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Research Article

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Antenatal Depression and Risk of Complications in the Mother and the Newborn: A Retrospective Cohort Study

Daniel Perejon Lopez, Laura Gasco Serna, Maria Catalina Serna Arnaiz*, Miriam Oros Ruiz, Julia Siscart Viladegut, Joaquim Sol and Blanca Salinas

Department of Family Medicine, University of Lleida, PC 25003 Lleida, Spain

Abstract

Objective: To analyse the relationship between depression and complications of pregnancy and the newborn in the Lleida health region.

Materials and methods: Retrospective observational cohort study in pregnant women between 2012-2018 in the Lleida health region. Variables included age, Body Mass Index (BMI), caesarean section, pre eclampsia, birth weight and Apgar score. We performed multivariate analysis, with linear regression coefficients and 95% Confidence Intervals (CI).

Results: Depression was diagnosed in 2.54% pregnant women from a total sample of 17,177. Depression is significantly associated with a miscarriage (OR 1.64), higher risk pregnancy (OR 4.9) and low birth weight (OR 2.2). Pre-eclampsia, 1-minute Apgar score and caesarean section were not significantly associated with depression.

Conclusion: Pregnancies in women with depression were more often classified as high-risk. In addition, depression in the mother increases the probability of miscarriage and low birth weight.

Keywords: Pregnancy; Depression; Preterm birth; Low birth weight

Introduction

Depression is one of the main causes of disability which affects approximately 280 million people globally [1].

Antenatal depression occurs during pregnancy, and can have consequences for both the mother and the newborn. It is estimated that the prevalence in Spain and neighbouring countries is around 10-15% [2-5], and that approximately 1.8-8% of pregnant women with depression use antidepressants [6-8].

Mental health problems impact pregnancy and childbirth and might also correlate with adverse outcomes for the newborn and the baby's development (HOWAR). One study, correlated depression in pregnant mothers under 35 years of age with hyperemesis, abortion, foetal malposition, caesarean section, and even intrauterine death [9]. Although they do not fully specify pathophysiological mechanisms, Aldane and colleagues concluded that maternal antenatal mental health disorders might be associated with a moderate increase in stillbirth and infant mortality [10].

In a systematic review comparing 20 cohort studies, Jahan, et al. conclude that untreated depression during pregnancy is associated with abortion, prematurity, Low Birth Weight (LBW, birth weight <2500 g), Small for Gestational Age (SGA), complications during delivery and postpartum depression [11].

Low birth weight is a predictor of short and long-term health. During the neonatal period, low birth weight is associated with a higher risk of infection, respiratory distress and mortality [12,13]. Later in life, it is associated with developmental delay, cardiovascular disease, and diabetes [14,15].

The aim of this study is to verify if antenatal depression has any deleterious effect on maternal and neonatal outcomes.

Materials and Methods

Study design and data collection

Retrospective, observational cohort study in pregnant women between 2012-2018 in the health region of Lleida.

Data were obtained from patients who had given birth at the Arnau de Vilanova Hospital between January 1, 2012 and December 31, 2018. The Arnau de Vilanova hospital is the only referral hospital in the region. Data were obtained from the CMBD database (Catalan acronym for minimum data set) in the E-CAP electronic medical records database, and from the Catalan health service database, which contains the electronic prescriptions made by Catalan health service professionals.

***Corresponding author:** Maria Catalina Serna Arnaiz, Department of Family Medicine, University of Lleida, PC 25003 Lleida, Spain, Tel: 675780132; E-mail: cserna.lleida.ics@gencat.cat

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This study is part of the ILERPREGNANT project, which aims to analyse the population prevalence of diseases, drug prescription and pharmacological adherence during pregnancy [16].

Participants

Women who had delivered between January 1, 2012 and December 31, 2018. Data from the date of the last period to the date of delivery were included. This means that data from 2011 were included for women with a last period date in 2011 and a delivery date in 2012. Women from health regions other than Lleida were excluded. To evaluate the representativeness of the sample, the percentage of births studied (births registered in the Arnau de Vilanova University Hospital in Lleida) was calculated with respect to the total number of births in the health region of Lleida according to the Statistics Institute of Catalonia (Idescat) (Table 1).

Year	Deliveries in Lleida sample	Deliveries from Idescat	Sample/Idescat
2012	3635	3788	96%
2013	3370	3535	95%
2014	3308	3592	92%
2015	3162	3426	92%
2016	3180	3283	97%
2017	3034	3197	95%
2018	3001	3029	99%

Table 1: Number of births registered in Lleida sample in comparison to the Lleida health region per year

The variables recorded were as follows: Depression (yes/no), which includes a diagnostic for depression according to the International Classification of Diseases, 9th revision (ICD-9) with codes 296.20 to 296.25, 296.30 to 296.35, 300.4, or 311, and in the 10th revision (ICD-10) with codes F32.0 to F32.9, F33.0 to F33.3, F33.8, F33.9, F34.1, or F41.2; age; Body Mass Index (BMI); diabetes mellitus (ICD-10 O24.9); risk of the pregnancy; duration of the pregnancy (miscarriage, preterm, term, prolonged); caesarean section; birth weight (<2500 g=underweight, between 2500 g and 3999 g=normal weight, and ≥ 4000 g=macrosomia), 1-minute and 5-minute Apgar score; and preeclampsia. Data were also collected on prescribed antidepressant drug, dispensation date, dose and amount. Antidepressants were classified into four classes following the Anatomical Therapeutic Chemical (ATC) classification system.

Data analysis

A descriptive analysis was performed, with numerical variables described by mean and standard deviation, and categorical variables by absolute and relative frequencies. To evaluate differences between groups, we used Student's t-test or *Chi-square* test for numerical and categorical variables, respectively. The association of the different variables with depression was evaluated with a multivariate linear model, using percentage of depression as the response variable, and the rest of the variables as predictors. Regression coefficients and odds rations and their 95% confidence interval were calculated.

Ethics

This study was approved by the Clinical Research Ethics Committee (CREC) of the Institut d'Investigació IDIAP Jordi Gol (code 19/196-P). The study follows the tenets of the Declaration of Helsinki. The information was extracted from centralized medical files in the E-CAP database by the department of research management and health evaluation. Informed consent from participants was not required. The variables in the E-CAP database were de-identified and processed following confidentiality guarantees established by the National Law and Regulation 2016/679 of the European Parliament and of the Council on personal data protection.

Results

Participants

Participants include a sample of 21,375 pregnant women who had given birth at the Arnau de Vilanova Hospital in Lleida between 2012 and 2018 (both included). Women who did not have a health card (n=1625) were excluded. Women with missing data in their medical records were also excluded (n=2573). The final sample consisted of 17,177 patients (Figure 1).

The average age of pregnant women during the study period was 30.5 years. A total of 436 women (2.54%) suffered from depression. In 20 women (0.13%), depression was considered gestational (Tables 2-4).

Figure 1: Sample of pregnant women.

Year of delivery	**17177**
2011	43 (0.25%)
2012	2740 (16.0%)
2013	2525 (14.7%)
2014	2491 (14.5%)
2015	2419 (14.1%)
2016	2418 (14.1%)
2017	2317 (13.5%)
2018	2224 (12.9%)
Age at pregnancy	**17177**
<30	6981 (40.6%)
>35	5733 (33.4%)
30-35	4463 (26.0%)
Body mass index	**16803**
≤ 25	11117 (66.2%)
>30	1986 (11.8%)
26-30	3700 (22.0%)
Number of pregnancies	**17177**
1	9009 (52.4%)
2	5181 (30.2%)
3	1870 (10.9%)
4	646 (3.76%)
>4	471 (2.74%)
Multiple pregnancy	**17177**
No	17145 (99.8%)
Yes	32 (0.19%)
Pre-eclampsia	**17177**
No	17018 (99.1%)
Yes	159 (0.93%)
Pregnancy risk	**15333**
Very high	316 (2.06%)
High	2912 (19.0%)
Intermediate	4527 (29.5%)
No risk	7578 (49.4%)
Birth weight	**15133**
Low birth weight	910 (6.01%)

Macrosomia	1020 (6.74%)
Normal birth weight	13203 (87.2%)
Apgar 1'	**15085**
High	14706 (97.5%)
Low	379 (2.51%)
Apgar 5'	**15087**
High	14970 (99.2%)
Low	117 (0.78%)
Caesarean section	**17177**
No	14201 (82.7%)
Yes	2976 (17.3%)

Table 2: General characteristics of the sample.

	No (N=16741)	**Yes (N=436)**
Year of delivery		
2012	2682 (97.9%)	58 (2.12%)
2013	2473 (97.9%)	52 (2.06%)
2014	2430 (97.6%)	61 (2.45%)
2015	2355 (97.4%)	64 (2.65%)
2016	2348 (97.1%)	70 (2.89%)
2017	2243 (96.8%)	74 (3.19%)
2018	2167 (97.4%)	57 (2.56%)

Table 3: Depression diagnosis in pregnant women for each study year.

Depression	**No (N=16741)**	**Yes (N=436)**	
Age at pregnancy (years)	30.5	32.2	p <0.001
<30	6850 (40.9%)	131 (30.0%)	
>35	5558 (33.2%)	175 (40.1%)	
30-35	4333 (25.9%)	130 (29.8%)	
Body mass index	24.8 (4.91)	25.6 (5.54)	p: 0.150
≤ 25	10851 (66.3%)	266 (62.6%)	
>30	1924 (11.7%)	62 (14.6%)	
26-30	3603 (22.0%)	97 (22.8%)	
Number of pregnancies			
1	8790 (52.5%)	219 (50.2%)	p: 0.413

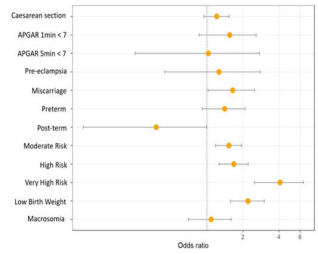
2	5053 (30.2%)	128 (29.4%)	
3	1815 (10.8%)	55 (12.6%)	
4	629 (3.76%)	17 (3.90%)	
>4	454 (2.71%)	17 (3.90 %)	
Multiple pregnancy			
No	16709 (99.8%)	436 (100%)	p: 1,000
Yes	32 (0.19%)	0 (0.00%)	
Caesarean section			
No	13854 (97.6%)	347 (2.44%)	0.097
Yes	2887 (97.0%)	89 (2.99%)	
Duration of pregnancy (qualitative)			
Miscarriage	545 (95.8%)	24 (4.22%)	0.004
Post-term	325 (99.1%)	3 (0.91%)	
Preterm	743 (96.6%)	26 (3.38%)	
Term	11024 (97.6%)	272 (2.41%)	
Pre-eclampsia			
No	16587 (99.1%)	431 (98.9%)	p: 0.606
Yes	154 (0.92%)	5 (1.15%)	
Pregnancy risk			
Very high	293 (1.96%)	23 (6.01%)	p<0.001
High	2820 (18.9%)	92 (24.0%)	
Intermediate	4399 (29.4%)	128 (33.4%)	
No risk	7438 (49.8%)	140 (36.6%)	
Birth weight			
Low birth weight	866 (5.87%)	44 (11.8%)	p<0.001
Macrosomia	993 (6.73%)	27 (7.24%)	
Normal birth weight	12901 (87.4%)	302 (81.0%)	
Apgar 1'			
High	14347 (97.5%)	359 (96.2%)	p: 0.167
Low	365 (2.48%)	14 (3.75%)	
Apgar 5'			
High	14600 (99.2%)	370 (99.2%)	p: 0.767
Low	114 (0.77%)	3 (0.80%)	
Caesarean section			
No	13854 (82.8%)	347 (79.6%)	p: 0.097
Yes	2887 (17.2%)	89 (20.4%)	

Table 4: Depression prevalence and relationship with other factors.

Table 3 shows percentage of depression for each year of study. The average prevalence of depression was 2.5%. Patients with depression have a higher average age, a higher body mass index, and are more often classified as high-risk pregnancy. The difference in prevalence of low birth weight is statistically significant, with 5.85% in children of patients without depression versus 11.7% of babies born to mothers with depression. No differences were found in relation to pre-eclampsia, Apgar score and number of caesarean sections.

Regarding pharmacological treatment, 14.9% of patients with depression received treatment, 71.3% drugs are selective serotonin reuptake inhibitors, followed by 12.1% serotonin-norepinephrine reuptake inhibitors, 7.89% non-selective monoamine oxidase inhibitors, and 6.58% atypical antidepressants. The most commonly prescribed drugs were paroxetine, followed by sertraline, citalopram and escitalopram. All patients diagnosed with depression received pharmacological treatment.

The regression model shows that pregnant women with depression have a significantly higher risk pregnancy, in particular in relation to low birth weight. In contrast, no significant differences were found regarding the 1-minute Apgar score, pre-eclampsia and number of caesarean sections (Figure 2).



	OR	CI 2.5-97.5	p value
Cesarean section	1.21	0.95-1.53	0.12
APGAR 1 min <7	1.55	0.86-2.58	0.11
APGAR5 min <7	1.03	0.25-2.75	0.96
Pre-eclampsia	1.26	0.45-2.79	0.60
Miscarriage	1.64	1.03-2.50	0.02
Preterm	1.41	0.92-2.08	0.09
Post-term	0.37	0.09-0.99	0.09
Moderate risk	1.52	1.18-1.96	0.001
High risk	1.67	1.27-2.21	<0.001
Veri high risk	4.09	2.50-6.40	<0.001
Low birth weight	2.20	1.57-3.02	<0.001
Macrosomia	1.08	0.70-1.60	0.701

Figure 2: Multiple linear regression: Prevalence of depression in relation to adverse variables.

Discussion

This study shows a prevalence of antenatal depression of 2.54%, 14.9% patients taking one or more antidepressant. Pregnancy of women with depression was more frequently classified as very high risk (4.9) and show more risk of miscarriage (1.64). For the new born, low birth weight (OR 2.2) was significantly more common in infant from women with depression (11.8%) compared to infant from women without depression (5.87%).

Results of adverse consequences vary in the studies on antenatal depression. A meta-analysis carried out by Ghimire, et al. found an increased risk of preterm birth (RR=1.35, 95% CI 1.19–1.52), low birth weight (RR=1.86, 95% CI 1.32–2.62) and intrauterine growth retardation (RR=4.39, 95% CI 2.45–7.86) [17,18]. Lang, et al. and Nasren, et al. also reported an increased risk of low birth weight [19,20]. However, other studies have not reported this association. The systematic review and meta-analysis by Fekadu Dadi, et al. attribute the higher prevalence of depression to the economic and psycho-social situation of pregnant women. This psycho-social situation might influence the relationship observed between anxiety/depression and prematurity. Women living in disadvantaged neighbourhoods have less access to quality food and health services, fewer leisure opportunities and more social and financial stress, which might determine the adverse effects on pregnancy.

In a systematic review of 20 studies on untreated antenatal depression published in 2021, Jahan, et al. underscored the relationship with low birth weight, and also with preterm delivery, death of the newborn (in addition to other perinatal complications), and postpartum depression.

Other studies point at the causative effect of antidepressant treatment rather than depression on birth weight. Specifically, in 2016 Nezvalová-Henriksen, et al. studied the effect of exposure to SSRIs during the 2nd and 3rd trimester pregnancy, concluding that it was associated with an average decrease of 4.9 days of pregnancy and of 205 g of birth weight.

In 2017, Mitchell, et al. conducted a systematic review to compare women who had taken antidepressants during their pregnancy with women diagnosed with depression and not treated. Regarding the average weight of the newborn, 6 of 9 studies did not find significant differences, two observed a higher risk of small for gestational age due to antidepressant treatment, and one study concluded that untreated depression was a risk factor for low birth weight. Only one study analysed abortion, and it was inconclusive. Another study found that children born to mothers who adhered to antidepressants weighed 71.9 g less than children of mothers who discontinued treatment (95% Confidence Interval (CI): −115.5, −28.3 g), with a larger difference for girls (−106.4 g, 95% CI: -164.6, −48.1) than boys (−48.5 g, 95% CI: −107.2, 10.3).

Among the limitations, we should consider that in this study, 14.9% of patients diagnosed with depression receive antidepressant treatment. Therefore, we have not analysed the influence of the treatment on the outcomes of the study or the adherence to it, which may condition different results. Importantly, this study has not stratified by socio-demographic variables that might affect pregnancy, but it is a population study conducted with data from a referral hospital that covers a high percentage of the population.

Conclusion

Antenatal depression is a risk factor for infant morbidity and mortality. In this study, maternal depression was associated with an increased risk of low birth weight, miscarriage and categorization of risk pregnancy. We underscore the relevance of early detection and treatment of depression in pregnancy. Further research is needed to evaluate the impact of depression on mother and child, taking into account severity, antidepressant treatment and other associated factors, in order to improve the management of pregnant women with depression.

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Author Contributions

All authors (M.O., M.L., J.S., D.P., M.C.S. and B.S.R.) contributed to the study conception and design. Material preparation, data collection and analysis were performed by M.O., M.L., J.S., D.P. and M.C.S. The first draft of the manuscript was written by B.S.R., M.L. and M.O.; and all authors commented on previous versions of the

manuscript. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement

Not applicable.

Informed Consent Statement

This study was approved by the ethics and clinical research committee of the "Institute for Primary Health Care Research Jordi Gol i Gurina (IDIAPJGol)" under the code 19/196-P. The study was conducted in accordance with the principles of the Declaration of Helsinki. Pseudonymized retrospective descriptive cross-sectional study adheres to Additional Provision 17.2.d LOPD-GDD for research purposes, without the need to obtain the consent of the data holders. There is a technical and functional separation between the research team and the performer pseudonymization, the data is only accessible to the research team, and technical measures have been taken to prevent such re-identification and access by third parties through the CMBD database ("Conjunt Minim de Base de Dades"), the E-CAP computerized medical history database and the Catalan Health Service database.

Data Availability Statement

Available upon request to corresponding author (dperejon.lleida.ics@gencat.cat).

Conflicts of Interest

The authors declare no conflict of interest.

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