https://doi.org/10.35845/kmuj.2025.24011

ORIGINAL ARTICLE

Effects of postprandial exercise timing on Irisin and metabolic responses in adults with prediabetes

Inayat Shah [1], Fazeelat Hajra Karim [2], Saman Tauqir [1], Zubia Shah [1,2]

1: Department of Physiology, Institute of Basic Medical Sciences, Khyber Medical University, Peshawar, Pakistan

2: Department of Physiology, Khyber Girls Medical College, Peshawar, Pakistan

Email: zubiashah1971@gmail.com

Contact #: +92-300-5942110

Date Submitted: April 21, 2025

Date Revised: December 14, 2025

Date Accepted: December 15, 2025

ABSTRACT

Objectives: To evaluate the effects of different postprandial exercise timings (30, 60, 90, and 120 minutes after meal intake) on serum irisin levels, lipid profile, anthropometric indices, and substrate metabolism in middle-aged adults with prediabetes.

Methods: This controlled, repeated-measures experimental study was conducted on twenty-five sedentary adults aged 30-40 years with prediabetes at Khyber Medical University, Peshawar, Pakistan, from July 2022 to December 2023. Participants served as their own controls and completed four treadmill-walking sessions (40 minutes at 50% predicted maximum heart rate), performed one week apart at varying postprandial intervals. Venous blood samples were collected at fasting, pre-exercise, and 60-, 90-, and 120-minutes post-exercise across the study weeks to assess serum irisin and lipid profile. Substrate metabolism (VO_2, respiratory quotient), perceived exertion, and anthropometric measures were assessed at baseline and at the end of the study.

Results: Exercise performed 30 minutes after meal produced maximum rise in serum irisin ($\Delta = +115$ pg/mL, $p<0.001$), and significant reductions in total cholesterol, LDL-C, and triglycerides, with an increase in HDL-C ($p<0.001$). Fat oxidation peaked at the 30-minute exercise condition ($p=0.015$), whereas carbohydrate oxidation was highest when exercise was initiated 120 minutes post-meal ($p = 0.026$). Anthropometric indices (BMI, waist circumference, body fat %) showed significant improvement over the study duration. Perceived stress remained largely unchanged, although participants subjectively reported better mood and energy following exercise.

Conclusion: Initiating postprandial exercise, particularly within 30–60 minutes after meals, optimally improves lipid metabolism, substrate utilization, and irisin response in prediabetes.

Clinical Trial Registration Number: NCT06656377

Keywords: Prediabetes State (MeSH); Irisin (Non-MeSH); Exercise (MeSH); Postprandial exercise (Non-MeSH); Lipids (MeSH); Lipid Profile (Non-MeSH); Cholesterol (MeSH); Triglycerides (MeSH); Cholesterol, LDL (MeSH); Cholesterol, HDL (MeSH); Chrono-Exercise (Non-MeSH); Cardiometabolic Health (Non-MeSH).

THIS ARTICLE MAY BE CITED AS: Shah I, Karim FH, Tauqir S, Shah Z. Effects of postprandial exercise timing on Irisin and metabolic responses in adults with prediabetes. Khyber Med Univ J 2025;17(4):456-64. https://doi.org/10.35845/kmuj.2025.24011

INTRODUCTION

Prediabetes (PD) is a growing global public health concern, characterized by blood glucose levels that exceed normal thresholds but do not meet diagnostic criteria for diabetes mellitus. This intermediate metabolic state is associated with a substantially increased risk of progression to type 2 diabetes mellitus (T2DM) and the development of cardiovascular diseases (CVD).[1,2] According to recent estimates from the Centers for Disease Control and Prevention (CDC) and the International Diabetes Federation (IDF), Pakistan ranks among the countries with the highest burden of PD, with approximately 33 million adults affected. This burden is expected to rise further in parallel with increasing sedentary lifestyles, obesity, and unhealthy dietary patterns.[3-5]

One of the key metabolic abnormalities in PD is dyslipidaemia, characterized by elevated triglyceride (TG) levels, reduced high-density lipoprotein cholesterol (HDL-C), and increased low-density lipoprotein cholesterol (LDL-C), all of which contribute to heightened cardiovascular risk.[6] Addressing these metabolic disturbances is essential to prevent progression from PD to overt diabetes and its associated complications. Non-pharmacological interventions, particularly regular physical activity, have been shown to significantly improve insulin sensitivity, lipid profiles, and glucose tolerance.[1,7]

Importantly, emerging evidence indicates that the timing of exercise relative to meal consumption, particularly during the postprandial phase, may play a critical role in modulating metabolic responses. The postprandial period is a metabolically vulnerable window characterized by transient surges in glucose, insulin, and circulating lipids, and dysregulated responses during this phase are closely linked to endothelial dysfunction and increased cardiometabolic risk.[8,9] Despite growing interest in postprandial exercise, most existing studies have primarily focused on glycaemic control, with limited mechanistic insight into hormone-mediated adaptations, especially among individuals with prediabetes. Consequently, the concept of chrono-exercise, time-specific physical activity tailored to metabolic rhythms, has emerged as a promising, personalized strategy for metabolic regulation.[10]

A novel focus of contemporary metabolic research is the investigation of irisin, an exercise-induced adipocytokine implicated in the

browning of white adipose tissue, improved glucose homeostasis, lipid modulation, and stress reduction.[11,12] However, evidence regarding the temporal dynamics of irisin release remains inconsistent. While some studies report pronounced exercise-induced increases, others demonstrate attenuated or variable responses, particularly in insulin-resistant or dysmetabolic states. Notably, the impact of postprandial exercise timing on irisin secretion has not been systematically explored in prediabetic populations, leaving an important physiological and clinical gap.

Although prior studies have examined the effects of exercise on lipid profiles or irisin levels independently, many have employed heterogeneous exercise protocols, varying intensities, or non-standardized nutritional conditions, thereby limiting interpretability. Moreover, few investigations have integrated hormonal responses with substrate utilization patterns, despite evidence that fat and carbohydrate oxidation are strongly influenced by the timing of exercise relative to meals.[13,14] This lack of an integrative approach constrains understanding of whether observed metabolic benefits are primarily hormonally mediated, substrate driven, or a combination of both.

Therefore, a critical unanswered question remains: does the timing of exercise within the postprandial window differentially influence irisin secretion, lipid metabolism, and substrate utilization in adults with prediabetes? Clarifying this relationship is essential for refining exercise prescriptions beyond generic recommendations toward mechanism-informed, precision lifestyle interventions.

To address these gaps, the present study evaluated the effects of four distinct postprandial exercise timings; 30, 60, 90, and 120 minutes after consumption of a standardized meal, implemented in a structured, week-by-week sequence. Using a repeated-measures design, each participant served as their own control, allowing direct within-subject comparisons across timing conditions. The study assessed changes in serum irisin levels, lipid profiles, anthropometric measures, perceived stress, and substrate metabolism, thereby extending existing evidence by integrating exercise timing with hormonal and metabolic mechanisms in a prediabetic population.

METHODS

Study design and ethical approval: This controlled, repeated-measures experimental study was conducted at the Sports Research Unit of Khyber Medical University, Peshawar, Pakistan, between July 2022 and December 2023. Ethical approval was obtained from the Graduate Study Committee (Ref. No. 62/2022), the Advanced Study and Research Board (Letter No. DIR/KMU-AS&RB/EA/001693), and the Institutional Review Board and Ethics Committee of the Institute of Basic Medical Sciences, KMU (Approval Nos. KMU/IBMS/IRBE/meeting/2022/8075 and KMU/IBMS/IRBE/3rd meeting/2023/9606-7). The study was registered with ClinicalTrials.gov (Identifier: NCT06656377).

Written informed consent was obtained from all participants prior to enrolment, and the study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Participants: A total of 25 middle-aged adults with prediabetes were recruited using non-probability purposive sampling. Sample size estimation was performed using G*Power software (version 3.1.9.2), assuming a significance level of $\alpha=0.05$, statistical power of $1-\beta=0.95$, and an effect size derived from previous exercise intervention studies. Participants were screened and diagnosed according to the American Diabetes Association criteria for prediabetes, defined by fasting plasma glucose levels of 100-125 mg/dL and glycated hemoglobin (HbA1c) values of 5.7%-6.4%.[15]

Participant eligibility, screening, and baseline assessment: Eligible participants were adults aged 30-40 years with a sedentary lifestyle, as determined using the International Physical Activity Questionnaire (IPAQ) short form, and were deemed physically fit to undertake exercise based on the Physical Activity Readiness Questionnaire (PAR-Q). Exclusion criteria included a prior diagnosis of diabetes mellitus; cardiovascular, pulmonary, or musculoskeletal disorders; pregnancy or lactation; current use of lipid-lowering medications; or participation in any other interventional studies.

At the initial visit, participants underwent comprehensive screening and baseline assessments. Anthropometric measurements, incl-uding height and weight, were recorded using a stadiometer and a calibrated digital weighing scale, and body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared (kg/m^2). Waist circumference was measured at the midpoint between the lowest rib and the iliac crest, while hip circumference was measured at the widest point of the hips; the waist-to-hip ratio (WHR) was subsequently derived. Fasting blood samples were also obtained to assess glycated hemoglobin (HbA1c) and lipid profiles as part of the baseline biochemical evaluation.

Study protocol

Overview: Participants served as their own controls and completed four exercise sessions scheduled for one week apart. Each session was performed at a different postprandial interval (30, 60, 90, and 120 minutes) following consumption of a standardized breakfast, with postpr-andial exercise timing serving as the primary variable of interest.

Standardized meal: At each visit, participants consumed a standardized 250-kcal isocaloric breakfast in the fasting state. The meal provided approximately 55% carbohydrates, 25% fat, and 20% protein, with an estimated moderate glycaemic index (GI≈55-60), and consisted of two slices of whole-grain bread, one boiled egg, and a measured portion of unsweetened low-fat milk tea. All meals were prepared under standardized conditions within the research facility and consumed within a fixed 20-minute period. Identical food items, portion sizes, preparation methods, and serving times were maintained across all visits

to ensure consistency of postprandial metabolic exposure. Participants were instructed to abstain from any additional food or beverages, except water, during the waiting period prior to exercise.

The exercise regimen consisted of treadmill walking performed at 50% of the predicted maximum heart rate (PMHR), calculated using the formula PMHR=220 -age. Each session lasted 40 minutes, including a 5-minute warm-up and a 5-minute cool-down. Exercise was initiated at four postprandial time points: 30 minutes (Visit 1), 60 minutes (Visit 2), 90 minutes (Visit 3), and 120 minutes (Visit 4) after meal consumption. Heart rate was continuously monitored using a Garmin HRM chest strap, and treadmill speed was adjusted as needed to maintain the target PMHR. Participants were advised to avoid vigorous physical activity for at least 24 hours prior to each session.

Blood sample collection and biochemical analysis: Venous blood samples were collected at four time-points during each visit: fasting (prior to breakfast), pre-exercise (immediately before the treadmill session), and at 30- and 60-minutes post-exercise. All samples were processed under aseptic conditions and centrifuged to separate plasma, which was stored at -80 °C until analysis.

Biochemical analyses included a lipid profile comprising total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglycerides. Serum irisin concentrations were measured using a commercially available enzyme-linked immunosorbent assay (ELISA) kit (manufacturer and catalogue number to be specified in the final version), with an analytical sensitivity of <1 ng/mL and a detection range appropriate for human serum. All samples were analyzed in duplicate, preferably within the same assay batch, to minimize inter-assay variability. Intra-assay and inter-assay coefficients of variation were maintained below 10% and 12%, respectively, in accordance with manufacturer specifications. Samples underwent only a single freeze–thaw cycle, and all analyses were conducted by the same trained laboratory personnel following standardized operating procedures.

Cardiorespiratory fitness assessment and gas analyzer: Cardiorespiratory variables were assessed using a breath-by-breath gas exchange analyzer (COSMED, Italy). Prior to each testing session, the metabolic cart was calibrated in accordance with manufacturer guidelines, including gas calibration with certified reference gas concentrations and flow calibration using a precision syringe. Ambient environmental conditions, including temperature, humidity, and barometric pressure, were recorded and incorporated into the calibration process. Calibration procedures were repeated before each participant session to ensure consistency and accuracy of measurements across all visits.

Measured parameters included oxygen consumption (VO_2), carbon dioxide production (VCO_2), respiratory quotient (RQ), metabolic equivalents (METs), heart rate (HR), energy expenditure (EEh; kcal/h), and fat and carbohydrate oxidation rates (kcal/day).

Psychological assessment: The Perceived Stress Scale (PSS) was administered before and after each exercise session to assess acute changes in psychological stress levels.

Chronobiological and temporal controls: All exercise testing sessions were conducted within a fixed morning time window (08:00 –11:00 AM), with individual testing times kept consistent across all four visits for each participant. Participants were instructed to maintain their usual sleep patterns and to refrain from strenuous physical activity for at least 24 hours prior to each session. Self-reported sleep duration and recent physical activity were verbally confirmed at each visit. Although formal chronotype assessment was not performed, the use of stable testing windows minimized circadian variability and supported interpretation of exercise timing effects within a chrono-exercise framework.

Ethical considerations related to repeated venepuncture: To minimize participant burden associated with multiple venous blood samples across study visits, a single peripheral intravenous cannula (three-way cannula) was inserted at the start of each visit, thereby avoiding repeated venepunctures. All subsequent samples during that visit were obtained through the same cannula under aseptic conditions. The cannula was flushed with normal saline after each sampling to maintain patency and prevent clot formation. All insertions were performed by an experienced phlebotomist using the smallest gauge compatible with adequate blood collection.

Participants were continuously monitored for discomfort, hematoma, dizziness, or vasovagal symptoms throughout each session. Potential risks and benefits, including those related to repeated blood sampling, were clearly explained during the informed consent process, and participants retained the right to withdraw at any time without penalty. The risk–benefit profile of this procedure was reviewed and approved by the Institutional Review Board prior to study initiation.

Statistical analysis: Data were analyzed using SPSS version 23 and GraphPad Prism version 8. Descriptive statistics were presented as mean± standard deviation (SD). Inferential analyses included paired t-tests to assess pre- and post-exercise changes within each visit and repeated-measures ANOVA with Bonferroni post hoc correction to evaluate trends across visits. Independent sample t-tests were applied to examine gender-based differences in anthropometric variables. A p value<0.05 was considered statistically significant. Graphical representations of lipid parameters and substrate metabolism were generated to improve clarity and support publication.

RESULTS

The participants had a mean age of 34.88±4.11 years. Male participants were significantly taller than females (172.70 cm vs. 164.25 cm; p=0.002), and waist circumference was also significantly higher in males compared with females (103.76 cm vs. 98.75 cm; p=0.035). No statistically significant gender differences were observed in hip circumference (p=0.467), body

weight (p=0.545), or body mass index (p=0.372), although females exhibited a slightly higher mean BMI than males (31.48 vs. 29.81 kg/m^2). Detailed anthropometric characteristics are presented in Table I. All the values in the table are presented as means± standard deviation (SD) values for the demographic and anthropometric parameters of the study participant's, categorized overall and by gender. Table II summarizes changes in lipid profiles at different postprandial exercise intervals. Across all visits, total cholesterol levels decreased significantly at 60 minutes of post-exercise compared with pre-exercise values, with the greatest reduction observed during the 30-minute postprandial exercise session (p< 0.001). Triglyceride levels demonstrated variable responses, with a significant reduction observed in Visit 2 (60-minute post-meal exercise; p=0.032), while changes during other visits did not reach statistical significance. High-density lipoprotein (HDL) levels increased consistently following exercise, with statistically significant elevations at 60 minutes across all four visits (p<0.05), most notably after the 30-minute postprandial session. Low-density lipoprotein (LDL) levels decreased significantly after exercise in Visits 1 through 3 but not in Visit 4, indicating a diminishing lipid-lowering effect with

Table I: Demographic and anthropometric profile of participants in the study

Participant Characteristics	Total	Female(n=8)	Male (n=17)	p-value
Age (years)	34.88±4.11	32.25±4.23	36.11±3.53	0.025
Height (cm)	170±6.70	164.25±2.91	172.70±6.28	0.002
Weight (kg)	87.85±14.56	85.21±13.77	89.1±13.77	0.545
Body Mass Index (kg/m^2)	30.34±4.27	31.48±4.30	29.81±4.28	0.372
Waist Circumference (cm)	102.16±12.22	98.75±17.10	103.76±10.73	0.035
Hip Circumference (cm)	105.13±12.43	106.41±9.93	102.42±17.10	0.467
Waist to hip ratio	0.97±0.04	0.92±0.05	1.01±0.02	0.659

m=meter; cm: centimeter

Table II: Changes in lipid profiles at various postprandial time points following exercise

Markers	Visits	Fasting	Waiting time (minutes)	Pre-exercise	30 min	60 min	p -values
Cholesterol	1	207.58±30.45	30	216.36±29.57	199.08±5.51	184.80±5.07	<0.001
	2	216.92±44.87	60	221.56±48.96	201.44±41.48	189.44±39.72	<0.001
	3	198.44±40.88	90	211.16±45.84	187.6±28.51	184.2±31.17	0.002
	4	201.36±30.77	120	207.72±32.66	188.76±22.26	179.88±20.84	<0.001
	p -value	0.314	-	0.636	0.274	0.738	-
TG	1	184.2±27.46	30	196.88±35.58	188.6±29.59	179.88±31.86	0.105
	2	183.88±26.71	60	200.2±33.59	185.52±27.56	174.04±23.10	0.032
	3	177.8±25.68	90	199.4±30.64	187.08±28.05	176.04±29.36	0.224
	4	174.36±21.02	120	187.28±23.59	178.96±19.52	173.08±17.54	0.27
	p-value	0.445	-	0.442	0.590	0.801	-
HDL	1	38.8±1.47	30	38.6±2.17	40.08±2.88	43.76±2.03	<0.001
	2	38.76±2.48	60	38.68±2.15	39.8±2.34	41.12±2.61	<0.001
	3	39±1.91	90	39.6±1.77	40.2±2.94	40.24±1.96	<0.001
	4	39.2±2.23	120	38.88±1.58	40.36±2.56	39.88±2.53	0.031
	p -value	0.867	-	0.255	0.901	<0.001	-
LDL	1	88.04±10.99	30	94±14.03	89.76±13.22	80.88±10.70	<0.001
	2	82.64±9.86	60	87.64±10.75	84.76±11.29	77±10.76	<0.001
	3	87.68±13.60	90	92.8±12.31	88.16±13.60	85.32±12.96	0.002
	4	87.4±12.46	120	92.88±11.33	89.48±11.02	86.24±9.95	0.198
	p -value	0.329	-	0.257	0.462	0.015	-

TG: Triglycerides; HDL: high-density lipoprotein; LDL: low-density lipoprotein

Table III: Dynamic changes in lipid profiles following postprandial exercise: a multi-visit analysis

Parameters	Blood Time points	Visit 1			Visit 2			Visit 3			Visit 4		
		Mean Difference	Std. Error	p -values	Mean Difference	Std. Error	p -values	Mean Difference	Std. Error	p -values	Mean Difference	Std. Error	p -values
Cholesterol	Pre-exercise vs 30 min	17.280*	4.430	.004	20.120*	3.615	.000	23.560*	4.913	.000	18.960*	3.272	.000
	Pre-exercise vs 60 mins	31.560*	4.051	.000	32.120*	4.309	.000	26.960*	4.605	.000	27.840*	4.294	.000
	30 mins vs 60 min	14.280*	2.373	.000	12.000*	1.606	.000	3.400	3.155	1.000	8.880*	1.999	.001
TG	Pre-exercise vs 30 min	8.280	2.990	.064	14.680	5.850	.116	12.320*	2.152	.000	8.320*	2.694	.030
	Pre-exercise mins vs 60 mins	17.000*	3.294	.000	26.160*	5.736	.001	23.360*	3.038	.000	14.200*	4.258	.017
	30 mins vs 60 min	8.720*	1.308	.000	11.480*	2.092	.000	11.040*	1.767	.000	5.880	2.324	.110
HDL	Pre-exercise mins vs 30 min	-1.480*	.444	.017	-1.120*	.353	.024	-.600	.583	1.000	-1.480*	.440	.016
	Pre-exercise mins vs 60 mins	-5.160*	.489	.000	-2.440*	.444	.000	-.640	.594	1.000	-1.000	.523	.407
	30 mins vs 60 min	-3.680*	.547	.000	-1.320	.479	.066	-.040	.607	1.000	.480	.530	1.000
LDL	Pre-exercise mins vs 30 min	4.240*	1.373	.030	2.880*	.930	.029	4.640*	.954	.000	3.400*	.993	.013
	Pre-exercise mins vs 60 mins	13.120*	1.925	.000	10.640*	1.278	.000	7.480*	1.211	.000	6.640*	1.283	.000
	30 mins vs 60 min	8.880*	1.403	.000	7.760*	1.241	.000	2.840*	.952	.039	3.240*	.906	.009

TG: Triglycerides; HDL: high-density lipoprotein; LDL: low-density lipoprotein

delayed exercise timing (p=0.198).

Bonferroni-adjusted post hoc analysis (Table III) confirmed significant reductions in total cholesterol and LDL cholesterol from pre-exercise to both 30- and 60-minutes post-exercise across study visits. Triglyceride levels demonstrated a comparable pattern, with significant reductions particularly evident in Visits 2 and 3. In contrast, HDL cholesterol showed modest decreases at certain time points, which may reflect acute fluid shifts or transient metabolic changes following exercise. Overall, LDL cholesterol reductions were consistent, demonstrating statistically significant declines across nearly all comparisons.

Table IV presents data on respiratory and metabolic parameters. While the number of steps and exercise duration remained statistically unchanged across different time intervals, oxygen consumption (VO_2) significantly increased with delayed exercise ($p<0.001$). Notably, fat oxidation was highest during the 30-minute post-meal exercise session and significantly declined with increasing wait times ($p=0.015$). Conversely, carbohydrate oxidation progressively increased, peaking at the 120-minute mark ($p=0.026$), indicating a metabolic substrate shift from fat to carbohydrate utilization as the postprandial period extended.

Timing protocol Human Irisin hormone concentration: Figure 1 illustrates Irisin hormone concentrations across the four exercise sessions. The highest increase in Irisin was observed when exercise commenced 30 minutes post-meal, with a statistically significant rise across all visits ($^{*}p<0.05$, $^{**}p<0.005$, $^{***}p<0.001$). This suggests that early postprandial exercise is most effective in stimulating Irisin secretion. Perceived stress levels, measured using the Perceived Stress Scale (PSS), showed no significant statistical change from baseline to the end of the study ($p>0.05$). However, subjective reports indicated that participants felt more relaxed and energized following exercise sessions, reflecting positive psychological responses even in the absence of statistically significant differences (Figure 2).

Collectively, these findings support the hypothesis that exercise timing significantly influences lipid metabolism, substrate utilization, and hormonal responses in individuals with prediabetes. Exercise performed within 30–60 minutes after meal consumption was most effective in improving lipid profiles, enhancing fat oxidation, and increasing irisin levels. These results provide strong evidence for incorporating time-specific physical activity into metabolic risk reduction and management strategies.

DISCUSSION

This study demonstrates that postprandial exercise timing significantly influences lipid metabolism, substrate utilization, and hormonal responses in adults with prediabetes. Exercise performed within 30-60 minutes after meal intake elicited the most favorable metabolic effects, including pronounced increases in circulating irisin, improved lipid profiles, and enhanced fat oxidation. By integrating metabolic, hormonal, and substrate utilization outcomes within a standardized nutritional context, these findings emphasize exercise timing relative to meals as a modifiable determinant of metabolic adaptation and support the role of chrono-exercise as a targeted, non-pharmacological strategy for reducing cardiometabolic risk in individuals with prediabetes.[11]

Irisin has been proposed as a key mediator linking skeletal muscle contraction to systemic metabolic regulation. First described by Boström P, et al., this exercise-induced myokine has emerged as a promising molecular link between physical activity and metabolic homeostasis.

In the present study, circulating irisin levels increased significantly when exercise was initiated 30 and 60 minutes after meal intake, a pattern consistent with previous reports by Parada-Sánchez SG, et al., and Rioux BV, et al., which demonstrated that both exercise modality and intensity influence irisin responses.[18,19] These findings may reflect enhanced muscle-adipose signaling within a postprandial metabolic milieu; however, they should be interpreted with caution.

Rather than suggesting a discrete "anabolic window," our results support the hypothesis that transient postprandial insulin availability and nutrient flux may permissively modulate exercise-induced irisin release. This interpretation aligns with experimental evidence indicating that irisin secretion is sensitive to both metabolic state and exercise context, although the underlying causal mechanisms remain incompletely understood. Future mechanistic studies incorporating insulin dynamics, glucose kinetics, and muscle tissue analyses are warranted to further elucidate these interactions.

These findings suggest that the postprandial anabolic milieu may enhance muscle-adipose signaling through improved insulin sensitivity and nutrient availability, thereby optimizing irisin secretion. This observation is consistent with findings by Aqeel M, et al., who highlighted the glycaemic benefits of post-meal exercise,[20] although the present study uniquely positions irisin as a central mechanistic mediator in prediabetic populations.

Our results demonstrated consistent and significant reductions in total cholesterol, LDL cholesterol, and triglycerides, particularly when exercise was performed 30-60 minutes after meal consumption. This temporal pattern suggests that exercise during peak postprandial lipaemia may facilitate lipid clearance, potentially through increased lipoprotein lipase activity and accelerated turnover of triglyceride-rich lipoproteins. The observed post-exercise increase in HDL cholesterol aligns with previous systematic reviews indicating that HDL is among the most responsive lipid fractions to aerobic exercise.[21] Collectively, these findings support the hypothesis that exercise undertaken during peak postprandial lipid excursions can acutely attenuate lipaemia, likely via enhanced lipoprotein lipase activity and upregulation of hepatic LDL receptor expression.[22,23]

Furthermore, the variability in triglyceride and LDL responses observed during the 90- and 120-minute exercise windows highlights the importance of individual metabolic

timing when designing exercise interventions. Evidence from studies by Bittel AJ, et al., and Shimada K, et al., demonstrates that postprandial lipid metabolism is highly time sensitive, reinforcing our observation that early post-meal exercise confers superior lipid-lowering effects. [24,25]

Analysis of substrate metabolism further clarifies the importance of exercise timing. Fat oxidation was greatest when exercise was performed early in the postprandial period, whereas delayed exercise favored carbohydrate utilization, reflecting progressive shifts in substrate availability as time elapsed after meal ingestion. These findings indicate that exercise timing influences not only hormonal responses but also acute metabolic fuel selection in individuals with prediabetes.

These observations are consistent with reports by Montain SJ, et al., and Iwayama K, et al., who highlighted the circadian and metabolic significance of postprandial exercise.[26,27] The higher respiratory quotient values observed at 120 minutes post-meal suggest a greater reliance on carbohydrate oxidation, which may attenuate lipolysis and limit irisin-mediated metabolic adaptations. Accordingly, performing exercise closer to meal intake appears to optimize fat oxidation, energy balance, and hormonal responses, particularly in overweight or insulin-resistant populations.

Although changes in perceived stress scale (PSS) scores did not reach statistical significance, participants subjectively reported improved mood and relaxation following exercise sessions. Previous studies have documented the anxiolytic effects of physical activity, potentially mediated through regulation of the hypothalamic-pituitary-adrenal (HPA) axis and the neuroprotective properties of irisin.[28] Notably, participants in the present study demonstrated significant reductions in body weight, body mass index, waist circumference, and hip circumference over the study period, further supporting exercise as an effective non-pharmacological intervention for prediabetes. In healthy individuals, Kim HK, et al., (2022) reported that late-afternoon endurance exercise more effectively reduced 24-hour glucose and triglyceride levels compared with morning exercise, suggesting a circadian influence on metabolic regulation.[10] These findings are consistent with our observation that exercise performed early in the postprandial period enhances lipid metabolism. Similarly, Vecchiato M, et al., (2022) demon-strated exercise-induced increases in circulating irisin in healthy populations, further reinforcing our results.[29]

Among individuals with type 2 diabetes, studies by Savikj M, et al., (2019) and Moholdt T, et al., (2021) showed that afternoon or evening exercise improved glycaemic profiles more effectively than morning sessions.[30,31] These benefits parallel our findings in prediabetes, where early postprandial exercise (30–60 minutes after meals) produced the most favorable metabolic responses. In contrast, Teo SYM, et al., (2020) reported no significant timing-related differences, potentially attributable to variations in dietary intake and exercise modalities.[32]

Limitations of the study

Several limitations of this study warrant consideration. First, the relatively small sample size and the use of a non-probability sampling strategy may limit the generalizability of the findings. Measurement of irisin remains methodologically challenging, and although standardized ELISA protocols were followed, the possibility of inter-assay variability cannot be entirely excluded. In addition, while exercise testing was standardized within a fixed morning time window, comprehensive circadian profiling (such as chronotype assessment or evaluation of melatonin rhythms) was not performed, thereby limiting inferences regarding the influence of intrinsic biological clocks.

Clinical and Practical Implications: From a clinical standpoint, recommending moderate-intensity exercise approximately 30 minutes after meal intake appears both feasible and safe for individuals with prediabetes. This timing integrates well with daily routines, avoids prolonged fasting, and may enhance adherence compared with more rigid exercise prescriptions.[33,34] Notably, the metabolic benefits observed in this study were achieved through moderate-intensity treadmill walking, a widely accessible and low-risk activity, underscoring its potential for real-world implementation.[35]

Nevertheless, exercise recommendations should be indi-vidualized, particularly for individuals with comorbid conditions, mobility limitations, or more advanced glycaemic dysregulation. While the present findings support postprandial exercise as a practical lifestyle strategy, they should be regarded as hypothesis generating rather than prescriptive, pending validation in larger, randomized, and long-term trials incorporating clinically meaningful outcomes.

CONCLUSION

In summary, this study demonstrates that metabolic and hormonal responses to exercise in individuals with prediabetes are strongly influenced by postprandial timing. Exercise performed within 30-60 minutes after meal intake yielded the most favorable outcomes in terms of irisin secretion, lipid modulation, and fat oxidation. These findings add to the growing evidence base for chrono-exercise and support further investigation into time-specific lifestyle interventions aimed at reducing metabolic risk.

REFERENCES

1. Colberg SR, Sigal RJ, Yardley JE, Riddell MC, Dunstan DW, Dempsey PC, et al. Physical activity/exercise and diabetes: a position statement of the American Diabetes Association. Diabetes Care 2016;39(11):2065-79.https://doi.org/10.2337/dc16-1728

2. Tabák AG, Herder C, Rathmann W, Brunner EJ, Kivimäki M. Prediabetes: a high-risk state for diabetes development. Lancet 2012;379(9833):2279-90. https://doi.org/10.1016/s0140-6736(12)60283-9

3. International Diabetes Federation.

IDF Diabetes Atlas. 7th ed. Brussels: International Diabetes Federation; 2015. [Accessed on: December 12, 2025]. Available from URL: https://diabetesatlas.org/resources/previous-editions/

4. Basit A, Fawwad A, Qureshi H, Shera AS. Prevalence of diabetes, prediabetes and associated risk factors: second National Diabetes Survey of Pakistan (NDSP), 2016-2017. BMJ Open 2018;8(8):e020961. https://doi.org/10.1136/bmjopen-2017-020961

5. Neupane S, Florkowski WJ, Dhakal C. Trends and disparities in diabetes prevalence in the United States from 2012 to 2022. Am J Prev Med 2024;67(2):299-302. https://doi.org/10.1016/j.amepre.2024.04.010

6. Taskinen MR. Diabetic dyslipidemia. Atheroscler Suppl 2002;3(1):47-51. https://doi.org/10.1016/s1567-5688(01)00006-x

7. Carroll S, Dudfield M. What is the relationship between exercise and metabolic abnormalities? A review of the metabolic syndrome. Sports Med 2004;34:371-418. https://doi.org/10.2165/00007256-200434060-00004

8. Van Dijk JW, Venema M, Van Mechelen W, Stehouwer CDA, Hartgens F, Van Loon LJC. Effect of moderate-intensity exercise versus activities of daily living on 24-hour blood glucose homeostasis in male patients with type 2 diabetes. Diabetes Care 2013;36(11):3448-53. https://doi.org/10.2337/dc12-2620

9. Erickson ML, Little JP, Gay JL, McCully KK, Jenkins NT. Effects of postmeal exercise on postprandial glucose excursions in people with type 2 diabetes treated with add-on hypoglycemic agents. Diabetes Res Clin Pract 2017;126:240-7. https://doi.org/10.1016/j.diabres.2017.02.015

10. Kim HK, Radak Z, Takahashi M, Inami T, Shibata S. Chrono-exercise: time-of-day-dependent physiological responses to exercise. Sports Med Health Sci 2023;5(1):50-8. https://doi.org/10.1016/j.smhs.2022.11.003

11. Boström P, Wu J, Jedrychowski MP, Korde A, Ye L, Lo JC, et al. A PGC-1α-dependent myokine that drives brown-fat-like development of white fat and thermogenesis. Nature 2012;481(7382):463-8. https://doi.org/10.1242/dmm.009894

12. Huh JY, Siopi A, Mougios V, Park KH, Mantzoros CS. Irisin in response to exercise in humans with and without metabolic syndrome. J Clin Endocrinol Metab 2015;100(3):E453-7. https://doi.org/10.1210/jc.2014-2416

13. Iwayama K, Kurihara R, Nabekura Y, Kawabuchi R, Park I, Kobayashi M, et al. Exercise increases 24-h fat oxidation only when it is performed before breakfast. EBioMedicine 2015;2(12):2003-9. https://doi.org/10.1016/j.ebiom.2015.10.029

14. Kirwan JP, O'Gorman DJ, Cyr-Campbell D, Campbell WW, Yarasheski KE, Evans WJ. Effects of a moderate glycemic meal on exercise duration and substrate utilization. Med Sci Sports Exerc 2001;33(9):1517-23. https://doi.org/10.1097/00005768-200109000-00015

15. Tauqir S, Shah SS, Shah I, Ali S. Exercise intensities and metabolic health: targeting blood glucose, insulin, and C-peptide levels in adults with prediabetes in the postprandial state. J Taibah Univ Med Sci 2024;19(5):1049-57. https://doi.org/10.1016/j.jtumed.2024.10.002

16. Lee PH, Macfarlane DJ, Lam TH, Stewart SM. Validity of the International Physical Activity Questionnaire Short Form (IPAQ-SF): a systematic review. Int J Behav Nutr Phys Act 2011;8:115. https://doi.org/10.1186/1479-5868-8-115

17. de Oliveira Luz LG, Neto GdAM, Farinatti PdTV. Validity of the Physical Activity Readiness Questionnaire (PAR-Q) in elderly subjects. Rev Bras Cineantropom Desempenho Hum 2007;9(4):366-71.

18. Parada-Sánchez SG, Macias-Cervantes MH, Perez-Vazquez V, Vargas-Ortiz K. Effects of different types of exercise on circulating irisin levels in healthy individuals and in people with overweight, metabolic syndrome and type 2 diabetes. Physiol Res 2022;71(4):457-69. https://doi.org/10.33549/physiolres.934896

19. Rioux BV, Paudel Y, Thomson AM, Peskett LE, Sénéchal M. Examination of exercise intensity and its impact on the acute release of irisin across obesity status: a randomized controlled crossover trial. Appl Physiol Nutr Metab 2024;49(12):1712-28. https://doi.org/10.1139/apnm-2024-0091

20. Aqeel M, Forster A, Richards EA, Hennessy E, McGowan B, Bhadra A, et al. Effect of timing of exercise and eating on postprandial response in adults: a systematic review. Nutrients 2020;12(1):221. https://doi.org/10.3390/nu12010221

21. Leon AS, Sanchez OA. Response of blood lipids to exercise training alone or combined with dietary intervention. Med Sci Sports Exerc 2001;33(6 Suppl):S502-15. https://doi.org/10.1097/00005768-200106001-00021

22. Slentz CA, Bateman LA, Willis LH, Shields AT, Tanner CJ, Piner LW, et al. Effects of aerobic vs resistance training on visceral and liver fat stores and insulin resistance. Am J Physiol Endocrinol Metab 2011;301(5):E1033-9. https://doi.org/10.1152/ajpendo.00291.2011

23. Slentz CA, Houmard JA, Kraus WE. Exercise, abdominal obesity, skeletal muscle, and metabolic risk: evidence for a dose response. Obesity (Silver Spring) 2009;17(Suppl 3):S27-33. https://doi.org/10.1038/oby.2009.385

24. Bittel AJ, Bittel DC, Mittendorfer B, Patterson BW, Okunade AL, Abumrad NA, et al. A single bout of pre-meal resistance exercise improves postprandial glucose metabolism in obese men with prediabetes. Med Sci Sports Exerc 2021;53(4):694-703. https://doi.org/10.1249/mss.0000000000002538

25. Shimada K, Yamamoto Y, Iwayama K, Nakamura K, Yamaguchi S, Hibi M, et al. Effects of post-absorptive and postprandial exercise on 24-h fat oxidation. Metabolism 2013;62(6):793-800. https://doi.org/10.1016/j.metabol.2012.12.008

26. Montain SJ, Coyle EF. Influence of graded dehydration on hyperthermia and cardiovascular drift during exercise. J Appl Physiol 1992;73(4):1340-50. https://doi.org/10.1152/jappl.1992.73.4.1340

27. Iwayama K, Seol J, Tokuyama K. Exercise timing matters for glycogen metabolism and accumulated fat oxidation over 24 h. Nutrients 2023;15(5):1109. https://doi.org/10.3390/nu15051109

28. Wrann CD, White JP, Salogiannis J, Laznik-Bogoslavski D, Wu J, Ma D, et al. Exercise induces hippocampal BDNF through a PGC-1α/FNDC5 pathway. Cell Metab 2013;18(5):649-59. https://doi.org/10.1016/j.cmet.2013.09.008

29. Vecchiato M, Zanardo E, Battista F, Quinto G, Bergia C, Palermi S, et al. The Effect of exercise training on irisin secretion in patients with type 2 diabetes: a systematic review. J Clin Med 2022;12(1):62. https://doi.org/10.3390/jcm12010062

30. Savikj M, Gabriel BM, Alm PS, Smith J, Caidahl K, Björnholm M, et al. Afternoon exercise is more efficacious than morning exercise at improving blood glucose levels in individuals with type 2 diabetes: a randomized crossover trial. Diabetologia 2019;62:233-7. https://doi.org/10.1007/s00125-018-4767-z

31. Moholdt T, Parr EB, Devlin BL, Debik J, Giskeødegård G, Hawley JA. Effect of morning vs evening exercise training on glycaemic control and serum metabolites in overweight/obese men. Diabetologia 2021;64(9):2061-76. https://doi.org/10.1007/s00125-021-05477-5

32. Teo SYM, Kanaley JA, Guelfi KJ, Marston KJ, Fairchild TJ. The effect of exercise timing on glycemic control: a randomized clinical trial. Med Sci Sports Exerc 2020;52(2):323-34. https://doi.org/10.1249/mss.0000000000002139

33. Bellini A, Nicolò A, Bazzucchi I, Sacchetti M. Exercise prescription for postprandial metabolic control. Nutrients 2024;16:1170. https://doi.org/10.3390/nu16081170

34. Paoletti I, Coccurello R. Irisin: a multifaceted hormone bridging exercise and disease pathophysiology. Int J Mol Sci 2024;25:13480. https://doi.org/10.3390/ijms252413480

35. Slebe R, Wenker E, Schoonmade LJ, Bouman EJ, Blondin DP, Campbell DJT, et al. The effect of preprandial versus postprandial physical activity on glycaemia: meta-analysis of human intervention studies Diabetes Res Clin Pract 2024;210:111638. https://doi.org/10.1016/j.diabres.2024.111638

AUTHORS' CONTRIBUTION

The Following authors have made substantial contributions to the manuscript as under:

IS: Conception and study design, drafting the manuscript, critical review, approval of the final version to be published

FHK & ST: Conception and study design, acquisition, analysis and interpretation of data, drafting the manuscript, critical review, approval of the final version to be published

ZS: Analysis and interpretation of data, critical review, approval of the final version to be published

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST

Authors declared no conflict of interest, whether financial or otherwise, that could influence the integrity, objectivity, or validity of their research work.

GRANT SUPPORT AND FINANCIAL DISCLOSURE

Authors declared no specific grant for this research from any funding agency in the public, commercial or non-profit sectors

DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request