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Impact of the severity of maternal depression, anxiety, and post-traumatic stress disorder, as well as alcohol consumption, on perinatal outcomes

Nayara López Carpintero[1*], Irene Caro-Cañizares[2], María Luisa Barrigón[3], Carolina Giráldez-García[4] and Rodrigo Carmona Camacho[5]

Abstract

Background Mental health disorders and substance use during pregnancy have been linked to adverse perinatal outcomes. Early identification may improve maternal and neonatal health. This study evaluated the impact of mental health disorder severity and alcohol consumption on perinatal outcomes.

Methods A cohort of 2,014 pregnant women was screened with the AC-OK instrument for mental health and substance use problems between July 2016 and December 2019. Of these, 193 screened positive and underwent assessment for anxiety, depression, post-traumatic stress disorder (PTSD), and alcohol use. Moderate-to-severe symptoms were defined as PHQ-9 ≥ 15 for depression, GAD-7 ≥ 10 for anxiety, and PCL-5 ≥ 33 for PTSD. Perinatal outcomes —including gestational monitoring, pregnancy complications, delivery outcomes, neonatal parameters, and postpartum complications— were compared between women with and without moderate-to-severe mental health disorders, and between alcohol users and non-users. Group differences were assessed using Student's t-test or chi-square test. Associations between head circumference < 10th percentile and mental health problems or alcohol consumption were evaluated using logistic regression. A p-value ≤ 0.05 was considered significant.

Results Neonates of mothers with moderate-to-severe anxiety more often required resuscitation (25.7% vs. 11.4%; $p = 0.05$) and had lower head circumference percentiles (34.38 vs. 46.72; $p = 0.016$). Infants of mothers with PTSD also had reduced head circumference percentiles (34.30 vs. 46.39; $p = 0.025$). Maternal alcohol consumption was associated with lower neonatal head circumference percentiles (37.65 vs. 48.12; $p = 0.014$). Anxiety, depression, PTSD, and alcohol use were significantly associated with neonatal head circumference below the 10th percentile ($p = 0.006$; $p = 0.002$; $p = 0.007$; $p = 0.026$, respectively). No significant associations were observed for other maternal or neonatal outcomes.

Conclusions Moderate-to-severe anxiety, depression, PTSD, and alcohol use during pregnancy were associated with reduced neonatal head circumference. These findings underscore the importance of early screening and intervention

*Correspondence:
Nayara López Carpintero
dralopezcarpintero@yahoo.es

Full list of author information is available at the end of the article

for maternal mental health and alcohol use. Further research is warranted to clarify long-term neurodevelopmental implications.

Trial registration WOMAP (Woman Mental Health and Addictions on Pregnancy), registered at ClinicalTrials.gov (NCT06965270) on March 20, 2025; retrospectively registered.

Keywords Perinatal care, Perinatal mental health, Alcohol, Perinatal outcomes

Background

The perinatal period, particularly pregnancy, is critical for both the physical and emotional development of the mother and the fetus. As a significant and potentially stressful life event, pregnancy can contribute to the onset or worsening of both mental health problems as well as substance use. The most prevalent mental disorders identified during pregnancy include mood disturbances, anxiety-related disorders, and Post-Traumatic Stress Disorder (PTSD) [1, 2]. Depression affects 5–25% of women in the perinatal period, anxiety up to 15%, and PTSD 2–24% [3–5]. Regarding substance use, the estimated prevalence among pregnant women is similar to that of the general population and remains relatively stable throughout pregnancy [6, 7]. Moreover, smoking tobacco and drinking alcohol during pregnancy have bidirectional interactions with mental health problems [8]. For instance, tobacco use during pregnancy can exacerbate symptoms of depression or anxiety, while untreated mental health problems can contribute to continued substance use and relapse [9, 10].

Mental health problems are among the leading causes of disability in pregnant women and contribute significantly to increased maternal mortality risk and adverse outcomes for the baby [2]. Evidence indicates that perinatal mental health problems in mothers are associated with abnormal neurological development and behavioral and mental health disorders in their offspring [11, 12]. Similarly, substance use has not only been linked to complications during pregnancy [9] but also to an increased risk of neonatal complications [13, 14], as well as neurodevelopmental problems in children [15–17]. Maternal alcohol consumption, as well as the use of illicit drugs (such as opioids and cocaine), tobacco, and cannabis during pregnancy, has been associated with adverse neonatal outcomes, including low birth weight, small for gestational age, preterm birth, admission to neonatal intensive care units, and sudden infant death [13, 14, 18–20]. While some substances, including tobacco, cannabis, and stimulants, have also been associated with neurodevelopmental delays, alcohol in particular is strongly implicated in long-term neurodevelopmental impairments [15–17] and is the leading cause of fetal alcohol spectrum disorder, characterized by cognitive deficits, dysmorphic facial features, and behavioral, emotional, and adaptive impairments [21, 22].

The co-occurrence of substance use and mental health problems, often termed dual pathology [23], poses significant challenges for clinical intervention [24]. In pregnant women, dual pathology is associated with non-compliance with prenatal care, health problems, and obstetric complications [8, 12]. While the effects of maternal mental health or substance use alone on infant perinatal outcomes are well documented, research on the impact of dual pathology during pregnancy on both maternal and neonatal outcomes remains limited.

The objective of this study is to evaluate the impact of moderate-to-severe anxiety, depression or PTSD and alcohol use on perinatal outcomes (both maternal and neonatal) in pregnant women screened to be at risk for dual pathology.

Methods

Sample and procedure

As part of the WOMAP (Woman Mental Health and Addictions on Pregnancy) clinical trial (NCT06965270, retrospectively registered on March 20, 2025), the study included 193 pregnant women over 18 years of age who were enrolled before 26 weeks of gestation, identified as at risk for co-occurring mental health and substance use problems (dual pathology). Participants were selected from an initial screening of 2,014 women attending routine obstetric consultations at five public hospitals in the metropolitan area of Madrid, Spain. Screening was conducted using the AC-OK questionnaire, a validated tool for detecting both mental health and substance use problems in clinical settings [25, 26].

Women were classified as at risk of dual pathology if they met the following criteria: (1) two or more positive responses on the AC-OK–Mental Health (AC-OK-MH) subscale; (2) one or more positive responses on the AC-OK–Substance Abuse (AC-OK-SA) subscale and/or reported smoking more than once per month; and (3) were not users of specialized services, defined as having no scheduled appointment within the next month and no medical visit in the previous three months. Women with psychotic or bipolar disorders were excluded.

Participants were recruited between July 2016 and December 2019 during their initial obstetric visits. Those who screened positive were invited to participate in the WOMAP clinical trial (ClinicalTrials.gov ID NCT06965270, retrospectively registered May 2025),

which tested a mindfulness-based cognitive behavioral intervention delivered remotely by trained psychologists via telephone or a digital platform. The intervention consisted of a structured program specifically developed for this trial and comprised eight sessions: (1) introduction to the program, motivation for change, and introduction to mindfulness; (2) psychoeducation on substance use and strategies for managing cravings; (3) exploration of maternal–fetal attachment and the bond with the baby; (4) psychoeducation on mental health disorders, including the triple response system and common thinking styles; (5) introduction to cognitive restructuring ('Evaluating My Thoughts') with practical exercises; (6) assertiveness training and effective communication skills; (7) reinforcement of substance use management strategies and relapse prevention; and (8) review of the self-care plan. Eligible participants were randomly assigned to treatment-as-usual, telephone, or digital intervention arms. For the purposes of this study, all women who screened positive—regardless of subsequent participation in the clinical trial, were included in the analysis (mean age 31.22 ± 5.99 years).

Assessments

After the positive screening for dual disorders risk, all participants underwent a comprehensive assessment protocol that included both obstetric and mental health/substance use evaluations.

Obstetric evaluations were performed as part of routine prenatal care. Maternal variables included age, body mass index (BMI) at the beginning of pregnancy, and tobacco use. Gestational monitoring recorded pregnancy complications, first-trimester combined screening results, and ultrasound-detected malformations. All antenatal ultrasound examinations were performed by specialists in perinatal medicine. Scans were routinely conducted during the first (11–13 weeks), second (19–21 weeks), and third (34–36 weeks) trimesters of pregnancy. Additional ultrasound examinations were performed when clinically indicated, depending on the findings. Delivery variables encompassed gestational age at delivery, labor onset (spontaneous, induced, or scheduled cesarean), and delivery type (vaginal, instrumental, or cesarean). Perinatal outcomes involved meconium-stained amniotic fluid, Apgar scores at 1 and 5 min, umbilical artery pH, and need for neonatal resuscitation. Neonatal assessments covered congenital malformations, complications (cardiac, respiratory, digestive, urological, neurological, and infectious) occurring during postnatal hospitalization, and biometric data at two hours of life—birth weight, length, and head circumference—adjusted for age and sex according to the reference tables of the Pediatric Endocrinology Service of Hospital La Paz [27]. Biometric measurements were performed by trained personnel: birth weight was measured naked on a calibrated electronic scale, birth length in the supine position using a rigid infantometer with the head in the Frankfurt plane (line passing through orbitale and porion) and the movable stop at the heel, and head circumference with a non-elastic tape around the most prominent occiput and forehead above the eyebrows, without compressing soft tissues. Biometric percentiles for estimated fetal weight, length, and head circumference were categorized as < 10th, 10th–90th, and > 90th, considering 10th–90th percentiles as the normal range [28]. Maternal outcomes included postpartum hospital stay and complications.

Regarding mental health, participants were assessed with a battery of validated instruments: the Patient Health Questionnaire (PHQ-9) for depressive symptoms [29, 30], the Generalized Anxiety Disorder 7-item scale (GAD-7) for anxiety [31, 32], and the Posttraumatic Stress Disorder Checklist for DSM-5 (PCL-5) [33, 34]. Furthermore, alcohol use was assessed and potential alcohol use disorder explored with the Alcohol Use Disorders Identification Test (AUDIT) [35].

To classify the severity of mental health and alcohol use problems and subsequent analysis, established cut-off scores from these instruments were used. Moderate-to-severe depressive symptoms were defined as a score of 15 or higher on the PHQ-9. For anxiety, a score of 10 or higher on the GAD-7 was used, reflecting moderate or greater symptom severity and a high probability of a clinically significant anxiety disorder. Clinically significant post-traumatic stress symptoms were defined as a score of 33 or higher on the PCL-5. For alcohol use, any reported consumption during pregnancy was considered positive, in line with recommendations for perinatal research and the absence of a safe threshold for alcohol use in pregnancy [1].

Data were collected and managed using the MeMind physician interface, an online platform that integrates physician and patient data [36].

Ethical considerations

The study was approved by the Clinical Research Ethics Committee of Fundación Jiménez Díaz (Ref. 2015/43) and conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent. Access to identifiable data was restricted to authorized personnel. All data were securely stored on an external server dedicated to research with AES-256 encryption and transmitted using SSL/TLS (Secure Socket Layer/Transport Layer Security) protocols. Compliance with the Spanish Data Protection Act was confirmed by an independent auditor.

Data analysis

First, descriptive analyses of the sample were performed. All obstetric variables were compared between two groups, classified according to alcohol consumption, anxiety, depression, and trauma symptoms, using the cut-off points described above.

Group differences were evaluated using Student's t-test for continuous variables and chi-square test for categorical variables ($p \leq 0.05$).

To evaluate the association between head circumference below the 10th percentile and alcohol consumption, anxiety, depression, or PTSD, the odds ratio was calculated using univariate logistic regression models, and multivariate models for each condition adjusted for alcohol consumption. The presence of interactions between alcohol, mental health variables, and therapy received was assessed using the Wald test, including interaction terms in the first step of each logistic regression model.

Statistical analysis was performed using IBM SPSS Statistics v30.0.0.

Results

Pregnant women who consumed alcohol had an increased risk of delivering infants with lower percentile head circumference at birth than non-users (37.65 versus 48.12;$p = 0.014$) (Table 1). Patients with moderate-to-severe anxiety, depression, or PTSD were alcohol consumers in a higher proportion than patients without these pathologies ($p = 0.026$, $p = 0.022$, and $p = 0.053$, respectively) (Tables 2, 3 and 4). Regarding anxiety, infants of mothers with moderate-to-severe anxiety tended to require more neonatal resuscitation (30% versus 15.3%;$p = 0.05$) and had lower head circumference percentile (34.38 versus 46.72;$p = 0.016$) (Table 2). Babies born to mothers positive for PTSD had lower head circumference percentile (34.30 versus 46.39;$p = 0.025$) than those negative (Table 3). No significant differences were found for depression, although there was a trend towards more spontaneous deliveries ($p = 0.08$) among patients with at least moderate depression (Table 4). As a cumulative effect, the existence of ≥ 2 mental health problems was associated with lower head circumference percentile at birth (32.72 versus 45.40;$p = 0.016$) and greater need for neonatal resuscitation (31% versus 20%;$p = 0.036$). A head circumference < 10th percentile was statistically significantly associated with alcohol consumption and the mental health problems studied (anxiety, depression, PTSD) in isolation (Tables 1, 2, 3 and 4). Two cases had a head circumference below the 3rd percentile; both were born to mothers who consumed alcohol, one with moderate-to-severe maternal mental health problems and the other without.

Analyses of the remaining maternal and neonatal variables studied showed no significant association with anxiety, depression, PTSD, or alcohol (Tables 1, 2, 3 and 4).

The distribution of pregnant women with and without therapy was similar for the alcohol consumption, anxiety, depression, and PTSD groups (Tables 1, 2, 3 and 4).

Pregnant women who consumed alcohol had a 6.077 times higher risk of having a newborn with a head circumference below the 10th percentile (Table 5). Moderate-to-severe anxiety, depression, and PTSD were independently associated with a head circumference below the 10th percentile (Table 6). Therapy did not modify the effect of mental health problems on a head circumference below the 10th percentile (Table 7).

Discussion

Maternal mental health and substance use during pregnancy are related to perinatal outcomes in both the mother and the infant. In this study, we evaluated whether alcohol consumption or the severity of anxiety, depression, and PTSD influence perinatal outcomes in pregnant women screened to be at risk for dual pathology.

Regarding substance use, although tobacco is a more recognized prenatal risk factor than alcohol, alcohol consumption is rising among women of childbearing age [1, 22] and often underdiagnosed during pregnancy, with some assuming low consumption is harmless [37]. Obstetricians should explicitly inquire about alcohol use, as many women seek counseling from healthcare professionals [38].

Some authors have associated prenatal alcohol exposure with low birth weight [39, 40] and preterm delivery [40, 41], risks that are exacerbated by combined alcohol and tobacco consumption [39]. Conversely, other studies fail to confirm these associations or detect a link between alcohol consumption and neonatal head circumference in the absence of smoking or illicit drug use [42]. In our study, although gestational age at delivery was slightly higher among mothers who consumed alcohol, the difference was not clinically relevant, as both groups delivered within the term gestation range. In biometric data, alcohol intake has also been linked to shorter birth length [43]. Fetal growth restriction induced by alcohol is aggravated by maternal undernutrition [44]. In our sample, the similar BMI —and generally adequate— between alcohol-consuming and non-consuming pregnant women may have mitigated the effects of undernutrition, possibly explaining the lack of fetal weight differences observed.

Regarding delivery outcomes, although alcohol consumption has been linked to lower rates of planned cesarean section and higher risks of gestational diabetes, preeclampsia, eclampsia, and postpartum hemorrhage [41], our study found no significant differences between alcohol-consuming and non-consuming

Table 1 Comparison of clinical, obstetric, and neonatal variables according to alcohol use

Variable	No alcohol use ($n=125$)	Alcohol use ($n=68$)	*P* Value
Smokers [% (n)]	58.4% (73)	67.6% (46)	0.134
BMI (mean ± SD)	24.70 ± 5.43	24.72 ± 6.31	0.986
Therapy Received [% (n)]	45.6% (57)	33.8% (23)	0.113
Gestational Follow-up			
Screening (High Risk) [% (n)]	9.6% (12)	5.9% (4)	0.268
Fetal Malformation [% (n)]	3.2% (4)	2.9% (2)	0.644
Gestational Complication [% (n)]	32.8% (41)	27.9% (19)	0.298
Placental Abruption	2.4% (1)	0.0% (0)	0.683
Placenta Previa	2.4% (1)	0.0% (0)	0.683
Threat of preterm labor	17.1% (7)	5.3% (1)	0.204
Premature Rupture of Membranes	12.2% (5)	0.0% (0)	0.137
Preeclampsia / Gestational Hypertension	4.9% (2)	5.3% (1)	0.688
Gestational Diabetes	34.1% (14)	36.8% (7)	0.530
Others	39.0% (16)	57.9% (11)	0.138
Week of gestation when complication appears (Mean ± SD)	26.84 ± 7.66	23.64 ± 10.68	0.270
Hospital Admission [% (n)]	12.8% (16)	5.9% (4)	0.101
Delivery Data			
Gestational Age at Delivery (weeks) (Mean ± SD)	38.66 ± 1.68	39.25 ± 1.31	0.024
Onset of labor [% (n)]			
Spontaneous	46.4% (58)	48.5% (33)	0.770
Induced	26.4% (33)	26.5% (18)	
Scheduled Cesarean	8.8% (11)	5.9% (4)	
Mode of Delivery [% (n)]			
Vaginal (Eutocic)	57.6% (72)	54.4% (37)	0.897
Instrumental	8.8% (11)	7.3% (5)	
Cesarean	16.0% (20)	17.6% (12)	
Intrapartum meconium [% (n)]	8.0% (10)	10.3% (7)	0.357
Arterial pH < 7.20 [% (n)]	22.4% (28)	29.4% (20)	0.146
Apgar Score 1 min (Mean ± SD)	8.56 ± 1.35	8.74 ± 0.81	0.500
Apgar Score 5 min (Mean ± SD)	9.59 ± 0.83	9.74 ± 0.66	0.397
Resuscitation at Birth [% (n)]	14.4% (18)	13.2% (9)	0.508
Neonatal data			
Birth Weight (g) (Mean ± SD)	3118.97 ± 407.23	3182.06 ± 447.89	0.387
Birth weight percentile (Mean ± SD)	42.66 ± 26.56	44.68 ± 29.35	0.671
Birth weight < 10th Percentile [% (n)]	8.8% (11)	7.3% (5)	0.656
Birth Weight < 2500 g [% (n)]	2.4% (3)	4.41% (3)	0.476
Length (cm) (Mean ± SD)	48.87 ± 2.12	49.25 ± 2.02	0.114
Length Percentile	35.82 ± 26.98	40.25 ± 27.90	0.374
Length < 10th Percentile [% (n)]	13.6% (17)	11.8% (8)	0.570
Head Circumference (cm) (Mean ± SD)	34.27 ± 1.29	33.88 ± 1.45	0.124
Head Circumference Percentile	48.12 ± 21.69	37.65 ± 25.25	0.014
Head Circumference < 10th percentile [% (n)]	1.8% (3)	13.2% (9)	0.006
Neonatal Malformations [% (n)]	1.6% (2)	1.7% (1)	0.700
Neonatal Complications [% (n)]	12.8% (16)	14.7% (10)	0.322
Puerperal Data			
Puerperal Complications [% (n)]	8.8% (11)	17.6% (12)	0.060
Infectious	45.5% (5)	38.5% (5)	0.527
Uterine Atony	27.3% (3)	7.7% (1)	0.233
Anemia	27.3% (3)	30.8% (4)	0.605
Others	45.5% (5)	23.1% (3)	0.235
Puerperium Hospital Stay (days) (Mean ± SD)	2.26 ± 0.51	2.35 ± 0.73	0.567

BMI Body Mass Index

Table 2 Comparison of clinical, obstetric, and neonatal variables according to anxiety

Variable	Anxiety no/<10 (*n* = 158)	Anxiety ≥ 10 (*n* = 35)	*P* Value
Smokers [% (n)]	62.7% (99)	57.1% (20)	0.336
Alcohol users [% (n)]	32.3% (51)	48.6% (17)	0.053
BMI (mean ± SD)	24.77 ± 5.86	24.43 ± 5.25	0.754
Therapy Received [% (n)]	42.4% (67)	37.1% (13)	0.567
Gestational Follow-up			
Screening (High Risk) [% (n)]	8.9% (14)	5.7% (2)	0.412
Fetal Malformation [% (n)]	3.2% (5)	2.9% (1)	0.702
Gestational Complication [% (n)]	31.6% (50)	28.6% (10)	0.445
Placental Abruption	2.0% (1)	0.0% (0)	0.833
Placenta Previa	2.0% (1)	0.0% (0)	0.833
Threat of preterm labor	14.0% (7)	10.0% (1)	0.600
Premature Rupture of Membranes	10.0% (5)	0.0% (0)	0.388
Preeclampsia / Gestational Hypertension	6.0% (3)	0.0% (0)	0.573
Gestational Diabetes	34.0% (17)	40.0% (4)	0.490
Others	44.0% (22)	50.0% (5)	0.497
Week of gestation when complication appears (Mean ± SD)	25.89 ± 8.46	25.80 ± 9.52	0.976
Hospital Admission [% (n)]	0.8% (17)	8.6% (3)	0.491
Delivery Data			
Gestational Age at Delivery (weeks) (Mean ± SD)	38.86 ± 1.68	38.90 ± 1.09	0.900
Onset of labor [% (n)]			
Spontaneous	44.3% (70)	60.0% (21)	0.208
Induced	28.5% (45)	17.1% (6)	
Scheduled Cesarean	7.0% (11)	11.4% (4)	
Mode of Delivery [% (n)]			
Vaginal (Eutocic)	56.3% (89)	57.1% (20)	0.475
Instrumental	7.0% (11)	14.3% (5)	
Cesarean	16.4% (26)	17.1% (6)	
Intrapartum meconium [% (n)]	7.0% (11)	17.1% (6)	0.085
Arterial pH < 7.20 [% (n)]	24.7% (39)	25.7% (9)	0.403
Apgar Score 1 min (Mean ± SD)	8.66 ± 1.16	8.43 ± 1.33	0.359
Apgar Score 5 min (Mean ± SD)	9.72 ± 0.61	9.43 ± 1.13	0.187
Resuscitation at Birth [% (n)]	11.4% (18)	25.7% (9)	0.059
Neonatal data			
Birth Weight (g) (Mean ± SD)	3165.93 ± 433.37	3048.83 ± 366.63	0.176
Birth weight percentile (Mean ± SD)	45.35 ± 27.58	35.80 ± 26.53	0.090
Birth weight < 10th Percentile [% (n)]	8.2% (13)	8.6% (3)	0.850
Birth Weight < 2500 g [% (n)]	2.53% (4)	5.71% (2)	0.429
Length (cm) (Mean ± SD)	48.98 ± 2.13	48.69 ± 1.80	0.622
Length Percentile	38.29 ± 27.63	34.12 ± 26.16	0.488
Length < 10th Percentile [% (n)]	12.6% (20)	14.3% (5)	0.622
Head Circumference (cm) (Mean ± SD)	34.25 ± 1.35	33.56 ± 1.41	0.017
Head Circumference Percentile	46.72 ± 23.33	34.38 ± 22.01	0.016
Head Circumference < 10th percentile [% (n)]	3.2% (5)	20.0% (7)	0.002
Neonatal Malformations [% (n)]	1.9% (3)	0.0% (0)	0.469
Neonatal Complications [% (n)]	12.0% (19)	20.0% (7)	0.338
Puerperal Data			
Puerperal Complications [% (n)]	11.4% (18)	14.3% (5)	0.513
Infectious	44.4% (8)	40.0% (2)	0.668
Uterine Atony	11.1% (2)	40.0% (2)	0.179
Anemia	33.3% (6)	20.0% (1)	0.538
Others	33.3% (6)	40.0% (2)	0.555
Puerperium Hospital Stay (days) (Mean ± SD)	2.28 ± 0.60	2.29 ± 0.53	0.946

BMI Body Mass Index

No/<10 versus ≥ 10 on the GAD-7 scale

Table 3 Comparison of clinical, obstetric, and neonatal variables according to PTSD

Variable	PTSD no/<33 (*n* = 163)	PTSD ≥ 33 (*n* = 30)	*P* Value
Smokers [% (n)]	63.2% (103)	53.3% (16)	0.206
Alcohol users [% (n)]	31.9% (52)	53.3% (16)	0.022
BMI (mean ± SD)	24.55 ± 5.81	25.48 ± 5.31	0.427
Therapy Received [% (n)]	43.6% (71)	30% (9)	0.166
Gestational Follow-up			
Screening (High Risk) [% (n)]	9.2% (15)	3.4% (1)	0.235
Fetal Malformation [% (n)]	2.5% (4)	6.7% (2)	0.235
Gestational Complication [% (n)]	33.7% (55)	16.7% (5)	0.046
Placental Abruption			
Placenta Previa	1.8% (1)	0.0% (0)	0.917
Threat of preterm labor	0.0% (0)	20.0% (1)	0.083
Premature Rupture of Membranes	14.5% (8)	0.0% (0)	0.476
Preeclampsia / Gestational Hypertension	9.1% (5)	0.0% (0)	0.637
Gestational Diabetes	5.5% (3)	0.0% (0)	0.767
Others	34.5% (19)	40.0% (2)	0.578
Week of gestation when complication appears (Mean ± SD)	26.12 ± 8.45	23.83 ± 10.05	0.541
Hospital Admission [% (n)]	11.7% (19)	3.3% (1)	0.145
Delivery Data			
Gestational Age at Delivery (weeks) (Mean ± SD)	38.87 ± 1.64	38.85 ± 1.26	0.956
Onset of labor [% (n)]			
Spontaneous	46.0% (75)	53.3% (16)	0.500
Induced	27.0% (44)	23.3% (7)	
Scheduled Cesarean	6.7% (11)	13.3% (4)	
Mode of Delivery [% (n)]			
Vaginal (Eutocic)	57.0% (93)	53.3% (16)	0.545
Instrumental	7.4% (12)	13.3% (4)	
Cesarean	16.0% (26)	20.0% (6)	
Intrapartum meconium [% (n)]	8.6% (14)	10.0% (3)	0.577
Arterial pH < 7.20 [% (n)]	25.1% (41)	23.3% (7)	0.477
Apgar Score 1 min (Mean ± SD)	8.63 ± 1.22	8.54 ± 1.06	0.750
Apgar Score 5 min (Mean ± SD)	9.66 ± 0.74	9.67 ± 0.82	0.987
Resuscitation at Birth [% (n)]	12.9% (21)	20.0% (6)	0.251
Neonatal data			
Birth Weight (g) (Mean ± SD)	3153.24 ± 425.34	3081.09 ± 407.36	0.454
Birth weight percentile (Mean ± SD)	44.53 ± 27.73	37.30 ± 26.13	0.249
Birth weight < 10th Percentile [% (n)]	8.6% (14)	6.7% (2)	0.750
Birth Weight < 2500 g [% (n)]	2.45% (4)	6.67% (2)	0.227
Length (cm) (Mean ± SD)	48.78 ± 2.08	49.28 ± 2.07	0.300
Length Percentile	36.18 ± 27.02	43.39 ± 28.41	0.252
Length < 10th Percentile [% (n)]	13.5% (22)	10.0% (3)	0.407
Head Circumference (cm) (Mean ± SD)	34.24 ± 1.35	33.57 ± 1.44	0.030
Head Circumference Percentile	46.39 ± 23.27	34.30 ± 22.52	0.025
Head Circumference < 10th percentile [% (n)]	3.7% (6)	20.0% (6)	0.007
Neonatal Malformations [% (n)]	1.8% (3)	0.0% (0)	0.589
Neonatal Complications [% (n)]	13.5% (22)	13.3% (4)	0.594
Puerperal Data			
Puerperal Complications [% (n)]	9.8% (16)	23.3% (7)	0.074
Infectious	50.0% (8)	28.6% (2)	0.357
Uterine Atony	16.6% (3)	14.3% (1)	0.672
Anemia	22.2% (4)	42.9% (3)	0.318
Others	22.2% (4)	57.1% (4)	0.134
Puerperium Hospital Stay (days) (Mean ± SD)	2.24 ± 0.58	2.48 ± 0.66	0.118

BMI Body Mass Index

No/<33 versus ≥ 33 on the PCL-5 scale

Table 4 Comparison of clinical, obstetric, and neonatal variables according to depression

Variable	Depression no/<15 (*n* = 173)	Depression ≥ 15 (*n* = 20)	*P* Value
Smokers [% (n)]	63.6% (110)	45% (9)	0.086
Alcohol users [% (n)]	4.6% (8)	20% (4)	0.026
BMI (mean ± SD)	24.77 ± 5.86	24.23 ± 4.67	0.694
Therapy Received [% (n)]	41.6% (72)	40% (8)	0.889
Gestational Follow-up			
Screening (High Risk) [% (n)]	8.7% (15)	5% (1)	0.510
Fetal Malformation [% (n)]	2.9% (5)	5% (1)	0.486
Gestational Complication [% (n)]	30.6% (53)	35% (7)	0.433
Placental Abruption			
Placenta Previa	1.9% (1)	0% (0)	0.883
Threat of preterm labor	1.9% (1)	0% (0)	0.883
Premature Rupture of Membranes	13.2% (7)	14.3% (1)	0.654
Preeclampsia / Gestational Hypertension	9.4% (5)	0% (0)	0.525
Gestational Diabetes	5.7% (3)	0% (0)	0.685
Others	43.4% (23)	57.1% (4)	0.386
Week of gestation when complication appears (Mean ± SD)	26.22 ± 8.40	23.43 ± 9.96	0.424
Hospital Admission [% (n)]	10.4% (18)	10% (2)	0.657
Delivery Data			
Gestational Age at Delivery (weeks) (Mean ± SD)	38.84 ± 1.64	39.11 ± 0.96	0.488
Onset of labor [% (n)]			
Spontaneous	43.9% (76)	75% (15)	0.088
Induced	28.3% (49)	10% (2)	
Scheduled Cesarean	7.5% (13)	10% (2)	
Mode of Delivery [% (n)]			
Vaginal (Eutocic)	56.6% (98)	55% (11)	0.585
Instrumental	7.5% (13)	15% (3)	
Cesarean	16.2% (28)	20% (4)	
Intrapartum meconium [% (n)]	7.1% (13)	20% (4)	0.110
Arterial pH < 7.20 [% (n)]	23.7% (41)	35% (7)	0.296
Apgar Score 1 min (Mean ± SD)	8.65 ± 1.15	8.29 ± 1.53	0.244
Apgar Score 5 min (Mean ± SD)	9.72 ± 0.63	9.24 ± 1.3	0.149
Resuscitation at Birth [% (n)]	12.7% (22)	25% (5)	0.173
Neonatal data			
Birth Weight (g) (Mean ± SD)	3147.23 ± 431.42	3101.18 ± 350.69	0.674
Birth weight percentile (Mean ± SD)	44.5 ± 27.61	35.0 ± 26.16	0.182
Birth weight < 10th Percentile [% (n)]	8.7% (15)	5% (1)	0.476
Birth Weight < 2500 g [% (n)]	2.89% (5)	5% (1)	0.695
Length (cm) (Mean ± SD)	48.8 ± 2.07	49.46 ± 2.12	0.262
Length Percentile	36.58 ± 26.96	44.71 ± 30.03	0.294
Length < 10th Percentile [% (n)]	13.3% (23)	1% (2)	0.619
Head Circumference (cm) (Mean ± SD)	34.18 ± 1.33	33.69 ± 1.57	0.202
Head Circumference Percentile	45.34 ± 23.41	35.29 ± 23.34	0.131
Head Circumference < 10th percentile [% (n)]	4.6% (8)	20% (4)	0.026
Neonatal Malformations [% (n)]	1.7% (3)	0% (0)	0.692
Neonatal Complications [% (n)]	13.3% (23)	15% (3)	0.608
Puerperal Data			
Puerperal Complications [% (n)]	12.1% (21)	10% (2)	0.448
Infectious	42.8% (9)	50% (1)	0.670
Uterine Atony	14.3% (3)	50% (1)	0.312
Anemia	33.3% (7)	0% (0)	0.493
Others	33.3% (7)	50% (1)	0.565
Puerperium Hospital Stay (days) (Mean ± SD)	2.30 ± 0.61	2.13 ± 0.35	0.136

BMI Body Mass Index

No/<15 versus ≥ 15 on the PHQ-9 scale

Table 5 Moderate-to-severe anxiety, depression, and PTSD and head circumference below the 10th percentile. Logistic Regression. Univariate Logistic Regression

Variable	Odds Ratio	95% Confidence Interval	*p*-value
Alcohol	6.077	1.56–23.72	0.009
Anxiety	7.295	2.09–25.42	0.002
Depression	5.400	1.38–21.12	0.015
PTSD	5.941	1.72–20.59	0.005
At least one mental disorder	7.833	2.18–28.21	0.002
Smoker	4.364	1.43–13.37	0.010

Table 6 Moderate-to-severe anxiety, depression, and PTSD and head circumference below the 10th percentile. Logistic Regression. Bivariate Logistic Regression

Variable	Odds Ratio	95% Confidence Interval	*p*-value
Alcohol	5.295	1.294–21.658	0.020
Anxiety	6.368	1.742–23.283	0.005
Alcohol	5.323	1.331–21.281	0.018
Depression	4.227	1.009–17.707	0.049
Alcohol	4.895	1.210–19.881	0.026
PTSD	4.559	1.251–16.620	0.021
Alcohol	5.507	1.338–22.661	0.018
At least one mental pathology	7.172	1.906–26.991	0.004
Alcohol	6.092	1.559–23.809	0.009
Tobacco	1.524	0.392–5.920	0.543

Table 7 Moderate-to-severe anxiety, depression, and PTSD and head circumference below the 10th percentile. Logistic Regression. Multivariate Logistic Regression

Variable	Odds Ratio	95% Confidence Interval	*p*-value
Alcohol	6.760	1.55–29.57	0.011
At least one mental disorder	8.199	2.06–32.62	0.003
Therapy Received	2.866	0.71–11.56	0.139

None of the interaction terms between alcohol and the mental health variables were statistically significant: Alcohol*Anxiety ($p=0.431$); Alcohol*Depression ($p=0.619$); Alcohol*PTSD ($p=0.883$); Alcohol*At least one mental disorder ($p=0.211$). In the models including therapy received, the interaction terms were also not significant: Alcohol*At least one mental disorder ($p=0.218$); At least one mental disorder*Therapy received ($p=0.533$); and, Alcohol*Therapy received ($p=0.752$). Accordingly, based on the principle of parsimony, interaction terms were excluded and the models were simplified to include only main effects

mothers in delivery outcomes or gestational and puerperal complications.

Prenatal alcohol exposure is a leading preventable cause of cognitive impairment, with no safe level or timing established [45]. Fetal alcohol spectrum disorder encompasses neurodevelopmental anomalies caused by maternal alcohol use [22]. Head circumference reflects central nervous system damage, potentially resulting in microcephaly (≥ 2 standard deviations below the mean or <3rd percentile). Prenatal alcohol exposure reduces mean head circumference, brain volume, and cognitive scores [45, 46]. Our findings confirm lower mean neonatal head circumference and a higher proportion of infants below the 10th percentile among alcohol-exposed neonates, which may indicate future neurobehavioral impairments.

In our sample, only two cases involved head circumference below the 3rd percentile; hence, we grouped neonates into those with head circumference < 10th percentile and ≥ 10th percentile, assuming biometric normality between the 10th and 90th percentiles [28]. Neonates with a head circumference below the 10th percentile require close postnatal follow-up to monitor growth and identify early signs of neurodevelopmental impairment. Although microcephaly and head circumference alterations have multiple etiologies [47], those related to alcohol are preventable, underscoring the imperative for proper identification and management.

Numerous factors may jointly influence perinatal outcomes. Births with high in utero alcohol exposure are more frequently associated with maternal psychiatric diagnoses, substance use, or smoking [41]. In light of the frequent co-occurrence of substance use and mental health problems, we studied patients at risk of dual pathology—particularly focusing on alcohol consumption, a frequently overlooked element during anamnesis.

The association between alcohol consumption and reduced neonatal head circumference has been previously documented; however, the link between smaller head circumference and maternal mental health problems is less well established than subsequent neurodevelopmental alterations [48]. In cases of perinatal anxiety and PTSD, some authors have reported an association with reduced neonatal head circumference [49, 50]. Our findings are consistent with these observations: in our sample, neonatal head circumference below the 10th percentile was associated with anxiety, depression, and PTSD. Other studies, however, have not confirmed these associations, instead reporting reduced birth length in infants of mothers with depression and anxiety, without differences in birth weight or head circumference [51].

In our sample, infants of mothers with moderate anxiety required more neonatal resuscitation, which further increased when two or more mental health conditions were present, exacerbating adverse perinatal outcomes. Similar findings have been reported in infants of mothers with anxiety and depression treated with psychotropic medications [52]. The association between anxiety and Apgar scores at birth is controversial: while some authors report lower Apgar scores in untreated anxious mothers [52], others find no association [49], consistent with our results. Existing literature indicates that infants

of mothers with untreated depression exhibit higher rates of hypoxia [52]; this contrasts with our findings, which showed no differences.

Mental health problems have been linked to prematurity and low birth weight. Prenatal depression has been associated with low birth weight and preterm birth [53], though there is conflicting evidence [54, 55]. In our sample, there were no differences in perinatal outcomes between patients with and without moderate-to-severe depression, although there was a trend toward more spontaneous deliveries. Prenatal anxiety has also been associated with preterm birth and lower mean birth weight [49]. Untreated prenatal anxiety and depression have been linked to higher induction rates, cesarean deliveries, longer hospital stays, and puerperal complications such as fever and postpartum hemorrhage [52]. These associations with delivery outcomes were not confirmed in our study, nor was the link between anxiety and cesarean delivery corroborated by others [49].

Regarding PTSD, previous findings suggest that prenatal PTSD is associated with an increased risk of low birth weight and preterm birth [50, 56], although the quality of evidence is considered low according to GRADE analysis [50]. Our results did not confirm this association. Other authors have reported that patients with probable PTSD and a major depressive episode are at higher risk of preterm birth, a risk that exceeds and is independent of antidepressant and benzodiazepine use [57].

Maternal PTSD was associated with reduced neonatal head circumference, consistent with previous studies [50, 58]. Unlike other studies that assess PTSD only perinatally or postpartum, our study determined PTSD risk using a graded scale early in pregnancy, which strengthens the relationship observed in our sample.

Global maternal psychological distress has been associated with reduced neonatal head circumference [59]. In contrast, our study assessed depression, anxiety, and PTSD independently, including their severity, and also evaluated alcohol consumption separately, allowing for a more precise evaluation of the individual contributions of each factor.

Other strengths of this study should also be highlighted. The use of the ACOK screening scale enabled rapid identification of pregnant women with substance use and mental health challenges, facilitating targeted further assessment. Administering the scales at the beginning of pregnancy allowed for early recognition of risks associated with both substance use and mental disorders, with particular attention to the severity of mental health conditions. Furthermore, the comprehensive evaluation of gestational follow-up, complications, delivery outcomes, neonatal parameters, and postpartum complications provided an integrated mother–infant perspective.

Nevertheless, some limitations should be acknowledged. The relatively modest sample size for certain variables may have limited statistical power, potentially affecting the robustness of some associations. Although the confidence intervals are wide and could indicate low precision due to the sample size, the consistency of the results across the different models presented is notable. Furthermore, the interaction terms were not statistically significant, providing no evidence of moderation and suggesting that the observed associations may be consistent across models. Additionally, although performed by trained personnel, interobserver differences in the measurement of birth biometric data should be considered a potential limitation. A subset of participants received psychotherapy during pregnancy, and those assigned to the treatment-as-usual group may or may not have received pharmacological treatment, although this was not documented. However, we observed no measurable effect of these interventions on neonatal head-circumference percentiles. Importantly, all women were informed of their mental health conditions and substance-use screening results—regardless of whether they received therapy. This awareness may have influenced their behaviour, engagement with care, or other unmeasured factors, potentially introducing bias. Finally, the lack of long-term follow-up beyond pregnancy, delivery, and the puerperium to assess the impact of maternal mental health problems and alcohol exposure on child outcomes should be considered an important limitation and an area for future research.

Future studies should systematically assess the impact of treatments on adverse perinatal outcomes in women with alcohol use and mental health disorders. The effect of anxiety treatment on perinatal outcomes remains unclear [49], and evidence linking prenatal antidepressant exposure to microcephaly is weak [60, 61]. In our study, psychotherapy did not appear to modify the association between neonatal head circumference < 10th percentile and maternal alcohol use or mental health disorders.

Timely identification and management of pregnant women with substance use and mental health problems should be prioritized as a public health measure: early intervention may improve maternal well-being and mitigate preventable complications, with important social and economic benefits [53].

Conclusion

Moderate-to-severe anxiety, depression, PTSD, and alcohol use during pregnancy were associated with reduced neonatal head circumference. Further research is needed to evaluate the impact of these biometric alterations on subsequent child neurodevelopment.

Abbreviations

AC-OK	Adult Screen for Co-Occurring Disorders
AUDIT	Alcohol Use Disorders Identification Test
BMI	Body Mass Index
GAD	Generalized Anxiety Disorder
PCL-5	Posttraumatic Stress Disorder Checklist for DSM-5
PHQ	Patient Health Questionnaire
PTSD	Post-Traumatic Stress Disorder
SSL/TLS	Secure Socket Layer/Transport Layer Security
WOMAP	Woman Mental Health and Addictions on Pregnancy

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Authors' contributions
NLC and RCC conceived and designed the original study, obtained the necessary approvals, and collected the data. The analysis plan was developed by NLC, RCC, ICC, MLB, and CGG, who also curated the dataset, while CGG performed the analyses. The first draft of the manuscript was written by NLC. All authors reviewed, contributed to, and approved the final manuscript.

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Data availability
The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
The study was approved by the Clinical Research Ethics Committee of Fundación Jiménez Díaz (Ref. 2015/43) and conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Obstetrics and Gynecology, FIIB_HUISHHEN (Fundación para la investigación e innovación biomédica. Hospital Universitario Infanta Sofía. Hospital Universitario del Henares), Alfonso X el Sabio University, Madrid, Spain
[2]Psychology and Health Sciences School, Universidad a Distancia de Madrid, UDIMA (Open University of Madrid), Madrid, Spain
[3]Institute of Psychiatry and Mental Health, Hospital General Universitario Gregorio Marañón, IiSGM, CIBERSAM, ISCIII, School of Medicine, Universidad Complutense, Madrid, Spain
[4]Department of Preventive Medicine, Hospital Universitario del Tajo, Madrid, Spain
[5]Department of Personality, Evaluation and Clinical Psychology, Faculty of Psychology, Universidad Complutense Madrid, Madrid, Spain

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References

1. Carmona Camacho R, López Carpintero N, Barrigón ML, Ruiz Nogales C, Menéndez I, Sánchez Alonso M, et al. Substance use, mental health and dual disorders on pregnancy: results of prevalence and treatment rates in a developed country. Adicciones. 2022;34:299–308. https://doi.org/10.20882/adicciones.1568.
2. Howard LM, Khalifeh H. Perinatal mental health: a review of progress and challenges. World Psychiatry. 2020;19:313–27. https://doi.org/10.1002/wps.20769.
3. Woody CA, Ferrari AJ, Siskind DJ, Whiteford HA, Harris MG. A systematic review and meta-regression of the prevalence and incidence of perinatal depression. J Affect Disord. 2017;219:86–92. https://doi.org/10.1016/j.jad.2017.05.003.
4. Fairbrother N, Young AH, Janssen P, Antony MM, Tucker E. Depression and anxiety during the perinatal period: prevalence, risk factors, and treatment options. J Clin Psychiatry. 2016;77:e525–34. https://doi.org/10.4088/JCP.15r10035.
5. Geller PA, Stasko EC. Effect of previous posttraumatic stress in the perinatal period. J Obstet Gynecol Neonatal Nurs. 2017;46:912–22. https://doi.org/10.1016/j.jogn.2017.04.136.
6. Blasco-Alonso M, González-Mesa E, Gálvez Montes M, Lonzano Bravo I, Merino Galdón F, Cuenca Campos F, et al. Exposición a tabaco, alcohol y drogas de abuso en gestantes. Estudio de prevalencia en gestantes de Málaga (España). Adicciones. 2015;27:1–11. https://doi.org/10.20882/adicciones.695.
7. Tavella RA, De Abreu VOM, Muccillo-Baisch AL, Da Silva Júnior FMR. Prevalence of illicit drug use during pregnancy: a global perspective. Anais Acad Bras Cienc. 2020;92:e20200302. https://doi.org/10.1590/0001-3765202020200302.
8. Caro-Cañizares I, López Carpintero N, Carmona-Camacho R. The elephant in the room: a systematic review of the application and effects of psychological treatments for pregnant women with dual pathology (mental health and substance-related disorders). Int J Environ Res Public Health. 2024;21:392. https://doi.org/10.3390/ijerph21040392.
9. Kruger ES, Rodriguez A, Leeman L, Sanjuan PM. Prenatal substance use and mental health comorbidities predicts continued use. Psychol Addict Behav. 2024. https://doi.org/10.1037/adb0001017. Advance online publication.
10. Martín-Agudiez N, Rodríguez-Muñoz MF. Revisión del tabaquismo en el embarazo: prevalencia, perfil sociodemográfico, depresión perinatal, variables psicológicas implicadas y tratamiento. Rev Esp Salud Publica. 2024;98:1–15. https://doi.org/10.23938/resp.923.
11. Kingston D, Kehler H, Austin MP, Mughal MK, Wajid A, Vermeyden L, et al. Trajectories of maternal depressive symptoms during pregnancy and the first 12 months postpartum and child externalizing and internalizing behavior at three years. PLoS ONE. 2018;13:e0195365. https://doi.org/10.1371/journal.pone.0195365.
12. Nonnenmacher N, Noe D, Ehrenthal JC, Reck C. Postpartum bonding: the impact of maternal depression and adult attachment style. Arch Womens Ment Health. 2016;19:927–35. https://doi.org/10.1007/s00737-016-0648-y.
13. Avalos LA, Adams SR, Alexeeff SE, Oberman NR, Does MB, Ansley D, et al. Neonatal outcomes associated with in utero cannabis exposure: a population-based retrospective cohort study. Am J Obstet Gynecol. 2024;231:e1321–13213. https://doi.org/10.1016/j.ajog.2023.11.1232.
14. Kim TH, Lee H, Woo S, Lee H, Park J, Fond G, et al. Prenatal and postnatal factors associated with sudden infant death syndrome: an umbrella review of meta-analyses. World J Pediatr. 2024;20:451–60. https://doi.org/10.1007/s12519-024-00806-1.
15. Gurka KK, Burris HH, Ciciolla L, Coles CD, Massey SH, Newman S, et al. Assessment of maternal health and behavior during pregnancy in the HEALthy Brain and Child Development Study: rationale and approach. Dev Cogn Neurosci. 2025;71:101494. https://doi.org/10.1016/j.dcn.2024.101494.
16. Jarque P, Carmona M, Roca A, Barcelo B, Pichini R, Elorza MA, et al. Evaluation of three-year neurodevelopmental outcomes in infants prenatally exposed to substance use. Drug Alcohol Depend. 2024;259:111284. https://doi.org/10.1016/j.drugalcdep.2024.111284.
17. Polanska K, Jurewicz J, Hanke W. Smoking and alcohol drinking during pregnancy as the risk factors for poor child neurodevelopment—a review of epidemiological studies. Int J Occup Med Environ Health. 2015;28:419–43. https://doi.org/10.13075/ijomeh.1896.00424.
18. O'Leary CM, Nassar N, Kurinczuk JJ, Bower C. The effect of maternal alcohol consumption on fetal growth and preterm birth. BJOG. 2009;116:390–400. https://doi.org/10.1111/j.1471-0528.2008.02058.x.
19. Patra J, Bakker R, Irving H, Jaddoe VW, Malini S, Rehm J. Dose-response relationship between alcohol consumption before and during pregnancy and risks of low birthweight, preterm birth and small for gestational age: a systematic review and meta-analyses. BJOG. 2011;118:1411–21. https://doi.org/10.1111/j.1471-0528.2011.03050.x.

20. Carter RC, Jacobson SW, Molteno CD, Jacobson JL. Fetal alcohol exposure, iron-deficiency anemia, and infant growth. Pediatrics. 2007;120:559–67. https://doi.org/10.1542/peds.2007-0151.
21. Greenfield SF, Back SE, Lawson K, Brady KT. Substance abuse in women. Psychiatr Clin North Am. 2010;33:339–55. https://doi.org/10.1016/j.psc.2010.01.004.
22. Popova S, Dozet D, Shield K, Rehm J, Burd L. Alcohol's impact on the fetus. Nutrients. 2021;13:3452. https://doi.org/10.3390/nu13103452.
23. Szerman N, Torrens M, Maldonado R, Balhara YPS, Salom C, Maremmani I, et al. Addictive and other mental disorders: a call for a standardized definition of dual disorders. Transl Psychiatry. 2022;12:446. https://doi.org/10.1038/s41398-022-02212-5.
24. Alegría M, Falgas-Bague I, Collazos F, Carmona Camacho R, Lapatin Markle S, Wang Y, et al. Evaluation of the Integrated Intervention for Dual Problems and Early Action Among Latino immigrants with co-occurring mental health and substance misuse symptoms: a randomized clinical trial. JAMA Netw Open. 2019;2:e186927. https://doi.org/10.1001/jamanetworkopen.2018.6927.
25. Chavez LM, Shrout PE, Wang Y, Collazos F, Carmona R, Alegría M. Evaluation of the AC-OK mental health and substance abuse screening measure in an international sample of Latino immigrants. Drug Alcohol Depend. 2017;180:121–8. https://doi.org/10.1016/j.drugalcdep.2017.07.042.
26. Cherry AL, Dillon ME. The AC-OK cooccurring screen: reliability, convergent validity, sensitivity, and specificity. J Addict. 2013;2013:573906. https://doi.org/10.1155/2013/573906.
27. Endocrinoped. Pediatric Endocrinology Service of Hospital La Paz. Anthropometric data. Web pediátrica.com. 2025. Available from: http://www.webpediatrica.com/endocrinoped/antropometria.php.
28. Cartwright RD, Anderson NH, Sadler LC, Harding JE, McCowan LME, McKinlay CJD. Neonatal morbidity and small and large size for gestation: a comparison of birthweight centiles. J Perinatol. 2020;40:732–42. https://doi.org/10.1038/s41372-020-0631-3.
29. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med. 2001;16:606–13. https://doi.org/10.1046/j.1525-1497.2001.016009606.x.
30. Diez-Quevedo C, Rangil T, Sanchez-Planell L, Kroenke K, Spitzer RL. Validation and utility of the patient health questionnaire in diagnosing mental disorders in 1003 general hospital Spanish inpatients. Psychosom Med. 2001;63:679–86. https://doi.org/10.1097/00006842-200107000-00021.
31. Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med. 2006;166:1092–7. https://doi.org/10.1001/archinte.166.10.1092.
32. Ruiz MA, Zamorano E, García-Campayo J, Pardo A, Freire O, Rejas J. Validity of the GAD-7 scale as an outcome measure of disability in patients with generalized anxiety disorders in primary care. J Affect Disord. 2011;128:277–86. https://doi.org/10.1016/j.jad.2010.07.010.
33. Blanchard EB, Jones-Alexander J, Buckley TC, Forneris CA. Psychometric properties of the PTSD Checklist (PCL). Behav Res Ther. 1996;34:669–73. https://doi.org/10.1016/0005-7967(96)00033-2.
34. Haghish EF, Sahuquillo J, Radoi A, Pomposo I, Lozano GC. Validating the Spanish translation of the posttraumatic stress disorder checklist (PCL-5) in a sample of individuals with traumatic brain injury. Front Psychol. 2024;15:1216435. https://doi.org/10.3389/fpsyg.2024.1216435.
35. Bohn MJ, Babor TF, Kranzler HR. The Alcohol Use Disorders Identification Test (AUDIT): validation of a screening instrument for use in medical settings. J Stud Alcohol. 1995;56:423–32. https://doi.org/10.15288/jsa.1995.56.423.
36. Barrigón ML, Berrouiguet S, Carballo JJ, Bonal-Giménez C, Fernández-Navarro P, Pfang B, et al. User profiles of an electronic mental health tool for ecological momentary assessment: MEmind. Int J Methods Psychiatr Res. 2017;26:e1554. https://doi.org/10.1002/mpr.1554.
37. Ujhelyi Gomez K, Goodwin L, Chisholm A, Rose AK. Alcohol use during pregnancy and motherhood: attitudes and experiences of pregnant women, mothers, and healthcare professionals. PLoS ONE. 2022;17:e0275609. https://doi.org/10.1371/journal.pone.0275609.
38. Pehlke-Milde J, Radu I, Gouilhers S, Hammer R, Meyer Y. Women's views on moderate and low alcohol consumption: stages of the subjective transition from pregnancy to postpartum. BMC Pregnancy Childbirth. 2022;22:902. https://doi.org/10.1186/s12884-022-05247-0.
39. Sbrana M, Grandi C, Brazan M, Junquera N, Nascimento MS, Barbieri MA, et al. Alcohol consumption during pregnancy and perinatal results: a cohort study. Sao Paulo Med J. 2016;134:146–52. https://doi.org/10.1590/1516-3180.2015.02040211.
40. Nykjaer C, Alwan NA, Greenwood DC, Simpson NA, Hay AW, White KL, et al. Maternal alcohol intake prior to and during pregnancy and risk of adverse birth outcomes: evidence from a British cohort. J Epidemiol Community Health. 2014;68:542–9. https://doi.org/10.1136/jech-2013-202934.
41. Broccia M, Hansen BM, Winckler JM, Larsen T, Strandberg-Larsen K, Torp-Pedersen C, et al. Heavy prenatal alcohol exposure and obstetric and birth outcomes: a Danish nationwide cohort study from 1996 to 2018. Lancet Public Health. 2023;8:e28–35. https://doi.org/10.1016/S2468-2667(22)00263-8.
42. Reynolds CME, Egan B, O'Malley EG, McMahon L, Sheehan SR, Turner MJ. Fetal growth and maternal alcohol consumption during early pregnancy. Eur J Obstet Gynecol Reprod Biol. 2019;236:148–53. https://doi.org/10.1016/j.ejogrb.2019.02.005.
43. Bakhireva LN, Ma X, Wiesel A, Wohrer FE, DiDomenico J, Jacobson SW, et al. Dose-response effect of prenatal alcohol exposure on perinatal outcomes. Alcohol Clin Exp Res. 2024;48:703–14. https://doi.org/10.1111/acer.15284.
44. Shankar K, Ronis MJ, Badger TM. Effects of pregnancy and nutritional status on alcohol metabolism. Alcohol Res Health. 2007;30:55–9.
45. Oei JL. Alcohol use in pregnancy and its impact on the mother and child. Addiction. 2020;115:2148–63. https://doi.org/10.1111/add.15036.
46. Treit S, Zhou D, Chudley AE, Andrew G, Rasmussen C, Nikkel SM, et al. Relationships between head circumference, brain volume and cognition in children with prenatal alcohol exposure. PLoS ONE. 2016;11:e0150370. https://doi.org/10.1371/journal.pone.0150370.
47. Chien SC, Chen CP. Genetic counseling in fetal microcephaly. J Med Ultrasound. 2024;32(1):1–7. https://doi.org/10.4103/jmu.jmu_18_23.
48. Wu Y, De Asis-Cruz J, Limperopoulos C. Brain structural and functional outcomes in the offspring of women experiencing psychological distress during pregnancy. Mol Psychiatry. 2024;29:2223–40. https://doi.org/10.1038/s41380-024-02449-0.
49. Grigoriadis S, Graves L, Peer M, Mamisashvili L, Tomlinson G, Vigod SN, Dennis CL, Steiner M, Brown C, Cheung A, Dawson H, Rector NA, Guenette M, Richter M. Maternal anxiety during pregnancy and the association with adverse perinatal outcomes: systematic review and meta-analysis. J Clin Psychiatry. 2018;79(5):17r12011. https://doi.org/10.4088/JCP.17r12011.
50. Zitoun NM, Campbell MK, Gagnier J, Kamalabadi YM, Garcia-Bournissen F. Associations between PTSD and pregnancy outcomes: systematic review and meta-analysis. BMC Pregnancy Childbirth. 2025;25:802. https://doi.org/10.1186/s12884-025-07545-9.
51. Broekman BF, Chan YH, Chong YS, Kwek K, Cohen SS, Haley CL, et al. The influence of anxiety and depressive symptoms during pregnancy on birth size. Paediatr Perinat Epidemiol. 2014;28:116–26. https://doi.org/10.1111/ppe.12096.
52. Ogunyemi D, Jovanovski A, Liu J, Friedman P, Sugiyama N, Creps J, et al. The contribution of untreated and treated anxiety and depression to prenatal, intrapartum, and neonatal outcomes. AJP Rep. 2018;8:e146–57. https://doi.org/10.1055/s-0038-1661379.
53. Dadi AF, Miller ER, Bisetegn TA, Mwanri L. Global burden of antenatal depression and its association with adverse birth outcomes: an umbrella review. BMC Public Health. 2020;20:173. https://doi.org/10.1186/s12889-020-8293-9.
54. Accortt EE, Cheadle AC, Dunkel Schetter C. Prenatal depression and adverse birth outcomes: an updated systematic review. Matern Child Health J. 2015;19(6):1306–37. https://doi.org/10.1007/s10995-014-1637-2.
55. Gentile S. Untreated depression during pregnancy: Short- and long-term effects in offspring. A systematic review. Neuroscience. 2017;342:154–66. https://doi.org/10.1016/j.neuroscience.2015.09.001.
56. Sanjuan PM, Fokas K, Tonigan JS, Henry MC, Christian K, Rodriguez A, et al. Prenatal maternal posttraumatic stress disorder as a risk factor for adverse birth weight and gestational age outcomes: a systematic review and meta-analysis. J Affect Disord. 2021;295:530–40. https://doi.org/10.1016/j.jad.2021.08.079.
57. Yonkers KA, Smith MV, Forray A, Epperson CN, Costello D, Lin H, et al. Pregnant women with posttraumatic stress disorder and risk of preterm birth. JAMA Psychiatry. 2014;71:897–904. https://doi.org/10.1001/jamapsychiatry.2014.558.
58. Engel SM, Berkowitz GS, Wolff MS, Yehuda R. Psychological trauma associated with the World Trade Center attacks and its effect on pregnancy outcome. Paediatr Perinat Epidemiol. 2005;19:334–41. https://doi.org/10.1111/j.1365-3016.2005.00676.x.

59. MacGinty RP, Kariuki SM, Barnett W, Wedderburn CJ, Hardy A, Hoffman N, et al. Associations of antenatal maternal psychological distress with infant birth and development outcomes: results from a South African birth cohort. Compr Psychiatry. 2020;96:152128. https://doi.org/10.1016/j.comppsych.2019.152128.
60. Sánchez N, Juárez-Balarezo J, Olhaberry M, González-Oneto H, Muzard A, Mardonez MJ, et al. Depression and antidepressants during pregnancy: craniofacial defects due to stem/progenitor cell deregulation mediated by serotonin. Front Cell Dev Biol. 2021;9:632766. https://doi.org/10.3389/fcell.2021.632766.
61. Koc D, Tiemeier H, Stricker BH, Muetzel RL, Hillegers M, El Marroun H. Prenatal antidepressant exposure and offspring brain morphologic trajectory. JAMA Psychiatry. 2023;80:1208–17. https://doi.org/10.1001/jamapsychiatry.2023.3161.

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