

## CLINICAL SCIENCE

# Depression during pregnancy in women with a medical disorder: risk factors and perinatal outcomes

Gláucia Rosana Guerra Benute,<sup>1</sup> Roseli Mieko Yamamoto Nomura,<sup>II</sup> Juliana Siracuza Reis,<sup>1</sup> Renério Fraguas Junior,<sup>III</sup> Mara Cristina Souza de Lucia,<sup>1</sup> Marcelo Zugaib<sup>II</sup>

<sup>1</sup>Division of Psychology, Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo, São Paulo, Brazil. <sup>II</sup>Department of Obstetrics and Gynecology, Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo, São Paulo, Brazil. <sup>III</sup>Department of Psychiatric, Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo, São Paulo, Brazil.

**BACKGROUND:** Approximately one-fifth of women present depression during pregnancy and puerperium, and almost 13% of pregnant women experience a major depressive disorder.

**OBJECTIVE:** The aim of this study was to identify risk factors for depression among pregnant women with a medical disorder and to evaluate the influence of depression on perinatal outcomes.

**METHODS:** Three hundred and twenty-six pregnant women with a medical disorder were interviewed. A semistructured interview was conducted for each participant using a questionnaire that had been developed previously. Major depression was diagnosed using the Portuguese version of the Primary Care Evaluation of Mental Disorders (PRIME-MD). The medical records of the participants were thoroughly reviewed to evaluate the perinatal results.

**RESULTS:** Major depressive disorder was diagnosed in 29 cases (9.0%). The prevalence of major depression was as follows: 7.1% for preeclampsia or chronic hypertension, 12.1% for cardiac disorder, 7.1% for diabetes mellitus, 6.3% for maternal anemia, 8.3% for collagenosis and 12.5% for a high risk of premature delivery. An univariate analysis showed a significant positive correlation between an average household income below minimum wage and a PRIME-MD diagnosis of major depression. A multiple regression analysis identified unplanned pregnancy as an independent predictor of major depression (86.2% in the group with a diagnosis of major depression by PRIME-MD vs. 68.4% in the group without major depression). A comparison between women who presented major depression and those who did not revealed no significant differences in the perinatal results (i.e., preterm delivery, birth weight and low Apgar scores).

**CONCLUSION:** In the present study, unplanned pregnancy in women with a medical disorder was identified as a risk factor for major depression during gestation. Major depression during pregnancy in women with a medical disorder should be routinely investigated using specific methods.

**KEYWORDS:** Depression; Pregnancy; Medical disorder; Perinatal outcome.

Benute GRG, Nomura RMY, Siracuza RJ, Fraguas Jr R, Lucia MCS, Zugaib M. Depression during pregnancy in women with a medical disorder: risk factors and perinatal outcomes. *Clinics*. 2010;65(11):1127-1131.

Received for publication on July 1, 2010; First review completed on July 26, 2010; Accepted for publication on August 23, 2010

E-mail: grguerra@uol.com.br

Tel.: 55 11 3069-6209

## INTRODUCTION

Depression is a significant public health concern. In addition to the suffering that is experienced by patients, there are costs associated with treatment due to a higher frequency of hospitalization and a loss of productivity.<sup>1</sup> In comparison to males, females demonstrate a higher incidence rate of major depressive disorder.<sup>2</sup> Approximately one-fifth of women present depression during pregnancy and puerperium,<sup>3</sup> and

almost 13% of pregnant women experience a major depressive disorder.<sup>4</sup> The American College of Obstetricians and Gynecologists recommends that women be screened for depression during pregnancy.<sup>5</sup> According to the Royal College of Obstetricians and Gynecologists (RCOG), health-care professionals should inquire about the mood of a pregnant woman to identify potential signs of depression during her first encounter with prenatal care services.<sup>6</sup>

Some symptoms of depression may overlap with those associated with the pregnancy, and therefore, the diagnosis of this disorder is difficult. Although the symptoms of anxiety and depression are often similar to complaints that are expected during pregnancy, a detailed evaluation of the patient would permit an adequate diagnosis of depression and an early intervention.<sup>7</sup>

**Copyright** © 2010 CLINICS – This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

The independent risk factors associated with antepartum depressive symptoms include stressful life events, a lack of social support and domestic violence.<sup>8</sup> According to Lovisi et al., poverty and violence are risk factors that are often experienced by pregnant women in Brazil and in other developing countries. In addition to pregnancy-specific vulnerability, women are also exposed to marked social inequality in these countries.<sup>9-10</sup>

Depression during pregnancy is a strong risk factor for postnatal depression, which indicates the need for interventions that are performed prior to childbirth.<sup>11</sup> Some studies have demonstrated that depression in pregnant women has negative effects on the birth outcome (e.g., low birth weight, preterm birth and impaired fetal development),<sup>12-13</sup> whereas others have reported that it does not interfere with the pregnancy.<sup>14</sup> Consequently, the aim of the present study was to identify risk factors for depression among pregnant women with a medical disorder and to evaluate the influence of depression on perinatal outcomes.

### SUBJECTS AND METHODS

This study was conducted between March 2005 and March 2006 at the largest public university hospital in the city of São Paulo in Brazil. High-risk pregnant women were referred for prenatal care and delivery. The local research ethics committee approved the study protocol and all of the women provided written informed consent prior to participating in the interview.

The criteria for inclusion in the study included singleton pregnancies, intact chorioamniotic membranes, an absence of fetal congenital and chromosomal abnormalities and an absence of pregnancy complications due to medical disorders. The exclusion criteria included fetal malformations and a lack of postnatal data. The gestational age was determined for all of the women based on the last menstrual period and according to the findings of an ultrasonography that was performed prior to the 20th week of gestation.

Each participant completed in a semistructured interview during which data were collected using a previously designed questionnaire. The women were interviewed either in the waiting rooms during prenatal outpatient visits or during hospitalization. Each interview lasted approximately one hour. The questionnaire consisted of closed-ended questions regarding demographic data such as age, religion (e.g., Catholic, Evangelical), average household income classified relative to the minimum wage, occupational status, relationship status (e.g., married, cohabiting, or unmarried), planned pregnancy, educational background and gestational age at the time of the interview (weeks).

Depression was diagnosed using the Portuguese version of the Primary Care Evaluation of Mental Disorders (PRIME-MD) classification system<sup>15</sup>. The present study focused specifically on major depressive disorder.

The medical records of the women were methodically reviewed for verification of the information regarding antenatal care and delivery. The gestational age at birth, type of delivery, birth weight and Apgar score were obtained from these records. Data were analyzed using the Statistica program for Windows (Release 4.3, Statsoft, Inc., 1993) and are reported as the mean and standard deviation. The Student's t-test was used to compare groups with or without a diagnosis of major depression. Categorical

data were compared using the chi-square test or Fisher's exact test where appropriate. Multiple regressions were performed using a standard procedure to identify independent variables that were related to the diagnosis of major depression according to the PRIME-MD. The level of significance was set at  $p < 0.05$  for all analyses.

### RESULTS

Three hundred and twenty-six pregnant women with a medical disorder participated in the present study. The women were interviewed at a mean gestational age of 28.2 weeks (SD = 10.5). The mean age of the participants was 30.2 years (SD = 7.1). The medical disorders presented by the women included preeclampsia or chronic hypertension (n = 142), heart disease (n = 66), diabetes mellitus (n = 84), anemia (n = 16), collagenosis (n = 24) and risk for preterm delivery (n = 16). Twenty-two (6.8%) women had two associated disorders.

Major depressive disorder was diagnosed in 29 cases (9.0%). None of the participants was taking a psychoactive medication. The prevalence of major depression among the women who were affected by a physical disorder was as follows: preeclampsia or chronic hypertension (7.1%), heart disease (12.1%), diabetes mellitus (7.1%), anemia (6.3%), collagenosis (8.3%) and risk for preterm delivery (12.5%). The symptoms of depression that were reported by the women are shown in Table 1. The most frequently reported symptoms were insomnia or hypersomnia and psychomotor agitation or retardation.

Table 2 shows the sociodemographic data and univariate analysis comparing pregnant women who presented major depression with those who did not. An average household income below minimum wage was positively correlated with a PRIME-MD diagnosis of major depression. Maternal depression was not associated with age, religion, occupational status, marital status, planned pregnancy, or educational level.

Standard multiple regressions were performed to differentiate the independent effects of the sociodemographic variables on the occurrence of major depression and to identify planned pregnancy as an independent predictor of major depression (Table 3).

No significant differences were observed with respect to perinatal outcomes between women who presented major

**Table 1 - Frequency of depressive symptoms reported by pregnant women with a medical disorder with or without diagnosis of major depression during pregnancy according to the PRIME-MD.**

Depressive symptoms	Diagnosis of Major depression	
	yes (n = 29)	no (n = 297)
Insomnia or hypersomnia	23 (79.3%)	64 (21.6%)
Fatigue or loss of energy	18 (62.1%)	38 (12.8%)
Decreased or increased appetite	14 (48.3%)	37 (12.5%)
Diminished interest in daily activities	21 (72.4%)	34 (11.5%)
Depressed mood	25 (86.2%)	37 (12.5%)
Feelings of worthlessness or inappropriate guilt	24 (82.8%)	29 (9.8%)
Diminished ability to think or concentrate	19 (65.5%)	38 (12.8%)
Psychomotor agitation or retardation	22 (75.9%)	54 (18.2%)
Recurrent thoughts of death	5 (17.2%)	4 (1.4%)

**Table 2** - Association of sociodemographic characteristics with a PRIME-MD diagnosis of major depression during pregnancy in women with medical disorders.

Characteristics	Diagnosis of Major depression		p
	yes (n = 29)	No (n = 297)	
Age (years), mean (SD)	29.4 (7.0)	30.3 (7.2)	0.54
Religion, n (%)			
Catholic	19 (65.5)	158 (53.7)	0.53
Evangelical	8 (27.6)	95 (32.3)	
Afro-Brazilian	0 (0)	5 (1.7)	
Others	2 (6.9)	39 (13.1)	
Average household income, n (%)			
< 1 minimum wage	3 (10.3)	10 (3.4)	0.04
1 to 6 minimum wage	15 (51.8)	211 (70.9)	
> 7 minimum wage	4 (13.8)	21 (7.2)	
No answer	7 (24.1)	55 (18.5)	
Employed, n (%)			
Yes	11 (38.0)	126 (42.3)	0.79
No	18 (62.0)	171 (57.7)	
Relationship status, n (%)			
cohabit with a partner	16 (55.2)	170 (57.1)	0.99
single	13 (44.8)	127 (42.9)	
Planned pregnancy, n (%)			
Yes	4 (13.8)	94 (31.6)	0.07
No	25 (86.2)	203 (68.4)	
Educational background, n (%)			
No schooling	1 (3.4)	2 (0.7)	0.15
Elementary school	8 (27.6)	118 (39.7)	
High school	19 (65.6)	150 (50.5)	
College	1 (3.4)	27 (9.2)	

depression during pregnancy and those who did not (Table 4). A nonadjusted univariate analysis revealed no significant association between the antenatal PRIME-MD diagnosis and an adverse neonatal outcome.

**DISCUSSION**

The findings of the present study suggest that unplanned pregnancy may be an independent risk factor associated with major depression during pregnancy in women with medical disorders. The concomitant occurrence of a medical disorder and an unplanned pregnancy was found to cause stress in the participants, especially those from low-income families. A previous systematic review<sup>8</sup> of 57 studies has concluded that stressful life events, a lack of social support and domestic violence are independently associated with antepartum depressive symptoms according to a multivariate analysis.

**Table 3** - Standard multiple regression analysis.

Variable	Coefficient	Standard error	t-value	p-value
Intercept	1.9626	0.1472	13.3329	0.00
Maternal age	0.00186	0.0024	0.7803	0.44
Relationship status	0.00236	0.0323	0.0714	0.94
Religion	0.03046	0.0221	1.3787	0.17
Planned pregnancy	-0.07286	0.0352	-2.0703	0.04
Educational background	-0.00196	0.0264	-0.0722	0.94
Occupational status	-0.00996	0.0336	-0.2961	0.77
Average household income	-0.0067	0.0192	-0.3473	0.73

**Table 4** - Association of perinatal outcomes with a PRIME-MD diagnosis of major depression during pregnancy in women with medical disorders.

Perinatal outcomes	Diagnosis of Major depression		p-value
	yes (n = 29)	no (n = 297)	
Gestational age at birth (weeks),			
mean (SD)	37.2 (1.8)	37.1 (2.6)	0.83
< 37, n (%)	16 (55.2)	158 (53.2)	0.99
≥ 37, n (%)	13 (44.8)	139 (46.8)	
Birth weight (g)			
mean (SD)	2700.7 (623.9)	2764.3 (775.1)	0.67
≤ 2,500, n (%)	6 (20.7)	96 (32.3)	0.28
> 2,500, n (%)	23 (79.3)	201 (67.7)	
1 <sup>st</sup> minute Apgar score, n (%)			
< 7	4 (13.8)	46 (15.5)	1.0
≥ 7	25 (86.2)	251 (84.5)	
5 <sup>th</sup> minute Apgar score, n (%)			
< 7	1 (3.5)	19 (6.4)	1.0
≥ 7	28 (96.5)	278 (93.6)	

The PRIME-MD classification system was developed to aid primary care physicians in screening, evaluating and diagnosing mental disorders. The agreement between the PRIME-MD diagnosis and that made by independent mental health professionals is excellent and it demonstrates a sensitivity of 83%, specificity of 88%, positive predictive value of 80% and an overall accuracy of 88%.<sup>16</sup> The PRIME-MD is considered a suitable tool to assess the relevance of psychiatric disorders in an obstetric outpatient setting because it is convenient and easy to use.

Andersson et al. used the PRIME-MD to assess the prevalence of psychiatric disorders during the second trimester of gestation in a population-based sample of pregnant women. The authors detected psychiatric disorders in 14.1% of the women and major depression in 3.3%. This proportion is lower than that observed in the present study, which only included pregnant women with a medical disorder.

Using the Edinburgh Postnatal Depression Scale (EPDS), Goodman<sup>18</sup> found a prevalence of depression of 8.6% in predominantly well-educated, high-income, married women from the northern United States who were in their third trimester of gestation.

In a study that employed the Spielberger State and Trait Anxiety Inventory and the EPDS, pregnant women with a medical disorder presented significantly higher scores on the state anxiety scale in comparison to those without a medical disorder. In addition, pregnant women with a medical disorder demonstrated a higher score on the EPDS in comparison to healthy controls; 26.7% had a score of 13 or higher (13 serves as the cut-off for probable major depression) compared to only 6.7% of the healthy controls.<sup>19</sup> The differences in the proportion of major depression in the study by King et al. compared to the present work may be explained in part by the observation that more than 50% of the women in that study were taking medication.

In a recent study of postpartum depression that was conducted in southern Brazil, both general health questionnaires and postpartum depression rating scales were found to be useful tools for the determination of depressive phenomena in women<sup>20</sup>. Although general health questionnaires were not used in the present study, this tool should be used in future research investigating depression in pregnant women.



Prior to this study, major depression in participants was likely to have gone unrecognized by an obstetrician. The high frequency of unrecognized major depression in obstetric patients suggests that the diagnosis of this condition is difficult due to the lack of a standard protocol.<sup>16</sup> The utilization of PRIME-MD can facilitate a reliable diagnosis of major depression in pregnant women with a medical disorder. Major depression is associated with substantial patient suffering, disability and loss of productivity.

The results of the present study suggest that perinatal outcomes (i.e., preterm delivery, low birth weight and low Apgar scores) are not related to the presence of major depression during pregnancy that is complicated by a medical disorder, which is consistent with the results reported by Andersson et al.<sup>14</sup> The samples assessed in these two studies (i.e., the present study and that performed by Andersson et al.) included pregnant women who had access to and frequently attended prenatal care appointments. The DSM-IV research criteria for psychiatric disorders were used to determine a clinical diagnosis of depression. Although the two samples were similar, high-risk pregnant women were enrolled in the present study, whereas Andersson et al. excluded women who presented any pathology.

In the present study, maternal exposure to major depression was not associated with a preterm birth. Nevertheless, a lack of social support constitutes an important risk factor for adverse effects on pregnancy outcomes,<sup>21</sup> and unplanned pregnancies are reported by 43.5% of pregnant women with a low level of social support. In the present study, unplanned pregnancy was found to be independently associated with a diagnosis of major depression during pregnancy.

Some studies have reported findings for the influence of depression on perinatal outcomes.<sup>12,13,22</sup> It is important to highlight the differences between the results reported by these studies and the present work in terms of the methods used, populations studied and the ways in which depression was evaluated. According to Hoffman et al<sup>12</sup> the score obtained using the Center for Epidemiological Studies Depression Scale indicated that depression was unrelated to fetal growth or the duration of gestation. Nevertheless, analyses of other potentially high-risk subgroups (e.g., women with a lower social class) have shown that a depressive mood may be associated with restricted fetal growth<sup>12</sup>. The Center for Epidemiological Studies Depression Scale evaluates depression based on the symptoms that are reported by the patients and does not distinguish between symptoms of pregnancy and those characteristic of depression. Orr et al. used this scale to evaluate depression in African American women, who are known to present a higher risk for preterm delivery.<sup>13</sup> Li et al. found that pregnant women with depressive symptoms have an increased risk for preterm delivery; however, this risk seemed to be exacerbated by a low level of education, fertility problems, obesity and stressful events.<sup>22</sup>

The limitations of the present study included the heterogeneity of the medical disorders and the wide range of medications that were used by the participants. Another limitation was that the psychiatric diagnoses were made on only one occasion during the pregnancy and it was unclear whether the symptoms were transitory. Despite these limitations, we were able to demonstrate that unplanned pregnancy is associated with a diagnosis of antenatal major depression in pregnant women with a medical disorder.

In conclusion, further studies that apply specific tools for the diagnosis of depression (instead of evaluating the presence of a disorder according to patient-reported symptoms) are necessary to clarify the influence of depression in pregnant women on perinatal outcomes. In this study, unplanned pregnancy in women with a medical disorder was identified as a risk factor for major depression during gestation. Thus, major depression during pregnancy in women with a medical disorder should be routinely investigated using specific instruments.

## REFERENCES

1. Stewart DE, Gagnon A, Saucier JF, Wahoush O, Dougherty G. Postpartum depression symptoms in newcomers. *Can J Psychiatry* 2008;53:121-4.
2. Essau CA, Lewinsohn PM, Seeley JR, Sasagawa S. Gender differences in the developmental course of depression. *J Affect Disord* 2010, in press.
3. Limlomwongse N, Liabsuetrakul T. Cohort study of depressive moods in Thai women during late pregnancy and 6-8 weeks of postpartum using the Edinburgh Postnatal Depression Scale (EPDS). *Arch Womens Ment Health*. 2006;9:131-8, doi: 10.1007/s00737-005-0115-7.
4. Gaynes BN, Gavin N, Meltzer-Brody S, Lohr KN, Swinson T, Gartlehner G, et al. Perinatal depression: prevalence, screening accuracy, and screening outcomes. *Evid Rep Technol Assess*. (Summ) 2005;119:1-8.
5. American College of Obstetricians and Gynecologists Committee on Health Care for Underserved Women. ACOG Committee Opinion No. 343: psychosocial risk factors: perinatal screening and intervention. *Obstet Gynecol*. 2006;108:469-77, doi: 10.1097/00006250-200608000-00046.
6. Royal College of Obstetricians and Gynaecologists. Antenatal care. Routine care for the healthy pregnant woman. London: RCOG Press; 2008.
7. American College of Obstetricians and Gynecologists. Committee on Obstetric Practice. Committee opinion no. 453: Screening for depression during and after pregnancy. *Obstet Gynecol*. 2010;115: 394-5, doi: 10.1097/AOG.0b013e3181d035aa.
8. Lancaster CA, Gold KJ, Flynn HA, Yoo H, Marcus SM, Davis MM. Risk factors for depressive symptoms during pregnancy: a systematic review. *Am J Obstet Gynecol*. 2010;202:5-14, doi: 10.1016/j.ajog.2009.09.007.
9. Lovisi GM, López JR, Coutinho ES, Patel V. Poverty, violence and depression during pregnancy: a survey of mothers attending a public hospital in Brazil. *Psychol Med*. 2005;35:1485-92, doi: 10.1017/S0033291705005362.
10. Manzolli P, Nunes MA, Schmidt MI, Pinheiro AP, Soares RM, Giacomello A, et al. Violence and depressive symptoms during pregnancy: a primary care study in Brazil. *Soc Psychiatry Psychiatr Epidemiol*. 2009, in press.
11. Patel V, Kleinman A. Poverty and common mental disorders in developing countries. *Bull World Health Organ*. 2003;81:609-15.
12. Hoffman S, Hatch MC. Depressive symptomatology during pregnancy: evidence for an association with decreased fetal growth in pregnancies of lower social class women. *Health Psychol*. 2000;19:535-43, doi: 10.1037/0278-6133.19.6.535.
13. Orr ST, James SA, Blackmore Prince C. Maternal prenatal depressive symptoms and spontaneous preterm births among African-American women in Baltimore, Maryland. *Am J Epidemiol*. 2002;156:797-802, doi: 10.1093/aje/kwf131.
14. Andersson L, Sundström-Poromaa I, Wulff M, Åström M, Bixo M. Neonatal outcome following maternal antenatal depression and anxiety: a population-based study. *Am J Epidemiol*. 2004;159:872-81, doi: 10.1093/aje/kwh122.
15. Fraguas R Jr, Henriques SG Jr, De Lucia MS, Iosifescu DV, Schwartz FH, et al. The detection of depression in medical setting: a study with PRIME-MD. *J Affect Disord*. 2006;91:11-7, doi: 10.1016/j.jad.2005.12.003.
16. Spitzer RL, Williams JB, Kroenke K, Hornyak R, McMurray J. Validity and utility of the PRIME-MD patient health questionnaire in assessment of 3000 obstetric-gynecologic patients: the PRIME-MD Patient Health Questionnaire Obstetrics-Gynecology Study. *Am J Obstet Gynecol*. 2000;183:759-69, doi: 10.1067/mob.2000.106580.
17. Andersson L, Sundström-Poromaa I, Bixo M, Wulff M, Bondestam K, Åström M. Point prevalence of psychiatric disorders during the second trimester of pregnancy: a population-based study. *Am J Obstet Gynecol*. 2003;189:148-54, doi: 10.1067/mob.2003.336.
18. Goodman JH. Women's attitudes, preferences, and perceived barriers to treatment for perinatal depression. *Birth*. 2009;36:60-9, doi: 10.1111/j.1523-536X.2008.00296.x.
19. King NM, Chambers J, O'Donnell K, Jayaweera SR, Williamson C, Glover VA. Anxiety, depression and saliva cortisol in women with a medical disorder during pregnancy. *Arch Womens Ment Health*. 2010, in press.

20. Zubaran C, Foresti K, Schumacher MV, Amoretti AL, Thorell MR, Müller LC. The Correlation Between Postpartum Depression and Health Status. *Matern Child Health J.* 2009, in press.
21. Elsenbruch S, Benson S, Rütke M, Rose M, Dudenhausen J, Pincus-Knackstedt MK, et al. Social support during pregnancy: effects on maternal depressive symptoms, smoking and pregnancy outcome. *Hum Reprod.* 2007;22:869-77, doi: 10.1093/humrep/del432.
22. Li D, Liu L, Odouli R. Presence of depressive symptoms during early pregnancy and the risk of preterm delivery: a prospective cohort study. *Hum Reprod.* 2009;24:146-53, doi: 10.1093/humrep/den342.