

Pregnancy-Onset Panic Disorder: Incidence, Comorbidity and Associated Factors

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ABSTRACT

Introduction: The present study aimed to investigate the incidence rate of pregnancy-onset panic disorder (POPD) among Turkish pregnant women using a diagnostic interview. Additionally, we examined whether the independent socio-demographic or clinical risk factors were associated with the risk of panic disorder in these women.

Methods: The study sample comprised 1475 consecutive pregnant women who presented to the obstetric outpatient clinics of two research centers. The rate of POPD in these participants was 1.3% (Group 1, n=20). The 20 women with POPD were compared with 250 pregnant women without pregnancy-onset depression or anxiety (Group 2; controls). Panic disorder and other anxiety or mood disorders were determined by means of the Structured Clinical Interview for DSM-IV. Comorbid Axis II disorders were diagnosed with the Structured Clinical Interview for DSM-III-R Personality Disorders.

Results: The incidence rate of panic disorder was 1.3% (n=20). In group 1, 55% (n=11) of the women with POPD had an additional mood or anxiety disorder. In addition, the prevalence rate of any cluster C personality disorder; including avoidant, passive-aggressive and obsessive-compulsive personality disorders, were significantly greater in the group 1 women with POPD than the control pregnant women without a panic disorder (group 2).

Conclusion: The women with POPD were more likely than the controls to have a cluster C Axis II disorder and a history of a pre-existing anxiety or mood disorder.

Keywords: Pregnancy, panic, comorbidity, personality

INTRODUCTION

The psychiatric disorders with the highest prevalence in women are depressive and anxiety disorders. Approximately 30% of women experience some type of anxiety disorder at some point in their lives (1). Panic disorder (PD), which is characterized by intense episodes of anxiety, is more common in women than in men (1). The prevalence of PD is the highest in women between the ages of 18 and 35 years (2). Thus, it is clear that at least some women with PD may have panic attacks during pregnancy. Studies also suggest that pregnant women with PD are at a risk of placental abruption, fetal distress, decreased nutrition, preterm birth, anemia and decreased fetal growth (3,4).

There are limited data regarding the impact of pregnancy on the course of PD. Some researchers have reported that panic attacks diminish during pregnancy (5,6,7), whereas others have described severe panic attacks occurring during pregnancy (3,8,9). Although a large group of women are likely to experience PD during their childbearing years, the incidence-prevalence and correlation of panic during the pregnancy period are not well defined. Limited data indicate that PD consequently affects approximately 1.5%–2.5% of pregnancies during pregnancy (10,11,12). Similarly, there are limited data on the comorbidity of PD, including Axis II disorders, during gestation. Previous investigations have consistently reported high prevalence rates of cluster C (“anxious-fearful cluster”) personality disorders among patients suffering from PD in community samples (13,14,15).

The present study aimed to determine the incidence rate of pregnancy-onset panic disorder (POPD) among Turkish pregnant women using a diagnostic interview. The second purpose of the current study was to investigate the possible association between PD during pregnancy and the independent socio-demographic or clinical (Axis I and Axis II comorbidities) risk factors.

METHODS

Subjects

Pregnant women were recruited from the obstetric outpatient clinic of two research centers. Participants with a history or existence of schizophrenia or related disorders, the existence of any gestational complications (e.g., imminent abortion, preeclampsia and placenta



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previa), a history of neurological disease and concomitant severe medical illnesses (e.g., uncontrolled endocrine abnormalities and cardiovascular or pulmonary diseases) were excluded from the study.

Our study included 1475 consecutive pregnant women who presented to the obstetric outpatient clinics of the two research centers. Of these 1475 pregnant women, 20 (1.3%) met the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) (16) for PD and these 20 women who did not have pre-existing PD and who showed an onset of PD during their current pregnancy were included in group 1. Of the remaining 1455 pregnant women, 250 consecutive pregnant women without any pregnancy-induced mood or anxiety disorder were included in the study in group 2. The women in group 2 were compared with those in group 1 to assess the factors associated with POPD.

Measurements

The gestational week was confirmed with ultrasound screening on the basis of the last menstruation date. The diagnosis of PD and comorbid mood and anxiety disorders in gravid women was ascertained by means of the Structured Clinical Interview for DSM-IV (SCID-I) (17). SCID-I was also used to determine mood and anxiety disorders at the onset of the current pregnancy in the pregnant women. The onset time of PD was established on the basis of the reports of the pregnant women. Personal and family history of major depression and PD were obtained based on SCID-I and the reports given by the pregnant women about their first-degree relatives, respectively. Cluster C personality disorders in the two study groups were diagnosed with the Structured Clinical Interview for DSM-III-R Personality Disorders (SCID-II) (18). SCID-I and SCID-II have been standardized for the Turkish population (19,20). In addition, a semi-structured interview form developed by the authors was used to determine the socio-demographic features and obstetric information.

Procedures

The objectives and procedures of the study were explained to all the women and written informed consent forms were provided. The study was approved by the Ethics Committee of the Medicine Faculty of Necmettin Erbakan University. After the socio-demographic characteristics and results of obstetric evaluation were recorded at the obstetric outpatient clinics, the women were referred to psychiatrists. Following the SCID-I interview, SCID-II was performed on the women in the study groups.

Statistical Analysis

All statistical analyses were conducted using Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA) version 13.0 for Windows. Continuous variables between the groups were compared with Student's t-test. Fisher exact test and χ^2 tests were used to analyze 2×2 and 3 (or more)×2 categorical variables between the groups. Independent factors associated with POPD were assessed using logistic regression analysis. Statistical significance was defined as $p < 0.05$.

RESULTS

The incidence rate of PD was 1.3% ($n=20$) in the women in group 1. The mean onset time of PD in the POPD group was 14.3 ± 8.0 gestational week. PD occurred during the first trimester of pregnancy in 10 women (50%), during the second trimester in 9 (45%) and during the third trimester in 1 (5%).

The mean age of the pregnant women (Group 1+Group 2, $n=270$) was 26.86 ± 5.85 years. The mean duration of pregnancy was 29.70 ± 9.37 weeks (range, 5–41 weeks) and the mean number of children was

0.89 ± 0.94 . Most of the women were married ($n=269$, 99.6 %) and they were mostly primary school graduates ($n=229$, 84.8%) and housewives ($n=249$, 99.2%). The trimester of the pregnancy among the pregnant women was as follows: first in 18 (6.7%) women, second in 63 (23.3%) and third in 189 (70.0%). The proportion of unplanned pregnancy was 17.7% ($n=48$). Seventy-nine (29.3%) women had a history of abortion. The number of primigravida women was 88 (32.6%) (Table 1).

There were no significant differences between pregnant women with and without PD in terms of age, marital and employment status, educational level, number of children, whether they were primigravida, history of abortion, smoking of cigarettes, planned or unplanned pregnancy, a family or personal history of MD and a family history of PD. Compared with the healthy pregnant women without POPD, the women with POPD had a higher rate of the existence of an anxiety or depressive disorder at the onset of pregnancy (Table 1).

Fifty-five percent ($n=11$, 55.0%) of the women with POPD had an additional mood or anxiety disorder. Comorbidity of any anxiety disorders (55.0%) was more prevalent than comorbidity of mood disorders (25.0%). The most common comorbid diagnoses were specific phobia (35.0%), generalized anxiety disorder (25.0%) and major depression (25.0%). The proportion of dysthymic disorder, obsessive-compulsive disorder and social phobia was 5%.

Of the 270 pregnant women included in this study, 47 (17.4%) met the criteria of at least one cluster C personality disorder. The most common diagnoses among these disorders were avoidant (7.40%) and obsessive-compulsive (5.55%) personality disorders. The proportion of dependent and passive-aggressive personality disorders was 4.8% and 3.7%, respectively. In addition, the prevalence rate of any cluster C personality disorder; avoidant, passive-aggressive and obsessive-compulsive personality disorders were significantly greater in the POPD group than that in the control pregnant women without PD (Table 2).

To determine the predictors of POPD, the variables of the existence of an anxiety disorder at the onset of pregnancy; major depression at the onset of pregnancy; and avoidant, obsessive-compulsive and passive-aggressive personality disorders were entered into a logistic regression model. Independent factors, including an anxiety disorder at the onset of pregnancy ($B=2.420$, Wald $\chi^2=5.738$, $df=1$, $p=0.017$), major depression at the onset of pregnancy ($B=3.116$, Wald $\chi^2=5.888$, $df=1$, $p=0.015$), obsessive-compulsive personality disorder ($B=2.348$, Wald $\chi^2=8.370$, $df=1$, $p=0.004$), avoidant personality disorder ($B=2.764$, Wald $\chi^2=15.883$, $df=1$, $p=0.000$) and passive-aggressive personality disorder ($B=2.286$, Wald $\chi^2=5.725$, $df=1$, $p=0.017$) were found to be associated with POPD.

DISCUSSION

In the current study, the primary research questions were as follows: what are the frequencies of POPD among pregnant women receiving prenatal care in the obstetrics sector? What demographic, clinical and obstetric factors of the pregnant women relate to the presence of POPD? Are women with antenatal personality disorders more likely to have POPD?

The prevalence of PD has been estimated through a series of epidemiological studies, including the National Institute of Mental Health (NIMH) Epidemiologic Catchment Area (ECA) Program and the National Comorbidity Survey (NCS). The lifetime prevalence of PD ranges from 1.7% in the ECA study to 3.5%–4.7% in NCS; the one-month prevalence was 0.5% in the ECA study and 1.5% in NCS (1,21,22,23). Most epidemio-

Table 1. The socio-demographic characteristics and psychiatric histories of pregnant women with and without POPD

	Women with POPD (Group 1) n=20	Women without POPD (Group 2) n=250	p value
Age, mean±SD, years	26.20±4.48	26.91±5.95	0.599 ^a
Education, n (%)			0.766 ^b
Primary school	17 (85.0)	212 (84.8)	
Secondary school	1 (5.0)	21 (8.4)	
University	2 (10.0)	17 (6.8)	
Employment status, n (%)			0.660 ^c
Unemployed	18 (90.0)	231 (92.4)	
Marital status			1.000 ^c
Married	20 (100)	249 (99.6)	
Planned pregnancy, n (%)	18 (90.0)	204 (81.6)	0.544 ^c
Number of children, mean±SD	0.70±0.86	0.90±0.94	0.342 ^a
Primigravida, n (%)	7 (35.0)	81 (32.4)	0.808 ^c
History of abortion, n (%)	6 (30.0)	73 (29.2)	1.000 ^c
Smoking of cigarettes, n (%)	2 (10.0)	10 (4.0)	0.220 ^c
Family history of major depression	0 (0)	6 (2.4)	1.000 ^c
Personal history of major depression	2 (10.0)	11 (4.4)	0.249 ^c
Family history of panic disorder	1 (5.0)	2 (0.8)	0.207 ^c
Major depression at the onset of pregnancy	2 (10.0)	2 (0.8)	0.026 ^c
Additional anxiety disorder at the onset of pregnancy	4 (20.0)	5 (2.0)	0.002 ^c

POPD: Pregnancy-onset panic disorder; SD: standard deviation; ^at-test, ^bχ² test, ^cFisher's exact test**Table 2.** Cluster C personality disorders in pregnant women with and without POPD, n (%)

	Women with POPD (Group 1) n=20	Women without POPD (Group 2) n=250	p ^a value
Avoidant	8 (40.0)	12 (4.8)	0.000
Dependent	3 (15.0)	10 (4.0)	0.062
Obsessive-compulsive	6 (30.0)	9 (3.6)	0.000
Passive-aggressive	5 (25.0)	5 (2.0)	0.000
Any personality disorder	13 (65.0)	34 (13.6)	0.000

POPD: Pregnancy-onset panic disorder. ^aFisher's exact test

logical studies, including those based on ECA and other data sources, have consistently shown lifetime rates between 1% and 2% (24). In these studies, PD is more commonly diagnosed in women than in men. The one-month prevalence rate of PD for women aged between 25 and 45 years was reported to be 1.1% in the NIMH and ECA studies (25). In the present study, the incidence rate of POPD was 1.3% (n=20) in an unselected population of pregnant women in various trimesters. The rate of PD we reported (1.3%) was within the range reported in community

samples. Similarly, reports (1,26,27,28,29) suggest that rates of psychiatric disturbances among pregnant women are similar to the rates for women in the general population.

To our knowledge, this is the first study to examine the incidence rate of POPD and to investigate comorbid conditions and predictors of POPD among pregnant women. Few studies have examined PD in OB/GYN clinics, particularly among pregnant patients and the detailed analyses of factors affecting POPD were not included. There is no uniformity worldwide for the observed prevalence of PD during pregnancy, which generally averages between 0.2% and 5.2% in multiple studies (10,11,12,29,30). One explanation for this diversity is that the screening and diagnostic instruments used in these studies vary in sensitivity. A second reason for the variability in the findings is that the studies assess pregnant women in different trimesters. Moreover, these studies mainly focused on specific risk groups, such as teenage mothers, women of low-income and certain ethnic groups (30,31). Additionally, many reports on PD in pregnancy are based on small sample sizes and do not include appropriate comparison groups.

The average incidence of POPD in our study was 1.3%, which was similar to our previous study that used the same type of instrument. We previously reported the current prevalence rate of PD as 2.5% (n=13) in 512 pregnant women during the third trimester of pregnancy (10). Of these 13 women who met the criteria for PD according to SCID-I, seven (1.3%) reported that their PD began during the 6th–28th weeks of their gestation. The panic symptoms of the remaining six women with PD were present prior to pregnancy (10).

Because there is no other study to examine the incidence rate of POPD, comparing our results with those of previous similar studies is difficult. Andersson et al. (30) studied 1566 consecutive women attending two obstetric clinics in Sweden during the second trimester of pregnancy. In this study, the point prevalence rate of anxiety disorders and PD was 6.6% and 0.2%, respectively. For the diagnosis of PD, Andersson et al. (30) used the Primary Care Evaluation of Mental Disorders (PRIME-MD) (32) system Brief Patient Health Questionnaire (BPHQ) and they conducted telephone interviews to confirm the positive results of PQ. In our study, the diagnosis of PD was made by face-to-face interviews using SCID-I. Kelly et al. (29), who utilized the medical record reviews in conjunction with PRIME-MD, found that the prevalence rate of anxiety disorders and PD are 5% and 1%, respectively in 186 women receiving prenatal care. In another study (11) of 387 pregnant women with low-income in which PD was measured by PRIME-MD and BPHQ, the authors noted that nine women (2%) had PD during pregnancy.

In a controlled study (33) of Nigerian women in late pregnancy (32 weeks and above), 172 gravid and 172 non-gravid women were evaluated using the Mini International Neuropsychiatric Interview (MINI), (34) a brief structured interview for the major Axis I psychiatric disorders in DSM-IV. Investigators showed that the rate of PD in pregnant women (5.2%) was three times more common than that in the non-pregnant (1.7%) controls. A small sample size is main limitation of that study and they assessed their subjects only during late pregnancy, whereas there may be differences in the rates of PD during the various stages of pregnancy. Recently, Spies et al. (12) assessed the K-10 screening test using SCID as the gold standard in a sample of 129 pregnant women who presented for care at midwife obstetric units in Cape Town, South Africa. The percentage of SCID-defined PD within 129 pregnant women was 1.5%.

In the current study, we found no association between the development of PD and being primigravid. The proportion of being primigravid was

35% among the pregnant women with PD. This finding is not supported by the retrospective study by Bandelow et al. (35) who noted that the number of women who had been pregnant with manifestations of PD is significantly lower during pregnancy and that women who had never been pregnant have an increased risk of panic manifestations during their lifetime when compared with women who had pregnancies. They do not have a simple explanation for this result. Although psychosocial influences, including the fear of safe delivery, may explain this difference, it remains speculative. The differences between our study and theirs may be explained on the basis of the type of patients recruited. Samples in the other studies comprised women with PD who presented to anxiety or PD clinics, whereas in our study, the patient sample was taken from obstetric outpatient clinics. In addition, they did not include a comparative control group of healthy pregnant women.

Cognitive factors are likely to be a contributing factor to POPD in pregnancy. POPD symptoms in women may be caused by their catastrophic cognitive assessment of bodily sensations, which are physiologically normative during pregnancy. Similarly, Cowley and Roy-Byrne (5) reported that increased heart and respiratory rates, which are physiologically normative during pregnancy, may also contribute to anxiety as panic attacks may result from catastrophic cognitive reactions to normal physiological events. Our opinion should be validated by further studies, including cognitive factors in women with POPD.

In the current study, the existence of any anxiety disorder and major depression at the onset of gestation was a strong factor in predicting the occurrence of POPD during pregnancy. These results suggest that a patient's past psychiatric history and current symptoms represented diatheses for POPD and that the past psychiatric history together with the current symptoms must be carefully assessed and factored into the treatment decisions.

In general, anxiety disorders frequently exhibit comorbidity with other Axis I diagnoses and this comorbidity may be common in the perinatal period as well (36,37), but we found no data regarding the comorbidity of specific Axis I disorders from the studies exploring an association between pregnancy and PD. Among the most common conditions comorbid with PD are depression and additional anxiety disorders (38,39). Although the overall comorbidity rate in our study is similar to the results of previous studies conducted among patients with general PD, it is difficult to interpret this finding without a control group. Clearly, further research is required with larger sample sizes of both pregnant and non-pregnant women with PD.

As a class, personality disorders are more prevalent in patients affected by PD with a prevalence rate ranging from 20% to 86% (40,41,42,43,44). Among patients with PD, several studies found a significant excess of personality disorders from the anxious cluster C (15,45,46). In the current study, the findings showed that the pregnant women with POPD were nearly five times more likely than the pregnant women without POPD to meet any cluster C personality disorder. The most common cluster C personality disorders described in patients with POPD are avoidant personality disorders followed by obsessive-compulsive, passive-aggressive and dependent personality disorders. Additionally, we found that these Axis II cluster C personality disorders were an independent determinant of POPD. These results are in agreement with several previous studies that investigated personality disorders in patients with PD (14,40,41,42,43,47,48). Considering the high frequency of comorbidity of PD and personality disorder, together with the fact that both tend to have a chronic course, the possible clinical impact of this association becomes important (49).

The results of this study should be interpreted in light of several limitations. 1) The onset time of POPD in pregnant women was established with retrospective recall rather than a prospective observation. However, when the entire pregnancy period was considered, it seemed unlikely that the pregnant women could misrecall the onset time of PD. 2) Although the number of pregnant healthy women was considerable (n=250), the sample size of the pregnant women with POPD (n=20) was small. Our results need to be validated in larger samples of women with POPD with and without specific comorbid disorders. 3) We did not perform interviews of the first-degree relatives of the pregnant women to determine the family history of major depression and PD. The family history was based on unstructured interviews with the pregnant women about their relatives because a structured diagnostic instrument assessing family history that is standardized for the Turkish population does not exist. 4) Finally, our study assessed pregnant women for disorders at one point in time. It would be important to have follow-up data on co-occurrence with Axis I and Axis II disorders because the patterns of co-occurrence may change over time.

In conclusion, despite some limitations, the results of the present study suggest the following: 1) The present study indicated that POPD is relatively common among pregnant women. 2) Axis I and Axis II comorbidities are observed in more than half of the women with POPD. 3) Cluster C personality disorders play a relevant role in POPD. Physicians should also be aware of potentially vulnerable groups for POPD, including women with avoidant, obsessive-compulsive and passive-aggressive personality disorders. Additionally, there is no question that a past history of psychiatric illness, including depression or any anxiety disorder, puts women at risk for POPD during pregnancy.

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