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Posttraumatic Stress Disorder Following Preeclampsia and PPROM: A Prospective Study With 15 Months Follow-Up

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Abstract

Objective: A prospective longitudinal evaluation of the prevalence of and risk factors for posttraumatic stress disorder (PTSD) in women with preeclampsia (PE) or preterm premature rupture of membranes (PPROM) compared to uncomplicated pregnancies. **Methods:** Participating women completed PTSD and depression questionnaires during pregnancy, 6 weeks, and 15 months postpartum. Data regarding psychiatric history and indices of obstetric care were collected from patient charts. **Results:** We included 57 PE, 53 PPROM, and 65 healthy pregnant women, of whom 137 also participated in the 15-month follow-up (PE 70%, PPROM 48%, and controls 95%; $P < .001$). At 6 weeks postpartum, the prevalence of PTSD, but not depression, following childbirth was significantly higher in patients than in controls (14% vs 3%; $P = .023$). A history of depression, depressive symptoms during pregnancy, and infant death were significantly associated with symptoms of postpartum PTSD. The maternal condition seems to be of less decisive value, as there was no difference between the prevalence of PTSD after PE and PPROM (11% vs 17%; $P = .324$). At 15 months postpartum, 11% of women with PE had PTSD, some of which did not have PTSD 6 weeks postpartum. The low response rate in the PPROM group at 15 months postpartum does not allow for definite conclusions. **Conclusion:** Pregnancies complicated by PE or PPROM are associated with PTSD in a substantial number of women. Especially women with proven vulnerability for psychological problems are at risk of developing PTSD postpartum, as are women whose children died in the perinatal period.

Keywords

preeclampsia, PPROM, preterm, posttraumatic stress disorder, depression

Introduction

Psychological problems in women during pregnancy and after childbirth are not uncommon. Approximately 1% to 2% of women develop a posttraumatic stress disorder (PTSD) following childbirth,[1] while 1 in 8 are depressed during pregnancy or postpartum.[2] These conditions affect not only the women involved but may also impair secure attachment of the infant and affect the partner relationship.[3] Posttraumatic stress disorder is an anxiety disorder that may develop following confrontation with a traumatic stressor. According to the *Diagnostic and Statistical Manual of Mental Disorders* [DSM-IV]), symptoms consist of reexperiencing the stressful situation, avoidance of reminders of that situation, and a persistent hyper-aroused state. The diagnosis of PTSD additionally requires that the threat elicited a subjective response of intense fear, horror, or helplessness; that the symptoms persist for at least a month; and that the symptoms impair daily life functioning.[4] Posttraumatic stress disorder commonly co-occurs with major depressive disorder.[5,6]

Little is known about the prevalence, course, and risk factors for PTSD following complicated pregnancies. A dose–response relationship between the intensity of the event and the risk of developing PTSD has been proposed.[7] Accordingly, one may hypothesize that that the prevalence of PTSD is higher among women with complicated pregnancies. Complications are often associated with interventions and lengthy

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hospitalization of the infant. Pregnancy may be complicated by conditions that are potentially life threatening for the fetus (eg, preterm premature rupture of membranes [PPROM]) or both mother and fetus (eg, preeclampsia [PE]). Very few studies have so far investigated PTSD following childbirth in a subgroup of women with PE, PPROM, or premature delivery. The prevalence of PTSD following PE was estimated as 28% in an exploratory retrospective study in Dutch patients with PE.[8] Three studies with sample sizes ranging from 30 to 80 women showed higher PTSD rates in women with premature delivery compared to those with uncomplicated pregnancies.[9-11]

Several studies suggest that vulnerability for psychological problems (ie, diagnosed psychiatric disorders in self or direct relatives, a history of self-reported mental symptoms, extreme fear of childbirth) and personality traits are the strongest predictors for (symptoms of) PTSD following childbirth.[8,12,13] A very limited number of studies have investigated the long-term course of PTSD following childbirth, and their findings are inconclusive; some report a decrease in symptoms,[14] while other researchers found little change over time.[10,12,15,16] In addition to studies with long-term follow-up being scarce, no study has yet followed women beyond 14 months following delivery. Data from long-term prospective studies may allow for identification of women vulnerable for developing PTSD following pregnancy complications, as well as identifying women with chronic PTSD who could benefit from treatment.

We, therefore, prospectively examined the prevalence and risk factors for PTSD and depression following PE and PPROM at 6 weeks and 15 months postpartum, and compared these to uneventful pregnancies. To increase the clinical relevance of the results, we used a naturalistic cohort and practical instruments that can easily be used to identify women at risk in clinical practice. We hypothesized that the prevalence of PTSD would be higher in women with pregnancy complications than in controls. Considering the association of PTSD with previous depression[17] and the comorbidity between PTSD and depression,[5] we expected to find that a history of depression and depression in pregnancy would be strong risk factors for PTSD following childbirth.[13] Additionally, we expected that among those women with PTSD shortly after delivery, many would still experience the condition at 15 months following childbirth.

Methods

Design and Setting

In this longitudinal study, pregnant women with PE, including those with severe PE (ie, Hemolysis, Elevated Liver Enzymes, Low Platelets (HELLP) syndrome) and PPROM were recruited in the obstetric clinic of the University Medical Center Groningen, The Netherlands (2005-2008). Preeclampsia and HELLP were defined according to the criteria of the International Society for the Study of Hypertension in Pregnancy.[18] Preterm premature rupture of membranes was defined according to the American Congress of Obstetricians and Gynecologists (ACOG) practice bulletin on PROM.[19] Healthy controls with uneventful pregnancies were recruited in an independent midwifery practice (2005-2006) by means of posters announcing the study. Based on a previous study,[8] we assumed a moderate effect size ($w = .30$). Combined with an α of .01 and a desired power (β) of .80, a minimal sample size (for the 3 groups combined) of 155 was required to detect a significant difference in PTSD levels between PE, PPROM, and controls.[20]

Many pregnancies and deliveries in The Netherlands are monitored by independent midwives. In case of (an increased risk of) complications or interventions during pregnancy or delivery (as defined by national guidelines[21]), women are referred to a gynecologist in a general hospital or academic referral center. The majority of women (66%) deliver under supervision of a gynecologist in a hospital.[22] When under supervision of an independent midwife, women can choose to deliver at home (23%), or in a homelike setting in a hospital or birth center (11%).[23] Referral during labor is not uncommon: 26% of women are referred to a gynecologist during labor.

Population

All women hospitalized with PE or PPROM were asked to participate in the study, unless their condition was so critical (as assessed by the clinician admitting them) that (a) they needed an immediate cesarean section, (b) they received magnesium sulfate infusions, or (c) they were too ill to complete questionnaires. Additional exclusion criteria in all groups were current multiple pregnancy, a history of intrauterine fetal death, and current alcohol or drugs dependence. Furthermore, women with preexisting medical conditions (diabetes mellitus, hypertension, cardiovascular or renal diseases, systemic lupus erythematosus) were excluded, as these women would be likely to anticipate pregnancy complications due to their preexisting condition. All women had singleton pregnancies, were native Dutch speakers, and gave written informed consent. Approval was obtained from the Medical Ethics Committee of the University Medical Center Groningen.

Procedure

On admission, the hospitalized women were informed about the study and were asked to consider their participation within 24 hours. Following signed consent, they were contacted by one of the researchers and tested as soon as possible to minimize the loss of participants due to delivery before testing. Participants were tested during pregnancy (t_1), 6 weeks postpartum (t_2), and 15 months postpartum (t_3). In order to obtain comparable intervals between t_1 and t_2 in the patient and control groups, participants in the control group were tested in the 38th week of pregnancy.

Measures

At t_1, participants completed a brief self-report measure of general demographic information. Data regarding current and past obstetric status were collected from the medical record.

Information regarding psychiatric history was obtained in an interview. The questions were derived from the screening questions of the *Structured Clinical Interview for DSM-IV* (SCID)[24,25] and were used to determine whether there was an indication for a previous depressive episode or previous posttraumatic stress symptoms. Questions were "In the past, did you ever experience one or more periods in which you felt depressed or down for most of the day or in which you lost interest in activities you usually enjoy?"; and "Have you ever witnessed or experienced a traumatic situation (such as experiencing or witnessing a life-threatening situation, physical or sexual abuse, a disaster or serious accident) and has this experience affected you afterward (eg, with nightmares or intrusive thoughts)?" Interviewers were blind to questionnaire results. At t_3 the participants were asked about the well-being of their children, and whether they had sought counseling for mental problems during the past years.

During all 3 test sessions, the PTSD Symptom Scale self-report questionnaire (PSS-SR)[26] and the Beck Depression Inventory, second edition (BDI-II),[27] were completed. The PSS-SR is a questionnaire containing 17 items corresponding to the 17 PTSD symptoms described in the DSM IV. These items are rated using 4-point scales asking for the frequency or intensity with which each symptom occurred over the past month (0 = *never/not at all*, 1 = *once a week/a little bit*, 2 = *2-4 times a week/somewhat*, 3 = *more than 5 times a week/very much*). The PSS-SR sum score ranges from 0 to 51. The retest reliability has been calculated .74.[26] In the present sample, the internal consistency was good ($\alpha = .86$ at t_1, $\alpha = .94$ at t_2, and $\alpha = .89$ at t_3). The PSS-SR that was administered at t_1 asked for PTSD symptoms in the preceding month that were related to any stressful event experienced before that still bothered the participants. At t_2 and t_3, the PSS-SR referred to PTSD symptoms in the preceding month that were specifically related to pregnancy and the perinatal period. In addition, at t_2, the participants rated the extent to which they had felt fear, helplessness, or horror during the pregnancy-related event they experienced as most shocking on three 100 mm Visual Analogue scales (VAS). In the present study, PTSD diagnosis at t_2 was based on a symptom profile reflected by the PSS-SR and VAS scores that was consistent with the *DSM-IV* criteria. For this, we used the criteria as used in the study of Engelhard et al.[8] More specifically, pregnancy-related PTSD was considered present when participants (1) scored 80 or more on 1 of the VAS for horror, fear, and/or helplessness at t_2 (subjective stress, *DSM-IV* A2 criterion); (2) reported at least 1 reexperiencing, 3 avoidance, and 2 hyper-arousal symptoms on the PSS (*DSM-IV*, B, C, and D criterion, respectively). Symptoms were considered present if an item was rated 2 (2-4 times a week) or more; (3) obtained a total PSS-SR score of 18 or higher (severity, *DSM-IV* F criterion). It should be noted that the duration criterion of 4 weeks (*DSM-IV* E criterion) was met because follow-up assessments were at 6 weeks and 15 months postpartum. At t_1 and t_3, the same criteria were used except for the VAS scores. Women with PTSD at t_3 but not at t_2 were only considered a case when they met criterion A2 at t_2.

The BDI-II[27] is a self-report measure of depressive symptoms during the preceding 2 weeks. It consists of 21 items containing 4 statements that reflect increasing symptom severity (scoring 0-3 per item). The sum score ranges from 0 to 63. The BDI-II is found to have good psychometric properties.[27-29] The internal consistency in the current sample was good ($\alpha = .88$ at t_1, $\alpha = .91$ at t_2, and $\alpha = .89$ at t_3). A cutoff score of 20 or more was used, corresponding with moderate depression according to the BDI manual.[27]

Statistical Analysis

Data were analyzed with Statistical Package for the Social Sciences (SPSS) 16.0, using a significance level of .05 (2-tailed). Group comparisons involved 3 groups: (1) PE, (2) PPROM, and (3) control (uneventful pregnancies). For the dichotomous data, χ^2 analyses were used. Comparing participants to nonresponders was done using nonparametric binomial tests. Exploration of the continuous data revealed that the PSS and BDI sum scores were not normally distributed. Therefore, for group comparisons nonparametrical Spearmans rho, Kruskal-Wallis, and Mann-Whitney *U* tests were used. In order to identify risk factors for PTSD and depression in the patient groups, hierarchical multiple regression (HMR) analyses were performed on the PSS and BDI sum scores. Where appropriate, nonnormally distributed variables were square root transformed (SQRT) to meet assumptions of normality, linearity, and homoscedasticity. Variables with a *P* value lower than .10 as found in univariate analyses were included in the multiple regression analysis.

Results

Patient Characteristics

A total of 197 women were willing to participate when approached during pregnancy. In all, 193 women were included at t_1 (Figure 1): 4 women did not meet the inclusion criteria (1 preexistent hypertension, 1 chronically ill, 1 drug dependence, and 1 previous intrauterine fetal death). At t_2 (6 weeks postpartum), 175 women completed the questionnaires, of whom 22 with HELLP, 35 with PE, 53 with PPROM, and 65 healthy pregnant women. A total of 18 women in the patient group dropped out after the first measurement: 4 women explicitly stated it was because they lost their infant in the postpartum period, 14 women did not specify a reason for their withdrawal. Comparison of these 18 women to the 110 patients who did take part at t_2 revealed that the age ($P = .023$) and educational level ($P = .039$) of the 18 nonresponders was slightly lower than that of the participants, but employment- and single parenthood rates were comparable. Additionally, no significant differences were observed in obstetric characteristics (proportion of women with primiparity, normal vaginal deliveries, cesarean deliveries, deceased infants, infants hospitalized at 6 weeks of age, extreme prematurity [<32 weeks gestation]) and psychological variables (proportion of women with depression and/or PTSD in history and/or pregnancy).

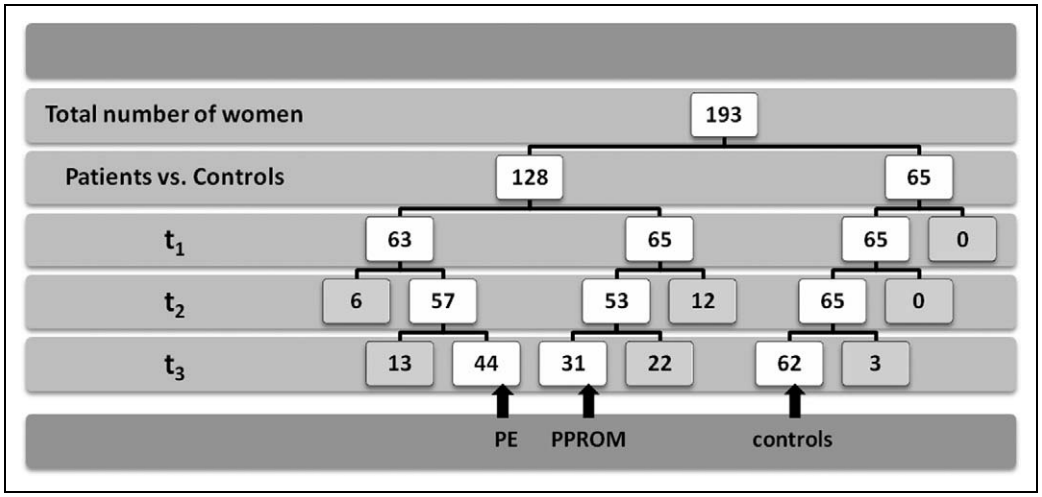

Figure 1. Overview of participation and dropout.
PE indicates preeclampsia; PPROM, preterm premature rupture of membranes.

At 15 months after delivery (t_3), 137 women completed the third set of questionnaires. This yielded a total response rate of 71%, with significant differences between the groups: PE 70%, PPROM 48%, and controls 95% ($P < .001$). For each of the 3 groups, potential discrepancies between women completing all 3 measurements and those only participating at t_1 and t_2 were evaluated. The same demographic, obstetric, and psychological variables as mentioned for the nonresponder analysis at t_2 were used, with the addition of the proportion of women with PTSD and depression at t_2. Women with PE who did not participate at t_3 were more often single (18% vs 0%; $P = .034$) and their children were less frequently hospitalized at 6 weeks of age (22% vs 50%; $P = .031$) than women with PE taking part at t_3. Women with PPROM not taking part in the 15-month follow-up had lower levels of education ($P < .001$) and reported more depression in history (47% vs 26%; $P = .007$) and during pregnancy (24% vs 3%; $P < .001$) as compared to women with PPROM taking part at t_3. No significant differences were found between the 3 controls not participating at t_3, as compared to the 62 healthy controls completing all 3 measurements.

Demographic and obstetric characteristics of the 175 women participating at t_2 are shown in Table 1. The patient and control groups differed in all obstetrical indices, as expected. The differences between the patient groups were not significant. As the HELLP and PE groups did not differ in their obstetric characteristics, they were pooled into 1 group for further analysis, labeled PE.

Prevalence

At t_1, 12% of women met the symptom criteria for PTSD (PE 21%; PPROM 14%; and controls 2%; $P = .003$). Figure 2 shows the prevalence of PTSD related to pregnancy and childbirth at t_2 and t_3. Pearson χ^2 tests indicated significant differences between the 3 groups in the prevalence of PTSD at both time points (t_2: $P = .039$; t_3: $P = .018$): the prevalence of PTSD was significantly higher in the patient group (PE and PPROM combined) than in the control group (t_2: $\chi^2 = 5.194$, $P = .023$; t_3: Fisher exact test $P = .032$). There were no significant differences in the prevalence of PTSD between the PE and the PPROM group (t_2: $\chi^2 = 0.972$, $P = .324$; t_3: Fisher exact test $P = .391$). Figure 3 shows the prevalence of depression at t_1, t_2, and t_3. The 3 groups did not differ significantly with respect to the prevalence of depression at either of the 3 time points.

At t_2, 9 (53%) of the 17 women with PTSD also had a comorbid depression. Further exploration of the data using nonparametric Mann-Whitney U tests revealed that at t_2, symptoms of PTSD and depression were associated with depression in history, depression at t_1, and PTSD at t_1 but not to a history of PTSD (all independent variables dichotomized). Women with PTSD and depression in history, during pregnancy (t_1) and at 6 weeks postpartum (t_2) reported more symptoms of PTSD and depression at t_3.

Of the 17 women with PTSD at t_2, 8 did not participate at t_3. Of the 9 women who did participate at t_3, 2 still met the criteria for PTSD at 15 months follow-up. In all, 7 women no longer met the PTSD criteria at t_3, 4 of whom had sought professional counseling. Additionally, 4 new cases of PTSD (3 in the PE group and 1 in the PPROM group) were identified at t_3, that is, women who did not meet the criteria for PTSD at t_2.

Risk Factors

As the death of an infant in the postpartum period is extremely stressful and can induce "grief-associated depressive symptoms,"[4] we investigated the effect of the death of the infant on the prevalence of depression and PTSD at t_2. The results, summarized in Table 2, indicate that the prevalence of depression and PTSD, as well as sum scores on the PSS-SR and BDI were significantly higher in women who had lost their infants (all Ps $< .01$). In order to evaluate whether removing the 12 women whose infants had died would influence the differences in prevalence rates, we repeated the χ^2 tests for PTSD at t_2 for $n = 163$. Prevalence rates decreased from 10.5% to 6.0% in

Table 1. Demographic, Psychiatric, and Obstetric Characteristics of Women Participating at t_2 (n = 175)[a]

	PE (n = 57)	PPROM (n = 53)	Control (n = 65)
Demographic characteristics			
Age, years (SD)[b]	29.4 (5.1)	30.7 (4.8)	31.9 (3.9)
Married or cohabiting, n (%)	54 (100%)	47 (92%)	61 (95%)
Completed college or university, n (%)[b]	19 (34%)	19 (36%)	54 (83%)
Not employed, n (%)	5 (9%)	10 (19%)	6 (9%)
Psychiatric history			
Reported history of depression, n (%)	22 (39%)	18 (34%)	17 (26%)
Reported history of PTSD, n (%)	7 (13%)	13 (25%)	9 (14%)
Obstetric characteristics			
Primipara[c]	43 (80%)	25 (49%)	48 (74%)
Hospitalization of mother, days (SD)[b]	9.4 (9.1)	18.6 (22.2)	0
Cesarean delivery, n (%)[b]	43 (77%)	15 (28%)	6 (9%)
Gestational age, week + day (SD)[b]	31 + 3 (3.9)	31 + 3 (3.2)	40 + 5 (1.0)
Birth weight, g (SD)[b]	1506 (846)	1686 (638)	3703 (500)
10-minute APGAR score (SD)[b]	7.5 (2.1)	7.7 (2.2)	9.4 (1.0)
Death of infant, n (%)[b]	7 (12.3%)	5 (9.4%)	0
Infant hospitalized at t_2, n (%)[b]	24 (43%)	20 (39%)	0

Abbreviations: PE = preeclampsia; PPROM = preterm premature rupture of membranes; PTSD = posttraumatic stress disorder.
[a] Demographic characteristics and psychiatric history collected at t_1. Obstetric characteristics collected at t_2.
[b] Significant difference between control group and patient groups.
[c] Significant difference between PPROM and all other groups.

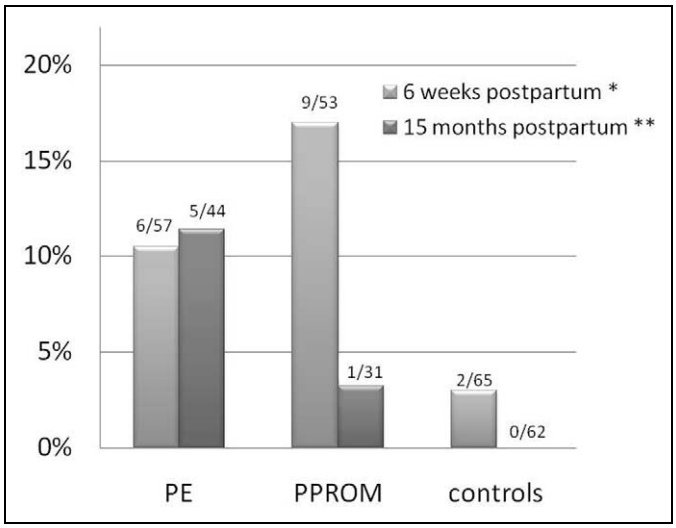

Figure 2. Prevalence of PTSD related to pregnancy and childbirth at t2 and t3.
*$\chi^2 = 6.499$, $P = .039$; **$\chi^2 = 8.063$, $P = .018$. PE indicates preeclampsia; PPROM, preterm premature rupture of membranes; PTSD, posttraumatic stress disorder.

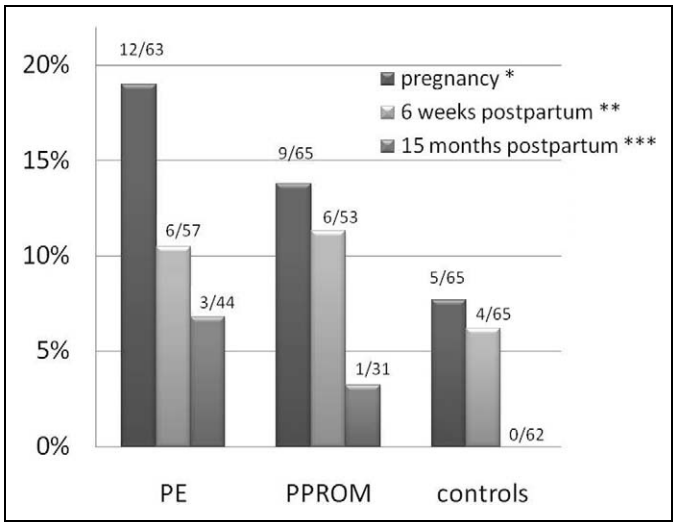

Figure 3. Prevalence of depression at t1, t2, and t3.
*$\chi^2 = 3.551$, $P = .169$; **$\chi^2 = 1.133$, $P = .567$; ***$\chi^2 = 4.234$, $P = .120$. PE indicates preeclampsia; PPROM, preterm premature rupture of membranes.

the PE group and from 17.0% to 14.6% in the PPROM group. As a consequence, initial differences between patients and controls in the prevalence of PTSD at t_2 did not persist ($P = .062$). However, the difference between women with PPROM and controls was significant (Fisher exact test 2-tailed: $P = .035$).

Finally, we evaluated the patient group for the contribution of psychological and obstetric risk factors to the PSS-SR and BDI scores at t_2 using 2 hierarchical linear regression analyses. Demographic variables age and education were not included, as no significant associations were found at t_2 between age and PTSD (independent samples t test, $P = .532$) or between education and PTSD (χ^2 test, $P = .473$). As we hypothesized that a history of depression and BDI scores during pregnancy would be the strongest risk factors for PTSD and depression postpartum (see introduction), these variables were entered in the first step (history of depression was dichotomized). In the second step, variables indicative of the well-being of both mother and infant were added, that is, death of infant between t_1 and t_2,

Table 2. Number (%) of Women With PTSD and Depression, and PSS-SR , BDI Sum Scores (Median, 25th-75th Quartile) in Women With Pregnancy Complications, as a Function of the Death of Their Infants (as measured at t2)

	Living Infant (n =98)	Infant Died (n = 12)
PTSD[a]	10 (10%)	5 (42%)
Depression[a]	7 (7%)	5 (42%)
PSS-SR score[a]	10.0 (6.0-17.2)	24.4 (18.2-37.5)
BDI score[a]	8.5 (5.0-12.4)	16.1 (9.8-30.2)

Abbreviations: BDI = Beck Depression Inventory; PSS-SR = PTSD Symptom Scale self-report questionnaire; PTSD = posttraumatic stress disorder.
[a] Significant difference between women with a living infant and women whose infant died between t_1 and t_2.

hospital admission of the infant at t_2, birth weight, diagnosis of the mother (PE vs PPROM), and cesarean delivery. We also added gestational age at delivery and length of hospitalization of the mother to the model. However, maternal hospitalization strongly correlated with the obstetric diagnosis of the mother and gestational age strongly correlated with birth weight, infant death, and infant hospitalization, which induced multicollinearity. Gestational age at delivery and maternal hospitalization were therefore removed from the model. BDI and PSS-SR scores were skewed and therefore square root transformed (SQRT).

The model for SQRT PSS-SR explained 29% of the variance in the first step ($P < .001$), and an additional 10% in the second step ($P = .004$), resulting in a model explaining 39% of the variance ($P < .001$). Significant risk factors were a high SQRT BDI score at t_1 ($\beta = .33$, $P < .001$), indication for a previous depressive episode ($\beta = .23$, $P = .007$) and the death of the infant ($\beta = .29$, $P = .001$). The other indicators for maternal or infant well-being in this period did not significantly contribute to the model. The model for SQRT BDI explained 38% of the variance in the first step ($P < .001$) and addition of the second step increased R^2 with 6% ($P = .032$), yielding a total of 44% ($P < .001$). As with PTSD, significant risk factors in the model for depression were the SQRT BDI at t_1 ($\beta = .42$, $P < .001$), indication for a previous depressive episode ($\beta = .30$, $P < .001$) and death of the infant ($\beta = .21$, $P = .008$).

Discussion

In this unique prospective study on psychological problems in women with pregnancies complicated by PE or PPROM, the prevalence of PTSD was found to be 11% (PE) and 17% (PPROM) at 6 weeks postpartum, which is significantly higher than following uneventful pregnancies in the control group (3%). Additionally, this is the first study to follow women up to 15 months postpartum, and we found that (at t_3) as much as 11% of women with PE met the criteria for PTSD, compared to none of the controls. The low response rate in the PPROM group at 15 months postpartum does not permit definite conclusions. The prospective design of this study allowed for identification of risk factors for posttraumatic stress symptoms and depressive symptoms. Risk factors were found to be a self-reported history of depression, a high BDI score during hospitalization, and infant death in the postpartum period. These risk factors together explained 39% and 44% of the variation in posttraumatic stress and depressive symptoms, respectively.

Our results should be considered in the light of several strengths and weaknesses. This is the first study reported to follow women longer than 14 months postpartum. Furthermore, among the limited studies on PTSD following PE, no articles with prospective designs have been published yet. Additionally, this study is one of the few studies focused at PTSD after preterm delivery and has a considerably larger sample size than previous studies (n = 175 vs 30-80).[9-11] Additional strengths include the use of a control group with uneventful pregnancies, and the assessment of both depression and PTSD with validated questionnaires. Furthermore, *DSM-IV* criteria A2, B, C, D, E, and F have been used, which is a stricter and more precise application of the *DSM-IV* than in many other studies.[30]

In retrospect, a number of procedural limitations of this study may be identified. Even though inclusion and exclusion criteria were clear, systematic reporting of women not willing to participate would have strengthened our assertion of having selected representative groups of women with PE, PPROM, and uncomplicated pregnancies. Additionally, the use of self-report questionnaires and the retrospective assessment of adversity/treat experienced during hospitalization may have influenced results. The response rate in the PPROM group at 15 months follow-up (48%) was significantly lower than among women with PE (70%) and controls (95%; $P < .001$). Moreover, selective dropout occurred in the PPROM group, as women with PPROM not taking part in the 15-month follow-up reported more depression in history (47% vs 26%; $P = .007$) and during pregnancy (24% vs 3%; $P < .001$), which may well have caused an underestimation of the prevalence rates of PTSD and depression at t_3 in the PPROM group. All in all, it should be concluded that the data on women with PPROM at 15 months follow-up are inconclusive. Finally, considering that the mean gestational age at delivery in the patient groups was 31 weeks, one may argue that the controls should have been assessed earlier than at 38 weeks' gestation. However, it was considered desirable to obtain comparable intervals between t_1 and t_2 in patient and control groups. Therefore, like most patients with PE and PPROM, participants in the control group also had to be tested toward the end of the pregnancy.

The prevalence of PTSD in our sample (at t_2) was somewhat lower than that found by Engelhard et al who reported a prevalence of 28% PTSD following preterm PE and preterm birth at 14 months postpartum. Engelhard et al retrospectively assessed posttraumatic stress symptoms fairly long after the index event occurred.[8] This might have resulted in an overestimation of symptoms, explaining the higher prevalence reported. In the present study, the majority of women with PTSD at 15 months postpartum developed (clinically relevant) symptoms after the t_2 measurement (6 weeks postpartum). This calls for long/longer follow-up in future studies relating to this topic and

awareness among clinicians that women may also develop PTSD (symptoms) several months after childbirth. The prevalence of PTSD at t_2 did not differ significantly between women with PE or PPROM, suggesting that PTSD is associated with the sequence of events accompanying preterm birth more than with the specific maternal condition, confirming our hypothesis. These findings are in accordance with those of Engelhard et al, reporting no difference in incidence of PTSD in women with PE or preterm birth.[8]

Since the prevalence of depression following complicated and uneventful pregnancies did not differ between the groups, depression does not seem to be a specific reaction to pregnancy complications. It should be noted that the sample size for this study was based on detecting differences between groups of a medium effect size. Indeed, this turned out to be the case for our primary outcome measure, PTSD. The observed effect size for depression was small (ie, smaller differences between the 3 groups). In order to detect such small differences, based on the current results, future studies should recruit large sample sizes (ie, n = 1388).[20] The slight decrease in depressive symptoms in the postpartum period has been reported before in uncomplicated pregnancies[31] and is probably related to a decrease in the level of worrying following the birth of a healthy infant. The prevalence of depression in the postpartum period in women with living children is within the normal range for depression in the postpartum period (period incidence of 7.1%).[32]

The scores of BDI and PSS-SR sum were already high at t_1. Although the time period specified in questionnaires includes several weeks prior to the onset of obstetric symptoms (ie, 2 weeks and 1 month for BDI and PSS-SR, respectively), it cannot be excluded that stress of the hospitalization has influenced t_1 symptom reports. Furthermore, it should be noted that, contrary to the PSS-SR administered during pregnancy, the PSS-SR questionnaire administered postpartum specifically referred to the peripartum period, signifying that prevalence rates of PTSD at t_1 and t_2 as found with the PSS-SR cannot be compared.

Significant risk factors for both PTSD and depression postpartum were high BDI scores during hospitalization, a self-reported previous depressive episode and the death of the infant in the postpartum period. In our study, risk factors such as cesarean delivery and hospitalization of the infant during follow-up did not significantly contribute to the regression models. These findings are in line with the recent study of Söderquist et al, who reported that experiencing depressive symptoms early in pregnancy is the main risk factor for PTSD following uncomplicated pregnancies.[13] Previous studies reporting associations between obstetric interventions and PTSD also indicated that psychological characteristics were much stronger risk factors for PTSD than the obstetrical characteristics,[33,34] which is in line with our findings. Therefore, we think that there is not one single obstetrical variable that is both necessary and sufficient for causing PTSD. Probably the whole constellation of events accompanying a complicated pregnancy (eg, maternal hospitalization, cesarean section, long-term infant hospitalization, and infant death) may put women who are already vulnerable at risk of developing PTSD. About 40% of the women who had lost their children developed depression and/or PTSD, compared to 10% in the women whose children survived. These findings extend the existing data on PTSD and depression following pregnancy loss and stillbirth to perinatal death[35,36] and illustrate the major impact of losing a infant in the postpartum period. For future research, we suggest to extend the list of potential risk factors for PTSD following childbirth to endocrine and immunological factors that could possibly mediate the relationship between PE/PPROM and PTSD (eg, hypothalamic-pituitary-adrenal [HPA] axis dysregulation or increased concentrations of inflammatory cytokines).

Regarding clinical practice, we hope the current findings will encourage gynecologists to be more alert on psychological problems in women with PE or PPROM. At various points in time, women ''at risk'' may be identified; next to asking for a history of depression (or other mental disorders) during pregnancy, all women hospitalized for PE or PPROM could be requested to complete a standard depression screening instrument (eg, BDI[26] or Edinburgh Postnatal Depression Scale[37]), as depression during pregnancy proved a risk factor for PTSD and depression postpartum in the women with PE/PPROM in this study; rather than focusing on the physical condition, current mental well-being, and experience of the delivery will hopefully become an integral part of the 6-week postpartum appointment. However, it may be too early for the implementation of large-scale screening programs for PTSD following childbirth. Even though effective treatments for postpartum depression have been well researched, this is not the case for PTSD[38]: the effects of debriefing/counseling are questionable, only one case report is available using cognitive–behavioral therapy and one using eye-movement desensitization and reprocessing (EMDR). The fact that there is limited evidence concerning the optimal management of women with PTSD following childbirth calls for a large study investigating possible treatment options.

In conclusion, this study shows that pregnancy complications can trigger posttraumatic stress symptoms in a substantial number of women. Especially women with proven vulnerability for psychological problems (through previous episodes of depression or depression during pregnancy) are at risk of developing PTSD, as are women whose children died in the perinatal period. Several women with PTSD at 6 weeks postpartum do no longer meet the criteria 15 months after childbirth, which is promising. However, this study also demonstrates that other women developed late onset PTSD following complicated childbirth. We suggest that clinicians be aware of these pathologic responses, not only to improve maternal mental health, but also because PTSD and depression influence maternal–infant attachment and infant development.[11,39] This study suggests that not the pregnancy complication itself (PE/PPROM), but the whole constellation of events accompanying a complicated pregnancy, in particular preterm delivery, may induce PTSD in vulnerable women.

Authors' Note

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