

PHYSIOLOGICAL AND BIOCHEMICAL EFFECTS OF INTERMITTENT FASTING ON INSULIN SENSITIVITY AND GLUCOSE METABOLISM: A SYSTEMATIC REVIEW

Hina Hakim¹, Sara Yar Khan¹, Muhammad Ishraq², Aizazullah³, Farzana Salman⁴, Marina Hidayat⁵

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²Lecturer, Department of Physiology, Peshawar Medical and Dental College, Peshawar

³Lecturer, Department of Biochemistry, Peshawar Medical and Dental College, Peshawar

⁴Professor, Department of Physiology, Peshawar Medical and Dental College, Peshawar

⁵Assistant Professor, Department of Physiology, Peshawar Medical and Dental College, Peshawar

Correspondence

¹Sara Yar Khan, Assistant Professor, Department of Biochemistry, Peshawar Medical and Dental College, Peshawar

☎: +92-332-4992929

✉: asad_sarwar77@gmail.com

INTRODUCTION

Intermittent fasting is a way of eating that involves alternating between fasting and eating. Intermittent fasting is a method of eating that primarily emphasises when to eat rather than how much to eat, in contrast to the other diet plans mentioned, which are calorie-restricted diets.¹ Commonly used methods include time-restricted eating, early time-restricted feeding, alternate-day fasting, modified fasting, 5:2 fasting, and periodic 24-hour fasts. The concept of IF has gained significant traction in recent years, sparking an interest in its use for weight management, metabolic control, and

cardiovascular disease prevention.² Many aspects of metabolic health involve insulin sensitivity and glucose metabolism. Lower insulin sensitivity is associated with hyperinsulinaemia, impaired fasting glucose, type 2 diabetes Mellitus, metabolic syndrome, fatty liver disease and cardiovascular risk. Standard therapies involve diet change, exercise, weight loss, and/or medications (where needed). Long-term sustaining continuous calorie restriction, however, is difficult. Intermittent fasting has thus been suggested as an alternative or adjunct lifestyle strategy that would yield beneficial metabolic effects by decreasing meal frequency, decreasing the amount of consumed energy,

ABSTRACT

OBJECTIVES

This study aimed to review the physiological and biochemical effects of intermittent fasting on insulin sensitivity and glucose metabolism in human studies published between 2019 and 2025.

METHODOLOGY

A literature search was conducted in electronic databases, such as PubMed, Google Scholar, ScienceDirect, SpringerLink, Wiley Online Library and Cochrane Library, for original human studies from January 2019 to December 2025. The studies included in the analysis were randomised controlled trials, randomised clinical trials, open-label randomised trials, randomised crossover trials and prospective interventional trials of intermittent fasting or time-restricted eating. There were no reviews, meta-analyses, narrative articles, case reports, animal or in vitro studies, nor pilot studies. The following data were collected for study characteristics, insulin sensitivity, glucose metabolism, physiological outcomes, biochemical markers, and risk of bias.

RESULTS

Twenty-one original studies were included. Most studies reported favourable effects of intermittent fasting on glucose regulation, fasting insulin, HOMA-IR, HbA1c, continuous glucose monitoring outcomes, body weight, waist circumference, lipid profile, and cardiometabolic markers. Benefits were more consistent among adults with obesity, metabolic syndrome, type 2 diabetes, polycystic ovary syndrome, and increased diabetes risk. Early time-restricted eating and 8–10-hour eating windows showed more promising metabolic effects than less structured fasting patterns. However, the magnitude of benefit varied across studies.

CONCLUSION

Intermittent fasting may improve insulin sensitivity, glucose metabolism, and related physiological and biochemical outcomes, especially in metabolically high-risk adults. However, heterogeneity in fasting schedules, intervention duration, population characteristics, and outcome measures limits direct comparison. Larger long-term randomised trials are needed to identify the safest and most effective fasting protocols.

KEYWORDS: Intermittent Fasting; Time-Restricted Eating; Insulin Sensitivity; Glucose Metabolism; HOMA-IR; HbA1c; Metabolic Syndrome; Type 2 Diabetes

increasing circadian rhythmicity, improving fat oxidation, and modifying insulin and glucose responses.³ There are several biological mechanisms that could account for the effect of intermittent fasting on glucose metabolism. Insulin drops during fasting, hepatic glycogen is depleted and lipolysis and fatty acid oxidation increase. Frequent fasting may lead to better metabolic flexibility, decreased ectopic fat deposition, better insulin signalling and decreased postprandial glucose exposure.⁴ Early time-restricted eating could be even more beneficial due to the fact that glucose tolerance and insulin sensitivity tend to be higher in the morning compared to the evening. Thus, the time of eating could be crucial as well as the length of the fast.¹ Intermittent fasting has been clinically tested across a diverse range of populations, such as healthy adults, overweight or obese individuals, metabolic syndrome patients, adults with type 2 diabetes, women with polycystic ovary syndrome and patients with non-alcoholic fatty liver disease. Results reported include fasting glucose, fasting insulin, HOMA-IR, HbA1c, postprandial glucose, continuous glucose monitoring, body weight, BMI, waist circumference, lipid profile, inflammatory markers, oxidative stress markers, blood pressure, and liver-related biochemical markers. There are beneficial effects reported in many studies, but the results are not entirely consistent. Some trials have reported significant improvements in glycaemic control and insulin resistance. In contrast, other trials have reported statistically significant but modest changes in glycaemic control and insulin resistance, particularly those trials where intervention duration was brief or calorie intake was controlled.^{5,6} Differences in the fasting schedule, eating window, intervention period, adherence, baseline metabolism, medication, physical activity, and study design could be responsible for the discrepancies among the reported results. For instance, an early eating window could yield different metabolic effects than a late eating window; fasting and calorie restriction or exercising could have a greater effect than fasting alone. Such differences render it difficult to be general when interpreting the results of each individual study and give arguments for the need for systematic synthesis of the available evidence.⁷ This systematic review was therefore conducted to evaluate the physiological and biochemical effects of intermittent fasting on insulin sensitivity and glucose metabolism. The review focused on original human studies published between 2019 and 2025 and excluded reviews, meta-analyses, narrative articles, case reports, animal studies, and pilot studies. The aim was to summarise the available evidence on fasting-related changes in glucose regulation, insulin sensitivity, HbA1c, body composition, lipid profile, inflammatory markers, oxidative stress markers, blood pressure, and tolerability,

while also considering variation in fasting protocols and study populations.

METHODOLOGY

A systematic review was performed to assess the physiological and biochemical changes in insulin sensitivity and glucose metabolism seen with IF. The review was developed as a qualitative systematic review without meta-analysis due to the differences in the characteristics of the population studied, fasting protocols, treatment duration, variables measured as outcomes, and study design. The methodology was designed following the general principles of reporting a systematic review, paying special attention to the transparent identification, selection, data extraction, and risk of bias assessment of studies. A comprehensive literature search was performed to identify original human studies published from January 2019 to December 2025. Electronic databases including PubMed, Google Scholar, ScienceDirect, SpringerLink, Wiley Online Library, and Cochrane Library were searched. The search terms were used alone and in combination: "intermittent fasting," "time-restricted eating," "time-restricted feeding," "early time-restricted feeding," "alternate-day fasting," "5:2 diet," "insulin sensitivity," "insulin resistance," "HOMA-IR," "fasting glucose," "fasting insulin," "HbA1c," "glucose metabolism," "type 2 diabetes," "metabolic syndrome," and "obesity." Boolean operators such as AND and OR were used to refine the search strategy. Reference lists of relevant articles were also screened manually to identify additional eligible studies. The studies included those that met the following criteria: They were original human studies published from 2019 to 2025, and examined the impact of IF or TRE on insulin sensitivity, glucose metabolism, or associated physiological or biochemical responses. Study designs that were eligible were randomised controlled trials (RCTs), randomised clinical trials (RCTs), randomised crossover trials, open-label randomised trials, and prospective interventional studies. Adults with obesity, overweight, metabolic syndrome, type 2 diabetes mellitus, non-alcoholic fatty liver disease, polycystic ovary syndrome or raised risk of diabetes were included in the studies. Studies in healthy adult subjects were also included if they mentioned glucose-related or metabolic outcomes. Systematic reviews, animal studies, in vitro studies, pilot studies, editorials, letters, commentaries, case reports, case studies, narrative and scoping reviews were excluded from the studies. Moreover, studies that did not evaluate intermittent fasting as a primary intervention and studies that did not report insulin sensitivity, glucose metabolism, or biochemical metabolic markers were excluded. Duplicate records and articles lacking methodological and/or outcome information were

removed during screening. The selection process for the study was done in a graduated manner. Captions and abstracts of the articles were first read to exclude those that were obviously out of scope. Second, full-text articles were screened for inclusion and exclusion based on the pre-established inclusion and exclusion criteria. Qualitative synthesis of studies included only those that met all the criteria. Twenty-one original studies were included in the final review. The studies featured a variety of different types of intermittent fasting, including 16:8, early time-restricted feeding, 8-hour fasting, 10-hour fasting, once-weekly 24-hour fasting, modified intermittent fasting, calorie restriction or exercise intermittently, and early time-restricted feeding. A structured format was used to extract data. The information extracted was author, year, country, study design, sample size, study population, age group, intervention period, fasting protocol, and feeding window. Data on fasting glucose, fasting insulin, HOMA-IR, insulin sensitivity, glycated haemoglobin (HbA1c), continuous glucose monitoring, adverse effects, postprandial glycemia, body weight, BMI, waist circumference, lipid profile, inflammatory markers, oxidative stress markers, blood pressure, and cardiometabolic markers were collected. Data were summarised in tabular form for comparison between studies. Insulin sensitivity and glucose metabolism were the major outcomes to be measured. These encompass changes in fasting blood glucose, fasting insulin, HOMA-IR, HbA1c, postprandial glucose, continuous glucose monitoring parameters and β -cell function (if reported). The secondary outcomes were physiological and biochemical parameters like body weight, BMI, waist circumference, body composition, lipid profile, inflammatory markers, oxidative stress markers, blood pressure, liver-related biochemical markers, and tolerability of intermittent fasting interventions. Due to the variability of the fasting schedules, fasting duration, participants' characteristics and reported results of the included studies, a meta-analysis was not conducted. Rather, findings were brought together in a "narrative" way. Study characteristics, glucose-related outcomes, and overall physiological and biochemical effects categorised the outcomes. This approach enabled the patterns to be interpreted across studies and the heterogeneity of the fasting protocols and populations. The methodological domains of the included studies that were deemed relevant to interventional studies were used to evaluate the risk of bias. These domains included randomisation process; selection bias; blinding or performance bias; completeness of outcome data; attrition bias; reliability of outcome measurement; selective reporting; and overall study conduct. In randomised studies, Cochrane RoB 2 style judgement was done with the categories of low risk, some concerns, and high risk. Selection of participants, comparability,

clarity of intervention, outcome measurement, and follow-up were the criteria for the assessment in the prospective interventional study. These domains were then used to determine an overall judgment for each study. Overall, this methodology was a systematic approach to identifying, selecting, extracting and synthesising evidence pertaining to the effect of intermittent fasting on insulin sensitivity and glucose metabolism. The use of predefined eligibility criteria, structured data extraction, and risk of bias assessment ensured that there was greater transparency and reliability of the review findings.

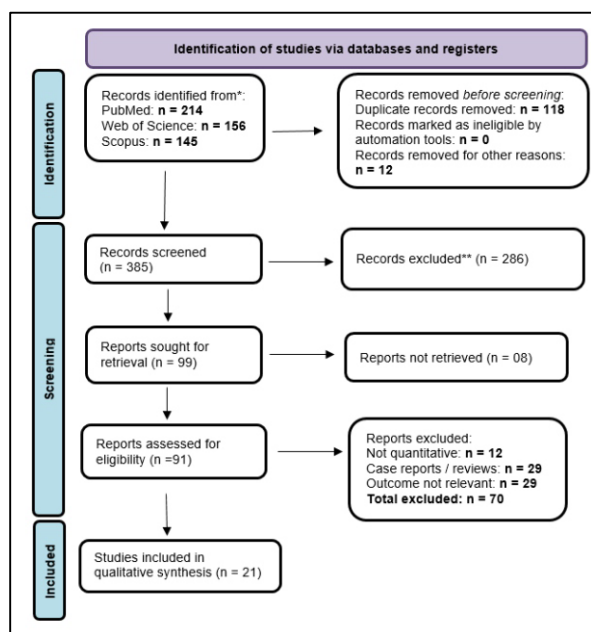


Figure 1: PRISMA Flow Diagram Showing the Study Selection Process for the Systematic Review

A total of 515 records were identified, 385 records were screened after removal of duplicates and other ineligible records, 91 full-text reports were assessed for eligibility, and 21 original studies were included in the final qualitative synthesis.

RESULTS

Table 1 summarises 21 original studies published between 2019 and 2025 that evaluated intermittent fasting and glucose-related metabolic outcomes. The majority of studies were randomised controlled trials or randomised clinical trials; some were crossover and a few were prospective interventional designs. Studies were carried out in various countries and involved various populations, including adults with obesity, metabolic syndrome, type 2 diabetes, non-alcoholic fatty liver disease, polycystic ovary syndrome and people who are at risk of developing type 2 diabetes. The sample sizes ranged from small to large, and the intervention

periods ranged from short-term studies to up to 6 months. The most frequently used intervention was time-restricted feeding, but the 5:2 fasting diet, modified intermittent fasting, once-weekly fasting and fasting

with exercise or calorie restriction were also employed. The table reveals a wide variety of evidence relevant to this study, and appropriate for narrative synthesis, but not for meta-analysis.

Table 1: Characteristics of Included Studies Evaluating Intermittent Fasting and Glucose-Related Metabolism

Study	Country	Design / n	Population	Duration	Fasting protocol
Jamshed et al., 2019 [8]	USA	Randomised crossover trial; n=11	Overweight adults	4 days	Early time-restricted feeding, eating between 8:00 am and 2:00 pm
Tinsley et al., 2019 [9]	USA	Randomised trial; n=40	Active/resistance-trained females (Young adults)	8 weeks	Time-restricted feeding with resistance training
Lowe et al., 2020 [10]	USA	Randomised clinical trial; n=116	Adults with overweight or obesity	12 weeks	16:8 time-restricted eating
Cienfuegos et al., 2020 [11]	USA	Randomised controlled trial; n=58	Adults with obesity	8 weeks	4-hour and 6-hour time-restricted feeding
Kunduraci and Ozbek, 2020 [12]	Turkey	Randomised controlled trial; n=70	Adults with metabolic syndrome	12 weeks	Energy-restricted intermittent fasting diet
Guo et al., 2021 [13]	China	Randomised clinical trial; n=39	Patients with metabolic syndrome (30–50 years)	8 weeks	Two-day modified intermittent fasting
Che et al., 2021 [14]	China	Randomised controlled trial; n=120	Overweight adults with type 2 diabetes mellitus (18–70 years)	12 weeks	10-hour time-restricted feeding, eating between 8:00 am and 6:00 pm
Li et al., 2021 [15]	China	Prospective interventional study; n=18	Women with anovulatory polycystic ovary syndrome (Reproductive age)	5 weeks	8-hour time-restricted feeding
Bartholomew et al., 2021 [16]	USA	Randomised controlled trial; n=103	Adults with elevated LDL-C and metabolic risk features (21–70 years)	26 weeks	Water-only 24-hour fasting twice weekly initially, then once weekly
Xie et al., 2022 [17]	China	Randomized controlled trial; n=90 randomized; 82 completed	Healthy adults without obesity	5 weeks	Early time-restricted feeding and mid-day time-restricted feeding
Zhang et al., 2022 [18]	China	Randomised controlled trial; n=60	Overweight and obese young adults (Young adults)	8 weeks	6-hour early or late time-restricted eating
Jamshed et al., 2022 [19]	USA	Randomised clinical trial; n=90	Adults with obesity	14 weeks	Early time-restricted eating plus energy restriction
Andriessen et al., 2022 [20]	Netherlands	Randomised crossover trial; n=14	Adults with type 2 diabetes mellitus	3 weeks	10-hour time-restricted eating
Kord Varkaneh et al., 2022 [21]	Iran	Randomised controlled trial; n=80	Patients with non-alcoholic fatty liver disease	12 weeks	5:2 intermittent fasting diet
Teong et al., 2023 [22]	Australia	Randomised controlled trial; n=209	Adults at increased risk of type 2 diabetes	6 months	Intermittent fasting plus early time-restricted eating
Pavlou et al., 2023 [23]	USA	Randomised clinical trial; n=75	Adults with type 2 diabetes mellitus and obesity	6 months	8-hour time-restricted eating
Parr et al., 2023 [24]	Australia	Randomised crossover trial; n=14	Adults with type 2 diabetes mellitus	Short-term intervention	Time-restricted eating compared with habitual eating pattern
Quist et al., 2024 [25]	Denmark	Open-label randomised controlled trial; n=100	Adults at high risk of type 2 diabetes	3 months plus follow-up	10-hour time-restricted eating
Manoogian et al., 2024 [26]	USA	Randomised controlled trial; n=108	Adults with metabolic syndrome	3 months	Personalised 8–10-hour time-restricted eating
Kramer et al., 2025 [6]	Canada	Randomised crossover trial; n=39	Adults with type 2 diabetes mellitus	Short-term intervention	Time-restricted eating
Bravo-Garcia et al., 2025 [27]	Australia	Randomised controlled trial; n=Not specified in abstract	Adults with type 2 diabetes mellitus	Short-term intervention	Time-restricted eating combined with exercise

Across studies, early TRE and 8-10-hour eating windows were most consistently associated with favourable changes in glucose regulation, fasting insulin, HOMA-IR/insulin sensitivity, HbA1c, or continuous glucose-monitoring outcomes. Effects were more apparent in metabolically high-risk populations than in healthy adults, although several trials reported modest or non-significant changes, demonstrating substantial between-study variability.

Table 2: Effects of Intermittent Fasting on Insulin Sensitivity and Glucose Metabolism

Study	Glycaemic control	Fasting insulin	HOMA-IR / insulin sensitivity	HbA1c
Jamshed et al., 2019 [8]	Improved 24-hour glucose profile	Reduced insulin response	Insulin-related metabolic response improved	NR
Tinsley et al., 2019[9]	No major adverse change reported	No clear change	No consistent improvement	NR
Lowe et al., 2020 [10]	No significant difference vs control	No meaningful change	No clear improvement	NR
Cienfuegos et al., 2020 [11]	Mild improvement in metabolic profile	Reduced fasting insulin	Insulin resistance improved	NR as a primary outcome
Kunduraci and Ozbek, 2020 [12]	Fasting glucose decreased	Variable	HOMA-IR improved	HbA1c decreased
Guo et al., 2021 [13]	Fasting glucose improved	Insulin level improved	Insulin resistance decreased	NR
Che et al., 2021 [14]	Blood glucose control improved	Fasting insulin decreased	Insulin sensitivity improved	HbA1c improved
Li et al., 2021 [15]	Glucose metabolism improved	Insulin level reduced	HOMA-IR improved	NR
Bartholomew et al., 2021 [16]	No strong consistent glucose benefit reported	Not consistently improved	No clear insulin-sensitivity benefit reported	No major improvement reported
Xie et al., 2022 [17]	Fasting glucose improved, especially with early eating	Insulin-related markers improved	Insulin sensitivity improved more with early eating	Not the main outcome
Zhang et al., 2022 [18]	Glucose markers improved modestly	Insulin response improved	Insulin sensitivity improved	Not clearly reported
Jamshed et al., 2022 [19]	No major independent fasting glucose advantage	No major independent improvement	No clear additional improvement beyond weight loss	Not strongly improved
Andriessen et al., 2022 [20]	Glucose homeostasis improved	Not clearly improved	Insulin sensitivity did not significantly improve	Not the main outcome
Kord Varkaneh et al., 2022 [21]	Glucose-related markers improved	Insulin markers improved	HOMA-IR improved	Not clearly reported
Teong et al., 2023 [22]	Postprandial glucose improved	Variable effect	Insulin-related response improved	Not the main primary outcome
Pavlou et al., 2023 [23]	Glycaemic control improved	Not consistently reported	Not clearly improved in all markers	HbA1c decreased
Parr et al., 2023 [24]	Daily glucose control improved	Not the main finding	Not clearly reported	CGM-based glucose control improved
Quist et al., 2024 [25]	Glucose markers showed limited or modest change	No consistent major improvement	No strong improvement reported	No clear sustained improvement
Manoogian et al., 2024 [26]	Glucose regulation improved modestly	No major change in fasting insulin	No major HOMA-IR improvement	HbA1c decreased slightly
Kramer et al., 2025 [6]	Glycaemic control improved in selected measures	Insulin-secretory response assessed	β-cell function improved	HbA1c/glucose markers assessed
Bravo-Garcia et al., 2025 [27]	Short-term blood glucose management improved	NR	NR	Short-term glucose indices improved

Physiological and biochemical effects extended beyond glycaemic outcomes. Many studies reported reductions in body weight or waist circumference and selected improvements in lipid or cardiometabolic markers, whereas changes in inflammatory and oxidative-stress outcomes were less consistently reported. Tolerability was generally acceptable, although adherence and intervention duration varied.

Table 3: Physiological and biochemical outcomes reported in the included studies

Study	Weight / body composition	Lipids	Inflammation / oxidative stress	BP / cardiometabolic	Tolerability
Jamshed et al., 2019 [8]	No major weight-loss effect due to short duration	No major lipid change reported	Markers related to circadian rhythm, aging, and autophagy were affected	Some improvement in metabolic rhythm was noted	Well tolerated
Tinsley et al., 2019[9]	Body weight was largely maintained; Lean mass was preserved with resistance training	No major harmful lipid change reported	NR	No major adverse cardiometabolic effect	Well tolerated among active females
Lowe et al., 2020 [10]	Modest weight reduction was observed; Lean mass reduction was a concern	No major lipid improvement reported	NR	No clear improvement in cardiometabolic markers	Generally acceptable, but metabolic advantage was limited
Cienfuegos et al., 2020 [11]	Decreased; Waist circumference and fat mass decreased	Triglycerides and oxidative-stress-related markers improved in some groups	Oxidative stress markers improved	Blood pressure and insulin resistance improved	Mild hunger and adjustment symptoms may occur
Kunduraci and Ozbek, 2020 [12]	Weight and BMI decreased; Central obesity markers improved	Total cholesterol, triglycerides, and LDL-C improved	Inflammatory markers showed favourable change	Blood pressure and metabolic syndrome components improved	Generally acceptable
Guo et al., 2021 [13]	Decreased; Abdominal obesity markers improved	Lipid parameters improved	Gut microbiota composition changed favourably	Cardiometabolic risk profile improved	No serious safety concern reported
Che et al., 2021 [14]	Decreased; Waist circumference decreased	Lipid profile showed improvement	NR	Blood pressure and metabolic risk markers improved	Well tolerated
Li et al., 2021 [15]	Weight and BMI decreased; Waist circumference improved	Lipid abnormalities improved	NR	Endocrine and metabolic markers improved	Well tolerated
Bartholomew et al., 2021 [16]	Weight change was modest	LDL-C and other lipid markers were assessed	NR	Cardiovascular risk markers were evaluated	Water-only fasting was feasible for selected participants
Xie et al., 2022 [17]	Modest decrease; Body fat and body composition improved	Lipid changes were modest	Inflammatory markers were not central outcomes	Blood pressure and metabolic rhythm improved, especially with early feeding	Generally safe
Zhang et al., 2022 [18]	Weight and BMI decreased; Fat mass and waist measures improved	Lipid profile improved in selected markers	NR	Cardiometabolic indicators improved	No major adverse effects reported
Jamshed et al., 2022 [19]	Weight decreased; Fat mass and body composition improved	Lipid changes were modest	Not the main focus	Blood pressure and mood-related outcomes improved	Generally acceptable
Andriessen et al., 2022 [20]	Weight decreased slightly	Lipid profile showed limited change	NR	Twenty-four-hour glucose profile improved	Feasible
Kord Varkaneh et al., 2022 [21]	Body weight and BMI decreased; Waist circumference improved	Lipid profile improved	Liver-related biochemical markers improved	Metabolic risk profile improved	Well tolerated
Teong et al., 2023 [22]	Decreased; Body fat and waist measures improved	Lipid response varied	Not central to the main outcome	Postprandial metabolic control improved	Acceptable adherence reported
Pavlou et al., 2023 [23]	Decreased; Waist circumference and fat mass improved	Lipid profile changes were variable	NR	HbA1c and metabolic health improved	Generally safe and acceptable
Parr et al., 2023 [24]	Not the main outcome; Not the main outcome	NR	NR	Continuous glucose monitoring outcomes improved	Short-term intervention was feasible

Study	Weight / body composition	Lipids	Inflammation / oxidative stress	BP / cardiometabolic	Tolerability
Quist et al., 2024 [25]	Modest decrease; Slight improvement	Limited change	NR	Modest/partly sustained	Well tolerated
Manoogian et al., 2024 [26]	Decreased; Waist circumference and body composition improved	Modest improvement	NR	Improved	Feasible with personalised schedule
Kramer et al., 2025 [6]	Weight change was not the central outcome; Not a main outcome	NR	NR	β -cell function and glucose regulation were assessed	Acceptable short term
Bravo-Garcia et al., 2025 [27]	Exercise-related body changes were assessed; Body composition outcomes were linked with exercise	Lipid outcomes were not the main focus	NR	Short-term glycaemic control improved when fasting was combined with exercise	Feasible

Risk-of-bias assessment classified 10 studies as low overall risk and 11 as having some concerns; no study was judged to be at high overall risk. The most frequent concerns related to the inability to blind behavioural dietary interventions, small samples, short intervention periods, limited adherence reporting, and incomplete follow up. Objective biochemical and clinical outcomes reduced concern regarding outcome measurement in many studies.

Table 4: Risk-of-Bias Assessment of Included Studies

Study	Design	Randomisation / selection	Blinding / performance	Missing data	Outcome measurement / reporting	Overall risk
Jamshed et al., 2019 [8]	Randomised crossover trial	Low	Some concerns	Low	Low / Low	Some concerns
Tinsley et al., 2019[9]	Randomised trial	Some concerns	Some concerns	Low	Low / Low	Some concerns
Lowe et al., 2020 [10]	Randomised clinical trial	Low	Some concerns	Low	Low / Low	Low
Cienfuegos et al., 2020 [11]	Randomised controlled trial	Low	Some concerns	Low	Low / Low	Low
Kunduraci and Ozbek, 2020 [12]	Randomised controlled trial	Low	Some concerns	Some concerns	Low / Some concerns	Some concerns
Guo et al., 2021 [13]	Randomised clinical trial	Low	Some concerns	Low	Low / Low	Low
Che et al., 2021 [14]	Randomised controlled trial	Low	Some concerns	Low	Low / Low	Low
Li et al., 2021 [15]	Prospective interventional study	Some concerns	Some concerns	Some concerns	Low / Some concerns	Some concerns
Bartholomew et al., 2021 [16]	Randomised controlled trial	Low	Some concerns	Some concerns	Low / Low	Some concerns
Xie et al., 2022 [17]	Randomised controlled trial	Low	Some concerns	Low	Low / Low	Low
Zhang et al., 2022 [18]	Randomised controlled trial	Low	Some concerns	Low	Low / Low	Low
Jamshed et al., 2022 [19]	Randomised clinical trial	Low	Some concerns	Low	Low / Low	Low
Andriessen et al., 2022 [20]	Randomised crossover trial	Low	Some concerns	Low	Low / Low	Some concerns
Kord Varkaneh et al., 2022 [21]	Randomised controlled trial	Low	Some concerns	Some concerns	Low / Some concerns	Some concerns
Teong et al., 2023 [22]	Randomised controlled trial	Low	Some concerns	Low	Low / Low	Low
Pavlou et al., 2023 [23]	Randomised clinical trial	Low	Some concerns	Low	Low / Low	Low
Parr et al., 2023 [24]	Randomised crossover trial	Some concerns	Some concerns	Low	Low / Low	Some concerns
Quist et al., 2024 [25]	Open-label randomised controlled trial	Low	Some concerns	Low	Low / Low	Some concerns
Manoogian et al., 2024 [26]	Randomised controlled trial	Low	Some concerns	Low	Low / Low	Low
Kramer et al., 2025 [6]	Randomised crossover trial	Low	Some concerns	Low	Low / Low	Some concerns
Bravo-Garcia et al., 2025 [27]	Randomised controlled trial	Low	Some concerns	Some concerns	Low / Low	Some concerns

DISCUSSION

The present systematic review found that intermittent fasting, especially time-restricted eating and early time-restricted feeding, was generally associated with favourable effects on glucose regulation, fasting insulin, HOMA-IR, HbA1c, continuous glucose monitoring outcomes, body weight, waist circumference, and broader cardiometabolic markers. These findings are supported by recent external evidence showing that fasting-based dietary approaches may improve metabolic control through reduced eating duration, lower total energy intake, circadian alignment, and improved substrate utilisation. For example, Oldenburg et al. reported that self-selected 8-hour time-restricted eating was comparable to calorie restriction for several glycaemic and body composition outcomes, although it did not produce superior metabolic flexibility compared with calorie restriction.²⁸ Similarly, Maruthur et al. showed in a controlled feeding randomised trial that isocaloric time-restricted eating alone may not produce marked weight loss when calories are held constant, suggesting that part of the benefit of fasting may depend on spontaneous calorie reduction rather than meal timing alone.²⁹ This supports the interpretation of the present review that intermittent fasting is beneficial, but its effect size depends on fasting protocol, calorie intake, and participant adherence. The review also identified potential greater benefits on glucose measures in adults with obesity, metabolic syndrome, prediabetes, type 2 diabetes, and polycystic ovary syndrome than in metabolically healthy adults. This is similar to other external studies of high-risk metabolic groups. In adults with early type 2 diabetes, an intermittent fasting meal-replacement diet resulted in a greater reduction in HbA1C compared to adults who were treated with metformin or empagliflozin, reported Guo et al.³⁰ Zheng et al. also discovered that the group receiving 8-hour time-restricted eating and the calorie-restricted eating regimen lost weight and had enhanced insulin resistance in overweight or obese women with PCOS.³¹ Our present review results are in line with the non-randomised controlled trial conducted by Ekberg et al., which found that a 5:2 diet led to a change in insulin secretion and insulin sensitivity markers in obese and overweight adults.³² They also indicate that the combined interventions, like fasting and calorie restriction or meal replacement, can lead to more pronounced metabolic effects than fasting. The timing of food intake appears to be an important factor in the metabolic response to intermittent fasting. The present review has noted that early time-restricted eating and 8–10 hour eating windows were most consistently linked to improvements in glucose regulation, while later or unrestricted eating

windows were not linked. This is plausible from a biological standpoint, as insulin sensitivity and glucose tolerance tend to be higher in the morning. This idea is further reinforced by external evidence. Karras et al. identified an improvement in body weight, lipid profile and glycaemic markers during Orthodox religious fasting and compared it with a combined energy- and time-restricted dietary pattern.³³ Based on recent metabolic evidence, Lange et al. concluded that although weight loss is beneficial, intermittent fasting's effects on glucose and lipid metabolism are not necessarily directly proportional to the actual amount of weight lost.⁵ Likewise, Horne et al. found that individual hormonal status, such as baseline human growth hormone (hGH), could influence the insulin-resistance response to repeated fasting.⁸ These results indicate the importance of taking into account the fasting timing, hormonal status and metabolic phenotype when interpreting results of different studies. The current review also confirmed that intermittent fasting can induce beneficial effects in other physiological and biochemical parameters, such as body weight, body mass index, waist circumference, lipid profile, blood pressure, liver-related parameters, oxidative stress, and inflammatory profile. External studies with models based on Ramadan or religious fasting confirm this more general effect. Among adults with obesity, Oueslati et al. found changes in cardiometabolic and inflammatory markers related to Ramadan intermittent fasting.³⁴ Ahmed et al. found that Ramadan fasting in individuals with metabolic dysfunction-associated steatotic liver disease was associated with changes in metabolic and liver-related parameters.³⁵ In addition, Faris et al. identified that there were significant plasma metabolomic differences in overweight and obese individuals during the Ramadan diurnal intermittent fasting period, and Shatila et al. demonstrated changes in dietary intake patterns during Ramadan fasting in healthy adults throughout the year.^{36,37} These results are consistent with the fact that fasting has been found to impact several biological pathways as observed in the current review: energy balance, lipid handling, oxidative stress, inflammation, and hepatic metabolism. Overall results were favourable; however, data were not consistent and should be viewed with caution. Inconsistent findings of robust effects of fasting and moderate effects have been attributed to variations in the fasting regimen (such as the number of hours or days of fasting), duration of fasting intervention, calorie intake, baseline metabolic health status, medication use, physical activity levels, sex, sleep pattern, and cultural fasting practices. This variation has also been identified by recent external research. The authors of the study reported by Nofal et al. observed positive outcomes of IF in metabolic syndrome, although the interventions took place in the context of a culturally

defined fasting cycle.³⁷ Pathan et al. demonstrated that patients with type 2 diabetes receiving ertugliflozin had good glycaemic control during Ramadan fasting, indicating that medication status affected glycaemic outcomes during the fasting period.⁷ Skarstad et al. showed that time-restricted eating was possible in breast cancer survivors, but feasibility and metabolic effects could be different from the group with diabetes or obesity.³⁸ Overall, the evidence is promising but heterogeneous. Differences in fasting duration and timing, intervention length, energy intake, adherence, baseline metabolic status, medication use, physical activity, sex, sleep, and cultural context limit direct comparison. Future trials should use standardized definitions, longer follow-up, objective adherence measures, continuous glucose monitoring where appropriate, and prespecified subgroup analyses.

LIMITATIONS

This review was limited by substantial clinical and methodological heterogeneity, which precluded meta-analysis. Many included trials had small samples or short intervention periods, and adherence reporting was variable. The review also applied a 2019-2025 publication window, which may have excluded earlier relevant evidence. These factors should be considered when interpreting the direction and magnitude of reported benefits.

CONCLUSIONS

Intermittent fasting may improve insulin sensitivity, glucose metabolism, body weight, and selected cardio metabolic outcomes, particularly in adults with obesity, metabolic syndrome, type 2 diabetes, non-alcoholic fatty liver disease, polycystic ovary syndrome, or increased diabetes risk. Early time-restricted eating and 8-10-hour eating windows showed the most consistently favourable patterns, but effects varied across populations and protocols. Larger, longer-term randomised trials are needed to determine the safest and most effective fasting strategies and to establish the durability of metabolic benefit.

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AUTHORS CONTRIBUTION

Hina Hakim - Concept & Design; Data Acquisition; Data Analysis/Interpretation; Drafting Manuscript; Critical Revision; Supervision; Final Approval

Sara Yar Khan - Concept & Design; Data Acquisition; Data Analysis/Interpretation; Drafting Manuscript; Critical Revision; Supervision; Final Approval

Muhammad Ishraq - Concept & Design; Data Acquisition; Data Analysis/Interpretation; Drafting Manuscript; Critical Revision; Supervision; Final Approval

Aizazullah - Concept & Design; Data Acquisition; Data Analysis/Interpretation; Drafting Manuscript; Critical Revision; Supervision; Final Approval

Farzana Salman - Concept & Design; Data Acquisition; Data Analysis/Interpretation; Drafting Manuscript; Critical Revision; Supervision; Final Approval

Marina Hidayat - Concept & Design; Data Acquisition; Data Analysis/Interpretation; Drafting Manuscript; Critical Revision; Supervision; Final Approval

The authors accept responsibility for all aspects of the work and will ensure that any concerns regarding the accuracy or integrity of any part are properly investigated and resolved.



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