan Body Fat Composition Analyzer; Omron Healthcare Co., Ltd., Japan) in the morning following an overnight fast. Heart rate and blood pressure were assessed utilizing the digital sphygmomanometer (Omron HEM-8712; Omron Healthcare Co., Ltd., Kyoto, Japan).

2.4.2 Blood Sampling and Biochemical Analysis

Biological samples were collected in the morning, within a similar menstrual cycle window, to minimize hormonal fluctuations. Fasting blood glucose (FBG) was measured following a 10-hour overnight fast. Subjects consumed their last meal at 10:00 p.m., and the blood samples were collected the next morning between 8:00 and 10:00 a.m. FBG was measured from fingertip capillary whole-blood samples using a plasma-equivalent glucometer (Easy Touch GCU ET322; Zhejiang Easy Touch Medical Instruments Co., Ltd., Zhejiang, China). The device has a measurement range of 20–600 mg/dL, with clinical validation showing a strong correlation with reference laboratory methods (YSI 2300 STAT analyzer), $r^2 = 0.9571$, and 98.3% of readings within ±20% of the reference values [45]. The coefficient of variation (CV) for repeated measurements ranged from 1.8% to 5.7%, indicating good reproducibility and compliance with the ISO 15197:2013 accuracy standards [45,46].

Blood samples for IGF-1 analysis were collected from the median cubital vein between 08:00 and 10:00 a.m. using a 10 mL Terumo syringe fitted with a 20 G needle. Samples were transferred into BD Vacutainer SST II Advance Plus blood collection tubes and centrifuged at 1000 rpm for 5 minutes at 23 °C to separate serum from cellular components. All processing steps were completed within 20 minutes of collection. Serum concentrations of IGF-1 were assessed utilizing the Human Insulin-like Growth Factor-1 ELISA kit (catalog No. E0103 Hu, Bioassay Technology Laboratory, Shanghai Korain Co., Ltd). The assay was a sandwich ELISA format with a detection range of 0.1–40 ng/mL and a sensitivity of 0.058 ng/mL. The intra-assay coefficient of variation (CV) was 5.1–7.4% and the inter-assay CV was < 8%, indicating good reproducibility [47].

2.5 Statistical Analysis

The sample size was calculated using G*Power version 3.1.9.7. A one-tailed paired-samples t-test was selected to detect the difference between two dependent means, consistent with the exploratory aim of evaluating short-term within-group metabolic responses rather than testing between-group superiority. The effect size (dz) was estimated at 0.8, based on the magnitude of change in fasting blood glucose and IGF-1 observed in a similar intermittent fasting study [48]. With $\alpha = 0.05$ and power $(1-\beta) = 0.80$, the minimum required sample size was 12 subjects. Considering potential attrition of ~20–25%, the target recruitment was increased to 15 subjects (5 per group). As this calculation was based on within-group effects, the study was not powered to detect between-group differences using ANOVA, and such comparisons are therefore interpreted as exploratory.

All statistical analyses were performed using IBM SPSS Statistics version 27. Data points with standardized Z-scores greater than +2 or less than -2 were classified as statistical outliers and excluded from the final analysis [49]. Normality and homogeneity were

assessed using the Shapiro–Wilk and Levene's tests, respectively. The Brown–Forsythe test was applied to normally distributed but non-homogeneous data. For normally distributed and homogeneous data, one-way ANOVA with Tukey's HSD post hoc test was used for between-group comparisons, and paired t-tests for within-group comparisons. For non-normally distributed data, the Kruskal–Wallis test with Dunn's post hoc test was used between groups, and the Wilcoxon signed-rank test within groups. Statistical data are presented as the mean ± standard deviation (SD) for normally distributed variables and as the median with interquartile range (IQR) for non-normally distributed variables. A p-value of less than 0.05 was considered statistically significant in all analyses.

3. Results

3.1. Subject Baseline Characteristics

A total of 22 subjects were included in the final analysis (Control n = 7, ADMF n = 7, TRF n = 8). The subjects had a mean age of 21.59 ± 1.84 years. Age, body weight, BMI, blood pressure, FBG, and IGF-1 serum levels did not exhibit statistically significant differences among the three groups at baseline ($p > 0.05$). The subject baseline characteristics are shown in Table 1.

Table 1. Baseline characteristics of subjects in the ADMF, TRF, and control groups.

Variable	ADMF (n=7)	TRF (n=8)	Control (n=7)	*p*-Value
Age, year [a]	21.14 ± 1.95	22.25 ± 1.98	21.28 ± 1.6	0.664
Systolic BP, mmHg [a]	111 ± 10.53	119.85 ± 9.45	114.66 ± 8.71	0.585
Diastolic BP, mmHg [a]	78 ± 3.80	81.42 ± 7.74	82.66 ± 8.14	0.564
Haemoglobin, g/dL [a]	12.62 ± 1.59	12.37 ± 1.33	12.50 ± 1.44	0.947
Weight, kg [a]	75.24 ± 9.33	76.4 ± 10.43	72.81 ± 12.27	0.809
BMI, kg/m^2 [b]	31.4 (27-33.2)	30.7 (27.2-32.07)	28.2 (25.2-30)	0.429
Body Fat, % [b]	38 (34.6-39.4)	38.05 (34.85-39.2)	36.5 (36.2-38.2)	0.936
Visceral fat rating [b]	11 (7-13.5)	10.5 (7.62-12.12)	8 (6-10)	0.337
Skeletal muscle, kg [b]	22.8 (22.4-24)	23 (22.55-25.1)	23.3 (22.1-24.7)	0.697
FBG, mg/dL [a]	102 ± 10.81	98.62 ± 11.21	101 ± 6.48	0.792
IGF-1,ng/mL [c]	207.38 ± 104.55	209.4 ± 40.92	131.62 ± 32.9	0.098

Data are reported as mean ± SD for normally distributed variables or as median (IQR1–IQR3) for non-normally distributed variables. [a] represents the p-value derived from the One-way ANOVA test. [b] represents the p-value derived from the Kruskal–Wallis test. [c] represents the p-value derived from the Brown–Forsythe test. Abbreviations: BMI, Body Mass Index; FBG, Fasting Blood Glucose; ADMF, Alternate Day Modified Fasting; TRF, Time-Restricted Feeding; IGF-1, Insulin-Like Growth Factor-1.

Following a 20-day fasting period, the ADMF group exhibited a notable decrease in body weight, from 75.24 ± 9.33 kg to 74.29 ± 9.61 kg ($p = 0.047$; n = 7; 95% CI: 0.02 to 1.8). In line with these findings, visceral fat in the ADMF group also significantly decreased from 11 (7–13.5) to 10.5 (7–13) ($p = 0.017$). However, no substantial alterations in bodyweight or visceral fat were observed in either the control or the TRF groups. The comparison of body composition data before and after the intervention is presented in Table 2.

Table 2. Comparison of body weight, body fat percentage, visceral fat rating, and skeletal muscle mass among the ADMF, TRF, and control groups.

Variable	Group	Pretest	Post-test	*p*-Value
Weight, kg	ADMF (n=7) [b]	75.24 ± 9.33	74.29 ± 9.61	0.047*
	TRF (n=8) [b]	76.4 ± 10.43	75.72 ± 10.47	0.222
	Control (n=7) [b]	72.81 ±12.27	73.4 ± 11.66	0.349
Body Fat, %	ADMF (n=7) [b]	38 (34.6-39.4)	37.4 (34.4-39.2)	0.370
	TRF (n=8) [b]	38.05 (34.85-39.2)	38.35 (35.7-38.92)	0.351
	Control (n=7) [a]	36.5 (36.2-38.2)	35.7 (35.1-39.4)	0.765
Visceral fat rating	ADMF (n=7) [b]	11 (7-13.5)	10.5 (7-13)	0.017*
	TRF (n=8) [a]	10.5 (7.62-12.12)	10.5 (7.45-11.87)	0.739
	Control (n=7) [a]	8 (6-10)	8 (6-10)	0.785
Skeletal muscle, kg	ADMF (n=7) [b]	22.8 (22.4-24)	22.7 (20.6-24)	0.498
	TRF (n=8) [b]	23 (22.55-25.1)	22.95 (22.75-23.32)	0.161
	Control (n=7) [a]	23.3 (22.1-24.7)	23.5 (22.1-24.3)	0.463

Data are reported as mean ± SD for normally distributed variables or as median (IQR1–IQR3) for non-normally distributed variables. [a] denotes the p-value derived from the Wilcoxon test. [b] denotes the p-value derived from the paired T-test. An asterisk (*) denotes statistical significance ($p < 0.05$). Abbreviation: ADMF, Alternate Day Modified Fasting; TRF, Time-Restricted Feeding.

3.2. The Effect of Intermittent Fasting on Fasting Blood Glucose

After 20 days of intervention, both the TRF and ADMF groups exhibited a statistically significant increase in FBG, whereas the control group did not change ($p = 0.066$). FBG levels in the ADMF group increased from 102 ± 10.81 mg/dL to 112.14 ± 6.06 mg/dL ($p = 0.036$; n = 7; 95% CI: −19.40 to −0.89). FBG levels in the TRF group increased from 98.42 ± 12.09 mg/dL to 113.71 ± 11.3 mg/dL ($p = 0.001$; n = 8; 95% CI: −24.11 to −9.38). Nevertheless, no statistically significant differences were observed when the changes in FBG between groups were compared ($p > 0.05$). The comparison of FBG levels before and after the intervention is presented in Table 3.

Table 3. The comparison of FBG levels before and after the intervention in each group.

Variable	Group	Pre-test	Post-test	*p*-Value
FBG (mg/dL)	ADMF (n=7)	102 ± 10.81	112.14 ± 6.06	0.036*
	TRF (n=8)	98.42 ± 12.09	113.71 ± 11.3	0.001*
	Control (n=7)	101.5 ± 6.16	108.37 ± 8.37	0.066

Data are reported as mean ± SD. The paired T-test was employed to analyse the discrepancy between the pretest and post-test data of FBG. An asterisk (*) is used to denote statistical significance ($p < 0.05$). Abbreviation: FBG, Fasting Blood Glucose; ADMF, Alternate Day Modified Fasting; TRF, Time-Restricted Feeding; IGF-1, Insulin-Like Growth Factor-1.

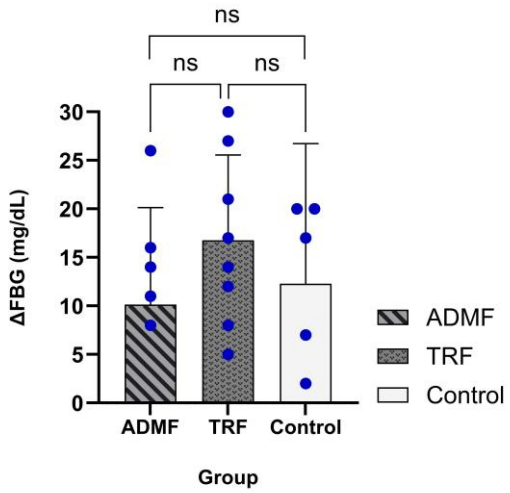

Figure 2. The comparison of changes in FBG levels (ΔFBG) among the three groups was assessed using the One-way ANOVA test. Abbreviation: IGF-1, Insulin-Like Growth Factor-1; ADMF, Alternate-Day Modified Fasting; TRF, Time-Restricted Feeding.

3.3. The Intermittent Fasting Effect on IGF-1 Serum

After 20 days of fasting, the TRF group demonstrated a significant decrease in serum IGF-1 levels, from 199.10 (183.32-220.12) ng/mL to 103.94 (83.36-112.27) ng/mL ($p < 0.001$; n = 8; 95% CI: 64.08 to 123.97). Conversely, the ADMF group did not exhibit any changes. In contrast, the control group showed a significant increase in serum IGF-1 levels, rising from 120.81 (92.50–164.20) ng/mL to 172.66 (158.49–211.01) ng/mL ($p = 0.043$).

The potential of TRF to reduce IGF-1 levels more effectively than no intervention was indicated by the significant difference in IGF-1 change between the TRF and control groups ($p < 0.014$) in between-group comparisons. The IGF-1 levels before and after the intervention are presented in Table 5.

Table 5. Comparative analysis of IGF-1 levels between pretest and posttest for each group

Variable	Group	Pre-test	Post-test	*p*-Value
IGF-1 (ng/mL)	ADMF (n=7)[b]	205.12 (97.19-312.48)	196.33 (182.45-217.38)	0.995
	TRF (n=8)[b]	199.10 (183.32-220.12)	103.94 (83.36-112.27)	< 0.001*
	Control (n=7)[a]	120.81 (92.50-164.20)	172.66 (158.49-211.01)	0.043*

Data are reported as median (IQR1–IQR3). The difference between pretest and post-test data of the IGF-1 serum was analysed using Wilcoxon test ([a]) or paired T test ([b]). Statistical significance ($p < 0.05$) is indicated by an asterisk (*). Abbreviation: IGF-1, Insulin-Like Growth Factor-1; ADMF, Alternate-Day Modified Fasting; TRF, Time-Restricted Feeding; IGF-1, Insulin-Like Growth Factor-1.

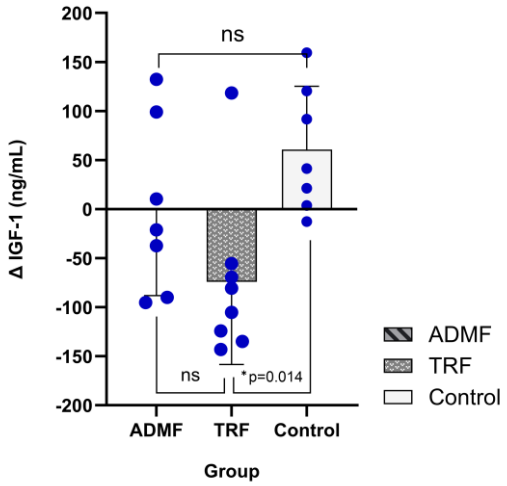

Figure 3. The comparison of changes in IGF-1 serum levels (ΔIGF-1) among the three groups was assessed using the Kruskal–Wallis test, followed by Dunn's post hoc analysis. Statistical significance ($p < 0.05$) is indicated by an asterisk (*). Abbreviation: IGF-1, Insulin-Like Growth Factor-1; ADMF, Alternate-Day Modified Fasting; TRF, Time-Restricted Feeding.

4. Discussion

This study aims to evaluate the short-term effects of two intermittent fasting (IF) regimens—TRF and ADMF—on FBG and IGF-1 serum levels in nondiabetic obese young women. The findings revealed a significant increase in FBG following TRF and ADMF interventions, while only TRF produced a significant reduction in IGF-1 levels. Furthermore, ADMF led to greater reductions in body weight and visceral fat, while the TRF group exhibited only a non-significant trend toward reduction in these parameters.

The 20-day duration of this intervention was intentionally designed to examine the effect of short-term ADMF and TRF, rather than their long-term physiological effects. Previous studies showed short intervention periods of fasting; for example, the survey by Hutchison et al. demonstrated that a 7-day TRF intervention in obese men resulted in a reduction in fasting glucose [50]. In addition, the study by Arnason et al. showed that a 14-day intermittent fasting protocol in adults with obesity led to a significant decrease in body weight and a downward trend in fasting insulin levels [51].

The observed rise in FBG contrasts with the expected reductions commonly associated with caloric restriction or prolonged fasting [30,32,52]. However, the effects of intermittent fasting remain inconsistent across populations, as they are influenced by fasting duration and timing [53]. Several studies have reported a transient elevation in blood glucose following short-term fasting [29,54]. The paradoxical findings observed in our study may be attributable to early changes in glucose regulation that occur during the short-term intermittent fasting [40,55].

Implementing a late eating period—where meals are consumed only after 16:00—has adversely affected postprandial glucose responses [53]. Intermittent fasting protocols that align food intake with the body's endogenous circadian rhythms enhance metabolic regulation. However, feeding during the biological evening—as seen in late TRF—induces circadian misalignment, leading to unfavorable postprandial outcomes and reduced insulin sensitivity [21,53]. The increase in blood glucose in this study is in contrast to the short-term intermittent fasting trial by Jamshed et al. Eight overweight individuals who followed a four-day early TRF schedule (eating between 8 a.m. and 2 p.m.) showed sufficient improvement in 24-hour glucose levels [31]. Circulating hormonal rhythms follow a circadian pattern that peaks in the morning to midday, during which insulin sensitivity is

highest; this temporal alignment enhances postprandial glucose regulation when food intake occurs earlier in the day [56].

Fasting has been shown to transiently impair first-phase insulin secretion, reflecting an adaptive rather than pathological response [29]. This early insulin release rapidly suppresses hepatic glucose output and subsequently facilitates peripheral glucose uptake. A reduction in this response is strongly associated with postprandial hyperglycemia, often evident in obese subjects and in those with impaired glucose tolerance [57]. However, Jørgensen et al observed that even healthy individuals exhibited reduced first-phase insulin secretion after 12- and 36-hour fasting, supporting the concept of β-cell rest as a physiological adaptation rather than dysfunction [58]. Likewise, Carlson et al reported a transient decline in first-phase insulin secretion with elevated glucose during an eight-week intermittent fasting regimen, which normalized once the intervention ceased [29]. In addition to affecting first-phase insulin secretion, another study by Heilbronn et al. reported that three weeks of alternate-day fasting reduced fasting insulin levels in adult men but impaired glucose tolerance in women due to decreased insulin sensitivity [59]. Reduced insulin levels and insulin sensitivity may also lower IGF-1 production, which subsequently affects glucose homeostasis, as both hormones regulate glucose through overlapping pathways [10,60].

Beyond changes in insulin dynamics, fasting also triggers neuroendocrine adaptations involving stress hormones, particularly cortisol. In humans, cortisol levels begin to rise immediately after the initiation of fasting [61]. A meta-analysis study demonstrated a strong association between fasting and increased serum cortisol [62]. During fasting, cortisol exerts key metabolic effects by inhibiting glucose uptake in peripheral tissues such as skeletal muscle and adipose tissue, thereby elevating circulating glucose levels. At the same time, it enhances glycogenolysis in the liver and muscle to sustain blood glucose availability [55]. Studies in rats subjected to 24-hour fasting showed an increase in the amplitude of cortisol secretion, whereas time-restricted feeding (TRF) with a 16/8 regimen for two weeks and TRF with a 22/2 regimen for 20 days increased cortisol levels and induced a shift in acrophase [63–65]. Studies in humans indicated an elevation of cortisol within the first 24 hours of fasting; similarly, TRF for four days also tended to increase cortisol levels [31,33,66]. However, other study showed that the cortisol levels returned to its usual pre-fasting concentrations approximately one month after fasting [67].

Interestingly, despite their differing fasting durations, an increase in FBG was observed in both the TRF and ADMF groups. The 20-day interventions employed in this study may reflect the early changes in glucose regulation to short-term intermittent fasting. These findings further underscore the necessity of more extended intervention periods to elicit more favorable glycemic effects, as glucose regulation during fasting is shaped by a complex interplay of factors, including body composition, neural inputs, metabolic hormones, and molecular signaling pathways [40,55].

Concerning the influence of short-term IF on IGF-1 in this study, a significant reduction was observed exclusively in the TRF group, but not in the ADMF group. Several meta-analyses and systematic reviews demonstrate that intermittent fasting is associated with reduced serum IGF-1 levels [68,69]. Multiple molecular pathways are thought to contribute to this effect, including increased hepatic IGFBP-1 expression, altered growth hormone receptor (GHR) expression, and impaired GH signaling [34,70,71].

A meta-analysis by Rahmani et al. reported that intermittent fasting increases IGFBP-1 levels [69]. Although nearly 99% of circulating IGFs are bound to IGFBP-3, the earliest detectable metabolic change is often a rise in IGFBP-1. IGFBP-1 binds IGF-1 with high affinity. During fasting, when insulin levels decline, IGFBP-1 concentrations increase, which consequently reduces the amount of free, biologically active IGF-1 [70,72,73]. Human studies support this evidence: 6 days of caloric restriction in healthy adults and 14

days in obese women elevated IGFBP-1 and lowered serum IGF-1 [74,75]. Similarly, a 5:2 diet with 75% energy restriction over six months in premenopausal women with obesity significantly increased IGFBP-1 while reducing IGF-1 [76]. However, the effects of specific intermittent fasting regimens, such as alternate-day modified fasting (ADMF) and time-restricted feeding (TRF), on IGFBP-1 remain unclear.

Fasting significantly lowers circulating insulin levels, causing a downregulation of hepatic growth hormone receptor (GHR) expression—a key mediator of GH-induced IGF-1 synthesis in hepatocytes [71,77]. In rodents, even 24-hour fasting reduced hepatic GHR and IGF-1 mRNA by 50% and 43%, respectively, with both returning to baseline after refeeding [36]. Fasting also impairs GH signaling, particularly the JAK-STAT pathway, where STAT5 plays a central role in hepatic IGF-1 production [34,78]. In humans, prolonged fasting (37.5 hours) reduced STAT5 and IGF-1 expression, indicating disrupted GH signaling [34]. However, the effects of ADMF and TRF on GHR expression and GH signaling remain unexplored.

Overall, the fasting durations applied—18 hours in TRF and 24 hours in ADMF—likely contributed to the observed reduction in IGF-1 levels [70]. Insulin declines about six hours after the last meal which promotes increased IGFBP-1 and reduced serum IGF-1 [24,72]. While TRF does not prescribe caloric restriction, the restricted daily eating window consistently reduces overall energy intake and insulin levels consistently [79]. In contrast, ADMF reduces calorie intake by up to 75% on fasting days, but intake on feeding days remains unchanged or only slightly reduced [80]. Thus, the continuous daily insulin reduction in TRF may produce a more sustained elevation of IGFBP-1 and a greater decline in IGF-1 than that achieved with ADMF.

This study also demonstrates that ADMF led to greater reductions in body weight and visceral fat compared to TRF, likely due to enhanced lipolysis during longer fasting periods [24]. While catecholamine levels typically begin to rise modestly after 12 hours of fasting, evidence indicates that substantial catecholamine-induced lipolysis occurs after approximately 15 hours of fasting. This may help explain the stronger lipolytic response in the 24-hour fasting period of ADMF compared to TRF [24,81]. The delayed activation could be further affected by impaired catecholamine sensitivity, a condition frequently reported in individuals with obesity [82,83]. Moreover, the marked reduction in visceral fat suggests a more pronounced lipolytic effect in intra-abdominal adipose tissue than subcutaneous fat depots [83]. Notably, intermittent fasting in this study did not result in lean mass loss, which may be attributed to an early metabolic shift toward fat and ketone utilisation—before significant protein catabolism—within the first 24 hours of fasting [24,53,59]. Additionally, the provision of 25% of daily caloric intake during fasting periods in the ADMF protocol does not appear to impair lipolysis or weight loss. On the contrary, this modest intake may improve compliance with the fasting regimen [80].

To our knowledge, this is the first study to evaluate the effects of distinct short-term intermittent fasting regimens on fasting blood glucose (FBG) and serum IGF-1 levels in non-diabetic, obese young women. Although this population remains underrepresented in the existing literature, investigating this group is particularly important, as women exhibit the highest global prevalence of obesity. Early intervention in cases of obesity is essential to prevent the progression to type 2 diabetes mellitus (T2DM) and other non-communicable diseases [2,7]. This study was designed to capture the early changes in glycemic regulation during short-term intermittent fasting in obese young women [40,55,84].

This research possesses several limitations that warrant consideration. Dietary intake was monitored only for adherence, without caloric or macronutrient quantification. Physical activity and sleep–circadian patterns were self-reported rather than objectively measured. Although samples were collected in a similar morning menstrual-cycle window, additional hormonal assessments (e.g., insulin, estradiol, progesterone, cortisol) were not

feasible, leaving residual hormonal variability possible. Fasting glucose was measured using a capillary glucometer instead of venous plasma assays, and intermediary metabolic regulators (insulin, cortisol, oral glucose tolerance) were not assessed, restricting mechanistic interpretation. Future studies should apply comprehensive metabolic profiling and more controlled monitoring of behavioral and hormonal confounders.

5. Conclusions

The 20-day intermittent fasting intervention produced distinct, protocol-specific effects: TRF significantly lowered IGF-1, whereas ADMF reduced body weight and visceral fat. Both regimens, however, led to increased fasting blood glucose levels, with no change observed in the control group. These findings suggest that early changes in glucose regulation are highly dependent on the specific dietary regimen used. These findings suggest that even short-term intermittent fasting may trigger an early response in obese young women. However, these findings must be interpreted cautiously due to several methodological constraints. Thus, the observed changes should be viewed as preliminary short-term responses rather than definitive regulatory effects. Future studies with larger samples, venous-based biochemical assays, comprehensive metabolic profiling, and more rigorous control of behavioural and physiological confounders are needed to clarify underlying mechanisms and strengthen causal inference.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/doi/s1, Figure S1: title; Table S1: title; Video S1: title.

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Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki. Ethical clearance was obtained from the Health Research Ethics Committee of the Faculty of Medicine, Universitas Airlangga (approval No. 36/EC/KEPK/FKUA/2024, dated 24 June 2024) as part of the project "Effect of Various Types of Intermittent Fasting (IF) on Several Markers: Aging, Working Memory, Inflammation, and Immune System in Obese Young Women."

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study. Written informed consent was obtained from the subjects to publish this paper.

Data Availability Statement: Data supporting the reported results can be obtained from the corresponding author upon reasonable request. The data are not openly accessible because of ethical considerations.

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