

Prenatal Maternal Psychiatric Disturbance and Offspring Neurodevelopmental Disorders: A Retrospective Case– Control Study from Egypt

Marwa El Karanshawy

melkaranshawy@aucegypt.edu

American University in Cairo

Sungsoo Chun

American University in Cairo

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Abstract

Background

Maternal mental health during pregnancy is an under-recognized predictor of offspring neurodevelopment, particularly in low-resource settings with limited perinatal mental health screening. This study investigated the association of the presence and diagnostic subtype of neurodevelopmental disorders (NDDs) in offspring with maternal depression, anxiety, stress, physical abuse exposure, and perceived social support during the last trimester of pregnancy in an Egyptian sample.

Methods

A retrospective case-control design was used to compare 200 mothers of children diagnosed with autism spectrum disorder, attention-deficit/hyperactivity disorder (ADHD) or attention deficit disorder (ADD) (cases) with 300 mothers of typically developing children (controls), frequency-matched at the group level on child age, sex and maternal socioeconomic status. Depression, anxiety and stress during pregnancy were measured retrospectively using the Depression Anxiety Stress Scales-21 and perceived support was measured using the Multidimensional Scale of Perceived Social Support. Physical abuse and emotional distress during the last trimester were documented, and the child's behavior was assessed using the Strengths and Difficulties Questionnaire. Chi-square tests, t-tests, and binary, ordinal, and multinomial logistic regressions were performed, with 95% confidence intervals reported for all regression estimates.

Results

Mothers had significantly higher severity of depression, anxiety and stress, more physical abuse (45.0% vs. 13.3%) and lower perceived social support than controls (all $p < .001$). In the final adjusted model, abuse (odds ratio [OR] = 5.16, 95% CI 2.75–9.65), depression (OR = 2.03, 95% CI 1.55–2.68), and anxiety (OR = 2.66, 95% CI 1.87–3.79) were independently associated with case status, whereas social support was associated with lower odds of case status (OR = 0.43, 95% CI 0.25–0.75; Nagelkerke $R^2 = .48$). The strongest association with autism diagnosis relative to ADHD was the severity of depression (relative risk ratio = 2.20, 95% CI 1.80–2.69).

Conclusion

Prenatal psychosocial adversity and maternal psychological distress, particularly depression and anxiety, were strongly and independently associated with offspring NDDs in this Egyptian sample. Because the design is retrospective and cross-sectional, these associations cannot be interpreted as causal, but they

support the embedding of screening for maternal mental health and violence within routine antenatal care in similar under-resourced settings.

Introduction

Maternal mental health during pregnancy is increasingly recognized as a modifiable determinant of offspring neurodevelopment but remains under-prioritized in routine antenatal care, particularly in low- and middle-income countries (Handa et al., 2024). Between 15% and 20% of pregnant women worldwide are estimated to suffer from a diagnosable psychiatric disturbance, most frequently depression and anxiety. Symptoms often worsen in the last trimester, when physiological, hormonal and psychosocial demands are highest (O'Hara & Wisner, 2014). In Egypt, community surveys have found that 15.3% of adults suffer from depression and psychiatric infrastructure is mostly found in major cities, with most pregnant women lacking access to perinatal mental health screening or care (Ragab et al., n.d.).

The prenatal period is a sensitive period for neurodevelopment of the fetus. The fetal programming hypothesis posits that maternal psychological distress could influence placental function, fetal glucocorticoid and cytokine exposure, and epigenetic regulation of stress-related genes, leading to long-term alterations in the brain structure and behavior of the offspring (Davis et al., 2018; Robakis et al., 2022). Meta-analytic evidence supports this model by showing associations between antenatal depression and anxiety and deficits in offspring socioemotional development (Madigan et al., 2018) and cognitive functioning (Lugo-Candelas et al., 2023).

Maternal psychological distress in pregnancy is rarely isolated. Mothers and children may be at greater risk when exposed to physical abuse, emotional distress, and low perceived social support (Burbach et al., 2024; O'Dea et al., 2023). It is important to understand the association between these psychosocial exposures and the offspring outcomes in tandem, and not just maternal mood, to be able to develop effective screening and intervention strategies in the antenatal period (Kinsella & Monk, 2009).

Despite this increasing evidence base, data from the Middle East and North Africa region remain limited (Robakis et al., 2022).

The present study therefore aimed to investigate, in a retrospective case-control sample of Egyptian mothers, (1) differences in prenatal depression, anxiety, stress, physical abuse and perceived social support during the last trimester of pregnancy between mothers of children with a diagnosed neurodevelopmental disorder (cases) and mothers of typically developing children (controls); (2) independent association of case status with these factors after mutual adjustment; and (3) whether maternal psychosocial risk factors differentiated diagnostic subtype (autism spectrum disorder [ASD] versus attention deficit hyperactivity disorder [ADHD] versus attention deficit disorder [ADD]) among cases. We hypothesized that higher levels of maternal psychological distress and physical abuse, and lower levels of perceived social support would be independently associated with offspring NDD status, and that depression severity would differentiate autism from the ADHD diagnoses. *Consistent with the*

observational, retrospective design, all hypotheses and analyses in this study concern statistical association rather than causal effect; this distinction is revisited throughout the Discussion.

Materials and Methods

Study design and setting

The present study used a retrospective case-control design to investigate the association between prenatal maternal psychiatric disturbance during the last trimester of pregnancy and NDDs in offspring. Study participants were recruited from a range of socioeconomic and cultural backgrounds and various social circles through Al Azhar University and medical convoys of Misr El Kheir, as well as private clinics. A case-control design was selected because it allows efficient assessment of a relatively rare, long-latency outcome without the resource burden of prospective cohort follow-up (Bangdiwala, 2019; Grimes & Schulz, 2005).

Participants

Cases were 200 mothers of children with a confirmed diagnosis of ASD, ADHD or ADD (cases) with 300 mothers of typically developing children (controls), recruited from the same source population.

Diagnostic definitions. Diagnoses of ASD and ADHD were confirmed against DSM-5-TR criteria through review of medical records. ‘ADD’ is not a current diagnostic category under DSM-5-TR or ICD-11; in this sample it denotes children whose medical records documented a clinician diagnosis of the predominantly inattentive presentation of ADHD, a label that remains in common clinical use in Egypt. These children are analyzed as a diagnostic group distinct from combined-presentation/hyperactive ADHD in order to preserve the clinical distinction made in their own medical records. Diagnoses were confirmed by child psychiatrists. The composition of the case group by diagnostic subtype is reported in Table 5a.

Control selection and matching. Controls were selected using frequency (group-level) matching rather than individual 1:1 or 1:n pairing: for each stratum of child age band (4–5, 6–7, 8–9 years), child sex, and maternal socioeconomic tertile (derived from maternal and paternal education and employment), controls were recruited from the same source population in approximately the same proportion as cases, yielding an overall case:control ratio of 2:3. Because matching was implemented at the group rather than the individual (matched-set) level, standard unconditional logistic regression — rather than conditional logistic regression, which is required only for individually matched sets — is the analytically appropriate approach (Bangdiwala, 2019; Banack et al., 2024). Because child age, child sex and maternal socioeconomic status were themselves the matching variables, they were not re-entered as covariates in the models predicting case status (Table 3), to avoid over-adjusting for factors already balanced by design; they were, however, retained as covariates in the multinomial model differentiating diagnostic subtype (Table 5), because subtype — unlike case status itself — was not a matching variable and could

plausibly be confounded by these factors. A formal balance check (e.g., standardized mean differences between cases and controls on the matching variables) is not available in the current dataset and is recommended as a supplementary table in any future revision.

Sample size was a priori calculated to have sufficient power ($\alpha = 0.05$, power = 0.80) to detect the expected association between prenatal maternal psychiatric disturbance and offspring NDD status.

Measures

The 21-item Depression Anxiety Stress Scales (DASS-21) are validated self-report measures that provide severity categories from normal to extremely severe on each subscale and were used to retrospectively assess prenatal maternal depression, anxiety and stress during the last trimester (Depression Anxiety Stress Scales – Short Form (DASS-21), n.d.). Perceived social support was measured by the Multidimensional Scale of Perceived Social Support (Zimet et al., 2011), which includes support from family, friends and significant other. Physical abuse and mental distress in the final trimester were individually categorized as binary (yes/no) variables from mother report and medical record review. The Strengths and Difficulties Questionnaire, completed by parents, was employed for assessing behavioral problems in children and grouped into normal, borderline and abnormal ranges (Danaei et al., 2021). The SDQ is copyrighted by Youthmind Ltd; it was used without modification, in its official Arabic translation parent-report version, in accordance with the developer's terms of use for non-commercial research (www.sdqinfo.org).

Justification for retrospective assessment. Because no prospective antenatal mental-health screening exists in routine care at the recruiting sites, prenatal depression, anxiety and stress could not be measured contemporaneously; the DASS-21 was therefore administered retrospectively, with mothers asked to rate their symptoms during the last trimester of the index pregnancy. Retrospective self-report of perinatal mood is an accepted approach in settings without prospective antenatal mental-health infrastructure, and validation work comparing retrospective with prospectively collected perinatal mood data shows moderate-to-good, though imperfect, agreement, indicating that retrospective report captures the general direction and relative severity of past symptoms while remaining subject to recall error (see Limitations). This limitation applies symmetrically to the abuse and emotional-distress items, which were likewise assessed retrospectively.

Statistical analysis

Descriptive statistics were used to summarize the sample, with continuous variables presented as means and standard deviations and categorical variables presented as frequencies and percentages. Associations between categorical variables were examined using Pearson's chi-square test of independence (with Yates' continuity correction for 2×2 tables), with Cramer's V reported as a measure of effect size (McHugh, 2013). Where expected cell counts were small, Fisher's exact test was considered. Independent samples t tests were conducted as supplementary analyses by treating the

ordered DASS-21 severity categories as numeric scores; these results were interpreted cautiously because ordinal categories do not necessarily represent equal intervals.

Binary logistic regression models were used to examine associations with case status. Model 1 included DASS-21 subscale severity categories, Model 2 additionally included perceived social support (with DASS-21 subscales entered as continuous scores), and Model 3 simultaneously included abuse exposure, all DASS-21 subscales, and perceived social support. Odds ratios and 95% confidence intervals were reported, and Nagelkerke's pseudo- R^2 was used to summarize the explanatory contribution of the final model. Ordinal logistic regression was used to examine group differences in perceived-support level, whereas multinomial logistic regression was used to examine whether maternal psychosocial risk factors, child age, child sex, and maternal education predicted ASD and ADD relative to ADHD as the reference category. Relative risk ratios and 95% confidence intervals were reported. All tests were two-tailed, with statistical significance set at $p < .05$. Analyses were conducted using IBM SPSS Statistics.

Missing data. Missing data were handled by pairwise (available-case) deletion; analysis-specific N's are reported alongside each test and therefore vary slightly (495–502 across the three DASS-21 subscales) depending on subscale-specific item completion. A sensitivity analysis under listwise deletion, and a supplementary table describing the pattern of missingness by variable, are recommended in any future revision.

Confidence intervals. 95% confidence intervals for all odds ratios and relative risk ratios are reported in Tables 3, 4 and 5. Where the underlying regression coefficient (B) and standard error (SE) were available but a CI had not previously been calculated, we report the Wald 95% CI, computed as $\exp(B \pm 1.96 \times SE)$; this is noted in the corresponding table footnotes.

Regression diagnostics. A sign and significance reversal is observed for the stress subscale across Table 3: non-significant in Model 1 (OR = 0.94), significantly protective in Model 2 (OR = 0.90, $p < .001$), and non-significant again in the final Model 3 (OR = 0.95). Because the three DASS-21 subscales are conceptually and empirically highly correlated, this pattern is most consistent with multicollinearity or suppression rather than a genuine protective effect of stress, and the Model 2 stress coefficient should not be interpreted causally or clinically. Formal collinearity diagnostics (variance inflation factors, tolerance) and a goodness-of-fit statistic.

Ethical considerations

The study protocol was reviewed and approved by the Institutional Review Board of the American University in Cairo (AUC IRB), Cairo, Egypt (case no. 2023-2024-137), and the study was conducted in accordance with the 1964 Declaration of Helsinki and its later amendments. Diagnoses were confirmed by review of medical records to minimize misclassification. Informed consent was obtained from all mothers enrolled in the study prior to data collection.

Results

The analytic sample consisted of 500 mothers (200 cases, 300 controls).

Psychosocial exposures in pregnancy

Physical abuse during pregnancy was reported by 45.0% of case mothers (90/200) compared with 13.3% of control mothers (40/300), a significant association, $\chi^2(1, N = 500) = 62.54, p < .001$, Cramér's $V = .35$ (Table 1). Case mothers were also significantly more likely than controls to report emotional distress in the last trimester (62.5%, 125/200 vs. 23.3%, 70/300), $\chi^2(1, N = 500) = 77.38, p < .001$, Cramér's $V = .39$ (Table 1).

DASS-21 severity according to case status

Mothers in the case group had significantly higher severity on all three subscales of the DASS-21 compared with control mothers (Table 2). For stress, $\chi^2(4, N = 495) = 105.14, p < .001$, Cramer's $V = .46, t(493) = 9.29, p < .001$; for anxiety, $\chi^2(4, N = 498) = 145.03, p < .001, V = .54, t(494) = 13.31, p < .001$; and for depression, the association was largest, $\chi^2(4, N = 502) = 217.18, p < .001, V = .66, t(499) = 14.59, p < .001$. In all three domains, case mothers were overrepresented in the moderate-to-extremely-severe categories, with the clearest separation in depression.

Associations with case status

In a binary logistic regression with DASS-21 severity categories as the only predictors (Model 1; Table 3), depression ($OR = 2.12, 95\% CI 1.67-2.68, p < .001$) and anxiety ($OR = 2.94, 95\% CI 2.17-3.98, p < .001$) were independently associated with case status, but stress was not ($OR = 0.94, 95\% CI 0.74-1.18, p = .584$). When perceived social support was added together with the DASS-21 subscales entered as continuous scores (Model 2), support was associated with lower odds of case status ($OR = 0.84, 95\% CI 0.77-0.92, p < .001$), while depression ($OR = 1.27, 95\% CI 1.20-1.35, p < .001$) and anxiety ($OR = 1.07, 95\% CI 1.02-1.13, p = .008$) remained significant; stress emerged as significant in this model ($OR = 0.90, 95\% CI 0.85-0.94, p < .001$), a reversal from Model 1 that is addressed as a probable multicollinearity artifact in the Statistical Analysis and Discussion sections rather than a genuine protective effect. An ordinal logistic regression further confirmed that case mothers reported significantly lower perceived support than control mothers ($OR = 0.20, 95\% CI 0.09-0.44, p < .001$; Table 4).

In the final multivariable model that included abuse exposure, all three DASS-21 subscales, and social support simultaneously (Model 3, Table 3), abuse during pregnancy showed the strongest independent association with case status ($OR = 5.16, 95\% CI 2.75-9.65, p < .001$), followed by anxiety ($OR = 2.66, 95\% CI 1.87-3.79, p < .001$) and depression ($OR = 2.03, 95\% CI 1.55-2.68, p < .001$). Stress was not significant ($OR = 0.95, 95\% CI 0.74-1.23, p = .71$), and social support remained associated with lower

odds (OR = 0.43, 95% CI 0.25–0.75, $p = .003$). The model accounted for approximately 48% of the variance in case status (Nagelkerke $R^2 = .48$).

Diagnostic subtype

Table 5 shows that, using ADHD as the reference category, abuse exposure, emotional distress, and the three DASS-21 subscales were independently associated with significantly greater relative risk of an autism diagnosis versus ADHD, with the strongest association for depression severity (RRR = 2.20, 95% CI 1.80–2.69, $p < .001$). The same predictors were significantly, but less strongly, associated with ADD versus ADHD (RRRs 1.25–1.62, see Table 5 for 95% CIs). Younger child age and male child sex were also associated with autism versus ADHD (both $p < .05$). The case group comprised 76 children with ASD (38.0%), 108 with ADHD (54.0%) and 16 with ADD (8.0%) (Table 5a).

Child behavioral outcome

In the case group, almost all children (200/200) were in the abnormal range on the SDQ, while 10.3% (31/300) of children in the control group were in the abnormal range and most control-group children were in the normal range (74.7%; Table 6).

Discussion and Conclusions

Interpretive framing. Throughout this Discussion, terms such as ‘predicted’ and ‘associated with’ are used in their statistical sense. The retrospective, cross-sectional case–control design cannot establish temporal precedence, cannot exclude reverse causation, and cannot separate in-utero, genetic, and postnatal environmental contributions to the observed associations; none of the findings reported here should be read as demonstrating a causal effect of maternal distress, abuse, or social support on offspring neurodevelopmental status.

This retrospective case-control study found that in an Egyptian sample, prenatal maternal depression, anxiety, physical abuse and perceived social support during the last trimester of pregnancy were each strongly and independently associated with offspring neurodevelopmental disorders, together accounting for almost half of the variance in case status. Relative to ADHD, depression had the strongest association with autism spectrum disorder, a pattern that is compatible with, but does not by itself establish, a cumulative-psychosocial-adversity gradient.

Maternal prenatal depression and anxiety predicted child and adolescent psychiatric symptoms in two independent cohorts (ALSPAC, UK; PREDO, Finland), independently and additively of children's polygenic risk scores, with no gene $\times$ environment interaction. Genetic confounding accounted for only part (~45%) of the association, supporting a genuine in-utero exposure effect in that genetically informed design. Prenatal mental health was identified as a potent, modifiable factor that should be more routinely screened and addressed, ideally in genetically informed trials (Chen et al., 2021).

Maternal mental health disorders, especially depression and anxiety, are associated with a range of adverse pregnancy outcomes, including preterm birth, low birth weight, impaired newborn self-

regulation, fetal growth restriction, lower Apgar scores, longer NICU stays, and increased infant emergency visits, particularly in resource-poor settings where services are inadequate. These risks are attenuated by psychosocial factors such as partner support and increased by stressors such as social isolation and low socioeconomic position. The literature recommends the inclusion of mental health assessments, psychosocial support, and evidence-based treatments in standard antenatal care, while acknowledging limitations from heterogeneous studies and the absence of quality assessment (Miguel et al., 2019; Tama et al., 2025).

These findings add to growing evidence, mostly from high-income cohorts, that maternal depression and anxiety are associated with neurodevelopmental risk in offspring even after adjustment for measured covariates (Chen et al., 2021; Madigan et al., 2018). We stress, however, that cross-sectional, retrospectively assessed associations cannot be interpreted as causal, and offer the following mechanistic literature as background for future hypothesis-testing rather than as an explanation the present data can adjudicate. The association with physical abuse (OR = 5.16) was particularly large compared with what is generally reported for maternal mood alone, consistent with the possibility that intimate partner violence may function as an upstream psychosocial stressor; however, because exposure and outcome were both measured retrospectively and cross-sectionally, the direction of this association cannot be established, and reverse causation — for example, mothers under greater strain being more likely to disclose abuse, or families under greater strain being more likely to seek and receive a diagnostic evaluation — cannot be excluded. This pattern is discussed alongside, though not confirmed by, the fetal programming hypothesis, in which chronic maternal stress may dysregulate the hypothalamic-pituitary-adrenal axis and affect placental and epigenetic pathways relevant to fetal brain development (Davis et al., 2018; Kinsella & Monk, 2009; Robakis et al., 2022). Our finding of an association between higher perceived social support and lower odds of case status (OR = 0.43 in the adjusted model) aligns with meta-analytic evidence indicating that supportive relationships buffer the effects of psychosocial adversity on maternal mental health and mother–infant bonding (Dekel et al., 2023).

Strengths and Difficulties Questionnaire distribution

The SDQ classifications showed an almost complete separation of groups: all 200 children in the case group were classified as abnormal, whereas 224 of 300 control children were classified as normal and 45 as borderline. This near-total separation, however, must be interpreted as a diagnostic-modeling issue as much as a substantive finding: the ordinal logistic regression analyzing SDQ category by group status yielded no statistical significance (coefficient = 18.60, $p = .944$); this discrepancy between the descriptive distribution and the model-based evaluation reflects quasi-complete separation — because every case child scored in the abnormal range, the maximum-likelihood estimate is unstable and standard errors are inflated, rendering the model itself uninformative rather than indicating an absence of group difference. The SDQ results should therefore be read as confirming the expected clinical distinction between groups rather than as an independent test of the prenatal-exposure hypothesis. Because all primary variables in this study — DASS-21 distress, perceived social support, abuse exposure, emotional distress, and child

SDQ status — were reported by the same respondent (the mother), shared-method variance may also inflate the observed associations among them, a limitation discussed further below. The findings of this study should be interpreted in light of an Egyptian mental health system that is limited in terms of psychiatric infrastructure and community-level surveillance data (Ghanem et al., 2009); much of the depression, anxiety and abuse identified in this sample had likely been undetected and unaddressed during pregnancy. This gap represents both a public health concern and an opportunity for intervention, and our findings support the integration of routine depression, anxiety, and abuse screening into antenatal care in similar low-resource settings (Handa et al., 2024; Mostafa et al., 2021).

Limitations

Design and temporality. First, the retrospective case-control design cannot establish temporal precedence and cannot exclude reverse causation: mothers of children with an NDD diagnosis may recall or report prenatal distress and abuse differently than control mothers, and the burden of caring for a child with an NDD is itself a recognized risk factor for maternal depression and anxiety that could be misattributed, retrospectively, to the prenatal period (Bangdiwala, 2019; Grimes & Schulz, 2005).

Retrospective recall of exposure. Retrospective assessment of a period several years earlier, using the DASS-21 administered to mothers of children now aged four to nine years, is vulnerable to at least three distinguishable biases that are likely to act in the same direction. First, ordinary recall decay affects all participants but is unlikely to be random with respect to case status. Second, mood-congruent recall means that mothers who are currently more distressed — plausibly a higher proportion of case mothers, given the burden of caregiving — tend to recall past mood as worse than it was, independent of their true prenatal state. Third, case mothers have typically undergone repeated diagnostic and developmental interviews in which the pregnancy history is revisited, which may lead them to reconstruct prenatal experiences through the lens of the child's later diagnosis. Because these processes should inflate rather than deflate the case-control contrast, the odds ratios reported here are more plausibly interpreted as upper-bound estimates of the true prenatal associations than as unbiased point estimates.

Matching and analysis. Because controls were frequency-matched rather than individually paired, unconditional logistic regression was the appropriate analytic choice, but no formal balance table (e.g., standardized mean differences on the matching variables) is available to confirm that matching succeeded as intended; we recommend this be added as a supplementary table before publication.

Measurement and common-method variance. Second, exposures were based on maternal self-report rather than prospectively collected clinical records and thus may be subject to measurement error and common-method variance, since a single respondent (the mother) provided data on distress, support, abuse, and child behavior. In addition, diagnoses were taken from clinician records without a formal inter-rater agreement assessment, and the ADD group was small ($n = 16$), so estimates for ADD relative to ADHD are imprecise.

Sampling and generalizability. Third, cases were recruited from clinical and university-affiliated settings using purposive and convenience sampling, which may limit generalizability to community populations and introduce selection bias if health-seeking behavior differs systematically across groups (Banack et al., 2024).

Confounding. Fourth, unmeasured genetic and shared-environment confounding cannot be entirely ruled out, although prior sibling-comparison studies suggest that antenatal maternal distress has effects on offspring above and beyond shared genetic liability in some cohorts (Miguel et al., 2019). Paternal mental health, obstetric complications, and finer-grained socioeconomic indicators (income, household crowding) were not assessed.

Finally, findings from one clinical sample in one country may not be generalizable to other populations in the region.

Conclusion

This retrospective case-control study of 500 Egyptian mother–child dyads (200 mothers of children diagnosed with ADHD, ADD, or autism spectrum disorder aged 3–17 years, and 300 matched controls) demonstrates that maternal psychiatric disturbance during the last trimester of pregnancy — measured retrospectively with the DASS-21 — is strongly and independently associated with offspring neurodevelopmental disorders: in adjusted logistic regression models, depression (OR = 2.03, 95% CI 1.55–2.68), anxiety (OR = 2.66, 95% CI 1.87–3.79), and exposure to physical abuse during pregnancy (OR = 5.16, 95% CI 2.75–9.65) were each independently associated with higher odds of case status, while perceived social support was independently associated with lower odds (OR = 0.43, 95% CI 0.25–0.75), with the final multivariable model accounting for approximately 48% of the variance in case status; multinomial analyses further showed that, relative to ADHD, maternal depression carried the strongest association with autism spectrum disorder (RRR = 2.20, 95% CI 1.80–2.69), a pattern consistent with, though not itself a test of, a cumulative-adversity gradient, and near-total separation on the Strengths and Difficulties Questionnaire (all 200 case children classified abnormal) indicated that maternal psychosocial vulnerability is mirrored in measurable child functioning, though this measure functioned in this study primarily as a manipulation check on case status rather than as an independent outcome (see Limitations). These findings are consistent with, but do not themselves test, an in-utero programming mechanism, given the absence of genetic or sibling-comparison data in the present design, and are also consistent with genetically informed cohort evidence showing that prenatal maternal depression and anxiety predict child psychiatric symptoms independently and additively of children's polygenic risk scores (Chen et al., 2021). Generated in a health system where perinatal mental illness is largely undetected (Ghanem et al., 2009), these findings support the integration of routine depression, anxiety, and violence screening, alongside evidence-based treatment and psychosocial support, into standard antenatal care in Egypt and comparable low-resource settings, while we reiterate that the retrospective, cross-sectional design establishes association rather than causation, and that prospective, genetically informed studies are required to test the in-utero mechanisms these data are compatible with.

Abbreviations

ADD

Attention deficit disorder (predominantly inattentive presentation of ADHD)

ADHD

Attention-deficit/hyperactivity disorder

ASD

Autism spectrum disorder

CI

Confidence interval

DASS-21

Depression Anxiety Stress Scales – 21 items

DSM-5-TR

Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision

ICD-11

International Classification of Diseases, 11th Revision

IRB

Institutional Review Board

NDD(s)

Neurodevelopmental disorder(s)

OR

Odds ratio

RRR

Relative risk ratio

SD

Standard deviation

SDQ

Strengths and Difficulties Questionnaire

SE

Standard error

SPSS

Statistical Package for the Social Sciences

Declarations

Ethics approval and consent to participate

The study protocol was reviewed and approved by the Institutional Review Board of the American University in Cairo (AUC IRB), Cairo, Egypt (case no. 2023-2024-137), and the study was conducted in

accordance with the 1964 Declaration of Helsinki and its later amendments. Informed consent was obtained from all mothers enrolled in the study prior to data collection.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Author Information

Dr. Marwa EL Karanshawy – Main Author, corresponding author. PhD Candidate, Department of Biological, Chemical, and Global Health Science, School of Science and Engineering, American University in Cairo, Egypt. melkaranshawy@aucegypt.edu.

City of Affiliation – Aff1: Cairo, Egypt.

Co-Author and research supervisor: Dr. Sungsoo Chun, MPH, PhD. Professor of Global Health, Department of Biological, Chemical, and Global Health Science, School of Science and Engineering, American University in Cairo, Egypt. Sungsoo.chun@aucegypt.edu.

City of Affiliation- Aff2: Cairo, Egypt.

Tables

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Author Contribution

M.K - wrote manuscript and conducted field work S.C - co-author and supervisor

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Data Availability

Research data were generated and analyzed in this study. The datasets analyzed during the current study are not publicly available due to the sensitive nature of the data collected (including disclosures of physical abuse and psychiatric symptom scores) and the confidentiality and anonymity provisions specified in the study's IRB approval (American University in Cairo IRB, Case #2023-2024-137). De-identified data are available from the corresponding author on reasonable request, subject to appropriate data protection and confidentiality safeguards.

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Tables

Table 1. Physical Abuse and Emotional Distress During the Last Trimester of Pregnancy by Case Status

Exposure	Cases n (%)	Controls n (%)	χ² (df)	p	Cramér's V
Physical abuse: Yes	90 (45.0)	40 (13.3)	62.54 (1)	< 0.001	0.354
Emotional distress: Yes	125/200 (62.5)	70/300 (23.3)	77.38 (1)	< 0.001	0.3

Table 2. DASS-21 Stress, Anxiety, and Depression Severity by Case Status

DASS-21 subscale	N	χ^2 (df), Cramer's V	t (df)	p
Stress	495	105.14 (4), .46	9.29 (493)	< .001
Anxiety	498	145.03 (4), .54	13.31 (494)	< .001
Depression	502	217.18 (4), .66	14.59 (499)	< .001

Case mothers scored significantly higher than control mothers on all three subscales. N's vary slightly across subscales because missing data were handled by pairwise deletion (see Statistical Analysis).

Table 3 (revised). Logistic Regression Models Predicting Case Status, with 95% CI

Predictor	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 (final) OR (95% CI)
Abuse during pregnancy	—	—	5.16 (2.75–9.65)***
Depression	2.12 (1.67–2.68)***	1.27 (1.20–1.35)***	2.03 (1.55–2.68)***
Anxiety	2.94 (2.17–3.98)***	1.07 (1.02–1.13)**	2.66 (1.87–3.79)***
Stress	0.94 (0.74–1.18), ns	0.90 (0.85–0.94)***	0.95 (0.74–1.23), ns
Perceived social support	—	0.84 (0.77–0.92)***	0.43 (0.25–0.75)**
Nagelkerke R ²	—	—	.48

Table 4 (revised). Ordinal Logistic Regression Predicting Level of Perceived Social Support

Predictor	B	SE	Wald	p	OR (95% CI)
Group (case vs. control)	-1.62	0.41	15.48	< .001	0.20 (0.09–0.44)

Case mothers were significantly less likely than control mothers to report higher levels of perceived psychological support. 95% CI is a Wald interval computed as $\exp(B \pm 1.96 \times SE)$.

Table 5 (revised). Multinomial Logistic Regression Predicting Neurodevelopmental Diagnosis Type from Maternal Psychosocial Risk (Reference: ADHD)

Predictor	Autism vs. ADHD RRR (95% CI)	ADD vs. ADHD RRR (95% CI)
Physical abuse (yes)	2.03 (1.45–2.84)***	1.32 (1.01–1.73)*
Prenatal emotional distress (yes)	2.29 (1.64–3.20)***	1.42 (1.05–1.92)*
Stress severity (DASS-21)	1.51 (1.26–1.80)***	1.25 (1.04–1.50)*
Anxiety severity (DASS-21)	1.75 (1.45–2.11)***	1.36 (1.12–1.65)**
Depression severity (DASS-21)	2.20 (1.80–2.69)***	1.62 (1.32–1.99)***
Child age (years)	0.91 (0.84–0.99)*	0.96 (0.88–1.05), ns
Child sex (male)	1.41 (1.02–1.96)*	1.13 (0.82–1.56), ns
Maternal education ($\geq$ secondary)	0.76 (0.58–0.99)*	0.83 (0.61–1.13), ns

RRR relative risk ratio; ns not significant ($p \geq .05$). Stress, anxiety, and depression severity entered as ordinal predictors. * $p < .05$, ** $p < .01$, *** $p < .001$.

Table 5a Diagnostic Subtype Composition of the Case Group (n = 200)

Subtype	n (%)	Mean age, y (SD)	% male	Diagnosing specialty
Autism spectrum disorder (ASD)	76 (38.0)	9.24 (3.63)	69.7	Child Psychiatrist
ADHD (combined/hyperactive presentation)	108 (54.0)	9.43 (3.07)	64.8	Child Psychiatrist
ADD (predominantly inattentive presentation)	16 (8.0)	10.06 (3.04)	31.2	Child Psychiatrist
Total	200 (100.0)	—	—	—

n, mean age, and % male are calculated directly from the case-level dataset (Gender, Age, Neurodevelopmental disorder; n = 200, matching the reported case total exactly).

Table 6. Distribution of Strengths and Difficulties Questionnaire (SDQ) Categories by Group

SDQ category	Cases n (%)	Controls n (%)
Normal	0 (0.0)	224 (74.7)
Borderline	0 (0.0)	45 (15.0)
Abnormal	200 (100.0)	31 (10.3)
Total	200 (100.0)	300 (100.0)

Nearly all children in the case group scored in the abnormal range. As discussed in the text, this near-complete separation renders the corresponding ordinal regression model uninformative (quasi-complete separation) and the SDQ result should be read as a manipulation check on case status rather than an independent test of the prenatal-exposure hypothesis.