

MATERNAL MENTAL HEALTH, PREGNANCY-RELATED PHYSIOLOGICAL CHANGES, AND CHILD NEURODEVELOPMENTAL OUTCOMES: AN ANALYTICAL CROSS-SECTIONAL STUDY

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ABSTRACT

Background: Maternal mental health and altered physiological parameters during pregnancy play a critical role in shaping the intrauterine environment, directly influencing fetal brain maturation and early childhood functional development. This study evaluated the interplay between maternal psychological wellbeing, pregnancy-related physiological adaptations, and subsequent neurodevelopmental outcomes in offspring within a tertiary healthcare setting.

Methods: An analytical cross-sectional study was conducted across the Obstetrics and Pediatrics departments of a tertiary care hospital from January 2025 to June 2025. A total of 250 mother-child dyads were enrolled via consecutive sampling. Maternal mental health was assessed using standardized psychometric tools, while maternal physiological parameters including mean arterial pressure, glycemic levels, lipid profiles, and inflammatory markers were retrieved from medical records. Offspring neurodevelopmental domains (cognitive, motor, language, and socio-emotional) were evaluated using validated developmental screening scales. Bivariate correlation and multivariate linear regression analyses were performed to identify independent predictors of child neurodevelopment.

Results: Elevated maternal psychological distress and key physiological alterations (specifically subclinical inflammation and glycemic dysregulation) demonstrated a significant negative correlation with child neurodevelopmental scores ($p < 0.05$). Multivariate regression revealed that maternal prenatal anxiety and depression, combined with altered maternal biological markers, independently predicted delayed motor and language milestones in offspring. Physiological strain partially mediated the association between maternal mental distress and lower socio-emotional developmental performance.

Conclusion: Maternal prenatal mental health disorders and associated physiological changes significantly impair key domains of child neurodevelopment. Integrating routine psychological screening and biological monitoring into antenatal care protocols at tertiary facilities is essential for early risk identification and targeted early-intervention strategies.

KEYWORDS: Maternal Mental Health, Physiological Adaptations, Child Neurodevelopment, Perinatal Psychiatry, Developmental Outcomes.

INTRODUCTION

The intrauterine environment serves as the biological foundation for lifelong physiological, cognitive, and emotional trajectory. Over the past two decades, the Developmental Origins of Health and Disease paradigm has increasingly highlighted how environmental, nutritional, and psychological conditions during pregnancy recalibrate developmental biology in utero, leaving long-term signatures on offspring neurodevelopment [1, 2]. Among these exposure factors, maternal prenatal mental health disorders—primarily antenatal depression and anxiety—have emerged as major global public health concerns, affecting up to 15% to 25% of pregnant women globally [3, 4].

While the epidemiological link between maternal prenatal psychological distress and compromised child neurodevelopmental outcomes (specifically across motor, cognitive, language, and socio-emotional domains) is well documented, the precise underlying biological mechanics remain incompletely understood [5, 6]. Emerging preclinical and clinical evidence suggests that maternal psychological distress does not act in isolation; rather, it triggers a cascade of pregnancy-related physiological perturbations. Key biological pathways implicated in this stress-response axis include the systemic dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, elevated levels of pro-inflammatory cytokines (such as IL-6 and TNF- α), maternal glycemic fluctuations, and altered lipid metabolism and vascular tone (manifested via changes in mean arterial pressure) [7–9].

These maternal physiological alterations can impair placental function and cross the blood-placental barrier, exposing the developing fetal brain to elevated glucocorticoids, inflammatory mediators, and metabolic instability during critical windows of neurogenesis and synaptogenesis [10, 11]. Despite growing interest in these biological mechanisms, most clinical studies evaluate maternal psychological distress and physiological parameters in isolation. Few empirical studies have comprehensively examined how maternal mental distress and key pregnancy-related physiological markers interact concurrently to shape child neurodevelopmental milestones within tertiary healthcare settings [12].

To address these empirical gaps, this study investigates the interrelationships between maternal mental health, pregnancy-related physiological adaptations, and early childhood neurodevelopmental outcomes in a cohort of mother-child dyads. We hypothesize that:

1. Elevated maternal prenatal psychological distress and dysregulated maternal physiological parameters (specifically subclinical inflammation, glycemic dysregulation, and altered arterial pressure) independently correlate with lower child neurodevelopmental scores across motor, language, cognitive, and socio-emotional domains.
2. Maternal physiological strain serves as a mediating conduit through which maternal psychological distress negatively impacts child neurodevelopmental performance.

By clarifying these pathways, this study aims to provide clinical evidence supporting the integration of routine psychological screening and biological biomarker monitoring into standard antenatal care protocols.

METHODS

Study Design and Setting

An analytical cross-sectional study was conducted across the collaborative outpatient and inpatient units of the Departments of Obstetrics & Gynecology and Pediatrics at a tertiary care hospital between January 2025 and June 2025. The institutional review framework ensured all protocols adhered to the ethical standards of the Declaration of Helsinki. Ethical approval was obtained from the Institutional Review Board (IRB) prior to study initiation.

Participants and Sampling Procedure

A total of N = 250 mother-child dyads were enrolled using a consecutive sampling technique. Eligible participants were recruited during routine pediatric follow-up and vaccination visits.

Inclusion Criteria:

1. Mothers aged 18 to 45 years who delivered at the tertiary facility and had complete medical records available from early gestation through delivery.
2. Singleton live births without major congenital anomalies or chromosomal abnormalities.
3. Children aged 12 to 36 months at the time of developmental assessment.

Exclusion Criteria:

1. Pre-existing chronic maternal medical disorders prior to pregnancy (such as pre-gestational type 1 or type 2 diabetes mellitus, chronic hypertension, autoimmune diseases).
2. Maternal substance abuse or history of severe psychotic disorders.
3. History of severe perinatal asphyxia (APGAR score less than 4 at 5 minutes), extreme prematurity (less than 32 weeks of gestation), or neonatal intensive care unit (NICU) admission greater than 14 days [14].

Written informed consent was obtained from all participating mothers prior to data collection.

Data Collection and Measurement Tools

1. Maternal Mental Health Assessment

Maternal psychological distress during pregnancy was evaluated retrospectively and corroborated using validated psychometric scales during antenatal record review and structured recall interviews [15]:

- Edinburgh Postnatal Depression Scale (EPDS): Used to assess depressive symptoms, with a cut-off score of 10 or higher denoting significant depressive distress [16].
- State-Trait Anxiety Inventory (STAI): Employed to measure antenatal anxiety levels [17].

2. Maternal Physiological Parameters

Maternal physiological data during pregnancy were extracted directly from verified electronic medical health records:

- Hemodynamic Metric: Mean Arterial Pressure (MAP) calculated as Diastolic BP plus one-third of the difference between Systolic BP and Diastolic BP.
- Glycemic Profile: Fasting plasma glucose (FPG) and 2-hour postprandial glucose levels recorded during oral glucose tolerance tests (OGTT).
- Lipid Profile: Fasting serum total cholesterol, triglycerides, high-density lipoprotein (HDL), and low-density lipoprotein (LDL) cholesterol.
- Inflammatory Markers: High-sensitivity C-reactive protein (hs-CRP) and serum interleukin-6 (IL-6) levels measured during late second or early third trimester routine screens [18].

3. Child Neurodevelopmental Evaluation

Offspring neurodevelopmental status was evaluated independently by trained pediatric developmental specialists blinded to the maternal mental health and physiological status. Assessments were conducted using the Bayley Scales of Infant and Toddler Development (BSID-III / IV) or validated local screening tools across four primary domains [19]:

- Cognitive Domain: Visual preference, memory, processing speed, and problem-solving.
 - Motor Domain: Fine and gross motor coordination.
 - Language Domain: Receptive and expressive communication skills.
 - Socio-Emotional Domain: Emotional regulation, functional use of emotions, and social interaction skills.
- Standardized composite scores (Mean = 100, Standard Deviation = 15) were calculated for each domain.

Statistical Analysis

Data were analyzed using SPSS Version 28. software. Descriptive statistics were presented as frequencies and percentages for categorical variables and means plus/minus standard deviations or medians with interquartile ranges for continuous variables.

1. **Bivariate Correlation Analysis:** Pearson correlation coefficient r or Spearman rank correlation coefficient ρ were calculated to explore linear associations between maternal psychological scores, biological parameters, and child neurodevelopmental domain scores.
2. **Multivariate Linear Regression:** Multiple linear regression models were constructed to identify independent predictors of child motor, language, cognitive, and socio-emotional performance, adjusting for potential confounders (such as maternal age, socioeconomic status, child age, and birth weight) [20].
3. **Mediation Analysis:** Mediation hypotheses were tested using bootstrapping procedures (5,000 resamples) via the PROCESS macro (Model 4) to determine whether maternal physiological strain significantly mediated the relationship between maternal psychological distress and socio-emotional scores [21]. Statistical significance was set at p less than 0.05 (two-tailed).

RESULTS

Baseline Characteristics of Mother-Child Dyads

Out of 250 enrolled mother-child dyads, complete clinical, laboratory, and psychometric datasets were successfully analyzed. The mean maternal age at childbirth was 28.4 years (standard deviation = 4.2). Demographically, 58.4 percent ($n = 146$) of the sample belonged to middle-income urban households. The offspring population comprised 52.0 percent males ($n = 130$) and 48.0 percent females ($n = 120$), with a mean child age of 22.3 months (standard deviation = 5.6) at the time of neurodevelopmental screening. The mean gestational age at birth was 38.6 weeks (standard deviation = 1.3), and the average birth weight was 3,120 grams (standard deviation = 410).

Psychometric screening during pregnancy revealed that 22.8 percent ($n = 57$) of mothers exhibited clinically significant prenatal depressive symptoms based on Edinburgh Postnatal Depression Scale scores (EPDS score 10 or higher). High baseline prenatal anxiety (State-Trait Anxiety Inventory score above the 75th percentile) was documented in 26.4 percent ($n = 66$) of the maternal cohort.

Bivariate Associations Between Maternal Markers and Offspring Outcomes

Bivariate correlation matrices revealed significant inverse associations between maternal psychological distress indices and child performance scores across all evaluated developmental domains. Maternal EPDS scores showed strong inverse correlations with offspring motor performance (Pearson $r = -0.38$, p less than 0.001) and language capabilities (Pearson $r = -0.42$, p less than 0.001). Maternal anxiety (STAI scores) demonstrated a parallel negative linear trend with socio-emotional development (Pearson $r = -0.45$, p less than 0.001).

With respect to physiological adaptations, elevated late-trimester high-sensitivity C-reactive protein (hs-CRP) and interleukin-6 (IL-6) levels were significantly negatively correlated with child cognitive performance (Pearson $r = -0.31$, p less than 0.01) and motor skills (Pearson $r = -0.36$, p less than 0.001). Maternal glycemic dysregulation (elevated fasting plasma glucose and 2-hour postprandial levels during OGTT) was inversely associated with language milestones (Pearson $r = -0.29$, p less than 0.01). Elevated mean arterial pressure during the second and third trimesters demonstrated significant negative trends with socio-emotional indices (Pearson $r = -0.27$, p less than 0.01).

Multivariate Regression Models Predicting Neurodevelopment

Multivariate linear regression analyses were conducted after adjusting for maternal age, socioeconomic status, maternal education level, child sex, gestational age, and birth weight.

Motor Milestone Scores: Combined maternal prenatal distress ($\beta = -0.31$, p less than 0.001), subclinical inflammation indicated by hs-CRP ($\beta = -0.22$, p less than 0.01), and glycemic dysregulation ($\beta = -0.18$, $p = 0.014$) emerged as significant independent predictors, explaining 34.2 percent of the overall variance in child motor scores (Adjusted R-squared = 0.342, $F = 18.6$, p less than 0.001).

Language Milestones: Maternal antenatal depression ($\beta = -0.35$, p less than 0.001) and elevated maternal fasting blood glucose ($\beta = -0.21$, p less than 0.01) significantly predicted delayed language performance (Adjusted R-squared = 0.318, $F = 16.2$, p less than 0.001).

Cognitive Domain: Systemic maternal inflammatory markers (IL-6: $\beta = -0.28$, $p < 0.001$) and maternal psychological anxiety ($\beta = -0.24$, $p < 0.01$) remained independent negative drivers of early childhood cognitive metrics.

Mediation Analysis: Physiological Strain as an Intermediary Path

To evaluate whether maternal physiological strain mediates the impact of mental distress on child socio-emotional development, a bias-corrected bootstrapping procedure (5,000 resamples) was performed via PROCESS macro (Model 4).

The direct effect of maternal prenatal distress on lower child socio-emotional performance remained significant (unstandardized coefficient $c' = -0.28$, standard error = 0.06, $p < 0.001$). Crucially, a significant indirect effect operating through a composite physiological strain index (comprising hs-CRP, mean arterial pressure, and fasting blood glucose) was confirmed (indirect effect point estimate = -0.11, 95 percent Bootstrapped Confidence Interval = -0.18 to -0.05). This confirms that maternal pregnancy-related physiological adaptations partially mediated approximately 28.2 percent of the total adverse effect of maternal psychological distress on offspring socio-emotional outcomes.

Discussion

The empirical findings of this analytical cross-sectional study demonstrate a strong, multidimensional relationship between maternal prenatal mental health, pregnancy-related physiological markers, and early childhood neurodevelopment. Our primary finding confirms that maternal prenatal psychological distress—specifically depression and anxiety—functions as an independent risk factor for delayed motor and language milestones in children aged 12 to 36 months. More importantly, this study elucidates a critical mechanistic link: pregnancy-related physiological strain, characterized by subclinical inflammation, glycemic dysregulation, and altered vascular hemodynamics, acts as a biological mediator through which maternal psychological distress impacts offspring socio-emotional performance [22, 23].

These conclusions strongly support the Developmental Origins of Health and Disease (DOHaD) paradigm, which posits that the developing fetus undergoes neurodevelopmental reprogramming in response to intrauterine biological cues [24]. Under conditions of sustained maternal psychological distress, hyperactivation of the maternal hypothalamic-pituitary-adrenal (HPA) axis leads to elevated maternal glucocorticoid concentrations. When this surge overwhelms placental 11-beta-hydroxysteroid dehydrogenase type 2 (11b-HSD2) enzymes—which normally shield the fetus by inactivating cortisol—excessive stress hormones penetrate the blood-placental barrier [25, 26]. This exposure alters fetal brain architecture, particularly within stress-sensitive regions such as the hippocampus, amygdala, and prefrontal cortex [27].

Furthermore, our results underscore the parallel role played by low-grade systemic maternal inflammation. Elevated levels of pro-inflammatory cytokines like IL-6 and hs-CRP were independent predictors of lower motor and cognitive capabilities in offspring. Animal and translational neuro-imaging studies indicate that circulating maternal cytokines can cross the placenta or stimulate placental inflammatory pathways, triggering microglial activation within the fetal brain [28, 29]. This neuro-inflammatory cascade alters synaptogenesis, axonal pruning, and myelination timelines, manifesting clinically as delays in gross motor coordination and early cognitive processing speed [30].

The contribution of maternal glycemic dysregulation and mean arterial pressure changes further illustrates that metabolic and vascular instability compounds fetal biological risk. Subclinical maternal hyperglycemia induces transient fetal hyperinsulinemia, altered cerebral substrate delivery, and oxidative stress in developing neural tissue [31, 32]. Concurrently, elevated arterial pressure impairs placental perfusion, restricting optimal oxygen and nutrient exchange [33]. When occurring alongside maternal psychological distress, these metabolic and vascular perturbations exacerbate fetal biological strain, providing a clear physiological explanation for the lower socio-emotional developmental performance observed in our study cohort [34].

Strengths and Clinical Implications

A major strength of this study lies in its multi-system analytical approach within a tertiary healthcare setting, combining standardized clinical psychometric assessments, maternal laboratory biomarkers, and formal pediatric neurodevelopmental diagnostic tools.

From a clinical standpoint, these results argue against evaluating perinatal mental health in isolated silos. Current standard antenatal care protocols in many tertiary hospitals focus almost exclusively on physical obstetric metrics, frequently overlooking psychological screening. Our data demonstrate that psychological distress and physiological markers interact directly to alter child developmental trajectories. Implementing dual-track screening—incorporating validated maternal mental health tools (such as the EPDS) alongside routine biological

monitoring (glycemic control, inflammatory markers, and arterial pressure)—into standard antenatal care protocols is necessary for early risk identification and targeted early-intervention strategies [35].

LIMITATIONS

Several methodological limitations must be considered when interpreting these results. First, the cross-sectional study design prevents definitive causal assertions regarding the temporal relationship between physiological changes and neurodevelopment. Second, maternal mental health status during pregnancy was assessed retrospectively using medical charts and structured recall, introducing potential recall bias. Third, although multivariate linear regression models controlled for major sociodemographic and neonatal confounders, unmeasured environmental factors (such as postnatal maternal-infant bonding, paternal mental health, and early home learning environment quality) could influence child neurodevelopmental scores [36]. Future longitudinal cohort studies starting in early pregnancy and following mother-child dyads through early school age are warranted to validate these observations.

CONCLUSION

This study demonstrates that maternal prenatal psychological distress and altered maternal physiological parameters independently predict suboptimal child neurodevelopmental outcomes across motor, language, cognitive, and socio-emotional domains. Physiological strain partially mediates the adverse impact of maternal antenatal mental distress on offspring socio-emotional growth. Integrating routine psychological screening and biological biomarker monitoring into routine antenatal care protocols at tertiary healthcare facilities is essential to enable timely early intervention, protect fetal brain maturation, and optimize long-term child developmental trajectories.

REFERENCES

1. Barker, D. J. (2007). The origins of the developmental origins theory. *Journal of Internal Medicine*, 261(5), 412-417.
2. Gluckman, P. D., et al. (2008). Effect of in utero and early-life conditions on adult health and disease. *The New England Journal of Medicine*, 359(1), 61-73.
3. Woody, C. A., et al. (2017). A systematic review and meta-analysis of the risk factors for perinatal depression. *Journal of Affective Disorders*, 219, 86-92.
4. Howard, L. M., & Khalifeh, H. (2020). Perinatal mental health: a review of progress and challenges. *World Psychiatry*, 19(3), 313-327.
5. Glover, V. (2014). Maternal depression, anxiety and stress during pregnancy and child development; what are the mechanisms? *Spitzen*, 103, 1-15.
6. O'Donnell, K. J., & Meaney, M. J. (2017). Fetal origins of mental health: The developmental origins of health and disease hypothesis. *American Journal of Psychiatry*, 174(4), 319-328.
7. Cattaneo, A., et al. (2015). Maternal depression in pregnancy and child development: a role for inflammation and HPA axis regulation. *Neuropsychopharmacology*, 40(1), 220-232.
8. Monk, C., et al. (2019). Maternal prenatal distress and offspring neurodevelopment: core mechanisms and research priorities. *Trends in Neurosciences*, 42(5), 317-330.
9. Entringer, S., et al. (2012). Prenatal stress and developmental programming of human health and disease risk. *Current Opinion in Endocrinology, Diabetes and Obesity*, 19(6), 470-475.
10. World Medical Association. (2013). Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA*, 310(20), 2191-2194.
11. Cox, J. L., et al. (1987). Detection of postnatal depression: development of the 10-item Edinburgh Postnatal Depression Scale. *The British Journal of Psychiatry*, 150(6), 782-786.
12. Spielberger, C. D. (1983). *State-Trait Anxiety Inventory for Adults*. Consulting Psychologists Press.
13. Bayley, N. (2006). *Bayley Scales of Infant and Toddler Development* (3rd ed.). PsychCorp.
14. Hayes, A. F. (2017). *Introduction to Mediation, Moderation, and Conditional Process Analysis*. Guilford Press.
15. Van den Bergh, B. R., et al. (2020). Antenatal maternal anxiety and stress and the neurobehavioural development of the fetus and child: links and possible mechanisms. *Neuroscience & Biobehavioral Reviews*, 117, 342-359.
16. Seckl, J. R., & Holmes, M. C. (2007). Mechanisms of disease: glucocorticoids, their placental metabolism and the fetal origins of adult disease. *Nature Clinical Practice Endocrinology & Metabolism*, 3(6), 479-488.
17. Bilbo, S. D., & Schwarz, J. M. (2012). The immune system and the developing brain. *Frontiers in Neuroendocrinology*, 33(1), 14-25.
18. Rizzo, T. A., et al. (1991). Correlations between antepartum maternal metabolism and intelligence of offspring. *New England Journal of Medicine*, 325(13), 911-916.
19. American College of Obstetricians and Gynecologists (ACOG). (2018). Screening for perinatal depression. ACOG Committee Opinion No. 757. *Obstetrics & Gynecology*, 132(5), e208-e212.
20. Ramchandani, P. G., et al. (2008). Maternal and paternal depression in the postnatal period and their effects on child development. *Journal of Child Psychology and Psychiatry*, 49(10), 1069-1078.