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Study of heart rate variability test in prediabetes, prehypertension and co-existing prediabetes with prehypertension subjects

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Abstract

Introduction: Cardiac autonomic neuropathy is common in people with diabetes and hypertension and increases the risk of heart disease. Heart rate variability (HRV) is a reliable method to assess cardiac autonomic function. However, limited information exists about HRV changes before these conditions develop. This study aimed to assess HRV changes in individuals with prediabetes, prehypertension, and both conditions together.

Method: A comparative cross-sectional study was conducted on 120 participants (both sexes, mean age 40.24±7.34 years) after ethical approval. Participants were categorized into four groups (n=30 each): control, prediabetes, prehypertension, and coexisting prediabetes with prehypertension, based on HbA1c and blood pressure measured on two occasions. HRV was recorded for 5 minutes in the sitting position using the Polar H10 device, and time- and frequency-domain parameters were analyzed and compared with controls.

Result: Total Power was significantly lower in the coexisting group and prehypertensive group compared to controls ($p<0.001$). Time-domain indices- RMSSD, NN50, pNN50, and SDNN were also markedly reduced in the coexisting and prehypertensive groups compared to controls ($p<0.001$ for all). The mean RR interval was shorter in the coexisting group ($p<0.001$), indicating a higher resting heart rate. Maximum and minimum heart rates were also significantly higher ($p = 0.032$ and 0.002, respectively). HRV parameters showed no significant difference between the prediabetes and control groups.

Conclusion: HRV was lowest in the coexisting group, moderately reduced in prehypertension, and unchanged in prediabetes. Coexistence of prediabetes and prehypertension causes greater autonomic dysfunction, highlighting the importance of early detection and prevention.

Keywords: Heart rate variability, Prediabetes, Prediabetes with prehypertension, Prehypertension

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Introduction

Prediabetes is a metabolic status between normal blood sugar levels and diabetes mellitus,[1] while prehypertension is an intermediate between normal blood pressure and hypertension.[2] People in these pre-stages are at a heightened risk of developing diabetes and hypertension respectively, both of which are major factors in cardiovascular disease (CVD), a widespread chronic illness with significant morbidity and mortality rates globally.[3,4] The increased risk of CVD in these individuals is often linked to the presence of certain pro-inflammatory molecules that, in turn have some influence on the autonomic nervous system (ANS).[5]

Heart rate variability (HRV) is considered a simple, sensitive, and noninvasive method for quantitatively assessing the sympathetic and parasympathetic branches of the autonomic nervous system. A heart rate that fluctuates and adjusts according to the body's needs is believed to provide a survival benefit. In contrast, lower HRV is associated with a higher risk of cardiovascular events.[6]

Although some studies have examined HRV in prediabetes and prehypertension subjects, revealing a decrease in HRV, [8-14] there have been few studies investigating HRV in subjects with co-existing prediabetes and prehypertension. This study aims to provide preliminary data on HRV in the Nepalese population among individuals with prediabetes, prehypertension, and those with both conditions. Comparing these groups with the control will provide insights into which one may pose a greater health risk, allowing for early intervention.

Method

This comparative cross-sectional observational study was carried out in the Physiology Laboratory of Patan Academy of Health Sciences (PAHS), Nepal, from Jun 2024 to Oct 2025. Participants were recruited using a convenience sampling method. The sample size was calculated based on a previous study using the mean and standard deviation of HRV parameters among control, prediabetes, prehypertension, and combined groups.[14] The calculation was performed using OpenEpi software.

Following ethical approval from the Institutional Review Committee of PAHS (Ref. bss2501171981), a total of 120 participants, including both males and females, were enrolled from the outpatient department and staff of a PAHS-affiliated tertiary care hospital. Prior to enrolment, participants were provided with a detailed information sheet outlining the study objectives, procedures, potential risks, and benefits, and written informed consent was obtained. Individuals with normal or prediabetic HbA1c levels based on hospital laboratory reports were initially recruited. Blood pressure was measured on two separate days, with at least two readings taken 1–2 minutes apart on each occasion, and the average value was recorded.

After obtaining a brief medical history and performing a physical examination to confirm eligibility, participants were allocated into four groups, with 30 individuals in each group. The control group consisted of age-matched healthy participants with normal glycaemic status (HbA1c <5.7%) and normal blood pressure (systolic <120 mmHg and/or diastolic <80 mmHg). Participants with HbA1c values between 5.7% and 6.4% were assigned to the prediabetes group, while those with systolic blood pressure of 120–139 mmHg and/or diastolic blood pressure of 80–89 mmHg were classified into the prehypertension group. The fourth group included individuals who met the criteria for both prediabetes and prehypertension. Participants were excluded if they had a known history of systemic illnesses such as diabetes, hypertension, thyroid disorders, cardiovascular or respiratory diseases, were taking medications for any chronic condition, or were pregnant.

On the day of HRV assessment, participants were instructed to avoid caffeine, alcohol, smoking, and strenuous physical activity for 24 hours prior to testing. Demographic and anthropometric data, including age, height, and weight, were recorded, along with cardiorespiratory variables such as blood pressure, pulse rate, and respiratory rate. Body mass index (BMI) was calculated accordingly.

Participants were then asked to rest in a seated position for five minutes before HRV recording. A five-minute HRV recording was obtained using an automated Polar H10 device in the physiology laboratory. The recorded HRV data were analysed using Kubios HRV software, which provides both time-domain and frequency-domain measures. Frequency-domain indices included total power (TP), low-frequency power (LF), high-frequency power (HF), and the LF/HF ratio. Time-domain indices included mean R–R interval (mean RR), standard deviation of normal-to-normal intervals (SDNN), root mean square of successive differences (RMSSD), number of NN intervals differing by more than 50 ms (NN50), percentage of NN intervals differing by more than 50 ms (pNN50), maximum heart rate, and minimum heart rate.

Data were entered into Microsoft Excel and analysed using SPSS version 26. HRV parameters were expressed as mean ± SD for normally distributed variables and as median (interquartile range) for non-normally distributed variables. Group comparisons were performed using one-way ANOVA followed by the

Tukey–Kramer post hoc test for normally distributed data, and the Kruskal–Wallis test with Dunn's post hoc test for non-normally distributed data. A p-value <0.05 was considered statistically significant

Result

The mean age, weight, BMI, and respiratory rate were comparable among the control and other groups (p > 0.05), showing no significant differences. However, significant differences were observed in basal heart rate and blood pressure parameters.

The basal heart rate was significantly higher in the prediabetes with prehypertension group (87.7±8.59 beats/min) compared to the control group (75.6± 9.51 beats/min; p<0.001). Systolic and diastolic blood pressures were also significantly elevated in both the prediabetes with prehypertension and prehypertensive groups compared with controls (p<0.001 for both). HbA1c levels were markedly higher in both the prediabetes with prehypertension (5.86 ± 0.04) and prediabetes groups (5.91 ± 0.35) than in the control group (5.09±0.27; p<0.001), confirming the glycemic status of these participants, Table 1.

Total power (TP) was significantly lower in the prediabetes with prehypertension group (261 [116.75–538.25] ms²) and the prehypertensive group (327.5 [183–591.75] ms²) than in controls (1118 [580.25–1756.75] ms²; p < 0.001 for both comparisons). Other frequency-domain parameters (LF, HF, LF/HF ratio) did not differ significantly compared with controls or other groups, although trends toward higher LF and LF/HF and lower HF were observed in the prediabetes with prehypertension group. Frequency-domain indices of HRV did not differ significantly between the prediabetes and control groups, Table 2.

The time-domain indices of HRV like RMSSD, NN50, pNN50, and SDNN were significantly reduced in the prediabetes with prehypertension group compared to controls (p<0.001 for all). The prehypertensive group also demonstrated significant declines in these parameters relative to controls (p<0.001 for all). The mean RR interval was significantly shorter in the prediabetes with prehypertension group (681.26 ± 83.27 ms) compared to controls (786.43 ± 99.67 ms; p<0.001), consistent with a higher resting heart rate. Maximum and minimum heart rates were also significantly elevated in the prediabetes with prehypertension group compared to controls (p=0.032 and p= 0.002, respectively). Time-domain indices did not differ significantly between the prediabetes and control groups, Table 3.

Discussion

In this study, the total power (TP) of the frequency-domain parameter was found to be significantly lower in both the prehypertensive and co-existing groups compared to the control group. This shows a clear reduction in heart rate variability (HRV), which reflects decreased vagal tone in these individuals, as TP generally indicates the strength of vagal control over the heart.[11]

The time-domain parameter SDNN, which represents overall HRV and includes both sympathetic and parasympathetic influences, was also lower in

Table 1. General and basal cardiovascular characteristics of the study groups (N=30)

Parameters	Control	Prediabetes	Prehypertensive	Prediabetes with prehypertension	p values
Age (years)	37.93 ± 5.76	39.6 ± 9.14	41.63 ± 6.58	41.8 ± 7.10	0.131
Weight (kg)	70.2 ± 10.7	69.13 ± 9.7	75.20 ± 8.87	73.23 ± 7.97	0.053
BMI (kg/m²)	25.72 ± 3.46	25.44 ± 3.3	27.53 ± 2.91	26.83 ± 2.53	0.034
Respiratory rate (per min)	16.93 ± 2.46	17.6 ± 2.2	18.13 ± 2.25	18.4 ± 2.35	0.078
Basal heart rate (beats/min)	75.6 ± 9.51	76.53 ± 7.58	76.17 ± 8.67	87.7 ± 8.59**	<0.001
Systolic blood pressure (mmHg)	115 (110–120)	111 (104–118)	136 (130–139)**	133 (130–138)**	<0.001
Diastolic blood pressure (mmHg)	76.5 (70–80)	70 (70–79)	86 (88–89)**	88 (86–89)**	<0.001
HbA1c (%)	5.09 ± 0.27	5.91 ± 0.35**	5.14 ± 0.25	5.86 ± 0.04**	<0.001

*Data presented as mean ± SD or median (Q1–Q3). p values represent overall significance from ANOVA or Kruskal–Wallis test.
*Indicates comparison of prediabetes, prehypertension, and co-existing groups with control. *p < 0.05; **p < 0.001.*

Table 2. Frequency-domain indices of HRV recorded in the sitting position of subjects in various groups

Parameters	Control	Prediabetes	Prehypertensive	Prediabetes with prehypertension	p values
TP (ms²)	1118 (580.25–1756.75)	733.5 (290.75–1244.5)	327.5 (183–591.75)**	261 (116.75–538.25)**	<0.001
LF (n.u.)	49.81 ± 21.87	53.59 ± 19.61	56.44 ± 21.63	61.78 ± 20.51	0.162
HF (n.u.)	50.02 ± 21.72	46.31 ± 19.67	43.41 ± 21.6	38.13 ± 20.51	0.165
LF/HF ratio	0.93 (0.43–2.1)	1.26 (0.70–2.59)	1.475 (0.67–3.09)	2.035 (0.88–3.525)	0.161

*Data presented as mean ± SD or median (Q1–Q3). p values represent overall significance from ANOVA or Kruskal–Wallis test.
*Indicates comparison of prediabetes, prehypertension, and co-existing groups with control. *p < 0.05; **p < 0.001.*

Table 3. Time-domain indices of HRV recorded in the sitting position of subjects in various groups

Parameters	Control	Prediabetes	Prehypertensive	Prediabetes with prehypertension	p values
Mean RR (ms)	786.43 ± 99.67	783.63 ± 85.71	782.93 ± 96.77	681.26 ± 83.27**	<0.001
SDNN (ms)	35.45 (27.22–45.52)	30.45 (21.4–38.9)	21 (17.25–29.37)**	18.55 (11.57–23.85)**	<0.001
RMSSD (ms)	34.18 ± 15.12	28.30 ± 11.84	22.16 ± 8.68**	15.78 ± 8.85**	<0.001
NN50 (beats)	51 (16.5–101)	38.5 (3.75–70)	6 (0–24.25)**	0 (0–6)**	<0.001
pNN50 (%)	14.2 (3.78–27.67)	9.99 (0.95–18.44)	1.4 (0–6.24)**	0 (0–1.31)**	<0.001
Max HR (beats/min)	88.87 ± 10.97	86.1 ± 10.6	85.3 ± 10.21	96.57 ± 11.13*	<0.001
Min HR (beats/min)	69.77 ± 10.63	70.37 ± 8.93	72.07 ± 9.58	80.57 ± 15.04*	0.001

*Data presented as mean ± SD or median (Q1–Q3). p values represent overall significance from ANOVA or Kruskal–Wallis test.
*Indicates comparison of prediabetes, prehypertension, and co-existing groups with control. *p < 0.05; *$p < 0.001$.

the prehypertensive and co-existing groups when compared to the control group. This suggests a reduction in total autonomic variability. Similarly, other parameters like RMSSD, NN50, and pNN50, which mainly reflect parasympathetic (vagal) activity, were reduced, supporting the idea of vagal withdrawal and autonomic imbalance in prehypertensive and co-existing groups. These findings are consistent with results from other studies.[9,11,14] The higher resting, mean RR, maximum, and minimum heart rates in the co-existing group during HRV testing further support this observation, indicating a shift toward sympathetic dominance as heart rate is at a higher level in the co-existing group than control. These changes in autonomic control may be early warning signs of cardiovascular dysfunction before full hypertension or diabetes develops.[9,15] The possible mechanisms behind these changes include low-grade inflammation, oxidative stress, insulin resistance, and impaired baroreflex sensitivity, all of which can disrupt autonomic regulation and weaken vagal tone.[6,16,17]

Time-domain measures mainly reflect total variability and short-term vagal activity, while frequency-domain parameters (LF, HF, LF/HF ratio) show the balance between sympathetic and parasympathetic activity.[15] In this study, frequency-domain findings (LFnu, HFnu, and LF/HF ratio) showed a trend toward higher sympathetic and lower parasympathetic modulation in the prehypertensive and co-existing groups, though these changes were not statistically significant. This agrees with earlier research suggesting that time-domain parameters are more sensitive to early autonomic changes, while frequency-domain shifts become more noticeable as the disease progresses further.[6,18]

Moreover, in this study, there was no significant difference between the control and prediabetic groups in HRV parameters. This is similar to other studies where most HRV variables were not significantly different in prediabetes.[19,20] Tarvainen et al. found that the greatest decrease in HRV occurred within the first 5–10 years of diabetes.[21] This suggests that mild disturbances in blood sugar alone may not cause major autonomic changes unless accompanied by high blood pressure. Still, when prehypertension and prediabetes occur together, autonomic dysfunction appears to worsen, likely due to the combined effects.

The strength of the study includes direct HRV measurement and comparison among four key groups: control, prediabetes, prehypertension, and co-existing conditions. Using a non-invasive HRV test provides a simple and reliable way to detect early autonomic changes before health problems appear. Future studies should explore whether lower HRV in people with prediabetes or prehypertension can predict the development of diabetes, hypertension, or heart disease. Research involving lifestyle interventions such as exercise, weight loss, or stress management could also help determine if improving health can restore HRV. Larger and well-designed studies are needed to confirm whether having both prediabetes and prehypertension together affects autonomic function more than having either one alone.

Conclusion

HRV measures (TP, RMSSD, NN50, pNN50, SDNN) were significantly lower in people with prehypertension and those with both prediabetes and prehypertension compared to the control group. However, there was no significant difference between the control group and the prediabetic group alone. Our findings show that people with co-existing prediabetes and prehypertension have the greatest reduction in overall HRV and parasympathetic activity, while those with only prehypertension show moderate reductions, and prediabetes alone does not show changes. This indicates that having both metabolic and blood pressure risk factors together leads to more severe autonomic dysfunction. Detecting and addressing these issues early could help maintain autonomic function and lower the risk of future cardiovascular problems.

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Conflicting Interest

None

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Author Contribution

Concept, design, planning: SM, SKM, SG, AP, PP, JB, IS; Literature review: SM; Data collection: SM, SKM, SG, AP, PP; Data analysis: SM; Draft manuscript: SM, SG; Revision of draft: SM, SKM, SG, AP, PP, JB, IS; Final manuscript: SM, SKM, SG, AP, PP, JB, IS; Accountability of the work: SM, SKM, SG, AP, PP, JB, IS; Guarantor: SM.

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