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Antibiotic Exposure during Pregnancy and Risk of Prenatal Depression

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Abstract

Depression during pregnancy is widespread and can have serious outcomes. Prior evidence has hinted that antibiotic treatment may be linked to depressive disorders. Because many pregnant individuals receive antibiotics, further study of this potential connection is necessary. This study used data from a nationwide, prospective online survey of pregnant participants in their third trimester. Antenatal depressive symptoms (ADSs) were identified by an Edinburgh Postnatal Depression Scale score of 13 or higher, or by a diagnosed depressive disorder. Among participants, 16.5% (n = 977) reported ADSs, and 37.9% of these individuals had a clinical diagnosis of depression. No significant association emerged between antibiotic exposure and the onset of ADSs. Four independent predictors of ADSs were identified: a prior history of depression, severe nausea and vomiting resulting in inability to eat, emotional abuse from a partner in the past year, and absence of a university qualification. The findings indicate no link between antibiotic use during pregnancy and depressive symptoms. Because undiagnosed depression remains common, new antenatal care strategies targeting individuals with identifiable risk factors may be needed.

Keywords: Pregnancy, Perinatal care, Depression, Antibiotic exposure, Risk factors, Maternal wellbeing

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Introduction

Depression affects roughly 322 million people worldwide, with a higher frequency among women than men (5.1% vs. 3.6%) [1]. During pregnancy, depressive symptoms are common, affecting up to one in five expectant individuals [2]. Although rates in the first trimester resemble those in non-pregnant women, the prevalence nearly doubles in the second and third trimesters [3].

Antenatal depressive symptoms (ADSs) can lead to considerable complications for both the mother and child. They are associated with higher maternal morbidity, obstetric complications, and increased rates of operative deliveries [4]. Evidence also points to a greater likelihood of preterm birth [5, 6] and low infant birth weight [5,7]. Babies born to parents with ADSs may experience lower rates of breastfeeding initiation [6] and poorer cognitive outcomes [8]. Furthermore, ADSs strongly predict postpartum depression [9], which can interfere with early bonding and child development [10].

Several social, psychological, and biological elements contribute to the development of ADSs [9,11]. A less explored potential factor is antibiotic exposure during pregnancy. Around 33% of pregnant individuals are

prescribed oral antibiotics, and roughly one-third of them receive multiple prescriptions [12]. Most are given for urinary, skin, respiratory, or ear infections, although some prescriptions occur without clear medical need [12]. Antibiotics alter the gut microbial environment, which plays a role in emotional regulation [13], and pregnancy itself modifies these microbial populations [14].

Previous research has noted a possible relationship between antibiotic use and depression [15]. For instance, Field et al. [16] investigated antibiotic exposure as a predictor of antenatal depression, but earlier studies have shown significant design flaws—particularly the omission of well-established predictors such as prior depression history [2,11]. Recognizing this gap, the present work was designed to re-examine the association in a more controlled manner.

The primary objective of this study was to determine whether antibiotic exposure during pregnancy is linked to depressive symptoms, after accounting for known risk factors. Secondary objectives included estimating the current rate of ADSs in Australia and identifying related variables. It was hypothesized that exposure to antibiotics during the antenatal period would be associated with an increased likelihood of ADSs.

Materials and Methods

Study framework and participant group

The information discussed here derives from a continuing nationwide, forward-looking cohort project in Australia titled "The Maternal Experience Study: Determinants of health and wellbeing after childbirth." Full methodological details are outlined elsewhere [17]. Briefly, the project involves four web-based questionnaires administered across pregnancy and the first postpartum year. The initial survey is completed during the latter part of the third trimester (approximately 32 weeks of gestation), while the remaining three are conducted at around 6 weeks, 6 months, and 12 months after delivery. The present paper reports findings from the antenatal phase. Although the study's original emphasis was on depressive symptoms after birth, that portion of data collection was still active during this analysis.

Participants were recruited through a voluntary response process. Recruitment was carried out using a variety of approaches, such as digital promotion on pregnancy-related Facebook communities (for example, Pregnancy Support Group Australia), paid advertisements across Facebook, Google, and Instagram, and the distribution of printed flyers in obstetric, radiology, and midwifery clinics, supermarkets, and prenatal wellness spaces (like yoga studios for expectant mothers). This multi-faceted strategy aimed to minimise recruitment bias, but it meant a response rate could not be determined. Incentives were offered via 41 gift-voucher prize draws for participants completing the study. Eligible pregnant people were enrolled between August 2021 and June 2022 and could give consent at any stage of their pregnancy. Antenatal questionnaires were distributed from 32 weeks' gestation onward (August 2021–November 2022). If the survey was not completed, two follow-up reminders were sent roughly two weeks apart.

The 32-week threshold was selected to examine the influence of antibiotic use during pregnancy on antenatal depression while maintaining consistency across participants, as physiological and emotional states differ by trimester. Collecting data later in pregnancy risked losing participants due to preterm labour, so that stage was avoided. Items related to antenatal depression were added several months into recruitment. Eligible participants were required to be aged 18 years or older and living in Australia. Surrogates were prospectively excluded. For this specific analysis, individuals who had experienced miscarriage or stillbirth before completing the questionnaire were excluded retrospectively. The University of Tasmania Human Research Ethics Committee approved the project (H0021790).

Variables and outcome assessment

Validated instruments or previously tested items were used wherever available [17], including the Edinburgh Postnatal Depression Scale (EPDS) [18]. The EPDS, a 10-item instrument originally designed to detect postpartum depressive symptoms, has also been validated for antenatal use [19]. A score of 13 or above—the accepted threshold for likely major depression—has been adopted in both Australian and global research [18,20–24]. According to the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG), those meeting or exceeding this score should be clinically reviewed, as it can indicate crisis-level distress [25]. The main variable of interest (depressive symptoms) was defined as an EPDS score of at least 13 and/or a clinical diagnosis of depression made or confirmed by a medical professional (general practitioner, psychiatrist, or obstetrician) during the pregnancy in question.

Participants were also asked if they had taken antibiotics while pregnant. Affirmative responses required further details, including the drug name, dose, treatment duration, number of courses, and the trimester in which they were used. To reduce confounding from infection-related illness, participants were screened for antibiotic use in the preceding 14 days. If they had recently finished or were still taking antibiotics, they were asked to delay survey completion until at least two weeks after the reported treatment end date. This two-week window allowed a week for recovery and another for mental health evaluation, consistent with the EPDS, which captures mood experiences over the prior seven days.

Analytical procedures

Survey construction and data collection were carried out using Research Electronic Data Capture (REDCap) [26], a secure web-based data management platform. Afterward, data were exported into Microsoft Excel for cleaning, including range and logic verifications. The anonymised dataset was then analysed using IBM® SPSS Statistics version 27.0 (Armonk, NY, USA). Quantitative variables were based on validated tools and scales (see [17] for protocol). Variables related to depression, anxiety, stress, sleep quality, social connectedness, and intimate partner abuse within the past 12 months were grouped according to established classification ranges. Other data points, such as antibiotic use and exercise participation, were coded dichotomously (yes/no). Frequency and percentage summaries were used for categorical data, and mean ± standard deviation for continuous variables such as age and gestational week.

Statistical testing began with bivariate analyses, followed by multivariable logistic regression. Missing data were handled through listwise deletion. Variables showing $p < 0.01$ at the bivariate level were tested for multicollinearity and interdependence ($p < 0.001$ considered significant) before inclusion in the regression model predicting depression. The sample size was determined using Peduzzi's equation [27], assuming ten independent predictors and an estimated antenatal depressive symptom (ADS) prevalence of 5.9% [28]. Accounting for a projected 30% attrition rate, the required sample size was 2203. Statistical significance for the final model was set at $p < 0.05$.

Because data were collected only in the third trimester, potential discrepancies in timing between antibiotic use and depressive symptom onset could not be ruled out. To account for this, a sensitivity test was performed using only the EPDS ≥13 criterion as the dependent variable, since its timing relative to any reported antibiotic exposure was precisely known within the same dataset.

Results

Participant profile and demographic summary

A total of 1,583 people agreed to join the research, of whom 977 completed the section concerning antenatal depression. Surveys were submitted between 31.9 and 42.0 weeks of gestation, with an average of 33.4 weeks (SD = 2.1). Most respondents held higher education qualifications, lived with a partner, and were Australian-born **(Table 1).** Ages ranged between 18 and 51 years, averaging 32.1 years (SD = 3.9). Participants were drawn from every Australian state and territory, with the largest representation from New South Wales (232; 23.8%) and Victoria (229; 23.5%), followed by Tasmania (162; 16.6%) and Queensland (159; 16.3%). Nearly all respondents self-identified as female, with one identifying as non-binary, another as both non-binary and female, and one person choosing not to specify gender.

Table 1. Basic participant demographics and relationship to depressive symptoms (n = 977)

Characteristics	n	No Depressive Symptoms (%)	With Depressive Symptoms (%)	p-Value	unadjOR (95% CI)
Age Groups					
18–25 years	963	24 (3.0)	11 (6.9)	0.010	
26–35 years		630 (78.4)	129 (81.1)		
36 years and older		150 (18.7)	19 (11.9)		
Indigenous Status					
Non-Aboriginal or Torres Strait Islander	976	805 (98.8)	155 (96.3)	0.035	
Aboriginal or Torres Strait Islander		10 (1.2)	6 (3.7)		
Migration Status					
Born in Australia	975	678 (83.3)	128 (79.5)	0.305	
Immigrated ≤ 10 years ago		53 (6.5)	16 (9.9)		
Immigrated > 10 years ago		83 (10.2)	17 (10.6)		
Relationship Status					
Married or cohabiting	976	791 (96.9)	150 (93.8)	0.061	
Single, separated, divorced, or in a relationship		25 (3.1)	10 (6.3)		
Household Income (Fortnightly, After Tax)					
< AUD 2000	940	70 (8.9)	27 (17.9)	<0.001	1.0
AUD 2000–5000		515 (65.3)	109 (72.2)		0.55 (0.34–0.90)
> AUD 5000		204 (25.9)	15 (9.9)		0.19 (0.10–0.38)
Education Level					
Non-university education #	977	169 (20.7)	57 (35.4)	<0.001	1.0
University degree		647 (79.3)	104 (64.6)		0.48 (0.33–0.69)
Employment Status					
Unpaid work, study, or other	977	96 (11.8)	37 (23.0)	<0.001	1.0
Paid employment		720 (88.2)	124 (77.0)		0.45 (0.29–0.68)

Totals may not reach 977 due to missing entries. CI = confidence interval; EPDS = Edinburgh Postnatal Depression Scale; unadjOR = unadjusted odds ratio.

Includes those with certificates/diplomas, apprenticeships, Year 10 or 12 qualifications, or no formal education.

A history of mental illness, including depression, was reported by 43.5% of respondents. Approximately one in five participants had used antibiotics during pregnancy **(Table 2)**, most frequently in the first or second trimester (Table S1). In contrast, probiotic intake peaked in the third trimester (Table S1). More than two-thirds of participants indicated that their pregnancy experience—such as appointments or birth planning—was influenced by the COVID-19 pandemic, and over half described the pandemic's isolation measures as having a moderate to severe negative effect on their mental wellbeing (Table S2).

Table 2. Medical and pregnancy-related factors and their association with depressive symptoms (n = 977)

Characteristics	n	No Depressive Symptoms (%)	With Depressive Symptoms (%)	p-Value	unadjOR (95% CI)
Pregnancy Planning					
Unplanned pregnancy	967	131 (16.2)	45 (28.5)	<0.001	1.0
Planned pregnancy		678 (83.8)	113 (71.5)		0.49 (0.33–0.72)
Pregnancy Type					
Singleton pregnancy	975	805 (98.8)	157 (98.1)	0.458	
Multiple pregnancy		10 (1.2)	3 (1.9)		
Gestational Diabetes Status					
No gestational diabetes	963	699 (87.0)	133 (83.1)	0.206	
Gestational diabetes		104 (13.0)	27 (16.9)		
Blood Pressure Status					
No hypertensive disorders	963	780 (97.1)	153 (95.6)	0.319	
Hypertensive disorders		23 (2.9)	7 (4.4)		
Pain Status					
No pain reported	977	369 (45.2)	65 (40.4)	0.261	
Pain reported		447 (54.8)	96 (59.6)		
Iron-Related Conditions					
No iron deficiency, anemia, or thalassemia	963	781 (97.3)	154 (96.3)	0.445	
Iron deficiency, anemia, or thalassemia		22 (2.7)	6 (3.8)		
Eating Ability					
Able to eat (with or without nausea/vomiting)	963	741 (92.3)	133 (83.1)	0.001	1.0
Nausea/vomiting preventing eating		62 (7.7)	27 (16.9)		2.43 (1.49–3.95)
Antibiotic Use					
No antibiotics used	970	663 (81.7)	125 (79.1)	0.504	
Antibiotics used during pregnancy		149 (18.3)	33 (20.9)		
Probiotic Use					
No probiotics used	971	627 (77.2)	124 (78.0)	0.837	
Probiotics used during preconception/pregnancy		185 (22.8)	35 (22.0)		

Totals may vary from 977 due to missing responses. CI = confidence interval; EPDS = Edinburgh Postnatal Depression Scale; unadjOR = unadjusted odds ratio.

Prevalence of antenatal depressive symptoms

During their pregnancy, 61 participants (6.2%) reported receiving a professional diagnosis of depression. An additional 100 respondents (10.2%, n = 977) recorded EPDS scores ≥13 during the third trimester. Taken together, the overall point incidence of depressive symptoms during the current pregnancy was 16.5% (161 of 977). Of those who reported a clinical diagnosis, 24 individuals (39.3%, n = 61) did not show elevated EPDS scores at the time of survey completion.

Bivariate findings

The central purpose of analysis was to explore whether antibiotic use during pregnancy correlated with depressive symptoms. No statistically meaningful link was found **(Table 2)**. Similarly, the use of probiotics either prior to conception or during gestation did not demonstrate any protective or predictive relationship with depressive outcomes.

A negative association emerged between depressive symptoms and several socioeconomic and psychosocial factors. Specifically, individuals with household incomes ≥AUD 2000 per fortnight post-tax **(Table 1)** or those reporting moderate to high levels of social support **(Table 3)** were less likely to experience depressive symptoms. Holding a tertiary qualification, being employed in paid work, and having a planned pregnancy were also related to lower odds of antenatal depression **(Tables 1 and 2)**. Furthermore, participants who engaged in physical activity during pregnancy showed reduced likelihood of depressive symptoms **(Table 4)**.

Table 3. Social and psychological characteristics before and during pregnancy in relation to depressive symptoms (n = 977)

Characteristics	n	No Depressive Symptoms (%)	With Depressive Symptoms (%)	p-Value	unadjOR (95% CI)
Personal Depression History					
No prior depression diagnosis	977	629 (77.1)	67 (41.6)	<0.001	1.0
Prior depression diagnosis		187 (22.9)	94 (58.4)		4.72 (3.31–6.72)
Family Mental Health History					
No family history of mental health issues	975	456 (56.0)	60 (37.3)	<0.001	1.0
Family history of mental health issues		358 (44.0)	101 (62.7)		2.14 (1.51–3.04)
Social Support Level					
Low social support	977	78 (9.6)	56 (34.8)	<0.001	1.0
Moderate social support		304 (37.3)	60 (37.3)		0.28 (0.18–0.43)
High social support		434 (53.2)	45 (28.0)		0.14 (0.09–0.23)
Emotional Abuse by Partner					
No emotional abuse by partner in past 12 months	966	649 (80.5)	107 (66.9)	<0.001	1.0
Emotional abuse by partner in past 12 months		157 (19.5)	53 (33.1)		2.05 (1.41–2.97)
Physical Abuse by Partner					
No physical abuse by partner in past 12 months	966	794 (98.5)	155 (96.9)	0.180	
Physical abuse by partner in past 12 months		12 (1.5)	5 (3.1)		

Totals may differ due to missing information. CI = confidence interval; EPDS = Edinburgh Postnatal Depression Scale; unadjOR = unadjusted odds ratio.

Table 4. Lifestyle, parity, and behavioural characteristics associated with depressive symptoms (n = 977)

Characteristics	n	No Depressive Symptoms (%)	With Depressive Symptoms (%)	p-Value	unadjOR (95% CI)
Parity Status					
No previous births #	977	452 (55.4)	87 (54.0)	0.111	
One previous birth		269 (33.0)	63 (39.1)		
Multiple previous births		95 (11.6)	11 (6.8)		
Pre-Conception BMI					
Underweight BMI before pregnancy	966	22 (2.7)	2 (1.3)	0.033	
Healthy BMI before pregnancy		380 (47.1)	61 (38.4)		
Overweight BMI before pregnancy		232 (28.7)	46 (28.9)		
Obese BMI before pregnancy		173 (21.4)	50 (31.4)		
Cigarette Smoking During Pregnancy					
Non-smoker during pregnancy	977	788 (96.6)	143 (88.8)	<0.001	1.0
Occasional or regular smoker during pregnancy &		28 (3.4)	18 (11.2)		3.54 (1.91–6.57)
Alcohol Consumption During Pregnancy					
No alcohol use during pregnancy	977	703 (86.2)	143 (88.8)	0.381	
Alcohol use during pregnancy		113 (13.8)	18 (11.2)		
Physical Activity During Pregnancy					
Not physically active during pregnancy	973	69 (8.5)	30 (18.9)	<0.001	1.0
Physically active during pregnancy		745 (91.5)	129 (81.1)		0.40 (0.25–0.64)

Totals may not add up to 977 due to missing data.
Nulliparous: never previously given birth (any outcome).
Primiparous: one prior birth, including stillbirth (loss after 20 weeks).
Multiparous: more than one prior birth, including stillbirth.
& Includes individuals who ceased smoking upon confirmation of pregnancy.
BMI = body mass index; CI = confidence interval; EPDS = Edinburgh Postnatal Depression Scale; unadjOR = unadjusted odds ratio.

Conversely, smoking during pregnancy and experiencing severe vomiting that interfered with eating were both associated with a higher likelihood of depressive symptoms **(Tables 2 and 4)**. Increased risk was also evident among those with a personal history of depression, a family history of mental health disorders, or who had endured emotional abuse from an intimate partner in the previous 12 months **(Table 3)**.

Adjusted statistical findings

This research examined a comprehensive array of variables previously linked to the onset of antenatal depressive symptoms (ADSs). To minimize bias, factors

entered into the multivariable logistic regression were chosen selectively. Some variables—such as those related to sleep disturbance, stress, and anxiety (Table S2)—though significant in the bivariate analysis, were excluded from the final model because they could reflect depressive symptomatology rather than independent risk factors.

Interrelationships among several predictors were also identified (Table S3). For instance, social support demonstrated strong correlations ($p < 0.001$) with six other independent measures, one being educational level. Similar relationships were found between planned pregnancy and physical activity. In the analysis, education was treated as a primary indicator of socioeconomic position, preferred over income or employment due to its closer association with smoking habits.

Among the overlapping mental health variables, personal history of depression was retained in preference to family mental health history, since (i) participants could more reliably report their own clinical background and (ii) previous evidence identifies personal depression history as a key predictor of antenatal mood disorders [2, 11, 29].

Consequently, the multivariate regression model included four significant predictors **(Table 5)**. Each variable maintained statistical significance. Participants reporting a history of depression, severe nausea or vomiting that hindered food intake, or emotional abuse by a partner during the prior 12 months were at heightened risk of developing ADSs. Conversely, university-level education showed a protective association. To confirm that antibiotic exposure was not masked by other factors, a sensitivity test reintroduced this variable into the regression, which again demonstrated no meaningful link with depressive outcomes **(Table 5)**.

Table 5. Logistic regression model for predictors of depressive symptoms during pregnancy (n = 977)

Characteristics	adjOR (95% CI)	p-Value	adjOR (95% CI) Including Antibiotic	p-Value Including Antibiotic
Education Level				
Non-university education #	1.0	0.005	1.0	0.007
University degree	0.57 (0.38–0.84)		0.58 (0.39–0.86)	
Personal Depression History				
No prior depression diagnosis	1.0	<0.001	1.0	<0.001
Prior depression diagnosis	4.21 (2.92–6.05)		4.05 (2.81–5.85)	
Emotional Abuse by Partner				
No emotional abuse by partner in past 12 months	1.0	0.001	1.0	0.001
Emotional abuse by partner in past 12 months	1.91 (1.28–2.84)		1.98 (1.33–2.95)	
Eating Ability				
No nausea/vomiting or able to eat despite nausea/vomiting	1.0	0.019	1.0	0.014
Nausea/vomiting preventing eating	1.91 (1.11–3.26)		1.96 (1.14–3.36)	
Antibiotic Use				
No antibiotics used			1.0	0.730
Antibiotics used during pregnancy			0.92 (0.58–1.46)	

adjOR: adjusted odds ratio; CI: confidence interval; EPDS: Edinburgh Postnatal Depression Scale.

Other education categories comprise certificates/diplomas, trade or apprenticeship qualifications, Year 10 or 12 equivalents, or no formal schooling.

When repeating the analysis using only EPDS ≥13 as the dependent outcome, findings remained largely consistent. Apart from the previously identified predictors, age emerged as significant ($p < 0.01$), indicating that depressive symptom likelihood declined with increasing maternal age. Only five variables showing initial significance were included in the refined logistic regression. In that adjusted model, age ceased to be significant, and the same four core predictors—prior depression, severe nausea/vomiting, recent partner abuse, and lack of tertiary education—remained independently associated ($p < 0.05$).

Discussion

This investigation represents the first comprehensive exploration of whether antibiotic use during pregnancy contributes to antenatal depressive symptomatology. The findings revealed no evidence of a causal or statistical relationship. The only comparable study, conducted in the United States (USA), found that antibiotic exposure in the first 20 weeks of gestation correlated with a 50% higher likelihood of depression at 20 weeks when compared with non-exposed pregnancies [16]. However, that study lacked multivariate adjustment, leaving many socioeconomic and

psychosocial factors unaccounted for. Its sample population also consisted largely of lower- to middle-income participants, whereas the current cohort primarily represented middle- to upper-income, tertiary-educated individuals.

The variation in reported depression rates is striking: Field et al. [16] documented a 42.0% prevalence of depressive symptoms, while the present analysis recorded only 16.5%. Differences in socioeconomic profile may partly explain this, since previous U.S. evidence links lower socioeconomic conditions with higher depressive symptom rates in later pregnancy [30].

A secondary goal of this research was to provide an updated estimate of antenatal depression incidence in Australia and contrast it with prior national data. Based on the criteria of either a clinical diagnosis or an EPDS score ≥13, the current point incidence was 16.5%. Pre-pandemic Australian studies reported substantially lower figures—5.9% to 8.9%—across cohorts ranging from 1,507 to 53,032 participants [24,28,31]. Those earlier investigations recruited from antenatal clinics [28,31] or via hospital invitation mailings [24] during 2002–2005 [24,31] and 2014–2016 [28]. Only one comparable study [32], also clinic-based, identified a similar rate of 15.2% (data from 2002–2004, n = 1,578).

Comparison with previous research

Since the beginning of the COVID-19 pandemic, multiple Australian investigations have reported on the frequency of antenatal depressive symptoms (ADSs), each applying an EPDS threshold of 13 and adopting comparable recruitment and data-collection methods (mainly paid or unpaid social media advertising and online surveys). In temporal sequence, based on their respective data collection periods, the reported prevalence rates were 26.5% (n = 1219, August 2020–February 2021) [33], 26.7% (n = 1607, July 2020–January 2021) [34], and 16.4% (n = 269, September 2020–November 2021) [35].

In the current research, 14.0% of respondents recorded an EPDS score ≥13 (n = 977, August 2021–November 2022). The comparatively higher figures in the studies by Lequertier et al. [33] and Davis et al. [34] may be linked to the period during which stringent lockdown measures and border closures were first introduced in Australia [33] and before the national COVID-19 vaccination program commenced [36]. Conversely, over half the data from Frankham et al. [35], and all of the data from the present analysis, were obtained after the vaccine rollout began in February 2021, which could explain the observed decline in ADS incidence.

Key predictors of antenatal depressive symptoms

Although antibiotic exposure was not identified as a determinant of ADSs, this study confirmed four independent predictors previously noted in the literature. A personal history of depression was found to strongly predict depressive symptoms during pregnancy, consistent with findings from earlier studies [37–40]. For instance, Bisetegn et al. [39] and Biratu et al. [40] reported comparable results (adjOR = 3.48, 95% CI 1.71–7.06, $p < 0.01$ and adjOR = 2.57, 95% CI 1.48–4.48, $p < 0.001$, respectively).

Similarly, emotional abuse by an intimate partner within the previous year was another significant correlate, aligning with a meta-analysis of 70 studies linking lifetime abuse experiences (including emotional abuse) to increased risk of ADSs [41]. Another variable associated with antenatal depression in this study was severe nausea or vomiting that impaired food intake. Prior research has demonstrated comparable outcomes, with individuals affected by hyperemesis gravidarum showing a higher likelihood of ADSs (OR = 2.99, 95% CI 1.17–7.64, $p = 0.022$ [42]; OR = 14.4, 95% CI 5.29–39.44, $p < 0.001$ [43]). In contrast, higher educational attainment appeared protective, echoing results from Abujilban et al. [44].

Clinical and public health implications

These findings represent associations rather than causal relationships. Nevertheless, they underscore the importance of routine and comprehensive depression screening during pregnancy—especially among those of lower socioeconomic status, those with a history of mental illness or abuse, or those suffering from severe nausea and vomiting.

In this study, 16.5% of participants experienced ADSs, yet only about 37.9% of these individuals had received a clinical diagnosis. This gap may reflect temporary mood disturbances, greater candor during anonymous surveys, or an underutilization of screening practices, particularly relevant given the well-established link between antenatal and postnatal depression [45].

Healthcare professionals—especially obstetricians, midwives, and general practitioners—are in a prime position to provide empathetic, confidential, and proactive screening. Routine integration of standardised tools such as the EPDS into prenatal visits is a minimum standard [29]. More advanced strategies employ multidisciplinary coordination, as demonstrated in New South Wales under the "SAFE START Strategic Policy" [46] and "Perinatal Integrated Psychosocial Assessment" [47]. These frameworks incorporate structured psychosocial questionnaires alongside the EPDS to identify individuals requiring further review.

However, neither framework currently screens for three of the additional predictors verified in this study—severe nausea/vomiting, lack of tertiary education, and recent emotional abuse. Future investigations could explore how incorporating these factors affects each model's sensitivity, specificity, and practicality.

Study limitations

Several limitations should be acknowledged. First, the study depended on self-reported data, introducing potential recall and cognitive biases. To counteract this, surveys were anonymous, and validated instruments were used wherever possible. Second, data concerning antibiotic usage were gathered during the late third trimester, while most reported use occurred in earlier trimesters, possibly affecting accuracy. Only six participants were uncertain about antibiotic use, and two misclassified antiviral or antifungal treatments as antibiotics. It remains possible that some participants misreported medication class, as many omitted specifying the drug names, preventing sub-analysis by antibiotic category.

Another constraint was the absence of data on pre-conception antibiotic exposure, which might be relevant since gut microbiota alterations can persist for months post-treatment [48]. Due to voluntary participation, it was also impossible to determine causes of attrition or non-completion, though the emergence of depression could have influenced these outcomes.

The study sample largely consisted of well-educated individuals with high socioeconomic standing, potentially biasing results toward a lower ADS incidence. Moreover, using the term "wellbeing" in recruitment materials may have drawn participants less likely to experience depression. These aspects limit the generalizability of findings. Despite not reaching the target sample size, this shortfall was mitigated by an observed ADS rate nearly triple the projected value.

Conclusions

This study found no significant relationship between antibiotic exposure during pregnancy and the onset of antenatal depressive symptoms. Nonetheless, four independent risk factors were reconfirmed: previous depression, emotional abuse, severe nausea or vomiting, and lower educational attainment.

The data also revealed that while ADSs are relatively common (16.5%), many affected individuals do not receive a formal diagnosis. Future studies should explore the barriers to recognition among those with elevated EPDS scores, ensuring improved detection and support pathways for maternal mental health.

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References

1. World Health Organization. Depression and other common mental disorders global health estimates [Internet]. Geneva: World Health Organization; 2017 [cited 2020 Apr 16]. Available from: https://apps.who.int/iris/bitstream/handle/10665/254610/WHO-MSD-MER-2017.2-eng.pdf
2. Yin X, Sun N, Jiang N, Xu X, Gan Y, Zhang J, et al. Prevalence and associated factors of antenatal depression: systematic reviews and meta-analyses. Clin Psychol Rev. 2021;83:101932.
3. Bennett HA, Einarson A, Taddio A, Koren G, Einarson TR. Prevalence of depression during pregnancy: systematic review. Obstet Gynecol. 2004;103(4):698-709.
4. Jahan N, Went TR, Sultan W, Sapkota A, Khurshid H, Qureshi IA, et al. Untreated depression during pregnancy and its effect on pregnancy outcomes: a systematic review. Cureus. 2021;13:e17251.
5. Grote NK, Bridge JA, Gavin AR, Melville JL, Iyengar S, Katon WJ. A meta-analysis of depression during pregnancy and the risk of preterm birth, low birth weight, and intrauterine growth restriction. Arch Gen Psychiatry. 2010;67(10):1012-24.
6. Grigoriadis S, VonderPorten EH, Mamisashvili L, Tomlinson G, Dennis CL, Koren G, et al. The impact of maternal depression during pregnancy on perinatal outcomes: a systematic review and meta-analysis. J Clin Psychiatry. 2013;74(06):e321-41.
7. Li X, Gao R, Dai X, Liu H, Zhang J, Liu X, et al. The association between symptoms of depression during pregnancy and low birth weight: a prospective study. BMC Pregnancy Childbirth. 2020;20:147.
8. Koutra K, Chatzi L, Bagkeris M, Vassilaki M, Bitsios P, Kogevinas M. Antenatal and postnatal maternal mental health as determinants of infant neurodevelopment at 18 months of age in a mother-child cohort (Rhea Study) in Crete, Greece. Soc Psychiatry Psychiatr Epidemiol. 2013;48(8):1335-45.
9. Howard LM, Molyneaux E, Dennis CL, Rochat T, Stein A, Milgrom J. Non-psychotic mental disorders in the perinatal period. Lancet. 2014;384(9956):1775-88.
10. Slomian J, Honvo G, Emonts P, Reginster JY, Bruyere O. Consequences of maternal postpartum depression: a systematic review of maternal and infant outcomes. Womens Health. 2019;15:e1745506519844044.
11. Míguez MC, Vázquez MB. Risk factors for antenatal depression: a review. World J Psychiatry. 2021;11(3):325-36.
12. Petersen I, Gilbert R, Evans S, Ridolfi A, Nazareth I. Oral antibiotic prescribing during pregnancy in

primary care: UK population-based study. J Antimicrob Chemother. 2010;65(10):2238-44.
13. Sherwin E, Sandhu KV, Dinan TG, Cryan JF. May the force be with you: the light and dark sides of the microbiota-gut-brain axis in neuropsychiatry. CNS Drugs. 2016;30(11):1019-41.
14. Su Y, Gan XP, Li FF, Zhang DY, Chen L, Cao YN, et al. Effect of exposure to antibiotics on the gut microbiome and biochemical indexes of pregnant women. BMJ Open Diabetes Res Care. 2021;9: e002321.
15. Pouranayatihosseinabad M, Bezabih Y, Hawrelak J, Peterson GM, Veal F, Mirkazemi C. Antibiotic use and the development of depression: a systematic review. J Psychosom Res. 2022;164:111113.
16. Field T, Hernandez-Reif M, Diego M. Risk factors and stress variables that differentiate depressed from nondepressed pregnant women. Infant Behav Dev. 2006;29(2):169-74.
17. Pouranayatihosseinabad M, Taylor M, Hawrelak J, Peterson GM, Veal F, et al. Maternal antibiotic exposure and the risk of developing antenatal or postpartum depressive symptoms: the maternal experience study protocol. Methods Protoc. 2023;6(3):98.
18. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. Br J Psychiatry. 1987;150:782-6.
19. Murray D, Cox JL. Screening for depression during pregnancy with the Edinburgh depression scale (EDDS). J Reprod Infant Psychol. 1990;8(1):99-107.
20. Boyce P, Stubbs J, Todd A. The Edinburgh Postnatal Depression Scale: validation for an Australian sample. Aust N Z J Psychiatry. 1993;27(4):472-6.
21. Murray L, Carothers AD. The validation of the Edinburgh Post-natal Depression Scale on a community sample. Br J Psychiatry. 1990;157:288-90.
22. Brooks J, Nathan E, Speelman C, Swalm D, Jacques A, Doherty D. Tailoring screening protocols for perinatal depression: prevalence of high risk across obstetric services in Western Australia. Arch Women's Ment Health. 2009;12(2):105-12.
23. Norhayati MN, Hazlina NH, Asrenee AR, Emilin WM. Magnitude and risk factors for postpartum symptoms: a literature review. J Affect Disord. 2015;175:34-52.
24. Woolhouse H, Gartland D, Mensah F, Brown SJ. Maternal depression from early pregnancy to 4 years postpartum in a prospective pregnancy cohort study: implications for primary health care. BJOG. 2015;122(3):312-21.
25. The Royal Australian and New Zealand College of Obstetricians and Gynaecologists. Mental health care in the perinatal period [Internet]. Melbourne: RANZCOG; 2019 [cited 2020 Jun 19]. Available from: https://ranzcog.edu.au/wp-content/uploads/2022/05/Mental-Health-Care-in-the-Perinatal-Period-C-Obs-48.pdf
26. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009;42(2):377-81.
27. Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A simulation study of the number of events per variable in logistic regression analysis. J Clin Epidemiol. 1996;49(12):1373-9.
28. Khanlari S, Eastwood J, Barnett B, Naz S, Ogbo FA. Psychosocial and obstetric determinants of women signalling distress during Edinburgh Postnatal Depression Scale (EPDS) screening in Sydney, Australia. BMC Pregnancy Childbirth. 2019;19:407.
29. Buist A, Bilszta J, Milgrom J, Condon J, Speelman C, Hayes B, et al. The Beyondblue national postnatal depression program, prevention and early intervention 2001–2005, final report. The National Depression Initiative [Internet]. Sydney: Beyondblue; 2006 [cited 2023 Aug 23]. Available from: https://studylib.net/doc/8396554/the-beyondblue-national-postnatal-depression-program-prev
30. Goyal D, Gay C, Lee KA. How much does low socioeconomic status increase the risk of prenatal and postpartum depressive symptoms in first-time mothers? Womens Health Issues. 2010;20(1):96-104.
31. Milgrom J, Gemmill AW, Bilszta JL, Hayes B, Barnett B, et al. Antenatal risk factors for postnatal depression: a large prospective study. J Affect Disord. 2008;108(1-2):147-57.
32. Bilszta JLC, Tang M, Meyer D, Milgrom J, Ericksen J, Buist AE. Single motherhood versus poor partner relationship: outcomes for antenatal mental health. Aust N Z J Psychiatry. 2008;42(1):56-65.
33. Lequertier B, McLean MA, Kildea S, King S, Keedle H, Gao Y, et al. Perinatal depression in Australian women during the COVID-19 pandemic: the Birth in the time of COVID-19 (BITTOC) study. Int J Environ Res Public Health. 2022;19(17):5062.
34. Davis D, Sheehy A, Nightingale H, de Vitry-Smith S, Taylor J, Cummins A. Anxiety, stress, and depression in Australian pregnant women during the COVID-19 pandemic: a cross sectional study. Midwifery. 2023;119:103619.

35. Frankham LJ, Thorsteinsson EB, Bartik W. The impact of COVID-19 related distress on antenatal depression in Australia. Int J Environ Res Public Health. 2023;20(8):4783.
36. Australian Government Department of Health and Aged Care. First COVID-19 vaccinations in Australia [Internet]. Canberra: Australian Government Department of Health and Aged Care; 2023 Jul [cited 2023 Jul 6]. Available from: https://www.health.gov.au/news/first-covid-19-vaccinations-in-australia
37. Duko B, Ayano G, Bedaso A. Depression among pregnant women and associated factors in Hawassa city, Ethiopia: an institution-based cross-sectional study. Reprod Health. 2019;16:25.
38. Rich-Edwards JW, Kleinman K, Abrams A, Harlow BL, McLaughlin TJ, Joffe H, et al. Sociodemographic predictors of antenatal and postpartum depressive symptoms among women in a medical group practice. J Epidemiol Community Health. 2006;60(3):221-7.
39. Bisetegn TA, Mihretie G, Muche T. Prevalence and predictors of depression among pregnant women in Debretabor town, northwest Ethiopia. PLoS One. 2016;11(3):e0161108.
40. Biratu A, Haile D. Prevalence of antenatal depression and associated factors among pregnant women in Addis Ababa, Ethiopia: a cross-sectional study. Reprod Health. 2015;12:99.
41. Shamblaw AL, Cardy RE, Prost E, Harkness KL. Abuse as a risk factor for prenatal depressive symptoms: a meta-analysis. Arch Women's Ment Health. 2019;22(2):199-213.
42. Beyazit F, Sahin B. Effect of nausea and vomiting on anxiety and depression levels in early pregnancy. Eurasian J Med. 2018;50(2):111-15.
43. Nicola MJ, Kim L, Shabnam B, Jessica Alice F, Aurelio T, Tom B, Cecilia B. Association between hyperemesis gravidarum and psychological symptoms, psychosocial outcomes and infant bonding: a two-point prospective case-control multicentre survey study in an inner-city setting. BMJ Open. 2020;10(10):e039715.
44. Abujilban SK, Abuidhail J, Al-Modallal H, Hamaideh S, Mosemli O. Predictors of antenatal depression among Jordanian pregnant women in their third trimester. Health Care Women Int. 2014;35(2):200-15.
45. Hutchens BF, Kearney J. Risk factors for postpartum depression: an umbrella review. J Midwifery Womens Health. 2020;65(1):96-108.
46. NSW Department of Health. NSW Health/Families, NSW Supporting Families Early Package–SAFE START strategic policy [Internet]. Sydney (NSW): NSW Department of Health; 2010 [cited 2023 Aug 7]. Available from: https://www1.health.nsw.gov.au/pds/ActivePDSDocuments/PD2010_016.pdf
47. Chambers GM, Botha W, Reilly N, Black E, Kingston D, Austin MP. The clinical performance and cost-effectiveness of two psychosocial assessment models in maternity care: the Perinatal integrated psychosocial assessment study. Women Birth. 2022;35(2):e133-e141.
48. Jernberg C, Löfmark S, Edlund C, Jansson JK. Long-term ecological impacts of antibiotic administration on the human intestinal microbiota. ISME J. 2007;1(1):56-66.