

RESEARCH ARTICLE

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Effects of intermittent fasting on blood glucose, lipid profile and renal-hepatic biomarkers of streptozotocin-induced rats fed with a high-fat diet

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Abstract

Objectives: Intermittent fasting (IF) is increasingly adopted as a dietary strategy for managing diabetes mellitus, yet its effects on vital metabolic organs such as the liver and kidneys remain unclear. This study investigated the impact of different IF regimens on hepatic and renal functions in streptozotocin-induced diabetic rats.

Methods: Fifty male Wistar rats were divided into five groups (n=10): control (group 1), diabetic (group 2), and three diabetic groups subjected to distinct IF protocols with a high-fat diet—time-restricted feeding (group 3), alternate-day fasting (group 4), and the 5:2 diet (group 5). The experiment lasted four weeks. Weekly body weight and blood glucose (BG) levels were monitored. Serum lipid profile, liver enzymes (ALT, AST, ALP), renal markers (urea, creatinine), and histopathological changes were assessed using standard methods. Data were analysed by one-way ANOVA at p<0.05.

Results: All groups gained weight, but BG and biochemical parameters varied significantly. Groups 2 and 5 showed the greatest BG reduction (104.0 ± 10.23 to 63.3 ± 15.37 mg/dL and 93.8 ± 6.65 to 42.8 ± 4.72 mg/dL, respectively; p=0.05). The 5:2 diet produced the lowest total cholesterol (3.0 ± 0.06 mg/dL), AST (56.5 ± 7.92 U/L), and urea (1.43 mg/dL), with elevated HDL and creatinine. Histological analysis showed varying degrees of hepatic alteration across IF groups.

Conclusion: Intermittent fasting, particularly the 5:2 regimen, improved glycemic and lipid profiles despite mild hepatic and renal stress. IF may support metabolic regulation in diabetes, though dietary fat modification and cautious fasting durations are advised to protect organ integrity.

Keywords: Intermittent fasting, Liver, Kidney function, diabetes mellitus, Streptozotocin-induced rats, diet

Plain English Summary

Diabetes is a common health condition that affects how the body controls blood sugar. One approach to managing diabetes is intermittent fasting, a pattern of eating that alternates between fasting and regular meals. This study explored how different types of intermittent fasting affect the liver and kidneys, which are vital for metabolism and waste removal.

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Researchers used fifty male rats to model diabetes by giving them a chemical called streptozotocin. The animals were then divided into groups that followed different fasting plans: time-restricted feeding (fasting for 16 hours daily), alternate-day fasting, and the “5:2 diet” (five days of eating normally and two fasting days each week). Over four weeks, the rats’ body weight, blood sugar, cholesterol, and markers of liver and kidney health were measured.

The results showed that intermittent fasting, especially the 5:2 diet, significantly lowered blood sugar and total cholesterol levels while improving “good” cholesterol. However, some fasting groups showed mild signs of stress in the liver and kidneys.

Overall, the study suggests that intermittent fasting may help control diabetes and improve heart health, but fasting should be carefully managed—particularly when combined with high-fat diets, to avoid possible harm to vital organs.

Background

Type 2 diabetes mellitus (T2DM) is a metabolic disorder characterised by chronic hyperglycemia due to insulin resistance or inadequate insulin secretion (1). The global prevalence of T2DM is increasing, particularly in low- and middle-income countries, with approximately 589 million adults aged 20-79 years living with diabetes as of 2024, and projections indicating that nearly 853 million will live with diabetes by 2050 (2, 3). It poses significant global health challenges, particularly in developing countries like Nigeria, where shifts to processed diets and sedentary lifestyles contribute to its rising prevalence. Complications such as diabetic kidney disease (DKD) significantly affect quality of life and mortality rates among diabetic patients (4). However, intermittent fasting (IF) has emerged as a popular dietary strategy for managing T2DM (5). The IF, including alternate-day fasting (ADF) and time-restricted feeding (TRF), has long been established to enhance metabolic health, improve glucose control, and facilitate weight loss through metabolic shifts involving reduced insulin levels and increased sensitivity (6, 7). The IF shows promise for managing T2DM, enhancing metabolic parameters, and lowering complication risks. With the rising T2DM prevalence and associated complications, the quest for effective therapies with minimal or no side effects is on the rise. Although intermittent fasting is effective in managing weight (8). However, the effects of weight cycling and its cardiometabolic impacts raise concern about factors which might negate the effectiveness of intermittent fasting in controlling weight gain, largely among obese diabetic individuals who use fasting as a means of obese weight management, especially in the case of (9, 10). This study investigates the effects of IF on the liver and kidney of Streptozotocin (STZ)-induced rats fed a high-fat diet, exploring its potential to mitigate high-fat diet-induced damage to these crucial metabolic organs. The STZ induction mimics aspects of diabetes and replicates some features of human T2DM,

providing insights into how IF may impact metabolic health in diabetic conditions exacerbated by dietary factors. Understanding IF's influence on liver and kidney health is crucial for comprehending its broader implications in metabolic homeostasis and the prevention of complications associated with type 2 diabetes. Therefore, the effects of IF on T2DM and diabetic complications in STZ-induced rats were examined in this study. It is believed that mechanistic insights into the impact of IF on liver and kidney function may offer new T2DM and DKD treatments.

Materials and Methods

Materials

Fifty male Wistar rats (90-120 g) were sourced from Babcock University Animal Facility, Ogun State, Nigeria, and housed in suitable cages at the Department of Physiology, Babcock University, Ilishan-Remo, Ogun State, Nigeria. They were acclimatised for a week with rat feed and water under a natural 12-hour light-dark cycle before the experiment began. Wistar rats, rat cages, standard rat feed, weighing scale, glucometer, test strips, cotton wool, methylated spirit, scissors, streptozotocin, syringes, butter, chloroform, and sample bottles.

Methods

An experimental study was conducted for a period of four (4) weeks in three phases. Fifty rats were randomly allocated into five groups (10 rats/group). There were two control groups (1 and 2). Group 1 (positive control group) was not injected with STZ and was placed on standard rat feed and water alone. Group 2 (negative control group) and other groups were injected with STZ to induce diabetes and were fed with a high-fat diet of 70% standard rat feed and 30% margarine with ad libitum access to water. Their weekly food intake and weekly body weights were recorded.

The weight of the rats was determined using a sensitive and calibrated scale. Before starting the experiment, each rat was weighed to establish a

baseline weight. The weighing was carried out weekly for four weeks to help in tracking weight changes over time. Weight gain was calculated for each rat by subtracting the baseline weight from the weight recorded at each measurement in grams.

Weight gain (g)= Weight (weekly measurements) – Initial weight (Baseline)

Treatments

The experimental animals were divided into five groups of 10 rats per group based on their weights. After one week of acclimatisation, the other four groups of animals were induced with streptozotocin (STZ) and treated for 21 days with intermittent fasting based on their groups, making a total of 28 days. Description of the experimental grouping is stated in Table 1.

Table 1: Descriptions of Experimental groups of the study

Experimental Groups	Description
Group 1	Standard rat feed and water alone (Positive control)
Group 2 (Streptozotocin alone)	Intraperitoneal administration of STZ at a dose of 50 mg/kg (Negative control)
Group 3 (Streptozotocin + IF 1)	Intraperitoneal administration of STZ at a dose of 50 mg/kg + with 16 hours fasting and access to food for 8 hours (time-restricted feeding)
Group 4 (Streptozotocin + IF 2)	Intraperitoneal administration of STZ at a dose of 50 mg/kg + alternate day fasting (alternating between feeding days and fasting days (alternate day fasting)
Group 5 (Streptozotocin +IF 3)	Intraperitoneal administration of STZ at a dose of 50 mg/kg + 5:2 diet (5 days of free feeding in a week with 2 non-consecutive fasting days)

STZ- Streptozotocin, IF- Intermittent fasting

The five groups were distinct based on the treatment that each one received. The first group (positive control), known as the control group, had access only to regular rat feed and water without fasting. The second group (negative control) received an intraperitoneal administration of streptozotocin (STZ) at a dosage of 50 mg/kg, without any additional modifications to their diet. The third group (time-restricted feeding) also administered STZ at the same dosage, but this was combined with a regimen of intermittent fasting; specifically, they underwent a fast for 16 hours and were allowed to eat for only 8 hours each day. In the fourth group (alternate day fasting), the same STZ dosage was administered, but the animals followed a different pattern, practising alternate day fasting for 16 hours, alternating between days of feeding and days of fasting. Finally, the fifth group (5:2 diet) was given the same STZ treatment, which allowed them five days of unrestricted feeding followed by two non-consecutive fasting days (16 hours/day) each week.

Induction of diabetes

Animals received their respective diets for 7 days for acclimatisation. On the 7th day, except for the positive control group, all animals in the treatment groups were injected intraperitoneally with 50 mg/kg streptozotocin (Sigma-Aldrich, St. Louis, MO, USA) after a 12-hour fast (11). In the post-injection, animals had ad libitum access to food and water to prevent hypoglycemic shock. Control

groups received vehicle (0.01 M citrate buffer, pH 4.5).

Before streptozotocin treatment, fasting blood glucose was measured from the tail vein blood using an Accu-Check glucometer. Blood glucose was measured again on the 16th day to confirm diabetes induction (blood glucose $\geq$ 250 mg/dl). Weekly records were kept for body weight, water intake, and food intake. Blood glucose levels were measured every three days from the tail vein. Standard rat feed was supplemented with margarine at a 70% to 30% ratio according to the method of Olufadekemi et al (12).

Evaluation of Lipid profile and Histopathological analysis

The blood was taken following an Institutional Animal Care and Use Committee (IACUC)-approved Animal Protocol, which was performed with a euthanasia procedure when the animal was under deep anaesthesia. The Blood was centrifuged at 3000 rpm for 20 minutes to obtain serum. Triglycerides, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), urea, and creatinine levels were determined using assay kits. The liver and kidneys were exercised, weighed, fixed in 10% formal saline, and processed for histopathological examination.

Organ samples were rinsed in ice-cold 1.15% KCl solution, blotted dry, and weighed. They were then sectioned for histology and fixed in Formalin. Meanwhile, harvested tissues were homogenised in 0.1M Phosphate buffer and centrifuged at 10,000 rpm for 15 minutes at 4°C to obtain post-mitochondrial fractions for biochemical analyses.

Liver and kidney tissues underwent dehydration in alcohol, with internal surfaces of embedding moulds treated with glycerine to aid paraffin embedding. After 48 hours of solidification, excess wax was trimmed from tissue blocks. Sections of 5 microns were cut using an automated microtome, floated on water, and straightened if folded. Slides coated with egg albumen facilitated section transfer and drying at 40°C.

Histological staining

Haematoxylin and Eosin (H&E) procedures were employed. Haematoxylin-stained nuclei blue-black, while Eosin imparted various colours to cytoplasm and connective tissue (13). Slides were examined under magnifications of 40x and 400x for histopathological evaluation.

Statistical analysis

Data were analysed using Statistical Package for Social Science (SPSS) version 22, and described by mean and standard deviation (SD). Mean

differences between the groups were determined using a one-way analysis of variance (ANOVA), and multiple comparisons were conducted using the Bonferroni post hoc test to control for Type I error. Statistically significant differences were set at values of $p < 0.05$.

Results

Water and food intake

Mean water intake was not consistent. While group 1 had a decline in water intake at the fourth week, groups 2 to 5 had an increase in water intake ($p > 0.05$). There was a decline in food intake in all groups in the third week. However, in the fourth week, food intake increased in all groups except group 3 ($177.3 \pm 27.99\text{g}$ to $168.9 \pm 19.08\text{g}$) (appendix).

Body weight of experimental animals

Figure 1 presents findings on water intake of the subjects. Throughout the period of study, all groups exhibited weight gain. The average weight of the rats in the first week ranged from $116.9 \pm 4.68\text{g}$ (in group 4) to $207.7 \pm 12.75\text{g}$ (group 1). Likewise, the increase in weight also occurred at the fourth week, with group 1 having the highest value ($242.1 \pm 4.97\text{g}$) and group 4 the least weight ($163.7 \pm 5.78\text{g}$).

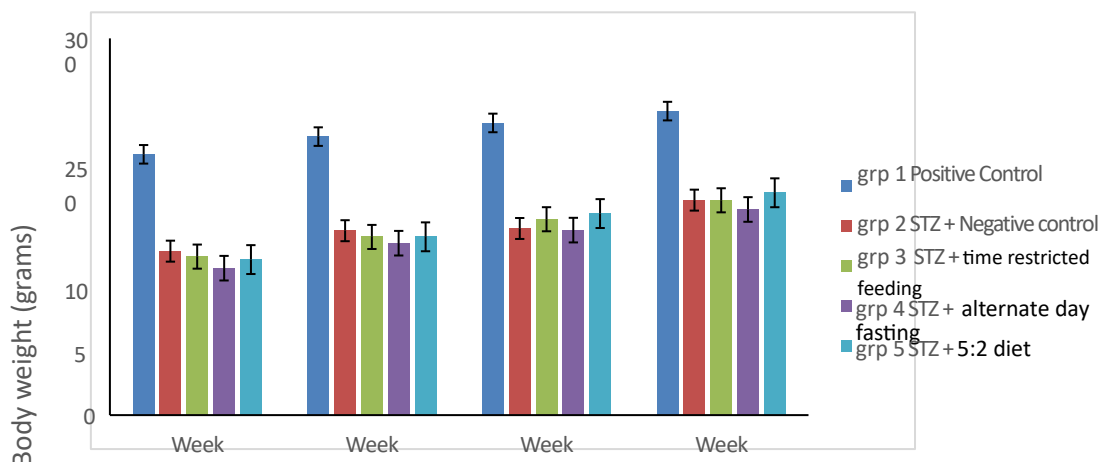


Figure 1: Weight trend of the rats in grams

Blood glucose level

The result of the blood glucose of the study animals is presented in Figure 2. At the initial stage, the blood glucose level of group 2 ($76.0 \pm 14.07\text{mg/dL}$) was the lowest, while group 3 had the highest value of blood glucose ($90.3 \pm 9.78\text{mg/dL}$). After inducing diabetes with STZ, all groups showed increased

blood glucose levels. Following treatment, a significant reduction was observed in blood glucose in group 2 ($104.0 \pm 10.23\text{mg/dL}$ to $63.3 \pm 15.37\text{mg/dL}$) and group 5 (93.8 ± 6.65 to $42.8 \pm 4.72\text{mg/dL}$) ($p < 0.05$).

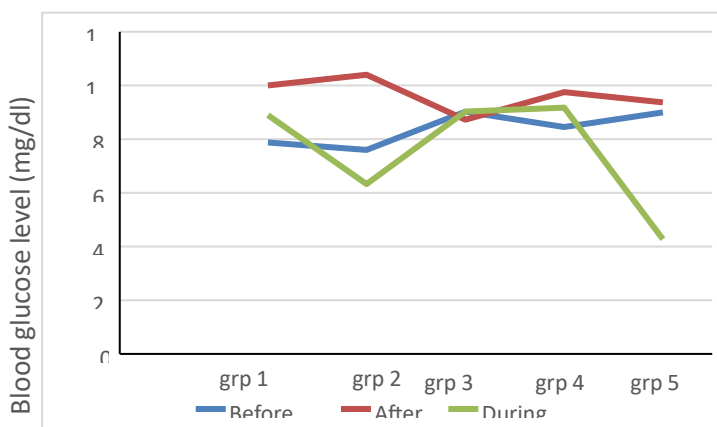


Figure 2: Blood glucose levels of study rats (mg/dl)

Plasma lipid profile

The findings on the plasma lipid profile of the experimental rats are presented in Table 2. The highest values of total cholesterol (7.2 ± 5.06 mg/dL) and triglyceride (13.7 ± 6.08 mg/dL) were found in group 1, while group 5 had the significantly highest values of high-density lipoprotein (34.4 ± 1.76 mg/dL) and low-density

lipoprotein (47.3 ± 1.95 mg/dL) ($p < 0.05$). Group 5 had the significantly lowest total cholesterol (3.0 ± 0.78 mg/dL). The least values of triglyceride (6.8 ± 1.71 mg/dL), high-density lipoprotein (5.7 ± 0.99 mg/dL) were found in group 3. The least value of low-density lipoprotein was found in group 4 (2.4 ± 1.29 mg/dL) ($p < 0.05$).

Table 2: Lipid profile of the experimental rats

Groups	TC (mg/dl)	TG (mg/dl)	HDL-C (mg/dl)	LDL-C (mg/dl)
1	$7.23^a \pm 0.05$	$13.72^a \pm 0.18$	$9.04^b \pm 0.03$	$4.56^b \pm 0.06$
2	$3.50^a \pm 0.07$	$7.88^a \pm 0.17$	$6.28^b \pm 0.49$	$4.25^b \pm 0.15$
3	$3.95^a \pm 0.03$	$6.78^a \pm 0.01$	$5.66^b \pm 0.09$	$3.06^b \pm 0.08$
4	$4.86^a \pm 0.04$	$7.09^a \pm 0.02$	$5.87^b \pm 0.08$	$2.43^b \pm 0.02$
5	$3.01^a \pm 0.06$	$7.57^a \pm 0.08$	$34.43^a \pm 1.76$	$47.33^a \pm 1.09$

Means with different superscripts along the column differ significantly at $p < 0.05$

Liver function profile

Table 3 presents the results of the liver function biomarkers test. The level of AST, ALT, and ALP was observed to be in varying degrees after treatment in groups 2,3,4 and 5 compared to the control group (group 1) which had the significant

highest values of AST (414.9 ± 303.63 mg/dL) and ALP (4529.8 ± 2177.67 mg/dL), while group 3 had the least amount of ALP (880.0 ± 28.19 mg/dL, $p =$). Group 5 had the least significant amount of AST (56.5 ± 22.92 mg/dL, $p =$) while group 4 had the least amount of ALT (0.2 ± 0.04 mg/dL).

Table 3: The liver function biomarkers test

Groups	AST	ALT	ALP
1	$414.96^a \pm 26.63$	$0.43^a \pm 0.09$	$4529.80^a \pm 77.67$
2	$221.16^{ab} \pm 19.57$	$0.52^a \pm 0.04$	$1712.70^b \pm 40.74$
3	$172.85^{ab} \pm 9.77$	$0.60^a \pm 0.07$	$880.00^b \pm 28.19$
4	$254.33^{ab} \pm 17.41$	$0.19^a \pm 0.04$	$2210.10^b \pm 10.09$
5	$56.45^b \pm 7.92$	$5.79^a \pm 0.13$	$1758.90^b \pm 18.68$

Means with different superscripts along the column differ significantly at $P < 0.05$

Kidney function profile

Table 4 shows the mean values of urea and creatinine levels in the blood samples of the rats in

each experimental group. The mean of urea across the group ranges from 1.43mg/dL to 3.35mg/dL, with group 5 having the lowest amount at

1.43mg/dL and group 1 having significant highest at a value of 3.35mg/dL. The mean value of creatinine level across all groups ranges from 9.67mg/dL to 86.75mg/dL, with group 4 having the lowest value of 9.67mg/dL and group 5 having the highest value of 86.75mg/dL ($p < 0.05$).

Histopathology Findings

Figures 3 and 4 present a photomicrograph representation of the liver sections from different experimental groups at lower and higher magnification. Micrographs of liver and kidney histological sections from different groups were

observed at lower and higher magnifications. In the liver (x400), Group 1 showed standard histological features with central vein, sinusoids, hepatocytes, and central vein haemorrhage. Group 2, treated with STZ only, displayed normal hepatocyte morphology without tissue degeneration. Group 3 exhibited dilated sinusoids, few inflammatory cells, and necrosis. Group 4 showed signs of degeneration with vacuolated cytoplasm and reduced hepatocyte count. Group 5 demonstrated less injury with improved cellular structure and uniform sinusoidal arrays, albeit has necrosis.

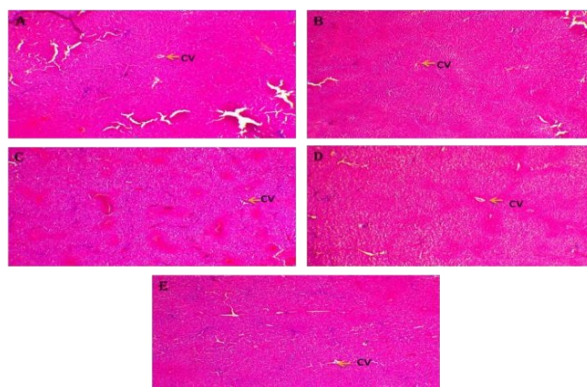


Figure 3: Magnification x40

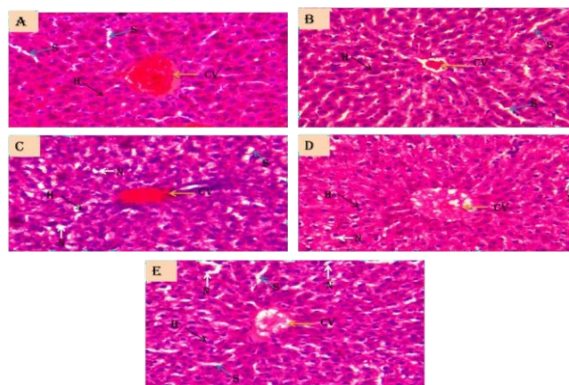


Figure 4: Magnification x400

In Figures 5 and 6, photomicrograph representations of the kidney sections from different experimental groups at lower and higher magnification are presented. In the kidney (x400), group 1 (A) displayed normal kidney architecture.

Group 2 (B) maintains normal kidney structure with no visible abnormalities. Group 3 (C) and 4 (D) showed hepatocellular necrosis and vacuolation, while Group 5 (E) exhibited partial preservation of architecture.

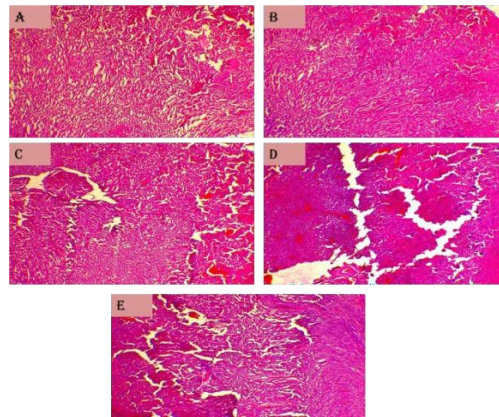


Figure 5: Magnification x40

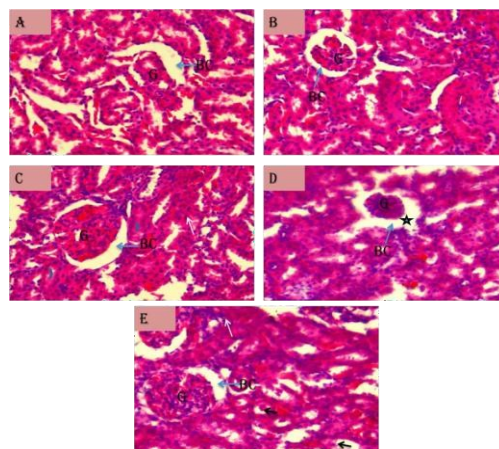


Figure 6: Magnification x400

CV = Central Vein (represented with a yellow arrow)
S = Sinusoids (represented with blue arrow)
N = Necrosis (represented with white arrow)
H = Hepatocytes (represented with black arrows)

Discussion

The findings of this study present significant insights into the impacts of intermittent fasting (IF) on various metabolic and health markers in diabetic model rats induced by streptozotocin (STZ). The results demonstrated notable changes in body weight, blood glucose levels, and lipid profiles, emphasising the potential benefits of dietary modifications for managing diabetes. Variations in water intake, food consumption, and associated metabolic variables highlighted the complexities between fasting regimens and metabolic outcomes, indicative of the multifaceted nature of IF (14, 15).

The study's observations of significant differences among treatment groups correlate with previous research indicating that IF can alleviate metabolic disturbances caused by diabetes and obesogenic

diets (16, 17). While fasting is typically linked to dietary intake restrictions, the observed increase in water consumption during fasting could prevent dehydration, which is critical for maintaining blood glucose levels (8, 18). This behavioural aspect could influence the efficacy of fasting regimens in managing diabetic conditions and necessitate further examination of hydration's role in fasting protocols.

The variations in body weight and food intake among the experimental groups further complicate the understanding of IF's effects; specifically, the 5:2 regimen led to unexpected weight gain, contradicting conventional expectations of fasting leading to weight loss (19, 20, 21). The results align with studies which reported that alternate-day fasting may not sufficiently address weight management due to compensatory caloric intake following fasting periods (22). This highlights the mechanism where the quality and quantity of food consumed post-fasting significantly influence weight outcomes, suggesting that merely employing IF without caloric oversight may yield limited success (23).

Additionally, blood glucose levels effectively illustrated the implications of fasting, particularly with the 5:2 diet, which registered significant reductions in glucose levels. This corresponds to the studies demonstrating IF's benefits in improving glucose metabolism and tolerance (24, 25, 26). However, varied experimental conditions underscore the critical nature of context in translating these results to broader human applications (27, 28, 29).

The lipid profiles observed showed intriguing results, with variations suggesting that intermittent fasting regimens could influence lipid metabolism. For instance, significant reductions in total cholesterol and improvements in HDL levels were pronounced in groups adhering to specific fasting protocols (30, 31, 32). While prior findings have typically associated IF with improved lipid levels, additional factors, such as the health status of experimental subjects and specifics of the fasting regimens, may contribute to observed metabolic profiles (33, 34, 35).

However, histological evaluations of kidney and liver function revealed mixed findings, with one group demonstrating improved renal function markers while concurrently exhibiting elevated creatinine levels, indicating hydration and dietary influences during fasting as potential confounding factors among animals placed on intermittent fasting. These findings resonate with previous studies highlighting intermittent fasting's effects on organ function, but they also emphasise the need for cautious interpretation given the diverse responses of metabolic pathways to fasting documented in previous literature (36, 37, 38).

In addition, this study presents evidence favouring intermittent fasting as a potential therapeutic avenue for managing Type 2 Diabetes Mellitus and its complications. However, limitations such as variability in responses among species, fasting duration, and dietary quality complicate the replicability of findings. Controlled dietary intake alongside fasting regimens is crucial to enhance these interventions' efficacy in clinical settings. Future studies should focus on delineating the mechanisms behind these results and implementing controlled human trials to evaluate the broader applicability of IF in diverse metabolic conditions.

Conclusion

This study demonstrates that the 5:2 intermittent fasting diet offers significant promise in managing diabetes-related metabolic disturbances, notably by markedly reducing blood glucose and cholesterol levels and improving lipid profiles, while

also providing protective effects on the liver and kidneys in a rat model. These findings contribute novel insights into the potential application of specific dietary regimens for metabolic health, highlighting the 5:2 diet as a particularly effective intervention despite associated weight gain and some elevation in renal and hepatic biomarkers.

However, limitations associated with the study include the observed organ-specific biomarker elevations, which could be due to physiological state of the study animals before the study or cumulative effects of fasting, dehydration and fat diet on metabolism (which were not accounted for), a short period of time spent to conduct the study and the use of an animal model, which may not fully translate to humans. Future research should explore long-term safety, optimise dietary protocols, and evaluate clinical efficacy in human populations to better inform potential therapeutic applications and mitigate risks associated with such dietary interventions.

List of Abbreviations

ADF:	Alternate-Day Fasting
ALP:	Alkaline Phosphatase
ALT:	Alanine Aminotransferase
ANOVA:	Analysis of Variance
AST:	Aspartate Aminotransferase
BG:	Blood Glucose
DKD:	Diabetic Kidney Disease
DM:	Diabetes Mellitus
H&E:	Haematoxylin and Eosin
HDL-C:	High-Density Lipoprotein Cholesterol
IF:	Intermittent Fasting
LDL-C:	Low-Density Lipoprotein Cholesterol
pH:	Potential of Hydrogen
SPSS:	Statistical Package for Social Science
STZ:	Streptozotocin
T2DM:	Type 2 Diabetes Mellitus

Declarations

Ethics approval and consent to participate

All procedures followed ethical guidelines for animal research. Ethical approval was obtained from the Babcock University Health Research Ethics Committee with reference number BUHREC 838/22.

Consent for publication

All the authors agreed to the publication of the work

Availability of data and materials

The data and materials used to write the article are available.

Competing interests

The authors declare no conflicts of interest.

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No grant was received from any external agency for this study.

Authors' contributions

AAR: conceptualisation, Data curation, Supervision, original draft writing, review
OE: Formal analysis, draft review
AE: Data curation and Methodology
OOO: formal analysis, draft writing, review, editing
OO: draft drafting, review and editing

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References

1. Ojo TK, Joshua OO, Ogedegbe OJ, Oluwole O, Ademidun A, Jesuyajolu D. Role of intermittent fasting in the management of prediabetes and type 2 diabetes mellitus. *Cureus*. 2022 Sep 5;14(9). <https://doi.org/10.7759/cureus.28800>
2. World Health Organization. Diabetes. World Health Organisation; WHO 2023. <https://www.who.int/news-room/fact-sheets/detail/diabetes>
3. Duncan BB, Magliano DJ, Boyko EJ. IDF diabetes atlas 11th edition 2025: global prevalence and projections for 2050. *Nephrology Dialysis Transplantation*. 2025 Aug 28;gfa177. <https://doi.org/10.1093/ndt/gfa177>
4. DCCT/EDiC Research Group. Intensive diabetes therapy and glomerular filtration rate in type 1 diabetes. *New England Journal of Medicine*. 2011 Dec 22;365(25):2366-76. <https://doi.org/10.1056/NEJMoa1111732>
5. Walker S, Tacinelli AM, Wu H, Pendergraft S, Horsfall K, Dridi S. Intermittent Fasting: A Potential Effective Strategy for Preventing Obesity and Type 2 Diabetes Mellitus. *Advances in Food Technology and Nutritional Sciences - Open Journal*. 2018 Nov 8;4(2):e9–12. <https://doi.org/10.17140/AFTNSOJ-4-e015>
6. Byrne MP, Pendergrass AG, Rapp AD, Wodzicki KR. Response of the intertropical convergence zone to climate change: Location, width, and strength. *Current climate change reports*. 2018 Dec;4(4):355-70. <https://doi.org/10.1007/s40641-018-0110-5>
7. Zang BY, He LX, Xue L. Intermittent fasting: potential bridge of obesity and diabetes to health?. *Nutrients*. 2022 Feb 25;14(5):981. <https://doi.org/10.3390/nu14050981>
8. Munhoz AC, Vilas-Boas EA, Panveloski-Costa AC, Leite JS, Lucena CF, Riva P, Emilio H, Carpinelli AR. Intermittent fasting for twelve weeks leads to increases in fat mass and hyperinsulinemia in young female Wistar rats. *Nutrients*. 2020 Apr 9;12(4):1029. <https://doi.org/10.3390/nu12041029>
9. Rhee EJ. Weight cycling and its cardiometabolic impact. *Journal of obesity & metabolic syndrome*. 2017 Dec 30;26(4):237. <https://doi.org/10.7570/jomes.2017.26.4.237>
10. Jacquet P, Schutz Y, Montani JP, Dulloo A. How dieting might make some fatter: modeling weight cycling toward obesity from a perspective of body composition autoregulation. *International Journal of Obesity*. 2020 Jun;44(6):1243-53. <https://doi.org/10.1038/s41366-020-0547-1>
11. Cerqueira FM, Chausse B, Kowaltowski AJ. Intermittent fasting effects on the central nervous system: how hunger modulates brain function. In *Handbook of Famine, Starvation, and Nutrient Deprivation 2019* (pp. 1243-1260). Springer, Cham. https://doi.org/10.1007/978-3-319-40007-5_29-1
12. Kunle-Alabi OT, Akindele OO, Odoh MI, Oghenetega BO, Raji Y. Comparative effects of coconut water and N-Acetyl cysteine on the hypothalamo-pituitary-gonadal axis of male rats. *Songklanakarin J Sci Technol*. 2017 Nov 1;39(6):759-64. <https://doi.org/10.14456/sjst-psu.2017.92>
13. Kim J, Choi W, Yoo D, Kim M, Cho H, Sung HJ, Choi G, Uh J, Kim J, Go H, Choi KH. Solution-free and simplified H&E staining using a hydrogel-based stamping technology. *Frontiers in Bioengineering and Biotechnology*. 2023 Nov 9;11:1292785. <https://doi.org/10.3389/fbioe.2023.1292785>
14. Gu L, Fu R, Hong J, Ni H, Yu K, Lou H. Effects of intermittent fasting in human compared to a non-intervention diet and caloric restriction: a meta-analysis of randomized controlled trials.

- Frontiers in nutrition. 2022 May 2;9:871682. <https://doi.org/10.3389/fnut.2022.871682>
15. Harris L, Hamilton S, Azevedo LB, Olajide J, De Brún C, Waller G, Whittaker V, Sharp T, Lean M, Hankey C, Ells L. Intermittent fasting interventions for treatment of overweight and obesity in adults: a systematic review and meta-analysis. JBI Evidence Synthesis. 2018 Feb 1;16(2):507-47. <https://doi.org/10.11124/JBISIRIR-2016-003248>
16. Janbozorgi N, Allipour R, Djafarian K, Shab-Bidar S, Badeli M, Safabakhsh M. Water intake and risk of type 2 diabetes: A systematic review and meta-analysis of observational studies. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2021 Jul 1;15(4):102156. <https://doi.org/10.1016/j.dsx.2021.05.029>
17. Osonuga IO, Olalekan SO, Olukade BA, Adedokun TA. Plain water intake in the prevention and management of type 2 diabetes mellitus (T2DM)—A study of biomarkers associated with insulin resistance in a black African population. Scientific African. 2024 Mar 1;23:e02114. <https://doi.org/10.1016/j.sciaf.2024.e02114>
18. Holcombe M. Intermittent fasting may not be as helpful for losing weight as once thought, study finds. 2023 Jan 19; Accessed 2025 March 15. Available at <https://edition.cnn.com/2023/01/19/health/eating-timing-weight-study-wellness/index.html>
19. Patterson RE, Laughlin GA, LaCroix AZ, Hartman SJ, Natarajan L, Senger CM, Martínez ME, Villaseñor A, Sears DD, Marinac CR, Gallo LC. Intermittent fasting and human metabolic health. Journal of the Academy of Nutrition and Dietetics. 2015 Aug 1;115(8):1203-12. <https://doi.org/10.1016/j.jand.2015.02.018>
20. Janaswamy R, Yelne P. A narrative review on intermittent fasting as an approachable measure for weight reduction and obesity management. Cureus. 2022 Oct 17;14(10). <https://doi.org/10.7759/cureus.30372>
21. Nye K, Cherrin C, Meires J. Intermittent fasting: exploring approaches, benefits, and implications for health and weight management. The Journal for Nurse Practitioners. 2024 Mar 1;20(3):104893. <https://doi.org/10.1016/j.nurpra.2023.104893>
22. Gallage S, Ali A, Avila JE, Seymen N, Ramadori P, Joerke V, Zizmare L, Aicher D, Gopalsamy IK, Fong W, Kosla J. A 5: 2 intermittent fasting regimen ameliorates NASH and fibrosis and blunts HCC development via hepatic PPARα and PCK1. Cell metabolism. 2024 Jun 4;36(6):1371-93. <https://doi.org/10.1016/j.cmet.2024.04.015>
23. Song DK, Kim YW. Journal of Yeungnam Medical Science. Journal of Yeungnam Medical Science. 2022 Apr 4;40(1):4-11. <https://doi.org/10.12701/jyms.2022.00010>
24. Gao Y, Tsintzas K, Macdonald IA, Cordon SM, Taylor MA. Effects of intermittent (5: 2) or continuous energy restriction on basal and postprandial metabolism: A randomised study in normal-weight, young participants. European journal of clinical nutrition. 2022 Jan;76(1):65-73. <https://doi.org/10.1038/s41430-021-00909-2>
25. Chijiokwu EA, Nwangwa EK, Oyovwi MO, Naiho AO, Emojevwe V, Ohwin EP, Ehiwarior PA, Ojugbeli ET, Nwabuoku US, Oghenetega OB, Ogheneyoma OO. Intermittent fasting and exercise therapy abates STZ-induced diabetotoxicity in rats through modulation of adipocytokines hormone, oxidative glucose metabolic, and glycolytic pathway. Physiological Reports. 2022 Oct;10(20):e15279. <https://doi.org/10.14814/phy2.15279>
26. Agbonifo-Chijiokwu E, Nwangwa KE, Oyovwi MO, Ben-Azu B, Naiho AO, Emojevwe V, Ohwin EP, Ehiwarior AP, Ojugbeli ET, Nwabuoku SU, Moke EG. Underlying biochemical effects of intermittent fasting, exercise and honey on streptozotocin-induced liver damage in rats. Journal of Diabetes & Metabolic Disorders. 2023 Jun;22(1):515-27. <https://doi.org/10.1007/s40200-022-01173-2>
27. Meng H, Zhu L, Kord-Varkaneh H, Santos HO, Tinsley GM, Fu P. Effects of intermittent fasting and energy-restricted diets on lipid profile: a systematic review and meta-analysis. Nutrition. 2020 Sep 1;77:110801. <https://doi.org/10.1016/j.nut.2020.110801>
28. Pammer A, Obermayer A, Stadler JT, Pferschy PN, Tripolt NJ, Habisch H, Madl T, Sourij H, Marsche G. Effects of dietary interventions and intermittent fasting on HDL function in obese individuals with T2DM: a randomized controlled trial. Cardiovascular Diabetology. 2024 Sep 12;23(1):339. <https://doi.org/10.1186/s12933-024-02426-5>
29. Li M, Li J, Xu Y, Gao J, Cao Q, Ding Y, Xin Z, Lu M, Li X, Song H, Shen J. Effect of 5: 2 regimens: energy-restricted diet or low-volume high-intensity interval training combined with resistance exercise on glycemic control and cardiometabolic health in adults with overweight/obesity and type 2 diabetes: a three-arm randomized controlled trial. Diabetes Care. 2024 Jun 4;36(6):1371-93. <https://doi.org/10.1016/j.cmet.2024.04.015>

- 2024 Jun 1;47(6):1074-83.
<https://doi.org/10.2337/dc24-0241>
30. Bakhit AA, Kurdi AM, Wadera JJ, Alsuwaida AO. Effects of Ramadan fasting on moderate to severe chronic kidney disease: a prospective observational study. Saudi medical journal. 2017 Jan;38(1):48.
<https://doi.org/10.15537/smj.2017.1.17566>
31. Karatas A, Canakci E, Arici YK, Kaya M, Sayim B. The effect of fasting during Ramadan on the kidney functions of stage III-IV chronic kidney disease patients. Pakistan Journal of Medical Sciences. 2021 Jul;37(4):972.
<https://doi.org/10.12669/pjms.37.4.3661>
32. Kalra A, Yetiskul E, Wehrle CJ, Tuma F. Physiology, liver. InStatPearls [internet] 2023 May 1. StatPearls Publishing.
<https://www.ncbi.nlm.nih.gov/books/NBK535438/>
33. Allaire M, Rautou PE, Codogno P, Lotersztajn S. Autophagy in liver diseases: time for translation?. Journal of hepatology. 2019 May 1;70(5):985-98.
<https://doi.org/10.1016/j.jhep.2019.01.026>
34. Cai H, Qin YL, Shi ZY, Chen JH, Zeng MJ, Zhou W, Chen RQ, Chen ZY. Effects of alternate-day fasting on body weight and dyslipidaemia in patients with non-alcoholic fatty liver disease: a randomised controlled trial. BMC gastroenterology. 2019 Dec 18;19(1):219.
<https://doi.org/10.1186/s12876-019-1132-8>
35. Xiao Y, Liu Y, Zhao L, Zhou Y. Effect of 5: 2 fasting diet on liver fat content in patients with type 2 diabetic with nonalcoholic fatty liver disease. Metabolic Syndrome and Related Disorders. 2022 Oct 1;20(8):459-65.
<https://doi.org/10.1089/met.2022.0014>
36. Tarabeih M, Qaddumi J, Hamdan Z, Hassan M, Jebrin K, Khazneh E, Bahar S, Ahmed N, Sawalha R, Sawalmeh O. Increasing overnight fluid intake and kidney function during ramadan fasting: a randomized controlled trial. InTransplantation Proceedings 2023 Jan 1 (Vol. 55, No. 1, pp. 80-86). Elsevier.
<https://doi.org/10.1016/j.transproceed.2022.10.059>
37. Ismail NA, Kumala ES, Pramaningtyas MD. Blood urea nitrogen levels increase after giving high-fat-high-fructose and lowered by islamic intermittent fasting, but not only ramadan fasting: Study in rats. Atherosclerosis. 2021 Aug 1;331:e237.
<https://doi.org/10.1016/j.atherosclerosis.2021.06.730>
38. Jang Y, Kim YS, Kim SR, Lee DW, Lee SB, Kim IY. Intermittent Fasting Protects Against the Progression from Acute Kidney Injury to Chronic Kidney Disease. Antioxidants. 2025 Jan 20;14(1):119.
<https://doi.org/10.3390/antiox14010119>