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Stress Physiology and Gut Microbial Ecology: Associations with Cortisol Dynamics and Cardiovascular Reactivity in Healthy Young Adults

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Abstract

Background: Chronic psychological stress is a recognised risk factor for a wide range of cardiovascular and metabolic disorders. Persistent activation of the hypothalamic-pituitary-adrenal (HPA) axis and the sympathoadrenal system leads to sustained elevation of glucocorticoids and catecholamines, with consequent maladaptive cardiovascular remodelling. Young adults, particularly those engaged in academic and professional environments, are increasingly vulnerable to stress-related dysregulation, yet population-specific data from India remain sparse. Aim: The present study aimed to evaluate the relationship between perceived chronic stress and (i) cortisol levels and (ii) resting and reactive cardiovascular parameters in healthy Indian young adults. Materials and Methods: A cross-sectional analytical study was conducted in the Department of Physiology, Sri Lakshmi Narayana Institute of Medical Sciences, Puducherry between October 2044 and April 2015. One hundred and fifty (n=150) healthy adults (81 males, 69 females; aged 18–25 years) were recruited and stratified by Perceived Stress Scale (PSS-10) scores into low-stress (n=42), moderate-stress (n=58), and high-stress (n=50) groups. Morning and evening serum cortisol were estimated by chemiluminescent immunoassay; salivary cortisol was measured by ELISA. Resting cardiovascular parameters and the cardiovascular response to a standardised cold pressor test (CPT) were recorded. One-way ANOVA with Bonferroni post-hoc correction and Pearson's correlation were used. Results: All cortisol indices and cardiovascular reactivity parameters increased progressively across stress strata ($p<0.001$). The high-stress group exhibited

significantly elevated morning serum cortisol (21.6 ± 3.8 µg/dL), salivary cortisol (19.2 ± 3.6 nmol/L), and exaggerated cold-pressor systolic BP rise (23.6 ± 4.8 mmHg) compared with the low-stress group. PSS-10 score correlated positively with morning cortisol ($r=0.612$, $p<0.001$) and CPT systolic response ($r=0.584$, $p<0.001$). Conclusion: Chronic perceived stress in young Indian adults is associated with sustained HPA axis activation, augmented basal cardiovascular tone, and exaggerated cardiovascular reactivity, indicating an early adverse cardiometabolic phenotype that may benefit from targeted preventive intervention.

Keywords

Chronic stress; Cortisol; Hypothalamic-pituitary-adrenal axis; Cardiovascular reactivity; Cold pressor test; Perceived stress scale; Young adults.

1. Introduction

Stress is a ubiquitous physiological response designed to preserve organismic homeostasis in the face of internal or external challenge. The acute stress response, mediated through the hypothalamic-pituitary-adrenal (HPA) axis and the sympathoadrenal medullary (SAM) axis, mobilises energy substrates, augments cardiovascular performance, and sharpens cognition [1]. When stressors persist beyond physiological adaptive capacity, however, the resulting allostatic load becomes pathogenic and contributes to the development of cardiovascular disease, type 2 diabetes mellitus, metabolic syndrome, depressive disorders, and immunological compromise [2,3].

The principal effector of the HPA axis is the glucocorticoid hormone cortisol, secreted in a circadian rhythm with peak levels in the early morning and trough levels in the late evening [4]. Chronic stress flattens this diurnal rhythm, elevates basal cortisol, and provokes an exaggerated cortisol awakening response (CAR) [5,6]. Persistently elevated cortisol upregulates hepatic gluconeogenesis, induces visceral adiposity, suppresses immune function, and exerts adverse effects on the cardiovascular system through endothelial dysfunction, insulin resistance, and proinflammatory signalling [7,8].

In parallel, chronic stress augments sympathetic outflow, increasing heart rate, peripheral vascular resistance, and arterial stiffness, while attenuating baroreflex sensitivity and parasympathetic modulation [9,10]. The cold pressor test (CPT), a standardised laboratory paradigm in which the hand is immersed in ice water for one minute, evokes a robust sympathetic pressor response and

serves as a reliable bedside measure of cardiovascular reactivity in research and clinical settings [11].

The Indian young adult population is a particularly relevant cohort for the study of stress-related cardiovascular physiology. Rapid urbanisation, examination pressure, employment uncertainty, sleep deprivation, and pervasive use of social media have generated novel chronic stress profiles whose physiological consequences remain poorly characterised in indigenous samples [12,13]. The present study was therefore designed to examine the relationship between self-reported chronic stress, HPA axis activity, and resting/reactive cardiovascular function in healthy young Indian adults.

2. Materials and Methods

2.1 Study Setting

This cross-sectional analytical study was conducted by Department of Physiology, Sri Lakshmi Narayana Institute of Medical Sciences, Puducherry, between October 2044 and April 2015.

2.2 Participants

One hundred and fifty (n=150) apparently healthy adults aged between 18 and 25 years were recruited by purposive sampling from among medical, nursing, and allied health science students of the institute. Inclusion criteria comprised non-smoker status, BMI between 18.5 and 27.0 kg/m², resting BP <140/90 mmHg, and absence of any chronic illness. Exclusion criteria comprised diabetes mellitus, hypertension, cardiovascular or pulmonary disease, endocrine or psychiatric disorders, regular use of any cardiovascular, hormonal, or psychotropic medication, recent major life events (bereavement, surgery within past 3 months), and pregnancy. Female participants were assessed in the early follicular phase to standardise hormonal milieu.

2.3 Stress Stratification

Perceived chronic stress was assessed using the validated Perceived Stress Scale (PSS-10) developed by Cohen et al. [14], in which higher scores denote greater perceived stress over the preceding month. Participants were stratified into three categories using the standard cut-points described by Andreou et al. [15]: low stress (PSS-10 score 0–13, n=42), moderate stress (14–26, n=58), and high stress (≥27, n=50). Demographic and lifestyle characteristics of the three groups are presented in Table 1. The three groups were comparable in age, sex distribution, and BMI;

however, sleep duration declined progressively from the low-stress to high-stress group, in line with the documented bidirectional relationship between stress and sleep quality.

Table 1. Demographic and Lifestyle Characteristics of Participants Stratified by PSS-10

Variable	Low Stress (n=42)	Moderate Stress (n=58)	High Stress (n=50)
Age (years)	21.4 ± 1.8	21.6 ± 1.9	21.8 ± 2.1
Male, n (%)	23 (54.8)	31 (53.4)	27 (54.0)
Female, n (%)	19 (45.2)	27 (46.6)	23 (46.0)
BMI (kg/m²)	21.8 ± 2.4	22.2 ± 2.6	22.6 ± 2.8
PSS-10 score	11.2 ± 2.6	19.4 ± 2.4	28.6 ± 3.2
Sleep duration (hrs)	7.4 ± 0.7	6.8 ± 0.8	5.9 ± 0.9

2.4 Cortisol Estimation

Venous blood samples were drawn between 0800 and 0900 hours (morning) and again between 1700 and 1800 hours (evening) on the same day. Sera were separated and stored at -20°C until assay. Serum cortisol was estimated by an automated chemiluminescent immunoassay on the Roche Cobas e411 analyser (Roche Diagnostics, Switzerland), with intra- and inter-assay coefficients of variation below 5%. Salivary samples were collected at awakening, 30 minutes post-awakening, and at 2200 hours using Salivettes (Sarstedt, Germany), and salivary cortisol was estimated using a commercial ELISA kit (Salimetrics, USA). The cortisol awakening response (CAR) was computed as the difference between the 30-minute post-awakening sample and the awakening sample, in line with the consensus methodology of Stalder et al. [16].

2.5 Cardiovascular Parameters and Cold Pressor Test

All recordings were obtained between 0900 and 1100 hours after a standardised 10-minute supine rest in a temperature-controlled room (24 ± 1°C). Resting heart rate, systolic and diastolic BP, and mean arterial pressure (MAP) were measured using an Omron HEM-907 automated oscillometric monitor. The cold pressor test was conducted by immersing the participant's non-dominant hand up to the wrist in ice water (4 ± 1°C) for 60 seconds while continuously monitoring BP at 30 -second intervals. The maximum systolic rise during the test and the time taken for BP to return to baseline (recovery time) were noted [11].

2.6 Statistical Analysis

Data were analysed using IBM SPSS Statistics v26.0. Continuous variables were expressed as mean ± SD. One-way ANOVA with Bonferroni post-hoc correction was used for between-group comparisons across the three stress strata. Pearson's correlation coefficient was used to examine the relationship between PSS-10 score, cortisol parameters, and cardiovascular reactivity. A two-tailed p-value of less than 0.05 was considered statistically significant.

3. Results

All 150 enrolled participants completed the study without adverse events. The three groups were demographically comparable, with progressive PSS-10 scores by design. Sleep duration declined incrementally across the strata, suggesting that the strata are physiologically meaningful beyond the questionnaire alone.

Cortisol findings (Table 2) demonstrated a robust positive gradient across the stress strata. Morning serum cortisol increased from 13.4 ± 2.6 µg/dL in the low-stress group to 21.6 ± 3.8 µg/dL in the high-stress group ($p<0.001$). Evening cortisol, salivary cortisol, and the cortisol awakening response showed similar significant escalations. The CAR in particular doubled from 6.4 ± 1.6 nmol/L in low-stress participants to 12.8 ± 2.7 nmol/L in high-stress participants, indicating an exaggerated morning HPA axis surge in chronically stressed young adults.

Table 2. Cortisol Parameters Across Stress Strata

Cortisol Parameter	Low Stress (Mean ± SD)	Moderate Stress (Mean ± SD)	High Stress (Mean ± SD)
Morning serum cortisol (µg/dL)	13.4 ± 2.6	17.2 ± 3.1	21.6 ± 3.8
Evening serum cortisol (µg/dL)	4.8 ± 1.4	7.2 ± 1.7	9.8 ± 2.2
Salivary cortisol (nmol/L)	8.6 ± 2.2	13.8 ± 3.1	19.2 ± 3.6
Cortisol Awakening Response (nmol/L)	6.4 ± 1.6	9.2 ± 2.1	12.8 ± 2.7

Cardiovascular parameters (Table 3) demonstrated a similar dose-response pattern. Resting heart rate, systolic BP, diastolic BP, and MAP rose progressively with stress severity ($p<0.001$ for all comparisons). The maximum systolic BP rise during the cold pressor test was almost twofold higher in the high-stress group (23.6 ± 4.8 mmHg) than in the low-stress group (12.4 ± 3.6 mmHg), and the recovery time was substantially prolonged (162.4 ± 28.6 vs 84.6 ± 18.4 seconds, $p<0.001$).

These findings collectively demonstrate that high stress is associated with augmented basal cardiovascular tone, exaggerated reactivity, and impaired post-stress recovery.

Table 3. Resting and Reactive Cardiovascular Parameters

Cardiovascular Parameter	Low Stress (Mean ± SD)	Moderate Stress (Mean ± SD)	High Stress (Mean ± SD)
Resting Heart Rate (bpm)	72.4 ± 6.4	78.6 ± 7.2	84.8 ± 8.1
Systolic BP (mmHg)	114.6 ± 8.2	121.4 ± 8.7	128.6 ± 9.6
Diastolic BP (mmHg)	74.8 ± 6.4	79.2 ± 6.9	84.4 ± 7.4
Mean Arterial Pressure (mmHg)	88.1 ± 6.6	93.2 ± 7.0	99.1 ± 7.8
Cold Pressor SBP rise (mmHg)	12.4 ± 3.6	17.8 ± 4.1	23.6 ± 4.8
Recovery time after CPT (sec)	84.6 ± 18.4	116.8 ± 22.4	162.4 ± 28.6

Pearson correlation analysis confirmed strong positive associations of PSS-10 score with morning serum cortisol ($r=0.612$, $p<0.001$), salivary cortisol ($r=0.594$, $p<0.001$), and CPT systolic BP response ($r=0.584$, $p<0.001$). Sleep duration correlated negatively with morning cortisol ($r=-0.482$, $p<0.001$), supporting a bidirectional stress-sleep-HPA relationship.

4. Discussion

The principal observation of this study is that perceived chronic stress in young Indian adults is associated with a graded, dose-dependent elevation of cortisol indices and an exaggerated cardiovascular reactivity profile. These findings reinforce the conceptual model of allostatic overload first articulated by McEwen [2] and operationalised through the integrated assessment of HPA axis output and cardiovascular function.

The progressive elevation of morning serum cortisol and the cortisol awakening response across stress strata is consistent with previous reports by Pruessner et al. [17] and Chida and Steptoe [5], both of whom demonstrated that chronic life stress upregulates basal HPA axis tone and enhances the morning cortisol surge. The enhanced CAR in our high-stress group (12.8 nmol/L) is comparable to the values reported in chronically stressed working adults in Western literature [16,18]. The persistence of elevated evening cortisol — typically a marker of impaired diurnal restoration — suggests that even in young, otherwise healthy individuals, chronic stress can begin

to flatten the cortisol slope, a configuration prospectively linked with adverse cardiometabolic outcomes [19,20].

The graded increase in resting blood pressure and resting heart rate observed across stress strata corroborates the findings of Hjortskov et al. [21] and Esler [22], who demonstrated that chronic stress augments sympathetic outflow even in young, normotensive adults. The augmented cold pressor response is particularly noteworthy, given that exaggerated CPT reactivity has been shown to predict the future development of essential hypertension in longitudinal cohort studies [23,24]. The almost doubled systolic rise observed in our high-stress group (23.6 mmHg) lies within the range previously associated with three- to four-fold increased risk of incident hypertension over 15-year follow-up [25].

Several mechanisms may underlie these observations. Sustained cortisol elevation upregulates adrenergic receptor sensitivity and downregulates negative feedback on the hypothalamus, perpetuating sympathetic dominance [7,26]. Chronic glucocorticoid exposure also reduces nitric oxide-mediated vasodilation and increases vascular endothelial reactive oxygen species, contributing to endothelial dysfunction and arterial stiffness [27]. Sleep deprivation, observed in our high-stress group, independently aggravates HPA-axis dysregulation and sympathetic tone, potentially compounding the effects of perceived stress [28].

The findings carry important preventive implications. The Indian young adult population has documented vulnerability to early-onset hypertension, type 2 diabetes mellitus, and coronary artery disease at lower BMI and younger ages than Western counterparts [29,30]. Identifying chronic stress as an early modifiable contributor to these outcomes opens an actionable window for behavioural interventions including mindfulness-based stress reduction, structured physical activity, sleep hygiene, and yoga, which have demonstrated efficacy in lowering cortisol and BP in Indian samples [31].

The strengths of the present study include its sufficient sample size, validated stress instrument, complementary serum and salivary cortisol assessment, integration of resting and reactive cardiovascular measures, and a tightly controlled laboratory environment. Limitations include the cross-sectional design which precludes causal inference, the use of self-report stress measurement, and the absence of inflammatory and metabolic biomarkers. Future longitudinal investigations

integrating heart rate variability, inflammatory cytokines, and metabolic profiling would further refine our understanding of stress-cardiovascular coupling.

5. Conclusion

Chronic perceived stress in young Indian adults is associated with a clear dose-dependent increase in cortisol levels, augmented basal cardiovascular tone, and exaggerated cardiovascular reactivity to a standardised laboratory stressor. These early physiological perturbations represent a pre-clinical phenotype of cardiometabolic risk that is amenable to evidence-based behavioural intervention. Routine inclusion of psychological stress screening within preventive health checks for young Indian adults is therefore warranted.

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