Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.69980/3h638y51

ASSOCIATION OF TELOMERASE ACTIVITY WITH OXIDATIVE STRESS AND ENDOTHELIAL FUNCTION IN PREHYPERTENSION.

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Abstract

Background: Prehypertension is an early blood pressure phenotype associated with increased cardiovascular risk; however, its cellular and vascular mechanisms in young adults remain incompletely defined. This study evaluated telomerase activity, oxidative stress, and endothelial function biomarkers in young adults with prehypertension compared to normotensive controls.

Methods: This analytical cross-sectional study included 91 young adults, comprising 47 normotensive controls and 44 individuals with prehypertension, classified according to the JNC 7 blood pressure criteria. Anthropometric parameters and blood pressure were measured using standardized methods. Serum telomerase activity, thiobarbituric acid reactive substances (TBARS), vascular cell adhesion molecule (VCAM), endothelin-1 (ET-1), soluble E-selectin, vascular endothelial growth factor (VEGF), and resistin levels were assessed. Between-group comparisons were performed using appropriate parametric and non-parametric tests. The correlations between telomerase activity, oxidative stress, and endothelial biomarkers were evaluated.

Results: Age and height were comparable between the groups. Prehypertensive participants had significantly higher body weight, body mass index, systolic blood pressure, and diastolic blood pressure than those of the controls. Compared with normotensive controls, the prehypertensive group showed significantly higher VCAM, ET-1, TBARS, telomerase activity, resistin, soluble E-selectin, and VEGF levels and lower NO levels. Telomerase activity was strongly positively correlated with VCAM, ET-1, VEGF, resistin, and soluble E-selectin levels. TBARS levels were also positively correlated with VCAM, ET-1, VEGF, and telomerase activity.

Conclusion: Young adults with prehypertension demonstrate a coordinated oxidative–endothelial–cellular stress phenotype characterized by elevated oxidative stress, endothelial activation, inflammatory vascular biomarkers, angiogenic response, and altered telomerase activity. Longitudinal studies are required to determine whether these biomarkers can predict the progression to established hypertension.

Keywords: Prehypertension, Telomerase activity, Oxidative stress, Endothelial dysfunction, Vascular aging, Endothelin-1.

Introduction

Prehypertension is an important intermediate phenotype in the continuum between optimal blood pressure and established hypertension. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure defined prehypertension as a systolic blood pressure of 120–139 mmHg and/or diastolic blood pressure of 80–89 mmHg in adults not receiving antihypertensive therapy(1). Although the 2017 American College of Cardiology/American Heart Association guidelines replaced the term "prehypertension" with the categories of elevated blood pressure and stage 1 hypertension, the biological relevance of this blood pressure range remains substantial because cardiovascular risk begins to increase well below the conventional diagnostic threshold for hypertension(2). Therefore, prehypertension should not be viewed merely as a numerical classification but as a clinically relevant vascular-risk state that may reflect early pathophysiological changes preceding overt hypertension.

The public health significance of prehypertension is considerable, particularly among young and middle-aged adults. Large epidemiological studies and meta-analyses have shown that prehypertension is associated with an increased risk of cardiovascular disease, coronary heart disease, myocardial infarction, and stroke, even after adjustment for traditional cardiovascular risk factors(3,4). This risk appears to be especially pronounced in individuals with high-range prehypertension, suggesting a graded relationship between blood pressure elevation and vascular injury(5). In South Asia, where cardiometabolic risk often appears earlier in life, population-based data indicate a high burden of prehypertension among economically active adults, including in India(6). These observations support the need to identify early biological markers that can explain why some individuals with prehypertension progress to hypertension and cardiovascular disease, whereas others remain clinically stable.

Endothelial dysfunction is considered one of the earliest detectable abnormalities in the pathogenesis of hypertension and atherosclerotic cardiovascular disease (CVD). The vascular endothelium regulates vasomotor tone, leukocyte adhesion, thrombosis, inflammation, oxidative balance, and vascular repair through the coordinated release of nitric oxide, prostacyclin, endothelin-1, adhesion molecules, and growth factors(7). In healthy individuals, nitric oxide maintains vasodilation and suppresses inflammation, platelet aggregation, and smooth muscle cell proliferation. In contrast, endothelial dysfunction is characterized by reduced nitric oxide bioavailability, increased vasoconstrictor activity, enhanced oxidative stress, and activation of proinflammatory pathways (8), suggesting that endothelial injury begins before the onset of sustained hypertension becomes clinically established. Studies have demonstrated impaired endothelial progenitor cell function and reduced endothelial repair capacity in individuals with prehypertension, linking early blood pressure elevation to defective vascular maintenance mechanisms(9).

Oxidative stress is a central mechanism that connects elevated blood pressure, endothelial dysfunction, and vascular remodeling. Excess generation of reactive oxygen species, particularly superoxide, reduces nitric oxide bioavailability through direct chemical interaction and formation of peroxynitrite, thereby impairing endothelium-dependent vasodilation(10). Reactive oxygen species also activate redox-sensitive inflammatory pathways, enhance vascular smooth muscle proliferation, increase extracellular matrix remodeling, and promote arterial stiffness(11). Thiobarbituric acid reactive substances, which largely reflect lipid peroxidation products such as malondialdehyde, are widely used as biochemical indicators of systemic oxidative stress and membrane lipid damage(12). In the context of prehypertension, increased oxidative stress may represent an early biochemical signal of vascular injury before irreversible vascular structural changes develop.

Endothelial activation can be further characterized by circulating biomarkers, such as vascular cell adhesion molecule-1, soluble E-selectin, endothelin-1, vascular endothelial growth factor, and resistin. Vascular cell adhesion molecule-1 and E-selectin are inducible adhesion molecules

expressed during endothelial activation that facilitate leukocyte rolling, adhesion, and transmigration into the vascular wall(13). Endothelin-1 is a potent vasoconstrictor peptide with mitogenic, inflammatory, and profibrotic actions and has been implicated in hypertension-related vascular damage(14). Vascular endothelial growth factor plays an important role in angiogenesis and endothelial repair; however, altered circulating levels may also reflect vascular stress or compensatory responses to endothelial injury(15). Resistin, initially described as an adipokine, is increasingly recognized as a pro-inflammatory mediator linked to endothelial dysfunction and vascular inflammation in hypertension(16).

In parallel with oxidative and endothelial mechanisms, cellular aging has emerged as a potentially important but less explored component of early cardiovascular risks. Telomeres are repetitive nucleotide sequences that protect chromosomal ends, whereas telomerase is a ribonucleoprotein enzyme complex that maintains telomere length and contributes to cellular replicative capacity(17). Beyond its canonical role in telomere maintenance, telomerase, particularly telomerase reverse transcriptase, has been implicated in mitochondrial protection, oxidative stress modulation, endothelial survival, and vascular homeostasis(18). Experimental and clinical evidence suggests that telomere dysfunction and impaired telomerase biology may contribute to endothelial senescence, vascular aging, atherosclerosis, and cardiometabolic diseases (19). Nitric oxide has also been shown to activate telomerase and delay endothelial cell senescence, indicating a biologically plausible link between endothelial health and telomerase activity(20).

Despite increasing evidence linking prehypertension with endothelial dysfunction and oxidative stress, the interaction between telomerase activity, oxidative stress, and endothelial activation in young adults with prehypertension remains insufficiently characterized. Most available studies have examined endothelial function, oxidative stress, and cellular aging markers in isolation. However, these processes are unlikely to operate independently of each other. Oxidative stress accelerates telomere damage and cellular senescence; endothelial senescence reduces nitric oxide bioavailability and impairs vascular repair; and endothelial activation amplifies inflammation and oxidative injury. Therefore, the simultaneous assessment of telomerase activity, oxidative stress, and endothelial biomarkers may provide a more integrated understanding of early vascular dysfunction in prehypertension.

This study aimed to evaluate telomerase activity, oxidative stress, and selected endothelial function markers in young adults with prehypertension compared to normotensive controls. We specifically examined serum telomerase activity, thiobarbituric acid reactive substances, vascular cell adhesion molecule-1, endothelin-1, soluble E-selectin, vascular endothelial growth factor, and resistin. By exploring the interrelationships among these markers, this study aimed to clarify whether prehypertension in young adults is associated with a coordinated cellular–vascular dysfunction phenotype. Such evidence may help identify early biological signatures of vascular aging and improve risk stratification before the development of hypertension.

Materials and Methods

This cross-sectional study was conducted among young adult volunteers at Sri Venkateswara Medical College, Tirupati, Andhra Pradesh, India. The study protocol was reviewed and approved by the Institutional Ethics Committee of Sri Venkateswara Medical College, Tirupati, India. All participants were informed of the study objectives, procedures involved, voluntary nature of participation, and confidentiality of data. Written informed consent was obtained from all participants prior to enrolment.

Young adult participants aged approximately 18–30 years were recruited from Sri Venkateswara Medical College in Tirupati. After screening for eligibility, the participants were divided into two groups based on their blood pressure status. The normotensive control group included participants with systolic and diastolic blood pressure between 100 and 119 mmHg and 60 and 79 mmHg, respectively. The prehypertensive group included participants with systolic blood pressure between 120 and 139 mmHg and/or diastolic blood pressure between 80 and 89 mmHg.

Apparently healthy young adults who were willing to participate and provide written informed consent were included in this study. Participants were eligible for inclusion in the normotensive group if their systolic and diastolic blood pressure values were within the normal range. Participants were eligible for inclusion in the prehypertensive group if their blood pressure values fulfilled the JNC 7 criteria. Individuals with known hypertension, diabetes mellitus, chronic kidney disease, endocrine disorders, established cardiovascular disease, acute or chronic inflammatory illness, or any systemic illness that could influence vascular, metabolic, oxidative, or inflammatory biomarkers were excluded. Participants receiving antihypertensive or any regular medication that could influence blood pressure, oxidative stress, endothelial function, inflammatory status, or metabolic parameters were also excluded.

Anthropometric measurements were performed using standardized procedures. Body weight was measured in kilograms using a calibrated weighing scale, with the participants wearing light clothing and without footwear. Height was measured in centimeters using a stadiometer, with the participants standing erect without footwear. Body mass index was calculated as weight in kilograms divided by height in meters squared and expressed in kg/m^2.

Blood pressure was measured using the auscultatory method with a calibrated sphygmomanometer. Measurements were obtained in a quiet room after the participants had rested in a seated position for at least 10 min. Participants were seated comfortably with their back supported, feet resting on the floor, and arms supported at the level of the heart. An appropriately sized cuff was placed on the upper arm. Systolic blood pressure was recorded at the appearance of the first Korotkoff sound, and diastolic blood pressure was recorded at the disappearance of the Korotkoff sounds. Three successive blood pressure readings were obtained at suitable intervals, and the mean value was used for the classification and statistical analysis. Participants were categorized into normotensive and prehypertensive groups based on their average blood pressure values.

After anthropometric assessment and blood pressure measurement, 5 mL of venous blood was collected from each participant under aseptic conditions. Blood samples were collected in the morning after overnight fasting. The collected samples were allowed to clot at room temperature and centrifuged for min to separate the serum. The separated serum was aliquoted into appropriately labelled microcentrifuge tubes and stored at −80°C until biochemical analysis. Repeated freeze–thaw cycles were avoided to minimize the preanalytical variability.

Serum samples were analyzed for telomerase activity, thiobarbituric acid reactive substances, vascular cell adhesion molecule-1, endothelin-1, soluble E-selectin, vascular endothelial growth factor, and resistin levels. Telomerase activity was assessed as a marker of cellular aging-related activity. Thiobarbituric acid reactive substances were measured as indices of lipid peroxidation and systemic oxidative stress. Vascular cell adhesion molecule-1 and soluble E-selectin levels were measured as markers of endothelial activation. Endothelin-1 was assessed as a marker of endothelial vasoconstriction. Vascular endothelial growth factor was measured as a marker of angiogenesis and vascular repair responses. Resistin was assessed as an inflammatory adipokine associated with cardiometabolic and endothelial dysfunction. Serum telomerase activity was measured using an enzyme-linked immunosorbent assay, according to the manufacturer's instructions. Oxidative stress was assessed by estimating serum thiobarbituric acid reactive substances (TBARS) using a spectrophotometric method. This assay reflects lipid peroxidation products, particularly malondialdehyde-like compounds, and is used as a biochemical indicator of the oxidative stress burden.

Statistical analyses were performed using R software (version 3.2.3) for Windows. Continuous variables were initially assessed for their distributional characteristics. Normality was evaluated using the Kolmogorov–Smirnov test. Normally distributed variables were summarized as mean ± standard deviation, whereas non-normally distributed variables were summarized as median with interquartile range, where appropriate. Categorical variables were expressed as frequencies and percentages. Between-group comparisons were performed between normotensive controls and prehypertensive participants. An independent samples t-test was used for normally distributed continuous variables, while the Mann–Whitney U test was used for variables that were not normally

distributed. Associations between telomerase activity, oxidative stress, and endothelial function biomarkers were assessed using correlation analyses. Pearson's correlation coefficient was used for normally distributed variables, and Spearman's rank correlation coefficient was used for non-normally distributed variables. Statistical significance was set at $p \leq 0.05$.

Results

The final analysis included 91 participants: 47 normotensive controls and 44 individuals with prehypertension. The baseline characteristics of the study participants are shown in Table 1. The two groups were comparable with respect to age and body height. The mean age of the control group was 18.95 ± 1.08 years, whereas that of the prehypertensive group was 18.65 ± 0.68 years, with no statistically significant difference between the two groups ($p = 0.122$). Similarly, the mean height did not differ significantly between the control and prehypertensive participants. In contrast, body weight and body mass index were significantly higher in the prehypertension group than in the control group. The systolic and diastolic blood pressure values were significantly higher in the prehypertension group.

A comparison of telomerase activity, oxidative stress, and endothelial function markers between normotensive controls and prehypertensive participants is shown in Table 2. The prehypertensive group demonstrated significantly higher levels of vascular cell adhesion molecules than the controls. The mean VCAM concentration was 3.83 ± 2.03 ng/mL in the control group and 14.32 ± 15.79 ng/mL in the prehypertensive group ($p < 0.001$), indicating increased endothelial activation among individuals with prehypertension.

Endothelin-1 levels were significantly elevated in the prehypertensive group. The mean ET-1 concentration was 36.09 ± 16.51 ng/L in the controls and 190.28 ± 192.56 ng/L in the prehypertensive participants ($p < 0.001$). This finding suggests increased endothelial vasoconstrictor activity in individuals with prehypertension.

Oxidative stress, assessed by thiobarbituric acid reactive substances, was significantly higher in the prehypertension group than in the control group. The mean TBARS concentration was 3.14 ± 1.12 nmol/mL among controls and 7.66 ± 6.53 nmol/mL among prehypertensive participants ($p < 0.001$), indicating increased lipid peroxidation and oxidative stress burden in the prehypertensive state.

Telomerase activity was significantly higher in the prehypertensive group than in the control group. The mean telomerase activity was 7.59 ± 2.96 IU/mL in the controls and 36.10 ± 35.01 IU/mL in the prehypertensive participants ($p < 0.001$). This finding indicates an altered telomerase activity in individuals with prehypertension.

Resistin levels were markedly elevated among prehypertensive participants. The mean resistin concentration was 144.46 ± 59.53 ng/mL in the control group and 1860.66 ± 2098.98 ng/mL in the prehypertensive group ($P < 0.001$). Similarly, soluble E-selectin levels were significantly higher in prehypertensive participants than in controls (77.71 ± 88.26 vs. 15.87 ± 6.16 ng/mL; $p < 0.001$).

Vascular endothelial growth factor levels were also significantly increased in the prehypertension group. The mean VEGF concentration was 37.03 ± 15.25 ng/L in the controls and 2716.49 ± 2795.32 ng/L in the prehypertensive participants ($p < 0.001$). These findings collectively indicate that prehypertension is associated with higher oxidative stress, a broad pattern of endothelial activation, and vascular biomarker alterations.

The association between telomerase activity and endothelial function markers is shown in Table 3. Telomerase activity was positively correlated with all measured endothelial and inflammatory vascular biomarkers. A strong positive correlation was observed between telomerase activity and vascular cell adhesion molecules ($r = 0.793$). Telomerase activity also showed a strong positive correlation with endothelin-1 ($r = 0.921$) and vascular endothelial growth factor ($r = 0.849$).

Among the measured biomarkers, the strongest correlation was observed between telomerase activity and resistin (r = 0.933). Telomerase activity was also positively correlated with the level of soluble E-selectin (r = 0.835). These findings suggest that higher telomerase activity is associated with higher levels of endothelial activation, vasoconstrictor activity, angiogenic response, and inflammatory vascular biomarkers in the study population.

The association between oxidative stress, as assessed by TBARS, and endothelial function markers is shown in Table 4. TBARS levels were positively correlated with endothelial and vascular biomarkers. A positive correlation was observed between TBARS and vascular cell adhesion molecules (r = 0.756), suggesting that higher oxidative stress is associated with greater endothelial activation. TBARS showed a strong positive correlation with endothelin-1 (r = 0.918), indicating an association between the oxidative stress burden and endothelial vasoconstrictor activity. TBARS was also positively correlated with vascular endothelial growth factor (r = 0.783), suggesting a relationship between lipid peroxidation and vascular repair/angiogenic response. In addition, TBARS levels showed a positive correlation with telomerase activity (r = 0.880), indicating that oxidative stress was closely associated with altered telomerase activity in the study population.

Table 1: Baseline characteristics of the study participants.

parameter	Controls(n=47)	Pre HTN (n=44)	P value
Age(yrs)	18.95 ± 1.08	18.65 ± 0.68	0.122
Height (cm)	162.42 ± 8.70	164.16 ± 8.43	0.336
Weight(kg)	54.94 ± 10.75	65.93 ± 12.14	0.000
BMI (kg/m^2)	20.87 ± 3.99	24.40 ± 3.73	0.000
SBP(mmHg)	112.21 ± 5.09	125.18 ± 2.90	0.000
DBP(mmHg)	74.12 ± 3.59	83.40 ± 3.87	0.000

Data expressed as Mean ± SD.
BMI: Body Mass Index, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure.

Table 2: Comparison of TE, oxidative stress and endothelial markers between the gropus.

parameter	Controls(n=47)	Pre HTN (n=44)	P value
VCAM (ng/ml)	3.83 ± 2.03	14.32 ± 15.79	0.000
ET 1 (ng/L)	36.09 ± 16.51	190.28 ± 192.56	0.000
TBARS (nmol/ml)	3.14 ± 1.12	7.66 ± 6.53	0.000
TE (IU/ML)	7.59 ± 2.96	36.10 ± 35.01	0.000
Resistin (ng/mL)	144.46 ± 59.53	1860.66 ± 2098.98	0.000
sE selectin (ng/mL)	15.87 ± 6.16	77.71 ± 88.26	0.000
VEGF (ng/L)	37.03 ± 15.25	2716.49 ± 2795.32	0.000

Data expressed as Mean ± SD.
VCAM: Vascular cell adhesion molecule, ET1: Endothelin, TBARS: Thibarbuturic acid reactive substances, TE: Telomerase, sE selectin: soluble E selectin, VEGF: Vascular Endothelial Growth Factor.

Table 3: Association of TE with endothelial markers

Sl. No	Parameter	TE (IU/ML)
		r value

1	VCAM (ng/ml)	0.793
2	ET 1 (ng/L)	0.921
4	VEGF (ng/L)	0.849
5	Resistin (ng/mL)	0.933
6	sE selectin (ng/mL)	0.835

VCAM: Vascular cell adhesion molecule ET1: Endothelin TE: Telomerase sE selectin: soluble E selectin, VEGF: Vascular Endothelial Growth Factor.

Table 4: Association of Oxidative stress with endothelial markers

Sl. No	**Parameter**	TBARS (nmol/ml)
		r value
1	VCAM (ng/mL)	0.756
2	ET 1 (ng/mL)	0.918
3	VEGF (ng/mL)	0.783
4	TE (IU/ML)	0.880

VCAM: Vascular cell adhesion molecule, ET1: Endothelin, TBARS: Thibarbuturic acid reactive substances, TE: Telomerase, sE selectin: soluble E selectin, VEGF: Vascular Endothelial Growth Factor.

Discussion

The present study demonstrated that young adults with prehypertension exhibit a distinct biochemical and vascular phenotype characterized by significantly higher oxidative stress, endothelial activation, inflammatory adipokine response, angiogenic marker elevation, and altered telomerase activity compared with normotensive controls. The prehypertensive group showed significantly higher body weight, body mass index, systolic blood pressure, and diastolic blood pressure than the normotensive group. In addition, TBARS, VCAM, endothelin-1, soluble E-selectin, VEGF, resistin, and telomerase activities were significantly elevated in individuals with prehypertension. Correlation analysis further demonstrated strong positive associations between telomerase activity and TBARS with several endothelial and vascular biomarkers. These findings suggest that prehypertension in young adults is not merely a borderline blood pressure category but may represent an early cellular–vascular stress state involving oxidative, endothelial, inflammatory, and telomerase-linked biological responses.

The clinical importance of prehypertension has been debated since its introduction in the JNC 7 classification; however, accumulating evidence indicates that blood pressure in this range is associated with increased cardiovascular risk compared with optimal blood pressure(21). Large meta-analyses have shown that prehypertension is associated with an increased incidence of cardiovascular disease, coronary heart disease, myocardial infarction, and stroke, particularly in individuals with high-range prehypertension(4). The present findings add mechanistic depth to this epidemiological association by demonstrating that young individuals with prehypertension already show measurable abnormalities in oxidative stress and endothelial function biomarkers. This is relevant because early vascular dysfunction may precede clinically apparent hypertension and contribute to later cardiovascular risk.

A major finding of this study was the significantly higher TBARS level in prehypertensive participants than in normotensive controls. TBARS reflects lipid peroxidation products and is widely used as a marker of oxidative stress in biological samples (22). Oxidative stress is a key mechanism in hypertension-related vascular dysfunction because reactive oxygen species reduce nitric oxide bioavailability, promote peroxynitrite formation, activate redox-sensitive inflammatory

pathways, impair endothelial-dependent vasodilation, and contribute to vascular remodeling(23). The strong positive correlations observed between TBARS and VCAM, endothelin-1, VEGF, and telomerase activity in the present study support the possibility that oxidative stress is closely linked to endothelial activation and cellular stress responses in prehypertension. However, because of its cross-sectional design, the present study could not establish whether oxidative stress is a cause, consequence, or parallel manifestation of early blood pressure elevation.

The elevation of endothelial biomarkers in the prehypertensive group was also biologically plausible. Endothelial dysfunction is characterized by a shift from a vasodilatory, anti-inflammatory, and antithrombotic vascular phenotype to a vasoconstrictive, inflammatory, proliferative, and prothrombotic phenotype(24). Previous studies have shown that endothelial repair capacity and endothelial progenitor cell function are impaired in prehypertension, suggesting that vascular injury and defective endothelial maintenance may begin before overt hypertension develops(25). In the present study, higher VCAM and soluble E-selectin levels indicated endothelial activation, whereas higher endothelin-1 levels suggested increased vasoconstrictor tone. Together, these findings support the interpretation that prehypertension in young adults is accompanied by early endothelial disturbances rather than isolated hemodynamic elevation.

The significant elevation of endothelin-1 levels in prehypertensive participants deserves particular attention. Endothelin-1 is a potent endothelial-derived vasoconstrictor peptide that contributes to vascular tone regulation, smooth muscle proliferation, inflammation, oxidative stress, and vascular remodeling(26). Increased endothelin-1 may therefore represent one pathway linking early blood pressure elevation with the progression toward sustained hypertension. The strong positive correlations between endothelin-1 and both TBARS and telomerase activity in the present study suggest that endothelial vasoconstrictor activation may coexist with oxidative stress and telomerase-linked cellular responses. This finding strengthens the view that prehypertension may involve a coordinated vascular stress phenotype rather than an isolated elevation of blood pressure.
The elevation of VCAM and soluble E-selectin further supports the presence of endothelial activation in patients with prehypertension. VCAM-1 and E-selectin are adhesion molecules involved in leukocyte adhesion, rolling, and transmigration across the endothelium, which are early events in vascular inflammation and atherogenesis(27). Their elevation in prehypertensive participants suggests that low-grade vascular inflammatory activation may already be present in young adults with modest blood pressure elevations. The strong positive correlations between telomerase activity and VCAM expression, as well as between TBARS and VCAM expression, are consistent with the concept that endothelial activation is closely linked to oxidative and cellular stress pathways. However, these biomarkers are not disease-specific, and their interpretation should be made in the context of other cardiometabolic variables, especially BMI.

Another important finding was the markedly higher resistin level in the prehypertensive group. Resistin is an inflammatory adipokine that has been associated with endothelial dysfunction, hypertension, cardiometabolic risk, and vascular inflammation(28). In human hypertension, higher resistin concentrations have been linked to inflammatory activation and endothelial dysfunction(29). A meta-analysis also reported higher serum resistin levels in hypertensive patients than in normotensive controls(30). In the present study, resistin showed the strongest positive correlation with telomerase activity among the endothelial and inflammatory markers examined. This may indicate that the telomerase signal observed in prehypertension is not isolated but occurs in parallel with adipokine-mediated inflammatory activation. Nevertheless, because BMI was significantly higher in the prehypertensive group, resistin elevation may partly reflect adiposity-related inflammation in this group. Therefore, adjusted regression analysis is essential before concluding that resistin is independently associated with prehypertension in this cohort study.

The finding of significantly elevated VEGF levels in prehypertension is also notable. VEGF is a key regulator of angiogenesis, endothelial survival, vascular permeability, and repair. Elevated

circulating VEGF levels have previously been proposed as markers of vascular damage in hypertension, including early hypertensive vascular injury(31). In the present study, VEGF levels were substantially higher in the prehypertensive group and showed positive correlations with telomerase activity and TBARS. This may represent a compensatory angiogenic or endothelial repair response to oxidative and vascular stresses. However, VEGF levels can be influenced by multiple biological processes, including inflammation, hypoxia, adiposity, platelet activation and endothelial injury. Therefore, VEGF elevation should be interpreted cautiously and preferably supported by additional adjusted analyses.

The most distinctive observation in this study was the significantly higher telomerase activity in prehypertensive participants. Telomerase biology is complex in cardiovascular disease. Telomeres and telomerase are involved in cellular aging, endothelial senescence, DNA damage responses, mitochondrial function, and vascular homeostasis(32). Experimental evidence suggests that NO can activate telomerase and delay endothelial cell senescence, indicating that telomerase may serve protective roles in endothelial biology(33). Conversely, chronic oxidative stress and telomere dysfunction promote endothelial senescence and vascular impairment(34). Therefore, the increased telomerase activity observed in this study should not be simplistically interpreted as either beneficial or harmful. We assume that elevated telomerase activity may reflect a compensatory cellular response to oxidative stress, endothelial activation, and early vascular injury in patients with prehypertension.

The positive correlation between telomerase activity and TBARS levels is particularly important. Since oxidative stress can damage telomeric DNA and accelerate endothelial senescence, an increase in telomerase activity may represent a counter-regulatory attempt to preserve cellular integrity under oxidative stress conditions(35). However, it is also possible that increased telomerase activity reflects increased cellular turnover, immune cell activation, inflammatory stimulation, or assay-related biological variability, rather than direct endothelial protection. As telomerase activity was measured in the serum rather than in specific vascular endothelial cells or leukocyte subpopulations, tissue-specific interpretation is limited. Future studies should consider measuring leukocyte telomere length, cell-specific telomerase activity, oxidative DNA damage markers, and nitric oxide bioavailability to clarify the mechanistic significance of telomerase elevation in prehypertension.

A central methodological issue in the present study was the significantly higher BMI observed in the prehypertensive group. BMI is not merely a descriptive variable; it is also a potential confounder. Higher adiposity may independently increase blood pressure, oxidative stress, resistin, VEGF, endothelial activation and inflammatory burden. Therefore, some of the observed group differences may be mediated or confounded by adiposity rather than by prehypertension alone.
The correlation pattern observed in this study supports an integrated model in which prehypertension is associated with oxidative stress, endothelial activation, inflammatory adipokine response, angiogenic signaling, and telomerase-linked cellular stress. TBARS correlated positively with VCAM, endothelin-1, VEGF, and telomerase activity, whereas telomerase activity correlated positively with VCAM, endothelin-1, VEGF, resistin, and soluble E-selectin. This pattern suggests that telomerase activity may be embedded within a broader vascular stress network, rather than acting as an isolated biomarker. From a pathophysiological perspective, oxidative stress may reduce nitric oxide bioavailability and activate endothelial inflammatory pathways; endothelial activation may increase adhesion molecules and vasoconstrictor mediators; and telomerase activity may change in response to cellular stress, repair demand or inflammatory stimulation. This integrated interpretation is more defensible than claiming a direct causal pathway from telomerase activity to prehypertension.

These findings have potential clinical implications. These findings support the concept that young adults with prehypertension may already have measurable endothelial and oxidative abnormalities

before the onset of hypertension. Oxidative stress and endothelial activation markers may help identify individuals at a higher biological risk within the prehypertensive range. The association between telomerase activity and oxidative and endothelial biomarkers raises the possibility that cellular aging pathways may be involved early in the development of hypertension. However, the data are insufficient to recommend these biomarkers for clinical risk prediction. For clinical translation, longitudinal studies are required to determine whether TBARS, telomerase activity, VCAM, endothelin-1, VEGF, soluble E-selectin, or resistin can predict the progression from prehypertension to sustained hypertension or cardiovascular events.

The strengths of this study include the selection of young adults, which reduces the confounding influence of advanced age and overt cardiovascular disease, and the simultaneous assessment of oxidative stress, endothelial activation, angiogenic response, inflammatory adipokine signaling, and telomerase activity. This multidimensional biomarker approach is valuable because prehypertension is unlikely to be driven by a single mechanism. This study also addresses an underexplored area by examining telomerase activity in relation to endothelial and oxidative stress markers in prehypertensive individuals.

This study has several limitations must be acknowledged. The cross-sectional design prevents the inference of causality or temporal sequence. The study was conducted in a single institutional setting among young adults, which may limit its generalizability to older populations or community-based cohorts. The significantly higher BMI in the prehypertensive group is an important potential confounder and should be addressed using appropriate statistical models.

Conclusion

In conclusion, this study showed that young adults with prehypertension have significantly higher oxidative stress, endothelial activation markers, resistin, VEGF, and telomerase activity than normotensive controls. The strong positive associations between TBARS and telomerase activity and endothelial biomarkers suggest that prehypertension is accompanied by a coordinated oxidative–endothelial–cellular stress phenotype. Rather than interpreting telomerase elevation as purely protective or pathological, the present findings support a more cautious interpretation that altered telomerase activity may reflect an early compensatory or stress-response mechanism in the setting of oxidative and endothelial disturbances. Longitudinal and mechanistic studies with appropriate adjustments for adiposity and other cardiometabolic confounders are needed to determine whether these biomarkers predict the progression of hypertension and future cardiovascular risk.

Acknowledgements

We extend our deepest appreciation to the esteemed MRU at SV Medical College, operating under the distinguished Department of Health Research, Government of India. This institution generously provided invaluable laboratory facilities and substantial financial support, facilitating the execution of our pioneering scientific investigations. We express our sincere gratitude for their unwavering support and acknowledge their pivotal contributions to scientific progress.

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