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Limited Depressive and Anxiety Symptoms Late in Pregnancy Are Not Related to Neonatal Outcomes

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Background: Prior studies have reported inconsistent findings regarding the link between antenatal depressive and anxiety symptomatology, with neonatal outcomes.
Objectives: The aim of the present study was to assess the possible association of prenatal depressive and anxiety symptoms, in the third trimester of pregnancy, with perinatal outcomes (birth weight of the newborn, Apgar score and the newborn's admission in neonatal intensive care unit) in a sample of pregnant women, in Greece.
Patients and Methods: A total of 117 women from Athens, during the 32nd to 35th week of pregnancy, participated in the study. Demographic and obstetric history data, as well as neonatal outcomes, were recorded. Three self-administered psychometric scales (Beck depression inventory (BDI), Edinburg postnatal depression scale (EPDS) and beck anxiety inventory (BAI)) were used to evaluate in detail the prenatal depressive and anxiety symptoms. Descriptive statistics, Spearman's Rho coefficients, Mann-Whitney U and Kruskal-Wallis testes were applied to analyze the data.
Results: On the basis of BDI, 81.1% of the sample showed minimal, 15.4% mild, 2.6% moderate and 0.9% severe depressive symptoms, respectively. Furthermore, 80.3% of the participants, scored on EPDS below the cut-off point for a likely diagnosis of depression. According to BAI scale, 43.6% showed minimal, 42.7% women mild, 10.3% moderate and 3.4% severe anxiety symptoms. No statistically significant correlations were found between depressive and anxiety symptoms and neonatal outcomes (birth weight, Apgar score and admission in neonatal intensive care unit).
Conclusions: Limited levels of prenatal depressive and anxiety symptoms do not seem to be associated with neonatal outcomes. In clinical practice, pregnant women, who suffer from low levels of prenatal depressive and anxiety symptoms, may be reassured, in respect of the adverse outcomes of these mood symptoms on the neonate.

Keywords: Depression; Anxiety; Prenatal; Intensive Care Units; Neonatal; Mood Disorders

1. Background

Although pregnancy and childbirth are often viewed as periods of emotional well-being, the perinatal period is a time of substantial vulnerability to affective illness. Pregnancy does not protect women from depression and anxiety (1, 2). Pregnancy is a period of great disruption and adjustment of biological, psychological and social aspects, which can be a risk factor for the development, occurrence or recurrence of mental disorders (3). Research from the past two decades has suggested a link between prenatal depression and anxiety and adverse obstetric and neonatal outcomes, such as infant's low birth weight (LBW) (4, 5). Prevalence rates of depressive symptoms, among women of childbearing age, range from 10% to 50% (6-10), depending on the instrument used and the demographic characteristics of the study population. Previous studies from Greece have indicated that rates of prenatal depressive symptoms range from 11.5% to 47% (11-13). Firm estimates for prenatal anxiety symptoms do not exist, although past studies suggest that prevalence rates of prenatal anxiety symptoms are similar to those in the general population, affecting 6.6% - 52.9% (14-17). According to the world health organization (WHO), elevated levels of prenatal anxiety are observed during the first and third trimesters of pregnancy (18). It therefore, appears that the estimates of prenatal depressive and anxiety symptoms prevalence rates vary. Comparisons across studies are complicated due to differences in study methodology and design, including use of various depression and anxiety screening instruments, variable time of depression and anxiety screening in pregnancy and differences in composition of the sample and sample sizes. As an example, in the study of Kurki et al. (14), prenatal anxiety symptomatology in 10 - 17 weeks of gestation was assessed by one question only (Are you tense or distressed?) and was observed in 16% of the study sample. On the other hand, in the study by Nasreen et al. (17), prenatal anxiety symptoms were estimated by a psychometric scale (STAI), during the third trimester of pregnancy and were observed in 26% (17).

Research findings are inconsistent regarding the association between prenatal depression anxiety symptomatology and adverse neonatal outcomes, such as the LBW of the newborn, the low Apgar score and the newborn's admission in neonatal intensive care unit (NICU). The allegations of possible association of psychological factors with LBW have been expressed for decades (4). Prenatal depression has been associated with LBW (17, 19, 20). However, contradicting findings have also been reported (21-25), possibly due to differences in study methodology and design (e.g. different psychometric tools, diverse study samples). In two of the studies (19, 20) confirming the association of prenatal depressive symptoms and LBW, the study samples recruited individuals from disadvantaged (low socioeconomic status or minority groups) populations. Anxiety symptoms during pregnancy have been reported to be associated with LBW in several studies (16, 17, 26), while others have not confirmed this association (22, 23, 27-29). A number of studies indicate an association between low Apgar score of the newborn and prenatal depression and anxiety (9, 22), while, in other studies, this association does not exist (22, 24, 25).

2. Objectives

The main aim of this investigation was to examine the association between prenatal depressive and anxiety symptoms with neonatal outcomes. Part of the aim of this study was the assessment of prenatal depressive and anxiety symptomatology in the third trimester of pregnancy, in a sample of pregnant women from Greece. As far as we know, no similar research has been conducted in Greece. The findings of this study will contribute to this research area, where there are conflicting research views, and will help even more health professionals in shaping a more comprehensive view on the issue, also in other countries besides Greece.

3. Patients and Methods

3.1. Study Design and Participants

During the study period, of all the pregnant women we encountered, 117 agreed to participate in this exploratory, longitudinal study. All of the subjects were recruited from the private medical sector and were in the third trimester of pregnancy. Inclusion criteria were pregnant women between 32^{nd} to 35^{th} weeks of gestation, which received routine prenatal care throughout pregnancy and were either of Greek origin or fluent in Greek language. We collected socio-demographic and obstetric data using a demographic questionnaire, which was administered to the women. The questionnaire included questions relating to age, ethnicity, education level, professional and economic status, number of pregnancies and children, and the health status of women. Prenatal depressive symptoms were assessed with the Beck depression inventory (BDI) and the Edinburg postnatal depression scale (EPDS). The BDI is a self-report rating scale, consisting of 21 categories of symptoms and behaviors. Each category describes a specific behavioral manifestation of depression and consists of 4 - 5 self-evaluation statements, sequentially classified. These statements are classified to reflect the variation in severity of symptoms from none to maximum importance. Numeric values from 0 to 3 were set for each statement, to determine the degree of importance. Items are scored on a 0 - 3 scale, yielding a score range of 0 - 63, where higher scores indicate greater depression severity. Scores in the range of 0 - 13 indicate minimal depression, 14 - 19 mild depression, 20 - 28 moderate depression and 29 - 63 severe depression (30). In the Greek version of the BDI, the internal consistency reliability is satisfactory and the Cronbach's index is $\alpha = 0.84$ (31). The EPDS is one of the most popular tools for perinatal depression evaluation. It is a widely used tool, with satisfactory validity and reliability, both in prenatal and postnatal period populations (32). The ten-topic version of EPDS scale consists of statements describing depressive symptoms and have four possible answers, each graded according to the complaint's severity or duration. The answers are graded from 0 to 3, while several of them are graded conversely and their total sum is calculated at the end. The instrument has been validated for Greece, with Cronbach's index being $\alpha = 0.9$ and cut off point 11 (33). Antenatal anxiety symptomatology was assessed using the Beck anxiety inventory (BAI). The BAI is a self-administered scale consisting of 21 entries of anxiety symptoms. The score of each entry ranges on a scale from 0 to 3, with an overall score range of 0 - 63, and the final rating scale consists of the sum of the degree of distress for each symptom. Scores of 0 - 7 represent minimal anxiety, 8 - 15 mild anxiety, 16 - 25 moderate anxiety and 26 - 63 severe anxiety (34).

Finally, a questionnaire containing questions about neonatal parameters (e.g. birth weight, admission to the NICU and Apgar score) was administered to the women to record neonatal outcomes.

3.2. Data Collection

The participants were recruited during their routine follow up in the private medical sector, in the time period between March to April 2012. Women completed questionnaires during their routine prenatal examination. The data collection process included two samplings in the same sample. The first sampling was carried out in the third trimester of pregnancy during 32^{nd} to 35^{th} week of pregnancy. The recording of demographic data and the completion of the BDI, EPDS and BAI were performed in this sampling. The second sampling was carried out on the first postpartum week, where the recording of neonatal parameters was performed and the sample consisted of 93 women. The reason of attrition probably could be attributed to the fact that the second phase of the study was taking place during the postpartum period. The requirements of this particularly sensitive period, such as the care of the newborn, may have played the main reason of attrition.

3.3. Ethical Considerations

The study protocol was approved by the assembly of Athens University Medical School, Athens, Greece, Medical School, approval number 6761, for scientific and ethical standards. Information about the study protocol and the confidentiality of the data and the identity of each participant were written to the informed consent form that was signed by each participant.

3.4. Data Analysis

Descriptive statistics were calculated for initial data analysis. Because of failure of all continuous variables in Kolmogorov-Smirnov normality tests, Spearman's Rho coefficients were calculated to define correlations between continuous variables and non-parametric tests (Mann-Whitney U and Kruskal-Wallis) were applied in order to define significant relationships between the continuous and categorical variables. The BDI, EPDS, and BAI scores were used as continuous variables. All association testing was conducted assuming a 5% significance level and a two-sided alternative hypothesis, while statistical analyses were performed using SPSS software package version 17.0 (SPSS Inc., Chicago, IL, USA).

4. Results

The initial sample of this study comprised 117 women from 32nd to 35th week of pregnancy. Their average age was 32.61 ± 4.06 years and the vast majorities of them were Greek (93.2%), graduates of higher-education (65.0%) and married (95.7%) (Table 1).

Table 1. Descriptive Statistics of the Initial Sample of Pregnant Women [a,b]

Participant Data Items	Values
Age, y	32.61 ± 4.06
Nationality	
Greek	109 (93.2)
Albanian	6 (5.1)
Other	2 (1.7)
Educational level	
Less than high school diploma	3 (2.6)
High school diploma	38 (32.4)
Bachelor's degree	76 (65.0)
Marital status	
Married	112 (95.7)
Unmarried	5 (4.3)
Professional status	
Employed	98 (83.8)
Unemployed	7 (6.0)
Housekeeping	12 (10.2)
Monthly family income, €	
0 - 1000	26 (22.2)
1000 - 3000	66 (56.4)
3000 - 5000	17 (14.6)
More than 5000	8 (6.8)
Planned pregnancy	
Yes	77 (65.8)
No	40 (34.2)
Fertilization *in vitro*	
Yes	10 (8.5)
No	107 (91.5)
Week of pregnancy	
32nd	55 (47.0)
33rd	25 (21.4)
34th	18 (15.4)
35th	19 (16.2)
Number of pregnancies	
First	67 (57.3)
Second	37 (31.6)
Third	11 (9.3)
Fourth	1 (0.9)
Fifth	1 (0.9)
Number of children	
None	74 (63.2)
One	36 (30.8)
Two	7 (6.0)
Hyperemesis (during pregnancy)	
Yes	16 (13.7)
No	101 (86.3)
Hypertension (during pregnancy)	
Yes	4 (3.4)
No	113 (96.6)
Diabetes mellitus (during pregnancy)	
Yes	17 (14.5)
No	100 (85.5)
Placental abruption	
Yes	14 (12.0)
No	103 (88.0)
Bleeding disorder (1st trimester)	
Yes	18 (15.4)
No	99 (84.6)
Bleeding disorder (2nd trimester)	
Yes	1 (0.9)
No	116 (99.1)
Bleeding disorder (3rd trimester)	
Yes	3 (2.6)
No	114 (97.4)
History of depression	
Yes	10
No	107
Received antidepressant treatment	
Yes	3 (2.6)
No	114 (97.4)
History of anxiety disorder	
Yes	11 (9.4)
No	106 (90.6)
Received anxiolytic treatment	
Yes	3 (2.6)
No	114 (97.4)

[a] N = 117.
[b] Values are presented as No. (%) except age that is presented as mean ± SD.

Furthermore, in a proportion of 83.8% they were employed, with most of them (56.4%) having a monthly family income from 1000 to 3000 €. Also, for 77 (65.8%) of the women in the sample this pregnancy was planned, while for 10 (8.5%) of them, *in vitro* fertilization was employed. The largest relative rate of the women (47.0%) in the sample in the initial phase of this study was at the 32nd week of pregnancy, which was the first for most of them (57.3%), while only 36 (30.8%) and seven (6.0%) of these women had one and two children, respectively. With regard to health problems experienced by women during pregnancy, hyperemesis was recorded at a rate of 13.7%, hypertension in 3.4%, diabetes mellitus in 14.5% and placental abruption in 12.0%. Similarly, bleeding disorders were experienced by 15.4% of the pregnant women, in the first trimester of pregnancy, 0.9% in the second and 2.6% in the third trimester. An important parameter of this study was the exploration of pregnant women's mental health. Therefore, 8.5% of the pregnant women reported a positive past history of depression, with three (2.6%) of them appearing to have received antidepressant treatment. Similarly, 9.4% of the pregnant women reported a history of anxiety disorder, with three (2.6%) of them reporting having followed anxiolytic treatment (Table 1).

The mean BDI score was 9.75 ± 4.67. Ninety-five (81.1%) participants were identified as experiencing minimal depressive symptoms, while 18 (15.4%) women showed mild, three (2.6%) moderate and one (0.9%), severe symptoms, respectively (Table 2).

The mean EPDS score was 6.77 ± 4.51. Ninety-four (80.3%) women showed absence of depression, while 23 (19.7%) indicated a likely diagnosis of depression (Table 2). The mean BAI score was 9.43 ± 6.37. Fifty-one (43.6%) participants showed minimal anxiety symptoms, while 50 (42.7%) women showed mild, 12 (10.3%) moderate and four (3.4%), severe, anxiety symptoms (Table 2). Participation in the second phase of the study (after childbirth) included 93 (79.48%) of the initial 117 women. Thereby, the average pregnancy week was 38 ± 1.35 weeks, for these women (N = 93), while births took place between the 34th and 40th week. The average duration of childbirth for all puerperants was 5.56 ± 4.55 hours. Fifty-three (57.0%) of them had a natural childbirth and 40 (43.0%) gave birth by cesarean section. Of the puerperants, who had natural birth (N = 53), 27 (50.9%) received analgesics and 43 (81.1%) received epidural anesthesia. Respectively, two (5.0%) of the women with cesarean section (N = 40) received general anesthesia, during childbirth, and 38 (95.0%) epidural anesthesia. At the same time, the average weight of the newborns (N = 93) was 3090.32 ± 456.13 gram. Admission to the NICU was deemed necessary for 18 (19.4%). One (1.2%) newborn had Apgar score 7, 19 (23.2%) had 8, 33 (40.2%) had 9 and 29 (35.4%) had Apgar score 10.

4.1. Associations of Prenatal Depressive and Anxiety Symptoms With Neonatal Parameters

According to BDI score, non-significant associations were found with the newborn's birth weight (Spearman's rho = -0.052, P = 0.623), with its admission in NICU (Mann-Whitney U test, P = 0.992) and the Apgar score (Kruskal-Wallis test, P = 0.307) (Table 3).

Table 2. Descriptive Statistics of Prenatal Depressive and Anxiety Symptoms Occurrence in Pregnant Women [a,b]

Mood Symptoms	No. (%)	Mean ± SD
BDI		9.75 ± 4.67
Minimal depressive symptoms	95 (81.1)	
Mild depressive symptoms	18 (15.4)	
Moderate depressive symptoms	3 (2.6)	
Severe depressive symptoms	1 (0.9)	
EPDS		6.77 ± 4.51
Total EPDS score < 11	94 (80.3)	
Total EPDS score > 11	23 (19.7)	
BAI		9.43 ± 6.37
Minimal anxiety symptoms	51 (43.6)	
Mild anxiety symptoms	50 (42.7)	
Moderate anxiety symptoms	12 (10.3)	
Severe anxiety symptoms	4 (3.4)	

[a] Abbreviations: BAI, Beck anxiety inventory; BDI, Beck depression inventory; EPDS, Edinburg postnatal depression scale.
[b] N = 117.

Table 3. Associations of Prenatal Depressive and Anxiety Symptoms With Neonatal Outcomes [a, b]

	BDI Score	P	EPDS Score	P	BAI Score	P
Birth weight, g (Rho)	-0.052	0.623	0.017	0.872	- 0.108	0.302
Admission in NICU	-	0.992	-	0.918	-	0.375
Yes [c]	10.06 ± 5.50	-	5.94 ± 3.40	-	10.33 ± 6.72	-
No [c]	9.48 ± 4.29	-	6.27 ± 4.29	-	8.68 ± 5.79	-
Apgar score		0.307		0.434		0.542
7 [c]	7.00 ± 0.00	-	6.00 ± 0.00	-	9.00 ± 0.00	-
8 [c]	11.89 ± 6.09	-	7.26 ± 4.54	-	10.42 ± 6.94	-
9 [c]	9.18 ± 4.26	-	6.42 ± 3.91	-	8.15 ± 4.32	-
10 [c]	9.14 ± 4.09	-	5.34 ± 4.11	-	7.79 ± 5.82	-

[a] Abbreviations: BAI, Beck anxiety inventory; BDI, Beck depression inventory; EPDS, Edinburg postnatal depression scale; NICU, neonatal intensive care unit.
[b] N = 93.
[c] The values are presented as mean ± SD.

According to EPDS scores, non-significant associations were found with the newborn's birth weight (Spearman's rho = 0.017, P = 0.872), with its admission in NICU (Mann-Whitney U test, P = 0.918), and the Apgar score (Kruskal-Wallis test, P = 0.434) (Table 3). Non-significant associations were found between prenatal anxiety symptoms, as assessed by BAI scale and the newborn's birth weight (Spearman's rho = -0.108, P = 0.302), its admission in NICU (Mann-Whitney U test, P = 0.375), and its Apgar score (Kruskal-Wallis test, P = 0.542) (Table 3).

5. Discussion

Our findings suggest that prenatal depressive and anxiety symptoms were not associated with neonatal outcomes, such as birth weight of the newborn, Apgar score and the newborn's admission in NICU. Therefore, in regard to the association of prenatal depression and anxiety symptoms with birth weight, our results mirror a number of previous studies (21-23, 25, 27-29). Other authors have found different results (16, 17, 19, 20, 26). There are several possible explanations for these discrepancies. First, there are differences in study methodology. More specifically, several of these studies include women who are of low income (16, 17, 20) or belong to minority groups (19), not all are of adult age and their level of education is basic (16). As we have already reported, the status of our sample was not low socioeconomic, all the participants were adults, the majority were graduates of higher education and received regular prenatal care. Probably, the difference in socioeconomic status, in health care systems and in maternal and neonatal profiles, may explain the adverse results. Another finding that we consider important in our study is that prenatal depressive and anxiety symptoms were not associated with Apgar score. This result is in agreement with previous studies (21, 22, 24, 25), although not all (9, 22). Several factors that may explain the inconsistency with our findings are the different moment at which took place the assessment of prenatal depression and anxiety symptomatology, the different screening instruments, as well as the different cultural background.

In this study, we also found no association between prenatal depressive and/or anxiety symptoms and the newborn's admission in NICU and we did not find any relationship. This concurs with the study of Setse et al. (2009) (10), although is contradicted by the study of Chung et al. (2001) (35). The sample of their study was 959 women from Hong Kong and they found that prenatal depressive symptoms were associated with increased risk of newborn's admission in NICU. Authors reported that it is unclear how a high score in a scale can interact with this indication and suggest further investigation.

The findings of our study should be interpreted with regard to a series of limitations. The sample size was not large enough, as well as the fact that, in the second phase, i.e. the period in which the recording of neonatal outcomes was performed, not all the initial sample participated. In addition, there was no selection in the population involved, i.e. no women were excluded from the study due to certain characteristics, such as pathological obstetric history. Also, our sample comes from a large urban center and the majority of the women had a high educational level. Furthermore, it should be mentioned that the majority of our sample reported the occurrence of limited depressive and anxiety symptoms that did not reach the cut-off point of a mood disorder. These attritions may compromise the generalization of the findings.

In conclusion, the evidence from our study suggests that limited depressive and anxiety symptoms during the third trimester of pregnancy do not appear to affect neonatal outcomes, such as the newborn's birth weight, the Apgar score and the newborn's admission in the NICU. This could be reassuring in clinical practice for pregnant women who suffer prenatally from low to moderate levels of prenatal depressive and anxiety symptoms. The present study confirms previous findings and contributes additional evidence in this field of research. As far as we know, no similar study has been conducted in Greece. One of the strengths of the study is that the assessment of prenatal depressive symptoms was based on two different psychometric scales, with similar results, therefore strengthening our conclusions. We hope our findings will stimulate further research that would yield evidence in antepartum depressive and anxiety symptomatology and its possible association with neonatal outcomes. Further research might assess prenatal depressive and anxiety symptoms using a combination of self-administrated scales and clinical interviews, in all trimesters of pregnancy. Another interesting area of future research would be to investigate possible associations between prenatal psychopathology with other neonatal and obstetric parameters, such as neonate small for gestational age (SGA), preterm birth and mode of delivery.

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Authors' Contributions

Study concept, design and data acquisition: Pinelopi Varela; data analysis and interpretation: Zacharias Kalogerakis; drafting of the manuscript: Pinelopi Varela, Martha Moraitou; critical revision of the manuscript for important intellectual content: Areti C. Spyropoulou; statistical analysis: Zacharias Kalogerakis; administrative, technical and material support: Areti C. Spyropoulou; study supervision: Iannis M. Zervas.

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