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ICMR -NATIONAL INSTITUTE OF NUTRITION

06th Feb 2024 - 30th Jun 2024

EFFECTIVENESS AND SUSTAINABILITY OF INTERMITTENT FASTING AMONG ADULTS: A SYSTEMATIC REVIEW AND META ANALYSIS

By

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Dissertation Completion Certificate

The certificate is awarded to

Dr Palla Gayatri

in recognition of having successfully completed her Internship in the Department of

Maternal and Child Health Nutrition Division

ICMR - National Institute of Nutrition

and has successfully completed her Project on

EFFECTIVENESS AND SUSTAINABILITY OF INTERMITTENT FASTING AMONG ADULTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

From 02 Feb 2024 to 30 Jun 2024

She comes across as a committed, sincere & diligent person who has a strong drive & zeal for learning.

We wish her all the best in her future endeavors.

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TO WHOMSOEVER IT MAY CONCERN

This is to certify that Dr Palla Gayatri, a student of PGDM (Hospital & Health Management) from International Institute of Health Management Research, New Delhi has undergone internship training at ICMR-NIN from 02 Feb 2024 to 30 Jun 2024

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The internship is in fulfillment of the course requirements.

I wish her all success in all her future endeavors.

Dr. Sumesh Kumar Dr Anandhi Ramachandran

Associate Dean, Academic and Student Affairs Professor

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The following dissertation titled "EFFECTIVENESS AND SUSTAINABILITY OF INTERMITTENT FASTING AMONG ADULTS: A SYSTEMATIC REVIEW AND META ANALYSIS" at 'ICMR -NIN' is hereby approved as a certified study in management carried out and presented in a manner satisfactorily to warrant its acceptance as a prerequisite for the award of PGDM (Hospital & Health Management) for which it has been submitted. It is understood that by this approval the undersigned do not necessarily endorse or approve any statement made, opinion expressed, or conclusion drawn therein but approve the dissertation only for the purpose it is submitted.

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This is to certify that Dr Palla Gayatri, a graduate student of the PGDM (Hospital & Health

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This dissertation has the requisite standard and to the best of our knowledge no part of it has been

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Dr Anandhi Ramachandran,

Professor

IIHMR, Delhi

Dr. Sai Ram Challa Scientist E

Maternal And Child Health. Divison

ICMR-NIN

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FEEDBACK FORM

FEEDBACK FORM

Name of the Student: Dr Palla Gayatri

Name of the Organisation in Which Dissertation Has Been Completed: ICMR -NIN

Area of Dissertation: Metabolic Disorders - Maternal and Child Health Nutrition Division

Attendance: Excellent; punctual and consistent.

Objectives achieved: Successfully met all dissertation objectives.

Deliverables: High-quality research report, comprehensive data analysis, and insightful findings.

Strengths: Strong analytical skills; Excellent research aptitude; Effective communication and teamwork; High level of dedication and initiative

Suggestions for Improvement: Enhance skills in advanced statistical methods; Increase engagement in interdisciplinary collaboration.

Suggestions for Institute: Provide more opportunities for hands-on training in fieldwork; Enhance access to advanced research tools and software.

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Date: 21-06-2024 Place: Hyderabad

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I hope to apply the knowledge and experience gained from this project to make meaningful contributions to the community in the future.

ORGANIZATION PROFILE

Introduction:

The ICMR - National Institute of Nutrition (NIN) is a premier institution under the Indian Council of Medical Research (ICMR), dedicated to conducting high-quality research in the field of nutrition and public health. Established in 1918, NIN has evolved into a leading research center, addressing key nutritional challenges and contributing significantly to national health policies and programs.

Vision and Mission:

Vision: To achieve optimal nutrition and health for all citizens.

Mission: To conduct research that generates scientific knowledge on nutritional requirements, dietary patterns, and the impact of nutrition on health, thereby informing and influencing public health policies and programs.

Research Focus Areas:

NIN's research activities encompass a wide range of topics within the field of nutrition, including but not limited to:

Nutritional Deficiencies: Investigating the prevalence and impact of micronutrient deficiencies such as anemia, vitamin D deficiency, and iodine deficiency disorders.

Diet and Chronic Diseases: Studying the relationship between dietary habits and the incidence of chronic diseases like diabetes, cardiovascular diseases, and obesity.

Food Safety and Toxicology: Assessing the safety of food items and the impact of environmental toxins on human health.

Maternal and Child Nutrition: Exploring nutritional interventions to improve maternal and child health outcomes.

Community Nutrition: Implementing and evaluating community-based nutrition programs aimed at improving dietary practices and nutritional status.

Facilities and Infrastructure:

NIN boasts state-of-the-art facilities and infrastructure to support its extensive research activities:

Laboratories: Equipped with advanced instruments for biochemical, clinical, and molecular nutrition research.

Clinical Research Unit: Facilitates human studies and trials to evaluate the efficacy of nutritional interventions.

Library and Information Center: A vast collection of scientific literature and databases to support research activities.

Community Nutrition Research Centers: Located in various regions to conduct field-based nutrition research and interventions.

Future Directions:

NIN is committed to continuing its legacy of excellence in nutrition research. Future directions include:

Expanding research on the impact of nutrition on non-communicable diseases.

Developing innovative dietary interventions to combat malnutrition and obesity.

Strengthening community-based nutrition programs to achieve sustainable health outcomes.

Enhancing capacity building and training programs for nutrition professionals and researchers.

The ICMR - National Institute of Nutrition (NIN) stands at the forefront of nutrition research in India, with a rich history of scientific achievements and a commitment to improving public health through evidence-based nutrition interventions. Its comprehensive research programs, state-of-the-art facilities, and strategic collaborations make it a pivotal institution in the quest for optimal nutrition and health for all.

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ABBREVIATIONS

IF – INTERMITTENT FASTING

ADF - ALTERNATE DAY FASTING

TRF – TIME RESTRICTED FEEDING

SMD – STANDARDIZED MEAN DIFFERENCE

CI – CONFIDENCE INTERVALS

BMI – BODY MASS INDEX

HOMA – IR - HOMEOSTATIC MODEL ASSESSMENT FOR INSULIN RESISTANCE

EFFECTIVENESS AND SUSTAINABILITY OF INTERMITTENT FASTING AMONG ADULTS: A SYSTEMATIC REVIEW AND META ANALYSIS

ABSTRACT

Objective: To examine the effectiveness and sustainability of intermittent fasting on weight loss and metabolic health factors as compared to normal diet in overweight or obese adults.

Methods: The following electronic databases were searched: PubMed, Scopus and Google scholar for published randomized controlled trials, cohort studies, case reports and descriptive studies. Two independent reviewers evaluated the methodological quality of included studies. Data were extracted from papers included in the review by two independent reviewers. Effect sizes were expressed as standardized mean differences, and their 95% confidence intervals were calculated for meta-analyses.

Results: Ten studies were included in this review. The intermittent energy restriction regimens varied across studies and included alternate day fasting, Time restricted feeding and 5:2 fasting. The duration of studies ranged from 5weeks to 3months.

Conclusions: In conclusion, intermittent fasting (IF) has been shown to significantly reduce BMI, body weight and waist circumference, as well as improve various metabolic health markers. Despite these promising findings, further long-term studies are essential to fully understand the effects of intermittent fasting as compared to normal diet.

EFFECTIVENESS AND SUSTAINABILITY OF INTERMITTENT FASTING AMONG ADULTS: A SYSTEMATIC REVIEW AND META ANALYSIS

The terms "overweight" and "obesity" refer to abnormal or excessive fat buildup that increases the risk of cardiovascular disease and diabetes. According to body mass index (BMI), a person over 25 is considered overweight and over 30 is obese. An estimated 5 million noncommunicable disease (NCD) deaths in 2019 have been related to higher-than-optimal body mass index (BMI).

Metabolic syndrome: Increased visceral fat mass and central obesity are important risk factors for chronic diseases such as insulin resistance and cardiovascular disease (CVD). A long-term follow-up study including US men and women that lasted more than 15 years found that for every kilogram increase in body weight, the risk of type 2 diabetes increased sevenfold in women and doubled in men. Furthermore, a major contributing element to the development of insulin resistance is inflammation of adipose tissue. An inflammatory cycle is facilitated by the development and hypertrophy of adipocytes. Thus, losing weight or reducing visceral fat can improve insulin sensitivity, which can help avoid diabetes and heart disease.

Intermittent fasting, a common dietary intervention adapted by humans for weight loss. Intermittent fasting (IF) is a dietary regimen alternates from designated periods of fasting and eating. IF emphasizes the timing of food intake. This approach aims to improve metabolic health and facilitate weight loss through various structured fasting schedules.

Aim -

- The objective of this study is to conduct a systematic review and meta analysis to understand the effectiveness of intermittent fasting as compared to normal diet in overweight or obese adults.
- Another objective is to understand the sustainability of intermittent fasting.

METHODOLOGY

SEARCH STRATEGY-

A systematic search on PubMed, Google scholar and Scopus was done independently by two reviewers. The terms used in the literature search are "Intermittent fasting" "Time restricted feeding" "Alternate day fasting" "Body mass index" "Weight loss" "Metabolic syndrome" "Metabolic health markers" "randomized controlled trials" "cohort studies" "case-control studies" "qualitative studies" "Longevity" "Effectiveness" "sustainability"

ELIGIBILITY CRITERIA-

INCLUSION CRITERIA

The intervention group included studies of intermittent fasting and the types- Alternate day fasting, 5:2, Time restricted feeding. The control group included normal eating or no other dietary intervention. Overweight and obese adults aged 18-64 years old

EXCLUSION CRITERIA

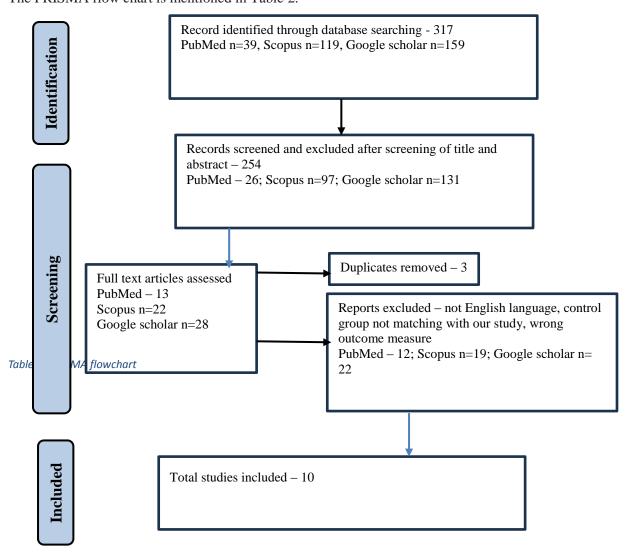
we excluded studies of -

- (1) Ramadan or any other type of religious fasting
- (2) if the comparison group included any other type of dietary intervention.
- (3) (3) The subject of the study was not human.
- (4) (4) The paper was not written in English
- (5) (5) There were duplicates
- (6) (6) Should the data not be accessible.

RESULTS

SEARCH RESULTS AND STUDY CHARACTERISTICS

Following the PRISMA search strategy, 317 studies were initially identified. After reviewing the abstracts and titles, 254 papers were not included for not fitting PICO requirements. Of the 63 remaining studies, 2 duplicates were removed. Ten papers from the 61 studies that underwent a full-text examination were included in the final analysis.. The PRISMA flow chart is mentioned in Table 2.



EVALUATION OF QUALITY AND EXTRACTION OF DATA

The Cochrane Collaboration's tool ROB -2 was used to assess the quality of screened RCTs (14). The risk of research bias was evaluated separately by two investigators. From the included studies, data and study details were retrieved. The ROB.2 tool has helped us reduce the possibility of bias in all of the investigations.

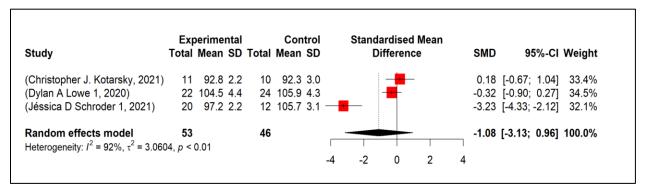
STATISTICAL ANALYSIS-

Software version 4.4.1 was utilized for statistical analysis. Together with the lead investigator, a qualified statistician completes the meta-analysis. For continuous data, the standard mean difference was computed. For every statistical finding, the 95% confidence intervals were given. The results' heterogeneity was represented by I2. We applied the random-effects model, where statistical significance was defined as p < 0.05. We conducted qualitative analysis for the studies that were not included in meta – analysis.

The study includes 10 articles, 7 are Randomized controlled trials, 1 case report, 1 descriptive prospective study and 1 experimental study .5 studies included TRF as experimental group ,2studies included 5:2 regimen, 2 studies included ADF regimen, one study included intermittent fasting with 12 - 16 hours of fast. Every person in the study is an adult who falls between the age range of 18 to 60 years and is overweight or obese.

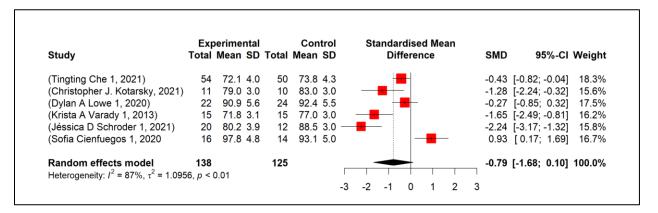
META – ANALYSIS

1. Intermittent fasting on BMI –



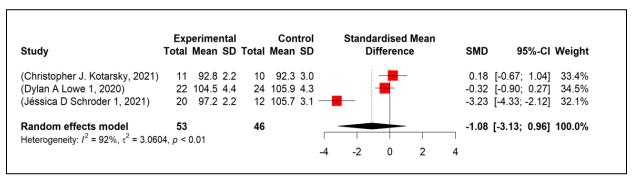
The sample in experimental group is 85 and the sample in the control group is 46. The (SMD) is -0.76, with a 95% confidence interval (CI) of [-1.10, -0.42]. The I² statistic is 91%, indicating high heterogeneity and substantial variation in study outcomes. The test for heterogeneity (Q = 2.3364, p < 0.01) suggests that the observed heterogeneity is statistically significant. These results imply that the meta-analysis demonstrates a moderate and statistically significant effect favoring the experimental group, despite considerable variability across the included studies.

2. Intermittent fasting on Weight-



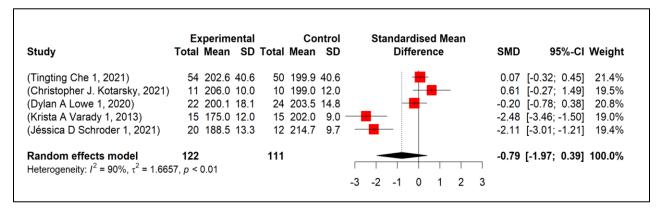
In total, 6 studies using a random effects model assigned 138 participants to the experimental groups and 125 people to the control groups. With a 95% confidence interval (CI) spanning from -1.68 to 0.10, the overall standardized mean difference (SMD) was -0.79, indicating that the experimental intervention tended to lower weight in comparison to the control group. Due to differences in intermittent fasting regimens, the I^2 score of 87% indicates considerable heterogeneity among the trials. The heterogeneity test (Q-test) yields significant results (p < 0.01).

3. Intermittent fasting on waist circumference –



In the meta-analysis, 46 individuals belonged to the control group and 53 to the experimental group. Difference in the overall standardized mean of -1.08, indicating a moderate effect size. The analysis revealed high heterogeneity ($I^2 = 92\%$, p < 0.01), suggesting significant variability among the studies. One study showed a significant effect favoring the control group, while the other two studies did not show significant effects. Despite these differences, the meta-analysis suggests that the experimental intervention tends to reduce waist circumference in relation to the group under supervision.

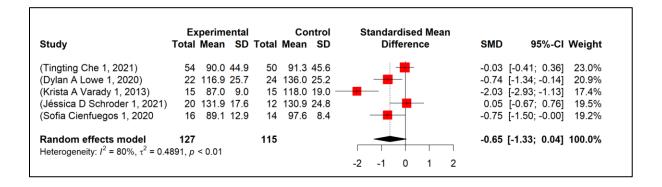
4. Intermittent fasting on total cholesterol -



In the meta-analysis, there were 122 people in the experimental group and 111 participants in the control group. Total SMD is -0.79, with a 95% CI of [-1.97, 0.39].

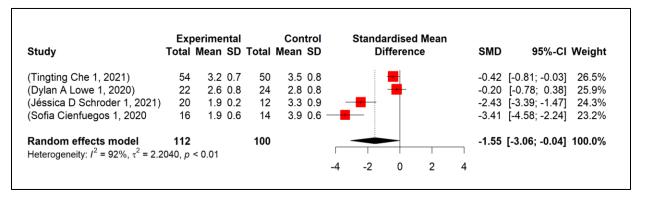
This implies a rather negative. Significant differences exist amongst the research, according to the heterogeneity statistics (I2 = 90%, φ 2 = 1.6657\tau^2 = 1.6657\2 = 1.6657, p < 0.01). This implies that there is a tendency for intermittent fasting to lower overall cholesterol levels. In Figure 4, the forest plot is displayed.

5. Intermittent fasting on triglycerides -



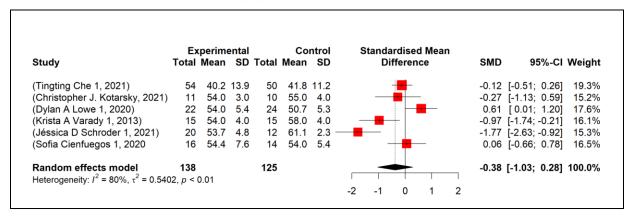
The overall SMD is -0.65, with a 95% CI of [-1.33, 0.04]. This suggests a moderate negative effect. The heterogeneity statistics indicate substantial variability among the studies ($I^2 = 80\%$, $\tau 2 = 0.4891 \times 2 = 0.4891 \times 2 = 0.4891 \times 2 = 0.4891$). The meta-analysis suggests a moderate negative effect overall. This suggests that intermittent fasting decreases triglyceride levels.

6. Intermittent fasting on HOMA-IR



The meta-analysis included 112 participants in the experimental group and 100 participants in the control group. The combined standardized mean difference (SMD) is -1.55, with a 95% confidence interval (CI) of [-3.06, -0.04], indicating a significant overall effect favoring the experimental intervention. The I² statistic of 92% signifies high heterogeneity among the studies. The test for heterogeneity (Q-test) is significant (p < 0.01). This meta-analysis suggests that the experimental intervention significantly reduces HOMA-IR levels compared to the control group. The forest plot is shown in Figure 6.

7. Intermittent fasting on High density Lipoprotein (HDL)-



The combined standardized mean difference (SMD) is -0.38, with a 95% confidence interval (CI) of [-1.03, 0.28], indicating a small and not statistically significant effect favoring the experimental group in terms of HDL levels. The I^2 statistic of 80% signifies high heterogeneity. The heterogeneity test (Q = 0.5402, p < 0.01) confirms significant variability across the studies, likely due to differences in study design, populations, or interventions.

QUALITATIVE ANALYSIS OF STUDIES NOT INCLUDED IN META-ANALYSIS -

In a 2019 case study an intermittent fasting schedule of 5:2 was followed for 5 weeks. Following the intervention, a significant 1.3 kg weight decrease was seen.

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Participants in a 2013 study adhered to an 8-week regimen that included two weeks of observation and six weeks of alternate-day fasting (ADF) diet. The findings demonstrated a significant drop in body weight from 84.3 ± 11.44 kg to 78.3 ± 10.18 kg (p < 0.0001) and waist circumference from 87.87 ± 9.74 cm to 82.86 ± 9.68 cm (p < 0.001).

Furthermore, there was a substantial decrease in systolic blood pressure from 114.8 ± 9.16 mmHg to 105.13 ± 10.19 mmHg (p < 0.001), and a decrease in diastolic blood pressure from 82.86 ± 10.6 mmHg to 74.5 ± 10.8 mmHg (p < 0.05).

Although not statistically significant, there were reductions in LDL cholesterol, total cholesterol, triglycerides, and fasting blood sugar levels (227.73 \pm 49.96 mg/dL to 214.67 \pm 43.27 mg/dL, 160.5 \pm 46.18 mg/dL to 143.9 \pm 22.77 mg/dL, 149.46 \pm 49.81 mg/dL to 131.3 \pm 50.97 mg/dL, and from 102 \pm 14.7 mg/dL to 96 \pm 11.79 mg/dL, respectively)..

Participants in a three-month trial saw a decrease in mean body weight from 88.5 ± 19 kg to 83.8 ± 17.6 kg. Male waist circumference dropped from 108.2 ± 11.3 cm to 103.6 ± 4.4 cm, while female waist circumference dropped from 98.9 ± 8.8 cm to 93.3 ± 3.3 cm. Furthermore, BMI decreased to 29.6 ± 5.1 kg/m² from 31.4 ± 5.3 kg/m²

In a study conducted by Kurt Widhalm, 2017 after a 12-week period, test subjects experienced an average weight loss of 7.19 kg (\pm 4.38 kg). Additionally, there was a reduction in total cholesterol and low-density lipoprotein (LDL) cholesterol by 9.20% (\pm 40.32%). (Kurt Widhalm, 2017)

The cumulative analysis explained in the table below of the studies indicates an average weight loss of -4.80 kg across four studies. (Sheryl Salis 1, 2022) (Samira Eshghinia 1, 2013) (Soo Liang Ooi 1, 2019) (Kurt Widhalm, 2017)Two studies reported an average waist circumference reduction of -5.06 cm (Samira Eshghinia 1, 2013) (Sheryl Salis 1, 2022), while one study observed a BMI decrease of -1.8 kg/m² (Sheryl Salis 1, 2022). Systolic and diastolic blood pressures were reduced by -9.67 mmHg and -8.36 mmHg, respectively, as indicated by one study each (Samira Eshghinia 1, 2013). One study reported a mean total cholesterol reduction of -13.06 mg/dL, triglycerides decrease of 16.6 mg/dL, and an LDL cholesterol reduction of 18.16 mg/dL. Additionally, HDL cholesterol increased by 8.26 mg/dL, and fasting blood sugar dropped by 6 mg/dL, each based on one study.

Parameter	Mean difference of all studies
Weight Loss (kg)	-4.80 kg
BMI Reduction (kg/m²)	-1.8 kg/m²
Waist Circumference Reduction (cm)	-5.06 cm
Systolic BP Reduction (mmHg)	-9.67 mmHg
Diastolic BP Reduction	-8.36 mmHg
Total Cholesterol Reduction	-13.06
Reduction of Triglycerides	-16.6
LDLCholesterol Reduction	-18.16
HDL Cholesterol Increase	-8.26
Fasting Blood Sugar Reduction	-6

DISCUSSION

Ten studies were thoroughly analyzed for this study in order to assess how IF affected weight and metabolic health markers. The pooled analysis showed that intermittent fasting showed a moderate and statistically significant reduction with a standardized mean difference (SMD) of -0.76 (95% CI: [-1.10, -0.42], $I^2 = 91\%$, p < 0.01) in BMI. Weight reduction was also moderate with an SMD of -0.79 (95% CI: [-1.68, 0.10], $I^2 = 87\%$, p < 0.01). Waist circumference showed a moderate effect size (SMD = -1.08, 95% CI: [-3.13, 0.96], $I^2 = 92\%$, p < 0.01), not statistically significant. Total cholesterol levels exhibited a moderate decrease (SMD = -0.79, 95% CI: [-1.97, 0.39], $I^2 = 90\%$, p < 0.01), while triglycerides showed a moderate negative effect (SMD = -0.65, 95% CI: [-1.33, 0.04], $I^2 = 80\%$, p < 0.01). Notably, IF significantly reduced HOMA-IR levels (SMD = -1.55, 95% CI: [-3.06, -0.04], $I^2 = 92\%$, p < 0.01). However, the effect on HDL was small and not statistically significant (SMD = -0.38, 95% CI: [-1.03, 0.28], $I^2 = 80\%$, p < 0.01).

Our study's meta-analysis showed that, in comparison to the control group, the experimental group's body weight and BMI were significantly lower after a period of intermittent fasting.

A study by Jing-Chao Sun et al. found that time-restricted eating (TRE) combined with calorie restriction (CR) significantly reduced waist circumference (WC) compared to the control group (SMD: -1.87; 95% CI: -3.47 to -0.26; I2: 67.25%). These results align with our study, which also demonstrated a significant reduction in waist circumference. (Jing-Chao Sun, 2023)

The typical pathological management of glucose and lipid metabolism emphasizes weight reduction, especially targeting insulin resistance and hyperinsulinemia caused by central obesity. Our meta-analysis demonstrated that intermittent fasting significantly reduced HOMA-IR levels in the experimental group compared to the control group. (SMD = -1.55, 95% CI: [-3.06, -0.04], $I^2 = 92\%$, p < 0.01). These results are consistent with a meta-analysis with 10 RCTs to understand of the effects of time restricted eating pre intervention as compared to post intervention, SMD-0.31;95% CIs: -0.44; -0.19) which showed similar outcomes to our study. (Xiaojie Yuan, 2022)

A study by Haiyan Meng MM et al. using a random-effects model revealed that intermittent fasting (IF) and energy-restricted diet (ERD) interventions led to significant changes in total cholesterol (TC) (SMD, -6.93 mg/dL; 95% CI, -10.18 to -3.67; P < 0.001; I2 = 78.2%), LDL cholesterol (LDL-C) (SMD, -6.16 mg/dL; 95% CI, -8.42 to -3.90; P < 0.001; I2 = 52%), and triglyceride (TG) concentrations (SMD, -6.46 mg/dL; 95% CI, -10.64 to -2.27; P = 0.002; I2 = 61%). However, HDL cholesterol (HDL-C) levels did not change significantly (SMD, 0.50 mg/dL; 95% CI, -0.69 to 1.70; P = 0.411; I2 = 80%).

CONCLUSION AND RECOMMENDATIONS

CONCLUSION

In conclusion, intermittent fasting (IF) significantly reduces body weight, BMI, waist circumference, and improves metabolic health markers which proves that intermittent fasting is an effective dietary strategy.

LIMITATIONS

- In the context of obesity research, BMI is a crucial metric for evaluating pre- and post-intervention changes. However, only three studies within our meta-analysis included BMI as a measured outcome, highlighting a significant gap in the current literature. This underscores the need for future studies to consistently incorporate BMI as a key parameter to better understand the efficacy of interventions on obesity-related outcomes.
- Studies that tracked patients for a year or more to evaluate the long-term impacts of intermittent fasting were not found.
- Another notable gap in the current literature is the short duration of the interventions in the selected studies, which ranged from 5 weeks to 3 months. This limited timeframe restricts our ability to assess the long-term sustainability and maintenance of the observed changes.
- The intervention group included various types of interventions, resulting in high heterogeneity in the metaanalysis. Despite this diversity, conducting a subgroup analysis was not feasible due to the insufficient number of studies. Furthermore, This study focused exclusively on refined studies with a control group that had either ad libitum or no dietary intervention.

5 RECOMMENDATIONS

• There is a critical need for longer-term studies to provide a more comprehensive understanding of the enduring effects of these interventions

The next study should look at the sustainability and long-term effects of intermittent fasting over a minimum of a year of follow-up. This will provide crucial information regarding whether the immediate benefits persist over time.

Use prospective cohort and longitudinal research to track people over time. With the help of these designs, results can be continuously monitored, leading to a comprehensive knowledge of the long-term impacts of intermittent fasting on weight, BMI, metabolic health markers, dietary adherence, and any negative consequences.

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