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Research report

Risk factors for Panic Disorder in pregnancy: A cohort study

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ABSTRACT

Background: The study investigates the prevalence of Panic Disorder (PD) with or without comorbid Major (MD) or Minor Depressive (md) disorder during pregnancy and focuses its attention on the different pattern of risk factors in these two subgroups in a sample of women attending two Centres for Prenatal Care of the Public Health Service.
Methods: Two-hundred and seventy-seven pregnant women were assessed monthly throughout the whole pregnancy period using the Primary Care Evaluation of Mental Disorders (PRIME-MD) for the screening of PD and the Hospital Anxiety and Depression Scale (HADS) for the evaluation of severity of anxious and depressive symptoms.
Results: Twenty-one women (7.5%) were diagnosed as affected by PD, of whom 12 (57.1%) showed MD or md comorbidity. The development of PD without depressive comorbidity is predicted by a history of previous episodes of Anxiety Disorders while the development of PD plus depressive comorbidity is predicted by a history of previous depressive episodes and by the lack of familiar support.
Limitations: Given the small sample size of our anxious and depressed women, the present data need to be verified by using larger samples.
Conclusions: The frequent association between PD and MD or md, the analysis of risk factors and of temporal relationship strongly suggests that the panic-depressive comorbidity might represent in fact depressive disorders with intense anxiety symptoms. These findings raise the question if the PD-depressive association is a true comorbidity or reveals the anxious symptomatology of a depressive disorder (MD or md).

1. Introduction

There is a consistent body of clinical research focusing on depression during the perinatal period, pregnancy and the first year postpartum, whereas anxiety disorders in these same periods have received less research attention. It was previously thought that pregnancy was a time of low risk for the new onset or exacerbation of an anxiety disorder. However, there is growing realization that symptoms of anxiety are common during pregnancy and postpartum and maternal symptoms of anxiety during pregnancy are associated with adverse fetal and developmental consequences.

Panic Disorder (PD) is one of the most prevalent and disabling anxiety disorders. According to the Epidemiological Catchment's Area population survey (Regier et al., 1990), lifetime prevalence for PD is estimated at 2.2%, and women are 2.5–3 times more likely than men to meet criteria for PD (3.4% vs. 0.9%). The Epidemiological Catchment's Area data also demonstrated an increased risk for PD in those under age 45 years (Regier et al., 1990). International reports confirm that women have significantly higher prevalence rates of PD (Kessler et al., 1994; Alonso et al., 2004).

It has been estimated that 3–12% of women experience symptoms related to PD at some time during their childbearing years, including pregnancy and the postpartum period (Wenzel et al., 2001; Smith et al., 2004; Andersson et al., 2006; Goodman and Tyer-Viola, 2010), and according to available data 3–11% of women with PD report the onset during perinatal period (Ross and McLean, 2006). PD is not only common but is also considered to be a chronic and debilitating illness associated with significant comorbidity (Ballenger et al., 1998; Yonkers et al., 1998). Noteworthy, approximately 50% of individuals with PD also have comorbid Major Depression (MD). Furthermore, several prospective studies have shown that a prenatal anxiety disorder is one of the strongest risk factors for developing postnatal depression (Andersson et al., 2003; Sutter-Dallay et al., 2004; Milgrom et al., 2008). Therefore, an

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anxiety disorder in pregnancy may be associated with significant maternal depressive morbidity.

Despite these important clues, there is lack of literature reporting risk factors for or predictors of antenatal PD and patterns of depressive comorbidity.

Therefore, the present study was aimed to investigate the prevalence of PD with or without comorbid depression at several times during pregnancy and to evaluate the pattern of risk factors in these two subgroups in a Italian sample of women attending two Centres for Prenatal Care of the Public Health Service.

2. Methods

Both the Local Ethical Committee (Comitato Unico della Provincia di Mantova e della Provincia di Reggio Emilia) approved the study protocol.

2.1. Sample

The study population was recruited among women who consecutively sought assistance at the Centres for Prenatal Care of the Public Health Service of District of Mantova (Italy) and Reggio Emilia (Italy), from September 2005.

Women participated in the study after the procedure had been fully explained and a written informed consent was obtained, if they were older than 18 years and completed all the evaluations from the beginning of their pregnancy.

2.2. Assessment

At each visit, all women were asked to complete (approximately every month) the following evaluations: (1) the Italian translation of the Primary Care Evaluation of Mental Disorders (PRIME-MD) (Spitzer et al., 1994) for the screening of PD; (2) the Italian translation of the Hospital Anxiety and Depression Scale (HADS) (Zigmond and Snaith, 1983) for the evaluation of severity of anxious and depressive symptoms.

Moreover, all women completed a brief questionnaire, performed ad hoc, to collect socio-demographic and medical history information, and to evaluate the presence (or absence) of problems with husband/partner, family, job, family support and whether the pregnancy was unwanted. The results of the questionnaire were discussed with the women (and when available with family members) to confirm their answers.

The PRIME-D is a structured interview for the diagnosis of mental disorders according to the criteria of DSM-IV (American Psychiatric Association, 1994). It has not been validated for the use in a pregnant population, however it showed good specificity and sensitivity in detecting PD (specificity 99%, sensitivity 57%) and MD (specificity 98%, sensitivity 57%) in primary care populations (Spitzer et al., 1994).

The interview was administered at each visit by the gynecologists, who were trained by a senior psychiatrist.

A woman was affected by PD if, at any evaluation during pregnancy, she fulfilled the criteria for a PD episode. A woman was defined non-anxious if she did not satisfy the criteria for PD or anxiety disorder not otherwise specified at any evaluation during pregnancy.

The duration and onset of PD (the month in which anxious symptoms firstly satisfied the diagnostic criteria for PD) throughout pregnancy were calculated. In women, who showed anxious symptoms at the first evaluation, the onset was arbitrarily considered the first month of pregnancy.

Concerning treatment of PD, only women with severe anxious symptoms (on clinical judgment) were referred by gynecologist to psychiatrist for a treatment. The gynecologists were properly trained to recognize this severe condition.

2.3. Statistical analysis

Comparisons between PD and non-anxious women were performed using the one-way analysis of variance with Bonferroni post-hoc analysis for continuous variables and with Fisher's exact test for categorical variables.

Stepwise logistic regression was used to evaluate which variables at the beginning of pregnancy could predict the development of depression. Two regression analysis were performed: the same independent variables entered in both analyses were occupation, number of childbirths, presence of problems with husband/partner, family, job, presence of family support and whether the pregnancy was unwanted, whereas the dependent variables were MD and no depression in one analysis and md and no depression in the other analysis.

3. Results

3.1. Sample

During the study period, 356 women attended the Centres of Prenatal Care. Thirty-two women (8.9%) were not included in the study because of language problems ($n=17$) or refusal to participate ($n=15$). Among the remaining 324 women, 25 (7.7%) were excluded from the study because they did not attend all the visits throughout pregnancy. Among non-completers, 15 dropped-out after the first evaluation, 7 attended another visit and 3 two more visits. At the beginning of pregnancy, the 25 non-completers showed the same socio-demographic features of the completers. Moreover, none of the non-completers showed anxious or depressive symptoms at any evaluation they attended.

Among the remaining 299 women, 22 women were excluded from the study because they presented during pregnancy anxious symptoms, which did not satisfy the diagnostic criteria of PD (anxiety disorder not otherwise specified). However, women with anxiety disorder not otherwise specified were considered when the prevalence of PD was calculated.

Therefore the study population included 277 women (mean age 30.7 ± 4.4 years; range 18–45 years. Twenty-one women were diagnosed as affected by PD and the remaining 256 did not present anxious symptoms during pregnancy (healthy controls) (C). PD and C women showed the same age, years of education and family or occupational status, whereas PD women had higher number of childbirths, more frequently reported an absence of family support and depressive or anxious episode before pregnancy (Table 1). Moreover, PD and C women showed the same number of assessments (PD $= 6.1 \pm 1.3$ vs. C $= 6.0 \pm 1.3$; $t=0.43$; $p=0.66$).

In anxious women, the PD symptoms became evident after 4.0 ± 2.1 months of pregnancy and they lasted 3.0 ± 2.0 months (Table 2).

3.2. Depressive comorbidity

PD women showed more depressive episodes during pregnancy that C (Table 1). Twelve PD women (57.1%) presented depressive episode during pregnancy: MD was diagnosed in 5 anxious women and md in 7. In seven women, PD was concomitant with MD ($n=3$) or md ($n=4$) whereas in 5 women PD preceded MD ($n=2$) or md ($n=3$).

Concerning treatments, no anxious or depressed women were treated with antidepressants or other psychotropic drugs. Only two women with MD received a psychological support.