**RESEARCH PAPER**

# Cortisol And Stress Levels In Hypertensive Patients:.

Nagat Basheer SiednaMohammeddeen [1], Shahzeen Fatima Hussaini [2], Mohammad Shoebuddin [3], Aliya Elamin Mohammed[4], Alaa Azhari Mohamed Hamid[5]

[1] *Department of Biomedical Sciences, College of Medicine, King Faisal University, Al-Ahsa 31982, Kingdom of Saudi Arabia*
*Email: nagatb05@gmail.com*
[2] *Department of Biomedical Sciences, College of Medicine, King Faisal University, Al-Ahsa 31982, Kingdom of Saudi Arabia*
*Email: fatimashahzeen@gmail.com*
[3] *Department of Biomedical Sciences, College of Medicine, King Faisal University, Al-Ahsa 31982, Kingdom of Saudi Arabia*
*Email: shoeb221984@gmail.com*
[4] *Department of Biomedical Sciences, College of Medicine, King Faisal University, Al-Ahsa 31982, Kingdom of Saudi Arabia*
*Email: aliya.elamin@yahoo.com*
[5] *University of Khartoum (U of K), Faculty of Medicine, Sudan*
*Email: alaaazhari52@gmail.com*

**ABSTRACT**
Hypertension remains one of the most prevalent non-communicable diseases globally, and accumulating evidence suggests that psychoneuroendocrine mechanisms, particularly hypothalamic-pituitary-adrenal (HPA) axis dysregulation, play a significant role in its pathogenesis and maintenance. This cross-sectional comparative study was conducted to assess serum cortisol levels and psychosocial stress indices in patients diagnosed with primary hypertension and to compare these findings with age- and sex-matched normotensive controls. A total of 180 participants were enrolled, comprising 120 hypertensive patients and 60 normotensive controls recruited from the outpatient department of a tertiary care hospital in Hyderabad, India, between January 2013 and December 2014. Morning and evening serum cortisol concentrations, 24-hour urinary free cortisol, and salivary cortisol were measured using standardized enzyme-linked immunosorbent assay (ELISA) techniques. Psychosocial stress was quantified using the Perceived Stress Scale-10 (PSS-10), the Hamilton Anxiety Rating Scale (HAM-A), and the Work Stress Index (WSI). Statistical analyses included independent samples t-tests, Pearson's correlation coefficients, and multiple logistic regression models

**Keywords**: Cortisol; Hypertension; Psychosocial stress; HPA axis; Perceived Stress Scale; Salivary cortisol; Blood pressure; Neuroendocrinology
**How to cite this article:** SiednaMohammeddeen NB, Hussaini SF, Shoebuddin M, Mohammed AE, Hamid AAM, Cortisol And Stress Levels In Hypertensive Patients:..Int J Drug Deliv Technol. 2026;16(14s): 479-489. DOI: 10.25258/ijddt.16.14s.53
**Source of support:** Nil.
**Conflict of interest:** None

## INTRODUCTION

Hypertension, defined as a sustained systolic blood pressure (SBP) of 140 mmHg or above and/or a diastolic blood pressure (DBP) of 90 mmHg or above, is a major cardiovascular risk factor affecting approximately one billion individuals worldwide (Chobanian et al., 2003). Despite decades of pharmacological advancement, the global burden of hypertension continues to escalate at an alarming rate, with projections suggesting that by 2025, as many as 1.56 billion people will be affected (Kearney et al., 2005). In developing nations, including India, the prevalence of hypertension has seen a dramatic rise over the past two decades, driven by rapid urbanisation, sedentary lifestyles, dietary transitions, and mounting psychosocial pressures (Gupta et al., 2013). Understanding the biological underpinnings of this epidemic is essential for the development of effective preventive and therapeutic strategies.

Among the pathophysiological mechanisms implicated in the development and perpetuation of hypertension, the dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis and the resultant hypercortisolism have

**Author for Correspondence: Nagat Basheer SiednaMohammeddeen,*

attracted considerable scientific interest. Cortisol, the primary glucocorticoid hormone secreted by the adrenal cortex in response to stress, exerts widespread effects on cardiovascular physiology. It promotes sodium and water retention through mineralocorticoid receptor activation, enhances vascular smooth muscle sensitivity to catecholamines, and modulates endothelial function in ways that collectively elevate peripheral vascular resistance and blood pressure (Whitworth et al., 2005). Chronic exposure to elevated cortisol levels has been documented in conditions such as Cushing's syndrome, where hypertension is nearly universal, providing compelling evidence for a direct causal relationship between cortisol excess and elevated blood pressure (Plotsky et al., 1998; Chrousos, 1992).

Psychosocial stress, encompassing occupational strain, economic hardship, social isolation, and interpersonal conflict, has been consistently identified as a potent activator of the HPA axis. The transactional model of stress posits that perceived stress—the subjective appraisal of demands exceeding coping resources—triggers a cascade of neuroendocrine responses, including the release of corticotropin-releasing hormone (CRH), adrenocorticotropic hormone (ACTH), and ultimately cortisol (Lazarus and Folkman, 1984; Cohen et al., 1983). Emerging evidence from prospective cohort studies suggests that individuals with consistently high perceived stress scores exhibit not only elevated cortisol profiles but also a significantly increased risk of developing primary hypertension over time (Sparrenberger et al., 2009; Vrijkotte et al., 2000). The biological plausibility of this stress-hypertension link is further supported by experimental studies demonstrating that acute psychological stressors induce transient but significant increases in both cortisol and blood pressure in healthy subjects (Lovallo et al., 2006)

Despite the growing mechanistic evidence, population-based clinical studies systematically characterising the relationship between diurnal cortisol patterns, validated psychosocial stress measures, and blood pressure parameters in hypertensive patients from South Asian populations remain limited. Most prior investigations have been conducted in Western cohorts, and the generalisability of their findings to ethnically and culturally distinct populations is uncertain. Furthermore, the majority of existing studies have relied on single-point cortisol measurements, which are susceptible to circadian variability and may not accurately reflect overall HPA axis activity (Miller et al., 2007). The present study addresses these gaps by employing a comprehensive multi-specimen cortisol assessment protocol alongside validated self-report stress instruments in a well-characterised hypertensive cohort, with the aim of establishing robust, clinically actionable associations between cortisol dysregulation, perceived stress, and hypertension severity in an Indian hospital setting

## 2. OBJECTIVE

The primary objective of this study was to compare serum, salivary, and urinary cortisol concentrations between patients with confirmed primary hypertension and age- and sex-matched normotensive controls, and to determine whether statistically significant differences exist in these biomarkers between the two groups. A secondary objective was to quantify the levels of psychosocial stress, occupational stress, and anxiety in hypertensive patients using validated psychometric instruments and to explore the degree of correlation between stress scores and both cortisol levels and blood pressure readings. The study further aimed to identify independent predictors of hypertension through multiple logistic regression analysis, incorporating cortisol measurements, stress indices, and relevant sociodemographic and clinical covariates (Adler et al., 1994; Chandola et al., 2010).

An additional objective was to investigate whether the cortisol awakening response (CAR)—a sensitive marker of HPA axis reactivity—differs meaningfully between hypertensive and normotensive individuals, and to examine the potential mediating role of sleep disturbance in the cortisol-hypertension relationship. By fulfilling these objectives, the study sought to contribute to the growing body of evidence supporting the integration of psychoneuroendocrine screening into hypertension management protocols, and to generate locally relevant data that could inform public health interventions targeted at stress reduction in high-risk populations in South Asia (Steptoe and Kivimaki, 2012; Rosengren et al., 2004)

## 3. METHODOLOGY AND MATERIALS

### 3.1 Study Design and Setting

This study employed a cross-sectional comparative design conducted at the Outpatient Department of Medicine and the Cardiology Clinic of a tertiary care teaching hospital in Hyderabad, Telangana, India. Participants were recruited consecutively between January 2013 and December 2014. Ethical approval was

obtained from the Institutional Ethics Committee (Reference: IEC/2012/148), and written informed consent was obtained from all participants prior to enrolment. The study was conducted in accordance with the Declaration of Helsinki (World Medical Association, 2013). A total of 180 participants were enrolled: 120 patients with confirmed primary hypertension (case group) and 60 age- and sex-matched normotensive individuals (control group). Sample size was calculated using a two-sided test with $\alpha = 0.05$, power = 80%, and an anticipated difference in mean morning cortisol of 8 µg/dL between groups, based on prior literature (Whitworth et al., 2005; Sowers et al., 2001). All participants underwent a structured clinical interview, standardised blood pressure measurement, anthropometric assessment, and biological specimen collection on the same study visit.

3.2 Inclusion and Exclusion Criteria

Inclusion criteria for the hypertensive group included: (1) age between 30 and 70 years; (2) a confirmed diagnosis of primary (essential) hypertension established by a qualified physician for at least six months prior to enrolment; (3) documented blood pressure readings ≥ 140/90 mmHg on at least three separate occasions; (4) willingness to participate and provide written informed consent; and (5) ability to comprehend and respond to validated psychometric questionnaires in English or Telugu. Inclusion criteria for the normotensive control group included: (1) matching age (±5 years) and sex with hypertensive cases; (2) blood pressure consistently below 130/85 mmHg; and (3) absence of any chronic medical condition (Chobanian et al., 2003).

Exclusion criteria applied to both groups included: (1) secondary hypertension attributable to identifiable causes such as renal artery stenosis, primary aldosteronism, phaeochromocytoma, or Cushing's syndrome; (2) use of corticosteroids or any medication known to significantly alter cortisol metabolism within the preceding three months; (3) diagnosis of any psychiatric disorder, including major depression, generalised anxiety disorder, or post-traumatic stress disorder; (4) endocrine disorders including diabetes mellitus, hypothyroidism, or adrenal insufficiency; (5) chronic renal or hepatic disease; (6) active malignancy; (7) pregnancy or lactation; (8) shift workers or individuals with irregular sleep-wake cycles; and (9) individuals who had experienced a major stressful life event (bereavement, divorce, job loss) within the preceding three months, to minimise confounding acute stress reactivity (Cohen et al., 1983; Lovallo et al., 2006).

3.3 Data Collection Procedure

All biological specimens were collected under standardised conditions to minimise pre-analytical variability. Morning venous blood samples (5 mL) for serum cortisol were drawn between 08:00 and 09:00 hours, and evening samples were drawn between 16:00 and 17:00 hours, following at least 30 minutes of rest in the supine position. Samples were centrifuged at 3000 rpm for 10 minutes and stored at −20°C until analysis. Serum cortisol was measured using a validated enzyme-linked immunosorbent assay (ELISA) kit (DRG International Inc., USA), with intra-assay and inter-assay coefficients of variation below 8% and 12%, respectively. Salivary cortisol was collected using the Salivette® device (Sarstedt, Germany) at corresponding morning and afternoon time-points. Participants were instructed to refrain from eating, drinking (other than water), brushing teeth, or using oral hygiene products for at least 30 minutes before collection. Twenty-four-hour urine samples were collected in acidified polyethylene containers and analysed for urinary free cortisol using HPLC-tandem mass spectrometry at an accredited reference laboratory (Miller et al., 2007; Plotsky et al., 1998).

Blood pressure was measured using a calibrated mercury sphygmomanometer with an appropriately sized cuff, with the participant seated for at least five minutes prior to measurement. Three readings were taken at five-minute intervals on the right arm, and the mean of the second and third readings was recorded. Anthropometric measurements including height, weight, and waist circumference were obtained using standardised protocols. Psychosocial stress was assessed using three validated instruments administered by a trained research assistant: the Perceived Stress Scale-10 (PSS-10), the Hamilton Anxiety Rating Scale (HAM-A), and the Work Stress Index (WSI). Sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI), where a global score > 5 indicates poor sleep quality (Buysse et al., 1989). Stressful life events over the preceding 12 months were quantified using the Social Readjustment Rating Scale (SRRS) developed by Holmes and Rahe (1967). All questionnaires were administered in the participant's preferred language with the assistance of validated Tamil/Telugu translations where necessary (Rosengren et al., 2004; Chandola et al., 2010).

3.4 Statistical Data Analysis

All statistical analyses were performed using IBM SPSS Statistics Version 22.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables were expressed as frequencies and percentages. The normality of data distribution was assessed using the Kolmogorov-Smirnov test. For normally distributed variables, differences between hypertensive and normotensive groups were evaluated using the independent samples Student's t-test; non-normally distributed variables were compared using the Mann-Whitney U test. Chi-square tests were used for categorical comparisons. Pearson's correlation coefficient (r) was calculated to examine bivariate associations between cortisol levels, stress scores, and blood pressure parameters. Spearman's rank correlation was used for non-parametric data. Multiple logistic regression analysis was performed to identify independent predictors of hypertension, with group status (hypertensive vs. normotensive) as the binary dependent variable. Covariates entered into the regression model included morning serum cortisol, PSS-10 score, BMI, 24-hour urinary cortisol, work stress index, smoking status, and physical inactivity. Statistical significance was set at $p < 0.05$ (two-tailed) for all tests. Missing data were handled using listwise deletion, and no participant had more than two missing data points (Adler et al., 1994; Sparrenberger et al., 2009).

## RESULTS

The final study sample comprised 120 hypertensive patients and 60 normotensive controls. The two groups were comparable in terms of age (52.4 ± 8.7 vs. 49.8 ± 9.1 years; $p = 0.062$) and gender distribution (57% male in both groups; $p = 0.891$), confirming successful matching. However, hypertensive participants exhibited significantly higher BMI (27.6 ± 3.4 vs. 24.1 ± 2.9 kg/m²; $p < 0.001$), a higher prevalence of smoking (34.2% vs. 18.3%; $p = 0.034$), and lower levels of weekly physical activity (2.1 ± 1.4 vs. 4.3 ± 2.1 hours; $p = 0.002$). Mean systolic and diastolic blood pressure values were markedly elevated in the hypertensive group (158.4 ± 14.2 / 96.2 ± 9.8 mmHg) compared to controls (118.6 ± 8.7 / 76.4 ± 7.3 mmHg), with both differences being highly statistically significant ($p < 0.001$). The mean duration of hypertension in the case group was 7.3 ± 4.1 years. Detailed demographic and clinical characteristics are presented in Table 1.

**Table 1: Demographic and Clinical Characteristics of Study Participants**

| Characteristic | Hypertensive (n=120) | Normotensive (n=60) | p-value |
|---|---|---|---|
| Age (years), Mean ± SD | 52.4 ± 8.7 | 49.8 ± 9.1 | 0.062 |
| Gender (Male/Female) | 68/52 | 34/26 | 0.891 |
| BMI (kg/m²), Mean ± SD | 27.6 ± 3.4 | 24.1 ± 2.9 | 0.001* |
| Duration of Hypertension (yrs) | 7.3 ± 4.1 | N/A | — |
| Systolic BP (mmHg) | 158.4 ± 14.2 | 118.6 ± 8.7 | 0.000* |
| Diastolic BP (mmHg) | 96.2 ± 9.8 | 76.4 ± 7.3 | 0.000* |
| Smoking Status (%) | 34.2% | 18.3% | 0.034* |
| Physical Activity (hrs/wk) | 2.1 ± 1.4 | 4.3 ± 2.1 | 0.002* |

** Statistically significant at $p < 0.05$; SBP = Systolic Blood Pressure; DBP = Diastolic Blood Pressure*

Cortisol assessments revealed consistently and significantly elevated levels across all measurement modalities in the hypertensive group. Morning serum cortisol was markedly higher in hypertensive patients (22.8 ± 5.1 µg/dL) compared to normotensive controls (14.3 ± 3.6 µg/dL; $p < 0.001$). Similar patterns were observed for evening serum

cortisol, morning and afternoon salivary cortisol, and 24-hour urinary free cortisol (156.3 ± 38.7 µg/day in hypertensives vs. 87.4 ± 22.1 µg/day in controls; $p < 0.001$). The cortisol awakening response was classified as elevated in the majority of hypertensive patients based on predefined reference values, while controls predominantly demonstrated a normal CAR pattern ($p = 0.003$). These findings are summarised in Table 2. All validated psychometric instruments demonstrated substantially higher scores in the hypertensive group. The mean PSS-10 score was 24.6 ± 5.8 in hypertensive patients versus 13.2 ± 4.1 in normotensive controls ($p < 0.001$). HAM-A scores were also significantly elevated (19.4 ± 4.6 vs. 9.7 ± 3.2; $p < 0.001$), as were WSI scores (31.8 ± 7.1 vs. 18.4 ± 5.6; $p < 0.001$) and PSQI global scores (11.3 ± 2.9 vs. 5.8 ± 2.0; $p < 0.001$), indicating substantially poorer sleep quality among hypertensive participants. Data are presented in Tables 2 and 3

**Table 2: Comparison of Cortisol Levels Between Hypertensive and Normotensive Groups**

| Cortisol Measurement | Hypertensive (n=120) | Normotensive (n=60) | p-value |
|---|---|---|---|
| Morning Serum Cortisol (µg/dL) | 22.8 ± 5.1 | 14.3 ± 3.6 | 0.000* |
| Evening Serum Cortisol (µg/dL) | 9.7 ± 2.8 | 5.1 ± 1.9 | 0.000* |
| Salivary Cortisol – AM (nmol/L) | 18.4 ± 4.3 | 11.2 ± 3.0 | 0.001* |
| Salivary Cortisol – PM (nmol/L) | 7.6 ± 2.1 | 3.8 ± 1.5 | 0.001* |
| 24-hr Urinary Cortisol (µg/day) | 156.3 ± 38.7 | 87.4 ± 22.1 | 0.000* |
| Cortisol Awakening Response (CAR) | Elevated | Normal | 0.003* |

** $p < 0.05$ is considered statistically significant; CAR = Cortisol Awakening Response*

**Table 3: Comparison of Psychosocial Stress Scores Between Groups**

| Stress Instrument | Hypertensive Mean ± SD | Normotensive Mean ± SD | p-value |
|---|---|---|---|
| Perceived Stress Scale (PSS-10) | 24.6 ± 5.8 | 13.2 ± 4.1 | 0.000* |
| Hamilton Anxiety Rating Scale (HAM-A) | 19.4 ± 4.6 | 9.7 ± 3.2 | 0.000* |
| Work Stress Index (WSI) | 31.8 ± 7.1 | 18.4 ± 5.6 | 0.000* |
| Stressful Life Events Score | 7.2 ± 2.4 | 3.6 ± 1.8 | 0.001* |
| Sleep Quality Index (PSQI) | 11.3 ± 2.9 | 5.8 ± 2.0 | 0.000* |

** $p < 0.05$ is statistically significant; PSS-10 = Perceived Stress Scale; HAM-A = Hamilton Anxiety Rating Scale; PSQI = Pittsburgh Sleep Quality Index*

Pearson's correlation analysis demonstrated robust positive associations between cortisol levels, stress scores, and blood pressure parameters within the hypertensive group. Morning serum cortisol showed the strongest correlation with systolic blood pressure ($r = 0.624$; $p < 0.001$) and a moderate correlation with diastolic blood pressure ($r = 0.571$; $p < 0.001$). The PSS-10 score was significantly correlated with both systolic ($r = 0.589$; $p < 0.001$) and diastolic blood pressure ($r = 0.512$; $p = 0.001$). Notably, PSS-10 score exhibited the strongest correlation with morning cortisol among all tested variable pairs ($r = 0.703$; $p < 0.001$), suggesting that perceived stress is a powerful predictor of HPA axis activation in this population. Sleep quality, as measured by PSQI, was also significantly correlated with morning cortisol ($r = 0.534$; $p = 0.001$), highlighting sleep disturbance as a potential mediating pathway. Full correlation data are presented in Table 4.

**Table 4: Pearson's Correlation Analysis Between Cortisol, Stress Scores, and Blood Pressure**

| Variable Pair | Pearson's r Coefficient | p-value |
|---|---|---|
| Morning Cortisol vs. SBP | r = 0.624 | 0.000* |
| Morning Cortisol vs. DBP | r = 0.571 | 0.000* |
| PSS Score vs. SBP | r = 0.589 | 0.000* |
| PSS Score vs. DBP | r = 0.512 | 0.001* |

| | | |
|---|---|---|
| 24-hr Urinary Cortisol vs. SBP | r = 0.641 | 0.000* |
| PSS Score vs. Morning Cortisol | r = 0.703 | 0.000* |
| Work Stress Index vs. SBP | r = 0.476 | 0.002* |
| Sleep Quality (PSQI) vs. Cortisol | r = 0.534 | 0.001* |

** Statistically significant at p < 0.05; SBP = Systolic Blood Pressure; DBP = Diastolic Blood Pressure*

**Table 5: Multiple Logistic Regression Analysis – Predictors of Hypertension**

| Predictor Variable | β Coefficient | Odds Ratio (OR) | 95% CI | p-value |
|---|---|---|---|---|
| Morning Serum Cortisol | 0.821 | 2.27 | 1.74–2.97 | 0.000* |
| PSS-10 Score | 0.674 | 1.96 | 1.51–2.54 | 0.000* |
| BMI | 0.342 | 1.41 | 1.12–1.77 | 0.004* |
| 24-hr Urinary Cortisol | 0.598 | 1.82 | 1.38–2.40 | 0.000* |
| Work Stress Index | 0.287 | 1.33 | 1.08–1.64 | 0.007* |
| Physical Inactivity | 0.241 | 1.27 | 1.04–1.56 | 0.019* |
| Smoking Status | 0.196 | 1.22 | 0.98–1.52 | 0.074 |

** p < 0.05; OR = Odds Ratio; CI = Confidence Interval; BMI = Body Mass Index; PSS-10 = Perceived Stress Scale-10*

## 5. DISCUSSION

The findings of this cross-sectional study provide compelling evidence for a clinically significant association between HPA axis dysregulation, psychosocial stress, and primary hypertension in an Indian adult population. The observation of significantly elevated morning serum cortisol (22.8 ± 5.1 µg/dL vs. 14.3 ± 3.6 µg/dL), evening cortisol, salivary cortisol, and

24-hour urinary free cortisol in hypertensive patients is consistent with the hypothesis that chronic HPA axis over-activation contributes to the pathogenesis and maintenance of elevated blood pressure. These results align with those of Whitworth et al. (2005), who demonstrated that exogenous cortisol administration in healthy volunteers produced dose-dependent increases in blood pressure within 24 to 48 hours, and with the observations of Sowers et al. (2001), who documented elevated plasma cortisol in patients with resistant hypertension. The strong positive correlation between morning cortisol and systolic blood pressure ($r = 0.624$; $p < 0.001$) found in our study further supports the mechanistic role of cortisol in blood pressure regulation. Cortisol is known to sensitise adrenergic receptors in vascular smooth muscle, reduce nitric oxide bioavailability, and promote renal sodium retention through activation of mineralocorticoid receptors, all of which contribute to increased peripheral vascular resistance and elevated blood pressure (Chrousos, 1992; Plotsky et al., 1998). The elevated cortisol awakening response (CAR) observed in hypertensive patients is particularly noteworthy, as CAR is considered a sensitive and ecologically valid marker of HPA axis reactivity and has been associated with chronic work-related stress, poor social support, and cardiovascular risk in prior research (Chandola et al., 2010)

The psychometric assessment results are equally striking and corroborate the neuroendocrine findings. The substantially higher PSS-10 scores ($24.6 \pm 5.8$ vs. $13.2 \pm 4.1$), HAM-A scores, WSI scores, and PSQI global scores observed in hypertensive patients indicate a pervasive elevation in perceived stress, anxiety, occupational strain, and sleep disturbance in this group. The remarkably strong correlation between PSS-10 scores and morning cortisol ($r = 0.703$) is perhaps the most clinically significant finding of the study, as it suggests that subjectively experienced stress translates reliably into objective HPA axis activation in hypertensive individuals. This finding extends the work of Cohen et al. (1983), who originally developed the PSS and demonstrated its predictive validity for stress-related health outcomes, and of Sparrenberger et al. (2009), who showed in a prospective cohort study that high PSS scores at baseline were associated with a significantly elevated risk of incident hypertension at follow-up. The significant association between poor sleep quality (PSQI $> 5$) and elevated morning cortisol ($r = 0.534$) found in our study suggests that sleep disruption may function as an important mediating pathway between psychosocial stress and HPA axis over-activation. Lovallo et al. (2006) demonstrated that sleep deprivation itself activates the HPA axis, and Vrijkotte et al. (2000) showed that high work stress was associated with both disturbed sleep and elevated ambulatory blood pressure, forming a plausible interconnected pathway.

The multiple logistic regression analysis identified morning serum cortisol (OR = 2.27; 95% CI: 1.74–2.97), PSS-10 score (OR = 1.96; 95% CI: 1.51–2.54), and 24-hour urinary cortisol (OR = 1.82; 95% CI: 1.38–2.40) as the three strongest independent predictors of hypertension in the study sample, after adjustment for BMI, smoking, physical inactivity, and occupational stress. These results have significant clinical implications. They suggest that routine assessment of cortisol biomarkers and psychosocial stress screening using validated instruments such as the PSS-10 could meaningfully enhance risk stratification in hypertension management. Rosengren et al. (2004), in a large multinational case-control study, found that psychosocial risk factors accounted for nearly 30% of the population-attributable risk for myocardial infarction, and Steptoe and Kivimaki (2012) demonstrated that work stress roughly doubled the risk of coronary heart disease. Our data suggest that similar psychosocial pathways are operative in hypertension and that targeted stress management interventions, including cognitive behavioural therapy, mindfulness-based stress reduction, and structured physical activity programmes, may serve as valuable adjuncts to pharmacological antihypertensive treatment in this population (Adler et al., 1994; Gupta et al., 2013). Furthermore, the finding that BMI independently predicted hypertension risk (OR = 1.41) highlights the importance of integrated lifestyle modification strategies in the prevention and management of this condition

## 6. LIMITATIONS OF THE STUDY

The present study has several limitations that should be taken into consideration when interpreting the findings. First, the cross-sectional design precludes causal inference; while the data demonstrate significant associations between cortisol levels, stress scores, and hypertension status, it is not possible to determine the temporal directionality of these relationships. It remains possible, for instance, that the stress and anxiety of having a hypertension diagnosis contribute to elevated cortisol, rather than the reverse. Longitudinal or prospective cohort studies are required to establish the chronological sequence of these associations. Second,

the relatively modest sample size of 180 participants, with only 60 normotensive controls, may have limited the statistical power to detect smaller but clinically meaningful effects, particularly in subgroup analyses stratified by gender or duration of hypertension. Third, selection bias may have been introduced by recruiting participants exclusively from a tertiary care hospital, which tends to attract more severe or complex cases; community-based sampling would improve the representativeness and generalisability of the findings to the general hypertensive population. Fourth, although participants were instructed to abstain from food and caffeine before sample collection, full compliance could not be verified, and uncontrolled dietary or lifestyle factors could have influenced cortisol readings. Finally, the study did not assess potentially important confounders such as antihypertensive medication class, which may differentially influence cortisol levels, nor did it measure aldosterone or ACTH concentrations, which would have provided a more complete characterisation of the HPA-renin-angiotensin axis interaction (Miller et al., 2007; Buysse et al., 1989).

## 7. ACKNOWLEDGMENT

The authors gratefully acknowledge the participants of this study for their time, cooperation, and willingness to contribute to clinical research. We extend our sincere gratitude to the nursing staff and phlebotomy team of the Outpatient Medicine and Cardiology Departments for their diligent support in specimen collection and logistics. We thank the Department of Biochemistry and the accredited reference laboratory for their expertise in cortisol assay analysis. Financial support for this study was provided by an internal research grant from the Nizam's Institute of Medical Sciences Research Fund (Grant No. NIMS-RF/2012/047). The authors declare no conflicts of interest. Statistical guidance was generously provided by the Biostatistics Division of the institution, and administrative assistance was rendered by the Clinical Research Coordination Office. We also acknowledge the contributions of Dr. Nalini Prasad and Dr. Samuel Obi, who assisted with participant recruitment and data verification

## 8. CONCLUSION

This cross-sectional comparative study provides substantive evidence that hypertensive patients exhibit significantly elevated cortisol levels across multiple biological specimens—morning and evening serum cortisol, salivary cortisol, and 24-hour urinary free cortisol—compared to normotensive controls. The elevated cortisol awakening response observed in hypertensive patients further substantiates the hypothesis that chronic HPA axis hyperactivity is a defining neuroendocrine feature of this population. Simultaneously, hypertensive patients demonstrated markedly higher scores on all validated psychosocial stress instruments employed in this study, including the PSS-10, HAM-A, WSI, and PSQI, indicating that the psychosocial burden experienced by these individuals is substantial and multidimensional, encompassing perceived stress, trait anxiety, occupational strain, and sleep disruption. The significant positive correlations between morning cortisol and blood pressure, between PSS-10 scores and blood pressure, and most notably between PSS-10 scores and morning cortisol, collectively support a biologically plausible and clinically meaningful pathway through which psychosocial stress activates the HPA axis and contributes to the pathogenesis of hypertension. The logistic regression analysis, which identified morning cortisol, PSS-10 score, and 24-hour urinary cortisol as the strongest independent predictors of hypertension after adjustment for lifestyle covariates, underscores the incremental predictive value of integrating neuroendocrine biomarkers and psychometric assessments into hypertension risk stratification frameworks (Kearney et al., 2005; Steptoe and Kivimaki, 2012).

From a clinical and public health perspective, the findings of this study have meaningful implications for the management of hypertension. The high prevalence of elevated perceived stress and suboptimal sleep quality observed in the hypertensive cohort suggests that non-pharmacological, psychosocial interventions—such as structured stress management programmes, mindfulness-based practices, cognitive behavioural therapy, and sleep hygiene counselling—should be considered as integral components of comprehensive hypertension care, rather than optional adjuncts. Routine screening for psychosocial stress using validated instruments such as the PSS-10 could feasibly be incorporated into primary care and specialist hypertension clinic workflows, enabling early identification of patients who might benefit most from targeted psychological support. Furthermore, the role of cortisol as an independent predictor of hypertension raises the possibility that morning serum cortisol, a readily measurable and widely available laboratory parameter, could serve as a useful biomarker for

monitoring HPA axis dysregulation in hypertensive patients and for assessing the efficacy of stress reduction interventions. Future research should include longitudinal studies to establish the causal directionality of the cortisol-hypertension relationship, randomised controlled trials evaluating the blood pressure-lowering effects of stress management interventions on cortisol levels, and multi-centre studies across diverse South Asian populations to enhance generalisability (Gupta et al., 2013; Chandola et al., 2010; Adler et al., 1994)..

**REFERENCE**


1. Adler, N. E., Boyce, T., Chesney, M. A., Cohen, S., Folkman, S., Kahn, R. L., & Syme, S. L. (1994). Socioeconomic status and health: The challenge of the gradient. American Psychologist, 49(1), 15–24.
2. Buysse, D. J., Reynolds, C. F., Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). The Pittsburgh Sleep Quality Index: A new instrument for psychiatric practice and research. Psychiatry Research, 28(2), 193–213.
3. Chandola, T., Britton, A., Brunner, E., Hemingway, H., Malik, M., Kumari, M., & Marmot, M. (2010). Work stress and coronary heart disease: What are the mechanisms? European Heart Journal, 29(5), 640–648.
4. Chobanian, A. V., Bakris, G. L., Black, H. R., Cushman, W. C., Green, L. A., Izzo, J. L., & Roccella, E. J. (2003). The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. JAMA, 289(19), 2560–2572.
5. Chrousos, G. P. (1992). Regulation and dysregulation of the hypothalamic-pituitary-adrenal axis: The corticotropin-releasing hormone perspective. Endocrinology and Metabolism Clinics of North America, 21(4), 833–858.
6. Cohen, S., Kamarck, T., & Mermelstein, R. (1983). A global measure of perceived stress. Journal of Health and Social Behavior, 24(4), 385–396.
7. Dekker, M. J., Koper, J. W., van Aken, M. O., Pols, H. A., Hofman, A., de Jong, F. H., & Tiemeier, H. (2008). Salivary cortisol is related to atherosclerosis of carotid arteries. Journal of Clinical Endocrinology & Metabolism, 93(10), 3741–3747.
8. Esler, M., Rumantir, M., Wiesner, G., Kaye, D., Hastings, J., & Lambert, G. (2003). Sympathetic nervous system and insulin resistance: From obesity to diabetes. American Journal of Hypertension, 14(11), 304S–309S.
9. Gupta, R., Guptha, S., Sharma, K. K., Gupta, A., & Deedwania, P. (2012). Regional variations in cardiovascular risk factors in India: India heart watch. World Journal of Cardiology, 4(4), 112–120.
10. Gupta, R., Sharma, A. K., Gupta, V. P., Bhatnagar, S., & Rastogi, S. (2013). Increased coronary heart disease prevalence and risk factors in an urban population of India. Indian Heart Journal, 54(1), 59–66.
11. Holmes, T. H., & Rahe, R. H. (1967). The Social Readjustment Rating Scale. Journal of Psychosomatic Research, 11(2), 213–218.
12. Kearney, P. M., Whelton, M., Reynolds, K., Muntner, P., Whelton, P. K., & He, J. (2005). Global burden of hypertension: Analysis of worldwide data. The Lancet, 365(9455), 217–223.
13. Lazarus, R. S., & Folkman, S. (1984). Stress, appraisal, and coping. Springer Publishing.
14. Lovallo, W. R., Farag, N. H., Vincent, A. S., Thomas, T. L., & Wilson, M. F. (2006). Cortisol responses to mental stress, exercise, and meals following caffeine intake in men and women. Pharmacology Biochemistry and Behavior, 83(3), 441–447.
15. Miller, G. E., Chen, E., & Zhou, E. S. (2007). If it goes up, must it come down? Chronic stress and the hypothalamic-pituitary-adrenocortical axis in humans. Psychological Bulletin, 133(1), 25–45.
16. Plotsky, P. M., Owens, M. J., & Nemeroff, C. B. (1998). Psychoneuroendocrinology of depression: Hypothalamic-pituitary-adrenal axis. Psychiatric Clinics of North America, 21(2), 293–307.
17. Rosengren, A., Hawken, S., Ounpuu, S., Sliwa, K., Zubaid, M., Almahmeed, W. A., & Yusuf, S. (2004). Association of psychosocial risk factors with risk of acute myocardial infarction in 11119 cases and 13648 controls from 52 countries. The Lancet, 364(9438), 953–962.
18. Sowers, J. R., Epstein, M., & Frohlich, E. D. (2001). Diabetes, hypertension, and cardiovascular disease: An update. Hypertension, 37(4), 1053–1059.
19. Sparrenberger, F., Cichelero, F. T., Ascoli, A. M., Fonseca, F. P., Weiss, G., Berwanger, O., & Fuchs, F. D. (2009). Does psychosocial stress cause hypertension? A systematic review of observational studies. Journal of Human Hypertension, 23(1), 12–19.
20. Steptoe, A., & Kivimaki, M. (2012). Stress and cardiovascular disease. Nature Reviews Cardiology, 9(6), 360–370.
21. Vrijkotte, T. G., van Doornen, L. J., & de Geus, E. J. (2000). Effects of work stress on ambulatory blood pressure, heart rate, and heart rate variability. Hypertension, 35(4), 880–886.

22. Weiner, H. (1992). Perturbing the organism: The biology of stressful experience. University of Chicago Press.
23. Whitworth, J. A., Williamson, P. M., Mangos, G., & Kelly, J. J. (2005). Cardiovascular consequences of cortisol excess. Vascular Health and Risk Management, 1(4), 291–299.
24. World Medical Association. (2013). Declaration of Helsinki: Ethical principles for medical research involving human subjects. JAMA, 310(20), 2191–2194.