Original Article

Impact of Intermittent Fasting on Reproductive Markers in PCOS

Huma Habib, Fatima Lajbar, Atif Ullah, Hamasa Gul, Fazal Rahim, Miraj Ahmad

Abstract

Objective: To evaluate the effect of a six-week time-restricted feeding (TRF) regimen on anthropometric, metabolic, and reproductive hormonal parameters in women with polycystic ovary syndrome (PCOS).

Study Design and Setting: Retrospective observational study conducted at Medical Teaching Institute Bacha Khan Medical College and Mardan Medical Complex, Mardan Pakistan.

Methodology: A total of 63 women diagnosed with PCOS according to Rotterdam criteria who completed a six-week TRF dietary regimen (8-hour feeding window from 1:00 p.m. to 9:00 p.m.) were included. Anthropometric measurements and laboratory parameters were recorded before and after the intervention. Variables assessed included body mass index (BMI), waist-to-hip ratio (WHR), insulin resistance using HOMA-IR, androgen profile (free androgen index, testosterone, SHBG), gonadotropins (LH and FSH), and ovarian reserve markers (estradiol and AMH). Paired t-tests were applied and $p < 0.05$ was considered statistically significant.

Results: Significant reductions were observed in BMI, WHR, HOMA-IR, fasting insulin, and free androgen index. Total and free testosterone levels decreased, while SHBG levels increased significantly. LH levels declined and FSH levels increased, improving the LH/FSH ratio. Estradiol levels increased whereas AMH levels showed a modest decline. Clinical improvement was observed in ovulatory function (60.4%), menstrual regularity (60.9%), and hyperandrogenism (63.6%). TRF showed high adherence (82.5%) with minimal side effects.

Conclusion: Time-restricted feeding appears to be a safe and effective lifestyle intervention for improving metabolic and reproductive hormonal parameters in women with PCOS. Further randomized controlled trials with longer follow-up are required.

Keywords: Hyperandrogenism; Insulin resistance; Intermittent fasting; Polycystic ovary syndrome; Time-restricted feeding

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INTRODUCTION

"Polycystic Ovary Syndrome (PCOS) is a common and multifaceted endocrine disorder among women of reproductive ages, and it is defined by hyperandrogenemia, anovulation, and polycystic ovaries. PCOS ranks among the major ethology of menstrual irregularities, infertility, and metabolic disorders.[1] The prevalence of PCOS ranges between 6% and 21% worldwide. This variation in prevalence may be due to differences in diagnostic criteria, genetic, and environmental influences.[2] PCOS manifests with a variety of reproductive disorders, including oligo- and anovulation, hyperandrogenism, and infertility in about 70% of women with PCOS.[3] PCOS is believed to have an intricate association with various metabolic disorders, including obesity, insulin resistance (IR), hyperinsulinemia, and an increased risk of T2DM. In this way, obesity adds to the pathophysiology of PCOS by leading to insulin resistance (IR), which in turn increases the levels of androgens and thereby hyperandrogenism and impairs ovarian function.[3] This highlights the importance of lifestyle changes, particularly dietary changes, in the management of PCOS.[4]

Intermittent fasting, a promising dietary intervention for the management of metabolic and endocrine abnormalities associated with PCOS, differs from the traditional method of caloric restriction by the inclusion of a window of fasting and eating, making it a more sustainable approach for dietary control. IF has been proven to improve insulin sensitivity, support weight maintenance, and influence reproductive hormones associated with PCOS.[5] However, the pharmacologic management with metformin and clomiphene citrate primarily targets IR and ovulatory problems but is associated with side effects and low adherence rates.[6] Similarly, caloric restriction has been proven effective with regard to metabolic parameters but is difficult to sustain over a prolonged period.[7] IF is a novel approach that not only treats metabolic problems but also has the advantage of practicality and physiological compatibility with the body's natural rhythms.[5] Among the different types of IF regimens, alternate day fasting, time restricted feeding, and the 5:2 diet are the most studied. In ADF, the cycles of fasting, with restricted caloric intake, alternate with the cycles of unrestricted feeding.[8,9] ADF has been found to decrease body weight, fasting glucose, and insulin levels, all of which are important for the management of PCOS.[10] In the 5:2 diet, 2 days of the week are set for fasting, with restricted caloric intake, while on the remaining 5 days, no restrictions are placed on food intake.[11] In the 5:2 diet, only non-caloric drinks such as water and black coffee are allowed on the fasting days. This regimen is attractive because of the importance of circadian rhythms, which are known to play an important role in the regulation of metabolic and endocrine functions.[12] On the other hand, the 5:2 diet, which is a variant of the ADF, involves two days of non-consecutive fasting with reduced caloric intake (20-25% of daily caloric requirements) and regular caloric intake for the remaining five days of the week.[13] This method incorporates moderate caloric restriction with sustainability to minimize the mental pressure of constant dieting.[14] Furthermore, Ramadan fasting involves a religious fast between dawn and dusk and provides an interesting model of long-term daily fasting, providing valuable information regarding the effects of fasting on metabolism and reproductive health. IF has been recognized as a holistic and pharmacological approach for the management of PCOS. It is believed to address the key issues associated with the condition, such as insulin resistance, hyperinsulinemia, and hyperandrogenism, which may normalize hormonal balance, menstrual cycles, and ovulatory capacity. However, the effect of intermittent fasting on the reproductive parameters of women with PCOS is still unknown. Thus, the present study is designed to evaluate the effect of intermittent fasting, also called time-restricted feeding, on the hormonal profile of women with PCOS.

METHODOLOGY

Ethical approval for this retrospective observational study was obtained from Bacha Khan Medical College Ethics Review Committee (Approval No: 774/024). The study was Conducted at Medical Teaching Institute Bacha Khan Medical College, and Mardan Medical Complex. The duration of the study was from August 2024 through 30 January 2025, and the conduct was in accordance with the principles set forth in the Declaration of Helsinki regarding ethical practice in human research. Women with Polycystic Ovary Syndrome (PCOS) diagnosed according to the Rotterdam criteria (16) were retrospectively screened. They were only included if they had undergone a time-restricted feeding (TRF) dietary regimen as a first-line intervention. Subjects were excluded if they had comorbidities that would likely affect dietary consumption or hormonal balance, such as but not limited to thyroid or adrenal disease, Cushing's syndrome, sex hormone-secreting tumours, hyperprolactinemia, diabetes mellitus, and severe cardiovascular, hepatic, renal, or gastrointestinal illness. Also excluded were those diagnosed with a history of regular alcoholism or smoking.

Other exclusion criteria included individuals who were less than 18 or more than 40 years old, and those with a body mass index (BMI) outside the range of 18–30 kg/m². Participants who were on hormonal contraceptives, antiandrogens, ovulation-inducing drugs, or insulin-sensitizing drugs were also excluded. Individuals who had a history (within 3 months) of receiving antiepileptic medications, psychotropic drugs, statins, or corticosteroids were not eligible. Additionally, pregnant, lactating, or perimenopausal women were excluded. Others that were disqualified included the use of antibiotics within the last 3 weeks, having active infection, or any gastrointestinal illness at the time of assessment. After application of the eligibility criteria, 83 women were identified for evaluation. Of these, 63 women who completed the 6-week time-restricted feeding (TRF) regimen and had complete pre- and post-regimen records were included in the final analysis.

All data were analysed using IBM SPSS Statistics (Armonk, NY, USA). Statistical significance was set at a two-tailed p-value of <0.05. The Shapiro–Wilk test was used to assess normality. Continuous variables were reported as mean ± standard deviation for normally distributed data and as median (interquartile range) for non-normally distributed data. Categorical variables were presented as frequencies and percentages. Paired t-tests were used to compare normally distributed continuous variables before and after the TRF regimen.

RESULTS

Sixty-three women with PCOS completed the 6-week Time-Restricted Feeding (TRF) program. Statistically significant improvements in anthropometric, metabolic, and reproductive hormonal parameters were found. There was a significant reduction in body mass index (BMI) from 26.74 ± 1.34 kg/m² to 25.59 ± 1.39 kg/m² ($p = 0.001$), and waist-to-hip ratio (WHR) also decreased significantly from 0.88 ± 0.05

to 0.84 ± 0.04 ($p = 0.001$). A marked improvement in insulin sensitivity was observed, as HOMA-IR values dropped from 3.22 ± 0.55 to 2.43 ± 0.53 ($p = 0.001$), accompanied by a significant decline in fasting insulin levels from 18.4 ± 2.7 ìIU/mL to 14.1 ± 2.4 ìIU/mL ($p = 0.001$). The Free Androgen Index (FAI) significantly decreased from 10.13 ± 2.02 to 7.64 ± 1.42 ($p = 0.001$), indicating reduced hyperandrogenism. Total testosterone levels also showed a meaningful decline from 72.5 ± 14.2 ng/dL to 61.8 ± 12.3 ng/dL ($p = 0.0015$), and free testosterone levels dropped significantly from 3.8 ± 0.7 pg/mL to 2.9 ± 0.6 pg/mL ($p = 0.001$). In parallel, sex hormone-binding globulin (SHBG) levels increased from 31.32 ± 4.60 nmol/L to 35.11 ± 4.29 nmol/L ($p = 0.001$), contributing to the reduction in bioavailable androgens. Luteinizing hormone (LH) levels decreased significantly from 8.11 ± 2.24 mIU/mL to 6.32 ± 1.93 mIU/mL ($p = 0.001$), while follicle-stimulating hormone (FSH) levels increased from 5.69 ± 1.31 mIU/mL to 6.39 ± 1.31 mIU/mL ($p = 0.0032$), thereby improving the LH/FSH ratio—a key marker in PCOS diagnosis.

Estradiol (E2) levels rose significantly from 58.69 ± 10.87 pg/mL to 63.93 ± 8.95 pg/mL ($p = 0.0128$), indicating enhanced follicular activity. Although Anti-Müllerian Hormone (AMH) levels decreased slightly from 6.21 ± 1.27 ng/mL to 5.72 ± 1.32 ng/mL ($p = 0.0265$), they remained within the diagnostic spectrum of PCOS, possibly reflecting improved follicular recruitment dynamics. There were also statistically significant reductions in other hormonal parameters. Dehydroepiandrosterone sulfate (DHEAS) decreased from 195.7 ± 28.3 ìg/dL to 182.4 ± 25.6 ìg/dL ($p = 0.002$). Thyroid-stimulating hormone (TSH) levels declined from 2.43 ± 0.74 ìIU/mL to 2.28 ± 0.65 ìIU/mL ($p = 0.041$), and prolactin levels dropped from 14.6 ± 3.1 ng/mL to 13.1 ± 2.9 ng/mL ($p = 0.036$), potentially reflecting reduced stress and hypothalamic-pituitary axis modulation. This table presents the mean ± standard deviation (SD) values of selected clinical and laboratory parameters measured at baseline and after a 6-week time-restricted feeding (TRF) intervention (8-hour feeding window). Paired t-tests were used to compare pre- and TRF values. BMI: Body Mass Index; WHR: waist to hip ratio HOMA-IR: Homeostatic Model Assessment of Insulin Resistance; FAI: Free Androgen Index; LH: Luteinizing Hormone; FSH: Follicle-Stimulating Hormone; E2: Estradiol; AMH: Anti-Müllerian Hormone; SHBG: Sex Hormone-Binding Globulin. A p-value 0.001 was considered statistically significant. This table shows the number and percentage of women with improved ovulatory status, menstrual regularity, and hyperandrogenism (defined as FAI = 8) after a dietary intervention with TRF. Improvement is defined as the change from abnormal to normal, while 'No Change' indicates the persistence of abnormal values after the intervention. This bar chart illustrates the mean values of the key anthropometric, metabolic, and reproductive hormonal markers prior to and after the 6-week Time-Restricted Feeding (TRF) intervention in women with PCOS, where the sample size was 63. Parameters measured include body mass index (BMI), insulin resistance (HOMA-IR), Free Androgen Index (FAI), luteinizing hormone (LH), follicle-stimulating hormone (FSH), estradiol (E2), anti-Mullerian hormone (AMH), and sex hormone-binding globulin (SHBG). Values prior to the intervention are indicated by the blue bars, while the values obtained after the intervention are indicated by the teal bars, showing significant improvements in all the parameters measured, where $p < 0.05$. Table 3 shows the Pearson correlation between the change in BMI and shifts in key metabolic and hormonal markers after 6 weeks of TRF. Notable findings include a strong negative correlation between weight loss and HOMA-IR ($r = -0.62$, $p < 0.001$), indicating improved insulin sensitivity. Table 4 summarizes adherence levels and side effect profiles during the TRF intervention. High compliance and low adverse event rates suggest that TRF was both feasible and well-tolerated in this cohort.

DISCUSSION

This retrospective observational study aimed to assess the effects of a 6-week, 8-hour Time-Restricted Feeding (TRF) regimen on anthropometric, metabolic, and reproductive hormonal parameters in women with Polycystic Ovary Syndrome (PCOS). The results of this study showed that Time-Restricted Feeding can improve insulin resistance, androgen levels, gonadotropin balance, and menstrual regularity in PCOS women. Obesity among PCOS women is a common condition and usually exacerbates the metabolic abnormalities associated with PCOS, mainly through its association with insulin resistance.[6] The concomitant presence of obesity and PCOS increases the risk of cardiovascular disease, menstrual irregularities, androgen levels, hirsutism, and decreases quality of life.[5] Even small reductions in body weight, usually between 5% and 10%, have been found to have a marked effect on cardiovascular risk factors, glucose metabolism, reproductive and endocrine functions in PCOS women. Weight loss in PCOS women increases the peripheral conversion of androgens to estrogens and helps to balance the hormonal levels.[4]

In our current investigation, we observed that following a six-week 8-hour TRF regimen led to notable reductions in BMI among PCOS patients. These findings are consistent with prior research demonstrating that intermittent fasting protocols can positively influence body weight, BMI, and waist circumference.[15] However, clinical evidence specifically focusing on TRF in PCOS remains limited. For instance, Li et al. reported significant improvements in most anthropometric markers following a 6-week TRF intervention.[13] Similarly, in an animal model of PCOS, an 8-hour TRF diet over eight weeks resulted in reduced body weight and adipose tissue mass compared to ad libitum

Table 1. Changes in Anthropometric, Metabolic, and Reproductive Hormonal Parameters Before and After Time-Restricted Feeding (TRF) in Women with PCOS (n = 63)

Parameter	Baseline Mean ± SD	Post-TRF Mean ± SD	p-value
BMI	26.74 ± 1.34	25.59 ± 1.39	0.001
WHR	0.88 ± 0.05	0.84 ± 0.04	0.001
HOMA_IR	3.22± 0.55	2.43 ± 0.53	0.001
FAI	10.13 ± 2.02	7.64 ± 1.42	0.001
Insulin (ìIU/mL)	18.4±2.7	14.1±2.4	0.001
Total Testosterone (ng/dL)	72.5±14.2	61.8±12.3	0.001
Free Testosterone (pg/mL)	3.8 ± 0.7	2.9 ±0.6	0.001
LH	8.11 ± 2.24	6.32 ± 1.93	0.001
FSH	5.69 ± 1.31	6.39 ± 1.31	0.0032
E2	58.69 ± 10.87	63.93 ± 8.95	0.0128
AMH	6.21 ± 1.27	5.72 ± 1.32	0.0265
SHBG	31.32 ± 4.60	35.11 ± 4.29	0.001
DHEAS (ìg/dL)	195.7 ±28.3	182.4 ± 25.6	0.002
TSH (ìIU/mL)	2.43 ± 0.74	2.28 ± 0.65	0.041
Prolactin (ng/mL)	14.6 ± 3.1	13.1 ± 2.9	0.036

Table 2. Categorical Improvements in Ovulatory Function, Menstrual Regularity, and Hyperandrogenism After TRF

Parameter	Improved (n, %)	No Change (n, %)
Ovulatory Status	29 (60.4%)	19 (39.6%)
Menstrual Regularity	28 (60.9%)	18 (39.1%)
Hyperandrogenism (FAI = 8)	35 (63.6%)	20 (36.4%)

Figure 1. Comparison of Mean Values of Clinical Parameters Before and After Time-Restricted Feeding (TRF)

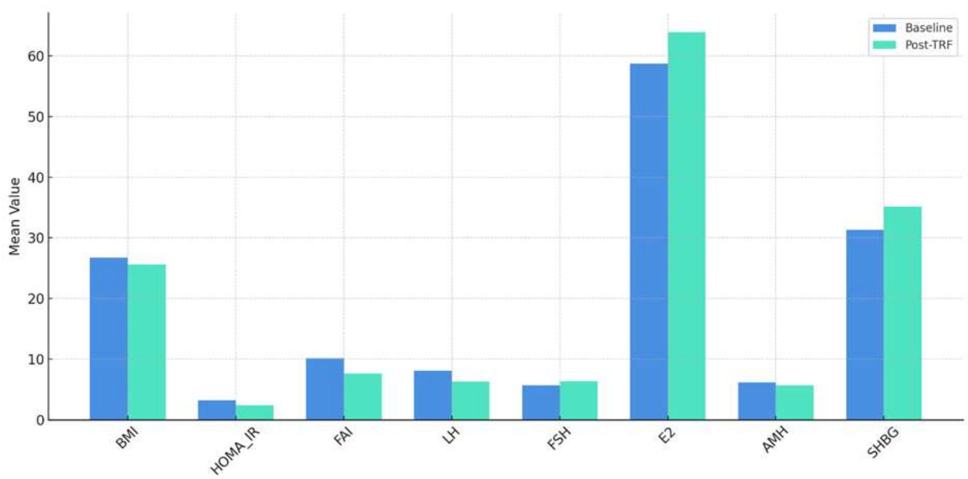

Table 3. Correlation Between ÄBMI and Changes in Hormonal and Metabolic Parameters

Parameter Change	Correlation with Ä BMI (r)	p-value
ÄHOMA_IR	0.06	0.622
ÄFAI	0.26	0.0376
ÄSHBG	0.04	0.7615
ÄLH_FSH_ratio	0.08	0.5492

Table 4. Adherence and Tolerability to TRF Regimen

Adherence Indicator	Value
Completed all 6 weeks	63/83 (75.9%)
Reported = 90% adherence to TRF	52 (82.5%)
Experienced adverse events	4 (6.3%)
Most common side effects	Headache (3.2%), Fatigue (3.1%)

feeding.[15] Other intermittent fasting strategies, such as the 5:2 diet (involving two calorie-restricted days per week), have also been shown to produce weight loss outcomes comparable to daily calorie restriction over a 6-month period in overweight young women.[16] Given the well-established connection between body composition and insulin resistance and the critical role that insulin resistance plays in the pathophysiology of PCOS our findings suggest that TRF could serve as an effective frontline intervention in the management of PCOS.

Insulin resistance (IR) is a central feature of PCOS and contributes to both its metabolic and reproductive disturbances.[17] In this study, TRF resulted in a significant reduction in HOMA-IR, aligning with previous interventional studies suggesting that intermittent fasting enhances insulin sensitivity by promoting ketogenesis, reducing oxidative stress, and modifying circadian insulin regulation.[18] This reduction in HOMA-IR levels from 3.22 to 2.43 ($p < 0.0001$) indicates an improvement in the condition and may prevent long-term risks of metabolic syndrome and type 2 diabetes. Hyperandrogenism, an essential feature of PCOS, was evaluated using the Free Androgen Index (FAI). This was found to have decreased significantly after the intervention. Insulin levels have been found to augment androgen secretion by ovarian theca cells and inhibit hepatic SHBG secretion, leading to an increase in free testosterone levels.[19] The reduction in FAI levels from 10.13 to 7.64, with a marked increase in SHBG levels, indicates hormonal rebalancing due to improved insulin levels and possible effects on hepatic SHBG secretion.[20]

The ratio of LH to FSH, which is usually high in PCOS due to increased frequency of pulsatile discharge of GnRH, was significantly reduced after TRF. This is due to decreased levels of LH and slightly increased levels of FSH, which restored homeostasis to the hypothalamic-pituitary-ovarian axis. This is important, as high levels of LH are associated with anovulation and impaired follicular development.[21] Our study is consistent with previous research that has shown that caloric restriction or intermittent fasting can modulate neuroendocrine function to improve ovulation cycles. Moreover, elevated estradiol levels and a slight decrease in AMH levels also support the idea of increased ovarian responsiveness and follicular recruitment post-TRF. AMH levels are usually elevated in women suffering from PCOS due to the presence of numerous pre-antral follicles. However, slight declines in AMH levels have been associated with better follicular dynamics and lower follicular arrest.[22] These hormonal changes were accompanied by clinical improvements in menstrual regularity and ovulation, which were achieved in over 60% of women. TRF was also associated with a significant reduction in BMI. This reduction was moderately correlated to changes in FAI ($r = 0.26$; $P = 0.0376$). Even though weight reduction was minimal, small weight losses are known to have a favorable effect on insulin and androgen levels. Notably, changes in BMI were not correlated to HOMA-IR and SHBG levels. This suggests TRF's effects on weight reduction and weight loss may not be solely responsible for its effects on metabolic parameters and may possibly include the regulation of metabolic hormones via the circadian rhythm.[23] Significantly, the TRF regimen showed good adherence rates (82.5%) and few side effects, such as fatigue and headaches. This confirms the literature that highlights the safety and tolerability of intermittent fasting regimens among women, even with hormonal imbalances.[24,25] The feasibility of the TRF regimen without the use of pharmacological agents makes it an interesting adjunct to lifestyle-based interventions for the management of PCOS. In the face of the global burden of PCOS and the limitations of pharmacological interventions, such as the side effects and poor adherence rates, the use of the TRF regimen appears to offer promise as a cost-effective and patient-centered approach to the management of PCOS, particularly in resource-scarce settings and among cultures that are resistant to pharmacological interventions. In addition, the simplicity of the dietary regimen, with an 8-hour feeding window, makes it a promising approach.

Limitations: However, some limitations have to be noted. Firstly, the non-randomized and retrospective nature of this study limits causal relationships. Secondly, the lack of control group and self-reported data on adherence might have created reporting and selection biases. Lastly, the duration of this study was only 6 weeks, and long-term effects cannot be generalized. Although the hormonal and metabolic effects of this treatment were substantial, conception and cardiovascular outcomes were not assessed. Further well-designed studies, like randomized controlled trials, with long-term follow-ups and mechanistic studies, like clock gene expression and cortisol levels, might provide further insights.

CONCLUSION

This research offers convincing proof of the benefits of a 6-week, 8-hour time-restricted feeding regimen, which has a positive impact on the metabolic and reproductive health of women living with PCOS. It was found that the regimen was effective in reducing insulin resistance, BMI, and androgens, while also facilitating the rebalancing of hormones, ovulation, and menstruation. Given the high adherence rate and lack of side effects, the TRF regimen offers promise as a non-pharmacological intervention that works in tandem with the natural rhythms of the human body, making it a suitable intervention for the management of PCOS, especially for women who are not responding to the usual treatments for the condition.

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Authors Contribution:
Huma Habib: Contributed To The Study Conception, Design, And Manuscript Drafting.
Fatima Lajbar: Participated In Data Collection, Literature Review, And Manuscript Preparation.
Atif Ullah: Assisted In Laboratory Data Interpretation And Statistical Analysis.
Hamasa Gul: Provided Clinical Supervision, Contributed To Study Design, And Critically Revised The Manuscript.
Fazal Rahim: Contributed To Data Interpretation, Clinical Correlation, And Manuscript Editing.
Miraj Ahmad: Supervised The Overall Study, Contributed To The Methodological Framework, And Served As The Corresponding Author Responsible For Final Manuscript Approval.

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