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REVIEW ARTICLE

IMPACT OF DIET RESTRICTION ON HEALTH AND DISEASE: A NOVEL APPROACH TO COUNTER PCOS AND OBESITY RELATED REPRODUCTIVE DYSFUNCTIONS

Ashutosh Ranjan*, Bhawna and Syed Mohd Atif

Depatment of Zoology, University of Lucknow, Lucknow-226007, UP, India

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***Corresponding author:**
Ashutosh Ranjan

ABSTRACT

Background: There has been a significant increase, to epidemic levels, of obese and overweight person of reproductive age, causing impairments to reproductive health. The prevalence of overweight and obesity among men and women of reproductive age is increasing. Obesity has a detrimental effect on male and female health, and of which a particular concern was paid on the reproductive disorders. TRF is being considered as a potential therapy for humans with obesity and related metabolic syndromes. There is strong evidence that high caloric intake has negative impacts on principal body functions, such as impaired endocrine effects, altered liver metabolism, and cholesterol imbalance. **Objective:** In this review we have listed out the potential benefits of different regimen of TRF to improve health and prevent disease progression. **Methodology:** The method used to write this manuscript is purely interpretative and descriptive in nature which is primarily based upon the primary and secondary sources of data like books, journals, and internet. **Conclusion:** Overall, dietary intervention along with TRF could be a novel therapeutic treatment approach for them suffering from metabolic disorders and infertility.

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INTRODUCTION

Nutritional imbalance arise when body does not process the digestion and distribution of macronutrients, such as protein, carbohydrates, fats etc. effectively leading to generation of nutritional deficiency or metabolic abnormality. According to World Health Organization (WHO) report 1 out of 8 people have obesity, in which adult individual of aged 18 years and above contribute 16% obesity (WHO, 2024). This rising metabolic disease have placed a tremendous burden on our healthcare system as well as general public (Narmkul *et al*., 2024). Diabetes and obesity are considered to be most common metabolic disease among adults. It is estimated that by the end of 2030, 439 million adults are expected to suffer with diabetes and obesity (Afshin *et al*., 2017). Other metabolic disease outcome includes cardiovascular disease, musculoskeletal conditions, endometrial cancer, PCOS, infertility in male and female, etc. Given these challenges, dietary modifications have been shown to play a pivotal role in management of metabolic abnormality thus, offering a non-pharmacological, sustainable treatment option (Bulsara *et al*., 2021). The two major dietary intervention include caloric restriction (CR) and intermittent fasting (IF) (Kalafi *et al*., 2024; Welton *et al*., 2020).The CR regimen include practice of reducing energy intake below normal level without causing malnutrition. It involves long-term daily reduction of food intake which result in improving metabolic biomarkers thus, potentially reducing the risk of chronic disease like obesity and diabetes. On the other hand, IF is an alternate strategy of CR that have been developed to effectively treat and monitor metabolic abnormality including obesity, diabetes, as well as infertility. The IF regimen include limiting the amount of time spent on food or drink intake for a specific period, and/or alternate period of fasting and feeding without imposing caloric restriction (Khalafi *et al*, 2024). There are three primary regimen of IF: time-restricted feeding (TRF), alternate-day fasting (ADF), the 5:2 diet, and other variations (Nye *et al*., 2024). TRF, food intake is performed in a specific time window, typically 4-10 h, with unrestricted caloric intake during that eating window. Outside this window, only non-caloric drink or beverages like water, unsweetened tea, or black coffee is allowed. Due to its practicality and ability to align with our circadian rhythm, TRF has been intrinsically linked to metabolic and endocrine regulation (Wilkinson at el., 2020). In ADF, on the day of fasting, energy intake is restricted to only water or minimal caloric intake that is interspersed with non-fasting days that allow unrestricted energy intake or food consumption. Recent findings have suggested that ADF regimen has a great potential in reducing body weight, improving insulin-sensitivity, fasting glucose level-factors that are crucial in the management of PCOS, diabetes etc. (Stekovic *et al*., 2020). The 5:2 diet is variation of ADF where two non-consecutive fasting days are restricted to

only 20-25% energy intake of daily requirement followed by 5 days of unrestricted food intake. This not only prevent metabolic and psychological stress of continuous dieting but balances the caloric restriction with sustainability (Carter *et al*., 2018). Today, a growing dietary trend in developed and developing countries is IF, which is now a days often encouraged and adopted to loose body weight, achieve optimum glycemic index, and improved metabolism. IF have also been shown to prevent apoptosis, autophagy, oxidative stress etc. (Golbidi *et al*., 2017). Looking into the long term potential of IF and its relevance in prevention of diseases, it could be implemented as an alternate strategy to counteract side effect arises due to disturbed metabolism. Therefore, a thorough understanding of IF is required to manage disorder arises due to disturb metabolism, life-style modifications, and also create public awareness of the potential outcomes of IF. In this article we have reviewed several aspect of IF in the implication of health and disease, and its potential challenges and future.

IF and PCOS: Rising prevalence of exposure to endocrine disruptors, life-style modifications, environmental changes, and genetic pre-dispositions have severely impacted the female reproduction viz. gynecological disorder, diabetes, cardiovascular disease, and most notably polycystic ovary syndrome (PCOS). Today, PCOS contributes to majority cause of female infertility. PCOS is characterized by morphological, hormonal, and metabolic abnormalities leading to characteristic symptoms like anovulation, hyperinsulinemia, and hyperandrogenism (Belenkaia *et al*., 2019). The coexistence of hormonal disturbances along with metabolic abnormality, including obesity, insulin resistance (IR), and hyperinsulinemia highlights the importance of life-style modifications or interventions in the management of PCOS. Recent findings have suggested the pivotal role of dietary modifications in amelioration of PCOS and mitigates its related complications. These interventions are beneficial in managing oxidative stress, inflammation, and metabolic abnormality. Thus, it is offering a non-pharmacological and sustainable treatment option (Bulsara *et al*., 2021; Juhasz *et al*., 2024).

Among the various dietary strategies, IF is proved to be a promising strategy in the mitigation of PCOS. Earlier studies have suggested the improvement in menstrual cycle abnormalities compared to placebo group following the IF regimen (Li *et al*., 2021; Talebi *et al*, 2024). The hormonal profile revealed that, IF lead to reduced Anti-Mullerian Hormone (AMH), follicle-stimulating hormone (FSH), and luteinizing hormone (LH) compared to healthy control females (Li *et al*., 2024; Cldwell *et al*., 2011; Feyzioglu *et al*., 2023). In contrast, there are certain report which suggest no changes in AMH, FSH and LH level (Methley *et al*., 2014; Ranneh *et al*., 2025). A notable reduction in testosterone (T), free androgen index (FAI), and estradiol (E2) were also observed in IF regimen (Cienfuegos *et al*., 2022). These findings suggest that IF could be an alternate strategy for the management of PCOS and its related complications. However, further research is needed to strengthen the effect of IF on hormonal profile like FSH, LH and T which are crucial in PCOS progression. An improved FSH and LH level are pivotal for menstrual cycle regulation and improved fertility. The hormonal concentration in PCOS female with and without IF is given in Table 1.

Table 1. Effect of intermittent fasting on reproductive hormonal profile of female

Hormone	Hormone concentration in PCOS	Hormone concentration after IF	Reference
Estradiol	High	Reduced	Jakubowicz, 2013
Androgens	Testosterone-High DHEA-S-High Androstenedione-High	Testosterone-Reduced DHEA-S-Reduced Androstenedione- Reduced	Li, 2021 Harvie 2011
SHBG	Low	Increased	Deswal 2018; Harvie 2011
Gonadotropins	LH & FSH-Reduced	LH & FSH-Unchanged	Li 2021
Prolactin	Not linked directly	Unchanged	Harvie 2011

IF can boost male fertility: Growing evidence is now suggesting that, approximately 10-20% of couple worldwide are unable to conceive due to male factor infertility. Around 50% cases of infertility is attributed to male partner. The male subfertility include low sperm count, sperm quality, sperm motility that are significantly affected by lifestyle changes (Kohn and Schuppe, 2021). Psychological stress including unfulfilled desire for children also creates a mental pressure leading to reduced fertility. The conventional method that are being prescribed for improving the sperm parameters are vitamins, Coenzyme Q10, zinc, selenium, carnitine nutrients rich diet etc. In addition to this fasting intervention have also now been shown to improve sperm quality and concentration. In a recent study by Zhang *et al*., 2025, IF has significantly improved the testicular morphology, and weight gain in obesity-induced male infertility mice model. There was increased reproductive competence and increased bioactive metabolites gene expression. Thus, IF can act as an alternate strategy in mitigation of male factor subfertility.

IF and obesity: Intermittent fasting (IF) is an increasingly popular strategy for weight loss and improved metabolic health. IF regimes involve deliberate implementation of fasting windows ranging from 12 to 72 hr. Please replace with this sentence: "Such strategies due to their promising results, are gaining social popularity but are not yet completely understood". Specifically, the effects of time-restricted feeding (TRF), a specific form of IF in which participants undergo daily fasting periods lasting about 16 hour, is among the most popular yet understudied regimens. A recent findings of Deota and Panda, 2020, found that mice who eat within a set amount of time (8-12 hour) resulted in slimmer, healthier mice than those who ate the same number of calories in a larger window of time, showing that the temporal pattern of eating may be as important as the nutritional content of the diet. If the benefits of this “time-restricted eating” (TRE) hold true in humans, it could have profound impacts on treating overeating disorders, diabetes and obesity. TRF has the potential for improving several key markers of health. One of the most consistent results reported showed a decrease in fasting insulin level, which supports the theory that TRF may improve insulin function. In a study reported by Gabel *et al*., 2018 showed that Twenty-three participants who were obese (20 women, 3 men) participated in a TRF regimen (ad libitum eating from 10 AM to 6 PM and water-only fast from 6 PM to 10 AM) every day for 12 weeks have more weight loss and reduced energy

intake, and decreased systolic blood pressure. This indicate that TRF produces a mild caloric deficit and weight loss without calorie counting and may lower blood pressure. In a study by Hutchison *et al*., 2019, fifteen men at risk for type-2 diabetes mellitus (T2DM) underwent 2 different 7-day TRF regimens, either an early TRF schedule (caloric intake confined to 8 AM to 5 PM) or a delayed TRF (caloric intake confined to 12 PM to 9 PM). The result showed reduced blood glucose, circulating fasting triglycerides and reduced insulin level. Overall, TRF improved glycemic responses in individual. Another very important study by Moro *et al*., 2019 where thirty-four resistance-trained men were randomly assigned TRF (caloric intake confined from 1 PM to 8PM) or normal diet (caloric intake confined to 8 AM to 8 PM). The result demonstrated that TRF, when combined with resistance training, significantly reduced fat mass while maintaining muscle mass.

This study particularly elucidates some of TRF's potential to encourage healthy body composition, especially when combined with physical activity. In a study of Sutton *et al*., 2018, eight men with prediabetes who were considered overweight underwent 5 weeks of TRF (water-only fast from 8 AM to 3 PM) compared with a normal diet (12 hour eating window, beginning 6:30 AM to 8:30 AM) in a randomized order, separated by a 7-week was houtperiod. The result showed that TRF elicited significant decrease in mean insulin and IR while also improving B-cell responsiveness. TRF also caused a notable decrease in mean (SD) systolic and diastolic blood pressure.

CONCLUSION

Our current lifestyle has led us to eating and increasing times/irregular hours and erratic patterns of eating increasing the risk of chronic diseases, including cancer, cardiovascular diseases, infertility, and other related chronic conditions. Shift in light–dark cycles curtails fertility competence in mice. Recently, dietary strategies that focus on the timing of eating and duration of fasting (i.e., chrono-nutrition) have been shown to improve metabolic health in humans. Specifically, TRF and calorie restriction (CR) limiting food access within the active phase is a dietary strategy that has emerged as a practical intervention for improving insulin resistance along with other markers of whole-body health such as reproductive health. Given the increased frequency of diabetes induced hypogonadism in male, lifestyle disorder like PCOS in female have resulted in reduced fertility. Therefore, it is crucial to understand the contribution of time restricted feeding (TRF) and calorie restriction (CR) regimen of feeding in order to mitigate health related issues in non-invasive way.

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