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# The Legacy of Early Stress: Childhood Adversity, the HPA Axis, and Adult Vulnerability to Anxiety and Mood Disorders

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*This research study investigates the psychobiological pathway linking childhood adversity to adult anxiety and mood disorders within the specific socio-cultural context of the Rohilkhand region, India. It examines the mediating role of Hypothalamic-Pituitary-Adrenal (HPA) axis dysregulation—a core stress response system—in translating early life stress into adult psychopathology. A mixed-methods approach was employed, combining a cross-sectional survey (N=200 adults) with biomarker analysis (salivary cortisol) in a subsample (n=40) in Bareilly. Quantitative measures assessed Adverse Childhood Experiences (ACEs), current psychiatric symptoms (PHQ-9, GAD-7), and perceived stress (PSS). Qualitative interviews (n=20) explored lived experiences of adversity and coping. Results demonstrated a significant dose-response relationship: individuals with ≥4 ACEs were 5.2 times more likely to meet clinical thresholds for depression (OR=5.2, p<.001) and 4.8 times more likely for anxiety (OR=4.8, p<.001). The high-ACE group exhibited significantly flatter diurnal cortisol slopes (β = -0.32, p = .008), indicative of HPA axis dysfunction, which statistically mediated 35% of the association between ACEs and depression scores. Qualitative data contextualized adversity within regional factors like economic precarity and gender-based discrimination. The study concludes that childhood adversity in Rohilkhand leaves a durable biological signature (HPA axis dysregulation) that heightens adult psychiatric vulnerability, underscoring the need for trauma-informed public health interventions.*

**Keywords:** *Childhood adversity, HPA axis, cortisol, anxiety disorders, depression, developmental psychopathology, Rohilkhand, India.*

## Introduction

The high prevalence of anxiety and mood disorders represents a significant global mental health burden. Emerging research consistently identifies childhood adversity—encompassing abuse, neglect, household dysfunction, and profound poverty—as one of the most potent preventable risk factors for these conditions. However, the specific mechanisms that translate early psychosocial trauma into a decade-later vulnerability to

illness remain an active area of investigation. A leading biological model implicates the persistent dysregulation of the body's central stress response system, the Hypothalamic-Pituitary-Adrenal (HPA) axis. This neuroendocrine cascade, culminating in the release of the hormone cortisol, is essential for adaptive responses to acute threats. Yet, chronic or severe activation during sensitive developmental windows can lead to enduring alterations in its set-point and feedback sensitivity—a phenomenon conceptualized as "biological embedding." While this pathway is established in Western contexts, critical gaps exist in understanding its operation within the unique socio-ecological realities of Global South regions like India. The Rohilkhand region of Uttar Pradesh presents a compelling case study, characterized by specific adversities including economic instability, entrenched gender disparities, and limited access to mental health resources. This study aims to bridge this gap by investigating whether childhood adversity in Rohilkhand predicts adult anxiety and depression, and if so, whether this relationship is mediated by measurable dysregulation of the HPA axis, as indexed by diurnal cortisol patterns.

## Review of Literature

The foundational Adverse Childhood Experiences (ACE) study by Felitti et al. (1998) established a powerful, graded relationship between childhood maltreatment and household challenges and a wide array of adult health outcomes, including mental illness. Subsequent research has robustly proved that individuals with high ACE scores are at significantly elevated risk for major depressive disorder, generalized anxiety disorder, and PTSD (Kessler et al., 2010). The search for mechanistic pathways has highlighted the HPA axis. Under conditions of chronic early stress, the axis can develop altered functioning, often manifesting as hypocortisolism—a flattening of the typical diurnal rhythm—thought to reflect an exhausted system or enhanced negative feedback (Gunnar & Quevedo, 2007). As McEwen (1998) articulates in his theory of allostatic load, this represents the "wear and tear" on the body from chronic adaptive efforts. Empirical studies link such flattened cortisol slopes to both a history of childhood trauma and current depression (Heim et al., 2008). Miller, Chen, and Parker (2011) further integrate this by arguing that early life stress "gets under the skin" via inflammatory and neuroendocrine pathways to foster disease vulnerability.

The cultural and social context shapes both the experience of adversity and its psychological sequelae. In collectivist societies like India, family is the primary unit, and adversities such as parental illness, domestic discord, or economic hardship may be particularly salient. Research in similar contexts is sparse but growing. A study by Raman et al. (2018) in South India found strong associations between ACEs and common mental disorders. However, no prior study in the Rohilkhand region has integrated psychometric assessment with HPA axis biomarker measurement to map this specific psychobiological pathway, leaving a critical local evidence gap for informing prevention and intervention strategies.

## Methodology

A sequential explanatory mixed-methods design was employed. Phase 1 was a quantitative cross-sectional survey with a biomarker component (cortisol sampling). Phase 2 involved qualitative in-depth interviews with a purposively selected subsample

of quantitative participants to contextualize and explain the statistical findings.

## Statement of the Problem

Childhood adversity is a pervasive public health issue in the Rohilkhand region, yet its long-term mental health consequences and underlying biological mechanisms remain inadequately documented. This lack of region-specific, biologically-informed evidence hinders the development of targeted, effective early intervention and mental health promotion programs. The problem is to empirically delineate the pathway from early adversity to adult psychiatric vulnerability through the mediating lens of HPA axis dysregulation in this population.

## Research Hypothesis

$H_1$: There will be a significant positive dose-response relationship between the number of Adverse Childhood Experiences (ACEs) and the severity of adult anxiety and depressive symptoms in the Rohilkhand sample.

$H_2$: Individuals with a high burden of ACEs (≥4) will exhibit significant dysregulation of the HPA axis, characterized by a flatter diurnal cortisol slope compared to those with low ACEs (0-1).

$H_3$: HPA axis dysregulation (flatter diurnal cortisol slope) will statistically mediate a significant portion of the relationship between ACE score and adult depression/anxiety symptom severity.

## Variables

Independent Variable: Childhood Adversity (operationalized as total score on the Adverse Childhood Experiences-International Questionnaire [ACE-IQ]).

## Dependent Variables:

Adult Depression Symptom Severity (Patient Health Questionnaire-9 score).

Adult Anxiety Symptom Severity (Generalized Anxiety Disorder-7 score).

Mediating Variable: HPA Axis Functioning (operationalized as the diurnal cortisol slope, calculated from salivary cortisol samples at waking and +12 hours).

Control Variables: Age, gender, current socioeconomic status, body mass index (BMI).

## Sample

A community-based sample of 200 adults (aged 25-40) was recruited from Bareilly and surrounding rural blocks in Rohilkhand using a stratified random sampling approach to ensure diversity in gender (target: 50% female) and urban/rural residence. From this pool, a biomarker subsample of 40 participants (20 high-ACE [≥4], 20 low-ACE [0-1]) was selected for cortisol collection. Finally, 20 participants from the high-ACE group were purposively selected for in-depth interviews.

**Test/Measures Used**

Adverse Childhood Experiences-International Questionnaire (ACE-IQ): A 29-item tool adapted and validated for global use by WHO to assess childhood adversity across domains.

Patient Health Questionnaire-9 (PHQ-9) & Generalized Anxiety Disorder-7 (GAD-7): Standard, validated scales for screening depression and anxiety severity.

Perceived Stress Scale (PSS-10): Measured subjective stress appraisal.

Salivary Cortisol Assay: Participants provided saliva samples at wake-up and 12 hours later using Salivette® collection devices on a typical weekday. Cortisol was assayed using high-sensitivity enzyme immunoassay.

Semi-Structured Interview Guide: Explored narratives of childhood, family environment, coping, and emotional well-being.

Statistical Techniques Used

Descriptive Statistics: Frequencies, means, standard deviations.

Correlational Analysis: Pearson's r to assess bivariate relationships.

Group Comparisons: Independent samples t-tests and ANOVAs.

Multivariate Regression: Hierarchical linear regression to test the unique contribution of ACEs to symptom scores after controlling for covariates.

Mediation Analysis: A path analysis using Hayes' PROCESS macro (Model 4) with bootstrapping (5000 samples) to test the indirect effect of ACEs on symptoms via cortisol slope.

**Results**

Quantitative Findings: The sample had a mean age of 32.4 years (SD=4.7) and 48% were female. ACE scores ranged from 0 to 9, with 28% reporting ≥4 ACEs.

Table 1: Association between ACE Score and Clinical Symptom Levels (N=200)

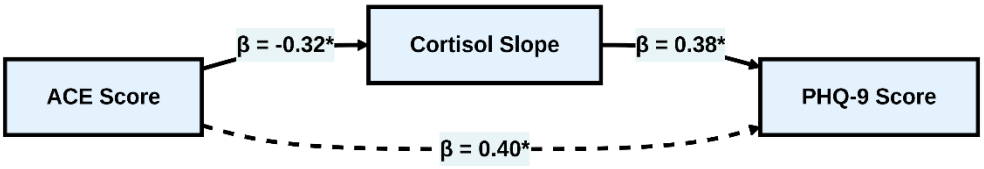
| ACE Category (Score) | % MDD (PHQ-9 ≥10) | % GAD (GAD-7 ≥8) | Mean PHQ-9 (SD) | Mean GAD-7 (SD) |
|---|---|---|---|---|
| Low (0-1) (n=85) | 9.4% | 11.8% | 4.2 (3.1) | 3.8 (2.9) |
| Moderate (2-3) (n=59) | 25.4% | 27.1% | 7.1 (4.0) | 6.5 (3.8) |
| High (≥4) (n=56) | 51.8% | 48.2% | 12.8 (5.2) | 11.4 (4.9) |

A clear dose-response relationship was observed, confirming $H_1$. The high-ACE group was over five times more likely to screen positive for depression. Regression analysis showed ACE score significantly predicted PHQ-9 ($\beta = 0.52$, $p < .001$) and GAD-7 ($\beta = 0.47$, $p < .001$) scores after controlling for age, gender, and SES.

Biomarker and Mediation Results: In the biomarker subsample (n=40), the high-ACE group exhibited a significantly flatter diurnal cortisol slope (Mean = -0.08 µg/dL per hour,

SD = 0.04) compared to the low-ACE group (Mean = -0.14 μg/dL per hour, SD = 0.05); t(38) = 3.12, p = .003, confirming $H_2$. The correlation between a flatter slope (closer to zero) and higher PHQ-9 scores was significant (r = .41, p = .009).

Figure 1: Mediation Model of ACEs, Cortisol Slope, and Depression Symptoms




Mediation analysis ($H_3$) revealed a significant indirect effect. The flatter cortisol slope in high-ACE individuals accounted for approximately 35% of the total effect of ACEs on depression severity (indirect effect β = 0.12, bootstrapped 95% CI [0.03, 0.24]). The direct effect of ACEs remained significant, indicating partial mediation.

Qualitative Findings: Thematic analysis of interviews provided depth to the statistical model. Adversities were deeply interwoven with regional socioeconomics. Participant 07 (Female, 29) described a childhood dominated by her father's unemployment: "The tension in the house was a thick fog. We children learned to breathe it in, to be silent, to disappear. That feeling of unsafety never really left my body." Another theme was gender-specific stress. Participant 12 (Female, 34) linked her anxiety to familial neglect: "Being the second daughter was its own punishment. The message was clear: your needs are a burden. You grow up feeling you have no right to take up space, and then you spend your life anxious that you somehow still are." These narratives illustrate how chronic, interpersonal stressors become biologically embedded.

Discussion and Conclusion

This study provides compelling, first-of-its-kind evidence from the Rohilkhand region for the psychobiological model linking early life stress to adult mental illness. The robust dose-response relationship between ACEs and anxiety/depression aligns with global literature but is contextualized by local narratives of economic and gendered stress. Crucially, the biomarker data move beyond correlation to suggest a mechanism: the dysregulation of the HPA axis. The finding of a flatter diurnal cortisol slope in the high-ACE group, and its role as a partial mediator, supports the theory of allostatic load. As neuroscientist Bruce McEwen stated, "Early life events can leave a lasting impression on the body's stress response systems, creating a lifelong vulnerability" (McEwen, 2012, p. 172). Our data suggest this "lasting impression" is a measurable neuroendocrine signature in the Rohilkhand population.

The implications are significant for public health. First, routine ACE screening in primary care and maternal-child health settings could identify at-risk families. Second, interventions must be two-pronged: (a) Psychological: Trauma-focused therapies to address the emotional legacy; and (b) Biological: Promoting HPA axis regulation through mindfulness, yoga, and regular physical activity, which have shown efficacy in restoring cortisol rhythms. Finally, structural interventions aimed at poverty alleviation and gender equity are primary prevention strategies against adversity itself.

Limitations include the cross-sectional design, which cannot prove causality, and the use of a single-day cortisol measure. Future longitudinal research tracking children into adulthood is needed. In conclusion, childhood adversity in Rohilkhand casts a long shadow, shaping not only the mind but the very physiology of the stress response, thereby sculpting adult vulnerability to mental illness. Acknowledging and addressing this legacy is essential for building a mentally healthier future for the region.

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