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Depression and anxiety in women during pregnancy and neonatal outcome: Data from the EDEN mother–child cohort

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ABSTRACT

Background: According to the World Health Organization, mental health disorders are the leading causes of disease burden in women from 15 to 44 years. These conditions in pregnant women may affect the offspring.
Aim: To analyze the relation between depression and anxiety of pregnant women and neonatal outcomes including gestational age and birthweight.
Study design: Observational cohort study.
Subjects: 2002 women recruited before the 20th gestational week.
Outcome measures: Gestational age at delivery in completed weeks of amenorrhea and preterm delivery defined as birth before 37 completed weeks of gestation. Spontaneous preterm birth (PB) defined as either spontaneous preterm labor or preterm premature rupture of the membranes. Medically indicated preterm delivery defined as delivery that begins by induction or cesarean section. Birthweight as a continuous variable and centiles of the customized fetal weight norms for the French population.
Results: From the 1719 women included in the study, 7.9% (n = 135) were classified as "anxious", 11.8% (n = 203) as "depressed", 13.2% (n = 227) as "depressed and anxious". After adjusting for potential confounders, depression combined with anxiety during pregnancy increased the risk of spontaneous PB (Odds Ratio: 2.46 [1.22–4.94]), but did not influence medically indicated PB nor birthweight.
Conclusion: In this study, comorbidity of depressive and anxiety symptoms was the worst condition during pregnancy. Further studies are needed to investigate depression and anxiety together to improve the comprehension of the biological modifications involved.

1. Introduction

According to the World Health Organization, mental health disorders are the leading causes of disease burden in women from 15 to 44 years [1]. The prevalence of mental health disorders during pregnancy is similar to the prevalence in the postpartum period [2]. Recent studies have estimated the prevalence of depression during pregnancy at between 10% and 30% [3,4]. This prevalence is higher in women of underprivileged socioeconomic classes, in very young women, and in women with a history of psychiatric disorders [5,6]. The prevalence of anxiety during pregnancy has not been widely studied to date. Its prevalence has been estimated to be between 5%, for generalized anxiety, and 54% for gravidic anxiety disorders [7,8]. The use of antidepressant drugs during pregnancy is estimated between 5% and 14% of women [9,10].

A number of studies have demonstrated that maternal stress during pregnancy has an impact on brain structures involved in mental health and can result in a general susceptibility to psychopathology [11,12]. High levels of depression during pregnancy seem to be associated with a higher risk of preterm birth or intrauterine growth restriction [13,14]. Depression is also an important risk factor for postpartum depression and related complications (mother–infant bonding difficulties, infant feeding difficulties and childhood overweight problems) [15–17]. High levels of anxiety in pregnant women

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have also been associated with adverse neonatal outcomes such as intrauterine growth restriction or preterm birth [18]. Moreover, Martini and al. demonstrated that the coincidence of anxiety before birth and self-perceived distress during pregnancy substantially increased the risk for preterm delivery and maternal depressive disorder after birth [19].

However, most of the studies have considered depression or anxiety as independent exposures, without considering that they may be confounding states [20]. Little is known about combined effects of depression and anxiety, although these disorders commonly co-occur in patients. In the general population, Pollack and al. noted that patients with depression and anxiety had more severe depressive symptoms than depressed patients alone, longer depressive episodes and an increased likelihood of substance abuse [21]. Some authors also suggested that comorbid depression and anxiety could be the worst condition in terms of cardiovascular morbidity or health care costs [22,23]. During pregnancy, Field et al. recently suggested that this comorbidity could lead to a higher incidence of preterm birth, compared to other vulnerable groups of women [24].

In this context, the purpose of the present study was to analyze the relationship between depression and anxiety of women during pregnancy and neonatal outcomes including gestational age and birthweight.

2. Methods

2.1. Participants

This analysis was carried out on the 'EDEN mother–child' cohort (study of pre- and early postnatal determinants of the child's development and health), the main objective of which is to assess the pre- and postnatal nutritional, social, and environmental determinants of infant and child development and health [25]. Women were recruited between September 2003 and January 2006 in two university maternity units, Nancy and Poitiers (France). Women were included at a prenatal visit if they were at less than 20 weeks of gestation. Women with a multiple pregnancy or a history of diabetes were excluded from the study. The other exclusion criteria were women who could not read French and women planning to deliver in a maternity ward other than the one considered or planning to leave the study region within the next 3 years. Among eligible women, 55% (2002) accepted to participate (1034 women in Nancy and 968 in Poitiers).

2.2. Measures and procedures

2.2.1. Depression

The Center for Epidemiological Studies-Depression scale (CES-D) and the State Trait Inventory Anxiety (the "state" component of the STAI) were administered to all the women in a self-administered questionnaire, between 24 and 28 gestational weeks. The CES-D is commonly used during pregnancy [13,26,27]. It was developed by the National Institute of Mental Health, translated into French by Fuhrer et al. in 1989 [28] and validated in various populations [29,30]. It includes 20 items that assess the different aspects of depression symptomatology: depressive mood, feelings of guilt, worthlessness and helplessness, psychomotor retardation, loss of appetite, and sleep difficulties. The questionnaire refers to the preceding week. Each response is scored from 0 (never) to 3 (all the time) according to the frequency of the symptoms. The maximum total score is 60. The threshold of 16 ($\geq$16) is commonly used to detect high levels of depression in women [31–33].

2.2.2. Anxiety

The STAI is one of the most frequently used scales to measure anxiety in the general population and in pregnant women [34,35]. It was created by Spielberger in 1970 and translated into French by Schweitzer in 1990 [36]. The state STAI measures the woman's "anxious state" at the time of the assessment. It includes 20 items, with responses scored 1 to 4, 1 corresponding to the lowest degree of anxiety, 4 to the highest degree. In the absence of a consensus on the threshold in the literature [37,38], the threshold of 37 ($\geq$37, i.e. the 80th percentile of our sample) was used to distinguish "anxious" from "non anxious" women [39].

2.2.3. Combination of depression and anxiety

The analyses on depression and anxiety included all women who responded to more than 95% of the questionnaire, i.e. at least 19 items of the 20 of the CES-D and the STAI. When one item only was missing, it was arbitrarily given the most favorable value, 0 for the CES-D and 1 for the STAI. The women were classified into four groups: "non depressed, non anxious" women, "depressed" women only, "anxious" women only, and "depressed and anxious" women. Those who did not respond to one of the two scales were classified as "non respondents". Women who did not respond to any of the two scales (= women who did not fulfilled the self-administrated questionnaire) were not included in the analyses as no information was available for them.

2.2.4. Neonatal outcomes

Gestational age at delivery (estimated from the date of the last menstrual period and early ultrasound assessment) and birthweight were extracted from medical records. Gestational age was assessed in completed weeks of amenorrhea. Preterm birth was defined as less than 37 weeks. Spontaneous preterm birth was defined as either spontaneous preterm labor or preterm premature rupture of the membranes. Medically indicated preterm delivery was defined as delivery that begins by induction or cesarean section in the absence of spontaneous labor or rupture of membrane as an initiating event. Birthweight was studied in two ways: birthweight as a continuous variable and centiles of birthweight according to customized fetal weight norms for the French population (<10th percentile, $\geq$10th percentile) [40]. To define customized fetal weight, a linear regression model determined the coefficients for the variables in a Gardosi's model birth weight using the sample from the French National Perinatal Survey [40]. Coefficients from the regression models were used to predict optimal fetal weight at 40 gestational. Hadlock's formula was then used to derive weight at each gestational age as a proportion of its expected value [41]. This standard was calculated by adjusting for physiological pregnancy variables such as maternal height, maternal weight in early pregnancy, parity and fetal gender. A weight below the 10th percentile was defined as small-for-gestational age (SGA).

2.2.5. Other characteristics

Sociodemographic and biomedical characteristics were obtained in a face to face interview and a clinical examination performed by a midwife in mid pregnancy. These included mother's age, educational level (no degree, end of secondary school, university degree after two years and university degree after three years or more), parity (0, 1, $\geq$2) and smoking during pregnancy (non smoking, less than 10 cigarettes per day, 10 cigarettes or more per day). Other data were extracted from the obstetrical and neonatal records and included pre-pregnancy BMI defined as weight (kg) divided by height (m^2), and hypertension during pregnancy.

2.2.6. Ethics

This study was approved by the Comité Consultatif pour la Protection des Personnes dans la Recherche Biomédicale, (Ethics Committee, Kremlin Bicêtre Hospital) and the Commission Nationale de l'Informatique et des Libertés (National Commission on Data Processing and Liberties). All women gave their written consent to participate in the study with their infant.

2.3. Statistical analysis

Descriptive statistics were used to summarize the characteristics of the sample. These characteristics were compared according to women's mental health using Chi-square, Student or ANOVA tests as appropriate. Respondents and non respondents to the two scales of mental health were compared.

Multivariate models were used to control for potential confounders (selected a priori): mother's age and educational level, parity, BMI pre-pregnancy, smoking during pregnancy, hypertension during pregnancy and the maternity unit. To test the association between women's mental health and birthweight, newborn's sex and gestational age were included in the multivariate analysis. To test the association between women's mental health and term of pregnancy (gestational age or preterm birth), newborn's sex was included in the multivariate analysis. Multiple linear regression models were used to test the statistical association between women's mental health, gestational age in weeks and birthweight. Logistic regressions were used to study preterm birth, and logistic regressions were used to test the statistical association between women's mental health and birthweight in centile groups. In a final step, we performed the same analyses adjusting for obstetric history: "previous preterm birth" or "previous SGA" as notified in the medical records and after increasing the threshold level of depression up to 23 (CES-D score $\geq$ 23).

Adjusted odds ratios with 95% confidence interval were computed. Statistical significance was defined as $p<0.05$.The data were analyzed using the SAS software, version 9.2 (Cary, NC, USA).

3. Results

Of the 2002 women recruited in the EDEN cohort, 1863 mother–infant pairs were initially available for the analysis. The 139 subjects who were not available comprised mother–child pairs with missing values (n = 110), stillbirth (n = 1) or fetal malformation (n = 28) (Fig. 1). Of these 1863 women, 114 and 135 were respectively given an arbitrarily value as 1 item was missing in the CES-D or the STAI. Finally, data were available for both scales (19 or 20 items) for 1719 (85.9%) women, who were included in the analysis.

Compared to these 1719 women, those whose depressed or anxious status was unknown had a higher score on the other scale of

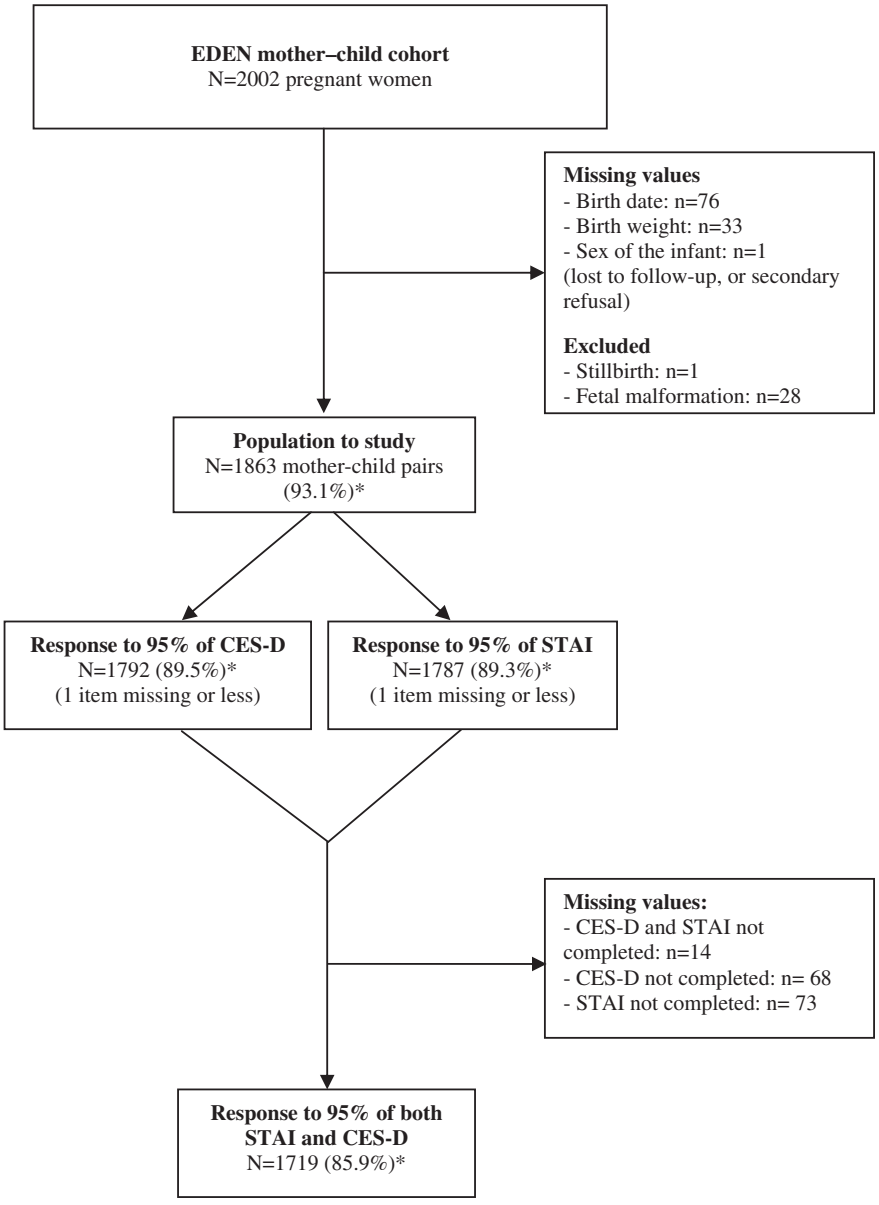

Fig. 1. Study population.

mental health and a lower educational level. The other characteristics of these 141 (7.0%) women are presented in Table 1. 14 (0.7%) women did not complete the self-administered questionnaire at all.

3.1. Depression and anxiety in women during pregnancy

In the sample, 7.9% of the women (n = 135) were classified as "anxious", 11.8% (n = 203) as "depressed", 13.2% (n = 227) as "depressed and anxious". The women classified as "depressed and anxious" had higher mean CES-D scores that women classified as "depressed" only ($p<0.001$), and higher mean STAI scores that women classified as "anxious" only ($p<0.001$).

There was no age difference between the four groups. Compared to women who were neither anxious nor depressed, the women classified as "anxious" or "depressed" had a lower educational level. The women classified as "depressed and anxious" had a lower educational level, a higher BMI and a higher parity. Moreover, these women were more frequently smokers ($p = 0.0003$).

3.2. Birthweight and preterm birth

The mean gestational age was 39.2 ± 1.7 weeks, and 5.6% (n = 104) of the infants were preterm. Spontaneous preterm birth occurred in 3.4% (n = 63) of women, indicated preterm birth in 2.1% (n = 40). Mean birthweight was 3280 g ± 510 g. According to the customized standards, 12.2% (n = 225) of the newborns were SGA.

There was a trend, although not statistically significant for "depressed and anxious" women to have a higher prevalence of preterm birth than "non depressed, non anxious" women: 7.5% versus 5.0%, $p = 0.13$. However, the difference for spontaneous preterm birth was significant: 6.6% versus 3.0%, $p = 0.007$ (Table 2). No differences were observed between depression, anxiety and indicated preterm birth or birthweight variables. There was no difference for other groups of women in preterm birth or birthweight compared to the reference group.

After adjusting for potential confounders, depression combined with anxiety during pregnancy increased the risk of spontaneous preterm birth (Odds Ratio (OR): 2.46 [1.22–4.94]), but did not influence medically indicated preterm birth. The associations between "all depressed" or "all anxious" women and spontaneous preterm birth were respectively OR: 1.72 [0.96–3.08], $p = 0.07$ and OR: 1.78 [0.97–3.21], $p = 0.06$. There was a trend for "depressed" women to have heavier babies: 3269 g versus 3185 g, $p = 0.10$, but there was no difference in SGA compared to the reference group. Finally, no association with neonatal outcomes was found for "anxious" women only (Table 3).

After adjusting for previous preterm birth or previous SGA, the results were not modified (data not shown). After increasing the threshold level of depression, mean length of gestation was shorter for "depressed and anxious" women than for "non depressed non anxious" women: 38.4 versus 38.8 weeks, $p = 0.01$. The association with heavy babies for "depressed" women disappeared: 3170 g versus 3155 g, $p = 0.72$. Other results were not modified.

4. Discussion

4.1. Summary

In the EDEN cohort, the associations between depressive and anxious states were similar to those described in women of the same age in the general population [42]. Women classified as "depressed and anxious" reported more severe depressive and anxious symptoms

Table 1
Depression, anxiety and women characteristics.

Characteristics	Non depressed, non anxious N = 1154	Anxious, non depressed N = 135		Depressed, non anxious N = 203		Depressed and anxious N = 227		Depression status unknown N = 68		Anxiety status unknown N = 73	
	m ± sd% (n)	m ± sd ou% (n)	p[1]	m ± sd ou% (n)	p[1]	m ± sd ou% (n)	p[1]	m ± sd ou% (n)	p[1]	m ± sd ou% (n)	p[1]
CES-D score	7.5 ± 3.9	11.8 ± 2.8	–	20.6 ± 5.0	–	24.5 ± 8.1	–	–	–	13.1 ± 9.0	<0.001
State STAI score	25.7 ± 4.5	42.5 ± 4.7	–	29.8 ± 4.2	–	48.0 ± 8.8	–	34.0 ± 10.4	<0.001	–	–
Mother's age (years)											
<25	14.5 (167)	17.0 (23)	0.73	19.2 (39)	0.19	18.5 (42)	0.11	20.6 (14)	0.54	12.3 (9)	0.44
[25–35]	70.3 (812)	68.2 (92)		65.0 (132)		63.4 (144)		66.2 (45)		67.1 (49)	
≥35	15.2 (175)	14.8 (20)		15.8 (32)		18.1 (41)		13.2 (9)		20.6 (15)	
Educational level											
No degree	24.0 (272)	35.8 (48)	0.03	27.1 (54)	0.01	36.6 (82)	<0.001	43.9 (29)	0.009	43.8 (32)	0.02
End of secondary school	17.4 (196)	16.4 (22)		25.6 (51)		16.9 (38)		21.2 (14)		13.7 (10)	
≤2 years degree university	23.1 (262)	17.9 (24)		19.6 (39)		24.1 (54)		15.2 (10)		16.5 (12)	
≥3 years degree university	35.5 (402)	29.9 (40)		27.7 (55)		22.3 (50)		19.7 (13)		26.0 (19)	
Parity											
0	47.8 (551)	46.7 (63)	0.81	39.1 (79)	0.02	38.9 (88)	0.02	35.8 (24)	0.12	33.9 (24)	0.03
≥1	52.3 (603)	53.3 (72)		60.9 (123)		61.1 (138)		64.2 (43)		66.1 (49)	
Smoking during pregnancy											
No	85.1 (971)	79.9 (107)	0.12	83.6 (168)	0.34	74.4 (168)	0.0003	74.6 (50)	0.17	80.6 (58)	0.71
1–9 cig/day	10.5 (120)	11.9 (16)		13.4 (27)		19.0 (43)		19.4 (13)		12.5 (9)	
≥10 cig/day	4.4 (50)	8.2 (11)		3.0 (26)		6.6 (15)		6.0 (4)		6.9 (5)	
Mother's BMI before pregnancy (kg/m^2)											
<18.5	9.2 (105)	3.0 (4)	0.01	8.1 (16)	0.50	7.3 (16)	0.15	12.5 (8)	0.44	8.7 (6)	0.84
[18.5–25]	66.7 (759)	64.9 (87)		64.0 (126)		62.7 (138)		65.6 (42)		62.3 (43)	
≥25	24.1 (275)	32.1 (43)		27.9 (55)		30.0 (66)		21.9 (14)		29.0 (20)	
Gestational weight gain (kg)											
<7	6.9 (78)	5.2 (7)	0.21	5.5 (11)	0.16	9.9 (23)	0.002	9.2 (6)	0.11	9.7 (7)	0.70
[7–15]	64.9 (736)	60.7 (82)		63.2 (127)		53.8 (123)		66.2 (43)		65.3 (47)	
[15–20]	20.0 (227)	20.7 (28)		18.4 (37)		21.5 (48)		9.2 (6)		16.7 (12)	
≥20	8.2 (93)	13.4 (18)		12.9 (26)		14.8 (33)		15.4 (10)		8.3 (6)	
Maternal height (cm)	163.6 ± 6.2	164.3 ± 5.7	0.19	163.8 ± 5.9	0.74	162.9 ± 6.1	0.10	162.4 ± 6.7	0.12	160.3 ± 6.0	0.01
Hypertension during pregnancy											
No	95.6 (1102)	93.3 (126)	0.24	92.6 (188)	0.07	95.2 (2)	0.78	94.1 (64)	0.75	95.9 (70)	0.73
Yes	4.4 (51)	6.7 (9)		7.4 (15)		4.8 (11)		5.9 (4)		4.1 (3)	
Gestational diabetes											
No	94.3 (1087)	91.9 (124)	0.26	92.6 (188)	0.36	93.8 (213)	0.79	91.2 (62)	0.38	86.3 (63)	0.01
Yes	5.7 (66)	8.1 (11)		7.4 (15)		6.2 (14)		8.8 (6)		13.7 (10)	

[1] Statistical comparison of this group with the "non depressed, non anxious" reference group (first column).

Table 2
Neonatal characteristics according to depression and anxiety during pregnancy.

	Non depressed, non anxious	Anxious, non depressed		Depressed, non anxious		Depressed and anxious		All depressed		All anxious	
	N = 1154	N = 135		N = 203		N = 227		N = 448		N = 231	
	m ± SD or% (n)	m ± SD or% (n)	p[a]	m ± SD or% (n)	p[a]	m ± SD or% (n)	p[a]	m ± SD or% (n)	p[b]	m ± SD or% (n)	p[c]
Mean gestational age	39.3 ± 1.6	39.1 ± 2.1	0.19	39.3 ± 1.8	0.63	39.1 ± 1.9	0.06	39.2 ± 1.9	0.16	39.1 ± 2.0	0.03
Preterm birth											
<37 weeks	5.0 (58)	5.9 (8)	0.65	5.9 (12)	0.60	7.5 (17)	0.13	6.7 (29)	0.20	6.9 (25)	0.20
Spontaneous preterm birth											
<37 weeks	3.0 (34)	2.2 (3)	0.63	3.0 (6)	0.98	6.6 (15)	0.007	4.9 (21)	0.04	5.0 (18)	0.06
Indicated preterm birth											
<37 weeks	2.0 (23)	3.7 (5)	0.20	3.0 (6)	0.38	0.9 (2)	0.25	1.9 (8)	0.70	1.9 (7)	0.81
Mean birthweight (g)	3278 ± 484	3256 ± 540	0.97	3358 ± 531	0.23	3252 ± 548	0.92	3302 ± 542	0.45	3254 ± 544	0.62
Centiles according to customized curves											
Small-for-gestational age	11.3 (129)	14.9 (20)	0.22	12.2 (24)	0.71	14.2 (31)	0.23	13.3 (55)	0.40	14.5 (51)	0.13

[a] Statistical comparison of this group with the "non depressed, non anxious" reference group (first column).
[b] Statistical comparison of this group with the "non depressed women" (anxious or not anxious women).
[c] Statistical comparison of this group with the "non anxious women" (depressed or not depressed women).

and were more frequently smokers than women "depressed" or "anxious" only. In addition, depression and anxiety during pregnancy were significantly associated with a two-fold increase in risk of spontaneous preterm birth. No association was found with intrauterine growth restriction. Women classified as "depressed" only or "anxious" only had no excess risk of preterm birth or intrauterine growth restriction.

4.2. Strength and limits of the study

This study used a prospective cohort of pregnant women in two maternity wards. Women's mental health, assessed between 24 and 28 gestational weeks, probably varied little throughout the pregnancy [3]. To our knowledge, very few studies have directly examined combined versus independent depressive and anxious symptoms as predictors of neonatal outcomes. This study is the first to demonstrate an effect of comorbid depression and anxiety disorders in a middle to privileged class population.

This study also has limitations. Compared with the French National Perinatal Survey performed in 2003 on a representative sample of women after delivery in France, the women who participated in the EDEN study had similar age, birthweight of the offspring and preterm birth rate but had a higher level education [43]. This social difference probably induces a lower proportion of women classified as "depressed" or/and "anxious" in our study and probably decreases the power of the study. In addition, 14 (0.7%) women did not complete the self-administered questionnaire at all and 141 (7.0%) women did not complete either one or the other of the mental scales. The selection of women having responded fully to the CES-D and the STAI scales may also have excluded "depressed" and/or "anxious" women and decreased the power of the study. Moreover, this study considered the state anxiety, it might have been useful to examine the outcome measures against the trait measure. The assessments of depression and anxiety were based on self-administered questionnaires that are likely to be less accurate than psychiatric examinations. Given the impossibility of a detailed psychiatric examination in large epidemiological studies, it is reasonable to trust the validated epidemiological scales available to date. Finally, we cannot exclude a residual confounding bias, for possible determinants of gestational age or growth (such as maternal epilepsy or other maternal conditions).

Table 3
Neonatal characteristics according to depression and anxiety during pregnancy: adjusted analysis.

	Non depressed, non anxious	Anxious, non depressed		Depressed, non anxious		Depressed and anxious		All depressed		All anxious	
	m ± SD or OR [96% IC]	m ± SD or OR [96% IC]	p[a]	m ± SD or OR [96% IC]	p[a]	m ± SD or OR [96% IC]	p[a]	m ± SD or OR [96% IC]	p[b]	m ± SD or OR [96% IC]	p[c]
Mean gestational age[d]	38.8 ± 1.6	38.6 ± 2.2	0.31	38.9 ± 1.9	0.71	38.6 ± 1.8	0.11	38.7 ± 2.0	0.49	38.6 ± 2.0	0.06
Preterm birth[d]											
<37 weeks	1	1.14 [0.52–2.49]	0.35	1.07 [0.54–2.14]	0.72	1.61 [0.88–2.94]	0.29	1.32 [0.81–2.14]	0.26	1.40 [0.85–2.30]	0.19
Spontaneous preterm birth[d]											
<37 weeks	1	0.74 [0.22–2.45]	0.62	0.88 [0.33–2.31]	0.79	2.47 [1.27–4.80]	0.008	1.72 [0.96–3.08]	0.07	1.78 [0.97–3.21]	0.06
Indicated preterm birth[d]											
<37 weeks	1	1.68 [0.60–4.72]	0.33	1.34 [0.51–3.52]	0.55	0.41 [0.09–1.86]	0.25	0.80 [0.35–1.84]	0.60	0.86 [0.36–2.07]	0.74
Mean birthweight[e] (g)	3185 ± 481	3180 ± 540	0.97	3269 ± 539	0.10	3199 ± 551	0.99	3229 ± 547	0.35	3184 ± 549	0.69
Centiles according to customized curves[f]											
Small-for-gestational age	1	1.26 [0.75–2.13]	0.38	1.02 [0.63–1.65]	0.97	1.18 [0.76–1.82]	0.46	1.07 [0.77–1.50]	0.70	1.21 [0.85–1.72]	0.30

[a] Statistical comparison of this group with the "non depressed, non anxious" reference group (first column).
[b] Statistical comparison of this group with the "non depressed women" (anxious or not anxious women, number of subjects in the model = 1691).
[c] Statistical comparison of this group with the "non anxious women" (depressed or not depressed women, number of subjects in the model = 1684).
[d] "Mean gestational age" and "Preterm birth" were adjusted for mothers' age, level of education, parity, pre-pregnancy BMI, smoking during pregnancy, hypertension during pregnancy, infant sex and center (number of women in the model = 1624).
[e] "Mean birthweight" was adjusted for mothers' age, level of education, parity, pre-pregnancy BMI, smoking during pregnancy, hypertension during pregnancy, infant sex, gestational age and center (number of subjects in the model = 1624).
[f] "Centiles according to customized curves" were adjusted for mothers' age, level of education, parity, pre-pregnancy BMI, smoking during pregnancy, hypertension during pregnancy and center (number of subjects in the model = 1624).

4.3. Comparisons with other studies

To our knowledge, only another study explored the combined effect of depression and anxiety on neonatal outcomes [24]. In that study, preterm birth occurred more frequently in pregnant women with comorbidity. Some other studies focused on spontaneous preterm birth [44–46]. The authors suggested that psychological factors could be associated with spontaneous preterm birth without involving mechanisms related to vascular troubles or intrauterine growth restriction. While the exact mechanisms underlying the association are not known at this point, various pathways have recently been suggested [47–53]. Response to stress involves a hormone system called the hypothalamic–pituitary–adreno–cortical axis (HPA). Comorbid depression and anxiety during pregnancy is probably the most vulnerable condition leading to an excessive stimulation of the HPA axis and an excessive secretion of stress hormones [48,49]. Several studies demonstrated that the synthesis and the release of placental corticotrophin-releasing hormone (CRH) were stimulated by stress hormones [50,51]. Excessive levels of placental CRH control a cascade of events, which lead to parturition [51]. Another hypothesis includes the role of smoking during pregnancy as a significant risk factor for spontaneous preterm birth [52,53]. Field et al. discussed additive effects of prenatal depression and anxiety on neonatal outcomes [24]. Another mechanism is the interaction between depression, anxiety and neonatal outcomes involving complex biochemical effects [24,54]. Our results rather support such interaction as no effect was observed in “depressed” or “anxious” groups.

We did not find any strong association between women's anxiety or depression and adverse pregnancy outcomes. It is possible that associations described in the literature require high levels of anxiety or depression [20]. It is also possible that effects on neonates require the co-existence of anxiety with depressive symptoms, as suggested in the prediction of cardiovascular events [22]. In the EDEN cohort, there was a trend for “mild depressed” women to have heavier babies, which disappeared when increasing the threshold level of depression. This association has already been described in the literature [55]. Further studies are needed on possible mechanisms and targets for biological effects of depression alone during pregnancy. These studies probably should probably take into consideration the pattern of food intake and physical activity of the “depressed” women only.

4.4. Conclusion

The psychological symptoms during pregnancy have consequences in terms of social, nutritional, medical behaviors and therefore probably on the development of the fetus. In this study, comorbidity of depressive and anxiety symptoms was the worst condition during pregnancy. Further studies are needed to understand the psychopathological relations between pregnant women's mental health and the growth of the fetus. These studies should probably investigate these two conditions together so as to reinforce the comprehension of the biomedical modifications involved.

Conflict of interest

The authors declare that they do not have any financial and personal relationships with other people or organizations that could inappropriately influence their work.

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