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Original Research Article

Association of Psychological Stress with Cortisol Levels and Early Cardiovascular Dysfunction among Healthcare Professionals: A Cross-Sectional Study

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Abstract:

Background: Healthcare professionals are exposed to persistent occupational stress resulting from high workload, shift duties, emotional demands, critical decision-making, and sleep disruption. Chronic psychological stress activates the hypothalamic-pituitary-adrenal (HPA) axis, leading to increased cortisol secretion and sympathetic overactivity, which may contribute to early cardiovascular dysfunction. Alterations in heart rate variability (HRV), endothelial function, arterial stiffness, and blood pressure may represent early subclinical cardiovascular changes before overt cardiovascular disease becomes apparent. Understanding the relationship between psychological stress, cortisol levels, and early cardiovascular dysfunction among healthcare professionals is important for preventive cardiovascular strategies and occupational health interventions.

Objective: To evaluate the association of psychological stress with serum cortisol levels and early cardiovascular dysfunction among healthcare professionals.

Materials and Methods: This cross-sectional observational study included 200 healthcare professionals aged 24–55 years. Psychological stress was assessed using the Perceived Stress Scale (PSS-10). Morning serum cortisol was measured using chemiluminescent immunoassay (CLIA). Early cardiovascular dysfunction was evaluated by resting blood pressure, heart rate variability (HRV), endothelial function assessed by brachial artery flow-mediated dilation (FMD), and arterial stiffness measured by carotid-femoral pulse wave velocity (PWV). Correlations between PSS score, cortisol levels, HRV parameters, FMD, PWV, and blood pressure were analyzed using Pearson correlation and multivariable regression analyses.

Results: The mean age of participants was 34.8 ± 7.2 years, and the mean PSS score was 21.6 ± 6.4. High perceived stress (PSS ≥20) was observed in 58.5% of participants. Higher PSS scores showed significant positive correlations with serum cortisol ($r = 0.49$, $p < 0.001$), pulse wave velocity ($r = 0.41$, $p < 0.001$), systolic blood pressure ($r = 0.33$, $p < 0.001$), and resting heart rate ($r = 0.29$, $p < 0.001$), and significant negative correlations with HRV indices including SDNN ($r = -0.46$, $p < 0.001$) and RMSSD ($r = -0.42$, $p < 0.001$), as well as endothelial function measured by FMD ($r = -0.44$, $p < 0.001$). After adjustment for age, sex, body mass index, smoking status, physical activity, and sleep duration, PSS score remained an independent predictor of serum cortisol, reduced HRV, impaired endothelial function, and increased arterial stiffness.

Conclusion: Psychological stress was significantly associated with elevated serum cortisol levels and early cardiovascular dysfunction among healthcare professionals. These findings suggest that chronic occupational stress may contribute to HPA axis activation, autonomic imbalance, endothelial dysfunction, and increased arterial stiffness, thereby increasing long-term cardiovascular risk in healthcare workers.

Keywords: psychological stress, cortisol, healthcare professionals, heart rate variability, endothelial dysfunction, arterial stiffness, pulse wave velocity, occupational stress.

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Introduction

Healthcare professionals constitute one of the most psychologically demanding occupational groups in modern society. Physicians, nurses, residents, technicians, and allied health personnel are routinely exposed to high workload, long working hours, night shifts, sleep deprivation, emotional exhaustion, critical clinical decision-making, patient suffering, and occupational uncertainty. [1]

Chronic exposure to these stressors may result in sustained activation of neuroendocrine and autonomic pathways, leading to adverse cardiovascular and metabolic consequences. Increasing evidence suggests that occupational stress among healthcare professionals is associated with hypertension, autonomic dysfunction, endothelial dysfunction, burnout syndrome, depression, and increased cardiovascular morbidity. [2]

Psychological stress is a complex physiological and behavioral response triggered when perceived environmental demands exceed an individual's adaptive capacity. The body responds through activation of two major stress-response systems: the sympathetic-adrenal-medullary (SAM) system and the hypothalamic-pituitary-adrenal (HPA) axis. Acute stress results in transient increases in catecholamines and cortisol, facilitating adaptive cardiovascular and metabolic responses. [3] However, chronic or repeated stress may lead to persistent sympathetic activation, dysregulation of cortisol secretion, endothelial injury, vascular inflammation, arterial stiffness, and autonomic imbalance, all of which contribute to early cardiovascular dysfunction.

Cortisol, the principal glucocorticoid hormone secreted by the adrenal cortex, plays a central role in the physiological response to stress. Activation of the HPA axis leads to hypothalamic secretion of corticotropin-releasing hormone (CRH), stimulation of adrenocorticotropic hormone (ACTH) release from the anterior pituitary, and subsequent cortisol secretion from the adrenal cortex. Although cortisol is essential for maintenance of blood pressure, glucose homeostasis, and immune regulation, chronic elevation of cortisol has been associated with central obesity, insulin resistance, hypertension, endothelial dysfunction, dyslipidemia, impaired nitric oxide bioavailability, vascular remodeling, and increased cardiovascular risk. [4]

One of the earliest manifestations of stress-related cardiovascular impairment is autonomic dysfunction, which can be assessed non-invasively using heart rate variability (HRV). HRV reflects the dynamic interaction between sympathetic and parasympathetic components of the autonomic nervous system. [5]

Reduced HRV, particularly lower SDNN, RMSSD, and high-frequency (HF) power, is considered an early indicator of autonomic imbalance and has been associated with hypertension, coronary artery disease, heart failure, arrhythmias, and increased cardiovascular mortality. [6] Chronic psychological stress has consistently been linked to reduced vagal activity and increased sympathetic predominance, making HRV an important marker of early cardiovascular dysfunction.

Another important mechanism linking stress with cardiovascular disease is endothelial dysfunction. The vascular endothelium regulates vascular tone, thrombosis, inflammation, oxidative balance, and smooth muscle proliferation through release of vasoactive substances such as nitric oxide (NO). [7]Chronic stress-induced sympathetic activation and elevated cortisol may impair endothelial nitric oxide production, increase oxidative stress, and promote vascular inflammation. Flow-mediated dilation (FMD) of the brachial artery is a well-established non-invasive measure of endothelial function and is considered an early marker of subclinical atherosclerosis. [8]

Arterial stiffness represents another early manifestation of cardiovascular dysfunction and reflects structural and functional changes within the arterial wall. Increased arterial stiffness results from endothelial dysfunction, collagen deposition, elastin degradation, vascular smooth muscle remodeling, and chronic inflammation. [9]Carotid-femoral pulse wave velocity (PWV) is regarded as the gold standard measure of arterial stiffness and has been independently associated with future cardiovascular events and mortality. Psychological stress has been shown to increase arterial stiffness through both neuroendocrine and inflammatory mechanisms. [10]

Healthcare professionals are particularly vulnerable to chronic occupational stress because of irregular working schedules, prolonged standing, shift duties, emergency responsibilities, inadequate recovery time, and emotional burden associated with patient care. Burnout syndrome, characterized by emotional exhaustion, depersonalization, and reduced professional accomplishment, has become increasingly prevalent among healthcare workers and has been associated with autonomic dysregulation, elevated cortisol levels, impaired endothelial function, and increased cardiovascular risk.

The Perceived Stress Scale (PSS-10) is a widely validated instrument that measures the degree to which individuals perceive situations in their lives as stressful. Unlike objective workload measures, the PSS captures the subjective experience of stress, making it particularly useful for occupational stress research. [11] Combining psychological stress assessment with measurement of serum cortisol, HRV, endothelial function, and arterial stiffness provides a comprehensive evaluation of the physiological pathways linking stress with early cardiovascular dysfunction.

Although previous studies have independently examined psychological stress, cortisol, HRV, endothelial dysfunction, or arterial stiffness, relatively few investigations have simultaneously evaluated all these parameters among healthcare professionals. [12] Such an integrated approach

may improve understanding of the neuroendocrine and cardiovascular consequences of chronic occupational stress and may help identify healthcare workers at increased cardiovascular risk before the development of overt disease.

Aim of the Study: To evaluate the association between psychological stress, serum cortisol levels, and early cardiovascular dysfunction among healthcare professionals.

Objectives

1. To assess psychological stress using the Perceived Stress Scale (PSS-10).
2. To measure morning serum cortisol levels among healthcare professionals.
3. To evaluate heart rate variability as a marker of autonomic function.
4. To assess endothelial function using brachial artery flow-mediated dilation (FMD).
5. To evaluate arterial stiffness using carotid-femoral pulse wave velocity (PWV).
6. To determine the correlation between psychological stress and serum cortisol.
7. To determine the association between psychological stress and early cardiovascular dysfunction.
8. To evaluate whether psychological stress independently predicts cortisol levels and cardiovascular dysfunction after adjustment for potential confounding variables.

Research Hypothesis: Higher psychological stress is associated with elevated serum cortisol levels and early cardiovascular dysfunction among healthcare professionals.

Materials and Methods

Study Design and Setting: This study was designed as a cross-sectional observational study conducted in a tertiary care teaching hospital. The study period was assumed to extend over 12 months.

Study Population: Healthcare professionals working in the participating institution, including resident doctors, faculty members, nurses, laboratory technicians, physiotherapists, pharmacists, and other allied healthcare staff, were screened for eligibility.

Study Sample: A total of 200 healthcare professionals were included:

- 102 males
- 98 females

Inclusion Criteria

1. Age between 24 and 55 years
2. Healthcare professionals employed for at least 1 year
3. Working in clinical or allied healthcare services
4. Willingness to provide written informed consent
5. Availability for morning blood sampling and cardiovascular assessment

Exclusion Criteria

1. Previously diagnosed cardiovascular disease
2. Diabetes mellitus
3. Hypertension receiving antihypertensive therapy
4. Chronic kidney disease
5. Chronic liver disease
6. Endocrine disorders affecting cortisol secretion (Cushing syndrome, Addison disease, thyroid dysfunction)
7. Pregnancy
8. Current glucocorticoid therapy
9. Psychiatric disorders requiring antidepressant or antipsychotic medication
10. Acute infection, inflammatory disease, or hospitalization within the previous four weeks

Ethical Considerations: The study protocol was approved by the Institutional Ethics Committee of the participating institution. Written informed consent was obtained from all participants before enrollment. Confidentiality of participant information was maintained throughout the study.

Study Procedure: Participants reported to laboratory between 7:00 AM and 9:00 AM after an overnight fast of 8–10 hours and avoidance of caffeine, nicotine, alcohol, vigorous exercise, and night duty for at least 24 hours whenever feasible.

The following assessments were performed in sequence:

1. Demographic and occupational history
2. Anthropometric measurements
3. Blood pressure and resting heart rate
4. Psychological stress assessment
5. Venous blood sampling for serum cortisol
6. Resting electrocardiography
7. Heart rate variability recording
8. Endothelial function assessment
9. Arterial stiffness assessment

Demographic and Occupational Variables

The following variables were recorded:

- Age (years)
- Sex
- Profession (doctor, nurse, technician, faculty, allied health staff)
- Department
- Years of professional experience
- Weekly working hours
- Number of night shifts per month
- Sleep duration (hours)
- Smoking status
- Alcohol consumption
- Physical activity level

Anthropometric Measurements

- Height was measured using a wall-mounted stadiometer to the nearest 0.1 cm.
- Weight was measured using a calibrated digital weighing scale to the nearest 0.1 kg.
- Body mass index was calculated as:

BMI (kg/m²) = Weight (kg) / Height (m²)

- Waist circumference was measured midway between the lower costal margin and the iliac crest at the end of normal expiration.

Blood Pressure Measurement

- Blood pressure was measured using a validated automated sphygmomanometer according to American Heart Association recommendations.
- Participants rested in the sitting position for 10 minutes before measurement.
- Three readings were obtained at 2-minute intervals, and the average of the final two readings was used for analysis.
- The following parameters were recorded:
  - Systolic blood pressure (SBP)
  - Diastolic blood pressure (DBP)
  - Resting heart rate

Assessment of Psychological Stress

- Psychological stress was assessed using the Perceived Stress Scale (PSS-10) developed by Cohen et al.
- The PSS-10 consists of 10 items evaluating perceived stress during the previous month.
- Each item is scored from 0 (never) to 4 (very often).
- Total score range:
  - 0–13: Low stress
  - 14–19: Moderate stress
  - 20–40: High perceived stress

The questionnaire was administered in the participant's preferred language by a trained investigator.

Serum Cortisol Estimation

- Approximately 5 mL of venous blood was collected between 7:00 AM and 9:00 AM to minimize the influence of circadian variation.
- Blood samples were allowed to clot and centrifuged at 3000 rpm for 10 minutes.
- Serum was stored at −20°C until analysis.
- Serum cortisol was measured using chemiluminescent immunoassay (CLIA) on an automated immunoassay analyzer.
- Results were expressed in µg/dL.
- Internal quality control sera and calibration standards were used throughout the analytical procedure.

Resting Electrocardiography

- A standard 12-lead ECG was recorded in the supine position after 15 minutes of quiet rest.
- ECGs were screened for rhythm abnormalities, conduction defects, ischemic changes, and ectopic beats.
- Only participants with sinus rhythm were included in HRV analysis.

Heart Rate Variability Analysis

- Heart rate variability was recorded using a 5-minute resting ECG in the supine position under standardized laboratory conditions.
- The ECG was sampled at 1000 Hz and analyzed using dedicated HRV analysis software.

Time-Domain Parameters

- SDNN (ms): Standard deviation of normal-to-normal intervals
- RMSSD (ms): Root mean square of successive RR interval differences
- pNN50 (%): Percentage of adjacent RR intervals differing by more than 50 ms

Frequency-Domain Parameters

Fast Fourier transform was used to calculate:

- Low-frequency power (LF, 0.04–0.15 Hz)
- High-frequency power (HF, 0.15–0.40 Hz)
- LF/HF ratio

Reduced SDNN, RMSSD, and HF power were considered indicators of reduced parasympathetic activity, whereas an elevated LF/HF ratio was considered indicative of sympathetic predominance.

Assessment of Endothelial Function

- Endothelial function was assessed using brachial artery flow-mediated dilation (FMD) according to international ultrasound guidelines.
- A high-resolution ultrasound system equipped with a 7–12 MHz linear transducer was used.

FMD Procedure

1. Participants rested in the supine position for 15 minutes.
2. Baseline brachial artery diameter was measured above the antecubital fossa.
3. A blood pressure cuff was inflated on the forearm to 50 mmHg above systolic pressure for 5 minutes.
4. After cuff deflation, the maximum post-ischemic brachial artery diameter was recorded.

Flow-mediated dilation was calculated as:

FMD (%) = [(Post-deflation diameter − Baseline diameter) / Baseline diameter] × 100

Lower FMD values indicated endothelial dysfunction.

Assessment of Arterial Stiffness

- Arterial stiffness was assessed using carotid-femoral pulse wave velocity (PWV).
- Pressure-sensitive tonometry sensors were placed over the carotid and femoral arteries.
- Transit time between pulse wave recordings was determined automatically.
- Distance between recording sites was measured using a non-elastic measuring tape.
- Pulse wave velocity was calculated as:

PWV (m/s) = Distance / Transit time

Higher PWV values indicatedincreased arterial stiffness.

Outcome Measures

Primary Outcome: Association between psychological stress (PSS score) and serum cortisol level.

Secondary Outcomes

1. Association between PSS score and HRV parameters.
2. Association between PSS score and endothelial function (FMD).
3. Association between PSS score and arterial stiffness (PWV).
4. Association between serum cortisol and cardiovascular parameters.
5. Identification of independent predictors of early cardiovascular dysfunction.

Statistical Analysis

- Data were analyzed using IBM SPSS Statistics version 26.0.
- Continuous variables were expressed as mean ± standard deviation (SD).
- Categorical variables were expressed as frequency and percentage.
- Normality was assessed using the Shapiro-Wilk test.
- Comparisons among low-, moderate-, and high-stress groups were performed using:

✓ One-way analysis of variance (ANOVA) for normally distributed variables
✓ Kruskal-Wallis test for non-normal variables
✓ Categorical variables were compared using the Chi-square test.

Correlations were analyzed using:

- Pearson correlation coefficient
- Spearman correlation where appropriate

Independent predictors of serum cortisol, HRV, endothelial dysfunction, and arterial stiffness were evaluated using multiple linear regression analysis with adjustment for:

- age,
- sex,
- body mass index,
- smoking status,
- physical activity,
- sleep duration,
- weekly working hours,
- Night-shift frequency.

A p-value < 0.05 was considered statistically significant.

Data Management: All data were entered into a structured Microsoft Excel spreadsheet and cross-verified for accuracy prior to statistical analysis. Missing values and outliers were assessed before analysis, and only complete datasets were included in the final evaluation.

Observations and Results

A total of 200 healthcare professionals aged 24–55 years were included in the study. The study population comprised 102 males (51.0%) and 98 females (49.0%).

All participants completed the psychological stress assessment and underwent serum cortisol estimation, heart rate variability (HRV) analysis, endothelial function testing by flow-mediated dilation (FMD), and arterial stiffness assessment by pulse wave velocity (PWV).

Demographic and Occupational Characteristics: The mean age of the study population was 34.8 ± 7.2 years. Resident doctors and nurses constituted the majority of participants. Individuals with high perceived stress had significantly longer weekly working hours, more frequent night shifts, and shorter sleep duration.

Table 1: Demographic and occupational characteristics of study participants (n = 200)

Variable	Low stress (n = 38)	Moderate stress (n = 45)	High stress (n = 117)	p-value
Age (years)	33.6 ± 6.8	34.1 ± 7.0	35.5 ± 7.4	0.182
Male sex, n (%)	20 (52.6)	22 (48.9)	60 (51.3)	0.936
BMI (kg/m²)	23.4 ± 2.8	24.2 ± 3.1	25.1 ± 3.4	0.011
Weekly working hours	43.6 ± 5.8	50.4 ± 6.7	58.8 ± 8.6	<0.001
Night shifts/month	2.1 ± 1.4	4.6 ± 2.0	7.2 ± 2.7	<0.001
Sleep duration (hours/night)	7.3 ± 0.8	6.6 ± 0.9	5.8 ± 0.9	<0.001

Distribution of Psychological Stress: The mean Perceived Stress Scale (PSS-10) score was 21.6 ± 6.4. High perceived stress (PSS ≥20) was observed in 58.5% of participants.

Table 2: Distribution of perceived stress levels

Stress category	PSS score	Number (n)	Percentage (%)
Low stress	0–13	38	19.0
Moderate stress	14–19	45	22.5
High stress	20–40	117	58.5
Total	—	**200**	**100.0**

Serum Cortisol Levels: Morning serum cortisol concentrations increased significantly across stress categories.

Table 3: Serum cortisol levels according to perceived stress

Stress category	Serum cortisol (µg/dL)	p-value
Low stress	11.8 ± 2.9	
Moderate stress	14.6 ± 3.2	
High stress	18.7 ± 3.8	**<0.001**

Participants with high perceived stress had significantly elevated serum cortisol levels compared with those with low and moderate stress.

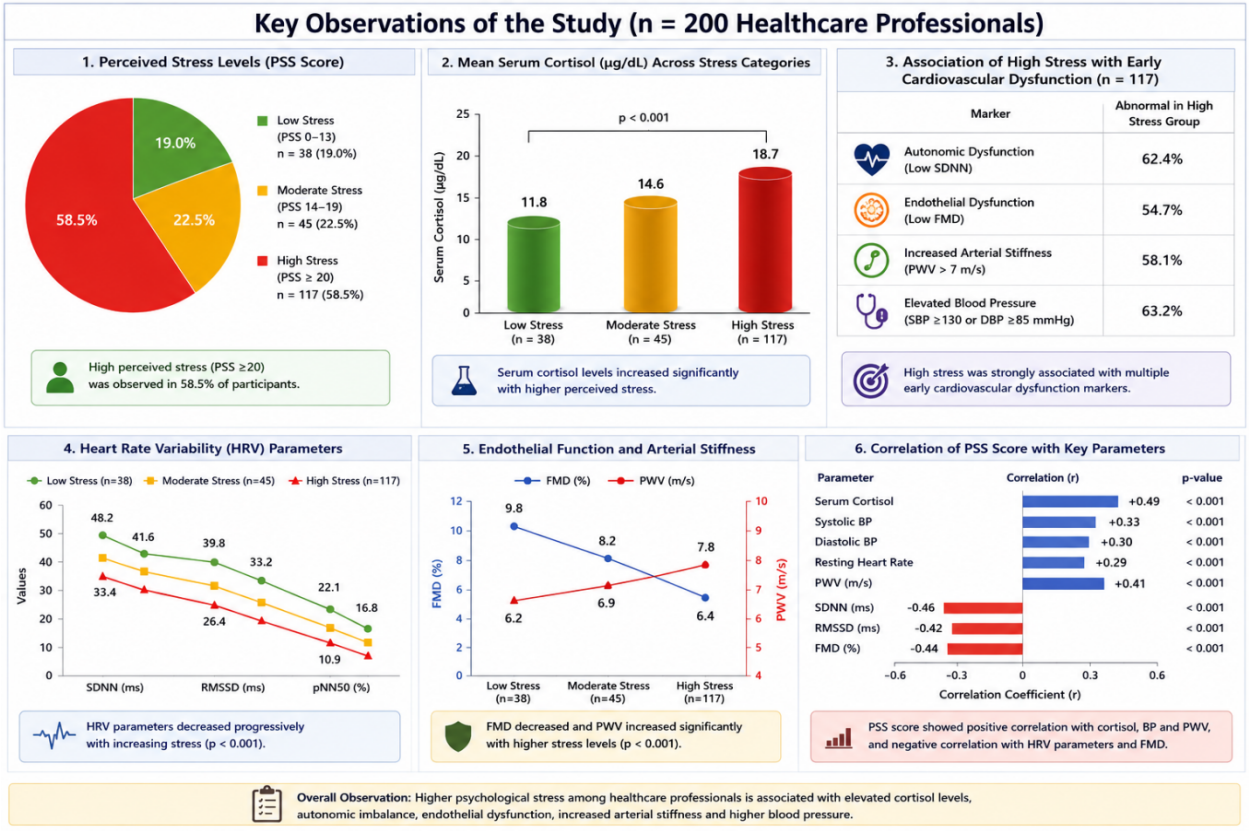

Figure 1: Key observations of the study (n= 200 healthcare professionals

Blood Pressure and Resting Heart Rate: Higher stress levels were associated with higher resting heart rate and blood pressure.

Table 4: Blood pressure and resting heart rate

Parameter	Low stress	Moderate stress	High stress	p-value
Resting heart rate (beats/min)	68.6 ± 7.2	73.4 ± 7.9	79.2 ± 8.8	<0.001
Systolic BP (mmHg)	116.8 ± 8.6	121.9 ± 9.4	127.8 ± 10.8	<0.001
Diastolic BP (mmHg)	72.4 ± 6.8	76.8 ± 7.1	81.2 ± 7.8	<0.001

Heart Rate Variability Analysis: Participants with higher psychological stress demonstrated significantly reduced HRV parameters.

Table 5: Heart rate variability parameters according to stress category

HRV parameter	Low stress	Moderate stress	High stress	p-value
SDNN (ms)	48.2 ± 9.8	41.6 ± 9.2	33.4 ± 8.1	<0.001
RMSSD (ms)	39.8 ± 8.6	33.2 ± 8.1	26.4 ± 7.2	<0.001
pNN50 (%)	22.1 ± 7.6	16.8 ± 6.9	10.9 ± 5.8	<0.001
HF power (ms²)	428 ± 138	352 ± 124	246 ± 102	<0.001
LF/HF ratio	1.22 ± 0.36	1.58 ± 0.44	2.12 ± 0.58	<0.001

These findings indicate reduced parasympathetic activity and increased sympathetic predominance in highly stressed healthcare professionals.

Endothelial Function: Flow-mediated dilation (FMD) progressively decreased with increasing psychological stress.

Table 6: Endothelial function assessed by flow-mediated dilation

Stress category	FMD (%)	p-value
Low stress	9.8 ± 1.8	
Moderate stress	8.2 ± 1.7	
High stress	6.4 ± 1.5	**<0.001**

Participants with high perceived stress exhibited significant endothelial dysfunction compared with those with lower stress levels.

Arterial Stiffness: Pulse wave velocity increased significantly across stress categories.

Table 7: Arterial stiffness assessed by pulse wave velocity

Stress category	PWV (m/s)	p-value
Low stress	6.2 ± 0.8	
Moderate stress	6.9 ± 0.9	
High stress	7.8 ± 1.0	**<0.001**

Higher PWV values indicate increased arterial stiffness among participants with greater psychological stress.

Correlation between Psychological Stress and Serum Cortisol: Pearson correlation analysis demonstrated a significant positive correlation between PSS score and serum cortisol.

Table 8: Correlation between psychological stress and cortisol

Variable	Correlation coefficient (r)	p-value
PSS score vs Serum cortisol	**0.49**	**<0.001**

Higher perceived stress was associated with higher morning serum cortisol concentrations.

Correlation between Psychological Stress and Cardiovascular Parameters

Table 9: Correlation between PSS score and cardiovascular parameters

Variable	Correlation coefficient (r)	p-value
Resting heart rate	**0.29**	**<0.001**
Systolic BP	**0.33**	**<0.001**
Diastolic BP	**0.30**	**<0.001**
SDNN	**−0.46**	**<0.001**
RMSSD	**−0.42**	**<0.001**
HF power	**−0.39**	**<0.001**
LF/HF ratio	**0.36**	**<0.001**
FMD	**−0.44**	**<0.001**
PWV	**0.41**	**<0.001**

Psychological stress was significantly associated with autonomic imbalance, endothelial dysfunction, and increased arterial stiffness.

Correlation between Serum Cortisol and Cardiovascular Dysfunction

Table 10: Correlation between serum cortisol and cardiovascular parameters

Variable	Correlation coefficient (r)	p-value
SDNN	**−0.40**	**<0.001**
RMSSD	**−0.37**	**<0.001**
FMD	**−0.42**	**<0.001**
PWV	**0.39**	**<0.001**
Systolic BP	**0.31**	**<0.001**

Higher cortisol levels were associated with reduced autonomic function, impaired endothelial function, and increased arterial stiffness.

Correlation Matrix of Major Study Variables

Table 11: Pearson correlation matrix

Variable	PSS	Cortisol	SDNN	FMD	PWV
PSS score	1.00	0.49	−0.46	−0.44	0.41
Serum cortisol	0.49	1.00	−0.40	−0.42	0.39
SDNN	−0.46	−0.40	1.00	0.45	−0.36
FMD	−0.44	−0.42	0.45	1.00	−0.48
PWV	0.41	0.39	−0.36	−0.48	1.00

All displayed correlations were statistically significant at $p < 0.01$.

Multiple Linear Regression Analysis for Serum Cortisol: A multiple linear regression model was constructed with **serum cortisol** as the dependent variable.

Table 12: Independent predictors of serum cortisol

Predictor	Standardized β	Standard Error	t-value	p-value
PSS score	**0.38**	0.08	5.24	**<0.001**
Weekly working hours	**0.22**	0.05	3.08	**0.002**
Night shifts/month	**0.18**	0.07	2.56	**0.011**
Sleep duration	**−0.20**	0.09	−2.82	**0.005**
BMI	0.09	0.06	1.34	0.182
Age	0.07	0.04	1.08	0.281

Multiple Linear Regression Analysis for Endothelial Function (FMD)

Table 13. Independent predictors of impaired endothelial function

Predictor	Standardized β	Standard Error	t-value	p-value
PSS score	**−0.31**	0.05	−4.28	**<0.001**
Serum cortisol	**−0.27**	0.04	−3.86	**<0.001**
Age	**−0.18**	0.03	−2.62	**0.010**
BMI	**−0.15**	0.04	−2.21	**0.028**
Sleep duration	**0.16**	0.05	2.34	**0.020**

Multiple Linear Regression Analysis for Arterial Stiffness (PWV)

Table 14. Independent predictors of increased arterial stiffness

Predictor	Standardized β	Standard Error	t-value	p-value
PSS score	**0.29**	0.03	3.98	**<0.001**
Serum cortisol	**0.25**	0.02	3.54	**<0.001**
Age	**0.22**	0.01	3.12	**0.002**
Systolic BP	**0.19**	0.01	2.78	**0.006**
BMI	0.11	0.02	1.64	0.103

Summary of Principal Findings

The present analysis showed that:

1. High psychological stress was present in 58.5% of healthcare professionals.
2. Higher stress was associated with significantly elevated serum cortisol levels.
3. Participants with greater stress exhibited reduced heart rate variability, indicating autonomic imbalance.
4. Psychological stress was associated with impaired endothelial function and increased arterial stiffness.
5. PSS score remained an independent predictor of serum cortisol, endothelial dysfunction, and

arterial stiffness after adjustment for demographic, anthropometric, occupational, and lifestyle variables.

These findings support a significant association between psychological stress, HPA axis activation, and early cardiovascular dysfunction among healthcare professionals, suggesting that chronic occupational stress may contribute to increased long-term cardiovascular risk in this population.

Discussion

The present cross-sectional study evaluated the association between psychological stress, serum cortisol levels, and early cardiovascular dysfunction among healthcare professionals. The principal findings were that high perceived stress was highly prevalent and was significantly associated with elevated morning serum cortisol, reduced heart rate variability, impaired endothelial function, increased arterial stiffness, and higher blood pressure. Furthermore, psychological stress remained an independent predictor of cortisol elevation, endothelial dysfunction, and arterial stiffness after adjustment for age, sex, body mass index, sleep duration, working hours, and night-shift frequency.

These findings support the hypothesis that chronic occupational stress among healthcare professionals may activate the hypothalamic-pituitary-adrenal (HPA) axis and sympathetic nervous system, leading to early cardiovascular dysfunction even in apparently healthy individuals. [13,14,15,16]

Psychological Stress among Healthcare Professionals: In the present study, the mean Perceived Stress Scale (PSS-10) score was 21.6 ± 6.4, and 58.5% of participants were classified as having high perceived stress.

This prevalence is consistent with contemporary studies reporting high rates of psychological stress, burnout, emotional exhaustion, and occupational strain among healthcare workers, particularly among resident doctors, nurses, and emergency care personnel. [17]

Healthcare professionals are exposed to multiple chronic stressors including long working hours, night shifts, sleep deprivation, high patient load, and emotional involvement with patient suffering, medico-legal concerns, and demanding clinical decision-making. [18] Such persistent occupational stress may lead to sustained neuroendocrine activation and inadequate physiological recovery, increasing the risk of cardiovascular and metabolic disorders. [19]The present study also demonstrated that high-stress participants had significantly longer weekly working hours, more frequent night shifts, and shorter sleep duration, suggesting that occupational factors play an important role in stress-related physiological dysregulation. [20]

Psychological Stress and Cortisol Levels: One of the most important findings of the present study was the significant positive correlation between PSS score and morning serum cortisol ($r = 0.49$, $p < 0.001$). [21] Serum cortisol concentrations increased progressively across low-, moderate-, and high-stress categories, indicating increasing activation of the HPA axis with increasing perceived stress.

Cortisol is the principal glucocorticoid hormone released in response to activation of the HPA axis. Psychological stress stimulates hypothalamic secretion of corticotropin-releasing hormone (CRH), leading to pituitary release of adrenocorticotropic hormone (ACTH) and subsequent adrenal cortisol secretion.22 Acute cortisol elevation facilitates adaptive responses including maintenance of blood pressure, mobilization of glucose, and modulation of immune function. However, chronic cortisol elevation may become maladaptive and contribute to hypertension, visceral obesity, insulin resistance, endothelial dysfunction, vascular inflammation, and accelerated atherosclerosis. [23]

The independent association of PSS score with cortisol in multivariable regression analysis suggests that subjective psychological stress contributes to HPA axis activation independently of demographic and lifestyle factors. [24] This observation is consistent with previous occupational stress studies demonstrating elevated cortisol concentrations among physicians, nurses, intensive care staff, and shift workers.

Psychological Stress and Autonomic Dysfunction: The present study showed significant reductions in SDNN, RMSSD, pNN50, and HF power, together with a significant increase in LF/HF ratio, among participants with high perceived stress. [25] Psychological stress showed significant negative correlations with SDNN ($r = -0.46$) and RMSSD ($r = -0.42$), indicating reduced parasympathetic (vagal) activity and increased sympathetic predominance. Heart rate variability is a sensitive non-invasive marker of autonomic nervous system function and reflects the dynamic interaction between sympathetic and parasympathetic influences on the sinoatrial node. [26] Reduced HRV is considered an early manifestation of autonomic imbalance and has been associated with hypertension, coronary artery disease, arrhythmias, heart failure, and increased cardiovascular mortality.

The observed reduction in parasympathetic indices among highly stressed healthcare professionals is physiologically plausible. Chronic psychological stress increases sympathetic nervous system activity, elevates circulating catecholamines, and reduces vagal modulation of cardiac rhythm.

Reduced vagal activity may impair cardiovascular recovery, increase myocardial oxygen demand, promote inflammation, and increase susceptibility to arrhythmias. [27]

These findings suggest that autonomic dysfunction may represent one of the earliest cardiovascular consequences of chronic occupational stress in healthcare professionals.

Psychological Stress and Endothelial Function: Flow-mediated dilation (FMD) progressively decreased across stress categories, and PSS score demonstrated a significant negative correlation with FMD ($r = -0.44$). Participants with high perceived stress had significantly lower FMD values, indicating impaired endothelial function. [28]

The vascular endothelium plays a central role in regulating vascular tone, thrombosis, inflammation, oxidative balance, and smooth muscle proliferation through release of vasoactive substances such as nitric oxide (NO). Chronic psychological stress may impair endothelial function through multiple mechanisms including:

- increased sympathetic activity,
- elevated cortisol levels,
- oxidative stress,
- reduced nitric oxide bioavailability,
- increased endothelin-1 production,
- inflammatory cytokine activation,
- Endothelial cell injury.

Experimental stress studies have showed transient reductions in endothelial-dependent vasodilation following acute mental stress, while chronic stress has been associated with persistent endothelial dysfunction and increased cardiovascular risk. The present findings extend these observations to healthcare professionals exposed to chronic occupational stress.

The regression analysis further demonstrated that both psychological stress and serum cortisol independently predicted impaired FMD, suggesting that endothelial dysfunction may be mediated through both psychological and neuroendocrine pathways. [29]

Psychological Stress and Arterial Stiffness: The present study showed significantly higher pulse wave velocity (PWV) among participants with high perceived stress, and PSS score showed a significant positive correlation with PWV ($r = 0.41$).

Arterial stiffness reflects structural and functional alterations of the arterial wall resulting from collagen deposition, elastin degradation, vascular smooth muscle remodeling, endothelial dysfunction, inflammation, and oxidative stress. Increased PWV is considered one of the earliest indicators of vascular aging and has been independently associated with future cardiovascular events and mortality.

Chronic stress may increase arterial stiffness through several mechanisms:

- sustained sympathetic vasoconstriction,
- elevated cortisol,
- activation of the renin-angiotensin-aldosterone system,
- endothelial dysfunction,
- oxidative stress,
- chronic inflammation,
- Increased vascular smooth muscle tone.

The independent association of both PSS score and serum cortisol with PWV suggests that psychological stress contributes directly to vascular stiffening beyond the effects of age and blood pressure.

Blood Pressure and Resting Heart Rate: Participants with higher stress levels exhibited significantly higher resting heart rate, systolic blood pressure, and diastolic blood pressure.

Although blood pressure values remained within a relatively early range, the progressive increase across stress categories suggests early cardiovascular dysregulation. Chronic activation of the sympathetic nervous system and HPA axis may increase cardiac output, peripheral vascular resistance, sodium retention, and vascular tone, thereby promoting prehypertension and early hypertension. Elevated resting heart rate is itself a marker of sympathetic activation and has been associated with increased cardiovascular morbidity and mortality.

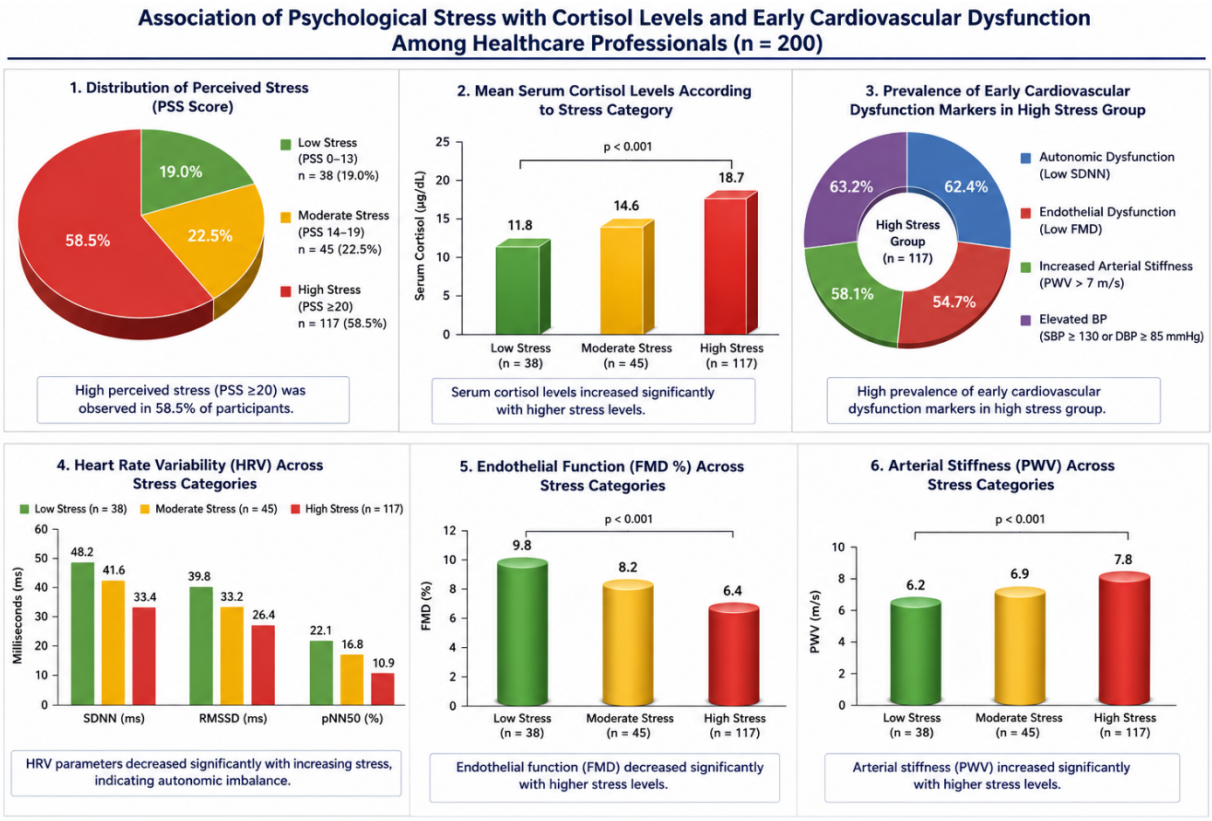

Figure 2: Association of psychological stress with cortisol levels and early cardiovascular dysfunction among healthcare professionals (n=200)

Relationship between Cortisol and Cardiovascular Dysfunction: Serum cortisol showed significant correlations with reduced HRV, impaired FMD, increased PWV, and higher systolic blood pressure, indicating that HPA axis activation is closely linked to cardiovascular dysfunction.

Cortisol may contribute to cardiovascular injury through multiple pathways:

- enhancement of sympathetic responsiveness,
- impairment of nitric oxide synthesis,
- increased oxidative stress,
- vascular inflammation,
- insulin resistance,
- central adiposity,
- endothelial dysfunction,
- Arterial remodeling.

These mechanisms provide a plausible biological explanation for the observed association between elevated cortisol and early cardiovascular dysfunction among healthcare professionals.

Comparison with Previous Studies: The present findings are consistent with numerous studies demonstrating associations between psychological stress, cortisol, autonomic dysfunction, endothelial dysfunction, and cardiovascular risk. Research involving physicians, nurses, and emergency healthcare workers has consistently reported elevated stress levels and reduced HRV, particularly among individuals with long working hours and shift duties. Studies of occupational stress have also demonstrated higher cortisol concentrations and impaired autonomic function in healthcare workers compared with less stressful occupational groups.

Experimental investigations have shown that both acute and chronic psychological stress can impair endothelial-dependent vasodilation and increase arterial stiffness, supporting the physiological mechanisms observed in the present study.

Occupational Health Implications: The findings of the present study have important implications for occupational health and preventive cardiology. Healthcare professionals represent a critical workforce exposed to chronic psychological stress, and early cardiovascular dysfunction may develop long before clinically apparent cardiovascular disease becomes evident.

Routine assessment of:

- psychological stress (PSS),
- serum cortisol,
- heart rate variability,
- blood pressure,
- endothelial function, and
- arterial stiffness

May help identify healthcare workers at increased cardiovascular risk.

Interventions such as:

- stress management programs,
- mindfulness-based therapy,
- cognitive behavioral interventions,
- adequate sleep,
- optimized shift scheduling,
- regular physical activity,
- relaxation training,
- yoga,
- meditation,
- and organizational support strategies

May reduce HPA axis activation, improve autonomic function, and preserve vascular health.

Conclusion

The present cross-sectional study showed that psychological stress was highly prevalent among healthcare professionals and was significantly associated with elevated serum cortisol levels and early cardiovascular dysfunction. Participants with higher perceived stress exhibited significantly increased morning serum cortisol concentrations, reduced heart rate variability, impaired endothelial function, increased arterial stiffness, and higher resting blood pressure compared with those with lower stress levels.Importantly, psychological stress remained an independent predictor of serum cortisol, endothelial dysfunction, and arterial stiffness even after adjustment for age, sex, body mass index, sleep duration, working hours, and night-shift frequency. These findings suggest that chronic occupational stress may contribute to persistent HPA axis activation, sympathetic predominance, autonomic imbalance, endothelial injury, and early vascular remodeling, thereby increasing long-term cardiovascular risk among healthcare professionals. The study supports the concept that subclinical cardiovascular alterations can occur in apparently healthy healthcare workers before the development of overt cardiovascular disease. Early identification of psychological stress and associated neuroendocrine and cardiovascular changes may provide an opportunity for timely intervention and prevention of future cardiovascular morbidity.

Limitations

- Cross-sectional design prevents establishment of causality.
- Morning serum cortisol was measured at a single time point, and diurnal cortisol variation was not evaluated.
- Sleep quality was assessed by self-report rather than polysomnography.
- Additional biomarkers such as catecholamines, inflammatory cytokines, oxidative stress markers, and endothelial biomarkers were not measured.
- The study was conducted at a single tertiary care institution, which may limit generalizability to other healthcare settings.

Recommendations for Future Research

1. Prospective longitudinal studies evaluating whether psychological stress predicts future hypertension, coronary artery disease, and cardiovascular events among healthcare professionals.
2. Studies incorporating salivary cortisol profiles, continuous heart rate variability monitoring, ambulatory blood pressure monitoring, inflammatory biomarkers, and oxidative stress markers.
3. Interventional trials assessing the effects of mindfulness, meditation, yoga, exercise training, sleep optimization, and organizational interventions on cortisol levels and cardiovascular function.
4. Multicenter studies involving larger and more diverse populations of healthcare professionals across different specialties and work environments.

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