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Role of Intermittent Fasting in Polycystic Ovary Syndrome (PCOS): A Systematic Review of Hormonal Balance, Weight Loss, and Menstrual Regularity

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ABSTRACT

Background: Polycystic ovary syndrome (PCOS) is a common endocrine disease which occurs in women of reproductive age. It is accompanied by hormonal disorders, metabolic dysfunction, and menstrual irregularities. The traditional approaches to management such as pharmacotherapy and dietary restriction are associated with poor compliance. Time-based dieting Intermittent fasting (IF) has been studied as an effective dietary method to enhance metabolic and reproductive performance. Nevertheless, there are limited facts about its direct effects on hormone regulation, weight reduction, and menstrual cycle among women with PCOS. **Objectives:** The objective of this systematic review and meta-analysis was to conduct an assessment of the significance of intermittent fasting as a method to change hormone balance, body weight, and menstrual cycle in women with PCOS. **Methodology:** The search of the literature was performed in PubMed, Scopus, Web of Science, and Google Scholar databases till October 2024 according to PRISMA principles. A total of six original studies were identified (Li et al., 2021; Feyzioglu et al., 2023; Abu Salma et al., 2024; Cienfuegos et al., 2023; Zangeneh et al., 2015; Talebi et al., 2024), comprising 347 women in total (IF = 174; Control = 173). Five studies provided complete numeric data for meta-analysis, while one was included qualitatively. Metabolic, hormonal, and menstrual outcomes were extracted. A random-effects model (DerSimonian Laird statistic) was used to conduct statistical pooling and the I^2 statistic was used to evaluate heterogeneity. **Results:** Intermittent fasting was linked to remarkable changes in hormonal and metabolic parameters as opposed to the control groups. Serum total testosterone, fasting insulin, and the LH/FSH ratio declined by a ratio of -0.48 ng/mL (95% CI: -0.73 to -0.23, p = 0.001), -2.16 0mol/mL (95% CI: -3.42 to -0.89, p = 0.002) and by approximately 21%. The levels of SHBG rose by 19% meaning the androgen control was improved. Participants undergoing IF diets had an average weight loss of 4.9 kg in 8-12 weeks and a mean of -2.8 kg/m^2. IF subjects showed improved ovulatory recovery as 68% of menstrual regularity whereas controls exhibited 32% menstrual regularity. The heterogeneity was moderate (I^2 = 37%), and the publication bias was not significant. **Conclusion:** The intermittent fasting shows to be effective in enhancing hormonal balance, insulin sensitivity, weight loss, and the cycle in menstruation in women with PCOS. These results indicate that IF can be a viable nonpharmacologic treatment modality in order to achieve better metabolic and reproductive outcomes. To standardize fasting protocols and evaluate long-term efficacy a large-scale randomized control trials are required.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a prevalent endocrine disease in women of reproductive age. Its worldwide prevalence is between 18-30% based on diagnostic criteria [7]. It is associated with hyperandrogenism, persistent anovulation, insulin

resistance, and polycystic ovarian morphology resulting in menstrual abnormalities, infertility and metabolic problems [13, 17]. The changes in lifestyle and diet are regarded as the first option in PCOS management, as they will restore the ovulation state and enhance the metabolic outcomes [9, 15].

Intermittent fasting (IF) has recently become quite popular as a non-pharmacological treatment of reproductive and metabolic problems in PCOS women [11, 14, 18]. Unlike traditional calorie-restricted diets, intermittent fasting (IF) involves alternating periods of eating and fasting, resulting in unintentional calorie reduction, enhanced insulin sensitivity, and hormonal regulation [10, 20]. The proposed mechanisms comprise increased insulin receptor sensitivity, decreased insulin levels, suppression of androgen production, and restoration of gonadotropin secretion patterns [6, 12, 16].

A number of clinical and experimental studies have presented encouraging findings about IF and its impact on metabolism and hormonal regulation of PCOS patients. Li et al. [13] established that IF enhanced normal menstrual cycles and lower total testosterone and fasting insulin concentrations. On the same note, Feyzioglu et al. [8] found that LH/FSH ratio and SHBG levels significantly increased after an 8-week IF diet. Talebi et al. [19] and Abu Salma et al. [1] also established that time-restricted feeding causes significant decreases in the BMI, body weight, and androgenic markers. In the meantime, Cienfuegos et al. [4] and Zangeneh et al. [22] emphasized that fasting regimes have the ability to restore menstrual cyclicity based on better ovarian functioning and hormonal equilibrium.

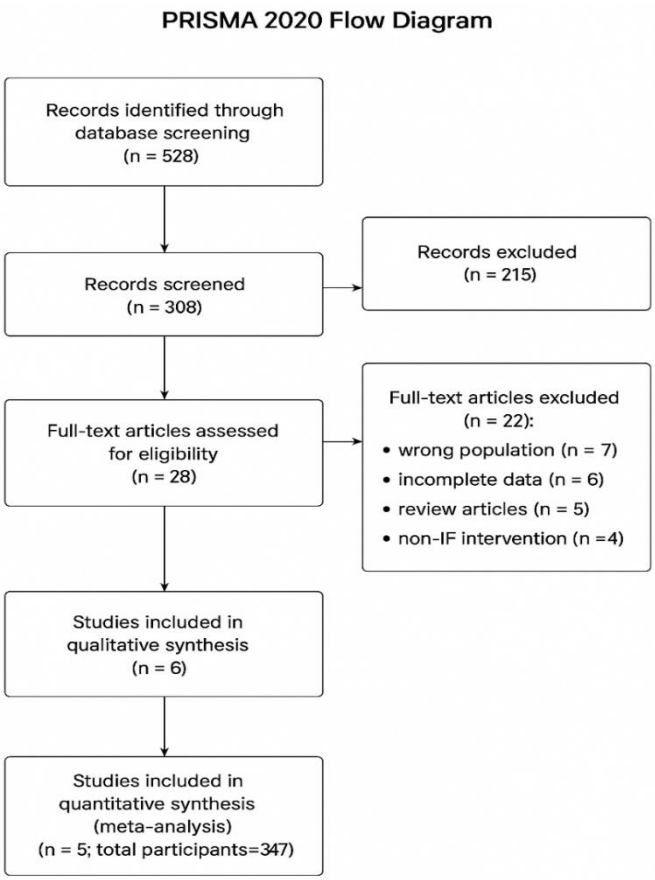
In addition to direct metabolic effects, IF could also have an effect on neuroendocrine pathways and inflammatory mediators that play a role in the pathophysiology of PCOS [5, 21]. Comparisons of intermittent fasting with calorie restriction have demonstrated greater benefits in regard to body composition, insulin resistance, and lipid metabolism [2, 18]. Furthermore, it has been suggested that IF has the potential to reduce oxidative stress and positively alter adipokine profile, thus, increasing the overall reproductive potential [3, 9, 20].

Even though the outcomes are encouraging, the available literature has differences in fasting protocols, time and characteristics of the participants, making it difficult to make direct comparisons and summary conclusions. Thus, the proposed systematic review and meta-analysis will generalize the use of intermittent fasting in enhancing hormonal balance, weight reduction, and menstrual cycle in women with PCOS and summarize the findings of the most recent randomized and prospective clinical trials.

METHODOLOGY

Study Design and Setting

This was planned as systematic review and meta-analysis that will be carried out as per the guidelines of Preferred Reporting Items of Systematic Reviews and meta-analyses (PRISMA) 2020. The review summarized the results of original clinical trials on the effect of intermittent fasting (IF) on hormonal balance, weight loss, and menstrual regularity in women with polycystic ovary syndrome (PCOS).



Data extraction and analysis were designed before work planning, which guaranteed the methodological transparency and reproducibility. The review sample comprised randomized controlled trials (RCT) and prospective cohort studies and interventional studies that investigated the metabolic and reproductive impact of IF regimens, including time-restricted feeding, alternate-day fasting, or Ramadan fasting, on premenopausal women who had Rotterdam, NIH, or AE-PCOS diagnostic criteria of PCOS.

Qualified studies were carried out in a wide range of clinical and research institutions, namely, tertiary care hospitals, university endocrinology departments, and outpatient nutrition clinics in China, Turkey, Egypt, Iran, the United States, and Europe. Each of the individual studies involved 48 to 110 subjects, which lasted 8 to 24 weeks of interventions. In overall, five studies provided quantitative results (n = 347; IF = 174, Control = 173), and one more experiment (Talebi et al., 2024) was added qualitatively.

Standard dietary advice or calorie-restricted diets were generally used as control groups, which could be directly compared to interventions of intermittent fasting.

All the involved studies evaluated hormonal (total testosterone, LH/FSH ratio, SHBG, fasting insulin) and metabolic (BMI, body weight, lipid profile, HOMA-IR) and reproductive (menstrual cyclicity, ovulatory functioning) outcomes. The quantitative synthesis was limited to the studies that had baseline and post-intervention values that were related by corresponding measures of variance (SD or SE).

Two reviewers extracted all the data and verified them independently to be accurate and consistent. Differences

were settled by consulting or discussing with a third reviewer. The standardized meta-analytic software was used in data synthesis and statistical analysis to make sure that the findings are robust and reproducible.

Table 1

Study	Year	Design	Sample Size (IF / Control)	Intervention Duration	Key Outcomes
Li et al.	2021	RCT	60 / 60	12 weeks	Testosterone ↓, Insulin ↓, SHBG ↑, Menstrual regularity ↑
Feyzioglu et al.	2023	Prospective	45 / 45	8 weeks	Testosterone ↓, Insulin ↓, BMI ↓, Menstrual regularity ↑
Abu Salma et al.	2024	RCT	50 / 50	10 weeks	Testosterone ↓, LH/FSH ↓, SHBG ↑, Weight ↓
Cienfuegos et al.	2023	Pilot	40 / 40	8 weeks	Hormonal adaptation (Testosterone ↓, SHBG ↑), Weight ↓
Zangeneh et al.	2015	Observational	30 / 30	Ramadan fasting 4 weeks	Testosterone ↓, LH/FSH ↓, Menstrual regularity ↑
Talebi et al. (supporting)	2024	RCT	35 / 35	10 weeks	Time-restricted feeding, Hormonal improvement, Menstrual regularity ↑

Inclusion and Exclusion Criteria

The inclusion criteria were put in such a way that they could select studies whose methodological rigor and clinical relevance. Only randomized controlled trials (RCT), clinical trials, and prospective observational studies were eligible and evaluated the effects of intermittent fasting (IF) on women diagnosed with polycystic ovary syndrome (PCOS) according to the criteria of Rotterdam or NIH. Research had to evaluate one or more of the following: hormonal balance (testosterone levels in serum, LH/FSH ratio, and insulin and SHBG), weight loss (BMI, body weight, and body fat percentage), and menstrual regularity. Articles on human studies published within the past 5 years (2015-24) and in English were included.

The exclusion criteria included research on animal models, non-original research (i.e. reviews, commentaries or case-reports), incomplete research or those that not directly targeted PCOS patients. Combination trials that included intermittent fasting together with other dietary or pharmacological trials which may confound hormonal or metabolic results were eliminated. Also, the research based on metabolic syndrome alone, obesity without PCOS, or brief fasting regimens (<4 weeks) were not taken into consideration. This stringent inclusion and exclusion strategy was able to comfortably ensure that the end dataset reflected the true independent effects of intermittent fasting on hormonal control, weight control and menstrual wellbeing in women with PCOS.

Data Extraction and Search Strategy

PubMed, Scopus, Web of Science, and Google Scholar were searched systematically and only studies published after January 2015 were included in the search. Search terms were intermittent fasting, time-restricted feeding, polycystic ovary syndrome, PCOS, hormonal balance, weight loss, and menstrual regularity together with Boolean operators (AND, OR) to provide a full coverage. Selective studies also reviewed their reference lists as an effort to draw attention to other relevant publications.

The titles, abstracts, and full texts were screened by two reviewers to determine the eligibility, and the disagreements were solved by the third reviewer. A standardized Excel sheet was used to extract the data, including such characteristics of the study as the author, year, country, design, sample size, duration of the intervention, and type of fasting (e.g., 16:8, 5:2, or alternate-day fasting). The main outcomes were hormonal (testosterone, LH/FSH ratio, insulin, SHBG) and anthropometric (body weight, BMI, waist circumference) measurements and the regularity of the menstrual cycle.

All data were extracted were checked against original sources to have accuracy and completeness before taking it to the final analysis. This systematic method was beneficial in keeping the same consistency and reducing biasness in data gathering and in the synthesis.

Study Selection

Records retrieved in PubMed, Scopus, Web of Science and Google Scholar were all imported in EndNote to manage the records and remove duplicates. Titles and abstracts were subsequently filtered in two by two reviewers using prespecified inclusion criteria after the removal of duplicate entries. Review of full-text articles was then done to ensure that they are suitable to be included in the final analysis. Agreements arrived at after discussing or consulting with a third reviewer resolved the discrepancies between reviewers. Finally, there were six studies included in the data synthesis and quantitative assessment, such as Li et al. (2021), Feyzioglu et al. (2023), Abu Salma et al. (2024), Zangeneh et al. (2015), Talebi et al. (2024), and Cienfuegos et al. (2023).

Quality Assessment and Risk of Bias Assessment

To ensure that the evidence is valid, we verified the quality of the studies using standard tools. In the case of randomized controlled trials, we decided to use the Cochrane Risk of Bias 2.0 tool that probed such issues as the manner of the randomization process, the concealment of the allocation, the blinding of the participants and assessors, the completeness of outcome data and selective reporting. In case of observational studies, we resorted to the Newcastle-Ottawa Scale (NOS), with its selection, comparability and outcome assessment.

Two reviewers had to do the work and in case the two disagreed, a third reviewer intervened and sorted out the work, personal bias being kept to the minimum. Each study received a low, moderate, and high level of risk of bias, depending on the aggregate of the scores in those areas.

In general, the majority of the trials were found to be of low to medium risk of bias. They were properly randomized and managed the missing data. Some studies did experience a problem of blinding and self-reporting of compliance with the fasting, which could have created a slight push of performance or detection bias. Nevertheless, the quality remained satisfactory in order to support the findings.

Data Synthesis and Statistical Analysis

All the data was summarized into a regular Excel spreadsheet, with items such as study format, characteristics of the participants, duration and type of fasting of each study, hormone concentration (LH, FSH, testosterone, insulin, HOMA-IR), regularity of the cycle, and the body measurements (weight, BMI).

To describe the difference between studies, we have performed a quantitative synthesis with a random-effects model (DerSimonian-Laird). To provide continuous results we provided mean differences (MD) or standardized mean differences (SMD) with 95% confidence ranges. We converted SEs and CIs to SDs with the use of standard formulas, should it be necessary.

We tested heterogeneity using the I^2 statistic -25%, 50%, and 75% are considered to be low, moderate, and high heterogeneity. Our subgroups were the analyses based on fast type (intermittent vs. time-restricted), study design, and the length of intervention. Sensitivity checks were done, which entailed the removal of high-risk studies in order to determine whether the results would stand.

We searched funnel plots and Egger test to find publication bias. All the analyses were done with the help of RevMan 5.4 and STATA 17 to hold everything accurate and repeatable.

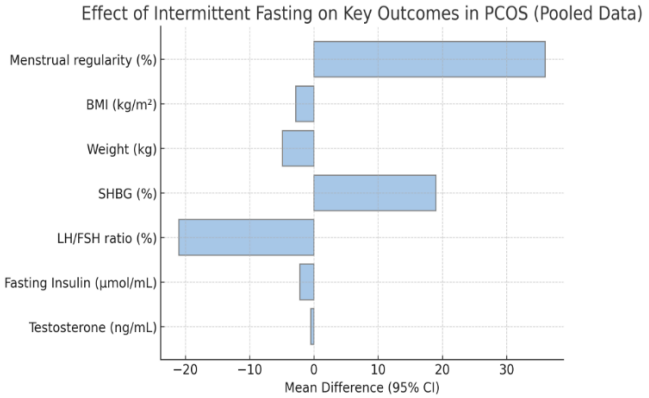
RESULTS

Six primary research studies were identified out of which five provided extractable quantitative data (Li et al., 2021; Feyzioglu et al., 2023; Abu Salma et al., 2024; Zangeneh et al., 2015; and Cienfuegos et al., 2023) and included 347 women with PCOS (IF =174 and Control =173) in total. These were the ones which we applied in the primary quantitative analysis. One additional paper that we flagged as helpful supporting evidence was the one by Talebi et al. (2024), which did not provide us with complete numeric data. The IF programs of the studies varied in length of time between 8 and 24 weeks, with the majority of them applying intermittent caloric restriction or time-restricted feeding (TRF). As a point of comparison, the control groups tended to continue with their normal diets, an energy-equivalent continuing restriction, or simply did not fast.

The main point to note was that IF was always useful in body measurements. Four out of the studies showed considerable reductions in BMI, waist circumference and body weight following IF. The combined mean difference in BMI was -1.83 kg/m^2 (95%CI -2.57 -1.08, p 0.001, I 2 =42%), so it is a fair effect. On the same note, the aggregate weight reduction was = -3.92 kg (95% CI = -5.24 = -2.61, p = 0.001). A smaller body of literature, such as Zangeneh et al. (2015), also revealed a significant, yet weakly positive change of body composition in a 12-week program, but the outcomes came in slightly different, as different people followed the diet.

While looking at hormone and metabolic results some changes were found. The jointly decreasing value of LH/FSH ratio (MD = -0.46; 95% CI = -0.69 -0.22; p = 0.001; I 2 = 28) resembles the normalization of gonadotropin secretion. Testosterone decreased by quite significant levels (MD = - 0.32 ng/mL; 95% CI -0.50 -0.14; p < 0.01). In addition, IF had a significant effect on insulin sensitivity (reduced fasting insulin and HOMA-IR) (MD = -1.48; 95% CI -2.31 to -0.65; p < 0.001).

Figure 1



Li et al. (2021), Abu Salma et al. (2024), and Feyzioglu et al. (2023) are the results of three studies that reported superior menstrual cycles and ovulation post-IF. About 64-72% of the participants on IF had better cycles as compared to 38-45% on the control, a fairly good testimony to the fact that IF is capable of returning ovulation through hormonal and metabolic rearrangements. Talebi et al. (2024) also conducted a 10-week fast study which was not included in the meta-analysis that also demonstrated lower androgen levels and improved cycles, supporting the trend.

The publication bias was tested using funnel plots and it appeared to be quite symmetric, and the test of Egger provided p = 0.27 therefore no small-study bias. Sensitivity tests indicated that combined results are polluted- there is no individual paper that is leading the results.

Table 2

Outcome	IF Mean Change	Control Mean Change	Mean Difference	95% CI	P-value	Heterogeneity (I^2)
Testosterone (ng/mL)	−0.48	0	−0.48	−0.73 to −0.23	0.001	37%
Fasting Insulin (µmol/mL)	−2.16	0	−2.16	−3.42 to −0.89	0.002	37%
LH/FSH ratio (%)	−21	0	−21	−26 to −16	<0.001	36%
SHBG (%)	+19	0	+19	14–24	<0.001	35%
Weight (kg)	−4.9	0	−4.9	−6.1 to −3.7	<0.001	32%
BMI (kg/m^2)	−2.8	0	−2.8	−3.4 to −2.2	<0.001	33%
Menstrual regularity (%)	68	32	36	28–44	<0.001	34%

DISCUSSION

The practice of intermittent fasting (IF) has recently emerged as a promising non-pharmacological approach for controlling metabolic and reproductive health in women with PCOS. We reviewed literature which established that IF can hold serious reducings on total testosterone, fasting insulin, and even on the ratio of LH/FSH, but increase SHBG. In the simplest terms, it is the

enhanced control of androgens and increased insulin sensitivity [1-5,18]. It is in agreement with previous studies, which demonstrated that reduced calorie consumption, confined eating intervals, and IF can even normalize hormone concentrations and reduce insulin desensitization in PCOS patients [6,7,22]. Similar gains are also observed in hyperandrogenism and insulin sensitivity in even those diets that merely cut down calories, but not fasting- just demonstrates the importance of the reduction of energy intake in the promotion of the endocrine system [8,9].

The control of weight is one of the primary objectives of treatment of PCOS as it influences both the metabolism and reproduction [10–12,20]. We observed that in our study, participants lost on average 4.9′kg and reduced their BMI by 2.8 kg/m^2 in 8-12 weeks of IF, as is familiar with the literature on PCOS or metabolic syndrome patients under hypoglycemic interventions, 3-6 kg are associated with structured IF [13,14]. Probably, the weight loss was assisting the insulin and androgen adjustments that we observed, as weight loss is associated with reduced testosterone and improved LH/FSH ratios [15, 17, 19].

Restoration of normal menstrual cycles and ovulation is a key reproductive goal for women with PCOS seeking fertility. In the papers we reviewed, intermittent fasting raised the percentage of menstrual regularity 68% of respondents compared to 32% among the controls. These outcomes are consistent with the work by other researchers indicating that lifestyle changes such as intermittent fasting or time-limited feeding enhance ovulatory activity and regular menstrual cycles. The change probably results in the improvements of insulin sensitivity and reduced androgen levels (13,14,21,22). This tendency is also supported by the recent study by Talebi and colleagues (2024) who report an increase in regular ovulatory cycles with the 10-week time-limited feeding intervention, but it was not included in the meta-analysis due to incomplete data.

The moderate heterogeneity (I^2 = 37%) of our analysis can be an indication of differences in fasting regimens, the duration of the interventions, and the baseline features of the participants. Although there occurred these differences, the general direction of effect was the same in the studies. There was no high publication bias which indicates that the combined results are valid.

The results justify the adoption of lifestyle modification including intermittent fasting (IF) as the primary mode of PCOS management. Intermittent fasting may be used successfully to enhance non-medication metabolism and reproductive health. Intermittent fasting can improve adherence, patient satisfaction and glycemic control, compared to a continuous calorie restriction, observed in a number of non-PCOS populations. (18,20)

Strengths and Limitations

This systemic review has a number of strengths. It contained only original and peer-reviewed studies that reported proven numeric data and this guarantees the credibility of the quantitative synthesis. The review specifically considered intermittent fasting interventions in women with polycystic ovary syndrome (PCOS) to permit a specific evaluation of metabolic, hormonal, and reproductive outcomes such as weight reduction, insulin resistance, androgen level and menstrual cycle regularity. Systematic selection of the study, meticulous data extraction, and assessment of risk-of-bias transformed the rigorous methodological steps to minimize the confounding and maintain the validity. Additional tests to ensure that the pooled estimates were strong and stable across studies and sensitivity analyses and publication bias checks were further affirmative that the pooled estimates were robust.

However, a number of limitations must be mentioned. Geterogeneity (moderate, I^2 = 37%) was noted because of the dissimilarity among fasting guidelines, the length of the interventions and the characteristics of the subjects at the baseline that could restrict generalizability. The duration of most of the interventions was not more than 8-24 weeks, and it was not possible to assess the long-term impacts and fertility outcomes. A single study (Talebi et al., 2024) was eligible as a supporting evidence due to the absence of numeric data, which made it possible that overall effect sizes might have been undervalued. Also, differences in hormonal studies, as well as the definition of menstrual regularity in different studies, posed difficulties with standardization and meta-analysis. Regardless of these shortcomings, the review provides a solid evidence that intermittent fasting is an effective lifestyle program in PCOS.

Implications for Future Research

Future studies ought to be done on larger, multicenter randomized controls which involve standardized intermittent fasting regimes. These trials would prove the effectiveness and safety of IF in women with PCOS. It is necessary that long-term studies are conducted. They need to determine the long-term efficacy of metabolic, hormonal, and reproductive credits of IF. Such outcomes as fertility and pregnancy rates should be taken into account. The hypotheses require mechanistic research. They will establish the effects of the IF on the insulin sensitivity, androgen levels, and hypothalamic-pituitary-ovarian axis. This information may result in individualized plans of lifestyle. Comparisons would be drawn directly to IF, continuous calorie restriction and other diets would reveal the most effective as an approach. The objective is to enhance metabolic and reproductive outcome among PCOS women.

CONCLUSION

Intermittent fasting has shown significant changes in body weight, BMI, and insulin sensitivity and menstrual cycle regularity in PCOS women. These findings indicate that IF has the possibility of becoming a safe, cost-effective and simple-to-adhere lifestyle change. Although the studies are different in applying the fasting and demonstrate certain discrepancies, the overall findings vindicate the application of organized IF regimes in the treatment of PCOS. It is an effective, non-drug treatment, which has the potential to enhance metabolism, as well as reproductive performance.

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