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Original Research

Effect of prenatal depression during late pregnancy on maternal and neonatal outcomes

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Summary

Aim: To determine whether prenatal depression during late pregnancy affect maternal and neonatal outcomes. *Methods*: The clinical data of 595 pregnant patients in our hospital during January 2016 to December 2017 were studied. These participants were assigned into three groups as mild-to-moderate depression group, severe depression group and non-depression group according to the Edinburgh postnatal depressive scale (EPDS). *Results*: Compared with the women without depression or with mild-to-moderate depression, pregnant patients with severe depression were likely to suffer from preterm birth ($p < 0.05$). There was no association between the mild-to-moderate depression, severe depression group and the non-depression group about neonatal outcomes (all $p > 0.05$). *Conclusion*: Severe prenatal depression during late pregnancy is significantly associated with increased risk of preterm birth, while mild-to-moderate prenatal depression would not affect maternal and neonatal outcomes.

Key words: Prenatal depression; Late pregnancy; Preterm birth.

Summary Statement

What is already known about this topic?

• An increasing number of pregnant patients exhibit symptoms of depression during the childbearing years. The current incidence of prenatal depression is much higher than that of postpartum depression.

• Previous studies have demonstrated that prenatal depression might be associated with adverse maternal and neonatal outcomes.

What this paper adds?

• Severe prenatal depression during late pregnancy is significantly associated with an increased risk of preterm birth, while mild-to-moderate prenatal depression would not affect maternal and neonatal outcomes.

The implications of this paper:

• Depression screening should be used as a routine prenatal screening program.

• Severe depression status during late pregnancy should be regarded as an important indicator for patients at risk for preterm birth.

Introduction

Depression is the leading cause of the global burden of mental health-related illnesses [1]. Women are at increased risk for depression as compared with men [2]. Pregnancy and postpartum are considered high risk periods [3]. A previous study showed that approximately 12% of pregnant patients were affected by prenatal depression with depression in the second and third trimester accounting for 12.8% and 12% of patients respectively [4].

On the basis of World Health Organizations [5], during the gestation or the postpartum period, 33.3%, 10% of pregnant women in developing and developed countries respectively, suffered from severe mental disorders.

The incidence of the postpartum depression is 17%, while the incidence of the prenatal depression is high as 20% to 40% [6]. Prenatal depression is similar to postpartum depression which should be diagnosed early with treatment initiated. However, prenatal depression is often not considered as a vital health issue [7]. The American College of Obstetricians and Gynecologists recommends that clinicians should screen for prenatal depression with a standard tool at least once during pregnancy [8]. Even if the pregnant patient was diagnosed with depression, treatment is often refused secondary to the concern about how the treatment will affect the infant's health [9]. Although there are several studies on prenatal depression [10-12], the research results of the depression on the pregnancy outcomes were inconsistent. Some studies showed that prenatal depression was associated with and preterm birth, low birth weight and intrauterine growth restriction Several reports found no association between prenatal depression and adverse pregnancy outcomes, such as preterm birth, low birth weight and low Apgar scores [13-15].

Therefore, it becomes meaningful to understand the correlation of prenatal depression and with maternal-neonatal outcomes. The aim of this study is to test the hypothesis that prenatal depression during late pregnancy can lead to adverse effects on maternal and neonatal outcomes. In the present the effect of prenatal depression during late pregnancy on maternal and neonatal outcomes in Chinese Han population is investigated.

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Table 1. — *Demographic characteristics between the depression group and non-depression group.*

Characteristics	Total (N = 595)	Non-depression group (N = 429)	Depression group (N = 166)	*p*-value	95% CI
Age (years old)				0.581[a]	0.772, 1.588
< 30 (%)	342	249 (72.8)	93 (27.2)		
≥ 30 (%)	253	180 (71.1)	73 (28.9)		
Domicile place				0.037[a]	1.036, 2.391
Zhejiang province (%)	468	347 (74.1)	121 (25.9)		
Non-Zhejiang province (%)	127	82 (64.6)	45 (35.4)		
Residence				0.001[b]	0.000, 0.001
City (%)	244	196 (80.3)	48 (19.7)		
Town (%)	216	147 (68.1)	69 (31.9)		
Village (%)	135	86 (63.7)	49 (36.3)		
Education background				0.452[b]	0.446, 0.465
Below the high school (%)	273	193 (70.7)	80 (29.3)		
Junior college (%)	93	63 (67.7)	30 (32.3)		
Undergraduate (%)	180	136 (75.6)	44 (24.4)		
Master or above (%)	49	37 (75.5)	12 (24.5)		
Occupation				0.126[a]	0.110, 0.122
Civil servant (%)	15	7 (46.7)	8 (53.3)		
Teacher (%)	73	51 (69.9)	22 (30.1)		
Doctor and nurse (%)	31	18 (58.1)	13 (41.9)		
Worker (%)	5	5 (100.0)	0 (0.0)		
Company employee (%)	336	246 (72.2)	90 (26.8)		
Housewife (%)	47	35 (74.5)	12 (25.5)		
Self-employed (%)	53	39 (73.6)	14 (26.4)		
Other (%)	35	28 (80.0)	7 (20.0)		
Personal character				0.028[a]	0.032, 0.039
Introvert (%)	212	141 (66.5)	71 (33.5)		
Extrovert (%)	383	288 (75.2)	95 (24.8)		
Planned pregnancy				0.042[a]	0.044, 0.052
Yes (%)	464	344 (74.1)	120 (25.9)		
No (%)	131	85 (64.9)	46 (35.1)		
Adverse pregnancy history				0.015[a]	0.014, 0.018
Yes (%)	200	132 (66.0)	68 (34.0)		
No (%)	395	297 (75.2)	98 (24.8)		
Monthly household income (yuan)				0.416[b]	0.414, 0.434
Below 3000 yuan (%)	140	96 (68.6)	44 (31.4)		
3001-4500 yuan (%)	163	115 (70.6)	48 (29.4)		
Above 4500 yuan (%)	292	218 (74.7)	74 (25.3)		
Family condition				0.048[b]	0.033, 0.040
Fair (%)	154	121 (78.6)	33 (21.4)		
General (%)	433	304 (70.2)	129 (29.8)		
Poor (%)	8	4 (50.0)	4 (50.0)		
Overall (%)	595	429 (72.1)	166 (27.9)		

a, Chi-square test; b, Kruskal-Wallis test.

Methods

Study design and participants

This study set up was illustrated in Figure 1. 630 pregnant women were recruited during their late second and third trimester of pregnancy (24-28 weeks) while attending routine prenatal examinations in the Department of obstetrics of Women's Hospital School of Medicine, Zhejiang University, between January 2016 and December 2017. The inclusion criteria were Chinese Han population, singleton gestation, age at least 18 years and without medical complications or mental disorders. Fifteen were excluded because they did not meet the inclusion criteria, 8 refused to participate and 12 had to be excluded because they labored in other hospitals. The remaining 595 participants were assigned into three groups and grouping criteria were shown below. After the participants had signed the informed consent form, they would receive two questionnaires including

Table 2. — *Maternal outcomes between the non-depression group and the depression group.*

Variable	Non-depression group (N = 429)	Depression group (N = 166)		*p*-value	95% CI
		Mild-to-moderate depression group (N = 142)	Severe depression group (N = 24)		
Labor induction mode				0.788[a]	0.791, 0.807
Labor onset (%)	303 (70.6)	101 (71.1)	18 (75.0)		
Cervical balloon (%)	18 (4.2)	6 (4.2)	2 (8.3)		
Propess pessary (%)	26 (6.1)	6 (4.2)	0 (0.0)		
Oxytocin (%)	82 (19.2)	29 (20.4)	4 (16.7)		
Delivery mode				0.957[a]	0.954, 0.962
Natural childbirth (%)	308 (71.8)	102 (71.8)	16 (66.7)		
Forceps-assisted vaginal birth (%)	25 (5.8)	8 (5.6)	1 (4.2)		
Cesarean section (%)	96 (22.4)	32 (22.5)	7 (29.2)		
Use of uteronic agents				0.622[a]	0.623, 0.642
Pitocin only (%)	39 (9.1)	8 (5.6)	1 (4.2)		
Pitocin plus other drugs (%)	114 (26.6)	43 (30.3)	7 (29.2)		
No use (%)	276 (64.3)	91 (64.1)	16 (66.7)		
Intrapartum hemorrhage or intraoperative hemorrhage (X ± SD)	261.96 ± 146.93	262.54 ± 132.19	258.33 ± 132.42	0.991[b]	
Preterm birth				0.010[a]	0.018, 0.023
Yes (%)	12 (2.8)	2 (1.4)	3 (12.5)		
No (%)	417 (97.2)	140 (98.6)	21 (87.5)		

a, Chi-square test; b, One-way ANOVA; X, mean; SD, standard deviation.

Table 3. — *Neonatal outcomes between the non-depression group and the depression group.*

Variable	Non-depression group (N = 429)	Depression group (N = 166)		*p*-value	95% CI
		Mild-to-moderate depression group (N = 142)	Severe depression group (N = 24)		
Apgar scores					
1 min	9.87 ± 0.61	9.89 ± 0.57	9.96 ± 0.20	0.748[b]	
5 mins	9.98 ± 0.14	9.95 ± 0.28	10.00 ± 0.01	0.142[b]	
Neonatal birth Weight (g)	3333.87 ± 391.63	3320.18 ± 434.91	3137.50 ± 508.26	0.072[b]	
NICU admission				0.917[a]	0.939, 0.948
Yes (%)	49 (11.4)	18 (12.7)	3 (12.5)		
No (%)	380 (88.6)	124 (87.3)	21 (87.5)		
Neonatal jaundice				0.545[a]	0.556, 0.576
Yes (%)	88 (20.5)	35 (24.6)	6 (25.0)		
No (%)	341 (79.5)	107 (75.4)	18 (75.0)		

a, Chi-square test; b, One-way ANOVA; CI, confidence interval.

social demography and the Chinese versions of the Edinburgh Postnatal Depression Scale (EPDS). Four obstetrical nurses were the professional interviewers who received a 2-month psychological training program prior to the start of the study. The interviewees were taken to the specific consulting room to finish the questionnaires with one obstetrical nurse present in order to keep the data as valid as possible.

Data of maternal and neonatal outcomes were gained from the Department of Obstetrics of Women's Hospital School of Medicine, Zhejiang University. All procedures performed in our study involving human participants were in accordance with the ethics committee of the hospital. All participants who volunteered for the complete study were free to pullback from the study at any time. We obtained informed consent of each participant and kept their data confidential.

Measurement instrument

Demographic characteristics examined include maternal age, place of household registration, residence, education background, occupation, personal character, monthly household income and family condition. Moreover, pregnancy intention (planned or unplanned pregnancy) and adverse pregnancy history were assessed by questionnaire during their prenatal examinations.

Depression was measured using Edinburgh postnatal depressive scale (EPDS). The EPDS is a self-assessment scale including ten items, scored from 0 to 3 (0 represented nor-

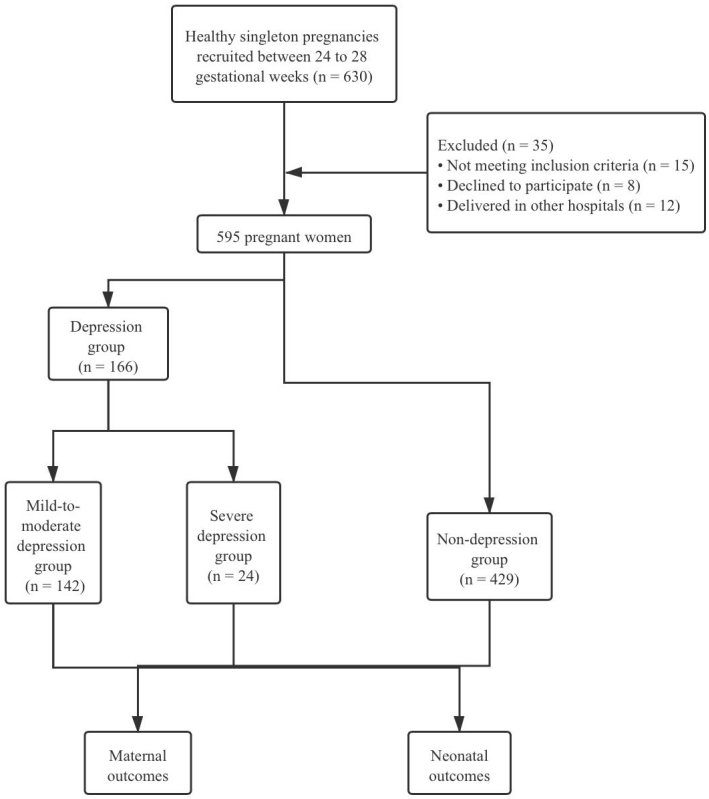

Figure 1. — The procedure of the present study. 630 pregnant women were recruited, 15 were excluded because they did not meet the inclusion criteria, 8 refused to participate and 12 had to be excluded because they labored in other hospitals. After informed consent, matching subjects received a set of questionnaires. 595 participants were divided into three groups according to EPDS scores. The maternal and neonatal outcomes were compared between mild-to-severe depression group, severe depression group and non-depression group.

mal and 3 represented severe) that has been effectively utilized for determining prenatal and postpartum depression [16]. The range of the total score is from 0 to 30 points, and interviewees whose scores are higher represent negative emotion. The recommended cutoff scores include less than 9 points for non-depression, 9 to 12 points for mild-to-moderate depression and more than 12 points for severe depression [17]. EPDS was initially used as a screening tool for the postpartum period [18]. Due to the sensitivity of the scale to assess the variation of depression, the sensitivity and specificity are 91% and 95% as a predictor for depression in pregnant patients [19]. Cronbach's α was 0.914 [20].

Data analysis

Data were analyzed using SPSS statistical software version 20.0 (IBM, NY, USA). All data input SPSS were cross-checked for verification. According to the type of data, baseline characteristics were compared using a Chi-square test and Kruskal-Wallis test which were presented as frequency with percentages. Chi-square test and One-way ANOVA were used to compare the variables of maternal and neonatal outcomes of the different groups. p value $<$ 0.05 was considered to reflect statistical significance.

Results

Demographic characteristics of depression group and non-depression group

From the Table 1, we can see that the incidence of prenatal depression is 27.9% (166/595). We divided the whole group into two as depression group and non-depression group according to 9 points.

Pregnant patients with domicile place of non-Zhejiang province, living in village, introvert personality and poor family condition were likely to develop depression (all $p <$ 0.05). Meanwhile, depressed women had unplanned pregnancies and adverse pregnancy histories ($p < 0.05$). There were no significant association between depression and education background, occupation and monthly household income.

Maternal-neonatal outcomes of mild-to-moderate depression, severe depression group and non-depression group

Compared with the women without depression or with mild-to-moderate depression, pregnant patients with severe depression were likely to suffer from preterm birth ($p < 0.05$). There was no statistically significant difference between mild-to-moderate depression, severe depression group and non-depression group about other maternal

outcomes including labor induction mode, delivery mode, use of uterotonic agents and hemorrhage (all $p > 0.05$).

Neonatal outcomes between the mild-to-moderate depression, severe depression group and the non-depression group

There was no association between the mild-to-moderate depression, severe depression group and the non-depression group about other neonatal outcomes including APGAR scores, neonatal birth weight, NICU admission and neonatal jaundice with depression (all $p > 0.05$).

Discussion

The main finding of this study shows that severe prenatal depression is significantly associated with the risk of preterm birth, however, mild-to-moderate prenatal depression in late pregnancy does not appear to affect the maternal and neonatal outcomes. It is not obvious to determine the specific association between prenatal depression and preterm birth. From a biological perspective, chronic stress can lead to the alteration of levels of inflammatory proteins [21], accordingly, these changes might cause early contractions and preterm birth [10]. Fransson *et al*. investigated prenatal depression and determined that a cut-off score of 12 or higher on the EPDS increased the risk for preterm birth (OR, 1.56 (95 % CI), 1.03-2.35) in a Swedish population [22]. Similarly, the research in Finland showed us that pregnancy outcomes were worse among women with severe depression than without [23]. However, other studies demonstrated no significant association between depression and preterm birth. Andersson *et al*. could not find any association between maternal depression and adverse neonatal outcomes [24]. In their study, depression was measured during the second trimester of pregnancy with the Primary Care Evaluation of Mental disorders (PRIME-MD) patient's questionnaire. Another study showed that subclinical-elevated depressive symptoms during pregnancy measured with self-rating scales were not significantly associated with preterm birth [13]. Evidence was found that different depression screening tools changed the association strength between prenatal depression and preterm birth [11]. In our study, depression was measured during the second and third trimester of pregnancy (24-28 weeks) and the different time point of depression screening was the factor affecting the association between prenatal depression and preterm birth.

In our study, we referred all of the pregnant patients with depression to the psychologists. As a general suggestion, anti-depressive medication exposure during pregnancy was associated with an increased risk of congenital malformations, preterm birth and fetal growth restriction [25]. A study suggested that it was important to take all the side effects of medications into consideration when pregnant patients took psychoactive drugs [26]. One study demonstrated that anger expression and suppression during pregnancy were vulnerable factors for perinatal mental disorders. Specifically anger expression was a predictive factor of mild prenatal depression [27]. A different report noted that anger suppression was associated with depression [28]. We suggested that the association between depression and anger experience and expression during the perinatal period is an interesting topic for further research.

We did not observe any associations of depression with Apgar scores, NICU (neonatal intensive care unit) admission and neonatal birth weight. The results of our study were consistent with the results of what Grigoriadis reported. Our study shows that depression may not influence the mode of the delivery. Similarly, Wu *et al.* has demonstrated that there was no association between mood and type of delivery [29].

There are still three limitations to our study. One limitation is that assessment of depression was only evaluated in the second or third trimester of pregnancy. We suggest that clinicians should assess depression at different points of time during the gestational period, because it is important to better understand the role that depression during pregnancy plays in fetal growth and development. The second limitation is that we used EPDS scale as the only screening tool to assess depression. It might be better to include face to face interview or other structured psychiatric interview schedules to diagnose depression. The third limitation is the lack of measurement of any blood levels such as blood cortisol.

In general, our finding indicate that prenatal depression screening could be regarded as a routine during perinatal care in China. It is helpful for obstetricians to identify the pregnant patient with severe depression and prevent mild and moderate depression from progressing to severe depression, which could optimize maternal and neonatal outcomes.

Conclusions

Our present study suggested that severe prenatal depression during late pregnancy measured with the EPDS increased the risk of preterm birth with no other specific adverse outcomes noted to the mother or the infant. Therefore, severe prenatal depression status during late pregnancy should be regarded as an important indicator for a potential adverse outcome in pregnancy and screening of all prenatal patients should be performed.

Ethics Approval and Consent to Participate

This study was approved by the Research Ethics Committee of Women's Hospital (IRB-20190020-R), Zhejiang University School of Medicine, Hangzhou, China. All participants were informed of the purpose of this study, and written consent was obtained from each participant prior to sample collection.

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Conflict of Interest

The authors declare no conflict of interest.

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