

Original article

Panic disorder during pregnancy and postpartum period

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Abstract

Background. – Earlier studies on the influence of pregnancy and postpartum period on the course of panic disorder have been inconsistent. The present study aims to quantify panic manifestations in these periods in large sample of women.

Method. – Panic manifestations, including exacerbations and new manifestations of panic disorder, were assessed retrospectively in a sample of 128 women with panic disorder with or without agoraphobia, 93 of whom had had 195 pregnancies.

Results. – Panic manifestations were fewer during pregnancy and more frequent in the postpartum period when compared with the control period. Women who had never been pregnant had significantly more panic manifestations than women with prior pregnancies. Breastfeeding and miscarriages did not have a significant effect. Women with postpartum panic reported more psychosocial stress events during this period.

Conclusions. – Possible reasons for postpartum panic and the protective effects of pregnancy are discussed, including psychosocial or hormonal factors and other neurobiological changes. Postpartum panic coincides with a sudden drop of hormones after delivery.

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1. Introduction

Initial case reports suggested that pregnancy protected against panic symptoms in patients with panic disorder, while the postpartum period seemed to increase the risk for onset or exacerbation of panic disorder [17,18,26,32,34]. Retrospective studies and case series have offered a more mixed picture. Some studies confirmed an improvement during pregnancy in the majority of women [14,31,36,48] (see also [27]). In contrast, according to other studies women continued to experience panic attacks or even worsened during pregnancy [11, 13,51], in particular during the last part of pregnancy [21,47]. All studies are summarized in Table 1.

During the postpartum period, a worsening of panic symptoms was consistently found in all studies, but the proportion of women showing a deterioration differed widely [12–14,36,

42]. In none of these studies it was tried to measure the degree of deterioration or improvement. All these studies except one [13] were retrospective.

The inconsistent findings in the available studies may have been due to their small sample sizes. Our objective was to investigate the impact of pregnancy and postpartum period on panic disorder in a larger sample and to quantify the degree of changes.

Panic disorder is twice as frequent in women than in men [1,53]. Studies on the influence of pregnancy and the postpartum period on panic symptoms may help to elucidate this phenomenon.

2. Patients and methods

Two-hundred and sixty-three women with a diagnosis of panic disorder with or without agoraphobia (PD) according to DSM-IV [2] ICD-10 [49] treated at the Anxiety Disorders Out-patient Unit at the Department of Psychiatry, University of Göttingen were selected consecutively from clinic admission

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Table 1

Main results of studies on the course of panic disorder during pregnancy and postpartum period in women with preexisting panic disorder (N = number of pregnancies, + = improvement, = no change, - = deterioration)

Authors	N	Pregnancy			Post-partum period		
		+	=	-	+	=	-
Cohen et al., 1994 [11]	48	10 (21%)	28 (58%)	10 (21%)	-	-	-
Cohen et al., 1994 [12]	40	-	-	-	3 (8%)	23 (57%)	14 (35%)
Cohen et al., 1996 [13]	10	1 (10%)	6 (60%)	3 (30%)	-	1 (10%)	9 (90%)
Cowley and Roy-Byrne, 1989 [14]	11	8 (73%)	1 (9%)	2 (18%)	1 (9%)	1 (9%)	9 (82%)
Fisch, 1989 [17]	5	5	-	-	-	-	5
George et al., 1987 [18]	3	3	-	-	-	-	3
Klein et al., 1994 [31]	33	14 (74%)	4 (21%)	1 (21%)	-	-	-
Kraus, 1989 [32]	2	2	-	-	-	-	2
Metz et al., 1988 [34]	3	3	-	-	-	-	3
Northcott and Stein, 1994 [36]	67	19 (43%)	16 (24%)	22 (33%)	12 (18%)	13 (19%)	42 (67%)
Sholomskas et al., 1993 [42]	64	-	-	-	7 (11%)	-	-
Verburg et al., 1994 [47]	4	-	-	3	-	-	-
Villeponteaux et al., 1992 [48]	22	14 (64%)	5 (23%)	3 (13%)	-	-	-
Wisner et al., 1996 [51]	45	12 (27%)	31 (69%)	2 (4%)	-	31 (69%)	14 (31%)

lists for the study. Forty-eight subjects could not be traced, four could not participate due to severe medical illnesses, and seven had died. Of the remaining 204 women, 128 gave written informed consent and were interviewed personally or by telephone. To again confirm a history or a present episode of PD and to exclude other relevant psychiatric disorders, a SCID (structured clinical interview for DSM-IV [52]) was performed. Exclusion criteria were a history of other mental disorders, including major depression (unless it was secondary to panic disorder or it occurred only within the postpartum period), bipolar disorder, generalized anxiety disorder, social phobia, obsessive-compulsive disorder, posttraumatic stress disorder, substance abuse or personality disorders. All participants were Caucasian.

To keep the participants blind to the intent of the study, they were asked to participate in an interview about stress and the onset of panic symptoms. The interviewers were not blind to the study hypothesis. All women completed a questionnaire about panic symptoms, and women with pregnancies were asked an additional set of 16 questions about panic manifestations during pregnancies and postpartum period. The definition of panic disorder according to DSM-IV/ICD-10 was explained to all participants. Participants had to indicate (1) the first appearance of panic symptoms according to both the ICD-10 and DSM-IV definition of panic attacks, (2) an exacerbation of preexisting panic disorder, assessed on a 1–4 scale from 1 = ‘mild’ to 4 = ‘very severe’. A ‘panic manifestation quotient (PMQ)’ was calculated, representing the proportion of panic manifestations per time unit. A ‘panic manifestation’ was defined as a first appearance of panic symptoms or an exacerbation of at least ‘moderate’ severity. The PMQ was defined as the ‘panic manifestation period’ (time with panic symptoms) divided by the observation period. The respective observation periods were 266 days for the pregnancy period, 180 days after childbirth for the postpartum period, or the days without pregnancies and postpartum period from age 15 to age 40 (or from 15 to the time of interview for participants under 40) for the non-pregnancy period, and, respectively, the non-postpartum period.

Participants had to indicate the duration of breast-feeding and were asked a set of questions regarding depressive symptoms in the postpartum period. They were also asked to indicate psychosocial stress situations during pregnancy. The degree of stress had to be assessed on a 0–4 scale from (0 = ‘no stress’ to 4 = ‘very severe stress’). Additionally, they had to describe the kind of stress (including marital discord, concomitant illness, unwanted pregnancy, financial problems etc.) in their own words. These descriptions were later analyzed and subdivided into different categories.

Women who had had miscarriages and abortions were compared with women who had normal deliveries.

To control for the confounding effect of panic treatments, women had to report treatment with psychopharmacological drugs and psychological therapies during pregnancy and postpartum period. Improvement under these treatments had to be assessed on a 1–5 scale (from 1 = very effective, to 5 = worsening). Participants currently on treatment were not excluded from the analysis.

The study was approved by the university ethics committee.

2.1. Statistical methods

Statistical analyses were performed by using the Statistical Analysis System SAS 8.01 (SAS[®] Institute, Heidelberg 2000). Differences in panic manifestations were analyzed with the non-parametric repeated measures analysis [8]. Ordinal data were analyzed using the Wilcoxon–Mann–Whitney U test, categorical data by using Fisher’s exact test. For testing the difference in PMQ between miscarriages and normal pregnancies, the asymptotic t -test for paired samples with missing values [7] was used.

3. Results

3.1. Pregnancy

Thirty-five (27.3%) of the 128 women had had no pregnancies, and 93 (72.7%) had been pregnant at least once in their

life, and together reported a total of 195 pregnancies. In 28 cases, miscarriages or abortions occurred. The women had on average 2.1 pregnancies and 1.8 children.

At the time of the interview, the mean age of the women was 43.4 years (S.D. 12.5; range 21.2–56.0). Seventy-seven patients (58%) had panic disorder with agoraphobia, the remaining had panic disorder without agoraphobia. Mean age at onset was 28.4 (S.D. 11.2) years for panic disorder with or without agoraphobia. As the mean age of women who had never been pregnant ($N = 35$) was different from the women with pregnancies, panic manifestations of the non-pregnant women were compared with the non-pregnancy period of an age-matched subsample ($N = 70$) of the women with pregnancies. The mean age of these two groups did not differ significantly (non-pregnant women, 38.0 ± 14.9 ; pregnant women, 40.9 ± 5.8 ; N.S.).

In women who had been pregnant, manifestations of panic disorder (with or without agoraphobia symptoms) were significantly lower during pregnancy (PMQ = 0.08) than during the non-pregnancy period (PMQ = 0.17; non-parametric ANOVA for repeated measures; $F = 7.03$; $df = 2,91$; $P < 0.0001$; Fig. 1). Seventeen (9%) women reported improvement in panic during pregnancy, 165 (84%) reported no change, and 13 (7%) reported an increase in panic symptoms.

3.2. Postpartum period

The postpartum period was associated with a fairly small but significant increase in manifestations of panic disorder with or without agoraphobia symptoms (PMQ = 0.19) in comparison to the non-pregnancy period (0.17; non-parametric ANOVA for repeated measures; $F = 4.42$; $df = 2,91$; $P < 0.0001$), and a substantial increase in comparison to the pregnancy period (0.08, $F = 3.84$; $df = 2,91$; $P = 0.0002$; Fig. 1).

For six pregnancies (3%), women reported improvement in panic postpartum, for 153 pregnancies (79%) no change was reported, and for 36 pregnancies (18%) an increase in panic symptoms was reported.

Ten of the 93 women (10.8%) who had been pregnant reported that they had had their first manifestation of panic dis-

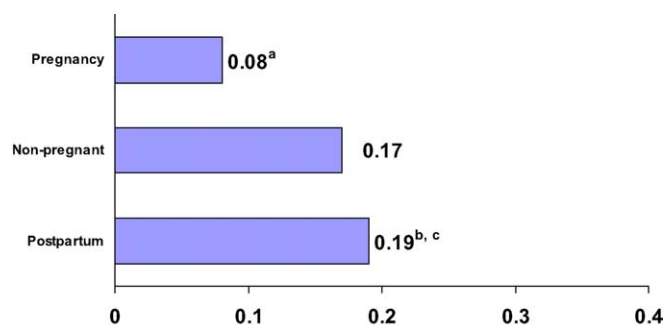


Fig. 1. Panic manifestation quotients during pregnancy, non-pregnancy and postpartum period (PMQ; means). Non-pregnant = non-pregnancy period in women who had been pregnant.

^a significantly different to non-pregnant; $P < 0.0001$

^b significantly different to non-pregnant; $P < 0.0001$

^c significantly different to pregnancy; $P < 0.0001$

order in their life during the postpartum period of one of their pregnancies. This is a 132-fold increased risk compared with the non-postpartum period. Five of these ten women reported onset of the first panic symptoms in their life within the first 5 days after childbirth.

3.3. Panic disorder with or without agoraphobia

Among women who had been pregnant, those who had panic disorder with agoraphobia (PDA) had a higher PMQ (0.19) than those who had panic disorder without agoraphobia (PD) (0.13; Wilcoxon–Mann–Whitney test; $U = 630$; $P = 0.0006$) during the non-pregnancy period. During pregnancy, both groups did not differ significantly ($P = 0.26$). During the postpartum period, PDA patients had significantly higher PMQs than those with PD (0.23 vs. 0.09; $U = 790$; $P = 0.033$).

3.4. Gravidae vs. nulligravidae

Women who had never been pregnant had significantly higher PMQs (0.32; range, 0–1.30) in comparison to the non-pregnancy period of age-matched women who had been pregnant (0.19; range, 0–0.97; $U = 2157$; $P = 0.04$) (Fig. 2).

3.5. Breast-feeding

During the postpartum period, PMQs were not significantly different between women who had breast-fed their children (125 pregnancies, PMQ = 0.22) and those who had not had a miscarriage and had not breast-fed their children (42 pregnancies; PMQ = 0.13; Wilcoxon–Mann–Whitney test, $U = 2234$, $P = 0.15$; N.S.).

3.6. Postpartum depression

In order not to increase the number of statistical comparisons, the occurrence of postpartum depression was only calculated for the first pregnancy of all women. Thirty-four (36.5%) of the women who had been pregnant reported postpartum depression and 19 (20.4%) had postpartum panic manifestations. Both disorders occurred in 11 women (11.8%). This was higher than the expected frequency (Fisher's exact test, $\chi^2 = 4.69$;

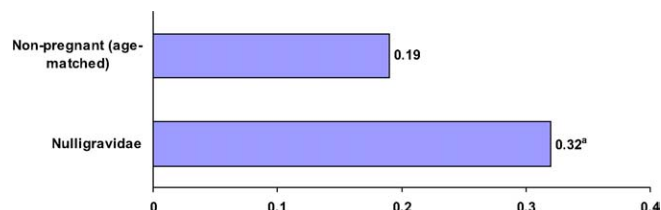


Fig. 2. Panic manifestation quotients in nulligravidae and women who had been pregnant (PMQ; means). Non-pregnant (age-matched) = non-pregnancy period in women who had been pregnant ($N = 70$), sample age-matched to nulligravidae ($N = 35$).

^a significantly different to non-pregnant; $U = 1075.0$; $P < 0.005$;

$P = 0.03$), showing that both disorders were not independent of each other.

3.7. Psychosocial stress factors

In 106 of 195 pregnancies (54%), the women reported that they had experienced psychosocial stress. The main reasons were problems with partnership (25.0% of all women who reported stress), family (20.8%), health (20.8%), financial or occupational problems (19.8%), and unwanted pregnancy (5.3%). In women who reported stress, the risk of developing panic manifestations was increased 1.7-fold for the first pregnancy (Fisher's exact test, $\chi^2 = 17.9$, $P = 0.002$).

3.8. Miscarriages and abortions

In the period after a miscarriage, no difference in panic manifestations was observed in comparison to the postpartum period after normal delivery (asymptotic t -test for paired samples with missing values; $T = 4.67$, $P = 0.68$; N.S.).

3.9. Antipanic treatment

Seven patients reported intake of psychopharmacological drugs for some period during pregnancy and postpartum period. Of these, five were treated with drugs with known efficacy in panic disorder (benzodiazepines, seven treatments; imipramine, one treatment), and two took preparations without known efficacy in panic disorder (1, St. John's wort; 1, a homeopathic preparation). Improvement with these treatments was reported to be 2.44 on average on a 1–5 scale. Non-pharmacological therapies (cognitive behavior therapy, psychodynamic therapy, client-centered therapy) were applied in eight pregnancies in seven women (of these treatments, efficacy proofs exist only for cognitive behavior therapy). On average, these treatments received a rating of 1.22 on a 1–5 scale. In two of these cases, the women were treated with a combination of a drug and psychological therapy.

4. Discussion

Our data, based on the largest sample investigated on this subject matter, suggested that during pregnancy panic manifestations are fewer, while the postpartum period seems to increase the risk for onset or exacerbation of panic disorder. In contrast to previous publications on this topic, the method used in this study not only allows us to assess the percentages of women experiencing increases or decreases of panic symptoms, but also to measure the amount of change. Although only few women reported improvement in panic symptoms, the overall quantity of these improvements was substantial.

Other authors found diverging results regarding the percentages of women experiencing changes in panic symptoms. For example, the rate for improvements varied between 7.5 and 74%. These differences may partly be explained by the low sample sizes used in some studies.

The improvement of panic symptoms during pregnancy and a worsening of panic symptoms during the postpartum period may be explained by psychosocial influences, hormonal changes, and the 'false suffocation alarm hypothesis'.

It can only be speculated how psychosocial factors may be responsible for the bipolar course of panic symptomatology. Improvement during pregnancy may be explained by the cheerful anticipation of the child, while fear of changes in the relation to the father, financial problems, an increased workload, or simply reduced sleeping time could be responsible for a deterioration after childbirth. In our sample, women who reported stress during pregnancy had a higher risk of panic manifestations. Marital disharmony and family, health, financial and occupational problems were reported most frequently. However, psychosocial stress factors may not be the only explanation for the postpartum panic phenomenon. For example, normal deliveries had the same high risk of panic manifestations as miscarriages.

Moreover, the sudden change from the positive influence of pregnancy to the negative impact of childbirth make another explanation more probable. While environmental influences are mostly present already during pregnancy and a sudden change of these factors after childbirth is unlikely for most women, hormonal changes may serve as a better explanation for the phenomenon.

During pregnancy, progesterone and estradiol concentrations rise to a maximum at term, when they are several hundred times higher than during the non-pregnancy period [33]. Around 4–5 days after delivery there is a precipitate drop in hormone concentrations [23]. This coincides with the peak symptoms of "maternity blues". Accordingly, we found an accumulation of new panic manifestations in the first 5 days after childbirth. As panic disorder and depression have many biological features in common [19], postpartum panic may have a similar neurobiological basis as postpartum depression [15,37]. In our sample there was a higher than by chance co-occurrence of postpartum depression and panic.

Estrogen and progesterone may influence mood by interacting with serotonin and norepinephrine neurotransmitter systems implicated in the treatment and pathophysiology of mood and anxiety disorders. Estrogen influences serotonin transporter sites, synthesis, receptor sensitivity, and metabolism of serotonin and decreases monoamine oxidase activity [10,22,41]. It also enhances noradrenergic neurotransmission by influencing synthesis, responsiveness of the α_2 -adrenergic receptor, and metabolism of norepinephrine [16,22,40]. Estrogen treatment may effectively treat [20], or prevent the recurrence [43] of postpartum depression.

Progesterone may have anxiolytic and sedative properties, mediated by benzodiazepine-like action at the GABA receptor-binding site [38], but may also lead to dysphoric and mood-destabilizing effects [9,39].

No consistent hormonal differences have been found in postpartum women with and without depression [23,24,50], suggesting that women with postpartum depression have normal endocrine function, but may have a differential sensitivity

to suddenly changing hormonal levels. When a sudden withdrawal of supraphysiologic gonadal steroid levels to a hypogonadal state is simulated, women with a history of postpartum depression develop significant mood symptoms in contrast to women without such a history [6].

While postpartum depression is not rare, pregnancy did not appear to be protective against depression, according to a prospective study [37].

According to Klein's false suffocation alarm theory [29], panic disorder may be due to a deranged suffocation alarm monitor misfiring an evolved suffocation alarm system because panic patients are abnormally sensitive to CO₂. During pregnancy, improvement may be explained by a respiration-stimulating effect of progesterone, which leads to hyperventilation and to a decrease in pCO₂. Therefore, according to this theory, pregnancy protects panic patients by increasing the distance of their pCO₂ levels from their thresholds. During the postpartum period, an abrupt progesterone decrease may lead to a sudden absence of its panic-suppressing effect, leading to an increase in panic, similarly to late luteal phase dysphoric disorder. Symptoms of the premenstrual syndrome can be relieved by administration of progesterone [53].

Not only estrogen or progesterone may play a role. Cortisol concentrations also rise during pregnancy to several times their normal values and then slowly return to normal within 15 days of delivery [23]. Abnormalities of the hypothalamus-pituitary-adrenal axis have been reported in patients with panic disorder. Cortisol was elevated mainly during nighttime [3,5] and during panic attacks [4].

In our sample, women who had never been pregnant had an increased risk of panic manifestations during their lifetime when compared to women who had had pregnancies. We do not have a simple explanation for this result. Although psychosocial influences may explain this difference, this remains speculative.

The confounding effect of medication, which was a problem in other related studies [30] was negligible in our study, most probably due to the reluctance of the women to take medication during pregnancy due to concerns regarding adverse effects on the developing fetus. Psychotherapeutic interventions were also reported rarely, so that these influences may have been insignificant.

The existence of the phenomenon of postpartum panic has implications for pregnancy counseling and management. Antipanic medication may be prophylactic for those women at greatest risk [12]. Treatment with tricyclic antidepressants or selective serotonin reuptake inhibitors seems to be compatible with breast feeding, although this view should be considered as preliminary due to the lack of data [35,44,45,25,46]. Regarding anxiolytic benzodiazepines, if high doses have to be used and long-term administration is required, breast-feeding should probably be discontinued [28,45].

Our study has some limitations. Due to the retrospective nature of the data, recall biases are possible, the interviewers were no blind to the intent of study, and the generalizability of

the findings is limited because only 63% individuals of the target sample participated in the study.

Altogether, our data support the theory that changes in panic symptoms during pregnancy and postpartum period may not only be influenced by psychosocial, but also by biological factors. Future prospective investigations on the phenomenon of postpartum panic, including studies on the role of hormonal alterations and psychosocial stress factors, may help to explain why panic disorder is twice as frequent in women than in men.

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