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Evaluation of the effects of intermittent fasting on clinical and laboratory parameters in metabolic syndrome

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ABSTRACT

Aim: Metabolic syndrome is associated with serious conditions, including obesity, type 2 diabetes mellitus, hypertension, and cardiovascular disorders. We aimed to study the effects of intermittent fasting on metabolic syndrome.

Methods: Patients with metabolic syndrome were enrolled in the study. Before the intervention, anthropometric measurements (body weight, body mass index [BMI], waist and hip circumferences) and laboratory parameters (fasting blood glucose, glycated hemoglobin [HbA1c], fasting insulin) were recorded. All participants were instructed to fast for 14–16 hours per day for three months, consuming two meals during the remaining 8–10 hours. After three months, anthropometric measurements were taken again, and laboratory parameters were reassessed. Data collected before the intervention and at the third month of intermittent fasting were compared.

Results: Twenty patients with metabolic syndrome completed the study protocol (7 men and 13 women). The mean age of the participants was 56±12 years. There was a statistically significant reduction in weight (from 94.4±16.7 kg to 89.1±15.9 kg), BMI (from 34.9±5.6 kg/m² to 33±5.5 kg/m²), waist circumference (from 113±13 cm to 105±11.3 cm), and hip circumference (from 118±11 cm to 113±10.4 cm) (p-values: <0.001, <0.001, <0.001, and 0.001, respectively). Moreover, fasting blood glucose (p=0.024), fasting insulin (p=0.001), and HbA1c (p=0.008) levels significantly decreased after three months of intermittent fasting.

Conclusion: Intermittent fasting should be considered a nutritional strategy to reduce BMI, waist circumference, and body weight and to improve metabolic parameters.

Keywords: Intermittent fasting, metabolic syndrome, fasting blood glucose, HbA1c, BMI.

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1. Introduction

Metabolic syndrome is a potentially life-threatening condition that begins with insulin resistance and is associated with systemic disorders such as abdominal obesity, glucose intolerance or diabetes mellitus, dyslipidemia, hypertension, and coronary artery disease. The prevalence of metabolic syndrome is reported to be approximately 22% in adults [1]. According to the diagnostic criteria for metabolic syndrome, a diagnosis requires at least two of the following criteria: hypertension (defined as systolic blood pressure >130 mmHg, diastolic blood pressure

>85 mmHg, or current use of antihypertensive medication), dyslipidemia (triglyceride level >150 mg/dL or HDL level <40 mg/dL in men and <50 mg/dL in women), and abdominal obesity (defined as a BMI >30 kg/m² or waist circumference >94 cm in men and >80 cm in women). Additionally, the presence of diabetes mellitus, impaired glucose tolerance, or insulin resistance is required [2].

Insulin resistance plays a fundamental role in the pathogenesis of metabolic syndrome. Therefore, treatment aims to control the risk factors contributing to insulin resistance through lifestyle modifications, and if necessary, pharmacological interventions to achieve clinical goals. The most effective approach includes weight loss, regular exercise, a healthy diet, and smoking cessation.

Intermittent fasting (IF), a form of time-restricted eating (typically involving 16 hours of fasting and an 8-hour eating window), has gained popularity in recent years due to its potential health benefits, including weight loss and reduced inflammation [3]. For many individuals, it is considered less restrictive than traditional calorie-restricted diets [4]. IF involves maintaining a regular daily caloric intake while incorporating short periods of strict calorie restriction [5].

Studies on IF and weight loss suggest a reduced risk of cardiovascular disease [3]. This is attributed to its modulating effects on various risk factors, including obesity, malnutrition, insulin resistance, type 2 diabetes, and arterial hypertension [6]. IF has been shown to reduce body fat and overall mass, thereby promoting optimal cardiovascular function and lowering the risk of myocardial infarction [7]. Additionally, it influences metabolic biomarkers such as insulin and glucose levels, thereby potentially reducing the risk of metabolic syndrome [8]. Since IF has been found to reduce insulin resistance, promote weight and fat loss, alleviate inflammation, improve blood pressure and lipid profiles, and regulate appetite, we hypothesize that it may offer significant benefits for patients with metabolic syndrome. Moreover, the simplicity and flexibility of IF may improve adherence compared to traditional calorie-restricted diets.

Present study aimed to evaluate the impact of prolonged intermittent fasting (14–16 hours per day) on the clinical and laboratory parameters of patients with metabolic syndrome presenting at our clinic.

2. Materials and methods

2.1. Study Design and Population: Patients diagnosed with metabolic syndrome who presented at our clinic were included in the study. All participants provided informed consent. Ethical approval was obtained from the local clinical studies ethics committee (approval no: 2021/100).

Participants were instructed to follow an 8–10 hour eating window of their choice while maintaining their usual number and content of meals, without any calorie restrictions or modifications to their ongoing treatments. They fasted for the remaining 14–16 hours of the day. Patients with metabolic syndrome who could adhere to this dietary regimen were included in the study, whereas those unable or unwilling to comply voluntarily were excluded. The study protocol involved monitoring participants for approximately three months.

Exclusion criteria included patients younger than 20 years or older than 75 years, individuals with type 2 diabetes mellitus using oral antidiabetic medications that induce hypoglycemia or receiving regular insulin therapy, patients with type 1 diabetes mellitus, those with stage 3–4 heart failure, advanced chronic obstructive pulmonary disease (COPD), stage 4–5 chronic kidney disease, or those

undergoing active cancer treatment (chemotherapy or radiotherapy). Additionally, individuals with active infections, liver failure, reactive hypoglycemia, or conditions predisposing to hypoglycemia were not eligible for participation.

At the end of the third month, participants were assessed for adherence to the intermittent fasting (IF) protocol, and laboratory measurements were repeated.

2.2. Laboratory Analyses: Clinical parameters, including age, gender, blood pressure, comorbidities, and medications used, as well as anthropometric measurements (weight, height, body mass index, waist circumference, and hip circumference), were recorded at baseline and at the end of the three-months study period.

Laboratory assessments included fasting glucose, urea, creatinine, uric acid, total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides, and complete blood count (leukocyte count, neutrophil count, lymphocyte count, hemoglobin, hematocrit, and platelet count). Additionally, insulin, HbA1c, homeostasis model assessment of insulin resistance (HOMA-IR), C-reactive protein (CRP), thyroid-stimulating hormone (TSH), and albumin levels were measured at baseline and after three months. Anthropometric and laboratory values were statistically compared between baseline and the third month.

Biochemical analyses were performed using an Abbott-8000 autoanalyzer with manufacturer-provided kits. Complete blood count tests were conducted using the Mindray BC-5380 analyzer. HbA1c and hormone tests were performed using the Lifotronic H9 device, while the Architect Plus i2000SR device was used for additional hormone assessments, employing kits from the respective manufacturers.

2.3. Statistical Analyses: For approximately 95% power, the required sample size for a 20% change was calculated as 18 using power analysis. To account for potential losses during follow-up and protect the study, an additional 10% was included, leading to a planned inclusion of 20 patients in the study. Statistical analyses were conducted using SPSS 20.0 for Windows (IBM Corp., Armonk, NY). The Kolmogorov–Smirnov test was used to assess whether variables followed a normal or skewed distribution. Normally distributed variables were expressed as mean ± standard deviation (SD) and analyzed using the paired samples t-test. Non-normally distributed variables were analyzed using the Mann–Whitney U test, with results presented as median (min–max). Categorical variables were compared using the Chi-square test, with results expressed as frequencies and percentages. A p-value <0.05 was considered statistically significant.

3. Results

The study included 20 participants, comprising 7 males and 13 females, with a mean age of 56±12 years.

A comparison of anthropometric measurements between baseline and the third month revealed statistically significant reductions in weight, BMI, waist circumference, and hip circumference. The mean weight decreased from 94.4±16.7 kg to 89.1±15.9 kg at the third month of the intervention (p<0.001). Similarly, the mean BMI was reduced from 34.9±5.6 kg/m² to 33±5.5 kg/m² by the end of the study (p<0.001). The mean waist circumference decreased from 113±13 cm to 105±11.3 cm (p<0.001), while the mean hip circumference was reduced from 118±11 cm to 113±10.4 cm at the third month (p=0.001).

Laboratory assessments also showed significant improvements. Fasting blood glucose

Table 1. The anthropometric and laboratory results of the study.

Parameters	**The initial value Mean ± SD**	**The 3rd month value Mean ± SD**	***p value***
Systolic Blood Pressure (mmHg)	132 ±12.1	130 ±9.9	*0.148*
Diastolic Blood Pressure (mmHg)	83 ± 6.3	81 ± 6	*0.163*
Weight (kg)	94.3 ± 16.7	89 ± 15.8	*<0.001*
Body Mass Index (kg/m^2)	34.9 ± 5.59	32.94 ±5.49	*<0.001*
Waist Circumference (cm)	112.9 ± 12.8	105 ± 11.2	*<0.001*
Hip Circumference (cm)	117.7 ± 10.9	113 ± 10.3	*<0.001*
Fasting Blood Glucose (mg/dL)	109.8 ± 16.1	100.2 ± 9.4	*0,024*
Insulin (µIU/mL)	16.2 ± 5.9	13 ± 5.2	*0.001*
HbA1c (%)	6.1 ± 0.79	5.8 ± 0.48	*0.008*
HOMA-IR	4,9 ± 2,01	3,3 ± 1,47	*<0.001*
Urea (mg/dL)	33 ± 7	28 ± 6	*0.004*
Creatinine (mg/dL)	0.82 ± 0.17	0.83 ± 0.17	*0.802*
Uric acid (mg/dL)	6.4 ± 1.5	5.8 ± 0.8	*0.032*
Sodium (mEq/L)	139 ± 2	138 ± 2	*0.787*
Potassium (mEq/L)	4.5 ± 0.3	4.2 ± 0.2	*0.001*
ALT (IU/L)	35 ± 25	24 ± 15	*0.007*
AST (IU/L)	23 ± 10	19 ± 6	*0.011*
TSH (mIU/L)	1.7 ± 0.9	2.2 ± 1.2	*0.14*
Albumin (g/dL)	4.6 ± 0.4	4.7 ± 0.4	*0.82*
CRP mg/L	4.98 ± 9.4	2.3 ± 2.8	*0.172*
Total cholesterol (mg/dL)	216 ± 40	216 ± 57	*0.99*
Triglyceride (mg/dL)	187 ±130	151 ±88	*0.04*
LDL (mg/dL)	129 ± 27	132,65 ± 48,62	*0.72*
HDL (mg/dL)	55 ± 12	60 ± 39	*0.58*
Leukocyte (k/µL)	6.99 ± 1.5	6.9 ± 1.4	*0.886*
Neutrophil (k/µL)	3.8 ± 0.99	3.8 ± 1.3	*0.987*
Lymphocyte (k/µL)	2.3 ± 0.8	2.4 ± 0.6	*0.776*
Hemoglobin (g/dL)	14 ± 1.3	13.8 ± 1.2	*0.278*
Hematocrit (%)	42 ± 3.6	41.7 ± 3	*0.416*
Platelet (k/µL)	285 ±61	294 ±62	*0.137*

levels decreased from 110±16 mg/dL to 100±9.5 mg/dL (p=0.02). Likewise, fasting insulin levels were reduced from 16.2±5.9 µIU/mL to 13.1±5.2 µIU/mL (p=0.001), HbA1c levels decreased from 6.2±0.8% to 5.8±0.5% (p=0.008), and HOMA-IR values declined from 4.9±2.02 to 3.31±1.47 (p<0.001).

Significant differences were also observed in triglyceride (p=0.04), blood urea (p=0.004), serum uric acid (p=0.03), plasma potassium (p=0.001), AST (p=0.01), and ALT (p=0.007) levels when comparing baseline and third-month values. In contrast, no significant differences were found in systolic or diastolic blood pressure measurements (p=0.15 and p=0.16, respectively).

No statistically significant changes were detected between baseline and third-month values for total cholesterol, LDL cholesterol, HDL cholesterol, leukocyte count, neutrophil count, lymphocyte count, hemoglobin, hematocrit, platelet count, serum albumin, CRP, serum creatinine, plasma sodium, and TSH. A summary of the anthropometric and laboratory data is presented in Table 1.

4. Discussion

The striking results of the present study revealed that intermittent fasting was highly effective in reducing fasting blood glucose, HbA1c, plasma insulin levels, and improving insulin sensitivity in subjects with metabolic syndrome. Furthermore, our data showed that intermittent fasting was also effective in decreasing anthropometric measures such as body weight, BMI, and waist and hip circumferences.

Intermittent fasting can have several positive effects on blood glucose levels and HbA1c, which are key indicators of blood glucose control. It can enhance insulin sensitivity, leading to more efficient glucose uptake by cells and lower blood glucose levels [9,10]. Many studies have reported that intermittent fasting can lower fasting blood glucose levels, which is particularly beneficial for individuals with insulin resistance or type 2 diabetes mellitus [11-13]. By reducing the frequency of meals, intermittent fasting can lead to more stable blood glucose levels throughout the day, avoiding spikes and crashes that can occur with frequent eating. Similarly, in the present study, we observed a reduction in fasting blood glucose in subjects with metabolic syndrome.

Intermittent fasting has been shown to reduce HbA1c levels, a marker of long-term blood glucose control. Decreased HbA1c levels are associated with a reduced risk of complications from diabetes mellitus [14]. The reduction in HbA1c can be sustained over time with consistent adherence to an intermittent fasting regimen, indicating long-term improvements in blood glucose management. Intermittent fasting often leads to a reduction in overall calorie intake, which can contribute to weight loss and improved metabolic health, indirectly affecting blood glucose and HbA1c levels [15]. In addition, intermittent fasting can influence hormones such as insulin, glucagon, and leptin, which play roles in glucose metabolism and appetite regulation [16]. These mechanisms may explain the reduced fasting blood glucose and decreased HbA1c levels observed in the present study.

The effects of intermittent fasting can vary depending on an individual's baseline metabolic health, the specific fasting regimen followed, and adherence to the fasting protocol. Different types of intermittent fasting (e.g., 16/8 method, 5:2 diet, alternate-day fasting) may have varying impacts on blood glucose and HbA1c levels [17]. We recommended at least 14-16 hours of fasting between meals to the participants enrolled in the present study. Several studies support the

benefits of intermittent fasting on blood glucose and HbA1c levels. For example, a recent study found that alternate-day fasting significantly reduced fasting glucose and insulin levels in participants [18]. Another study in the United States reported that time-restricted feeding improved insulin sensitivity and reduced HbA1c levels in men with prediabetes [19]. These findings suggest that intermittent fasting can be an effective strategy for improving blood glucose control and reducing HbA1c levels, particularly in individuals with insulin resistance or type 2 diabetes.

We demonstrated that body weight, BMI, waist circumference, and hip circumference improved after 3 months of intermittent fasting. This intervention often leads to a reduction in overall calorie intake, contributing to weight loss. Various studies have shown that intermittent fasting can be an effective strategy for reducing body weight [20]. Another mechanism of the beneficial effects of intermittent fasting on anthropometric measures may be the reduction in fat mass. Intermittent fasting can help reduce body fat percentage by promoting the use of fat as an energy source during fasting periods [21]. Additionally, weight loss through intermittent fasting leads to a reduction in BMI. Recent reports have shown reductions in waist circumference, which is an indicator of abdominal fat [22]. A reduction in waist circumference is associated with a decreased risk of metabolic diseases, including metabolic syndrome, type 2 diabetes mellitus, and hypertension [23-25]. Furthermore, intermittent fasting may specifically target visceral fat, the fat stored around internal organs, which is linked to higher medical risks [26]. Although the effect on hip circumference might be less pronounced than on waist circumference, intermittent fasting can still lead to reductions in hip measurements [27]. This is associated with an improved waist-to-hip ratio. These findings align with the results of the present study.

Other possible mechanisms for the benefits of intermittent fasting include reduced calorie intake due to the limited eating window, leading to a negative energy balance and weight loss. Additionally, intermittent fasting can improve metabolism by enhancing insulin sensitivity, increasing fat oxidation, and modulating hormone levels (e.g., ghrelin and leptin) that regulate hunger and fat storage [8]. During fasting periods, the body shifts from glucose to fat as the primary energy source, promoting fat loss. Several studies support these effects: one study in an obese population found that participants following an intermittent fasting regimen experienced significant reductions in body weight, BMI, and waist circumference [28]. Another study revealed that intermittent fasting led to reductions in visceral fat and improvements in metabolic health markers [29]. A meta-analysis concluded that intermittent fasting was an effective strategy for weight loss and improving body composition [30]. All of these mechanisms could contribute to the beneficial effects of intermittent fasting on the laboratory and anthropometric measures reported in our study.

The limited study population and the single-center nature of our work are some of the limitations of the present study. Another limitation is that lifestyle habits and daily physical activity of the participants were not controlled, just asked not to make gross change of daily routine. Yet, the findings in our report support the current medical literature regarding the benefits of intermittent fasting on metabolic and anthropometric parameters.

4.1. Conclusion: In conclusion, intermittent fasting may prevent the development of diabetes and other metabolic conditions in patients with metabolic syndrome by reducing blood glucose

and HbA1c, improving insulin sensitivity, and decreasing body weight, BMI, and waist circumference. Therefore, we believe that intermittent fasting should be considered as one of the nutritional interventions for this population.

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