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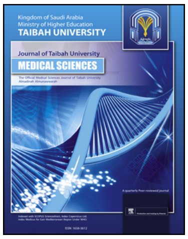

Original Article

Exercise intensities and metabolic health: Targeting blood glucose, insulin, and C-peptide levels in adults with prediabetes in the postprandial state

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الملخص

أهداف البحث: تعمل التمارين الرياضية على تحسين نسبة السكر في الدم بعد الأكل وحساسية الأنسولين لدى الأفراد المصابين بمرض السكري، ولكن تظل الكثافة المثلى لهذا التنظيم الأيضي غير واضحة. تهدف الدراسة الحالية إلى استكشاف تأثير كثافات التمارين المختلفة على مستويات الجلوكوز في الدم والأنسولين والببتيد سي لدى الأفراد المصابين بمرض السكري لتحديد الكثافة المثلى لتحسين هذه المؤشرات الأيضية.

طريقة البحث: في هذه الدراسة المتقاطعة، شارك 25 فردا مصابا بمرض السكري في جلسات تمرين بأربع كثافات مختلفة بنسبة 50% و60% و70% و80% من أقصى معدل ضربات قلب متوقع باستخدام جهاز المشي. استمرت كل جلسة لمدة 30 دقيقة، بما في ذلك فترة إحماء لمدة 5 دقائق وفترة تهدئة لمدة 5 دقائق. تم جمع عينات الدم في أربع نقاط زمنية مميزة: أثناء الصيام، وقبل التمرين مباشرة، وبعد التمرين بـ 30 و60 دقيقة. تم تحليل هذه العينات لمعرفة مستويات الجلوكوز والأنسولين والببتيد سي. تم تقييم تأثيرات شدة التمرين على هذه المعلمات باستخدام تحليل التباين المتكرر، مع إجراء اختبارات لاحقة لتحديد الاختلافات المحددة بين الشدة.

النتائج: كان متوسط أعمار المشاركين 34.88 عاما، ومتوسط طولهم 170 سم، ومؤشر كتلة الجسم 30.34 كجم/م2. لوحظ انخفاض كبير في مستويات الأنسولين والجلوكوز بعد التمرين بنسبة 70%. وعلى الرغم من ارتفاع مستويات الجلوكوز في الدم أثناء الصيام (110-115 مجم/ديسيلتر)، فقد لوحظ انخفاض كبير بعد 30 و60 دقيقة من التمرين. اقتربت مستويات الأنسولين من خط الأساس عند 70% من الشدة، من الصيام إلى 60 دقيقة بعد التمرين، مما يشير إلى استجابة إيجابية عند هذه الشدة. أظهرت مستويات الببتيد سي أيضًا تغييرات كبيرة، حيث جعل التمرين بنسبة 70% من الشدة أقرب إلى مستويات الصيام بعد 60 دقيقة من التمرين.

الاستنتاجات: تسلط هذه الدراسة الضوء على أهمية شدة التمارين الرياضية في تحسين المعايير الأيضية لدى الأفراد المصابين بمرض السكري. وعلى وجه التحديد، كان 70% من الحد الأقصى لمعدل ضربات القلب المتوقع مفيدا، مما أدى إلى تحسين حساسية الأنسولين وتقليل خطر الإصابة بمرض السكري من مرحلة ما قبل السكري.

الكلمات المفتاحية: سكر الدم؛ الببتايد-سي؛ النشاط البدني؛ شدة التمرين؛ الأنسولين؛ مقدمات السكري

Abstract

Objective: Exercise improves postprandial glycaemia and insulin sensitivity in individuals with prediabetes, but the optimal intensity for this metabolic regulation remains unclear. The current study aims to explore the impact of various exercise intensities on metabolic markers in prediabetic individuals to identify the optimal intensity for improving these indicators.

Methods: In this crossover study, 25 prediabetic individuals participated in exercise sessions at 50 %, 60 %, 70 %, and 80 % intensities of their predicted maximum heart rate using a treadmill. Each session lasted for 30 min, including a 5-min warm-up and a 5-min cool-down period. Blood samples were collected at four distinct time points: during fasting, immediately before exercise, and 30 and 60 min post-exercise. These samples were analyzed for glucose, insulin, and C-peptide levels. The effects of exercise intensity on these parameters were evaluated

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using repeated measures ANOVA, with post hoc tests conducted to determine specific differences between the intensities.

Results: The participants had an average age of 34.88 years, a mean height of 170 cm, and a BMI of 30.34 kg/m^2. A significant reduction in insulin and glucose levels post-exercise was observed at 70 % intensity ($p \leq 0.001$). Despite high fasting blood glucose levels (110−115 mg/dL), significant reductions were noted at 30 and 60 min post-exercise ($p \leq 0.001$). Insulin levels approached near baseline at 70 % intensity, from fasting (26.74 ± 20.83) to 60 min post-exercise (28.47 ± 20.79), indicating a positive response at this intensity. C-peptide levels also showed significant changes, with the 70 % intensity exercise bringing them closest to fasting levels by 60 min post-exercise.

Conclusion: This study highlights the importance of exercise intensities in enhancing metabolic parameters in prediabetic individuals. Specifically, 70 % of the predicted maximum heart rate was beneficial, optimizing insulin sensitivity and potentially reducing the risk of progressing from prediabetes to diabetes.

Keywords: Blood glucose; C-peptide; Exercise; Exercise intensities; Insulin; Prediabetes

Introduction

Prediabetes is characterized by impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT); it signifies a stage where the body's capability to regulate glucose declines.[1] The World Health Organization categorizes fasting blood glucose (FBG) levels between 6.1 and 6.9 mmol/L after overnight fasting as IFG,[2] whereas IGT is characterized by elevated blood glucose levels post-meal.[3] Both IFG and IGT are generally attributed to insulin resistance and dysfunction of pancreatic β-cells.[4] People with IFG have a 20−30 % greater risk of developing type 2 diabetes (T2DM) within 5−10 years.[3]

Regular aerobic exercise is essential for lowering the risk of developing T2DM. Its efficacy is primarily attributed to positive effects on postprandial metabolism, as it increases the sensitivity of skeletal muscles to insulin for up to 48 h post-exercise.[5] The significant role of exercise in managing prediabetes and T2DM is well-established and widely acknowledged.[6] However, the intensity of exercise that optimally improves insulin sensitivity still needs to be clearly defined. The American Diabetes Association (ADA) recommends that adults with prediabetes perform at least 150 min of moderate-intensity physical activity or 90 min of vigorous-intensity activity weekly.[5] While both moderate and vigorous exercises offer health benefits, the specific outcomes can vary based on the intensity of the activity.[7] High-intensity exercise (HIE) is often associated with more immediate and noticeable improvements in cardiometabolic health compared to moderate-intensity exercise (MIE).[5,8,9]

Recent medical care standards have underscored the importance of including exercise in treatment plans for prediabetes, emphasizing its role in effectively managing this condition.[9] However, the clinical guidelines do not specify the most effective exercise intensity for blood sugar control in individuals with prediabetes.[9] Thus, determining the optimal intensity of exercise necessary for enhancing insulin sensitivity in patients with prediabetes is of paramount importance.

Therefore, the current study assessed the impact of varying exercise intensities on glucose, insulin, and C-peptide levels in patients with prediabetes after they consumed an isocaloric breakfast.

Materials and Methods

Study approvals, participants, and location

This crossover study was approved by the ethical review board of the Institute of Basic Medical Sciences (IBMS) of Khyber Medical University (Reference No. KMU/IBMS/IRBE/meeting/2022/8075; Pesahwar, Pakistan), and was carried out according to the Declaration of Helsinki. The study was conducted from July 2022 through December 2023, and written informed consent was obtained from all participants. Using G Power 3.1.9.2 software, and maintaining a significance level (α) of 0.05 and statistical power of 0.80, a sample size of 12 was calculated. However, to increase the power of the study, 25 participants were recruited.[10] Participants were both males and females aged 25−35 years. Prediabetic status was diagnosed by fasting plasma glucose levels ranging from 100 to 125 mg/dL, and/or glycosylated hemoglobin (HbA1c) levels between 5.7 % and 6.4 %. All procedures were conducted at the Sports Research Unit (SRU) of Khyber Medical University at 8:00 AM after participants fasted for 10−12 h overnight.

Screening and baseline tests

In the screening phase, participants visited the SRU for evaluations, including fasting plasma glucose and HbA1c levels. Their previous physical activity status was assessed using the short form of the International Physical Activity Questionnaire (IPAQ).[11] Participants who met the ADA[12] prediabetes criteria were invited to participate in the study. The exclusion criteria were participants with a history of ischemic heart disease, hypertension, diabetes, or any respiratory or musculoskeletal disorder hindering physical activity; and females who were pregnant or breastfeeding. The CONSORT flowchart showing the participant recruitment and baseline assessment is shown in Figure 1.

Borg rating of perceived exertion

The Borg Rating of Perceived Exertion (RPE) scale[13] is a standard tool for evaluating an individual's subjective experience of effort and strain during physical activity. The scale ranges from 6 to 20, indicating different categories of no to light exertion, moderate exertion, hard to very hard exertion, and maximum exertion. The RPE for each participant was recorded after each exercise session.

Exercise protocol and participation preparation for the study

Participants were scheduled for four separate morning sessions in a fasting state at the SRU, each starting at about 8:00 AM, spaced 1 week apart with a 7-day washout period between sessions. Before the scheduled exercise day, they were advised not to engage in any strenuous physical activities for at least 24 h. To maintain dietary uniformity and account for prestudy nutritional factors, they were interviewed about food consumption the day before exercise session, using a 24-h dietary recall questionnaire. During this period, participants were asked to avoid junk food and non-healthy items such as sugary beverages, sweets, and fizzy drinks during the study period, to reduce acute dietary variability that could influence the exercise outcomes. The goal of the study was to assess the effects of exercise independent of dietary modifications on parameters under investigation.

Exercise intensities were calculated as predicted maximum heart rate (PMHR) percentages. Intensities of 50 %, 60 %, 70 %, and 80 % of PMHR were selected to cover the spectrum from moderate to high intensity to assess the impact of different exercise levels on the study outcomes. Each exercise session lasted 40 min (including a 5 min warm-up and cool-down period) and was performed 30 min after a standardized 250 calorie isocaloric breakfast. The exercise sessions were designed and aligned with the durations and intensities evaluated elsewhere.[14,15] Before starting the exercise session, the participants were acquainted with the treadmill's (Revo fitness treadmill Model no. RT-115 serial no. ZYT102-581501007) controls and speeds. Each participant wore a heart rate monitor (HRM-Run Garmin, Sports Research Unit of Khyber Medical University, Peshwar, Pakistan), which used short-range telemetry technology to monitor and transmit heart rate data in real time, ensuring that exercise was performed at the intended intensities. The speed of the treadmill (Revo RT100; Taiwan) was adjusted incrementally to reach the desired maximum heart rate. The first session involved a total of 40 min of exercise at 50 % of the PMHR, including 5-min warm-up and 5-min cool-down periods. Blood samples were collected at fasting, before exercise, and 30 and 60 min after exercise. The subsequent sessions followed a similar pattern, with exercise intensities at 60 %, 70 %, and 80 % PMHR for the second, third, and fourth visits, respectively, maintaining the same duration and blood sampling routine, as shown in Figure 2. However, the final session required greater fitness from participants. In the final visit, the participants were instructed to stop exercising if they could not continue. The PMHR for all participants was calculated from the following formula: PMHR = 220 − age in years.[16]

Laboratory procedures and data analyses

After collecting whole blood samples, they were immediately centrifuged for plasma glucose evaluation using standardized kits (FreeStyle blood glucose meter; Abbott Diabetes Care Inc., Alameda, CA, USA). Serum insulin levels were determined with the enzyme-linked immunosorbent assay (ELISA) (Insulin ELISA, IN374S and C-peptide ELISA, CP179S; Calbiotech, El Cajon, CA, USA), with tests conducted in duplicate for accuracy.

SPSS version 23 and GraphPad Prism version 8 were used for data analyses. The Shapiro−Wilk test was used to assess the normality of the data. Demographic variances were examined using the independent samples *t*-test to identify sex-based differences. Repeated measures analysis of variance (ANOVA) was applied to discern differences across the various exercise intensity levels. Furthermore, to understand the relationships between different time points and diabetes-related parameters, a post hoc test was conducted, utilizing a general linear model complemented by Bonferroni correction for multiple comparisons.

Results

Demographic details of the participants

This study recruited a total of 25 participants with a mean age of 34.88 ± 4.11 years. The mean height, weight, and body mass index of the participants were (170 cm ± 6.70, 87.85 kg ± 14.56, and 30.34 kg/m^2 ± 4.27), respectively, indicating a prevalence of overweight and obesity. Similarly, mean waist circumference was 102.16 ± 12.22 cm, and mean hip circumference was 105.13 ± 12.43 cm, with a mean waist-to-hip ratio of 0.97 ± 0.04. As shown in Table 1, these values provide a comprehensive overview of the physical characteristics of the study participants, highlighting the general trends in age and body size that are more prone to developing diabetes. Analysis of the IPAQ showed that most participants (88 %) were living a sedentary lifestyle fitting in the 'low' physical activity category, as shown in Table 2. Only 12 % of the participants reported 'moderate' physical activity, whereas no participant reported vigorous, active activity.

Differential response to exercise intensities

Pre-exercise blood glucose levels increased across all exercise intensities due to breakfast consumption, as shown in Table 3. Within 60 min post-exercise, a significant decrease in glucose levels was observed at all intensities ($p \leq 0.001$), with more pronounced reductions at 60 % and 70 % intensities. Insulin levels showed significant fluctuations, with 70 % intensity bringing levels closest to fasting benchmarks within 60 min post-exercise. At 80 % intensity, improvements in glucose and insulin levels were noted, but sustaining this intensity was challenging for participants. Therefore, 70 % intensity was considered optimal.

C-peptide levels demonstrated significant changes at 50 % and 70 % intensity levels ($p \leq 0.001$), with less pronounced changes at 60 % and 80 % intensities. The 70 % intensity exercise brought C-peptide levels closest to fasting levels by 60 min post-exercise.

Figure 3A to 3D visually summarizes these responses, highlighting the body's intensity-dependent metabolic response. Specifically, Figure 3A shows the trend of decreasing glucose levels, and Figure 3B illustrates the variability of

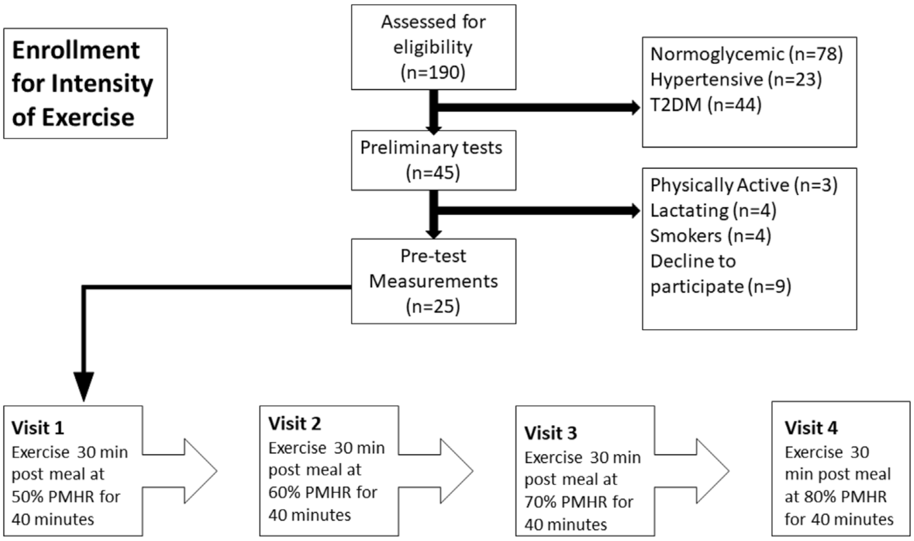

Figure 1: Consort flowchart showing the details of each visit.

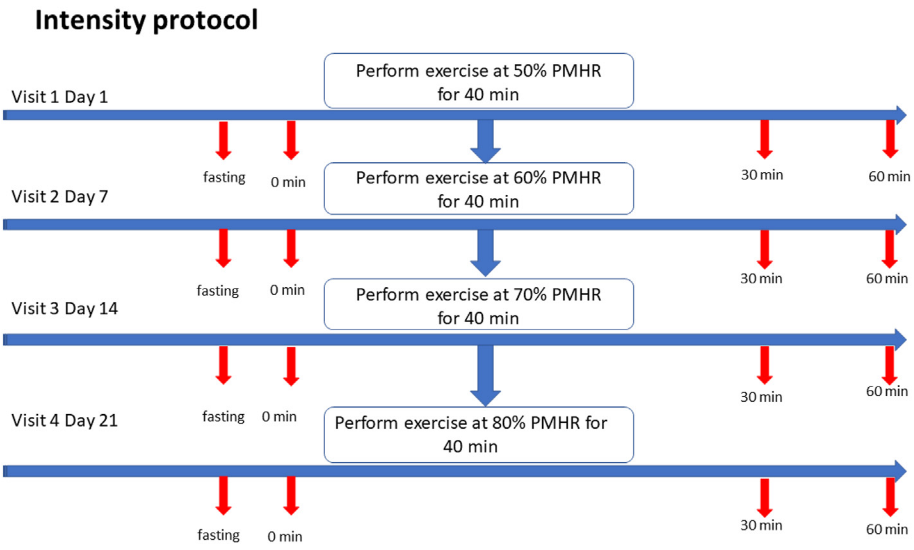

Figure 2: Consort flowchart showing the details of the exercise intensity protocol.

insulin levels, especially at 70 % intensity, suggesting that the body's metabolic response to exercise is intensity-dependent.

C-peptide levels, indicative of insulin production, demonstrated significant changes at 50 % and 70 % intensity levels ($p \leq 0.001$), but at 60 % and 80 % intensities, the changes were less pronounced ($p = 0.068$ and $p = 0.359$, respectively). The patterns suggest that exercise at all intensities affects C-peptide levels, but the return to fasting levels varies. The 70 % intensity exercise brought C-peptide levels closest to fasting levels by 60 min post-exercise, indicating a potentially more significant impact of MIE to HIE

Table 1: Demographic and anthropometric profile of participants in the study.

Demographics	Total	Female (n = 8)	Male (n = 17)	P-value
Age	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	102.42 ± 17.10	106.41 ± 9.93	0.467
Waist-to-hip ratio	0.97 ± 0.04	0.96 ± 0.05	0.97 ± 0.02	0.659

All values in the table are presented as the mean ± standard deviation.

Table 2: Baseline physical activity of the participants with prediabetes as determined by the IPAQ questionnaire.

Physical Activity	Frequency	Percentage of Participants
Low	22	88 %
Moderate	3	12 %
High	0	0 %
Total	25	100 %

IPAQ = International Physical Activity Questionnaire.

on C-peptide levels. Figure 3C depicts a rise in insulin utilization or reduced secretion over time in response to varied exercise intensities.

Figure 3D illustrates the correlation between the BORG exertion scale and the levels of exercise intensity. The data clearly show that, as exercise intensity increase, so does the RPE. Higher scores on the Borg Scale are indicative of increased exertion levels. Workouts of moderate intensity, which register an RPE of approximately 12—13, align with 60—70 % of the maximum exercise intensity. This link between RPE and varying levels of exercise intensity is

Table 3: Differential response of blood glucose levels, insulin, and C-peptide to various exercise intensities.

Markers	Intensity	Fasting	Pre-exercise	30 min	60 min	P-values
Glucose (mg/dL)	50 %	115.08 ± 3.45	190.48 ± 6.81	161.64 ± 11.19	157.36 ± 11.66	≤0.001
	60 %	113.48 ± 7.45	184.48 ± 6.05	155.32 ± 12.03	149.36 ± 11.33	≤0.001
	70 %	112 ± 3.29	177.12 ± 5.83	137.92 ± 5.99	120.64 ± 2.28	≤0.001
	80 %	110.28 ± 3.24	172.28 ± 13.66	145.72 ± 10.94	141.12 ± 10.42	≤0.001
Insulin (μU/mL)	50 %	22.84 ± 25.76	63.62 ± 48.70	41.58 ± 43.77	36.13 ± 42.74	≤0.001
	60 %	24.69 ± 25.50	74.25 ± 43.72	46.76 ± 38.58	33.53 ± 29.00	≤0.001
	70 %	26.74 ± 20.83	70.98 ± 43.27	51.95 ± 37.31	28.47 ± 20.79	≤0.001
	80 %	20.39 ± 17.33	69.27 ± 39.36	40.05 ± 29.33	36.18 ± 33.52	≤0.001
C-peptide (ng/mL)	50 %	3.03 ± 0.26	4.16 ± 0.37	4.01 ± 0.37	3.89 ± 0.37	≤0.001
	60 %	2.96 ± 0.29	3.58 ± 0.65	3.38 ± 0.63	3.27 ± 0.63	0.068
	70 %	2.83 ± 0.27	3.25 ± 0.39	2.09 ± 0.23	2 ± 0.29	≤0.001
	80 %	2.29 ± 0.23	3.08 ± 0.36	2.54 ± 0.26	2.42 ± 0.28	0.359

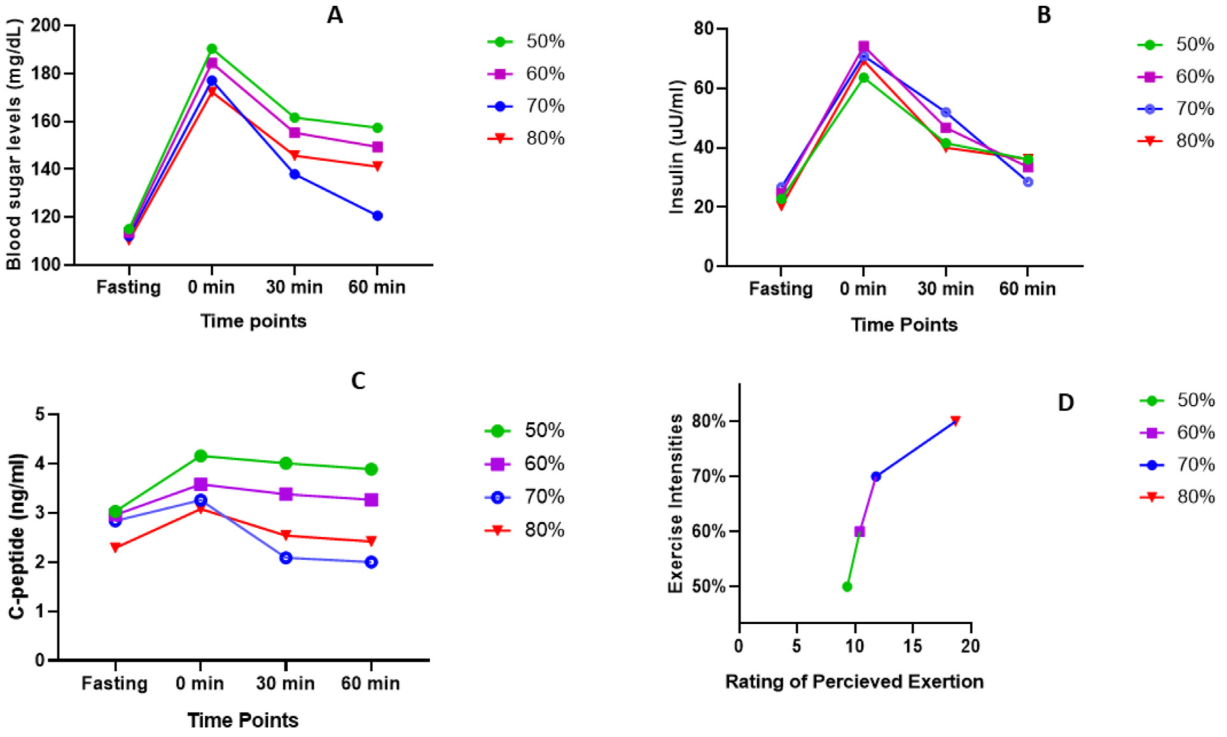

Figure 3: Graphs presents the mean ± standard error of the mean of blood glucose levels (A), insulin (B), and C-peptide (C) at 50 %, 60 %, 70 % and 80 % maximum heart rate with sampling at four time points: baseline, before exercise, and 30 and 60 min after post-prandial exercise. (D) Represents the Borg rating of perceived exertion for participants at the end of each visit.

Table 4: Effects of different exercise intensities on blood glucose levels, insulin, and C-peptide pre-exercise and post-exercise.

Parameters	Time points	50 %			60 %			70 %			80 %		
		Mean Difference	Std. Error	P-Values	Mean Difference	Std. Error	P-Values	Mean Difference	Std. Error	P-Values	Mean Difference	Std. Error	P-Values
Blood glucose levels (mg/dL)	Fasting vs PE	−75.4	1.653	≤0.001	−71	1.463	≤0.001	−65.12	1.295	≤0.001	−62.00	3.02	≤0.001
	Fasting vs 30 min	−46.56	2.385	≤0.001	−41.84	2.458	≤0.001	−25.92	1.459	≤0.001	−35.44	2.22	≤0.001
	Fasting vs 60 min	−42.28	2.448	≤0.001	−35.88	2.340	≤0.001	−8.64	0.838	≤0.001	−30.84	2.13	≤0.001
	PE vs 30 min	28.84	2.09	≤0.001	29.16	2.19	≤0.001	39.2	1.52	≤0.001	26.56	2.65	≤0.001
	PE vs 60 min	33.12	2.25	≤0.001	35.12	2.02	≤0.001	56.48	0.95	≤0.001	31.16	2.64	≤0.001
	30 min vs 60 min	4.28	0.37	≤0.001	5.96	0.32	≤0.001	17.28	1.10	≤0.001	4.60	0.32	≤0.001
Insulin (μU/mL)	Fasting vs PE	−40.78	7.73	≤0.001	−45.55	10.58	0.001	−43.84	7.92	≤0.001	−48.87	6.97	≤0.001
	Fasting vs 30 min	−18.74	7.04	0.082	−10.07	15.66	1.000	−24.81	6.73	0.007	−19.65	6.16	0.024
	Fasting vs 60 min	−13.28	6.93	0.402	−8.84	6.33	1.000	−1.32	3.29	1.000	−15.78	6.77	0.172
	PE min vs 30 min	22.04	5.91	≤0.001	35.48	8.29	0.002	19.02	4.56	0.002	29.22	5.88	≤0.001
	PE min vs 60 min	27.5	7.06	≤0.001	36.72	8.15	0.001	42.51	6.62	≤0.001	33.09	6.17	≤0.001
	30 min vs 60 min	5.45	3.55	0.41	1.23	13.61	1.000	23.48	4.86	≤0.001	3.87	5.26	>0.999
C-peptide (ng/mL)	Fasting vs PE	−1.12	0.06	≤0.001	−0.62	0.13	≤0.001	−0.42	0.06	≤0.001	−0.788*	0.06	≤0.001
	Fasting vs 30 min	−0.98	0.06	≤0.001	−0.42	0.13	0.017	0.74	0.07	≤0.001	−0.248*	0.05	≤0.001
	Fasting vs 60 min	−0.86	0.06	≤0.001	−0.312	0.13	0.131	0.83	0.07	≤0.001	−0.124	0.06	0.215
	PE min vs 30 min	0.14	0.01	≤0.001	0.2	0.02	≤0.001	1.16	0.07	≤0.001	0.54	0.04	≤0.001
	PE min vs 60 min	0.26	0.01	≤0.001	0.31	0.02	≤0.001	1.25	0.09	≤0.001	0.66	0.04	≤0.001
	30 min vs 60 min	0.12	0.01	≤0.001	0.1	0.01	≤0.001	0.09	0.06	0.78	0.12	0.01	≤0.001

PE: Pre-exercise.

Table 4 summarizes statistical data comparing post hoc analysis with blood glucose levels, insulin, and C-peptide at four different time points (fasting vs pre-exercise, 30 and 60 min; pre-exercise vs 30 min; pre-exercise vs 60 min, and 30 vs 60 min) under different exercise intensities (50 %, 60 %, 70 %, 80 %).

valuable for researchers in creating personalized fitness programs. Such tailored approaches ensure that physical training regimens are safe and effective for individuals' needs.

Effects of exercise intensities on metabolic parameters over time

The post hoc analysis in the study focused on the effects of different exercise intensities on the metabolic parameters over specific time intervals, as shown in Table 4.

Analyzing blood glucose levels, a consistent decrease from pre-exercise to 30 min after exercise across all intensities were noted, with the mean differences ranging from 26.56 to 29.16 mg/dL ($p \leq 0.001$), indicating a robust response to exercise. The response from 30 to 60 min was comparatively minimal, suggesting a continued effect of exercise on blood glucose.

Similarly, a marked reduction in mean insulin and C-peptide levels at both 30 and 60 min after exercise across all visits was noted, with a more pronounced effect at 70 % intensity. This indicates a significant response to MIE to HIE, as shown by the lower standard errors given in Table 3.

Discussion

This study reinforces the importance of physical activity in improving the metabolic parameters associated with progression of prediabetes to diabetes. Varied exercise intensities demonstrated a dose-response relationship in improving the metabolic parameters. However, based on the feasibility and ease of performance, MIE to HIE, specifically at 70 %, emerged, as an effective method for improving glucose regulation in individuals with prediabetes.

The findings of the current study are consistent with the results reported by Kang et al.,[17] Nybo et al.,[18] and Sandvei et al.,[19] who all demonstrated the effect of different exercise intensities on modulation of the insulin level, insulin sensitivity, and blood glucose concentration in patients with diabetes. All of these findings point towards the positive effects of exercise on the metabolic parameters in patients with diabetes; however, better effects are extracted with enhanced intensities, a finding that is in line with the current study and the overload principal of exercise. However, it is also important to understand that the prediabetic population usually presents a picture of central obesity and least active lifestyle; thus, exercise incorporation into their lifestyle should be supervised, incremental, and submaximal for extraction of maximum effects.[19] Similarly, previous findings on the effects of a single session on insulin sensitivity and glucose metabolism have also been validated by the current study. Specifically, the benefits of exercise do not require an active lifestyle. Corey et al.[20] reported that even a single session of physical activity can reduce blood sugar levels postprandially and ameliorate insulin sensitivity, in individuals with prediabetes, depending on the exercise intensity.[20] The authors proposed that exercise can lower blood sugar levels and the effects could be detected even in an hour following exercise.

Exercise triggers a complex interaction between hormonal and cellular mechanisms in the body, essential for regulating blood glucose levels.[21] A key component in this process is the role of skeletal muscles in glucose absorption after eating. Transporting glucose into muscles is a vital step for utilization which is mainly done through glucose transporter type 4 (GLUT4) isoforms.[21] Both insulin and exercise are important facilitators for the movement of GLUT4 to the muscle cell membrane, thereby enhancing glucose absorption and improving insulin sensitivity.[21] During aerobic activities, muscle glucose uptake is increased as exercise not only boosts the presence of GLUT4 in the muscles but also promotes its translocation, assisting in the insulin-independent uptake of blood glucose.[5,21] Post-exercise, there is sustained high uptake of glucose, driven by muscle contraction, which can continue for several hours[5]; the current study observed a decrease in blood glucose levels at 30 and 60 min after exercise ($p \leq 0.001$).

Engaging in HIE is challenging for individuals with a greater body mass. People with prediabetes tend to be obese; therefore, exercising at a high intensity was challenging, despite the fact that a positive response was observed from the participants. However, they found exercise at 70 % PMHR to be easily manageable and thus sustainable for longer periods of time when exercise was prescribed for prediabetes.

In the current study, an initial increase in C-peptide levels followed by stabilization or a decline has been observed. This pattern reflects a complex interaction between the intensity of exercise and the body's insulin utilization and production. Such interplay has been previously reported.[22] It is widely acknowledged that physical activity enhances insulin sensitivity. From the findings of our study, it appears that the reduction in both insulin and C-peptide levels might be associated with improved β-cell function due to heightened physical activity.[22] Supporting our observations, Ha et al.[23] also noted a significant reduction in C-peptide levels following an aerobic exercise regimen, underscoring the substantial influence of exercise. These outcomes contribute to the fact that physical activity decreases the burden on the pancreatic β-cells and promote transport of the insulin-independent uptake of glucose by the cells.[23]

Contrary to the findings of the current study, Manders et al.[9] reported that HIE does not lower glucose levels. Their results indicated that low-intensity exercise (LIE) may be more effective at reducing hyperglycemia. The difference in effectiveness between LIE and HIE might be attributed to the fact that the immediate glucose-lowering effects of exercise may vary between individuals with prediabetes and diabetes. Variability in responses can be attributed to different mechanisms including insulin resistance, insulin-independent uptake, and peripheral utilization of glucose. Type 2 diabetes usually presents as peripheral insulin resistance and lower glucose utilization, which may require a more physically active lifestyle for efficient glucose metabolism. Moreover, the participants in their study[9] were encouraged to implement dietary modifications, whereas the participants in our study were directed to maintain customary dietary habits.

Overall, our research offers compelling evidence supporting the efficacy of targeted exercise intensity interventions in improving physical health. For individuals with prediabetes, engaging in physical activities at 70 % of their PMHR can produce an immediate beneficial effects on postprandial blood glucose levels and insulin sensitivity.

Consistent with our results, Zubia et al.[24] and Liu et al.[25] suggest that increased physical activity, particularly at 70 % of PMHR, has a significant impact on reversing insulin resistance, underscoring the importance of exercise as a potential alternative to pharmacological treatments in managing prediabetes. Notably, 48 % of the participants with prediabetes in their study exhibited HbA1c levels within the normal range following the intervention period. Given that the exercise intervention in our study was limited to 4 weeks, extending the duration could potentially result in even greater benefits.

By integrating exercise prescription strategies informed by these findings, healthcare professionals can more effectively customize interventions to mitigate the risk of progression to type 2 diabetes in individuals with prediabetes. This approach underscores the crucial role of exercise intensity in the management and potential reversal of prediabetes. One of the key strengths of this study is its focus on adults with prediabetes, a population that has been relatively underrepresented in existing research. The range of exercise intensities assessed (from 50 % to 80 % of PMHR) provides a thorough evaluation of how varying levels of physical activity influence critical metabolic indicators, an area not extensively explored in prior studies. Additionally, the crossover design represents a significant advantage, enabling direct individual comparisons and minimizing interparticipant variability.

Despite its contributions, this study had several limitations. It focused exclusively on the immediate post-exercise period, neglecting the potential stabilization or variation of metabolic parameters over hours or days, which is essential for understanding long-term metabolic health benefits. Additionally, the study did not include dietary modifications, thus not exploring how dietary changes might interact with exercise to affect metabolic outcomes. The small sample size of 25 participants, constrained by financial limitations, restricts the generalizability of the findings and the scale of the study. These limitations indicate that while the study offers valuable preliminary insights, further research with larger samples, long-term observations, and dietary considerations is needed to comprehensively evaluate the impact of exercise on metabolic health.

Conclusion

MIE to HIE, particularly at 70 % of PMHR, demonstrated a marked reduction in postprandial glucose spikes. The findings underscore the substantial and immediate impact of physical activity on key metabolic markers, including blood glucose, insulin, and C-peptide levels, with the most pronounced effects observed at this intensity. While HIE (80 %) also yielded notable metabolic benefits, its long-term practicality is uncertain due to increased physical demands. Consequently, exercise at 70 % intensity offers an optimal balance between efficacy and sustainability.

Future research should aim to include diverse ethnic populations to further validate these findings. Additionally, it is crucial to monitor metabolic markers over extended periods following exercise to gain a comprehensive understanding of how these parameters fluctuate or stabilize over time.

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Conflict of interest:

The authors have no conflicts of interest to declare.

Ethical approval

The study was approved on June 29, 2022 by the ethical review board of the Institute of Basic Medical Sciences of Khyber Medical University (Reference No. KMU/IBMS/IRBE/meeting/2022/8075).

Authors contributions

ST and IS conceived the study, conducted the review and research, provided materials, collected and organized the data, and wrote the initial and final drafts of the article.

SA and SS conducted the literature search, assessed the quality of the sources, refined the manuscript in terms of language and style, and wrote the initial and final drafts of the article.

The manuscript underwent a final revision and received approval from all the authors. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

References

1. Yip WCY, Sequeira IR, Plank LD, Poppitt SD. Prevalence of pre-diabetes across ethnicities: a review of impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) for classification of dysglycaemia. **Nutrients 2017**; 9(11): 1273. https://doi.org/10.3390/nu9111273.
2. Aw TC, Lim WR, Mattar N, Teo WL, Phua SK, Tan SP. What constitutes impaired fasting glucose (ifg) levels? **Pathology 2009**; 41: 68. https://doi.org/10.1097/01268031-200941001-00157.
3. Bock G, Dalla Man C, Campioni M, Chittilapilly E, Basu R, Toffolo G, et al. Pathogenesis of pre-diabetes: mechanisms of fasting and postprandial hyperglycemia in people with impaired fasting glucose and/or impaired glucose tolerance. **Diabetes 2006**; 55(12): 3536–3549. https://doi.org/10.2337/db06-0319.
4. Heikes KE, Eddy DM, Arondekar B, Schlessinger L. Diabetes Risk Calculator: a simple tool for detecting undiagnosed diabetes and pre-diabetes. **Diabetes Care 2008**; 31(5): 1040–1045. https://doi.org/10.2337/dc07-1150.
5. Colberg SR, Sigal RJ, Fernhall B, Regensteiner JG, Blissmer BJ, Rubin RR, et al. Exercise and type 2 diabetes: the American College of Sports Medicine and the American Diabetes Association: joint position statement executive summary. **Diabetes Care 2010**; 33(12): 2692. https://doi.org/10.2337/dc10-9990.
6. Babraj JA, Vollaard NBJ, Keast C, Guppy FM, Cottrell G, Timmons JA. Extremely short duration high intensity interval training substantially improves insulin action in young healthy males. **BMC Endocr Disord 2009**; 9(1): 1–8.
7. Lee SJ, Tjonna A, Rognmo O, Stolen T, Bye A, Haram P. Aerobic interval training versus continuous moderate exercise as a treatment for the metabolic syndrome. **Circulation 2008**; 118(4): 346–354. https://doi.org/10.1161/CIRCULATIONAHA.108.772822.
8. Irving BA, Davis CK, Brock DW, Weltman JY, Swift D, Barrett EJ, et al. Effect of exercise training intensity on abdominal visceral fat and body composition. **Med Sci Sports Exerc 2008**; 40(11): 1863. https://doi:10.1249/MSS.0b013e3181801d40.
9. Manders RJ, Van Dijk JW, Van Loon LJ. Low-intensity exercise reduces the prevalence of hyperglycemia in type 2 diabetes. **Med Sci Sports Exerc 2010**; 42(2): 219–225.
10. American Diabetes A. Standards of medical care in diabetes—2010. **Diabetes Care 2010**; 33(Suppl 1): S11. https://doi.org/10.1249/mss.0b013e3181b3b16d.
11. Hagströmer M, Oja P, Sjöström M. The International Physical Activity Questionnaire (IPAQ): a study of concurrent and construct validity. **Publ Health Nutr 2006**; 9(6): 755–762.
12. Sherwood Z. Prediabetes: definition, diagnostic criteria and management. **Diabetes Nursin 2018**; 22(4).
13. De Souza D, Campos E, Gonçalves R, Viana J, De Lima J, Santos T, et al. Validity of the Borg 6–20 categories obtegories obtained in incremental testing for prescribing aerobic exercise intensity: a systematic review. **Hum Mov 2023**; 24(1): 46–55.
14. Liu Y, Li J, Zhang Z, Tang Y, Chen Z, Wang Z. Effects of exercise intervention on vascular endothelium functions of patients with impaired glucose tolerance during prediabetes mellitus. **Exp Ther Med 2013**; 5(6): 1559–1565. https://doi:10.3892/etm.2013.1064.
15. Khan A, Iftikhar M, Baxendale RH, Arif T, Shah I. The effect of different exercise intensities on plasma endostatin in healthy volunteers. **Journal of Pharmaceutical Research International 2021**; 33(13): 30–38.
16. Cruz-Martínez LE, Rojas-Valencia JT, Correa-Mesa JF, Correa-Morales C. Maximum Heart Rate during exercise: reliability of

the 220-age and Tanaka formulas in healthy young people at a moderate elevation. **Rev Fac Med 2014**; 62(4): 579–585.

17. Kang J, Robertson RJ, Hagberg JM, Kelley DE, Goss FL, Dasilva SG, et al. Effect of exercise intensity on glucose and insulin metabolism in obese individuals and obese NIDDM patients. **Diabetes Care 1996**; 19(4): 341–349. https://doi:10.2337/diacare.19.4.341.
18. Nybo L, Sundstrup E, Jakobsen MD, Mohr M, Hornstrup T, Simonsen L, et al. High-intensity training versus traditional exercise interventions for promoting health. **Med Sci Sports Exerc 2010**; 42(10): 1951–1958. https://doi:10.1249/MSS.0b013e3181d99203.
19. Sandvei M, Jeppesen PB, Støen L, Litleskare S, Johansen E, Stensrud T, et al. Sprint interval running increases insulin sensitivity in young healthy subjects. **Arch Physiol Biochem 2012**; 118(3): 139–147. https://doi:10.3109/13813455.2012.677454.
20. Rynders CA, Weltman JY, Jiang B, Breton M, Patrie J, Barrett EJ, et al. Effects of exercise intensity on postprandial improvement in glucose disposal and insulin sensitivity in prediabetic adults. **J Clin Endocrinol Metabol 2014**; 99(1): 220–228. https://doi.org/10.1210/jc.2013-2687.
21. Adams OP. The impact of brief high-intensity exercise on blood glucose levels. **Diabetes, Metab Syndrome Obes Targets Ther 2013**: 113–122. https://doi:10.2147/DMSO.S29222.
22. Li Y, Meng L, Miao Q, Sato Y. Association between physical activity and serum C-peptide levels among the elderly. **Geriatr Gerontol Int 2014**; 14(3): 647–653. https://doi:10.1111/ggi.12152.
23. Ha M-S, Cho W-K, Kim J-H, Ha S-M, Lee J-A, Yook JS, et al. Effects of an exercise program on health-related physical fitness and IGF-1, C-peptide, and resistin levels in obese elementary school students. **Journal of the Korean Applied Science and Technology 2018**; 35(3): 956–962. https://doi.org/10.12925/jkocs.2018.35.3.956.
24. Shah Z, Shah I, Malik MO, Ullah I. Effect of short duration moderate intensity physical activity on glycemic control and antioxidant status of prediabetic population. **Saudi Med J 2021**; 42(6): 660. https://doi.org/10.15537/smj.2021.42.6.20210019.
25. Liu Y, Ye W, Chen Q, Zhang Y, Kuo C-H, Korivi M. Resistance exercise intensity is correlated with attenuation of HbA1c and insulin in patients with type 2 diabetes: a systematic review and meta-analysis. **Int J Environ Res Publ Health 2019**; 16(1): 140. https://doi.org/10.3390/ijerph16010140.

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